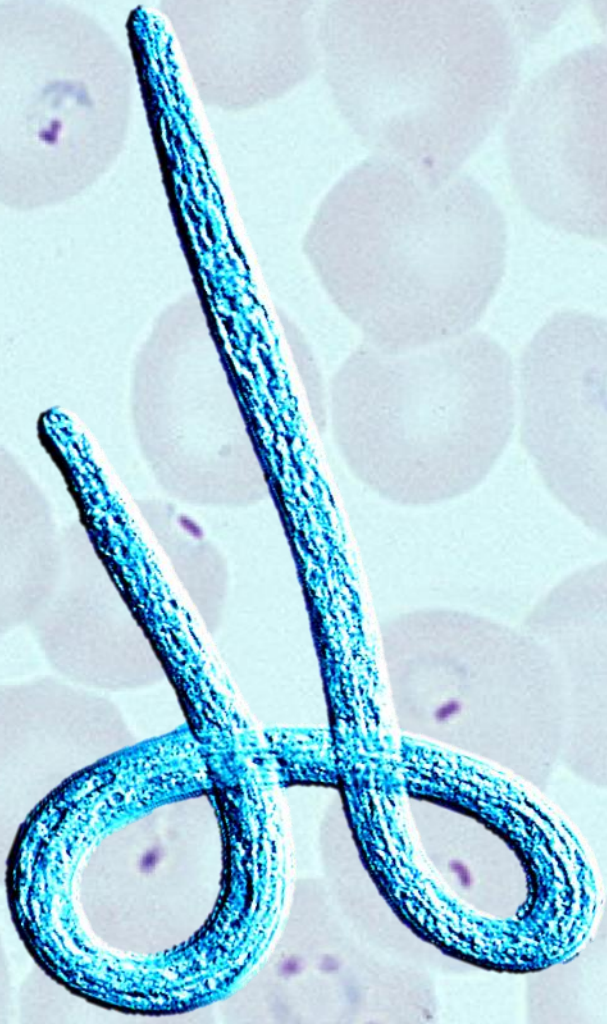
British Society for Parasitology

Spring Meeting 16- 18 April 2015



Abstract Book

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This list has hyperlinks to the selected abstract.

Programme by Session days

Day 1 Thursday 16th April 2015 Sessions 1,2 and 3 by Stream -hyperlinks to the abstracts.

Timeslot 16/04/15	Stream A Room 1B	Stream B Room 1C	Stream C Room 11B	Stream D Room 11A	Stream E Room 11C
8.00 am	**REGISTRATION** in the Foyer & throughout the day				
9.00 –10.30 am	**Plenary Sessions 1,2,3 (Room 1A) - Chair** - Prof M Taylor, Liverpool School of Tropical Medicine **Malaria:** Prof D. Kwiatkowski - Malaria genomics: tracking a diverse and evolving parasite population **NTDs:** Prof J. Utzinger - *Neglected tropical diseases: from application to innovation* **Vectors:** Prof J. Hemingway - *Overcoming Major Impediments to success Vector-borne disease control.* **Room 1A (650)**				
10.30 –11.00 am	**Tea & coffee (*viewing exhibitions& Poster Session setup*)**				
11.00 –12.30 pm	**A1 - (Room 1B) - Malaria - Hot Topics/Advance** **Chair:** Prof A Bell	**B1 - (Room 1C) - NTDs - Hot Topics/Advance** **Chair:** Prof D Molyneux	**C1 - (Room 11B) - Vectors - Hot Topics/Advance** - **Chair:** Prof M. Donnelly		
12.30 –2.00 pm	**Lunch & drinks (*viewing exhibitions & Poster Session setup*)**				
2.00 –3.30 pm	**A2 - (Room 1B) - Malaria - Molecular & Cellular Biology I** **Chair:** E Salcedo-Sora **Keynote:** M. Blackman - *Dissecting the regulation and dynamics of malaria parasite egress*	**B2 - (Room 1C) - NTDs - Diagnostics I** – **Chair:** E Adams Keynote: L. van Lieshout - *Under the microscope: new approaches in the diagnosis of intestinal worms and schistosomiasis.*	**C2 - (Room 11B) - Vectors -Molecular & Cellular Biology I** **Chair:** H Ranson **Keynote:** M. Lawniczak - *The male mosquito contribution to malaria transmission: mating increases female susceptibility to human malaria parasites.*	**D2 - (Room 11A) - Parasites - Ecology I** **Chair:** J Cable **Keynote:** M. Begon - *Infectious diseases: from wild rodents to universal truths*	**E2 - (Room 11C) - Parasites - Immunology & Pathology I** **Chair:** J Turner **Keynote:** P. Fallon - *Schistosoma mansoni: potent immune modulator for the parasites, not our, needs*
3.30 –4.00 pm	**Tea & coffee (*viewing exhibitions & Poster Session setup*)**				
4.00 –5.30 pm	**A3 - (Room 1B) - Malaria - Molecular & Cellular Biology II** **Chair:** E Salcedo-Sora	**B3 - (Room 1C) - NTDs - Diagnostics II** **Chair:** E Adams	**C3 - (Room 11B) - Helminth- Molecular & Cellular Biology** **Chair:** R Stothard	**D3 - (Room 11A) - Parasites - Ecology II** **Chair:** J Cable	**E3 - (Room 11C) - Parasites - Immunology & Pathology II** **Chair:** J Turner
5.30 –7.00 pm	**Evening drinks with Poster Session viewing** ***from 7.30pm Young Parasitologists' Evening at Tribeca's, Liverpool***				

Day 2 Friday 17th April 2015 Sessions 4,5,6 and 7 by Stream

Timeslot 17/04/2015	Stream A Room 1B	Stream B Room 1C	Stream C Room 11B	Stream D Room 11A	Stream E Room 11C
8.15 am	**REGISTRATION** in the Foyer & throughout the day				
9.00 he Foyer	A4 - (Room 11A) - Malaria - Drugs I **Chair:** G Biagini **Keynote:** S. Ward - *The trials and tribulations of generating fully synthetic peroxide based antimalarials.*	B4 - (Room 11B) - NTDs - Molecular Biology I **Chair:** A Acosta-Serrano **Keynote:** N. Hall - *Genomics of Entamoeba: dissecting populations and species.*	C4 - (Room 11C) - Vectors - Emerging diseases and zoonose **Chair:** S Torr **Keynote:** C. Drakeley - *An integrated research programme to understand the epidemiology of Plasmodium knowlesi*	D4 - (Room 13) - Parasites - Geospatial Ecology I **Chair:** L Rinaldi **Keynote:** G. Cringoli 3)*Geographical Information Systems and Cystic Echinococcosis*	E4 - (Room 14 - Parasites - Co-infections **Chair:** D Blake **Keynote:** A. Fenwick - *Present and future control of co-infections with schistosomiasis and STH*
10.30 t and futu	**Tea & coffee (*viewing exhibitions*)**				
11.00 g exhibit	A5 - (Room 11A) - Malaria - Drugs II **Chair:** G Biagini	B5 - (Room 11B) - NTDs - Molecular Biology II **Chair:** A Acosta-Serrano	C5 - (Room 11C) - Vectors – Zoonesis **Chair:** S Torr	D5 - (Room 13) - Parasites - Geospatial Ecology II **Chair:** L Rinaldi	E5 - (Room 14) - Parasites - One Health & Zoonosis **Chair: R Stothard** **Keynote:** J. Dupouy-Camet - *Travel medicine allows advances on the knowledge of Neglected meat & fish borne Parasitic Diseases*
12.30 medicine	**BSP Annual General Meeting: 12.45 - 1.15pm Room 11B**				
1.00 nnual Ge	**Lunch & drinks (*viewing exhibitions)***				
2.00 ng exhib	A6 - (Room 11A) - Malaria - Molecular Biology **Chair:** A Craig **Keynote:** J. Baum - *Imaging malaria parasite cell biology from whole cells down to single atoms…. towards achieving superb resolution*	B6 - (Room 11B) - NTDs – Modelling **Chair:** P Lamberton **Keynote:** D. Hollingsworth -	C6 - (Room 11C) - Vectors - Vector/Parasite Interactions I **Chair:** L Reimer **Keynote:** S. Sinkins - *Wolbachia-mosquito interactions and pathogen transmission*	D6 - (Room 13) - Parasites - Wildlife & Aquatic **Chair:** M Betson	E6 - (Room 14) - Parasites - Evolution I **Chair:** R Post **Keynote:** A. Waeschenbach - *Untangling the molecular phylogeny of tapeworms*
3.30 gling th	**Tea & coffee (*viewing exhibitions*)**				
4.00 ng exhib	A7 - (Room 11A) - Malaria - Epidemiology **Chair:** P Horrocks	B7 - (Room 11B) - NTDs – Drugs **Chair:** O Millington **Keynote:** J. Keiser - *Towards better drugs for trematode infections: field successes from pharmacokinetics to clinical trials*	C7 - (Room 11C) - Vectors - Host/Parasite Interactions II **Chair:** L Reimer	**D7 - (Room 13A) - Students - Career tips** **Chair:** S MacDonald **Workshop:** Caroline Ash (Senior Editor for Science) Kate Hawkins (Science Comms) David Johnson (HSE specialist inspector) Valerie Decraene (Senior Epidemiologist PHE)	E7 - (Room 14) - Parasites - Evolution II **Chair:** R Post

5.30 t oom 14	***from 7.30pm BSP Conference Dinner at the Maritime Museum***

Timeslot **18/04/2015**	
8.30 am	**REGISTRATION** in the Foyer
9.00 he Foyer P	**Plenary session 4,5,6,7:** **Chairs** hairsy session 4,5,6,7 **2015 Wright Medallist** Julian Rayner ulian Rayneredallist 7:_Sessions_ **Panelists:** Julie Jacobson - *Research on neglected tropical disease:progress and planning towards control and elimination.* Robert Don - *Developing drugs for neglected tropical diseases* Jeremy Burrows – *Medicines for Malaria Venture*
11.00 -11.30 am	**Tea & coffee**
11.30 coffee am	**Open Question Time Debate**: **Chair** - Peter Sissons "**Conflict, environment & Ebola: Barriers to parasite control & eliminationr** Panellists: Moses Bockarie – LSTM Janet Hemingway – LSTM Judy Smith - WHO-AFRO, Cameroon Anthony Bettee - Ministry of Health, Liberia Louis-Albert Tchuem -Tchuente : WHO-AFRO, Cameroon
1.00 pm	**Exit and sight seeing around Liverpool**

The Full Programme

Day 1 Conference Opens 8:00 am

Registration 8:42 AM - 4:59 PM (497 mins)

Day 1 Plenary Sessions 1,2,3 (Room 1A) - Chair - Prof M Taylor, Liverpool School of Tropical Medicne

Plenary Session 1 - Prof Dominic Kwiatkowski - Malaria 9:00 AM - 9:30 AM (30 mins)

Malaria genomics: tracking a diverse and evolving parasite population (Dominic Kwiatkowski)

Plenary Session 2 - Prof Jurg Utzinger - Neglected Tropical Diseases 9:30 AM - 10:00 AM (30 mins)

Neglected tropical diseases: from application to innovation (Jürg Utzinger)

Plenary Session 3 - Prof J Hemingway - Vectors 10:00 AM - 10:30 AM (30 mins)

Overcoming Major Impediments to success Vector-borne disease control. (Janet Hemmingway)

Day 1 Conference Break

Coffee and Tea Break 10:30 AM - 11:00 AM (30 mins)

Day 1 Session A1 - (Room 1B) - Malaria - Hot Topics/Advance - Chair: Prof A Bell

A1-O1 11:00 AM - 11:15 AM (15 mins)

Lack of evidence to support EPCR as a major cytoadherence receptor (Yvonne Azasi)

A1-O2 11:15 AM - 11:30 AM (15 mins)

Coping with stress: fight or flight in the malaria parasite Plasmodium chabaudi (Petra Schneider)

A1-O3 11:30 AM - 11:45 AM (15 mins)

P-selectin is a host receptor for Plasmodium MSP7 ligands (Abigail Perrin)

A1-O4 11:45 AM - 12:00 PM (15 mins)

Watching the clock: the story of circadian rhythms in malaria parasites (Kimberley Prior)

A1-O5 12:00 PM - 12:15 PM (15 mins)

Genome-wide population analysis of human Plasmodium knowlesi infections reveals extreme diversity and signatures of recent strong selection (Samuel Assefa)

Day 1 Session B1 - (Room 1C) - NTDs - Hot Topics/Advance - Chair: Prof D Molyneux

B1-O1 11:00 AM - 11:15 AM (15 mins)

EUROLEISH-NET: Control of leishmaniasis, from bench to bedsite and community (Albert Picado)

B1-O2 11:15 AM - 11:30 AM (15 mins)

Monitoring Transmission of Lymphatic Filariasis Post-Mass Drug Administration in Ghana (Irene Offei Owusu)

B1-O3 11:30 AM - 11:45 AM (15 mins)

Introducing COUNTDOWN: a multidisciplinary implementation research consortium for control of NTDs (Russell Stothard)

B1-O4 11:45 AM - 12:00 PM (15 mins)

Microfluidics for drug-assays and diagnostics on Trypanosoma brucei (Axel Hochstetter)

B1-O5 12:00 PM - 12:15 PM (15 mins)

A Genome on the Verge of Extinction (Caroline Durrant)

Day 1 Session C1 - (Room 11B) - Vectors - Hot Topics/Advance - Chair: Prof M. Donnelly

C1-O1 11:00 AM - 11:15 AM (15 mins)

Interspecific Variation of the Microbiota in Natural Tsetse Fly Populations (Frances Blow)

C1-O2 11:15 AM - 11:30 AM (15 mins)

Shooting swoops: video-tracking Anopheles gambiae flight around insecticide treated bed nets (Josephine Parker)

C1-O3 11:30 AM - 11:45 AM (15 mins)

Are topical insect repellents effective against malaria in endemic populations? A systematic review and meta-analysis (Anne Wilson)

C1-O4 11:45 AM - 12:00 PM (15 mins)

The Anopheles gambiae 1000 genomes project (Tiago Antao1)

C1-O5 12:00 PM - 12:15 PM (15 mins)

Mosquito-parasite interactions influence vectorial capacity for lymphatic filariasis (Lisa Reimer)

Day 1 Conference Break

Lunch & Poster session A setup, Posters 1-200 12:30 PM - 2:00 PM (90 mins)

Day 1 Session A2 - (Room 1B) - Malaria - Molecular & Cellular Biology I - Chair: E Salcedo-Sora

A2-IS - Invited speaker Prof M Blackman, MRC National Institute for Medical

Research 2:00 PM - 2:30 PM (30 mins)

Dissecting the regulation and dynamics of malaria parasite egress (Michael Blackman)

A2-O1 2:30 PM - 2:45 PM (15 mins)

Increased adhesion of Plasmodium falciparum infected erythrocytes to intercellular adhesion molecule 1 in children with acute intestinal injury (James Church)

A2-O2 2:45 PM - 3:00 PM (15 mins)

Structural Characterisation of Chromatin Proteins in the Human Malarial Parasite (Ashley Jordan)

A2-O3 3:00 PM - 3:15 PM (15 mins)

Structural conservation despite huge sequence diversity allows EPCR binding by the PfEMP1 family implicated in severe childhood malaria (Clinton Lau)

A2-O4 3:15 PM - 3:30 PM (15 mins)

Merozoite antigens of Plasmodium falciparum elicit strain-transcending opsonising immunity (Danika Hill)

Day 1 Session B2 - (Room 1C) - NTDs - Diagnostics I - Chair: E Adams

B2-IS - Invited speaker Dr L van Lieshout, Leiden University Medical Center (LUMC)

2:00 PM - 2:30 PM (30 mins)

Under the microscope: new approaches in the diagnosis of intestinal worms and schistosomiasis. (Lisette van Lieshout)

B2-O1 2:30 PM - 2:45 PM (15 mins)

Comparison of individual and pooled samples for the assessment of soil-transmitted helminth, Schistosoma mansoni and S. haematobium infection intensity in children, Ethiopia (Bruno Levecke)

B2-O2 2:45 PM - 3:00 PM (15 mins)

IgG1 as a Potential Biomarker of Post-Chemotherapeutic Relapse in Visceral Leishmaniasis, and Adaptation to a Rapid Diagnostic Test (Tapan Bhattacharyya)

B2-O3 3:00 PM - 3:15 PM (15 mins)

Performance Evaluation of Enzyme Linked Immunosorbent Assay and Lineblot for Serological Diagnosis of Chagas (Trypanosoma Cruzi) Disease (Andreas Latz)

B2-O4 3:15 PM - 3:30 PM (15 mins)

Validity of Polymerase Chain Reaction (PCR) Versus Coproscopic Examination for DiagnosingInfection with Schistosoma mansoni in Low Intensity Endemic Area in Egypt. (Hassan Bassiouny)

Day 1 Session C2 - (Room 11B) - Vectors - Molecular & Cellular Biology I - Chair: H Ranson

C2-IS - Invited speaker Dr M Lawniczak, Wellcome Trust Sanger Institute 2:00 PM - 2:30

PM (30 mins)

The male mosquito contribution to malaria transmission: mating increases female susceptibility to human malaria parasites. (Mara Lawniczak)

C2-O1 2:30 PM - 2:45 PM (15 mins)

T345M, an additional mutation associated with insecticide resistance in the Anopheles gambiae GABA receptor, Rdl (Jennina Taylor-Wells)

C2-O2 2:45 PM - 3:00 PM (15 mins)

Analysis of the transcriptome of the major malaria vector Anopheles funestus. (Gareth Weedall)

C2-O3 3:00 PM - 3:15 PM (15 mins)

Successful application of a hybrid sequence-based genomewide association study (GWAS) design to detect the genetic basis of pyrethroid resistance in Anopheles arabiensis. (David Weetman)

C2-O4 3:15 PM - 3:30 PM (15 mins)

The isolation and identification of potential vaccine antigens against the poultry red mite (James Pritchard)

Day 1 Session D2 - (Room 11A) - Parasites - Ecology I - Chair: J Cable

D2-IS - Invited speaker Prof M Begon, University of Liverpool 2:00 PM - 2:30 PM (30 mins)

Infectious diseases: from wild rodents to universal truths (Mike Begon)

D2-O1 2:30 PM - 2:45 PM (15 mins)

On the origins of Schistosoma turkestanicum in Eastern Europe; an agent of zoonotic and veterinary schistosomiasis in a wildlife reservoir (Scott Lawton)

D2-O2 2:45 PM - 3:00 PM (15 mins)

Dynamics of plague (Yersinia pestis) in the wildlife system of the Kazakh pre-Balkhash desert. (Bethany Levick)

D2-O3 3:00 PM - 3:15 PM (15 mins)

The study of the great gerbil populations (Rhombomys opimus Licht 1823) from different habitats of the Kazakhstan area. (Aidyn Yeszhanov)

D2-O4 3:15 PM - 3:30 PM (15 mins)

Biased sex ratio among worms of the family Heligmosomidae – looking for a mechanism (Agnieszka Kloch)

Day 1 Session E2 - (Room 11C) - Parasites - Immunology & Pathology I - Chair: J Turner

E2-IS - Invited speaker Prof P Fallon, Trinty College Dublin 2:00 PM - 2:30 PM (30 mins)

Schistosoma mansoni: potent immune modulator for the parasites, not our, needs. (Padraic Fallon)

E2-O1 2:30 PM - 2:45 PM (15 mins)

Protective immunity against filarial infective larvae requires skin resident neutrophils (Nicolas Pionnier)

E2-O2 2:45 PM - 3:00 PM (15 mins)

Class switched antibody is necessary for efficient worm expulsion during a primary Trichuris muris infection (Emma Murphy)

E2-O3 3:00 PM - 3:15 PM (15 mins)

TLR2 stimulation of canine DH82 cells reduced the rate of Leishmania infantum infection in vitro and stimulated the production of IL-6 and TNF-alpha (Shazia Hosein)

E2-O4 3:15 PM - 3:30 PM (15 mins)

Leishmania major infection has a significant effect on atherogenesis and cytokines pattern in resistant mice (Marc Karam)

Day 1 Conference Break

Tea & Coffee 3:30 PM - 4:00 PM (30 mins)

Day 1 Session A3 - (Room 1B) - Malaria - Molecular & Cellular Biology II - Chair: E Salcedo-Sora

A3-O1 4:00 PM - 4:15 PM (15 mins)

Red blood cells preconditioned with hemin are less permissive to Plasmodium invasion. (Véronique Gaudreault)

A3-O2 4:15 PM - 4:30 PM (15 mins)

Quantification of Plasmodium-host protein interactions on intact, unmodified erythrocytes by backscattering interferometry (Abigail Perrin)

A3-O3 4:30 PM - 4:45 PM (15 mins)

Structure of malaria invasion protein RH5 with erythrocyte basigin and blocking antibodies (Katherine Wright)

A3-O4 4:45 PM - 5:00 PM (15 mins)

Enhanced clearance of infected red blood cells: A novel mechanism for malaria resistance in mice carrying a mutation in the host cytoskeletal protein, beta spectrin (Patrick Lelliott)

A3-O5 5:00 PM - 5:15 PM (15 mins)

A new tool for the chemical genetic investigation of Pfnek2 in Plasmodium falciparum (Deborah Mitcheson)

Day 1 Session B3 - (Room 1C) - NTDs - Diagnostics II - Chair: E Adams

B3-O1 4:00 PM - 4:15 PM (15 mins)

Lessons learnt from TB – molecular diagnostics for NTDs (Thomas Edwards)

B3-O2 4:15 PM - 4:30 PM (15 mins)

North American paragonimiasis as model for the development of improved serodiagnosis of paragonimiasis globally. (Peter Fischer)

B3-O3 4:30 PM - 4:45 PM (15 mins)

Novel LAMP assay for the diagnosis of Leishmaniasis (Emily Adams)

B3-O4 4:45 PM - 5:00 PM (15 mins)

Development and assessment of a point of care isothermal nucleic acid amplification test for the diagnosis of urogenital schistosomiasis (Bonnie Webster)

B3-O5 5:00 PM - 5:15 PM (15 mins)

Circulating antigen tests and urine reagent strips for diagnosis of active schistosomiasis in endemic areas (Poppy Lamberton)

Day 1 Session C3 - (Room 11B) - Helminth- Molecular & Cellular Biology - Chair: R Stothard

C3-O1 4:00 PM - 4:15 PM (15 mins)

Sensory Protein Kinase Signalling in Schistosoma mansoni Cercariae and Implications for Human Host Infection (Anthony Walker)

C3-O2 4:15 PM - 4:30 PM (15 mins)

Developing Neuropeptides as Transgenic Nematicides (Leonie Wilson)

C3-O3 4:30 PM - 4:45 PM (15 mins)

Defining the molecular target for fruit cysteine proteinases on the cuticle of Caenorhabditis elegans and parasitic nematodes (Victor Njom)

C3-O4 4:45 PM - 5:00 PM (15 mins)

Molecular Characterization of Fasciola parasites from Nigeria. (Nusirat Elelu)

C3-O5 5:00 PM - 5:15 PM (15 mins)

Heads or tails: Functional investigations of gene regulatory networks controlling planarian AP patterning in the model tapeworm Hymenolepis microstoma (Francesca Jarero)

Day 1 Session D3 - (Room 11A) - Parasites - Ecology II - Chair: J Cable

D3-O1 4:00 PM - 4:15 PM (15 mins)

Partitioning host species contributions to parasite persistence in multi-host communities (Andy Fenton)

D3-O2 4:15 PM - 4:30 PM (15 mins)

The Infections and Genetics of Wild House Mice, Mus Musculus domesticus (Luke Lazarou)

D3-O3 4:30 PM - 4:45 PM (15 mins)

D3-O4 4:45 PM - 5:00 PM (15 mins)

Interactions between multiple helminths and the gut microbiota in wild rodents (Sarah Perkins)

D3-O5 5:00 PM - 5:15 PM (15 mins)

Neuropeptides and sociality behaviours in plant parasitic nematodes (Emily Robb)

Day 1 Session E3 - (Room 11C) - Parasites - Immunology & Pathology II - Chair: J Turner

E3-O1 4:00 PM - 4:15 PM (15 mins)

The association of STAT6, IL33, IL10 and CHI3L1 polymorphisms on schistosomiasis infection and related morbidity (Alexandra Sparks)

E3-O2 4:15 PM - 4:30 PM (15 mins)

Immune-dependence of chemotherapy: characterization of Schistosoma mansoni tegument antigens exposed by praziquantel to host antibody reactivity (Joseph Igetei)

E3-O3 4:30 PM - 4:45 PM (15 mins)

Changes in antibody levels after schistosomiasis chemotherapy: a systematic review and metaanalysis (Mizuho Fukushige)

E3-O4 4:45 PM - 5:00 PM (15 mins)

Ovar-MHC Class II Haplotypes and Nematode Resistance in Sheep (Nur Mahiza Md Isa)

E3-O5 5:00 PM - 5:15 PM (15 mins)

DNA vaccination with Onchocerca volvulus Glyceraldehyde-3-Phosphate Dehydrogenase leads to protection in a mouse model of human filariasis (Vera Steisslinger)

Day 1 Poster Session

Poster session - Drinks and Viewing 5:30 PM - 7:00 PM (90 mins)

Day 1 Society Event

Young Parasitologists' Evening at Trebeca's, Liverpool 7:30 PM - 11:59 PM (269 mins)

Day 2 Opens 8:00 am

Registration 8:30 AM - 5:00 PM (510 mins)

Day 2 Session A4 - (Room 11A) - Malaria - Drugs I - Chair: G Biagini

A4-IS - Invited speaker Prof S Ward, Liverpool School of Tropical Medicine 9:00 AM -

9:30 AM (30 mins)

The trials and tribulations of generating fully synthetic peroxide based antimalarials. (Stephen A Ward)

A4-O1 9:30 AM - 9:45 AM (15 mins)

Atovaquone-Emetine dihydrochloride hydrate: a novel drug combination for malarial (Holly Matthews)

A4-O2 9:45 AM - 10:00 AM (15 mins)

Predictors of cardiac safety of artemisinin-based combination therapy in human immunodeficiency virus infected adults stabilized on antiretroviral therapy in Malawi (Eva Maria Hodel)

A4-O3 10:00 AM - 10:15 AM (15 mins)

Exploring the In vitro and In vivo activity of the aqueous and methanolic bark extract of Bridelia ferruginea using fluorescent based assays and the mouse animal model. (Maryam Shehu Idris-Usman)

A4-O4 10:15 AM - 10:30 AM (15 mins)

Overcoming drug-resistant malaria using structure-based drug design - P67 (SP) (Michael Capper)

Day 2 Session B4 - (Room 11B) - NTDs - Molecular Biology I- Chair: A Acosta-Serrano

B4-IS - Invited speaker Prof N Hall, University of Liverpool 9:00 AM - 9:30 AM (30 mins)

Genomics of Entamoeba: dissecting populations and species. (Neil Hall)

B4-O1 9:30 AM - 9:45 AM (15 mins)

Investigation of amino acid utilisation in Leishmania and its impact on host metabolism. (Archana Nayak)

B4-O2 9:45 AM - 10:00 AM (15 mins)

Investigating stage-specific trans-regulators in Leishmania spp. (Pegine Walrad)

B4-O3 10:00 AM - 10:15 AM (15 mins)

Genome plasticity and copy number variation determine gene expression differences in Leishmania (Stefano Iantorno)

B4-O4 10:15 AM - 10:30 AM (15 mins)

DNA repair proteins MRE11 and RAD50 are involved in genome plasticity in Leishmania (Marie-Claude Laffitte)

Day 2 Session C4 - (Room 11C) - Vectors - Emerging diseases andzoonose - Chair: S Torr

C4-IS - Invited speaker Prof C Drakeley, London School of Hygiene and Tropical

Medicine 9:00 AM - 9:30 AM (30 mins)

An integrated research programme to understand the epidemiology of Plasmodium knowlesi (ChrisDrakeley)

C4-O1 9:30 AM - 9:45 AM (15 mins)

The risk of mosquito-borne disease emergence in the UK (Matthew Baylis)

C4-O2 9:45 AM - 10:00 AM (15 mins)

Recent experiences controlling zoonotic diseases: Market traffic and risks of introduction of controlled pathogens (Richard Selby)

C4-O3 10:00 AM - 10:15 AM (15 mins)

Japanese encephalitis virus in Bangladesh: who's infecting whom? (Jennifer Lord)

C4-O4 10:15 AM - 10:30 AM (15 mins)

Quantifying wildlife host density and feeding preferences of tsetse (Glossina swynnertoni and G.pallidipes) in Serengeti National Park, Tanzania (Harriet Auty)

Day 2 Session D4 - (Room 13) - Parasites - Geospatial Ecology I - Chair: L Rinaldi

D4-IS - Invited speaker Prof G Cringoli, University of Naples 9:00 AM - 9:30 AM (30 mins)

Geographical information systems and cystic Echinococcosis (Giuseppe Cringoli)

D4-O1 9:30 AM - 9:45 AM (15 mins)

Mapping the burden of schistosomiasis and soil-transmitted helminthiasis in the context of integrated preventive chemotherapy in Nigeria (Uwemedimo Ekpo)

D4-O2 9:45 AM - 10:00 AM (15 mins)

Spatial epidemiology of co-infecting amphibian diseases (Kirsten McMillan)

D4-O3 10:00 AM - 10:15 AM (15 mins)

Rabbits In Space (Joanne Lello)

D4-O4 10:15 AM - 10:30 AM (15 mins)

Genome-scale phylodynamics of an endemic zoonotic virus: canine rabies virus in Tanzania (Kirstyn Brunker)

Day 2 Session E4 - (Room 14) - Parasites - Co-infections - Chair: D Blake

E4-IS - Invited speaker Prof A Fenwick, Imperial College London 9:00 AM - 9:30 AM (30 mins)

Present and future control of co-infections with schistosomiasis and STH (Alan Fenwick)

E4-O1 9:30 AM - 9:45 AM (15 mins)

ParaDesign: towards an online tool to design surveys for monitoring mass drug administration programmes implemented to control soil-transmitted helminthiasis in public health (Bruno Levecke)

E4-O2 9:45 AM - 10:00 AM (15 mins)

Do geohelminth co-infections affect outcomes of treatment for Trichuris trichuria? (Mark Booth)

E4-O3 10:00 AM - 10:15 AM (15 mins)

Age-distribution of soil-transmitted helminth infection after repeated annual school-based deworming: a community-wide cross sectional study in Western Kenya (Rita Oliveira)

E4-O4 10:15 AM - 10:30 AM (15 mins)

Global research on eight neglected zoonoses 1950 to 2014 (Mahmoud Abo-Shehada)

Day 2 Conference Break

Tea and Coffee Break 10:30 AM - 11:00 AM (30 mins)

Day 2 Session A5 - (Room 11A) - Malaria - Drugs II - Chair: G Biagini

A5-O1 11:00 AM - 11:15 AM (15 mins)

DDD107498: A Novel Preclinical Candidate for Malaria (Irene Hallyburton)

A5-O2 11:15 AM - 11:30 AM (15 mins)

Malaria transmission blocking drugs: new assays and new hits. (Donatella Taramelli)

A5-O3 11:30 AM - 11:45 AM (15 mins)

Assessment of the Haematological Profile of Children with Malaria Parasitaemia Treated with Three Different Artemisinin-Based Combination Therapies (Uchechukwu Chukwuocha)

A5-O4 11:45 AM - 12:00 PM (15 mins)

Screening the Malaria Box using a rapid in vitro Bioluminescence-Rate-of-Kill (BRoK) assay (Imran Ullah)

A5-O5 12:00 PM - 12:15 PM (15 mins)

Multiple Approaches towards understanding Artemisinin Pharmacodynamics (Matthew Phanchana)

Day 2 Session B5 - (Room 11B) - NTDs - Molecular Biology II - Chair: A Acosta-Serrano

B5-O1 11:00 AM - 11:15 AM (15 mins)

Proteomic analysis of trypanosome-infected tsetse saliva unravels a novel family of invariable GPIanchored surface glycoproteins from Trypanosoma brucei. (Aitor Casas-Sanchez)

B5-O2 11:15 AM - 11:30 AM (15 mins)

Development of an in silico pipeline for prioritizing novel Schistosoma mansoni drug targets. (Kezia Whatley)

B5-O3 11:30 AM - 11:45 AM (15 mins)

Schistosoma mansoni excretes/secretes extracellular vesicles containing definable populations of small non-coding RNAs (sncRNA) and proteins (Fanny Nowacki)

B5-O4 11:45 AM - 12:00 PM (15 mins)

G protein coupled receptors in the Fasciola hepatica genome - new opportunities for flukicide discovery? (Paul McVeigh)

B5-O5 12:00 PM - 12:15 PM (15 mins)

Circulating microRNAs represent species-specific biomarkers of Dirofilaria immitis infection (Erin McCammick)

Day 2 Session C5 - (Room 11C) - Vectors - Zoonesis - Chair: S Torr

C5-O1 11:00 AM - 11:15 AM (15 mins)

Ticks are knocking at our door - changes in agriculture and density of ticks (Anna Bajer)

C5-O2 11:15 AM - 11:30 AM (15 mins)

What do tsetse and trypanosomes tell modellers about the elimination of human African trypanosomiasis? (Kat Rock)

C5-O3 11:30 AM - 11:45 AM (15 mins)

Recombinant salivary proteins as a host exposure marker to sand fly bites (Petr Volf)

C5-O4 11:45 AM - 12:00 PM (15 mins)

Development of a xenomonitoring tool to monitor sleeping sickness (Lucas Cunningham)

C5-O5 12:00 PM - 12:15 PM (15 mins)

Admixture in humans of two divergent Plasmodium knowlesi populations associated with different macaque host species (Paul Divis)

Day 2 Session D5 - (Room 13) - Parasites - Geospatial Ecology II - Chair: L Rinaldi

D5-O1 11:00 AM - 11:15 AM (15 mins)

Sheep and Fasciola hepatica in Europe: the GLOWORM experience (Laura Rinalfi)

D5-O2 11:15 AM - 11:30 AM (15 mins)

Geographical information systems to plan cross sectional surveys of helminths in sheep farms: an example from southern Italy (Antonio Bosco)

D5-O3 11:30 AM - 11:45 AM (15 mins)

A spatially explicit mathematical model of Plasmodium knowlesi malaria transmission in Southeast Asia (Mary Parmiter)

D5-O4 11:45 AM - 12:00 PM (15 mins)

Investigation of a new focus of cutaneous leishmaniasis in Ghana (Godwin Kwakye-Nuako)

D5-O5 12:00 PM - 12:15 PM (15 mins)

Cryptosporidiosis in Gaza Strip (Adnan Al-Hindi)

Day 2 Session E5 - (Room 14) - Parasites - One Health & Zoonosis - Chair: R Stothard

E5-IS - Invited speaker Prof J Dupouy-C, Université Paris Descartes 11:00 AM - 11:30 AM (30 mins)

Travel medicine allows advances on the knowledge of Neglected meat & fish borne Parasitic Diseases (Jean Dupouy-Camet)

E5-O1 11:30 AM - 11:45 AM (15 mins)

Understanding the mechanisms of a zoonotic reservoir: leptospire infection in Rattus norvegicus in urban slums Brazil. (Amanda Minter)

E5-O2 11:45 AM - 12:00 PM (15 mins)

Insights into the molecular epidemiology and phylogeography of Echinostoma revolutum (Frölich, 1802): a zoonotic agent of human echinostomiasis (Egie Enabulele)

E5-O3 12:00 PM - 12:15 PM (15 mins)

Schistosoma haematobium and urogenital schistosomiasis; genetics, epidemiology and biological complexities (Bonnie Webster)

E5-O4 12:15 PM - 12:30 PM (15 mins)

Leishmaniasis in Suriname – outcomes of an integrated research programme (Henk Schallig)

Day 2 Society Event

British Socity for Parasitology AGM (Room 1B) 1:15 PM - 2:00 PM (45 mins)

Day 2 Conference Break

Lunch - Poster B setup 1:00 PM - 2:00 PM (60 mins)

Day 2 Session A6 - (Room 11A) - Malaria - Molecular Biology - Chair: A Craig

A6-IS - Invited speaker Dr J Baum, Imperial College London 2:00 PM - 2:30 PM (30 mins)

Imaging malaria parasite cell biology from whole cells down to single atoms…. towards achieving

superb resolution (Jake Baum)

A6-O1 2:30 PM - 2:45 PM (15 mins)

A role for the pir gene family in establishing chronic infection in malaria (Adam Reid)

A6-O2 2:45 PM - 3:00 PM (15 mins)

Effect of malaria infection on lipid profile and oxidative stress in children (Olusegun Matthew Akanbi)

A6-O3 3:00 PM - 3:15 PM (15 mins)

Rapid and inducible protein degradation system reveals Calcineurin phosphatase function at multiple stages during Plasmodium life-cycle (Nisha Philip)

A6-O4 3:15 PM - 3:30 PM (15 mins)

PfPKG - a signalling hub that regulates egress and invasion of the malaria parasite from erythrocytes (Mohammad Mahmood Alam)

Day 2 Session B6 - (Room 11B) - NTDs - Modelling - Chair: P Lamberton

B6-IS - Invited speaker Dr D Hollingsworth, University of Warwick 2:00 PM - 2:30 PM (30

mins)

Using mathematical models to inform the design of effective control of neglected tropical diseases (Déirdre Hollingsworth)

B6-O1 2:30 PM - 2:45 PM (15 mins)

Development of a Markov transition probability model to predict changes in Schistosomiasis infection following treatment (Arminder Deol)

B6-O2 2:45 PM - 3:00 PM (15 mins)

How effective is school-based deworming on the elimination of soil-transmitted helminths? (Jie Yang)

B6-O3 3:00 PM - 3:15 PM (15 mins)

Multiple ivermectin doses are macrofilaricidal: implications for the elimination of onchocerciasis (Maria-Gloria Basáñez)

B6-O4 3:15 PM - 3:30 PM (15 mins)

Longitudinal investigation of trends in Echinococcus coproantigen and PCR positivity during a control scheme (Alexander Mastin)

Day 2 Session C6 - (Room 11C) - Vectors - Host/Parasite Interactions I - Chair: L Reimer

C6-IS - Invited speaker Prof S Sinkins, Lancaster University 2:00 PM - 2:30 PM (30 mins)

Wolbachia-mosquito interactions and pathogen transmission (Steven Sinkins)

C6-O1 2:30 PM - 2:45 PM (15 mins)

Unravelling the sandfly salivary glycome (Karina Mondragon-Shem)

C6-O2 2:45 PM - 3:00 PM (15 mins)

A Review of the Importance of the Vertical Transmission of Dengue Viruses by Mosquitoes (Martin Grunnill)

C6-O3 3:00 PM - 3:15 PM (15 mins)

Studies on common ectoparasites of one humped camels (camelus Dromedarius) in cholistan desert (Muhammad Fiaz Qamar)

C6-O4 3:15 PM - 3:30 PM (15 mins)

Innate immunity as a structuring mechanism of parasite communities within and between withinhost infection sites (Evelyn Rynkiewicz)

Day 2 Session D6 - (Room 13) - Parasites - Wildlife & Aquatic - Chair: M Betson

D6-O1 2:00 PM - 2:15 PM (15 mins)

Worms, MHC and fish speciation: lessons from Lake Tanganyika (Pascal I. Hablützel)

D6-O2 2:15 PM - 2:30 PM (15 mins)

Parasites and invasive species: transmission during inter-specific interactions and potential effects on invasion dynamics (Jo James)

D6-O3 2:30 PM - 2:45 PM (15 mins)

Predation by crabs facilitates castrating trematodes in snails (Anieke van Leeuwen)

D6-O4 2:45 PM - 3:00 PM (15 mins)

Eco-Immunology: the effects of thermal variation on fish hosts of Saprolegnia parasitica (Alexander Stewart)

D6-O5 3:00 PM - 3:15 PM (15 mins)

The effects of inbreeding on disease susceptibility: Gyrodactylus turnbulli infection of guppies, Poecilia reticulata (Willow Smallbone)

Day 2 Session E6 - (Room 14) - Parasites - Evolution I - Chair: R Post

E6-IS - Invited speaker Dr A Waeschenbach, Natural History Museum, London 2:00

PM - 2:30 PM (30 mins)

Untangling the molecular phylogeny of tapeworms (Andrea Waeschenbach)

E6-O1 2:30 PM - 2:45 PM (15 mins)

Diversity and divergence of immune genes in wild rodents (Andrew Turner)

E6-O2 2:45 PM - 3:00 PM (15 mins)

Extensive nucleotide diversity within the mitochondrial genome of Schistosoma mansoni. (Andrew Briscoe)

E6-O3 3:00 PM - 3:15 PM (15 mins)

South African tortoise haemogregarines: with special focus on Haemogregarina parvula Dias, 1953 (Courtney Cook)

E6-O4 3:15 PM - 3:30 PM (15 mins)

Babesia behnkei sp. nov., a novel rodent Babesia species from the Sinai Mountains, Egypt (Anna Bajer)

Day 2 Conference Break

Tea and Coffee Break 3:30 PM - 4:00 PM (30 mins)

Day 2 Session A7 - (Room 11A) - Malaria - Epidemiology - Chair: P Horrocks

A7-O1 4:00 PM - 4:15 PM (15 mins)

Going in under the radar: Cryptic populations of infectious Plasmodium falciparum clones (Lynn Grignard)

A7-O2 4:15 PM - 4:30 PM (15 mins)

Development of a novel malaria antibody assay utilizing antigens from all 5 human pathogenic plasmodium species (Andreas Latz)

A7-O3 4:30 PM - 4:45 PM (15 mins)

Revealing a chronic high burden of non-Plasmodium falciparum infection in Uganda: a longitudinal survey in Bukoba village, Mayuge District (Russell Stothard)

A7-O4 4:45 PM - 5:00 PM (15 mins)

Performance of Rapid Diagnostic Test for Malaria Diagnosis at the Different Specialized Hospitals in Wad Medani, Gezira State, Sudan (Bakri Nour)

A7-O5 5:00 PM - 5:15 PM (15 mins)

A simplified molecular diagnostic platform for malaria: the direct on blood PCR-NALFIA system. (Henk Schallig)

Day 2 Session B7 - (Room 11B) - NTDs - Drugs - Chair: O Millington

B7-IS - Invited speaker Assistant Prof J Keiser, Swiss Tropical Institute 4:00 PM - 4:30 PM (30 mins)

Towards better drugs for trematode infections: field successes from pharmacokinetics to clinical trials (Jennifer Keiser)

B7-O1 4:30 PM - 4:45 PM (15 mins)

On the way to new drugs against schistosomiasis (Noemi Cowan)

B7-O2 4:45 PM - 5:00 PM (15 mins)

A lack of adaptive mutations in the gene coding for the multi-drug transporter SMDR2 suggests that it does not directly confer resistance to praziquantel in the human blood fluke Schistosoma mansoni (Billie Francesca Norman)

B7-O3 5:00 PM - 5:15 PM (15 mins)

The benefits of collaboration between pharma and academia: the antiwolbachia drug discovery story (Rachel Clare)

B7-O4 5:15 PM - 5:30 PM (15 mins)

PK/PD Modelling Predicts High Dose Rifampicin Can Achieve Rapid Elimination of Wolbachia from filarial nematodes (Ghaith Aljayyoussi)

Day 2 Session C7 - (Room 11C) - Vectors - Host/Parasite Interactions II - Chair: L Reimer

C7-O1 4:00 PM - 4:15 PM (15 mins)

Multihost pollinator pathogens: old and new (David Pascall)

C7-O2 4:15 PM - 4:30 PM (15 mins)

Onchocerciasis transmission in Ghana: effect of vector species on biting rates, transmission potentials and the human blood index (Poppy Lamberton)

C7-O3 4:30 PM - 4:45 PM (15 mins)

A cross-sectional survey of fly populations and latrine condition in trachoma-hyperendemic communities of the Bijagos Archipelago of Guinea-Bissau (Lucy Stubbs)

C7-O4 4:45 PM - 5:00 PM (15 mins)

Development of a new generation vaccine against Dermanyssus gallinae, the poultry red mite (Tatiana Kuster)

C7-O5 5:00 PM - 5:15 PM (15 mins)

The importance of freshwater snails in local transmission of urogenital schistosomiasis and the identification and characterization of transmission hot-spots in Zanzibar (Tom Pennance)

Day 2 Session D7 - (Room 13) - Students - Career tips - Chair: S MacDonald

Workshop - Caroline Ash (Senior Editor for Science) Kate Hawkins (Pamoja Communications - Science Comms) David Johnson (HSE specialist inspector) Valerie Decraene (Senior Epidemiologist PHE) 4:00 PM - 5:30 PM (90 mins)

Day 2 Session E7 - (Room 14) - Parasites - Evolution II - Chair: R Post

E7-O1 4:00 PM - 4:15 PM (15 mins)

Host range of RNA viruses predicts transmission and virulence of human infections (Liam Brierley)

E7-O2 4:15 PM - 4:30 PM (15 mins)

The Hepatozoon species (Adeleorina: Hepatozoidae) of African bufonids (Edward Netherlands)

E7-O3 4:30 PM - 4:45 PM (15 mins)

Host barriers to cross-species emergence of rabies virus (Nardus Mollentze)

E7-O4 4:45 PM - 5:00 PM (15 mins)

The molecular basis of parasitism in the nematode Strongyloides ratti (Vicky Hunt)

E7-O5 5:00 PM - 5:15 PM (15 mins)

The evolution of life history traits in response to drug selection (Alan Reynolds)

Day 2 Society Event

BSP Gala Dinner at the Maritime Museum 7:30 PM - 11:59 PM (269 mins)

Day 3 Opens 8:00 am

Registration 8:00 AM - 5:00 PM (540 mins)

Day 3 Plenary Sessions 4,5,6,7 - (Room 1A) - Chairs - Prof J Smith - Salford & Prof M Taylor - Liverpool School of Tropical Medicne

Plenary Session 4 - Wright Medal Lecture 2015 - Professor Julian Rayner 9:00 AM - 9:30 AM (30 mins)

Plenary Session 5 - Julie Jacobson, Bill & Melinda Gates Foundation - NTD research priorities 9:30 AM - 10:00 AM (30 mins)

Plenary Session 6 - Robert Don - Drugs for Neglected Diseases Initiative 10:00 AM - 10:30 AM (30 mins)

Plenary Session 7 - Jeremy Burrows - Medicines for Malaria Venture 10:30 AM - 11:00 AM (30 mins)

Drugs to eradicate malaria – future reality or fantasy island? (Jeremy Burrows)

Day 3 Conference Break

Coffee and Tea Break 11:00 AM - 11:30 AM (30 mins)

Day 3 Open Question Time Debate - "Conflict, environment & Ebola: Barriers to parasite control & elimination" Chair Peter Sissons

Panellists:

Julie Jacobson - Bill and Melinda Gates Foundation,

Judith Smith - Salford University,

Luis Albert Tchuenté - University of Yaounde, Cameroon,

Janet Hemmingway - LSTM,

Moses Bockarie – LSTM Anthony Bettee – Ministry of Health, Liberia

11:30 AM - 12:45 PM (75 mins)

Day 3 Conference Close

Exit and sight seeing around Liverpool 1:00 PM - 1:00 PM (0 mins)

Plenary Sessions 1, 2, 3 (Room 1A – Main Auditorium)

Chair - Prof M Taylor, BSP Vice-President, Liverpool School of Tropical Medicine

Malaria genomics: tracking a diverse and evolving parasite population

Dominic Kwiatkowski

Oxford University and the Wellcome Trust Sanger Institute

Malaria parasites are continually evolving to evade the immune system and human attempts to control the disease. To eliminate malaria from regions where it is deeply entrenched we need ways of monitoring what is going on in the parasite population, detecting problematic changes as soon as they arise, and executing a prompt and effective response based on a deep understanding of this natural evolutionary process. Powerful new tools to address this problem are emerging from the fast-growing field of genomic epidemiology, driven by new sequencing technologies and computational methods that allow parasite genome variation to be studied in much greater detail and in many more samples than was previously considered possible. These new tools will provide a deep understanding of what is going on in the parasite population, generating actionable knowledge for strategic planning of control interventions, for monitoring their effects and steering them for greatest impact, and for raising the alert if things start to go wrong.

16/04/2015 Plenary Sessions 1, 2, 3 (Room 1A) - Chair - Prof M Taylor, Liverpool School of Tropical Medicne 9:00 AM - 9:30 AM (30 mins)

Neglected tropical diseases: from application to innovation

Jürg Utzinger

Swiss Tropical and Public Health Institute

Quite logically, the neglected tropical diseases (NTDs) come to the fore only after one of the “big three” has been discussed – malaria, in the current British Society of Parasitology Spring Meeting 2015. Importantly though, over the past decade, the NTDs have gained visibility – in terms of numbers and faces. What are the main drivers explaining the growing interest in the NTDs? What is the true burden of the NTDs? Do we have the necessary tools to detect, control and eliminate the NTDs? These issues will be discussed within the frame of a rapidly changing landscape of global health initiatives, coupled with profound demographic and epidemiological transitions in many parts of the world. It will be argued that, along the value chain from discovery to large-scale implementation, there are unique opportunities for reverse advances. Indeed, applications can drive innovation, which, in turn, will move the NTD control and elimination agenda ahead.

16/04/2015 Plenary Sessions 1, 2, 3 (Room 1A) - Chair - Prof M Taylor, Liverpool School of Tropical Medicne 9:30 AM - 10:00 AM (30 mins)

Overcoming major impediments for success in vector-borne disease control.

Janet Hemingway

Liverpool School of Tropical Medicine

Prevention of malaria, and to a lesser extent a raft of the NTDs is heavily dependent on effective vector control. For diseases such as Chagas, malaria and visceral leishmaniasis the optimal vector control strategies are relatively clear. For others, such as dengue and chikungunya a number of different interventions have been tried over many years but none of these are particularly effective. Most of the cost-effective interventions that we have are insecticide based, relying heavily or in some cases exclusively on pyrethroids. Resistance to these insecticides has been spreading rapidly, particularly in Africa. The short, medium and long term plans for counteracting this resistance will be described.

16/04/2015 Plenary Sessions 1, 2, 3 (Room 1A) - Chair - Prof M Taylor, Liverpool School of Tropical Medicne 10:00 AM - 10:30 AM (30 mins)

Session A1 - (Room 1B) - Malaria - Hot Topics/Advances

Chair: Prof A Bell, Trinty College Dublin

Lack of evidence to support EPCR as a major cytoadherence receptor – (SP)

Yvonne Azasi and J. Alexandra Rowe

Centre for Immunity, Infection and Evolution, Institute of Immunology and Infection Research, University of Edinburgh

Sequestration of mature *Plasmodium falciparum* infected erythrocytes (IEs) in the microvasculature of the brain is mediated by adhesins from the *Plasmodium falciparum* Erythrocyte Membrane Protein, PfEMP1 family, encoded by var genes. A subset of PfEMP1, known as Domain Cassettes (DC) 8 and 13, has been shown to bind to Human Brain Endothelial Cells (HBEC), and Endothelial Protein C Receptor (EPCR) suggested as the host receptor on HBEC for DC8- and DC13-binding. EPCR is a transmembrane glycoprotein also found in plasma, which has anti-coagulation, anti-inflammatory, neuroprotective and anti-apoptotic effects. These protective effects are via its activation of protein C. The binding of IEs to EPCR may interfere with protein C binding and hence abrogate its protective functions, contributing to severe malaria pathology. We used three well-characterized DC8 or DC13 PfEMP1-expressing IEs to investigate the role of EPCR in HBEC-binding. Static binding assays and live immunofluorescence assays showed that parasites expressing IT4var19 (DC8) bind to EPCR. However, parasites expressing HB3var03 (DC13) or IT4var07 (DC13), did not bind EPCR. Furthermore, EPCR antibodies, soluble protein and EPCR siRNA knockdown inhibited adhesion of IT4var19 to HBEC by >80%, but had no significant effect on binding of the other two. These data show that not all DC8- and DC13-expressing IEs bind to EPCR, even though recombinant HB3var03 and IT4var07 proteins had previously shown high affinity EPCR-binding. This points to a mismatch between data from recombinant proteins and live IEs, and suggests that additional receptors, other than EPCR, are required for HBEC-binding.

16/04/2015 Session A1 - (Room 1B) - Malaria - Hot Topics/Advance - Chair: Prof A Bell 11:00 AM - 11:15 AM (15 mins)

Coping with stress: fight or flight in the malaria parasite *Plasmodium chabaudi*

Petra Schneider, Charlotte Repton, Sarah E. Reece

Institute of Evolutionary Biology, University of Edinburgh

Malaria parasites replicate asexually within the host, but require sexual stages for between-host transmission. During infection, parasites adjust their level of investment into sexual stages (reproductive effort) in response to changes in the in-host environment, including the availability of red blood cell resources, presence of competing parasite strains, and drug treatment. Until recently, it was assumed that plasticity in reproductive effort is explained by parasites maximising investment into transmission when in-host conditions deteriorate to such an extent that the survival of the infection is at risk (i.e. "terminal investment"). However, we have shown that parasite strategies are more 'sophisticated' because they can also increase investment into in-host survival by restraining reproductive effort in response to mild stress such as treatment with low drug doses. Life history theory predicts that parasites should evolve to allocate resources to sexual stages according to a trade off between the likely fitness returns from of current versus future transmission opportunities. We exposed the rodent malaria parasite *Plasmodium chabaudi* to increasing doses of antimalarial drugs to test whether they increase investment into transmission as in-host survival becomes decreasingly likely. We also investigate whether parasites measure their replicative state to assess their prospects of surviving in the host and to weigh up the value of current versus future transmission.

16/04/2015 Session A1 - (Room 1B) - Malaria - Hot Topics/Advance - Chair: Prof A Bell 11:15 AM - 11:30 AM (15 mins)

P-selectin is a host receptor for *Plasmodium* MSP7 ligands

Abigail Perrin, S. J. Bartholdson, G. W. Wright

Cell Surface Signalling Laboratory, Wellcome Trust Sanger Institute, Hinxton, Cambridge, United Kingdom CB10 1SA.

Plasmodium parasites, the etiological agents of malaria, typically elicit a non-sterile but protective immune response in human host populations. P-selectin is a cell surface receptor expressed in mammals that is a known component of the inflammatory response against pathogens and has been previously identified as a host factor that influences malaria-associated pathology both in human patients and rodent infection models. To better understand the molecular mechanisms underlying the involvement of P-selectin in the pathogenesis of malaria, we used a systematic extracellular protein interaction screen to identify *Plasmodium falciparum* MSP7, best known as a component of the MSP1 complex, as a binding partner of human P-selectin. We showed that the two proteins bound each other directly via the P-selectin C-type lectin and EGF-like domains and N-terminus of MSP7, which is not found on the merozoite surface. We also showed that multiple *P. falciparum* MSP7-related proteins bound to

P-selectin and that orthologous proteins in the murine parasite *P. berghei* (PbMSRP1 and PbMSRP2) interacted with mouse P-selectin. P-selectin binding is the first described function of the secreted N-terminus of PfMSP7, and its conservation across the *Plasmodium* MSP7 family implies an important biological function. Finally, we demonstrate that P-selectin, when complexed with MSP7, could no longer bind to its endogenous carbohydrate ligand, Sialyl-LewisX providing a possible mechanism for the known immunomodulatory effects of both MSP7 and P-selectin in malaria infection models.

16/04/2015 Session A1 - (Room 1B) - Malaria - Hot Topics/Advance - Chair: Prof A Bell 11:30 AM - 11:45 AM (15 mins)

Watching the clock: the story of circadian rhythms in malaria parasites – (SP)

Kimberley Prior, Aidan J. O'Donnell, Nicholas J. Savill, Sarah E. Reece

University of Edinburgh

The evolution and ecology of infectious diseases is a growing and dynamic field of research. A novel area within this field involves integrating chronobiology, immunology, parasitology, and evolutionary theory with mathematical models to investigate the circadian rhythms of malaria parasites. These parasites live within red blood cells of the mammalian host. Recent work indicates that mismatching the biological (developmental) rhythms of parasite and host, via a means of jet lagging parasites, results in a loss of parasite fitness. This highlights the importance of synchrony and timing of parasite developmental rhythms with its host. Major questions arising from this finding are "to what extent are parasites and hosts in control of synchrony and timing of parasite developmental rhythms" and "what roles do parasite developmental rhythms play in strategies for parasite offence and host defence"? To start to answer these questions a three day time series was performed to measure parasite and host factors every three hours, then twice per day sampling until the end of the infection. Integrating this large dataset with mathematical models it is possible to 1) characterise parasite development in terms of timing and synchrony 2) assess genetic variation in parasite rhythms and 3) ask whether rhythms co-vary with variation in the in-host environment. A better understanding of parasite and host dynamics during malaria infections means one can start to examine whether hosts or parasites are in charge, identify the factors responsible for rhythms and ultimately what the costs and benefits are to parasite and host.

16/04/2015 Session A1 - (Room 1B) - Malaria - Hot Topics/Advance - Chair: Prof A Bell 11:45 AM - 12:00 PM (15 mins)

Genome-wide population analysis of human *Plasmodium knowlesi* infections reveals extreme diversity and signatures of recent strong selection

Samuel Assefa[1], Caeul Lim[2], Mark D Preston[1], Craig W Duffy[1], Jonathan E Goldberg[2], Dan Neafsey[3], Paul CS Divis[1,4], Taane G Clark[1], Manoj T Duraisingh[2], David J Conway[1, 4], Arnab Pain[2, 4] and Balbir Singh[4]

[1] Pathogen Molecular Biology Department, London School of Hygiene and Tropical Medicine, Keppel St, London, WC1E 7HT United Kingdom [2] Department of Immunology and Infectious Diseases, Harvard School of Public Health, Boston, MA 02115, USA [3]Broad Institute, 415 Main St, Cambridge, MA 02142,

USA [4] King Abdulah University of Science and Technology, Thuwal, Jeddah, Kingdom of Saudi Arabia 5 Malaria Research Centre, Universiti Malaysia Sarawak, Kuching, Sarawak, Malaysia

Over the last ten years, there has been an increase in the reported numbers of human infections with the simian malaria parasite, *P. knowlesi*, including a proportion involving severe complications and death. Here, we have undertaken a whole genome survey of parasite diversity to test for evidence of recent selection or population structure that could indicate recent adaptation, analysing sequences of 50 clinical isolates from Malaysian Borneo and 5 lines from rhesus macaques. The overall diversity (π =6.3 x 10-3) was higher than previously reported in *P. falciparum* and *P. vivax*, suggesting the diversity in human patients reflects a large population reservoir in macaques. Allele frequency-based scans on clinical samples indicate that orthologues of known human malaria vaccine candidate genes including the circumsporozoite protein (csp), thrombospondin related adhesive protein (trap) and merozoite surface protein 1 (msp1) are targets of balancing selection. A number of genomic regions were found to be under strong positive selection using haplotype homozygosity scans, but as expected for a zoonotic parasite, the orthologues of drug resistance genes in endemic human malaria parasites were not under selection.

16/04/2015 Session A1 - (Room 1B) - Malaria - Hot Topics/Advance - Chair: Prof A Bell 12:00 PM - 12:15 PM (15 mins)

Session B1 - (Room 1C) - NTDs - Hot Topics/Advances

Chair: Prof D Molyneux, Liverpool School of Tropical Medicine

EUROLEISH-NET: Control of leishmaniasis, from bench to bedsite and community

Albert Picado[1], Michael Miles[3], Marleen Boelaert[2], Pascal Mertens[4], Petr Volf[5], José Luis Oliveira[6], Orin Courtenay[7], Jean-Loup Lemesre[8], Vicente Larraga[9], Elisa Sicuri[1], Montserrat Gállego[1], Mary Cameron[3], Simon Croft[3], Philippe Buscher[2], Jean-Claude Dujardin[2]

[1] Barcelona Institute for Global Health, Spain [2] Institute of Tropical Medicine, Belgium [3] London School of Hygiene and Tropical Medicine, UK [4] Coris Bioconcept, Belgium [5] Prague University, Czeck Republic [6] BMD Software, Portugal [7] Warwick University, UK [8] Institut de Recherche pour le Développement, France [9] Consejo Superior de Investigaciones científicas, Spain

Leishmaniasis control is the topic for EUROLEISH-NET, a Marie Sklodowska-Curie – Innovative Training Network. Leishmaniasis is a neglected infectious disease and a major public health and veterinary problem that afflicts both developing countries and Europe. The current technological and epidemiological advances underpin the necessity to develop training programmes aiming at developing new tools and strategies to control of leishmaniasis. An excellent group of academic and non-academic institutions in Europe and abroad will host 15 PhD students who will receive training in this programme. The expertise and training that will be offered ranges from parasitology to molecular science, genetics, epidemiology and strategic interventions. The 15 research projects designed encompass drug discovery, drug resistance, diagnostics and vaccine development, population genetics, vector control and integrated control programmes. The designated project supervisors have proven track records of

success in research and in training. The incorporation of trainee mobility into the network, together with the commitment, strong affiliations and technology transfer between the participants provide a highly synergistic framework for success. The EUROLEISH-NET coordinators have proven experience in laboratory, field, administrative and financial management, supported by a meticulously planned series of meetings and diligent monitoring of the progression of each researcher. We anticipate an extremely productive training and research output from EUROLEISH-NET. We expect to train the next generation of leading research scientists in this field, endowed with skills that are broadly and internationally transposable. We will present the EUROLEISH-NET training network.

16/04/2015 Session B1 - (Room 1C) - NTDs - Hot Topics/Advance - Chair: Prof D Molyneux 11:00 AM - 11:15 AM (15 mins)

Monitoring transmission of lymphatic filariasis post-mass drug administration in Ghana

Irene Offei Owusu, Francis Anto, Moses Bockarie, John Gyapong

School of Public Health, University of Ghana,Accra,Ghana: Liverpool School of Tropical Medicine, University of Liverpool, United Kingdom

Transmission Assessment Surveys is recommended by the WHO in the decision to stop Mass Drug Administration and for post-MDA surveillance in lymphatic filariasis elimination programs. In Ghana, four districts have stopped MDA after 9 rounds, TAS has been conducted and they have passed; therefore the need for post-MDA surveillance. This study aimed to monitor transmission of lymphatic filariasis Post-MDA in Ghana using periodic surveys. Two surveys were conducted; school-based and household surveys. A xenomonitoring study was also undertaken alongside using Indoor Residual Spraying. 1,600 children (6-10 years) from selected schools and 1,200 community members (11-60 years) participated in four annual school-based and household surveys respectively. Daytime finger-prick blood samples were collected from all consenting participants and tested using ICT, ELISA and PCR. Night time blood was collected for microscopy. Mosquitoes were captured from households, and LAMP assay performed to detect *W. bancrofti* parasites. Results obtained show that prevalence of LF in humans is fairly stable [2010=0.13%; 2012=0%; 2013=0.06%; 2014=0.1%] among children and the general population [2010=0.1%, 2012=0%, 2013=0.1%, 2014= 0.1%]. 5,609 mosquitoes were captured over a period of 2 years; 4277 *Anopheles* spp., 2287 *Culex* spp. and 45 *Mansonia* spp. Mosquitoes were pooled by community and species with an average pool size of 15. Six (0.1%) pools were positive for W. bancrofti, (5 *An. gambiae* spp. and 1 *Culex* spp.). Surveys in both humans and mosquitoes revealed very low antigen, antibody and microfilaria prevalence four years after last MDA. Monitoring should continued in post-MDA areas to detect early recrudescence

16/04/2015 Session B1 - (Room 1C) - NTDs - Hot Topics/Advance - Chair: Prof D Molyneux 11:15 AM - 11:30 AM (15 mins)

Introducing COUNTDOWN: a multidisciplinary implementation research consortium for control of NTDs

Russell Stothard, S Theobald, M Taylor

Liverpool School of Tropical Medicine

In the last decade control of NTDs has expanded with preventive chemotherapy campaigns and WHO has set ambitious targets within their 2020 Roadmap for disease control. To respond to the need for implementation research to foster scale-up of control of NTDs, the Department for International Development (DfID), UK funded a five year project entitled COU**NTD**OWN. The formation of this research consortium is set to conduct multidisciplinary investigations ranging from health system analyses, applied social science, field epidemiology and economical evaluations in Liberia, Ghana, Nigeria and Cameroon. Launched in November 2014, the consortium has been active during the inception year initial activities will be reported here.

16/04/2015 Session B1 - (Room 1C) - NTDs - Hot Topics/Advance - Chair: Prof D Molyneux 11:30 AM - 11:45 AM (15 mins)

Microfluidics for drug-assays and diagnostics on *Trypanosoma brucei*

Axel Hochstetter, Thomas Pfohl

Departement Chemie Universität Basel Basel Switzerland

Microfluidics is a scientific field, where small quantities of fluids are studied in a microscopic setting. Emerging from the interface between chemistry, physics and engineering, microfluidic applications for biological problems allow for high-speed analysis on the single cell level. Exploiting the laminar flows in this microscopic regime (at low Reynolds numbers) we present a rapid drug-assay based on chemical gradient microfluidics and optical micromanipulation. Here, we used this combination to in situ monitor the effects of drugs and chemicals on the motility of the flagellated unicellular parasite *Trypanosoma brucei*; specifically, the local cell velocity and the mean squared displacements (MSD) of the cell trajectories. With our method, we are able to record in situ cell fixation by glutaraldehyde, and to quantify the critical concentration of 2-deoxy-D-glucose required to completely paralyzing trypanosomes. In addition, we detected and quantified the impact on cell propulsion and energy generation at much lower 2-deoxy-D-glucose concentrations. Our microfluidics-based approach advances fast cell-based drug testing in a way that allows us to distinguish cytocidal from cytostatic drug effects, screen effective dosages, and investigate the impact on cell motility of drugs and chemicals. Using suramin, we could reveal the impact of the widely used drug on trypanosomes: suramin lowers trypanosome motility and induces cell-lysis after endocytosis. [1] 1.A. Hochstetter, E. Stellamanns, S. Deshpande, S. Uppaluri, M. Engstler and T. Pfohl, Lab Chip, (2015), DOI: 10.1039/c5lc00124b

16/04/2015 Session B1 - (Room 1C) - NTDs - Hot Topics/Advance - Chair: Prof D Molyneux 11:45 AM - 12:00 PM (15 mins)

Dracunculus medinensis: a genome on the verge of extinction

Caroline Durrant, Nancy Holroyd[1], Matthew Berriman[1], Mark L. Eberhard[2], Ernesto Ruiz-Tiben[3], James A. Cotton[1]

[1] The Wellcome Trust Sanger Institute, Hinxton, UK [2] Division of Parasitic Diseases and Malaria, Centers for Disease Control and Prevention, Atlanta, Georgia [3] The Carter Center, Atlanta, Georgia

Dracunculus medinensis (Guinea worm) is a nematode that causes the disease dracunculiasis. This was once a major parasitic infection, widespread across tropical Africa and Asia. However, infection is entirely preventable, through provision of clean water and behaviour change, leading to a drop in cases from around 3.5 million cases annually in the 1980s to 126 cases in 4 countries in 2014. The aim is that dracunculiasis will be the second human disease to be eradicated, the first parasitic disease and the first disease to be eradicated without the use of a vaccine or drug. However, dracunculiasis was believed to be extinct for a decade in Chad until new cases emerged in 2010. The current outbreak in Chad does not cluster by village or water source and many dogs are also infected. It appears that dogs are now the main host in Chad, with human cases being sporadic, perhaps transmitted by a common paratenic host. Building on de-novo genome assemblies for *D.medinensis* and *D.insignis*, we demonstrate the challenges of studying a genome that is on the verge of extinction and describe genome-wide patterns of diversity in *D.medinensis* samples from Chad and other parts of the range. While we show that the canine and human cases in Chad are more similar to each other than to human and animal cases from other parts of Africa, the small number of samples genotyped to date means we cannot conclusively show that transmission between dog and human cases is occurring.

16/04/2015 Session B1 - (Room 1C) - NTDs - Hot Topics/Advance - Chair: Prof D Molyneux 12:00 PM - 12:15 PM (15 mins)

Session C1 - (Room 11B) - Vectors - Hot Topics/Advances

Chair: Prof M Donnelly, Liverpool School of Tropical Medicine

Interspecific variation of the microbiota in natural tsetse fly populations – (SP)

Frances Blow[1], Ian Goodhead[3], Alistair C Darby[2]. George Tsiamis[3]. Kostas Bourtzis[1]

[1.] Department of Functional and Comparative Genomics, University of Liverpool, Crown Street, Liverpool, L69 7ZB 2. Department of Environmental and Natural Resources Management, University of Patras, [2] Seferi Street, Agrinio 30100, Greece [3.] Insect Pest Control Laboratory, Joint FAO/IAEA Programme of Nuclear Techniques in Food and Agriculture, Seibersdorf, Vienna, Austria

Tsetse flies belonging to the Genus *Glossina* are vectors of *Trypanosoma* protozoa: the causative agents of trypanosomiasis in humans and animals. Tsetse flies are known to harbor three microbial symbionts; *Wigglesworthia glossinidia*, *Sodalis glossinidius* and *Wolbachia* species. The tsetse fly microbiota is essential to host fitness, particularly during development, and is implicated in trypanosome transmission rate. Knowledge of the microbiota is critical in understanding the factors that make tsetse a successful

vector for trypanosomes and in developing control strategies. 16S rRNA sequencing by Illumina MiSeq of the bacterial communities of hundreds of insects from natural populations was used to study the diversity of bacteria associated with different species of tsetse from multiple locations across sub-Saharan Africa. This method was able to distinguish tsetse species based upon their associated bacterial communities, and host genotype was found to be more influential in distinguishing bacterial communities than geographic location. This can be attributed not only to the strict congruence between host phylogeny and that of their vertically transmitted *Wigglesworthia* symbionts, but also to fluctuating presence and abundance of other key members of the bacterial community. These features may contribute to the effectiveness of different species of tsetse as vectors of trypanosomes, and provide natural examples to study and improve our understanding of host-parasite-microbiota interactions.

16/04/2015 Session C1 - (Room 11B) - Vectors - Hot Topics/Advance - Chair: Prof M. Donnelly 11:00 AM - 11:15 AM (15 mins)

Shooting swoops: video-tracking *Anopheles gambiae* flight around insecticide treated bed nets – (SP)

Josephine Parker[1], Natalia Angarita-Jaimes[2], Mayumi Abe[1], Fabian Mashauri[3], Jackline Martine[3], Catherine E Towers[2], David Towers[2] & Philip J McCall [1]

[1] *Vector Biology Department, Liverpool School of Tropical Medicine, UK* [2] *Optical Engineering Group, Dept of Mechanical Engineering, University of Warwick, UK* [3] *National Institute of Medical Research, Mwanza, United Republic of Tanzania*

Large scale distribution of long lasting insecticide treated nets (LLINs) is a key part of many malaria control programs worldwide. However little is known about how mosquitoes interact with nets, or how insecticide treatment affects their behaviour. In order to gain a better understanding of this topic, the flight of *Anopheles gambiae* s.s. mosquitoes around human-baited bednets was tracked and recorded using a novel large scale camera system. Four behavioural flight modes were characterized: exploratory 'swooping' flight, 'visiting' in which mosquitoes made infrequent net contacts interspersed with long flight tracks, high contact 'bouncing' flight, and 'resting' on the net. A high proportion of activity was focussed on the roof of the net, in the area above the volunteer's torso, suggesting mosquitoes were attracted to the volunteer's breath and body odours. There was no evidence for any repellent action: mosquitoes were attracted to the LLIN by the human volunteer, but following a short initial period of insecticide contact (17-96 seconds per mosquito) net attack rapidly dropped to near negligible levels. This fall in activity did not occur at untreated nets, and may be attributed to contact irritant or toxic effects of insecticide on behaviour. Tracking experiments using wild mosquitoes in Tanzania revealed similar patterns of behaviour in lab and field settings. The results will be useful in designing and testing the next generation of bednets, potentially leading to new approaches to vector control.

16/04/2015 Session C1 - (Room 11B) - Vectors - Hot Topics/Advance - Chair: Prof M. Donnelly 11:15 AM - 11:30 AM (15 mins)

Are topical insect repellents effective against malaria in endemic populations? A systematic review and meta-analysis – (SP)

Anne Wilson[1], Vanessa Chen-Hussey[2], James G Logan[2], Steve W Lindsay[1]

[1] *School of Biological and Biomedical Sciences, Durham University, South Road, Durham DH1 3LE, UK*
[2]*London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK*

Recommended vector control tools for malaria such as long-lasting insecticidal nets act indoors and are therefore unable to tackle outdoor biting mosquitoes. Topical insect repellents may be able to reduce outdoor biting and morbidity from malaria. A systematic review and meta-analysis was conducted to assess the efficacy of topical repellents against malaria. Studies were identified using systematic literature search methods. Randomized and non-randomized controlled trials were included that assessed the effect of topical repellents (all active ingredients and concentrations) on *Plasmodium falciparum* or *Plasmodium vivax* malaria or infection in malaria-endemic populations. Meta-analysis of clinical data was conducted in order to generate summary risk ratios. Results Ten trials met the inclusion criteria. Topical repellents showed a non-significant 18% protective efficacy (95% CI: -8%, 38%) against *P. falciparum* malaria. Similarly, the average protective efficacy of topical repellents against *P. vivax* malaria did not reach significance (20%, 95% CI: -37%, 53%). Exclusion of non-randomized trials from the meta-analysis did not alter the findings. Although there is good evidence that topical repellents can provide individual protection against mosquitoes, this meta-analysis indicates that topical repellents are unlikely to provide effective protection against malaria in endemic populations. Studies were heterogeneous (e.g. study locations, follow-up periods, participant characteristics, topical repellents used, user compliance, and co-interventions) which may explain the variation in the efficacy of topical repellent between studies. Further well-designed trials of topical repellents at appropriate doses and alternative modes of repellent delivery, such as spatial repellents and long-lasting insecticide-treated clothing, are required.

16/04/2015 Session C1 - (Room 11B) - Vectors - Hot Topics/Advance - Chair: Prof M. Donnelly 11:30 AM - 11:45 AM (15 mins)

The *Anopheles gambiae* 1000 genomes project

Tiago Antao, on behalf of the *Anopheles gambiae* 1000 genomes consortium

Department of Vector Biology, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool

The *Anopheles gambiae* 1000 genomes Project (Ag1000G) is a consortial project using whole genome deep sequencing to provide a high resolution view of genetic variation in natural populations of *Anopheles gambiae*, the principal vector of *Plasmodium falciparum* malaria in Africa. A preliminary analysis of the 1st phase dataset, which includes 765 individual *Anopheles gambiae* and *Anopheles coluzzii* populations from eight sub-Saharan countries, will be presented. Preliminary results suggest that this dataset can provide valuable insights from both an epidemiological (i) and evolutionary biology perspective (ii): i. Successful vector control interventions associated with severe population reductions may leave clear genomic traces; for example runs of homozygozity or marked increases of the frequency of genes involved in resistance to insecticides. A representative case, involving a Kenyan population sampled after a successful control intervention will be discussed. ii. The impact of the ongoing

speciation process on the genomes of the *Anopheles gambiae* species complex will also be assessed. The dataset reveals clear signals of reproductive isolation between sympatric *An. coluzzii* (formerly M-form) and *An. gambiae* s.s. (formerly S-form) in Burkina Faso. The benefits of dense genotyping will be illustrated by presenting existing markers of form differentiation and the potential to find new loci involved in speciation.

16/04/2015 Session C1 - (Room 11B) - Vectors - Hot Topics/Advance - Chair: Prof M. Donnelly 11:45 AM - 12:00 PM (15 mins)

Mosquito-parasite interactions influence vectorial capacity for lymphatic filariasis

Lisa Reimer[1], Katherine Gleave[1], Darren Cook[1], Bruce Christensen[2], Mark Taylor[1]

[1] *Liverpool School of Tropical Medicine, Liverpool, UK* [2] *University of Wisconsin, Madison, USA*

The capacity of a vector population to transmit disease is a function of vector biting rates, vector population age structure and vector competence. Vector-parasite interactions can influence mosquito behavior and physiology, which in turn influence overall capacity. Through a series of labarotary and field-based experiments, we explored the impacts of filarial worm infection on mosquito longevity, fecundity, host-seeking and blood-feeding behavior. Laboratory-based experiments were conducted on *Aedes aegypti* infected with *Brugia malayi*. Mosquitoes were categorized as unexposed controls, exposed, infected or infective depending on parasite stage. We observed a significant decrease in receptivity to human odours when mosquitoes were at the infected stage (positive for developing worms) and a significant increase when mosquitoes were infective with L3 larvae. The response in the short-range host-seeking assay was density dependent: responders had a significantly higher L3 burden than non-responders. We observed a decrease in the mean number of eggs produced by infected mosquitoes and a significant increase in mortality by the infective stage. No differences were observed in probing and bloodfeeding behaviour in infected mosquitoes. Field-based exposures of anopheline mosquitoes with Wuchereria bancrofti further support the observation that vector competence and longevity are strongly influenced by parasite density.

16/04/2015 Session C1 - (Room 11B) - Vectors - Hot Topics/Advance - Chair: Prof M. Donnelly 12:00 PM - 12:15 PM (15 mins)

Session A2 - (Room 1B) - Malaria - Molecular & Cellular Biology I –

Chair: E Salcedo-Sora, Liverpool Hope Univeristy

Dissecting the regulation and dynamics of malaria parasite egress

Michael Blackman, Christine R Collins[1]*, Sujaan Das[1]*, Chrislaine Withers-Martinez[1], Fiona Hackett[1], Abigail Perrin[2], Robert Stallmach[1], Gavin Wright[2] and Michael J. Blackman[1]

[1] *Division of Parasitology, MRC National Institute for Medical Research, London NW7 1AA, UK*
[2] *Cell Surface Signalling Laboratory, Wellcome Trust Sanger Institute, Cambridge CB10 1HH*

The malaria parasite replicates in a parasitophorous vacuole (PV) within infected red blood cells. Egress of malaria merozoites from the host red cell is a tightly regulated event that is essential for completion of the parasite life cycle and for disease progression. However, little is known about how egress is controlled and how the bounding PV membrane and red cell membrane and cytoskeleton are disrupted to enable egress. Previous work from this lab has shown that egress is preceded by the cGMP-dependent discharge of a serine protease called SUB1 from the intracellular parasite into the lumen of the PV1,2. There, the protease rapidly modifies several abundant parasite proteins, including two soluble papain-like proteins called SERA53 and SERA64, and an abundant merozoite surface protein called MSP1. All three of these SUB1 substrates are essential but of unknown function. In this talk I will present a snapshot of recent published and unpublished data that provide exciting new insights into how the SUB1 pathway contributes in unexpected ways to the kinetics and efficiency of malarial egress. 1. Yeoh et al. (2007) Cell 131, 1072-1083. 2. Collins et al. (2013) PLoS Pathogens 9:e1003344. 3. Stallmach et al. (2015) Mol Microbiol doi: 10.1111/mmi.12941. [Epub ahead of print]. 4. Ruecker et al. (2012) J Biol Chem 287, 37949-37963.

16/04/2015 Session A2 - (Room 1B) - Malaria - Molecular & Cellular Biology I - Chair: E Salcedo-Sora 2:00 PM - 2:30 PM (30 mins)

Increased adhesion of *Plasmodium falciparum* infected erythrocytes to intercellular adhesion molecule 1 in children with acute intestinal injury

James Church[1,2] Lydia Nyamako[2], Peter Olupot-Olupot[3,4], Kathryn Maitland[2,5], Britta C. Urban[2,6]

[1.] Centre for Paediatrics, Blizard Institute, Queen Mary University of London, UK [2.] KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya [3.] Mbale Regional Referral Hospital, Clinical Research Unit (MCRU), Mbale, Uganda [4.] Busitema University, Faculty of Health Sciences, Mbale Campus, Mbale, Uganda [5.] Wellcome Trust Centre for Clinical Tropical Medicine, Imperial College, London, UK [6.] Liverpool School of Tropical Medicine, Parasitology Department, Liverpool, UK

Children with *Plasmodium falciparum* malaria are at increased risk of concomitant invasive bacterial infection particularly with enteric gram-negative organisms. These co-infections are associated with a poor prognosis. The preponderance of gram-negative bacteraemias in malaria is suggestive of an intestinal barrier dysfunction however the precise mechanism of intestinal damage remains poorly understood. We hypothesised that sequestration of infected red blood cells (iRBCs) in the intestinal microvasculature contributes to tissue damage and subsequent microbial translocation. RBCs of 109 children hospitalised with malaria were taken into culture and allowed to grow to maturity. Of the 109 children, iRBCs of 48 (44%) children survived to maturity. By means of a static adhesion assay, we measured adhesion of these iRBCs to recombinant proteins constitutively expressed on the gut endothelial cell surface. Adhesion phenotypes from the 48 samples were then correlated with biochemical evidence of gut compromise (defined as the presence or absence of endotoxaemia or elevated plasma I-FABP). The majority of iRBCs demonstrated binding to the endothelial receptors CD36 and to a lesser extent to ICAM-1, consistent with previous studies. Adhesion of iRBCs to CD36 and ICAM-1 as well as rosetting was similar in children with or without endotoxemia. By contrast, we observed increased adhesion of iRBCs to ICAM-1 in children who had elevated plasma concentrations of I-FABP (Spearman rho = 0.36, p= 0.022), a marker of acute enterocyte damage. These findings suggest that the adhesion of iRBCs could contribute to increased susceptibility to gram-negative bacteraemia in children with malaria in sub-Saharan Africa.

16/04/2015 Session A2 - (Room 1B) - Malaria - Molecular & Cellular Biology I - Chair: E Salcedo-Sora 2:30 PM - 2:45 PM (15 mins)

Structural characterisation of chromatin proteins in the human malarial parasite – (SP)

Ashley Jordan, Juliette Devos, Michael Haertlein, Edward Mitchell, Trevor Forsyth, Catherine Merrick

Keele University, School of Life Sciences, Newcastle-Under-Lyme, Staffordshire, ST5 5BG, UK Institut Laue-Langevin, Life Sciences Group, 71 Avenue des Martyrs, 38042 Grenoble, France

Malaria remains a global public health burden with approximately 600,000 deaths per year, predominantly among young children in sub-Saharan Africa. The human malarial parasite, *Plasmodium falciparum*, causes illness by infecting human red blood cells. Chronic infections depend on antigenic variation of cell surface antigens expressed on these cells. *P. falciparum* erythrocyte membrane protein 1 (PfEMP1) is the major surface antigen and this protein mediates sequestration of infected cells within host blood vessels, which leads to severe malaria. Expression of this protein is controlled by a family of 'var' genes which are regulated via an epigenetic process through modifications to the encoding chromatin. The sirtuin enzyme, PfSir2a, is a NAD+ dependent histone deacetylase whose disruption has been shown to affect the expression of PfEMP1. It has a putative binding partner, PfAlba3, that is a DNA binding protein and may provide a bridge between PfSir2a and DNA, facilitating PfSir2a activity to help to silence var genes. We are using small angle neutron and X-ray solution scattering (SANS/SAXS) techniques to characterise the interactions between PfSir2a, PfAlba3 and DNA. This work will give us a better understanding of the molecular mechanisms underlying antigenic silencing and switching - key virulence processes in the malaria parasite.

16/04/2015 Session A2 - (Room 1B) - Malaria - Molecular & Cellular Biology I - Chair: E Salcedo-Sora 2:45 PM - 3:00 PM (15 mins)

Structural conservation despite huge sequence diversity allows EPCR binding by the PfEMP1 family implicated in severe childhood malaria – (SP)

Clinton Lau[1], Louise Turner[2], Jakob S. Jespersen[2], Edward D. Lowe[1], Bent Petersen[3], Christian W. Wang[2], Jens E. V. Petersen[2], John Lusingu[4], Thor G. Theander[2], Thomas Lavstsen[2] and Matthew K. Higgins[1]

[1] Department of Biochemistry, University of Oxford, South Parks Road, OX1 3QU, Oxford, UK [2] Centre for Medical Parasitology, Department of International Health, Immunology & Microbiology, University of Copenhagen and Department of Infectious Diseases, Rigshospitalet, 1017 Copenhagen, Denmark. [3] Center for Biological Sequence Analysis, Technical University of Denmark, 2800, Kgs. Lyngby, Denmark [4]National Institute for Medical Research, Tanga, 2448, Ocean Road, P.O. box 9653, Dar es Salaan, Tanzania.

The PfEMP1 family of surface proteins is central for *Plasmodium falciparum* infection and must retain their ability to bind to host receptors while also diversifying to aid immune evasion [1]. The interaction between CIDRalpha1 domains of PfEMP1 and endothelial protein C receptor (EPCR) is associated with

severe childhood malaria [2]. We combine crystal structures of CIDRalpha1:EPCR complexes with analysis of 885 CIDRalpha1 sequences, showing that the EPCR-binding surfaces of CIDRalpha1 domains are conserved in shape and bonding potential, despite dramatic sequence diversity. The binding surface of the CIDR domains consists of a central hydrophobic residue which protrudes into a hydrophobic groove in EPCR, surrounded by a ring of hydrophilic residues. This surface mimics features of the natural EPCR ligand, protein C, and can block this ligand interaction [2]. Using peptides corresponding to the EPCR-binding region, antibodies can be purified from individuals in malaria-endemic regions that block EPCR binding of diverse CIDRalpha1 variants. This highlights the extent to which such a surface protein family can diversify while maintaining ligand-binding capacity and identifies features that should be mimicked in immunogens to prevent EPCR binding. 1. Smith, J. D., Rowe, J. A., Higgins, M. K. & Lavstsen, T. Malaria's deadly grip: cytoadhesion of *Plasmodium falciparum*-infected erythrocytes. Cell. Microbiol. 15, 1976–83 (2013). 2. Turner, L. et al. Severe malaria is associated with parasite binding to endothelial protein C receptor. Nature 498, 502–5 (2013).

16/04/2015 Session A2 - (Room 1B) - Malaria - Molecular & Cellular Biology I - Chair: E Salcedo-Sora 3:00 PM - 3:15 PM (15 mins)

Merozoite antigens of *Plasmodium falciparum* elicit strain-transcending opsonising immunity – (SP)

Danika Hill[1,2], Danny W. Wilson[1,2,3], Emily M. Eriksson[1,2], Alex D. Uboldi[1,2], Diana S. Hansen[1,2], Peter Siba[4], Alan F. Cowman[1,2], Ivo Mueller[1,2], Louis Schofield[1,2,5]

[1.] The Walter and Eliza Hall Institute of Medical Research, Parkville, Australia [2.] Department of Medical Biology, University of Melbourne, Parkville, Australia [3.] Research Centre for Infectious Diseases, School of Molecular and Biomedical Science, University of Adelaide, Adelaide, Australia [4.] Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea [5.] Australian Institute of Tropical Health and Medicine, James Cook University, Douglas, Australia

It is unclear whether naturally acquired immunity to *Plasmodium falciparum* results from antibodies produced against multiple, diverse antigens or fewer highly conserved antigens. Moreover, specific antibody functions required for protective immunity remain poorly understood. These considerations are highly relevant to vaccine design. In this study, we investigated whether merozoite opsonisation was associated with naturally acquired immunity, and displayed strain-specific or strain transcending specificities. Using our validated assay of merozoite phagocytosis, opsonisation responses in a cohort of plasma from Papua New Guinea (PNG) were measured to a panel of 15 diverse parasite strains. Highly correlated opsonisation responses were observed across all parasite strains, as were strong associations with protection (Hazard ratio, 0.15, 95% confidence interval 0.04-0.63). No strain-specific acquisition of opsonising antibodies was observed, and MSP-3, MSP-6, MSPDBL1 or PfMSP1-19 were not dominant antigens for opsonisation. We observed opsonising antibodies to transcend the antigen diversity between strains, and suggest that conserved domains within merozoite surface antigens may be important vaccine candidates.

16/04/2015 Session A2 - (Room 1B) - Malaria - Molecular & Cellular Biology I - Chair: E Salcedo-Sora 3:15 PM - 3:30 PM (15 mins)

Session B2 - (Room 1C) - NTDs - Diagnostics I

Chair: DR E Adams, Liverpool School of Tropical Medicine

Under the microscope: new approaches in the diagnosis of intestinal worms and schistosomiasis

Lisette van Lieshout

Leiden Clinical Parasitology Group; Dept. of Parasitology; Leiden University Medical Center (LUMC); The Netherlands

Reliable laboratory tests to diagnose intestinal helminths and *Schistosoma* infections are essential for appropriate individual patient management, as well as for prevalence mapping at the community level. The traditional method, meaning microscopic examination of stool and urine samples, is relatively simple to perform, but also has some major disadvantages including lack of sensitivity as well as being observer dependent. With the elimination of these helminths on the horizon, highly sensitive and reproducible diagnostic tools become increasingly important. In this presentation new diagnostic approaches will be discussed, with a focus on the detection of parasite DNA in clinical samples via multiplex real-time PCR. Examples of the application of these tests in different study populations will be shown, ranging from usage as a routine diagnostic test in European hospital laboratories, to the outcome of high-throughput population-based surveys in low-resource communities in endemic regions. Special attention will be paid to PCR-based diagnosis of genital schistosomiasis. In addition, the value of immunodiagnostic assays will be discussed for schistosomiasis. Although serology can be used as a reliable first line diagnostic test in travellers with acute infection, it has its limitations in population based surveys as antibodies remain detectable for many years after treatment. Alternatively, tests to detect the schistosome circulating antigens CCA and CAA are increasingly used to diagnose active infections. The value of these user-friendly urine-based point-of-care CCA and CAA detection assays will be briefly discussed and compared with PCR data, being either for population-based prevalence mapping or for the diagnosis of individual patients.

16/04/2015 Session B2 - (Room 1C) - NTDs - Diagnostics I - Chair: E Adams 2:00 PM - 2:30 PM (30 mins)

Comparison of individual and pooled samples for the assessment of soil-transmitted helminth, *Schistosoma mansoni* and *S. haematobium* infection intensity in children, Ethiopia

Abraham Degarege[1], Ashenafi Kure[2], Zeleke Mekonnen[3], Daniel Dana[3], Mitiku Bajiro[3], Mio Ayana[3], Mengistu Legesse[1], Yohannes Negash[1], Jozef Vercruysse[4], Berhanu Erko[1], Bruno Levecke[4]

[1]Aklilu Lemma Institute of Pathobiology, Addis Ababa University, Addis Ababa, Ethiopia [2]South Health Bureau, Public Health Laboratory, Hawassa, Ethiopia. [3]Department of Medical Laboratory Sciences and Pathology, Jimma University, Jimma, Ethiopia [4]Department of Virology, Parasitology and Immunology, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium

We have recently shown that pooling of stool samples allows rapid assessment of intensity of soil-transmitted helminth (STH, *Ascaris lumbricoides*, *Trichuris trichiura* and hookworms) infections using the McMaster. In the present study we evaluated our pooling strategy for the assessment of the

intensity of STH, *Schistosoma mansoni* and *S. haematobium* infections. Two cross-sectional surveys were conducted in school-aged children in Ethiopia. In the first survey, a stool sample of 360 subjects was examined for STH and *S. mansoni* infections using Kato-Katz in southwest Ethiopia. In addition, we compared the time between an individual and pooled examination strategy. In the second survey, a urine sample of 580 subjects was examined for *S. haematobium* infection using urine filtration in northeast Ethiopia. In both surveys individual and pooled samples (pools sizes of 5, 10 and 20) were examined. Except for hookworms, there was a significant positive correlation between the mean of the individual egg counts and the egg counts of the pooled samples, regardless of the pool size. There was no significant difference in infection intensity between the examination of individual and pooled stool samples, except for hookworms and *S. haematobium*. For these helminths, pools of 5 (*S. haematobium*) and 10 (hookworms) resulted in lower levels of infection intensity. A pooled examination strategy reduced the time in the laboratory by 71.5% (pool size of 5), 77.5% (pool size of 10) and 81% (pool size of 20). We conclude that samples holds promise as a cost-effective strategy for assessing infection intensity.

16/04/2015 Session B2 - (Room 1C) - NTDs - Diagnostics I - Chair: E Adams 2:30 PM - 2:45 PM (15 mins)

IgG1 as a potential biomarker of post-chemotherapeutic relapse in visceral leishmaniasis, and adaptation to a rapid diagnostic test

Tapan Bhattacharyya[1], Armon Ayandeh[1], Andrew K. Falconar[2], Shyam Sundar[3], Sayda El-Safi[4], Marissa A. Gripenberg[1], Duncan E. Bowes[1], Caroline Thunissen[5], Om Prakash Singh[3], Rajiv Kumar[3,6], Osman Ahmed[4,7], Osama Eisa[4], Alfarazdeg Saad[4], Sara Silva Pereira[1], Marleen Boelaert[8], Pascal Mertens[5], Michael A. Miles [1].

[1] Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, United Kingdom, [2] Departamento de Medicina, Universidad del Norte, Barranquilla, Colombia, [3] Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India, [4] Faculty of Medicine, University of Khartoum, Khartoum, Sudan, [5] Coris BioConcept, Gembloux, Belgium, [6] Immunology and Infection Laboratory, Queensland Institute of Medical Research, Herston, Queensland, Australia, [7] Department of Laboratory Medicine, Karolinska Insitutet, Stockholm, Sweden, 8 Department of Public Health, Institute of Tropical Medicine, Antwerp, Belgium

Symptomatic visceral leishmaniasis (VL) is usually fatal without effective chemotherapy. Distinction of asymptomatic carriage from progressive disease and the prediction of relapse following treatment are hampered by the lack of prognostic biomarkers for use at point of care. Here, IgG isotype and subclass levels were determined using unpaired samples from Indian and Sudanese patients with differing clinical VL status, including pre-treatment active VL, post-treatment cured, post-treatment relapsed, and post kala-azar dermal leishmaniasis, and seropositive and seronegative endemic healthy controls. *L. donovani* antigen-specific IgG1 levels were significantly elevated in relapsed versus cured VL patients ($p<0.0001$). Using paired Indian VL sera, IgG1 levels had not decreased significantly at day 30 after the start of treatment ($p = 0.8304$), but were dramatically decreased by 6 months compared to day 0 ($p = 0.0032$) or day 15 ($p<0.0001$) after start of treatment. Similarly, Sudanese sera taken soon after treatment did not show a significant change in the IgG1 levels ($p = 0.3939$). Prototype lateral flow mmunochromatographic rapid diagnostic tests (RDTs) were developed to detect IgG1 levels following VL treatment: more than 80% of the relapsed VL patients were IgG1 positive; at least 80% of the cured VL patients were IgG1 negative ($p <0.0001$). Thus, six months after treatment of active VL, elevated levels of specific IgG1 were

associated with treatment failure and relapse, whereas no IgG1 or low levels were detected in cured VL patients. A lateral flow RDT was successfully developed to detect anti-*Leishmania* IgG1 as a potential biomarker of post-chemotherapeutic relapse.

16/04/2015 Session B2 - (Room 1C) - NTDs - Diagnostics I - Chair: E Adams 2:45 PM - 3:00 PM (15 mins)

Performance evaluation of enzyme linked immunosorbent assay and lineblot for serological diagnosis of Chagas (*Trypanosoma cruzi*) Disease

Andreas Latz[1], P. Conception[2], D. M. Bustamante Zamora[3], J. Völger[1]
[1]NovaTec Immundiagnostica GmbH, R+D, Dietzenbach, Germany [2]Pontificia Universidad Javeriana, Laboratorio de Parasitología Molecular, Bogotá, Colombia [3]Universidad de San Carlos, Escuela de Biología, Colonia Santa Rosa, Guatemala

Chagas disease, caused by infection with the protozoan parasite *Trypanosoma cruzi*, affects 8-11 million individuals worldwide. It is endemic from the south of the US to Central America and South America. The disease is commonly transmitted by an insect vector but may also be spread through blood transfusion and organ transplantation, ingestion of food contaminated with parasites and from a mother to her fetus. Early diagnosis is essential so etiological treatment can be administered. Screening of donated blood, blood components, and solid organ donors, as well as donors of cells, tissues, and cell and tissue products for *T. cruzi* is mandated in all Chagas-endemic countries and has been implemented. Here we describe a new Novalisa ELISA and lineblot for diagnosis of Chagas disease. These test systems are taking advantage of the chimeric multiepitope antigen TcF (IDRI). The test was evaluated in endemic countries like Colombia and Guatemala with chronic patients (symptomatic and asymptomatic), regnant women and newborns and a Chagas negative control group. Overall performance of both testsystems, ELISA and blot, was excellent. In addition both new test systems were the only one who could reliably detect congenital transmission of Chagas from a mother to the child, making it essential for screening of new borns in endemic countries to provide treatment as early as possible. In our hands NovaTec Immundiagnostica ELISA and blots can reveal positive patients that currently used in house tests can not detect. Results were confirmed by qRT-PCR and compared with results of other commercial kits.

16/04/2015 Session B2 - (Room 1C) - NTDs - Diagnostics I - Chair: E Adams 3:00 PM - 3:15 PM (15 mins)

Validity of Polymerase Chain Reaction (PCR) versus coproscopic examination for diagnosing infection with *Schistosoma mansoni* in low intensity endemic area in Egypt.

Hassan Bassiouny[1], Safaa M. Eassa[1], Walaa A. Hazzah[2], Engy O. El-Komy[1]
Departments of [1] Tropical Health and [2]Microbiology, High Institute of Public Health, Alexandria University, Egypt

Introduction: Egypt is one of the most highly endemic countries with localized transmission foci of schistosomiasis. Aim of work: This study assessed the validity of conventional PCR (cPCR) versus coproscopic techniques as gold-standard for diagnosing of *S. mansoni* infection in low intensity endemic area in Kafr El-Sheikh governorate, Egypt. Methodology: It was a cross-sectional study. The study examined faecal samples of 120 primary schoolchildren [74 (61.7%) males and 46 (38.3%) females] with

mean age 10.16±0.798 years (range: 9-12 years). Three fresh stool samples were collected on three consecutive days from each study subject and examined by FECS (3 slides from one fecal sample of the first day), Kato-Katz (10 slides from 3 fecal samples on 3 consecutive days- 6 slides on the first day and 2 slides on 2nd and 3rd days samples respectively) and cPCR (one sample of the fecal specimen of the first day). Results: The prevalence *S.mansoni* infection was 40.0 %, 69.2% and 80.8% by the three techniques respectively. All infected cases were of low intensity of infection. The Kappa index and diagnostic parameters showed a good diagnostic value of cPCR as compared to coproscopic examination. Conclusion: cPCR demonstrated a good diagnostic performance for the detection of *S. mansoni* in low intensity endemic area versus coproscopic examination as gold-standard.

16/04/2015 Session B2 - (Room 1C) - NTDs - Diagnostics I - Chair: E Adams 3:15 PM - 3:30 PM (15 mins)

Session C2 - (Room 11B) - Vectors - Molecular & CellularBiology I

Chair: Prof H Ranson, Liverpool School of Tropical Medicine

The male mosquito contribution to malaria transmission: mating increases female susceptibility to human malaria parasites.

Mara Lawniczak

Wellcome Trust Sanger Institute

Mating has profound consequences on physiology and behavior in many organisms. In many organisms, mating also reduces ability of females to defend against infections. In many Anopheline mosquitoes, females tend to mate once in their lifetime, receiving sperm and a mating plug comprising seminal fluid proteins and a steroid hormone. The receipt of the steroid hormone in particular both induces females to lay eggs and reduces their ability to remate. We explored the impact of mating on female susceptibility to *Plasmodium falciparum* infection and discovered that mated females develop significantly higher infection loads than virgins. The impact of mating on parasite transmission does not appear to be mediated by midgut microbiota. Males may contribute to malaria transmission by rendering females more susceptible to *Plasmodium falciparum*. We are now exploring what factors underlie this difference between virgin and mated females.

16/04/2015 Session C2 - (Room 11B) - Vectors - Molecular & Cellular Biology I - Chair: H Ranson 2:00 PM - 2:30 PM (30 mins)

T345M, an additional mutation associated with insecticide resistance in the *Anopheles gambiae* GABA receptor, Rdl

Jennina Taylor-Wells[1], Basil Brooke[2], Isabel Bermudez[1], Andrew Jones[1]

[1]Department of Biological and Medical Sciences, Faculty of Health and Life Sciences, Oxford Brookes University, Oxford, OX3 0BP, UK [2]Centre for Opportunistic, Tropical and Hospital Infections, National Institute for Communicable Diseases/NHLS, Sandringham, Johannesburg, SA

Cys-loop ligand gated ion channels contain the molecular targets for insecticides, including the γ-aminobutyric acid (GABA)-gated chloride channel Rdl ('resistance to dieldrin'). In *Anopheles gambiae* Rdl the A296G mutation is associated with insecticide resistance. We report a further mutation, T345M, identified in insecticide resistant *An. gambiae* mosquitoes. An *An. gambiae* s.s strain containing phenotypic resistance to dieldrin was colonised using wild material collected from the Democratic Republic of Congo. Samples of adult females were exposed to 4% dieldrin and were sorted according to resistant or susceptible phenotype 24 h post exposure. From both phenotypes the complete coding sequence of Rdl was amplified. In all resistant samples, two mutations were identified, A296G, the classic mutation within the second transmembrane domain, and a novel T345M mutation, present in the third transmembrane domain. Susceptible samples did not contain either mutation. This mutation has also been identified in *Drosophila simulans* (T350M), whereby both mutations also appeared simultaneously. Two-electrode voltage-clamp electrophysiology was applied to Xenopus laevis oocytes expressing *An. gambiae* Rdl with the single and double mutations. Results showed that GABA sensitivity was not significantly altered in the presence of the mutations, however sensitivity to the insecticide fipronil was significantly reduced in the A296G and double mutation, from that of the wild type. This study provides insights into the mechanisms of insecticide resistance. Also, functional expression of mosquito specific Rdl isoforms may provide a useful tool for testing compounds on a validated target, in the search for novel pesticides for major disease control.

16/04/2015 Session C2 - (Room 11B) - Vectors - Molecular & Cellular Biology I - Chair: H Ranson 2:30 PM - 2:45 PM (15 mins)

Analysis of the transcriptome of the major malaria vector *Anopheles funestus*

Gareth Weedall[1], Helen Irving[1], Margaret Hughes[2], Charles Wondji[1]

[1]Vector Biology Department, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5QA, UK. [2]Centre for Genomic Research, University of Liverpool, Crown Street, Liverpool L69 7ZB, UK.

Insecticide resistance presents a challenge for malaria control. *Anopheles funestus*, a major African malaria vector, shows increasing insecticide resistance, the genetic bases of which remain largely uncharacterised. Application of genomic technologies such as RNAseq and differential gene expression analysis can help elucidate the molecular mechanisms of insecticide resistance by identifying resistance-associated genes. In a pilot study to optimise our application of RNAseq, we sequenced the fully insecticide-susceptible *An. funestus* laboratory colony FANG, to compare the effects of mRNA enrichment by poly(A)-selection and ribosomal-RNA depletion on transcriptome composition and profiling. We found that while the enrichment method makes only a small difference to the amount of aligned data, after accounting for rRNA, it makes a substantial, replicable difference to transcriptome

composition. This is at least partly due to the representation of non-polyadenylated transcripts. The most over-represented genes in the rRNA-depleted libraries include ncRNAs (signal recognition particles), and histone genes, known to display complex 3'-end processing. The most over-represented genes in poly(A)-enriched libraries include ribosomal protein and transcription-associated genes. These substantial differences in composition mean great care should be taken in comparing gene expression data among studies. The analysis also highlighted many incorrect gene models in the draft genome annotation. We performed targeted annotation improvement, including editing gene models and transferring functional annotation from *Anopheles gambiae*, to substantially improveme the annotation of detoxification genes such as P450 and GST gene families. Further, community-led gene curation will benefit future studies of this important malaria vector.

16/04/2015 Session C2 - (Room 11B) - Vectors - Molecular & Cellular Biology I - Chair: H Ranson 2:45 PM - 3:00 PM (15 mins)

Successful application of a hybrid sequence-based genomewide association study (GWAS) design to detect the genetic basis of pyrethroid resistance in *Anopheles arabiensis*

David Weetman

Vector Biology Department, Liverpool School of Tropical Medicine

Driven by advances in marker availability and screening technologies, the last eight years has seen an explosion of genome-wide association studies (GWAS) in humans, most aimed at detecting genetic variants linked to common diseases. Malaria vectors within the *Anopheles gambiae* complex represents a natural target for GWAS in insects, with insecticide resistance a phenotype of primary importance for investigation. However, several properties of the genomes of natural mosquito populations present extreme challenges for GWAS to the extent that their feasibility has been questioned, a doubt that seems warranted for the simple, standard design widely applied in human genetics. Here we present results from a novel hybrid GWAS design founded on advances in *Anopheles* population genomics, falling sequencing costs and successes from microarray experiments. Focussing on relatively recent and increasing pyrethroid resistance in *Anopheles arabiensis*, now the primary malaria vector throughout much of East Africa, we sequenced multiple pools of partially or fully resistant and susceptible females from northern Tanzania and Zanzibar. Following a stringent analysis pipeline, emphasising replication of results we identify strong association signals in the genome around clusters of genes likely involved in metabolic resistance, with evidence for commonalities in the basis of pyrethoid resistance across a broad geographical area. This first successful application of a full GWAS *in Anopheles* suggests that with appropriate experimental design GWAS is both a feasible and powerful option to identify the genetic basis of medically-relevant phenotypes and discover markers for wider application.

16/04/2015 Session C2 - (Room 11B) - Vectors - Molecular & Cellular Biology I - Chair: H Ranson 3:00 PM - 3:15 PM (15 mins)

The isolation and identification of potential vaccine antigens against the poultry red mite – (SP)

James Pritchard, Tatiana Kuester, Fiona Tomley & Olivier Sparagano

The Royal Veterinary College, University of London, Hawkshead Lane, North Mymms, AL9 7TA Coventry University, Coventry, CV1 5FB

The poultry red mite (PRM), *Dermanyssus gallinae*, is the most economically important ectoparasite affecting laying hens throughout the world. Current acaricidal controls are not sufficiently effective due to increased resistance promoting the study of alternative control strategies. We aim to purify 'concealed' membrane proteins from homogenated mites in order to identify potential vaccine candidates following the success of the BM86 gut protein in the tick vaccine TickGARD®. Our purified 'membrane protein enriched' fraction has produced peptides via 2D LC-MS hitting >1500 contigs against a PRM transcriptome (Illumina 100bp paired-end sequencing: 36Gb sequence from 36 billion reads: assembled into 200K contigs). 54% of peptides related to other mite species whilst 34% appear to be unique to *D. gallinae*. This fraction was used to select for mite-specific antibodies from a phagemid antibody library (Tomlinson J, 1.37 x 108 phage with 1000 fold coverage) via biopanning. Several libraries showed binding to PRM via ELISA and immunohistochemistry and will be further selected to pull down targeted mite proteins. These proteins will be identified via mass spectrometry and tested in future in vivo rodent models. The immunogenic capacity of antibodies of vaccinated rodent hosts to kill biting mites as well as reducing surviving mite oviposition will be analyzed and potential vaccine candidates will be studied further.

16/04/2015 Session C2 - (Room 11B) - Vectors - Molecular & Cellular Biology I - Chair: H Ranson 3:15 PM - 3:30 PM (15 mins)

Session D2 - (Room 11A) - Parasites - Ecology I

Chair: Prof J Cable, Univeristy of Cardiff

Infectious diseases: from wild rodents to universal truths

Mike Begon

The University of Liverpool

What determines the size of a host population that is sufficient to sustain a parasite within it? How do parasites mediate the interaction between host species that share that parasite? How does being infected with one parasite affect a host's chances of becoming infected with another parasite? Or affect the length or intensity of that second infection? Or the fitness consequences of being infected? Under what circumstances to hosts tolerate rather than resist the parasites infecting them? Why, when infected, do some hosts get sick while others remain healthy? These are key questions whatever host-parasite system we work on: medical, veterinary or wildlife. I shall argue that wild rodents offer the best opportunities for addressing them

16/04/2015 Session D2 - (Room 11A) - Parasites - Ecology I - Chair: J Cable 2:00 PM - 2:30 PM (30 mins)

On the origins of *Schistosoma turkestanicum* in Eastern Europe; an agent of zoonotic and veterinary schistosomiasis in a wildlife reservoir

Scott Lawton[1] & Gabor Majaros[2]

[1.] Kingston University London, Surrey, UK [2.] University of Budapest, Hungary

Schistosomiasis is a debilitating parasitic infection caused by *Schistosoma* blood flukes infecting over 200 million people worldwide and over 165 million heads of cattle globally, with particular high prevalence in Africa and Asia. A natural foci of infection caused by Schistosoma turkestanicum was found infecting red deer populations in the Gemenc forest of Hungary and comparisons of parasite populations using cytochrome oxidase 1 (cox1) sequences showed the Hungarian populations to be exceptionally diverse as well as being closely related to Iranian populations rather than those from China. Molecular clock analysis suggested that the Hungarian populations diverged from those in Iran around 63,000 years ago during the last ice age, coinciding with the invasion of Hungary by red deer from the near East and North Africa and establishing populations in Eastern Europe. Further, DNA sequencing analysis reveals the Hungarian population of *S. turkestanicum* to be extremely genetically diverse and unique with no haplotypes being shared with populations from Asia. Also, high levels of positive selection in the cox1 were detected between Hungarian and Asian parasite populations indicating the presence of potential metabolic adaptations in specific geographical localities again illustrating the long periods of isolation. This is one of the first and most detailed molecular studies of schistosomisis in wildlife and highlights the importance of understanding the biology causative agents of such diseases in populations of wild animals which could potentially act as reservoirs of diseases of public health concern.

16/04/2015 Session D2 - (Room 11A) - Parasites - Ecology I - Chair: J Cable 2:30 PM - 2:45 PM (15 mins)

Dynamics of plague (*Yersinia pestis*) in the wildlife system of the Kazakh pre-Balkhash desert – (SP)

Bethany Levick, Anne Laudisoit, Stephen Cornell, Mike Begon

Institute of Integrative Biology Biosciences Building Crown Street University of Liverpool, Liverpool, Merseyside L69 7ZB

Infamous for its devastating historical impact, plague (*Yersinia pestis* infection) remains endemic in several distinct foci worldwide. Spillover of disease from zoonotic reservoirs into human populations continues in the present day, providing a pressing need for better understanding of the dynamics of zoonotic plague reservoirs. Further, previous theoretical work have shown that findings in this system to have applications in our general understanding of wildlife disease. Epizootic events in the plague focus in the pre-Balkhash desert of Kazakhstan have previously been demonstrated to be controlled by a threshold density of the asymptomatic rodent host (*Rhombomys opimus*) and their burden of *Xenopsylla* spp. fleas. However, despite much progress, the dynamics of the system remain not yet fully characterised. Here new field records and newly accessed historical records allow for the system to be examined at the level of the individual burrow to identify trends in distribution of the host, vector and

bacterium. These findings are used to inform a burrow specifi c metapopulation model. Our ultimate aim is to improve our current ability to project epizootic events in the system, and identify key factors controlling such events.

16/04/2015 Session D2 - (Room 11A) - Parasites - Ecology I - Chair: J Cable 2:45 PM - 3:00 PM (15 mins)

The study of the great gerbil populations (*Rhombomys opimus* Licht 1823) from different habitats of the Kazakhstan area – (SP)

Aidyn Yeszhanov[1],Nurtazin S.T.[1], M.Begon[2], Beljayev A.I[3], Beljayev I.A.[4], Bekmanov B.O.[5], Salmurza R.[1], Nelika Hughes[6]

[1] al-Farabi Kazakh National University, Almaty, Kazakhstan, [2.] University of Liverpool, United Kingdom, [3.] Taldykorganantiplague station, Taldykorgan, Kazakhstan, [4.] Altai State University, Barnaul, Russia, [5.] Institute of Genetics, Almaty, Kazakhstan, [6.] University of Antwerp, Anwerp, Belgium.

The great gerbil (*Rhombomys opimus*), is the main carrier of a number of extremely dangerous zoonotic infections, including plague (*Yersinia pestis*) in the Central-Asia. Meanwhile, some aspects of the biology of this species are still unclear. Material for this study was collected in the lower reaches of the Ural River in Akzhayik district of West Kazakhstan region, as well as in the desert Moiynkum on the territory of Balkhash-Alakol depression, located on the territory of Almaty region. Total for morphological and molecular genetic analyses were processed data from 683 adult animals of both sexes. To study the morphology using traditional morphological and physiological techniques, restriction enzyme analysis of mitochondrial cytochrome b gene was performed using 4 restriction enzymes (Alu I, HaeIII, HinFI, SspI). For the extraction of total DNA was used the reagent kit QIAamp DNA MiniKit (Qiagen, USA). The greatest similarity between them revealed in gerbils from the desert Taukum, the right bank of the Ili River and Bakanas plain (Balkhash-Alakol depression). Gerbils of Zhalanashkol differ from the above populations, possible reason can be the geographic isolation. The population of the Akzhayik district statistically significantly differ from these populations, different habitat conditions may serve the cause of it. Moyinkum population morphologically stand out from all populations we studied. The reason may be some differences in environmental conditions although both populations live in the subzone of northern deserts.

16/04/2015 Session D2 - (Room 11A) - Parasites - Ecology I - Chair: J Cable 3:00 PM - 3:15 PM (15 mins)

Biased sex ratio among worms of the family Heligmosomidae - looking for a mechanism

Agnieszka Kloch[1], Anna Bajer[1], Aleksander Michalski[2], and Jerzy Behnke[3]

*[1.] University of Warsaw, Faculty of Biology [2.] perlism.org [3.] University of Nottingham, School of Life Sciences *corresponding author*

According to Fisher's Principle, an equal sex ratio is an evolutionary stable strategy. Yet, in many parasites biased sex ratios have been reported but the causes and mechanisms of the observed bias are poorly understood. In the present study, we analysed sex ratios in long-term data-sets from three populations of bank voles (*Clethrionomys* (=*Myodes*) *glareolus*) infected with *Heligmosomum mixtum*

and *Heligmosomoides glareoli*. The overall sex ratios of both species were female-biased but in contrast to previous reports the proportion of females did not change with infection intensity. Higher female-bias was observed in older hosts, and as infections with Heligmosomidid worms have been found to be long-lasting, this implies that the sex ratio changes over time within a host. Single-sex infections were more frequent than expected based on a random infection process, but females in female-only infections bore eggs, suggesting a regulatory processes of sex ratios occurring at an infrapopulation level.

16/04/2015 Session D2 - (Room 11A) - Parasites - Ecology I - Chair: J Cable 3:15 PM - 3:30 PM (15 mins)

Session E2 - (Room 11C) - Parasites - Immunology & Pathology I

Chair: Dr J Turner, Liverpool School of Tropical Medicine

Schistosoma mansoni: potent immune modulator for the parasites, not our, needs

Padraic Fallon

Trinity College Dublin, Ireland.

As helminth parasites have co-evolved with man they have exerted marked selection pressure on the human genome. The immunome of modern man is thus a product of such helminth programming of the human immune system. *Schistosoma mansoni* is one such immune modulating helminth parasite with extensive studies shown how infected individuals in endemic countries have altered immunological responses. In animal models modulation by *S. mansoni* during infection has been shown to be a requisite for the parasite's survival and the continuation of its lifecycle. Furthermore, infection of mice with *S. mansoni* has been shown to alter the disease course in a range of unrelated inflammatory conditions such as models of anaphylaxis, allergic lung inflammation and inflammatory bowel disease. Similarly, molecules from *S.mansoni*, such as omega-1 and SmCKBP or IPSE-1, are potent immune modulators. In this talk the modulation of immunity by *S. mansoni* in mouse models will be considered with the purpose of such regulation presented in the context of the parasites requirements.

16/04/2015 Session E2 - (Room 11C) - Parasites - Immunology & Pathology I - Chair: J Turner 2:00 PM - 2:30 PM (30 mins)

Protective immunity against filarial infective larvae requires skin resident neutrophils

Nicolas Pionnier[1,2], Brotin Emilie[2], Karadjian Gregory[1], Hemon Patrice[3], Gaudin-Nome Françoise[2,3], Vallarino, Lhermitte Nathaly[1], Nieguitsila Adélaïde[1], Aknin Marie-Laure[2], Marin-Esteban Viviana[2], Chollet-Martin Sylvie[2], Schlecht-Louf Géraldine[2], Martin Coralie[1]*, Bachelerie Françoise[2]*
(* equal contribution)

[1] UMR 7245 MCAM MNHN-CNRS Muséum National d'Histoire Naturelle, France [2]UMR-S996 INSERM - LabEx LERMIT Inflammation, Chemokines and Immunopathology, France [3] Plateforme Histologie PHIC UnivSud SFR-UMS IPSIT Faculté de Pharmacie, France

Filariases are chronic diseases affecting 200 million people worldwide. Despite considerable effort to reduce disease burden, filarial infections remain a major public health problem requiring new therapeutic approaches. In our study, we used *Litomosoides sigmodontis* as a well-established murine model of filarial infections. We have previously shown that the CXCL12 chemokine and its receptor CXCR4 participate to the resistance mechanisms to filarial infection in mice, pointing out this pair as potential therapeutic targets. To better characterize their roles, we used mice harboring a CXCR4-gain-of-function that models the anomaly of the rare human WHIM immunodeficiency disorder. Consequently, considering the CXCL12/CXCR4 control over neutrophils and lymphocytes homeostasis, WHIM mice display a profound lympho-neutropenia. Unlike what we were expecting considering this leucopenia, the filarial parasitic success was dramatically decreased in the WHIM mice compared to their wild-type (wt) littermate. We provided manifold evidence pointing to a key role played by neutrophils in the resistance into the early steps of filarial infection. First, albeit being neutropenic, WHIM mice displayed a constitutive skin neutrophils infiltrate; second, filarial infection promoted within a few hours neutrophils recruitment in the skin of WHIM and wt littermate; and third, neutrophils depletion normalized the filarial parasitic success in WHIM mice. We also unraveled that neutrophils undergone a process of neutrophil extracellular traps (NETs) in response to L3 whatever mice are mutated or wt. This is the first evidence that netosis, considered as an adaptive process set in motion by neutrophils in response to pathogens size, is involved in antifilarial defense.

16/04/2015 Session E2 - (Room 11C) - Parasites - Immunology & Pathology I - Chair: J Turner 2:30 PM - 2:45 PM (15 mins)

Class switched antibody is necessary for efficient worm expulsion during a primary *Trichuris muris* infection – (SP)

Emma Murphy, Kathryn Else, Nicola Harris, and Ari Waisman

Faculty of Life Sciences, University of Manchester, A. V. Hill Building, Oxford Road, Manchester, UK; Swiss Vaccine Research Institute, Lausanne, Switzerland, UNIVERSITÄTSMEDIZIN der Johannes Gutenberg-Universität Institut für Molekulare Medizin

Gastrointestinal helminths infect over 1 billion people worldwide and are associated with high levels of morbidity, creating large economic burdens where infections are endemic. *Trichuris muris*, a naturally occurring intestinal parasite of mice has been an invaluable tool in helping to understand the different components involved in immunity to *Trichuris* infection. It is well established that resistance to *T. muris* infection is tightly associated with the generation of T helper 2 (Th2) immune responses, whereas susceptibility is associated with T helper 1 (Th1), immune responses. Despite a good understanding of the role of T cells in immunity to *Trichuris*, the involvement of B cells and class switched antibodies in resistance to a primary *T. muris* infection is unclear. To determine the importance of class switched antibody in immunity to *T. muris*, two different mouse models, both unable to class switch their immunoglobulin from IgM, were infected with *T. muris*, and the progress of infection monitored. Surprisingly, both transgenic mouse models lacking class switched antibody did not expel a primary parasite infection, and were unable to make Th2 responses. Depletion of Th1 polarising cytokines in vivo revealed that once the Th1 response was blocked in mice lacking class switched antibody expulsion of T. muris occured. Thus lack of expulsion appears to be due to inefficient Th2 priming of the immune

response rather than lack of secreted class switched antibody. These results suggest B cells play a unique role in the generation of an efficient Th2 response against primary *T. muris* infection.

16/04/2015 Session E2 - (Room 11C) - Parasites - Immunology & Pathology I - Chair: J Turner 2:45 PM - 3:00 PM (15 mins)

TLR2 stimulation of canine DH82 cells reduced the rate of *Leishmania infantum* infection in vitro and stimulated the production of IL-6 and TNF-alpha

Shazia Hosein[1], Daniel Ngugi[1], Karin Allenspach[1], Damer Blake[1], Laia Solano-Gallego[1,2]

[1]*Royal Veterinary College, University of London, Hawkshead Lane, North Mymms, AL9 7TA, UK.*
[2]*Universitat Autonoma de Barcelona, Facultat de Veterinaria, 08193 Cerdanyola del Valles, Barcelona, Spain*

Canine leishmaniosis (CanL) caused by the protozoan parasite *Leishmania infantum* is a chronic zoonotic systemic disease resulting from complex interactions between the parasite and the host immune system. Toll-like receptors (TLRs) are essential components of the innate immune system and facilitate the early detection of many infections. The impact of the commercial ligand Pam3CSK4, a TLR2 agonist, was determined for *L. infantum* macrophage invasion and replication at 12, 24 and 48 hours post infection. Infection rate and parasite load were calculated by counting the number of infected cells per 100 macrophages and the number of amastigotes per infected cell. Stimulation responses were assessed by measuring (1) gene transcription of TLRs 2, 3, 4 and 9 by qRT-PCR (2) cytokine production for IL-6, IL-10, IL-12 and TNF-alpha by ELISA and (3) nitric oxide (NO) production using Griess reagent. Pam3CSK4 stimulation resulted in fewer infected cells at every time point in comparison to unstimulated infected cells and the development of a lower number of intracellular amastigotes per infected cell. Pam3CSK4 stimulation resulted in the significant increase in the production of pro-inflammatory cytokines TNF-alpha and IL-6 in infected and non-infected cells. The findings from these assays highlight possible mechanisms by which L. infantum may modulate the host immune system and establish infection providing new insights into the pathogenesis of the immune-mediated alterations associated with CanL. This experimental model could be applied under several other conditions to improve the understanding of this disease and to suggest novel therapeutic opportunities.

16/04/2015 Session E2 - (Room 11C) - Parasites - Immunology & Pathology I - Chair: J Turner 3:00 PM - 3:15 PM (15 mins)

***Leishmania major* infection has a significant effect on atherogenesis and cytokines pattern in resistant mice**

Marc Karam[1], Mirna Chahine[2], Amani Shahine[1]

[1.]*University of Balamand – Lebanon;* [2.]*Lebanese University - Hadath - Lebanon*

The outcome of the infection with *Leishmania major* depends on the type of the immune response mounted by the host. This response is either cell mediated or humoral making the host resistant (as humans and C57BL/6 mice) or susceptible (BALB/c mice) respectively. Activation of either branch of the

immune system depends on other factors such as genetic makeup of the host, the infecting dose and the cytokine milieu. In BALB/c mice, the early production of Th2 cytokines (IL-4, IL-5, IL-10 and IL-13) inhibits IL-12 function and natural killer (NK) favoring the exacerbation of the disease. On the other hand, L. major infection in resistant hosts results in Th1 cells activation with production of IL-2, Interferon-γ (IFN-γ) and Tumor Necrosis Factor-α (TNF-α) favoring self-healing. Conversely, in therosgenesis T helper cells seem to play a role in the plaque development. Th1 cells produce mainly IFN-γ, TNF-α and IL-2 and are considered to be proatherogenic. However, Th2 cells produce mainly IL-4, IL-5, IL-10 and IL-13 and seem to have an atheroprotective role. In this study we investigated the effect of L. major infection on atherogenesis in C57BL/6 mice as well as the levels to some atherosclerosis related cytokines in the plasma and aorta of the mice. Our results show that *L. major* infection increases significantly the plaque size, especially at weeks 3 and 8 postinfection in the mice infected with the parasite accompanied by significant changes in the levels of the atherosclerosis related cytokines in the plasma as well as in the aorta.

16/04/2015 Session E2 - (Room 11C) - Parasites - Immunology & Pathology I - Chair: J Turner 3:15 PM - 3:30 PM (15 mins)

Session A3 - (Room 1B) - Malaria - Molecular & Cellular Biology II

Chair: DR E Salcedo-Sora, Liverpool Hope University

Red blood cells preconditioned with hemin are less permissive to *Plasmodium* invasion

Véronique Gaudreault[1], Jakob Wirbel[2], Armando Jardim[2], Petra Rohrbach[2] and Tatiana Scorza[1]

[1]*Département des Sciences Biologiques, Université du Québec à Montréal, Montréal, Québec, Canada*
[2]*Institute of parasitology, McGill University, Montréal, Québec, Canada*

Blood stage malaria causes severe hemolytic anemia in *Plasmodium*-infected host, which results in the release and accumulation of oxidized heme (hemin; HE). We previously reported impaired establishment of *Plasmodium* immunity concurrent to HE pre-treatment in vitro and in vivo. Nonetheless, mice preconditioned with HE develop lower parasitemia when challenged with *Plasmodium chabaudi adami* blood stage parasites. Fluorescence microscopy of ring-stage infection revealed a delayed merozoites invasion and an increased *P. c. adami* red blood cells (RBCs) selectivity, characterized by an increased multiple infection per RBCs. Discrimination of HE-treated from de novo generated RBCs was achieved with an in vivo biotinylation technique. Fluorescence-activated cell sorting analysis of biotynylated-RBCs revealed a decreased permissibility of the HE-conditioned RBCs population for parasite invasion. These effects were also apparent in in vitro *P. falciparum* cultures using HE-preconditioned human RBCs. These findings suggest that HE alters an unidentified membrane component that restricts *Plasmodium* invasion capacity, extends merozoites extra-erythrocytic journey and favors multiple-ring infection. Our results assign a function for HE as a protective agent against high parasitemia, and suggest that the hemolytic nature of blood stage malaria may be beneficial for the infected host.

16/04/2015 Session A3 - (Room 1B) - Malaria - Molecular & Cellular Biology II - Chair: E Salcedo-Sora

4:00 PM - 4:15 PM (15 mins)

Quantification of *Plasmodium*-host protein interactions on intact, unmodified erythrocytes by back-scattering interferometry

Abigail Perrin, Phoonthawee Saetear, Abigail J Perrin, S Josefin Bartholdson, Madushi Wanaguru, Amanda Kussrow, Darryl J Bornhop and Gavin J Wright

Cell Surface Signalling Laboratory and Malaria Programme, Wellcome Trust Sanger Institute, Hinxton, Cambridge, UK (AJP, SJB, MW, GJW) Department of Chemistry and the Vanderbilt Institute for Chemical Biology, Vanderbilt University, 4226 Stevenson Center, Nashville 37235, Tennessee, USA (PS, AK, DJB)

Invasion of host erythrocytes by *Plasmodium falciparum* is central to the pathogenesis of malaria and involves key recognition events between erythrocyte receptors and merozoite ligands. Identification and characterisation of these host-parasite interactions is often impeded by the biochemical challenges of working with isolated or recombinant membrane glycoprotein receptors, such that it is desirable to perform binding assays with receptors embedded within the membranes of intact human erythrocytes. Here we introduce backscatting interferometry (BSI) as a novel platform for the detection and measurement of protein interactions at the erythrocyte surface. BSI is a unique optical detection method that can be used to infer binding events in tiny volumes of solution based on changes in refractive index. We have used BSI to obtain equilibrium binding measurements for known host-parasite interactions involved in erythrocyte invasion. Purified recombinant proteins constituting the entire ectodomains of *P. falciparum* merozoite ligands PfRH5 and PfEBA175 bound to the erythrocyte surface with KDs of 1.1µM and 50nM respectively, in good agreement with previous biophysical measurements of the PfRH5/BSG and PfEBA175/GYPA interactions. These results demonstrate that BSI can be used to detect and quantify the interactions of free-solution merozoite invasion ligands with their receptors on intact human erythrocytes with a very high sensitivity, without the need for labelling and requiring only nanomoles of recombinant *Plasmodium* protein. Hence BSI can be used to investigate host-parasite protein interactions without the limitations of other assay platforms, and represents a valuable new method to investigate the molecular mechanisms underlying erythrocyte invasion by *P. falciparum*.

16/04/2015 Session A3 - (Room 1B) - Malaria - Molecular & Cellular Biology II - Chair: E Salcedo-Sora
4:15 PM - 4:30 PM (15 mins)

Structure of malaria invasion protein RH5 with erythrocyte basigin and blocking antibodies

Katherine Wright[1], Kathryn A. Hjerrild[2], Jonathan Bartlett[1], Alexander D. Douglas[2], Jing Jin[2], Rebecca E. Brown[2], Joseph J. Illingworth[2], Rebecca Ashfield[2], Stine B. Clemmensen[3], Willem A. de Jongh[3], Simon J. Draper[2] and Matthew K. Higgins[1]

[1]*Department of Biochemistry, University of Oxford, South Parks Road, Oxford, OX1 3QU* [2]*Jenner Institute, University of Oxford, Old Road Campus Research Building, Roosevelt Drive, Oxford, OX3 7DQ* [3]*ExpreS2ion Biotechnologies, SCION-DTU Science Park, Agern Allé 1, DK-2970 Horsholm, Denmark*

Erythrocyte invasion by *Plasmodium* is a pivotal stage of the parasite lifecycle, during which the symptoms and pathology of malaria arise. Central to this process are two families of parasite proteins,

the reticulocyte-binding protein homologue (RH) and erythrocyte-binding like (EBL) proteins, that mediate host-parasite interactions1. RH5 from *Plasmodium falciparum* (PfRH5) is the only member of either family shown to be necessary for erythrocyte invasion in all tested strains, through its interaction with erythrocyte surface protein basigin2,3. Since antibodies targeting PfRH5 block parasite invasion and subsequent growth, PfRH5 is an exceptionally promising vaccine candidate4. To gain insight into the molecular basis of the PfRH5—basigin interaction, we solved the crystal structure of PfRH5 bound to basigin, and to two different antibodies that prevent parasite invasion5. PfRH5 adopts a novel fold in which two three-helical bundles come together in a kite-like architecture, presenting binding sites for basigin and inhibitory antibodies at one tip. Few basigin side chains participate in the PfRH5 interaction, reducing the potential for basigin escape mutants that abolish PfRH5 binding. Invasion-inhibitory antibodies bind at or near the basigin binding site, thereby identifying PfRH5 epitopes that will be important components of a vaccine to prevent erythrocyte invasion. This provides the first structural insight into erythrocyte binding by the *Plasmodium* RH family. 1Tham, W.H. et al. Trends Parasitol 28,23-30 (2012). 2Baum, J. et al. Int.J.Parasitol. 39,371-380 (2009). 3Crosnier, C. et al. Nature 480,534-537 (2011). 4Douglas, A.D. et al. Cell Host & Microbe 17,130-139 (2015). 5Wright, K.E. et al. Nature 515,427-430 (2014).

16/04/2015 Session A3 - (Room 1B) - Malaria - Molecular & Cellular Biology II - Chair: E Salcedo-Sora
4:30 PM - 4:45 PM (15 mins)

Enhanced clearance of infected red blood cells: A novel mechanism for malaria resistance in mice carrying a mutation in the host cytoskeletal protein, beta spectrin

Patrick Lelliott, BJ McMorran, SJ Foote, G Burgio

The John Curtin School of Medical Research, ANU

The malaria parasite, *Plasmodium*, invades and grows within its host's red blood cells (RBCs) to avoid detection and clearance by the immune system. Mutations in RBC proteins can interfere with one or more aspects of this process, and thereby provide a protective advantage to the host (e.g. sickle cell trait). Using a mouse model, we sought to identify changes in malaria susceptibility due to mutations in RBC proteins, and their mechanism of action. We investigated an ENU mutagenized mouse line containing a nonsense mutation in Sptb, which encodes the host RBC cytoskeletal protein, beta spectrin. Homozygous mice contained no detectable beta spectrin and were not viable. Heterozygotes expressed normal amounts of protein and displayed only a mild haematological phenotype, which included reduced RBC volume and increased RBC fragility. Heterozygotes infected with *Plasmodium chabaudi* adami DS displayed reduced parasitaemia and a dramatic increase in survival (80% vs. 17%, $p<0.001$). Using a novel in vivo invasion assay (1), we determined parasites were able to invade and grow normally in mutant RBCs. In contrast, clearance of infected RBCs within 30 minutes of invasion was enhanced by 27% ($p<0.001$). This study presents the first evidence that mutations in Sptb can lead to malaria resistance in mice. Surprisingly, these mutations had no effect on parasite invasion or growth but instead led to increased clearance of infected RBCs, thus providing a novel perspective on the host/parasite interaction. (1) Lelliott et al. Malar J. 2014;13:100

16/04/2015 Session A3 - (Room 1B) - Malaria - Molecular & Cellular Biology II - Chair: E Salcedo-Sora
4:45 PM - 5:00 PM (15 mins)

A new tool for the chemical genetic investigation of Pfnek2 in *Plasmodium falciparum*

Deborah Mitcheson[1], Andrew R. Bottrill[2], Katherine Carr[3], Roger J. Griffith[4], Sharon Yeoh[3], Andrew M. Fry[3], Christian Doerig[5], Richard Bayliss[3] and Andrew B. Tobin[6]

[1.] Department of Cell Physiology and Pharmacology, University of Leicester, Hodgkin Building, Lancaster Road, Leicester, LE1 9HN, UK, [2.] Protein and Nucleic Acid Chemistry Laboratory, University of Leicester, Hodgkin Building, Lancaster Road, Leicester LE1 9HN, UK, [3.] Department of Biochemistry, University of Leicester, Henry Wellcome Building, Lancaster Road, Leicester, LE1 9HN, UK, [4.] Newcastle Cancer Centre, Northern Institute for Cancer Research, School of Chemistry, Bedson Building, Newcastle University, Newcastle upon Tyne, NE1 7RU, UK, [5.] Department of Microbiology, Building 76, Monash University, Wellington Road, Clayton, Victoria 3800, Australia, [6.] Medical Research Council Toxicology Unit, University of Leicester, Hodgkin Building, Lancaster Road, Leicester, LE1 9HN, UK

The NIMA-related serine/threonine malarial protein kinase, Pfnek2, is present in the gametocyte stage of the life cycle of *Plasmodium falciparum*. Its role is unknown although it may play a part in cell cycle progression due to its similarity to the human NEK proteins. To investigate the role of Pfnek2, we have developed a chemical biology strategy which involves the design of a chemical probe which can inhibit a genetically altered Pfnek2 kinase at specific stages in the *Plasmodium falciparum* life cycle. This strategy involved the generation of a chemical probe, NCL-00016066, which covalently binds to a modified Pfnek2 (valine 24 to cysteine) in the glycine rich loop. The first part of this strategy is to generate an inhibitor, identify its probable mode of inhibition and ascertain the dose response of the purified enzyme in vitro. This inhibitor, NCL-00016066, at 20 µM, slightly decreases the activity of wild type Pfnek2 in vitro in a reversible manner while the same concentration completely inhibits the activity of a Pfnek2 V24C mutant. In contrast to the small inhibition observed with the wild type Pfnek2, the inhibition of the mutant Pfnek2 was irreversible. Mass spectroscopy data confirmed that this inhibition is through modification of the introduced cysteine at position 24. These results pave the way for the introduction of a Pfnek2 V24C mutant into *Plasmodium falciparum* that will enable probing of Pfnek2 function via NCL-00016066 inhibition of this mutant.

16/04/2015 Session A3 - (Room 1B) - Malaria - Molecular & Cellular Biology II - Chair: E Salcedo-Sora
5:00 PM - 5:15 PM (15 mins)

Session B3 - (Room 1C) - NTDs - Diagnostics II

Chair: DR E Adams, Liverpool school of Tropical Medicine

Lessons learnt from TB – molecular diagnostics for NTDs

Thonas Edwards, Emily Adams

Liverpool School of Tropical Medicine, Pembroke Place, Liverpool

There has been a paradigm shift in diagnostic testing for Tuberculosis in the last 5 years, with the emergence of a range ofnovel molecular tests. Although considered game changers, their requirement for a laboratory, computers and reliable electricity supply have restricted their use. The first fully integrated molecular test for TB, GeneXpert, uses self-contained cartridges, requires minimum sample processing and identifies Mycobacterium tuberculosis and genetic

Rifampicin resistance markers within 2 hours. Despite rapid expansion, its impact on patient outcome has been limited because health staff initiate treatment without waiting for results. It is important to apply the lessons learnt from diagnostic development in other disease areas, and work towards affordable, integrated devices that can be used in close to community settings. The development of molecular tests for NTDs should be carefully considered in order to ensure suitability for the intended test setting and position in the diagnostic algorithm, to make certain of true clinical benefit. Here we will talk about future developments in molecular diagnostics for NTDs and the need for intelligent design.

16/04/2015 Session B3 - (Room 1C) - NTDs - Diagnostics II - Chair: E Adams 4:00 PM - 4:15 PM (15 mins)

North American paragonimiasis as model for the development of improved serodiagnosis of paragonimiasis globally.

Peter Fischer, Kurt C. Curtis, Kerstin Fischer, Samantha N. McNulty, Makedonka Mitreva, R. Reid Townsend and Gary J. Weil

Washington University School of Medicine, St. Louis MO

Paragonimiasis is a foodborne trematode infection that affects 23 million people mainly in Asia. In North America paragonimiasis is caused by *Paragonimus kellicotti* and affects rarely humans. Parasites cause chronic cough with fever and hemoptysis, and lung fluke infection is often confused with tuberculosis. We used a systems biology approach of adult *P. kellicotti* worms to identify antigens that might lead to improved diagnostic tests. Antibodies from patients with *P. kellicotti* infection were used to isolate antigens for proteomic analysis, and RNAseq data enabled protein identification. Among the 22 most abundant identified proteins were a number of orthologues to known diagnostic antigens as well as novel candidates. Sequences for these proteins have 80-90% identity with amino acid sequences for orthologues in *P. westermani*. We expressed five *P. kellicotti* proteins in E. coli, and used them to raise antibodies. Immunolocalization of the antigensin adult worms showed that four of them were present in the tegument, at the parasite host interface. In contrast, a known egg yolk antigen was absent from the tegument but present in developing and mature eggs. We evaluated the diagnostic potential of these antigens by Western blot with sera from patients with paragonimiasis (from Missouri, the Philippines), fascioliasis, and schisosomiasis and with sera from healthy North American controls. A recombinant cysteine protease and a myoglobin showed the highest sensitivity and specificity as diagnostic antigens. In conclusion, this study has identified two promising *P. kellicotti* antigens that might be useful for the diagnosis of paragonimiasis globally.

16/04/2015 Session B3 - (Room 1C) - NTDs - Diagnostics II - Chair: E Adams 4:15 PM - 4:30 PM (15 mins)

Novel LAMP assay for the diagnosis of Leishmaniasis

Emily Adams[1,2], Inge Versteeg[1], Maria Adelaïda Gomez[3], Yasuyoshi Mori[4], Nancy Saravia[3], Audrey Albertini[5], Henk Schallig[1]

[1] Royal Tropical Institute, Amsterdam, 1105 AZ, The Netherlands [2] Liverpool School of Tropical Medicine, Liverpool, L3 5QA, UK [3] CIDEIM, Cra 125 # 19-225 Cali, Colombia [4] Eiken Chemical Company, Tokyo, Japan [5] Foundation for Innovative New Diagnostics, Switzerland

Introduction: A novel Pan-*Leishmania* LAMP assay was developed for diagnosis of both cutaneous and visceral leishmaniasis. Primers were designed on the 18S rDNA and the kDNA selected for their high copy number. Methods: Prototype LAMP assays were tested for cutaneous leishmaniasis (CL) in a prospective cohort trial of 105 clinical suspects in South-West Colombia. Swab samples from 105 CL suspects were processed for DNA extraction using the Qiagen Blood and Tissue kit; coupling a non-invasive sampling method to a standardised extraction. Microscopy was performed on skin scrapings of ulcers, aspirate samples were cultured, LAMP and qPCR performed on extracted DNA. A composite gold standard comprising of microscopy AND/OR culture positivity was used to calculate the diagnostic accuracy of LAMP and qPCR. Results and conclusions: LoopAMP (Eiken Chemical, Japan) was 95% sensitive (95% CI: 87.22 % to 98.53 %) and 86% specific (95% CI: 67.32 % to 95.88 %). This molecular test is more sensitive and specific than microscopy and culture alone. Presenting author: Emily Adams: emily.adams@lstmed.ac.uk

16/04/2015 Session B3 - (Room 1C) - NTDs - Diagnostics II - Chair: E Adams 4:30 PM - 4:45 PM (15 mins)

Development and assessment of a point of care isothermal nucleic acid amplification test for the diagnosis of urogenital schistosomiasis

Bonnie Webster, Rosser A, Forrest M, Rollinson D

Natural History Museum, London

Infection with *Schistosoma haematobium* causes urogenital schistosomiasis, a major health problem across Africa. Research into this pathogen is neglected and substantial uncertainties surround the effectiveness of diagnostic tests for infection. Diagnosis mainly relies on microscopic detection of S. haematobium eggs in urine but many factors affect sensitivity. Amplification of schistosome DNA in urine by PCR has proved to be sensitive and specific but its application is limited, requiring infrastructure, financial resources and skilled personnel often not available in an endemic setting. Recombinase Polymerase Amplification (RPA) is a novel isothermal DNA amplification/detection technology offering an alternative to PCR and represents a revolution in DNA diagnostics. This technology combines superior speed, portability and accessibility with exquisite sensitivity and specificity, and is practical in nearly any setting, making it an ideal candidate for POC (Point-Of-Care) diagnostics. Here we have developed a RPA assay that can currently amplify *S. haematobium* DNA at a lower limit of 100 fg with sufficient amplification taking place in 10 minutes at 37°C. The assay can withstand inhibitors and *S. haematobium* DNA can be amplified from within crude urine, up to 5% of the total reaction volume. The assay was further developed into a lateral flow RPA (LF-RPA) assay where *S. haematobium* DNA amplicons can easily be detected using oligochromatographic lateral flow strips. This LF-RPA produces quick reproducible results that are easy to interpret with comparable sensitivity to competing methods. The assay requires little infrastructure and is a promising POC test for the field diagnosis of urogenital schistosomiasis.

16/04/2015 Session B3 - (Room 1C) - NTDs - Diagnostics II - Chair: E Adams 4:45 PM - 5:00 PM (15 mins)

Circulating antigen tests and urine reagent strips for diagnosis of active schistosomiasis in endemic areas

Eleanor A Ochodo[1,2],Gowri Gopalakrishna[1],Bea Spek[3], Johannes B Reitsma[4], Lisette van Lieshout[5], Katja Polman[6], Poppy Lamberton[7], Patrick MM Bossuyt[1], Mariska MG Leeflang[1]

[1]Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Academic Medical Centre, University of Amsterdam, Amsterdam, Netherlands. [2]Centre for Evidence-based Health Care, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa. [3]Department of Speech and language pathology, Hanze University Groningen, Groningen, Netherlands. [4]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, Netherlands. 5Department of Parasitology,Leiden UniversityMedical Center, Leiden, Netherlands. [6]Department of Biomedical Sciences, Institute of Tropical Medicine, Antwerp, Belgium. [7]Department of Infectious Disease Epidemiology, Imperial College London, London, UK.

Schistosomiasis is a parasitic disease common in the tropical and subtropics. Point-of-care tests and urine reagent strip tests are quicker and easier to use than microscopy. We estimate how well these point-of-care tests are able to detect schistosomiasis infections compared with microscopy. We included 90 studies involving almost 200,000 people, with 88 of these studies carried out in Africa in field settings. Study design and conduct were poorly reported against current expectations. Results: Among the urine strips for detecting urinary schistosomiasis, the strips for detecting blood were better than those detecting protein or white cells (sensitivity and specificity for blood 75% and 87%; for protein 61% and 82%; and for white cells 58% and 61%, respectively). For urinary schistosomiasis, the parasite antigen test performance was worse (sensitivity, 39% and specificity, 78%) than urine strips for detecting blood. For intestinal schistosomiasis, the parasite antigen urine test, detected many infections identified by microscopy but wrongly labelled many uninfected people as sick (sensitivity, 89% and specificity, 55%). Conclusions: Among the evaluated tests for *S. haematobium* infection, microhaematuria correctly detected the largest proportions of infections and non-infections identified by microscopy in comparison to protein or white cell tests. The parasite antigen test is not accurate. The CCA POC test for *S. mansoni* detects a very large proportion of infections identified by microscopy, but it misclassifies a large proportion of microscopy negatives as positives in endemic areas with a moderate to high prevalence of infection, possibly because the test is potentially more sensitive than microscopy.

16/04/2015 Session B3 - (Room 1C) - NTDs - Diagnostics II - Chair: E Adams 5:00 PM - 5:15 PM (15 mins)

Session C3 - (Room 11B) - Helminth- Molecular & Cellular Biology –

Chair: Prof R Stothard, Liverpool School of Tropical Medicine

Sensory protein kinase signalling in *Schistosoma mansoni* cercariae and implications for human host infection

Anthony Walker, Margarida Ressurreição, Ruth S. Kirk, David Rollinson, Aidan M. Emery, Nigel M. Page, Anthony J Walker

Molecular Parasitology Laboratory, School of Life Sciences, Kingston University, United kingdom; and Department of Life Sciences, The Natural History Museum, London, United Kingdom

Through sensing their environment, schistosome cercariae display extraordinary behavioural responses to abiotic and biotic stimuli that enable them to locate and subsequently infect the vertebrate definitive host. Here we have studied the effect of such stimulants on protein kinase signalling pathways of cercariae in the context of human host infection, using *Schistosoma mansoni*. Cercariae exposed to various light and temperature regimes displayed modulated protein kinase C (PKC), extracellular signal-regulated kinase (ERK) and p38 mitogen-activated protein kinase (p38 MAPK) activities, with distinct responses observed at 37°C and intense light or dark, when compared to those maintained at 24°C under normal light. In addition, confocal laser scanning microscopy of cercariae revealed the activated protein kinases associated with regions including the sensory papillae, acetabular tubules, tegument, acetabular glands, and nervous system. Exposure to the human skin component linoleic acid (LA) also resulted in altered temporal protein kinase activation, particularly for PKC and ERK, which occurred concurrently with release of acetabular gland components revealed by staining with the fluorescent probe CFDA-SE. Attenuation of PKC, ERK and p38 MAPK activity resulted in significantly reduced release of gland components, particularly in response to LA, demonstrating the importance of these signalling pathways to host penetration mechanisms. Collectively, these findings highlight the importance of protein kinase signalling pathways to location and infection of the definitive host by schistosome cercariae.

16/04/2015 Session C3 - (Room 11B) - Helminth- Molecular & Cellular Biology - Chair: R Stothard 4:00 PM - 4:15 PM (15 mins)

Developing Neuropeptides as Transgenic Nematicides – (SP)

Neil D. Warnock[1], Leonie Wilson[1], Cheryl Patten[2], Colin C. Fleming[3], Aaron G. Maule[1], Johnathan J. Dalzell[1]

[1]Queen's University Belfast, UK; [2]University of New Brunswick, Canada; [3] Agri-Food and Biosciences Institute, UK.

Plant parasitic nematodes (PPNs) seriously threaten global food security. It is estimated that they are responsible for a 12.3% reduction in agricultural productivity worldwide. This equates to $120 billion annually and highlights the significant economic burden they impose on society. Conventionally, an integrated approach to PPN management has relied heavily on various nematicides. As environmental concerns rise over the systemic effects of sustained nematicide use, withdrawal has left a significant shortcoming in our ability to manage this problem and highlights the need for novel and robust control methods. It has been discovered that nematodes can assimilate exogenous peptides through retrograde transport along the chemosensory amphid neurons. These peptides accumulate within cells of the central nerve ring and can elicit physiological effects when released to interact with receptors on adjoining cells. We are harnessing bioactive neuropeptides from the neuropeptide-like protein (NLP) and FMRFamide-like peptide (FLP) families of plant parasitic nematodes as novel nematicides. We have identified numerous discrete neuropeptides that negatively impact chemosensation, stylet thrusting, neuromuscular activity and infectivity of the root knot nematode *Meloidogyne incognita*, and of the potato cyst nematode *Globodera pallida*. Transgenic secretion of these peptides from the rhizobacterium, *Bacillus subtilis*, and the terrestrial microalgae *Chlamydomonas reinhardtii* reduce plant

infection levels by up to 90% when compared with controls.

16/04/2015 Session C3 - (Room 11B) - Helminth- Molecular & Cellular Biology - Chair: R Stothard 4:15 PM - 4:30 PM (15 mins)

Defining the molecular target for fruit cysteine proteinases on the cuticle of *Caenorhabditis elegans* and parasitic nematodes – (SP)

Victor S Njom[1], Oumu Diallo[1], Ian Duce[2], Mark Dickman[3], and David Buttle[1].

[1.] Department of Infection and Immunity, [2.] Biological and Chemical Engineering University of Sheffield, [3.] School of Biology University of Nottingham.

Parasitic nematodes cause enormous public health, agricultural and economic problems worldwide, as pathogens of humans, livestock and crops. Their impact is increasing due to lack of full efficacy of current anthelmintics and development of resistance by the nematodes. We are developing friut cysteine proteinases as alternatives to currently available anthelmintics. We have demonstrated anthelmintic potency of plant cysteine proteinases from papaya ("papain"), fig (ficin), and pineapple (bromelain) on gastrointestinal (GI) nematodes of mouse, sheep and pig, in vivo. The enzymes have a novel mechanism, digesting the cuticle of the nematode leading to blistering, rupture and death. The nematode cuticle is composed of proteins such as collagens and cuticlins but the specific molecular target(s) of the proteinases have yet to be identified. For example, there are about 158 collagen and 8 cuticlins genes in the *C. elegans* genome. Our study aim to identify the molecular target(s) and thereby define the mechanism of action of this new class of anthelmintics. Methodology: *Caenorhabditis elegans* and murine GI nematode *Heligmosomoides bakeri* are our initial target organisms. The cuticles were isolated by washing in denaturing buffers. They were digested with papain and other homologous enzymes. The supernatant was taken, run on SDS-PAGE and individual bands were analysed by LCMSMS. Results: Initial experiments have confirmed the suitability of our approach, with cuticle globin paramyosin and actin-related proteins identified in papain-digested cuticle supernatants. Conclusion: Preliminary data suggest that our approach is a practical one. However, structural cuticle proteins attacked by cysteine proteinases have yet to be identified.

16/04/2015 Session C3 - (Room 11B) - Helminth- Molecular & Cellular Biology - Chair: R Stothard 4:30 PM - 4:45 PM (15 mins)

Molecular characterization of *Fasciola* parasites from Nigeria – (SP)

Nusirat Elelu, Tristan Cogan & Mark C. Eisler

Department of Veterinary Clinical Science, University of Bristol. UK.

Background Fasciolosis is a parasite of veterinary and medical importance. It has a worldwide distribution with two distinct species (*F. hepatica* and *F. gigantica*) and an intermediate form. The ribosomal DNA internal transcribed spacers (ITS) and mitochondrial cytochrome oxidase (COI) genes are useful in speciation and understanding genetic origin of *Fasciola*. Genetic studies for *F. gigantica* have been carried out in various African countries including Mauritania, Egypt and Niger but no studies have

been carried out in Nigeria where the parasite commonly occurs in livestock. Methods Genomic DNA was extracted from adult *Fasciola* collected from abattoir cattle and genetically characterized based on ITS and COI gene. These were compared to Fasciola sequences previously published in GenBank by alignment and construction of phylogenetic trees. Results All ten isolates from Nigeria belonged to the F. gigantica cluster, except for a single specimen (Nigeria_Fg9), which had a nucleotide transition from C to T at ITS1 position 17. Alignment of the COI gene from Nigerian samples revealed high genetic diversity differing in 4 distinct positions of clipped PCR products (178, 203, 319 and 331). This was different from any Fasciola sequences available in GenBank, including both *F. gigantica* and *F. hepatica*. Conclusions This study confirmed that *F. gigantica* occur in cattle from Kwara State, Nigeria and are genetically distinguishable from *F. gigantica* described elsewhere in Africa. There was no evidence of *F. hepatica* or intermediate forms. The genetic diversity reported within the parasites reflects the need for further genetic studies, including genes possibly associated with anthelmintic resistance, such as the beta-tubulin gene.

16/04/2015 Session C3 - (Room 11B) - Helminth- Molecular & Cellular Biology - Chair: R Stothard 4:45 PM - 5:00 PM (15 mins)

Heads or tails: functional investigations of gene regulatory networks controlling planarian AP patterning in the model tapeworm *Hymenolepis microstoma* – (SP)

Francesca Jarero, & Peter Olson

Natural History Museum, Department of Life Sciences, Cromwell Road, London, SW7 5BD

Tapeworms are a medically and economically important group of flatworms for which, like most parasitic animals, we remain ignorant of their basic developmental pathways. By contrast, an increasingly sophisticated and instructional model of developmental gene regulation has formed over the last decade from studies of free-living planarians. Gene regulatory networks (GRN) controlling anteroposterior (AP) patterning during planarian growth and regeneration are centred on Beta-catenin-dependent Wnt signalling, showing that continual expression of βcat results in posteriorisation, whereas suppression of βcat production via RNA interference, small molecule inhibition, or through the expression of Wnt antagonists results in anteriorisation of tissues. In turn, Wnt signalling is found to be regulated by Hedgehog signals, while downstream Wnt targets includes Hox and other genes. We examine quantitative and spatial expression of Wnt and Hedgehog signalling components throughout the complex life cycle of the model tapeworm *Hymenolepis microstoma*. In addition, we present functional investigations of Wnt repression during larval development by injecting inhibitors directly into the haemocoel of the beetle intermediate host. Initial results of these studies indicate that tapeworm AP patterning, although highly modified, is controlled by the same underlying GRN found in free-living flatworms, and is most broadly comparable to other animals during larval development, while being co-opted and modified during strobilar, adult growth.

16/04/2015 Session C3 - (Room 11B) - Helminth- Molecular & Cellular Biology - Chair: R Stothard 5:00 PM - 5:15 PM (15 mins)

Session D3 - (Room 11A) - Parasites - Ecology II –

Chair: Prof J Cable, Univeristy of Cardiff

Partitioning host species contributions to parasite persistence in multi-host communities

Andy Fenton, Daniel Streicker, Owen Petchey, Amy Pedersen

Institute of Integrative Biology, University of Liverpool, Biosciences Building, Crown Street, Liverpool, L69 7ZB, UK. Institute of Biodiversity, Animal Health, and Comparative Medicine, University of Glasgow, Glasgow, G12 8QQ, Scotland, UK. Medical Research Council-University of Glasgow Centre for Virus Research, Glasgow, G61 1QH, Scotland, UK. Institute of Evolutionary Biology and Environmental Studies, University of Zurich, Winterthurerstrasse 190, CH-8057, Zurich, Switzerland. Institute of Evolutionary Biology and Centre for Immunity, Infection and Evolution (CIIE), School of Biological Sciences, University of Edinburgh, West Mains Road, Edinburgh, EH9 3JT, UK.

Many parasites circulate endemically within communities of multiple host species. To understand disease persistence within these communities it is essential to know the contributions of each species to parasite transmission and maintenance. However, quantifying those contributions is challenging. We present a modified conceptual framework for classifying multi-host sharing by environmentally-transmitted parasites, based on key thresholds for parasite persistence. We then develop a generalised technique to quantify each species' contribution to parasite persistence, allowing natural systems to be located within the framework. We illustrate this approach using data on gastrointestinal parasites circulating within rodent communities and show that, although many parasites infect several host species, persistence is often driven by just one species. In some cases, however, parasites require multiple host species for maintenance. Our approach provides a quantitative method for differentiating these cases using minimal reliance on system-specific parameters, enabling informed decisions about parasite management within poorly understood multi-host communities.

16/04/2015 Session D3 - (Room 11A) - Parasites - Ecology II - Chair: J Cable 4:00 PM - 4:15 PM (15 mins)

The infections and genetics of wild house mice, *Mus musculus domesticus* – (SP)

Luke Lazarou, Stephen Abolins, Laura Weldon, Mark Viney

University of Bristol

The laboratory mouse is very well known, but the infection and immunobiology of wild mice is much less well explored. To address this we have sampled c.500 wild mice from south-west England, as well as from Skokholm Island and the London Underground. We characterised these mice for ecto- and endo-parasites, and for evidence of microbial infections. These infections differed among the sample sites; mice from London Underground were completely free of worm infections, yet showed the highest prevalence of microbial infections. We have also multi-locus genotyped these mice to understand their population structure. FST analyses suggest that mice from different sample sites are genetically separated. STRUCTURE clustering analysis detects 10 sub-populations among the 16 sample sites. We

are now seeking to identify mouse genotypes associated with particular infection phenotypes.

16/04/2015 Session D3 - (Room 11A) - Parasites - Ecology II - Chair: J Cable 4:15 PM - 4:30 PM (15 mins)

Hosts alter habitat use in response to parasitic infection – (SP)

David Daversa[1,2], David R Manica[1], Andrea M Garner[2], Trenton WJ Bosch[3], Jaime Jolles[1], Jolle W

[1.] Department of Zoology, University of Cambridge, Downing Street, Cambridge CB2 3EJ [2.] Institute of Zoology, Zoological Society of London, Regents Park, London NW1 4RY [3.] Museo Nacional de Ciencias Naturales, CSIC c/ Jose Gutierrez Abascal 2 28006 Madrid. SPAIN

Host activity among different habitats strongly influences both the extent of exposure to parasites and parasite development on hosts. Therefore, individuals may adjust activity to minimize time in habitats posing high infection risk. Alternatively, parasites may manipulate hosts into occupying habitats most suitable for infection development. We experimentally tested whether the fungal parasite *Batrachochytrium dendrobatidis* (*Bd*) induces such behavioural changes in a semi-terrestrial amphibian host, the alpine newt (Ichthyosaura alpestris). While *Bd* is confined to moist environments, alpine newts frequently move among habitats with varying moisture levels, from aquatic breeding ponds to dry terrestrial habitat. We introduced newts to an environment comprised of equal parts aquatic and terrestrial habitat. For one week we added varying concentrations of active *Bd* to the aquatic habitat on a daily basis while continuously tracking newt activity. This design allowed us to determine whether individuals alter activity among these habitats in response to either different degrees of exposure or to the onset of infection. While we detected strong dose-dependent infection dynamics, exposure to even high concentrations of *Bd* did not induce alterations in habitat use. However, newts responded to the onset of infection by increasing time in low-risk terrestrial habitat, suggesting that hosts detect infections and adjust activity patterns to inhibit infection development. These findings highlight the behavioural effects posed by *Bd* infections and emphasize the role of parasites in driving patterns of host activity.

16/04/2015 Session D3 - (Room 11A) - Parasites - Ecology II - Chair: J Cable 4:30 PM - 4:45 PM (15 mins)

Interactions between multiple helminths and the gut microbiota in wild rodents

Sarah Perkins[1,2], Kreisinger, J.[1], Bastein, G.[1], Marchesi, J.[2,3], Hauffe, H.[1]

[1.] Department of Biodiversity and Molecular Ecology, Centre for Research and Innovation, Fondazione Edmund Mach, Via E. Mach 1, 38010 S. Michele all'Adige (TN), Italy [2.] School of Biosciences, Cardiff University, Sir Martin Evans Building, Museum Avenue, Cardiff, CF10 3AX, UK [3.] Centre for Digestive and Gut Health, Department of Surgery and Cancer, Faculty of Medicine, Imperial College London, London SW7 2AZ, United Kingdom.

The gut microbiota is vital to host health and, as such, it is important to elucidate the mechanisms altering its composition and diversity. Intestinal helminths are host immunomodulators and have evolved both temporally and spatially in close association with the gut microbiota, resulting in potential mechanistic interplay. Host-helminth and host-microbiota interactions are comparatively

well-examined, unlike microbiota-helminth relationships, which typically focus on experimental infection with a single helminth species in laboratory animals. Here, we examined the association between microbiota and natural infection of multiple helminth species in wild mice (*Apodemus flavicollis*), using 16S rRNA gene catalogues (metataxonomics). Variation in the composition and abundance of gut microbial taxa associated with helminths was specific to each helminth species and occurred both up- and downstream of that helminth's niche (gut position). The most pronounced helminth-microbiota association was between the presence of tapeworms in the small intestine and increased Bacteriodetes spp. in the stomach. In addition, helminths themselves appear to harbour a microbiota that is unique and different to its host, leading us to question whether helminths directly or indirectly alter the gut microbiota. Regardless, helminths clearly have the potential to alter gut homeostasis. Free-living rodents with a diverse helminth community offer a useful model system that enables both correlative (present study) and manipulative inference to elucidate helminth-microbiota interactions.

16/04/2015 Session D3 - (Room 11A) - Parasites - Ecology II - Chair: J Cable 4:45 PM - 5:00 PM (15 mins)

Neuropeptides and sociality behaviours in plant parasitic nematodes – (SP)

Emily Robb[1], Ivan Vokřál[2], Johnathan Dalzell[1], Colin Fleming[3], Angela Mousley[1], Aaron G. Maule[1] and Nikki J. Marks[1]

[1.]*Institute for Global Food Security, School of Biological Sciences, Queen's University Belfast, UK;* [2.]*Department of Pharmacology and Toxicology, Charles University, Prague, Czech Republic;* [3.]*AgriFood Biosciences Institute< Newforge Lane, Belfast, UK*

Plant parasitic nematodes significantly reduce crop production such that their control is a significant issue for global food security. Little effort has centred on understanding the behaviour of pre-parasitic J2-stage nematodes in soil prior to host infection. We hypothesize that sensory input and inter-J2 signalling modulate behaviour and set out to investigate social behaviours such as dispersal, and the role of FMRFamide-like peptides (FLPs) in such behaviours. The role of environmental factors (population density, CO2) on J2 dispersal was examined. Results showed nematodes derived from higher density populations dispersed more effectively than nematodes derived from less dense populations; after 6h, 43% of *Globodera pallida* J2s derived from high density populations had dispersed compared to 14% from low density populations (similar results for *Meloidogyne incognita*). CO2 also impacted dispersal; after 6h, 31% of a low density population of *G. pallida* had dispersed after 5% CO2 incubation, compared to 11% incubated in atmospheric CO2. FLPs are known to modulate sensory and motor functions in nematodes and qPCR analyses revealed marked FLP diversity in plant nematode J2s. Those flp genes most highly expressed (flp-6, -7, -14, -16 & -18) were selected to determine their impact on dispersal. Peptide exposed worms were analysed in motility assays and displayed a significant reduction in motility (~40%) after 16 hours in flp-6, flp-14 and flp-16. Neuromuscular function is a well-established target for parasite control and we aim to better understand J2 behaviour and FLP signalling to help seed

16/04/2015 Session D3 - (Room 11A) - Parasites - Ecology II - Chair: J Cable 5:00 PM - 5:15 PM (15 mins)

Session E3 - (Room 11C) - Parasites - Immunology & Pathology II

Chair: DR J Turner, Liverpool School of Tropical Medicine

The association of STAT6, IL33, IL10 and CHI3L1 polymorphisms on schistosomiasis infection and related morbidity – (SP)

Alexandra Sparks[1], Norman Nausch[1], Katharina Stenzel[1], Laura J. Appleby[1], Eleanor Strong[1], Nicholas Midzi[2], Takafira Mduluza[3], Francisca Mutapi[1]

[1.] Institute of Immunology and Infection Research, Centre for Immunity, Infection and Evolution, School of Biological Sciences, University of Edinburgh, Kings Buildings, Ashworth Laboratories, Edinburgh EH9 3JT, Edinburgh, UK [2.] National Institute of Health Research, PO Box CY 573, Causeway, Harare, Zimbabwe [3.]Department of Biochemistry, University of Zimbabwe, PO Box 167, Mount Pleasant, Harare, Zimbabwe

Urogenital schistosomiasis, caused by the parasitic helminth *Schistosoma haematobium*, is a disease of major public health importance in sub-Saharan Africa. Within endemic regions, there is a large variation in worm burden and morbidity, and there is evidence that host genetics play an important role in explaining this host heterogeneity. The type of T helper cell response to the parasite, particularly the eggs, is crucial in determining susceptibility and severity of disease and this response is likely to be influenced by genetic variation in immune genes. The aim of this study was to determine whether variation in immune genes is associated with susceptibility to schistosome infection and morbidity. In a Zimbabwean population of 926 individuals, 4 single nucleotide polymorphisms were genotyped: rs3024495 in IL10, rs3939286 in IL33, rs324013 in STAT6 and rs4950928 in Chitinase 3-like 1 (CHI3L1), and these were related to *Schistosoma haematobium* infection. In addition, genotypes were related to levels of morbidity markers: CHI3L1, a marker of a range of inflammatory diseases, and the markers of liver damage, aspartate transaminase (AST) and alanine transaminase (ALT). Preliminary analysis found an association with the CC genotype at rs4950928 (CHI3L1) and increased CHI3L1 levels and the TT genotype at rs3939286 (IL33) and increased AST levels, but no association of genotype with susceptibility to infection. These results suggest that levels of the inflammatory marker CHI3L1 and the liver damage biomarker AST are associated with host genetic variation.

16/04/2015 Session E3 - (Room 11C) - Parasites - Immunology & Pathology II - Chair: J Turner 4:00 PM - 4:15 PM (15 mins)

Immune-dependence of chemotherapy: characterization of *Schistosoma mansoni* tegument antigens exposed by praziquantel to host antibody reactivity – (SP)

Joseph Igetei[1], Marwa Elfaham[1], Susan Liddell[1,2], Jan Bradley[1] and Michael J. Doenhoff[1]

[1.] School of Life Sciences, University of Nottingham, Nottinghamshire, NG7 2RD, UK. [2.] School of Biosciences, University of Nottingham, Sutton Bonington Campus, LE12 5RD, UK.

The tegument antigens of *S. mansoni* worms play an important role in the survival of the parasite in its definitive hosts. Here, the tegumental antigens that are exposed by sub-curative doses of praziquantel were investigated using serum from a rabbit that had been infected percutaneously with *S. mansoni* cercariae. The antiserum had previously shown synergistic action with praziquantel in killing adult worms. IgG antibodies in this antiserum reacted with two antigens of, respectively, ~30 kDa and ~40 kDa in Western immunoblots of a detergent extract of *S. mansoni* adult worms. Both antigens were purified by repeated immunoelectrophoresis in, and elution from, one dimensional sodium dodecyl sulphate polyacrylamide gel electrophoreses (SDS-PAGE). After each electrophoresis the part of the gel containing the respective antigen was excised, eluted and re-electrophoresed. The purified ~30 kDa and ~40 kDa antigens were analysed by tandem mass spectrometry (TMS). Data from the purified ~30 kDa antigen was significant for two entries in the NCBInr database, corresponding to two *S. mansoni* tegument antigens: Sm29 and fructose 1, 6-bisphosphate aldolase. TMS analysis of the 40 kDa antigen revealed the presence of *S. mansoni* malate dehydrogenase. In indirect immunofluorescence both the unfractionated rabbit antiserum and anti-30 kDa antigen antibodies purified from the same antiserum reacted on the surface of adult worms treated with a sub-lethal dose of praziquantel, but such reactivity was not observed on the surface of control untreated worms. These results provide tentative identification of the *S. mansoni* tegument antigens which induce production of host antibodies.

16/04/2015 Session E3 - (Room 11C) - Parasites - Immunology & Pathology II - Chair: J Turner 4:15 PM - 4:30 PM (15 mins)

Changes in antibody levels after schistosomiasis chemotherapy: a systematic review and meta-analysis – (SP)

Mizuho Fukushige[1], Mark E.J. Woolhouse[1], Francisca Mutapi[1,2]

[1]Centre for Immunity, Infection and Evolution, College of Medicine and Veterinary Medicine, University of Edinburgh, Edinburgh, UK [2]Institute of Immunology and Infection Research, Centre for Immunity, Infection and Evolution, School of Biological Sciences, University of Edinburgh, Edinburgh, UK

Previous studies have demonstrated that schistosomiasis chemotherapy boosts protective antibody responses against *S. mansoni* and *S. haematobium*, which is otherwise occur slowly with age. A considerable number of studies have been conducted measuring schistosome-specific antibody levels before and after chemotherapy. Using these reports, the objective of this study is to conduct a meta-analysis to identify predictors affecting the direction of change in antibody levels after chemotherapy. Following a systematic review, we identified in total 155 observations from 40 articles (published 1981-2013), all these studies measured post-treatment antibody levels within 6 months after chemotherapy. Observations were grouped according to antibody types (anti-egg/anti-worm) and

isotypes for the analysis. Classification and regression tree (CART) models, weighted by the sample size were used to identify predictors. We used potential predictors of age, prevalence, infection intensity, drug type (praziquantel, oxamniquine, or others), schistosome species (*S. mansoni*, *S. haematobium*, or co-infection) and the time after chemotherapy for this analysis. The results reveal variable temporal dynamics of antibody levels following treatment. The results show a sustained increase in anti-worm IgA, IgE, and IgG4 (praziquantel treatment group), whereas decrease in anti-egg IgG4 (praziquantel treatment group). The results show elevation of several antibodies (anti-worm IgG, IgG1, anti-egg IgE) shortly after chemotherapy and subsequent decrease to below pre-treatment levels approximately 2-6 months after chemotherapy. There results indicate the 'normal' patterns of change in antibody responses to human schistosome infection that are induced by chemotherapy, but they also illustrate that there can be considerable variability within and between different human populations.

16/04/2015 Session E3 - (Room 11C) - Parasites - Immunology & Pathology II - Chair: J Turner 4:30 PM - 4:45 PM (15 mins)

Ovar-MHC Class II haplotypes and nematode resistance in sheep

Nur Mahiza Md Isa & Michael Stear

Institute of Biodiversity, Animal Health & Comparative Medicine, College of Medical, Veterinary & Life Sciences, University of Glasgow, Bearsden Road G61 1QH

Overcoming drug resistance in sheep farms involves finding alternative methods such as selective breeding of nematode resistant sheep. However, selective breeding requires identification of superior sheep. Identification of loci associated with nematode resistance could help. Several groups have reported the existence of alleles within the Ovar-DRB1 that are associated with enhanced resistance to nematode infection. However, high linkage disequilibrium (the tendency of alleles at distinct loci to occur together) among MHC Class II genes makes it difficult to identify causal mutations. We performed haplotype analysis of Ovar-MHC Class II genes (Ovar-DRB1, DQA1, DQA2, DQA2-like, DQB1 and DQB2) and its association with faecal egg counts. The haplotype analysis revealed only 20 haplotypes from a flock of Texel sheep. Interestingly, the Ovar-DQB2 locus has a major influence on nematode resistance in this study as well as the Ovar-DRB1 locus. The study emphasizes the importance of haplotype characterisation of the MHC genes in studying the role of the genes in nematode resistance.

16/04/2015 Session E3 - (Room 11C) - Parasites - Immunology & Pathology II - Chair: J Turner 4:45 PM - 5:00 PM (15 mins)

DNA vaccination with *Onchocerca volvulus* Glyceraldehyde-3-Phosphate Dehydrogenase leads to protection in a mouse model of human filariasis

Vera Steisslinger, Norbert Brattig[1] , Simone Korten[1,2], Alfons Renz[3,4], Daniel Achukwi[4], Norbert W. Brattig[1], Klaus D. Erttmann[1]

[1.] Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany [2.]Department of Microbiology, MVZ Laboratory Lademannbogen, Germany [3.]Institute of Evolution and Ecology, University of Tübingen, Germany [4.]Institute of Agricultural Research for Development, Wakwa Regional Centre, Cameroon

The filaria Onchocerca volvulus is the causative agent of river blindness (onchocerciasis). Over the last decades control programs successfully prevented tens of millions of onchocerciasis cases worldwide, mostly by mass drug administration of ivermectin. This strategy, however, has its limitations, which might be overcome by the additional use of a vaccine. Previously our group cloned and characterized Onchocerca volvulus (Ov)-Glyceraldehyde-3-phosphate Dehydrogenase (GAPDH) and conducted a small scale DNA vaccination study with OvGAPDH.DNApl in cattle as compatibility test [1]. The infection of the susceptible Balb/c mouse with the rodent filaria Litomosoides sigmodontis serves as a model of human filariasis, in which we tested the protective potential of OvGAPDH. Three different vaccine formulations were used to immunize BALB/c mice: (i) the DNA-construct OvGAPDH.DNApl, (ii) a combination of the DNA-construct plus recombinant OvGAPDH protein, and (iii) OvGAPDH peptides in alum. After challenge infection of immunized and control mice with L. sigmodontis, the formulations including the DNA-plasmid, led to significant reduction of adult worm load (up to 57% reduction) and microfilaraemia (up to 94% reduction) in the immunized animals. Our results indicate that vaccination with OvGAPDH has protective potential against filarial challenge infection in the mouse model thus allowing to proceed to the Onchocerca ochengi /cattle model. This natural host-parasite system has previously provided evidence for natural cross-protection in a co-endemic system [2,4] and for the protective effect of vaccination against O. ochengi under field conditions [3,4]. [1] BBA 2005;6:85; [2] Parasitology 1998;116:349; [3] Parasite Immunol 2007;29:113; [4] PNAS 2006;103:5971

16/04/2015 Session E3 - (Room 11C) - Parasites - Immunology & Pathology II - Chair: J Turner 5:00 PM - 5:15 PM (15 mins)

Session A4 - (Room 11A) - Malaria - Drugs I

Chair: Prof G Biagini Liverpool School of Tropical Medicine

The trials and tribulations of generating fully synthetic peroxide based antimalarials.

Stephen A Ward, Paul M O'Neill, Richard Amewu

Liverpool School of Tropical Medicine

Malaria is a curable and preventable but often fatal disease that affects 40% of the world's population. Available drugs are becoming increasingly ineffective due to resistance and the number of truly novel antimalarial compounds in the drug development pipeline may be insufficient to meet future treatment needs. This challenge is even more critical now that the community has accepted the challenge to move towards a malaria eradication agenda. The artemisinins are currently the frontline agents in the treatment of malaria due to their ability to rapidly reduce parasite biomass. However the first generation analogues such as artesunate and artemether have limitations and the emergence of what appears to be artesunate resistant strains of *P. falciparum* at the Thai-Cambodia border raises serious concerns over the future of all semi-synthetics in this class. We have been engaged in the design and development of fully synthetic alternatives to the semi-synthetic artemisinins based on a core tetraoxane pharmacophore. From a library of over 150 1,2,4,5-tetraoxanes we have developed a potential candidate molecule, E209 through three generation of design and evaluation. E209 has

outstanding in vitro activity against sensitive and resistant strains of *P. falciparum* (IC50=2.4nM (K1), 4.7nM (3D7) and TI>14000) and retains this level of activity against S.E Asian isolates that failed standard artemisinin based combination chemotherapy. This compound has excellent in vivo activity (ED50=1.33 mg/kg and ED90=4.18 mg/kg), acceptable oral bioavailability (F%) and DMPK and blood stability superior to currently available peroxides. E209 may have potential as a single dose cure. The drug discovery and development pathways through three generations of analogies to E209 will be described.

17/04/2015 Session A4 - (Room 11A) - Malaria - Drugs I - Chair: G Biagini 9:00 AM - 9:30 AM (30 mins)

Atovaquone-Emetine dihydrochloride hydrate: a novel drug combination for malarial – (SP)

Holly Matthews[1], Jon Deakin[1], Maryam Idris-Usman[1], Martin Read[2], Farid Khan[3], Niroshini Nirmalan[1]

[1.] *School of Environment and Life Sciences, University of Salford, M5 4WT, Salford, Manchester, UK*
[2.] *Manchester Institute of Biotechnology, University of Manchester, M1 7DN, Manchester, UK*
[3.] *Lumophore Ltd. Manchester Science Park, M15 6SE, Manchester, UK*

Malaria is one of the most significant parasitic diseases that afflicts mankind. Recent reports estimate there were around 600,000 fatalities in 2012. Treatment mainly relies on chemotherapy and Artemisinin based Combination Therapy (ACT) is the current frontline recommendation by the WHO. Unfortunately, most combinatory options are compromised by resistance. Despite efforts to contain resistance to the important artemisinin class, its trajectory is following that of the previous treatments, chloroquine and sulfadoxine-pyrimethamine, with reports already reaching the Indian border. It is therefore imperative that novel therapeutics are developed quickly. Recent high-throughput phenotypic screens, against predominantly erythrocytic-stage malaria, have identified a multitude of active compounds. Repositioned from their previous indications, these compounds diversify antimalarial targets and have shorter drug development times. The anti-amoebic compound emetine dihydochloride hydrate was identified as a potent inhibitor (IC50 = 47 nM) of the multidrug resistant *Plasmodium falciparum*, strain K1. Second-phase characterization has revealed in vitro pharmacokinetic matching and synergy with the existing antimalarial atovaquone. Furthermore, killing profile data along with mitochondrial staining has provided some indication about the, potentially multiple, mechanistic actions of emetine in the malaria parasite. In the current climate, such an option definitely warrants further investigation as an antimalarial candidate.

17/04/2015 Session A4 - (Room 1B) - Malaria - Drugs I - Chair: G Biagini 9:30 AM - 9:45 AM (15 mins)

Predictors of cardiac safety of artemisinin-based combination therapy in human immunodeficiency virus infected adults stabilized on antiretroviral therapy in Malawi

Eva Maria Hodel, Clifford G Banda[1], Mavuto Mukaka[1], Richard Kamwezi[2], Maxwell Yohane[2], Fraction Dzinjalamala[1,2], Jane Mallewa[1,2], Dianne J Terlouw[1,3], Victor Mwapasa[1,2]

[1.] *Malawi Liverpool Wellcome Trust Clinical Research Programme, Blantyre, Malawi;* [2.] *University of Malawi, College of Medicine, Blantyre, Malawi;* [3.] *Liverpool School of Tropical Medicine, Liverpool, United Kingdom*

Co-infections with *Plasmodium falciparum* malaria and human immunodeficiency virus (HIV) occur frequently in sub-Saharan Africa but there is limited data on the safety of artemisinin-based combination therapy (ACT) in individuals taking antiretroviral (ARV) drugs. Several ACT partner drugs have been associated with cardiac abnormalities in a concentration dependent manner and thus triggered a call for more safety data from various high risk sub-populations. On the other hand, ARV drugs such as protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs) affect the activity of cytochrome P450 isoenzymes and may alter plasma concentrations of ACTs. As part of a pharmacokinetic trial assessing safety of ACTs among malaria-free but HIV infected individuals stabilised on ART, we compared the incidence and severity of QTc prolongation and cardiac related adverse events in ARV-naïve individuals (n=41) and those taking NNRTIs (n=71) and PIs (n=42) in combination with a standard three-day regimen of dihydroartemisinin-piperaquine, artesunate-amodiaquine or artemether-lumefantrine. The effect of predictors such as age, gender, electrolyte levels and intake of cotrimoxazole prophylaxis on QTc prolongation across study arms were assessed using logistic regression. The safety data of ACTs in HIV infected populations will help inform treatment guidelines and support national malaria control programs considering large ACT mass drug administration campaigns.

17/04/2015 Session A4 - (Room 11A) - Malaria - Drugs I - Chair: G Biagini 9:45 AM - 10:00 AM (15 mins)

Exploring the *in vitro* and *in vivo* activity of the aqueous and methanolic bark extract of *Bridelia ferruginea* using fluorescent based assays and the mouse animal model.

Maryam Shehu Idris-Usman[1], Joshua Howard-Taylor[1], Holly Mathews[1], Godwin Akuodor[2], Uche Osunkwo[2] and Niroshini Nirmalan[1]

[1.] *School of environmental and life sciences, University of Salford, Manchester, United Kingdom*
[2.] *Department of Pharmacology and Toxicology, National Institute for Pharmaceutical Research and Development (NIPRD), Idu industrial estate, Abuja, Nigeria.*

Advances in high-throughput screening technologies and extensive funding have failed to deliver affordable anti-malarial options. The mainstay of drug-based malaria control continues to be largely reliant on the fortuitous discovery of natural compound remedies informed by traditional medical practices. The WHO has recently encouraged African countries to commence the development of Traditional African medicines (TAM) especially in relation to diseases like malaria that are endemic in these regions. One of the main bottlenecks with traditional medicine usage is the lack of standardized dosing, proper extraction and purification methods and hence the need for more research into the scientific validation and standardisation of these practices. Hence the purpose of this study is to ascertain the antimalarial activity of *Bridelia ferruginea* in line with its traditional usage for malaria. In the study, fluorescent based assays including flow cytometry (FCM) and the SYBR green microtitire assay (SG) were used to evaluate invitro antiplasmodial activity of the aqueous and methanolic bark extracts of *Bridelia ferruginea*. In vivo antiplasmodial activity was also, evaluated using the *Plasmodium berghei* mouse model. The results revealed that both the aqueous and methanolic extracts showed inhibitory activity against the *Plasmodium falciparum* K1 resistant and 3D7 chloroquine sensitive strain. This study hence validates the traditional usage of the plant extract for malaria.

17/04/2015 Session A4 - (Room 11A) - Malaria - Drugs I - Chair: G Biagini 10:00 AM - 10:15 AM (15 mins)

Misuse of antimicrobials: Could we be supporting malaria parasite development in the mosquito host?

Jewelna Osei-Poku, Mathilde Gendrin, Dorothy Yeboah-Manu, George K. Christophides, Michael D. Wilson

Department of Parasitology, Noguchi Memorial Institute for Medical Research, College of Health Sciences, University of Ghana. Division of Cell and Molecular Biology, Imperial College, London, UK

Some bacteria inhabiting the guts of mosquito vectors are known to be effectively involved in killing *Plasmodium* parasites. Treating mosquitoes with antibiotics/antimicrobials clears these gut bacteria, allowing for enhanced development and transmission of *Plasmodium*. We hypothesize therefore, that the overuse of antibiotics/antimicrobials among human populations may inadvertently impact on efforts to control malaria transmission. This study seeks to investigate the effect of human serum concentrations of commonly administered antibiotics/antimicrobials on the gut microbiota of *Anopheles gambiae* s.l, and the consequential effect on *Plasmodium falciparum* development. We have used 454-pyrosequencing to catalogue the core gut microbiome of *Anopheles gambiae* s.l. sampled from two regions in Ghana, and investigated the effects of varying levels of commonly administered antimicrobials; Amoxicillin, Metronidazole, and Tetracycline, on the *An. gambiae* gut microbiota, using quantitative PCR and 454-pyrosequencing. Our results show that *An. gambiae* mosquitoes sampled from the two regions in Ghana have similar gut microbiome, dominated by bacterial species belonging to the family Halomonadaceae (average 71.6%). When mosquitoes from one of the sites were treated with our antibiotics under investigation, Amoxicillin showed the greatest effect in reducing the gut microbiota (average 85.1% bacterial clearance). Metronidazole and Tetracycline cleared 32.2% and 60.1% bacteria, respectively. The bacteria profile of this antibiotic clearance is yet to be confirmed by sequencing. Further studies will investigate the consequential effects on *Plasmodium falciparum* development. The results from this study are expected to inform on possible negative effects of the unbridled use of antimicrobials on the control of malaria.

17/04/2015 Session A4 - (Room 11A) - Malaria - Drugs I - Chair: G Biagini 10:15 AM - 10:30 AM (15 mins)

Session B4 - (Room 11B) - NTDs - Molecular Biology I

Chair: DR A Acosta-Serrano, Liverpool school of Tropical Medicine

Genomics of *Entamoeba*: dissecting populations and species.

Neil Hall[1], Kanok Preativatanyou[1], Ian Wilson[1], Gareth Weedall[2]

[1.] *Department of Functional and Comparative Genomics, University of Liverpool, Liverpool, L69 7ZB*
[2.] *Liverpool School of Tropical Medicine, Liverpool*

The genus *Entamoeba* contains pathogenic species as well as many apparently commensal species. *Entamoeba histolytica* is the causative agent of amoebiasis, which causes significant levels of death and disease worldwide. More recently related species, such as *E. bangladeshi*, and *E. moshkovskii* have been associated with human disease. For a long time, the genetics *Entamoeba histoytica* was unresolved due

to the lack of genetic tools and we have few clues as to the role of parasite genetics in determining if an infection leads to a virulent or asymptomatic infection. Our data have demonstrated that *E. histolytica* can recombine and suggests that meiosis occurs during encystation. However there is little evidence to extensive recombination in *E. moshkovski* which may be a species complex. We have also sequenced the genome of a number of *Entamoeba* isolates and compared the gene content and genetic variation with other species to better understand how these organisms have adapted to their various environmental niches. Our results suggest that the reptile pathogen *E. invadens* and *E. moshkovski* have a much more diverse armoury of host interaction genes compared to *E. histolytica*. This may be due to a wider range of hosts or environmental niches that they are able to inhabit.

17/04/2015 Session B4 - (Room 11B) - NTDs - Molecular Biology I- Chair: A Acosta-Serrano 9:00 AM - 9:30 AM (30 mins)

Investigation of amino acid utilisation in *Leishmania* and its impact on host metabolism. – (SP)

Archana Nayak, Michael P Barrett, Richard Burchmore

Institute of Infection, Immunity and Inflammation; Glasgow Polyomics; College of Medical, Veterinary and Life Sciences; University of Glasgow; Glasgow; G12 8TA; U.K.

The plant sap and blood meal consumed by the female sand fly serves as major source of amino acids utilised by the parasites *Leishmania* for its viability, osmoregulation and transmission. Amino acids and its transporters could act as major gateway for drugs to combat this disease. Here, we studied the importance of natural amino acids by individually deleting each one from the medium composition. This was achieved by formulating chemically defined medium for the culture of *Leishmania mexicana*. Addition of co-factors and metals made a significant difference to support continuous growth in the defined medium. Glutamine, phenylalanine and tryptophan were found to be most important for growth even in the first passage in the culture medium. Absence of isoleucine, histidine, threonine, arginine, lysine, tyrosine, leucine, proline and valine significantly compromised growth. Unexpectedly, lack of methionine did not affect parasites growth. This study outlines the key medium components required to maintain continuous culture in vitro and highlights the importance of amino acids in the order of their essentiality and its contribution to pathogenicity. We plan to extend these data by applying metabolomics and proteomics approaches and enlist the differences of mammalian and parasitic enzymes that could serve as potential drug targets.

17/04/2015 Session B4 - (Room 11B) - NTDs - Molecular Biology I- Chair: A Acosta-Serrano 9:30 AM - 9:45 AM (15 mins)

Investigating stage-specific trans-regulators in *Leishmania* spp.

Luis De Pablos Torro and Pegine B. Walrad

Centre for Immunology and Infection, Dept of Biology, University of York

Leishmania spp. are the causative agent of leishmaniasis, the second deadliest parasitic disease. Like the other kinetoplastid parasite diseases, no vaccine currently exists for Leishmaniasis and there is a

growing resistance to the limited treatments available. Despite this urgency, relatively little is known of the molecular mechanisms which drive virulence in these parasites and enable their swift adaptation upon transmission between the sandfly vector and mammalian hosts. Gene regulation in kinetoplastid parasites is overwhelmingly post-transcriptional as undefined promoter regions drive polycistronic arrays of genes with negligible transcriptional control. Accordingly, there is an emphasis upon trans-regulator RNA binding proteins (RBPs) in *Leishmania* spp. parasites relative to the proteomes of other eukaryotes. These regulatory RBPs and their transcript target complexes (mRNPs) promote the swift adaptation to new host environments and enable the *Leishmania* parasite's lifecycle progression to human-infective forms. Despite the vital role of such regulatory mRNPs, very little is known of the role of these complexes in *Leishmania* spp. gene regulation. We have optimised a cutting edge crosslinking strategy to isolate RBPs which bind mRNAs of different stage *Leishmania mexicana* parasites and identified them by high sensitivity mass spectroscopy. We have confirmed the stage-specific mRNA expression of select proteins via qPCR and are currently endogenously tagging regulatory candidates. While gene regulation varies substantially between *Leishmania* spp. parasites, we seek to utilise the optimised tools and techniques to investigate the function of candidate regulators in *L. mexicana* as well as other *Leishmania* species.

17/04/2015 Session B4 - (Room 11B) - NTDs - Molecular Biology I- Chair: A Acosta-Serrano 9:45 AM - 10:00 AM (15 mins)

Genome plasticity and copy number variation determine gene expression differences in *Leishmania* – (SP)

Stefano Iantorno, Caroline Durrant, James Cotton, Mandy Sanders, Michael Grigg, David Sacks, Matt Berriman

Wellcome Trust Sanger Institute, Hinxton CB10 1SA

Leishmania is a genus of unicellular eukaryotic parasites responsible for a wide range of human diseases, from cutaneous (CL) and mucocutaneous leishmaniasis (MCL) to life-threatening visceral leishmaniasis (VL). *Leishmania tropica* is responsible for significant CL and VL in endemic areas in North and East Africa, the Middle East, and the Indian subcontinent. Global RNA-seq analysis of 12 *Leishmania tropica* isolates revealed considerable intraspecific differences in gene expression. Comparison with whole-genome sequence data generated from the same 12 isolates using a new reference genome assembly suggests that most variation in gene expression is explainable by variation in copy number at the level of individual genes, or at the level of the whole chromosome. Most field isolates appear to be near diploid, with some degree of aneuploidy seen in all isolates. Cloning of single cells from 4 of these isolates shows variable ploidy within the same isolate, a condition that in *Leishmania* has been called mosaic aneuploidy. Gene annotation analysis suggests that the most significant differentially expressed genes in this set of isolates are membrane-bound transporter proteins, which are known to be involved in uptake of nutrients and drug compounds from the extracellular environment. We identify copy number variation in these genes suggesting that a certain degree of plasticity is observed in natural populations of *Leishmania*, creating the conditions necessary for rapid downregulation or upregulation of different transporter proteins over a limited number of mitotic generations in the presence of environmental stressors.

17/04/2015 Session B4 - (Room 11B) - NTDs - Molecular Biology I- Chair: A Acosta-Serrano 10:00 AM - 10:15 AM (15 mins)

DNA repair proteins MRE11 and RAD50 are involved in genome plasticity in *Leishmania* – (SP)

Marie-Claude Laffitte, Philippe Leprohon, Danielle Légaré, Marc Ouellette

Centre de recherche en infectiologie Centre hospitalier universitaire de Québec (CHUQ), Pavillon CHUL 2705 boul. Laurier, Local RC-709 Québec (Québec) Canada G1V 4G2

Genome plasticity is a powerful mechanism to face stressful conditions in *Leishmania* parasites. Variations in chromosome organization and copy number are used by this parasite to rapidly generate diversity in response to antileishmanial drug exposure. We hypothesized that genomic plasticity in *Leishmania* would imply a leading role of DNA repair proteins, considering the need of DNA processing in this phenomenon. Here we investigated the role of MRE11 and RAD50 genes encoding for two DNA repair proteins part of the complex MRN, in chromosomal integrity and genome plasticity. We first generated *Leishmania infantum* MRE11 null mutants and observed an altered capacity to perform extra-chromosomal linear amplification relevant to drug-resistance. This result confirmed a novel MRE11-dependent repair pathway used by *Leishmania* to amplify portion of its genome in response to drug pressure. We then tried to generate RAD50 null mutants in both WT and MRE11-/- strains. Interestingly, inactivation of RAD50 was successfully obtained in the MRE11 null mutant strain while it was not possible in the WT background, suggesting a possible hierarchy in the MRN complex assembly. Analysis of the MRE11-/-RAD50-/- strain by whole genome sequencing revealed multiple chromosomal translocations and highlighted microhomology sequences between the translocated chromosomes at the level of the breakpoint regions. These results demonstrate a possible microhomology-mediated end-joining mechanism in the MRE11-/-RAD50-/- cells and therefore a prominent role of MRE11 and RAD50 in genome plasticity. The thorough characterization of the MRN complex should help in deciphering the genomic molecular plasticity involving inter and intrachromosomal recombinations in *Leishmania* parasites.

17/04/2015 Session B4 - (Room 11B) - NTDs - Molecular Biology I- Chair: A Acosta-Serrano 10:15 AM - 10:30 AM (15 mins)

Session C4 - (Room 11C) - Vectors - Emerging diseases and zoonoses

Chair: Prof S Torr, Liverpool School of Tropical Medicine

An integrated research programme to understand the epidemiology of *Plasmodium knowlesi*

Chris Drakeley, KM Fornace, NM Anstey, MJ Grigg, TH Chua, H Ferguson, SJ Torr, M Salgado-Lynn, DJ Stark, I Vythilingam, E Espino, T William, J Cox

London School of Hygiene & Tropical Medicine

The simian parasite, *Plasmodium knowlesi* is an increasing cause of human malaria in parts of Southeast Asia, particularly in Malaysian Borneo where it is associated with a higher risk of severe and fatal disease than *P. falciparum*. In Sabah, Malaysia there has been a marked and rapid increase in *P. knowlesi* cases numbers, the reasons for which are not yet clear. One credible hypothesis is that deforestation and

resulting habitat fragmentation have increased the amount of contact between people, mosquito vectors and primate hosts. However, to date, no detailed study of risk factors for *P. knowlesi* infection has been conducted and substantial knowledge gaps exist in relation to the transmission system and the role of ecological factors in determining spatial and temporal patterns of risk. This presentation will focus on a multidisciplinary programme being carried out in Sabah to elucidate the epidemiology of P. knowlesi and characterise interactions between ecological factors and vector/human/macaque populations. The programme incorporates a variety of approaches from the fields of clinical epidemiology, primatology, social science, parasitology, entomology, ecology, geography and modelling. An overview of the multidisciplinary framework will be presented and specifically the integration of these different data sources with information on land cover generated from multi-temporal drone imagery. The aim being to combine approaches to assess the probability of human exposure with zoonotic *P. knowlesi* and characteristics of individuals and places associated with increased probability of exposure.

17/04/2015 Session C4 - (Room 11C) - Vectors - Emerging diseases and zoonose - Chair: S Torr 9:00 AM - 9:30 AM (30 mins)

The risk of mosquito-borne disease emergence in the UK

Matthew Baylis, Jolyon Medlock

Institute of Infection and Global Health; & Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool MRA- Emergency Response Department, Health Protection and Medical Directorate, Public Health England, Porton down, Salisbury

Malaria was prevalent in parts of the UK until the first half of the 20th century, with changes to our physical landscape, farming practices, housing and medicine all contributing to its eventual demise. The UK has not experienced other mosquito-borne diseases to date but this may be a future risk. The risk arises from two main sources: indigenous mosquitoes, which may happen to be competent for certain pathogens and are awaiting their introduction; and invasive mosquitoes, which may bring a pathogen with them or be able to transmit when a pathogen subsequently arrives. There are important precedents for both of these risks in other settings, and the risks are expected to increase with climate change. Of particular concern is the recent discovery of populations of the West Nile vector, Culex modestus in the southeast, and the slow but steady spread of the Asian Tiger mosquito, *Aedes albopictus*, further north in mainland Europe. The recent discovery that a UK mosquito, *Ochleratatus detritus*, is a competent vector for some flaviviruses is also important especially as such species, in their native environment and climate, may be surprisingly good vectors if presented with the opportunity.

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Recent experiences controlling zoonotic diseases: Market traffic and risks of introduction of controlled pathogens

Louise Hamill, Kevin Bardosh, Christine A. Acup, Jenna Fyfe, Kim Picozzi, Charles Waiswa, Sue Welburn and Richard Selby

University of Edinburgh

Rhodesian (acute) HAT in Uganda has steadily moved northwards towards the area of *gambiense* (chronic) HAT over the past two decades around Lake Kyoga. Migration of this acute form of sleeping sickness into districts that had not previously experienced disease has been ascribed to unrestricted movements of infected cattle from established disease foci to naïve areas. In 2006 a large-scale intervention aimed to treat the majority of cattle in 5 districts west of Lake Kyoga to halt HAT's progression. Trypanocidal treatment successfully reduced *T. b. rhodesiense* prevalence within cattle from the baseline of 0.81% to 0.11% at three months post intervention. In the absence of enforcement of policy for trypanocidal treatment at point of sale, and application of methods to prevent reinfection, sustained protection from migration of HAT to new districts cannot be maintained. Using data mapping traffic of cattle through major markets from SE Uganda around the shores of Lake Kyoga between 2006 and 2008 this study assesses the relative risk posed by migration of infected cattle for introduction of disease. Relocated cattle are infected with a suite of hematoparasites, trypanosomes and Tick Borne Diseases, consideration should be given not only to treating animals to remove trypanosome infections but also to address migration of *T. parva* and other Tick Borne diseases. While responsibility lies with Government for enforcement of policy to treat animals at the point of sale, awareness between traders, farmers and communities of diseases that affect humans and animals, One Health

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Japanese encephalitis virus in Bangladesh: who's infecting whom?

Jennifer Lord[1], Emily S. Gurley[2], Juliet R. C. Pulliam[3,4,5]

[1.] Vector Group, Liverpool School of Tropical Medicine, Liverpool, United Kingdom [2.] Centre for Communicable Diseases, icddr,b, Mohakhali, Dhaka, Bangladesh [3.] Department of Biology, University of Florida, Gainesville, Florida, United States of America [4.] Emerging Pathogens Institute, University of Florida, Gainesville, Florida, United States of America [5.] Fogarty International Center, National Institutes of Health, Bethesda, Maryland, United States of America

In 1950's Japan, annual epidemics of human encephalitis were attributed to the mosquito-borne pathogen- Japanese encephalitis virus (JEV). Subsequent extensive field and laboratory studies in Japan accumulated empirical evidence for the primary role of pigs and the mosquito *Culex tritaeniorhynchus* in JEV transmission, with a minor role for ardeid birds. Since these initial studies, empirical data including numbers of *Cx. tritaeniorhynchus* relative to other mosquito species caught during entomological surveys and pig seroconversion rates have contributed to the theory that across Asia the JEV cycle primarily involves these species. However, in some regions of Asia reporting cases of Japanese encephalitis (JE), including Bangladesh, the pig population density is low relative to other domesticated animals. Are pigs and *Cx. tritaeniorhynchus* still the primary host and vector of JEV in these regions? As

part of a multidisciplinary project I am working toward integrating quantitative and empirical approaches to enable the relative roles of potential host and vector species in JEV transmission to be elucidated. I discuss parameters that contribute to the basic reproduction number (R0) of a mosquito-borne pathogen including host species density, the estimation of mosquito species relative abundance, the proportion of bloodmeals taken on each host species and the probability of host to mosquito transmission as evidence that other species may be important to JEV transmission in some regions of Asia.

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Quantifying wildlife host density and feeding preferences of tsetse (*Glossina swynnertoni* and *G. pallidipes*) in Serengeti National Park, Tanzania

Harriet Auty[1], Sarah Cleaveland[2], Imna Malele[3], Stephen J. Torr[4] , Susan C. Welburn[5], Kim Picozzi[5]

[1.] Epidemiology Research Unit, SRUC, Drummondhill, Stratherrick Road, Inverness. [2.] Boyd Orr Centre for Population and Ecosystem Health, Institute of Biodiversity, Animal Health and Comparative Medicine, College of Medical, Veterinary and Life Sciences, University of Glasgow, Glasgow. [3.] Tsetse & Trypanosomiasis Research Institute (TTRI), Box 1026 Tanga, Tanzania. [4.] Department of Vector Biology, Liverpool School of Tropical Medicine, Liverpool, UK, Warwick Medical School, University of Warwick, Coventry. [5.] Division of Pathway Medicine and Centre for Infectious Diseases, School of Biomedical Sciences, College of Medicine and Veterinary Medicine, University of Edinburgh, Chancellor's Building, Edinburgh.

Identifying hosts of blood-feeding insect vectors is a crucial part of understanding the role of different host species in disease transmission cycles. Rhodesian human African trypanosomiasis is commonly associated with wilderness areas of east and southern Africa. Such areas hold a diverse range of host species which form the host community responsible for disease maintenance. However, the relative contribution of different wildlife host species in transmission and maintenance remains unclear. This study quantified the feeding preferences of the tsetse vector in a wilderness area of great host species richness, Serengeti National Park, Tanzania. *Glossina swynnertoni* and *G.pallidipes* were collected from six sites. The sources of blood meals were identified through matching Cytochrome B sequences amplified from blood meals to published sequence data. The density of large mammal species was assessed and feeding indices calculated to assess the relative selection or avoidance of each host species by tsetse. The host species most commonly identified in G.swynnertoni blood meals were warthog (40% of meals identified), buffalo (23%) and giraffe (22%), despite being found at low densities. In contrast, wildebeest, zebra, impala and Thomson's gazelle , found at the highest densities, were never identified in blood meals. *G.pallidipes* showed different feeding patterns, with buffalo, giraffe and elephant most commonly identified. Although *G.swynnertoni* and *G.pallidipes* can feed on a range of wildlife species, they are highly selective. These feeding patterns, along with the ability of the key host species to maintain and transmit *T. b. rhodesiense*, drive the epidemiology of HAT in wilderness areas.

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Session D4 - (Room 13) - Parasites - Geospatial Ecology I

Chair: Prof L Rinaldi, Univeristy of Naples

Geographical information systems and cystic echinococcosis

Giuseppe Cringoli[1],Maria Paola Maurelli[1], Vincenzo Musella[2], Antonio Bosco[1], Laura Rinaldi[1]

[1.] Unit of Parasitology and Parasitic Diseases, Department of Veterinary Medicine and Animal Productions, University of Naples Federico II, Regional Center for Monitoring Parasitic Infections (CREMOPAR, Campania Region), Naples, Italy; [2.] Department of Health Sciences, University Magna Graecia of Catanzaro, Italy

Cystic echinococcosis (CE) is one of the most widespread parasitic zoonoses, caused by the larval stages of Echinococcus granulosus. The life cycle of *E. granulosus* includes canids as definitive hosts and a wide range of domestic and wild mammals and humans as intermediate hosts. Disability Adjusted Life Years (DALYs) resulting from human CE have been calculated as high as 1 million, similar to Dengue, Chagas Disease and Trypanosomiasis. Standardisation and harmonisation of novel diagnostics (e.g. FLOTAC technique for detection and isolation of eggs from dog faeces followed by molecular tools for species identification) and epidemiological approaches (e.g. geographical information systems, GIS) are very useful for the control of this zoonosis. GIS are advantageous to visualize and analyze large numbers of datasets in a geographical context at various spatial scales (local, national, regional and global). Representation of epidemiological data in the form of a map facilitates interpretation, synthesis and recognition of any changing frequency and pattern of CE and the appearance of clusters infections. Moreover, maps are convenient tools to foster discussion and dialogue among different stakeholders and the health authorities. GIS was very useful to better understand the chain of transmission of E. granulosus in southern Italy. GIS is proposed as a key tool to control the distribution of CE in animals and humans, based on: 1) information, dissemination and health education for dogs' owners, farmers and school-age children; 2) treatment of dogs in sheep farms; 3) diagnosis of CE in livestock and humans.

17/04/2015 Session D4 - (Room 13) - Parasites - Geospatial Ecology I - Chair: L Rinaldi 9:00 AM - 9:30 AM (30 mins)

Mapping the burden of schistosomiasis and soil-transmitted helminthiasis in the context of integrated preventive chemotherapy in Nigeria

Uwemedimo Ekpo[1], Akinola Oluwole[1], Dimitrios-Alexios Karagiannis-Voules[2], Eniola Abe[3], Obiagele Nebe[4], Jürg Utzinger[2], Penelope Vounatsou[2]

[1.] Department of Biological Sciences, Federal University of Agriculture, Abeokuta Nigeria; [2.] Department of Epidemiology and Public Health, Swiss Tropical and Public Health Institute, Basel, Switzerland; [3.] Department of Zoology, Federal University Lafia, Nigeria; [4.] Department of Public Health, Federal Ministry of Health, Abuja, Nigeria

Nigeria is regarded as the most endemic country in Africa for schistosomiasis and soil transmitted

helminthiasis (STHs). These two neglected tropical diseases are found many rural and semi-urban communities in Nigeria. The current control strategy involves preventive chemotherapy treatment with Praziquantel and albendazole using the school system since school-aged children are the high-risk group for the two diseases. For effective implementation of preventive chemotherapy treatment, the spatial distribution of the two diseases is required for a nationwide integrated deworming programme. We used systematic reviews, current survey infection data, remote sensed environmental data and socio-economic data with Bayesian geostatistical modelling to produced high resolution maps of the spatial distribution of schistosomiasis and soil transmitted helminthiasis for Nigeria. Schistosomiasis is endemic in 35 of the country's 36 states, including the federal capital territory of Abuja. Prevalence estimates, adjusted for school-aged children in 2010, showed that the prevalence is <10% in most states with a few reaching as high as 50%. An estimated 11.3 million school-aged children require Praziquantel annually. STHs are endemic in 20 of the country's 36 states, including the Federal Capital Territory of Abuja. An estimated 6.7 million school-aged children were infected in 2011. Among them, 2.0 million are located in 184 Districts in 20 states deserving annual preventive chemotherapy.

17/04/2015 Session D4 - (Room 13) - Parasites - Geospatial Ecology I - Chair: L Rinaldi 9:30 AM - 9:45 AM (15 mins)

Spatial epidemiology of co-infecting amphibian diseases – (SP)

Kirsten McMillan[1,2], Trenton W. J. Garner[2], Christl A. Donnelly[3], and David Lesbarrères[1]

[1.] Genetics and Ecology of Amphibians Research Group, Laurentian University, Sudbury, Ontario, Canada P3E 2C6 [2.] Institute of Zoology, Zoological Society of London, London NW1 4RY, United Kingdom
[3.] Department of Infectious Disease Epidemiology, Imperial College London, School of Public Health, St Mary's Campus, Norfolk Place, London W2 1PG, United Kingdom

Emerging infectious diseases have significant effects on biological communities. In some cases, pathogens have caused host extinctions. The majority of research has focused on a 'one host – one pathogen framework'. However, individual hosts encounter multiple pathogens simultaneously, which may lead to additive, antagonistic or synergistic effects on hosts. The dynamic interaction between pathogens is an important issue when modeling infectious diseases, as it can increase infection prevalence and severity. While establishing the cause of extinction is difficult and candidate model species are few, amphibians appear to be an ideal specimen as increasing evidence suggests that we are facing a global population decline. Ranavirus (family Iridoviridae) and the Chytrid fungus (*Batrachochytrium dendrobatidis*) are the primary pathogens associated with amphibian mortalities. While there have been several reports of ranavirus and chytrid infection within Europe, both pathogens have become prominent in North America and particularly in Canada. We aim to investigate the distribution and severity of both pathogens in Ontario, Canada. We will test 3,500 post metamorphic and adult Northern Leopard frogs (*Lithobates* (formerly *Rana*) *pipiens*) for the presence of infection. We will collect our samples annually, from 50 different sample sites, throughout the summer months of 2012-2015. Utilising these results, we hope to model the dynamics of both pathogens simultaneously. We are interested in evaluating how environmental heterogeneity, seclusion and disease-induced mortality alter a pathogen community. This provides us with a mechanism in which to study competitive dynamics on the scale of individuals, and their large-scale consequences.

17/04/2015 Session D4 - (Room 13) - Parasites - Geospatial Ecology I - Chair: L Rinaldi 9:45 AM - 10:00

AM (15 mins)

Rabbits in space

Joanne Lello[1], Vaughan I. P.[1] & Boag B[2].

[1.]*Cardiff University, School of Biosciences;* [2.]*Hutton Institute*

We examine the role of geographic proximity, and connectivity of rabbit warrens on the prevalence and mean intensity of a range of rabbit parasites. We find that the proximity and connectivity are important predictors of both parasite measures but that the relationship is not always straightforward, varying between parasites in relation to factors such as rabbit age, sex and estimated relative density. We also ask whether the inclusion of such geographic information alters our previous findings regarding the network of helminth interspecific interactions observed in this host dataset.

17/04/2015 Session D4 - (Room 13) - Parasites - Geospatial Ecology I - Chair: L Rinaldi 10:00 AM - 10:15 AM (15 mins)

Genome-scale phylodynamics of an endemic zoonotic virus: canine rabies virus in Tanzania

Kirstyn Brunker, Katie Hampson, Denise Marston, Anthony Fooks, Daniel Horton, Roman Biek

Institute of Biodiversity, Animal Health and Comparative Medicine, University of Glasgow; The Boyd Orr Centre for Population and Ecosystem Health, University of Glasgow; Animal Health and Veterinary Laboratories, Weybridge, UK

Many of the pathogens perceived to pose the greatest risk to humans are viral zoonoses, accounting for a range of emerging and endemic infectious diseases. In order to determine a basis for their management and control it is important to understand the spatial structure of viral pathogens. Phylogeography is a useful tool to develop a quantitative understanding of the processes that give rise to spatial patterns and drive pathogen dynamics. Moreover, whole genome information is increasingly being used to offer more complete resolution to uncover these patterns but it is unclear how much resolution can be achieved and down to what scale. We use canine rabies virus, a rapidly evolving RNA virus, as a case study using a phylogeographic approach to uncover the landscape epidemiology of a viral zoonoses. Rabies is a globally distributed zoonotic disease that kills ~55,000 people every year: mostly children in Asia and Africa where the virus circulates endemically in domestic dogs. We know little about the dynamics of rabies virus in dogs, or the underlying mechanisms that allow the disease to persist. Hence, effective control is hindered by our limited understanding of the key drivers of viral transmission, particularly the role of humans and the effect of landscape heterogeneity. Using full genome data we resolve spatio-temporal patterns of endemic rabies virus in Tanzania and assess the scale of resolution afforded by full over partial genome data.
17/04/2015 Session D4 - (Room 13) - Parasites - Geospatial Ecology I - Chair: L Rinaldi 10:15 AM - 10:30 AM (15 mins)

Session E4 - (Room 14) - Parasites - Co-infections

Chair: Dr D Blake, Royal Veterinary College

Present and future control of co-infections with schistosomiasis and STH

Alan Fenwick,

SCI, Imperial College London

In 2015, the pharmaceutical company Merck KGaA have donated 105 million tablets of praziquantel through WHO for the treatment of schistosomiasis in school aged children in Africa. In 2016 and thereafter their donation will be 250 million tablets annually – enough to treat 100 million children. But this is not all – praziquantel is also purchased by Crown Agents (using DFID funding), by World Vision and by RTI (using USAID funding). This means that by 2016 praziquantel supply for the first time will not be the bottleneck to treating those who need treatment against schistosomiasis. Indeed supply might even exceed demand. Meanwhile the pharmaceutical companies GSK and Johnson and Johnson have committed to providing against country requests up to 400 million tablets of abendazole annually and 200 million tablets of mebendazole annually respectively. The challenge for the African countries Ministries of Health and Education and the NGO's which support them, is providing the logistical support to ensure that these donations are effectively and economically utilised. This presentation will summarise the current treatment achievements in Africa and speculate how the donated drugs can be best utilised to achieve the World Health Assembly targets of reaching elimination as a public health problem and then elimination of transmission.

17/04/2015 Session E4 - (Room 14) - Parasites - Co-infections - Chair: D Blake 9:00 AM - 9:30 AM (30 mins)

ParaDesign: towards an online tool to design surveys for monitoring mass drug administration programmes implemented to control soil-transmitted helminthiasis in public health

Bruno Levecke[1], Anderson R.M.[2], Berkvens D.[3], Charlier J.[1], Devleesschauwer B.[1,4], Speybroeck N.[4], Vercruysse J.[1], Van Aelst S.[5,6]

[1]Department of Virology, Parasitology and Immunology, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium [2]Department of Infectious Disease Epidemiology, Faculty of Medicine, Imperial College London, London, United Kingdom [3]Department of Biomedical Sciences, Institute of Tropical Medicine, Antwerp, Belgium [4]Institute of Health and Society (IRSS), Faculty of Public Health, Université catholique de Louvain, Brussels, Belgium [5]Department of Applied Mathematics, Computer Science and Statistics, Faculty of Sciences, Ghent University, Ghent, Belgium [6]Department of Mathematics, Faculty of Sciences, KU Leuven University, Leuven, Belgium

Roundworms (*Ascaris lumbricoides*), whipworms (*Trichuris trichiura*) and hookworms (*Ancylostoma duodenale* and *Necator americanus*) infect millions of children in sub-tropical and tropical countries, resulting in malnutrition, growth stunting, intellectual retardation, and cognitive deficits. To fight these

worms, large-scale deworming programmes are implemented in which anthelmintic drugs are administered. This world wide upscale of deworming programmes creates the need for a monitoring system that allows programme managers, policy-makers and donors of the drugs to assess whether the objectives are being met and, if necessary, to adjust the implemented strategy. Thus, it will be imperative to periodically assess worm infections by means of prevalence and infection intensity to determine whether the deworming programme progresses as anticipated. We developed a mathematical framework based on worm egg counts in stool allowing health-care decision makers to adapt their survey design according to both local worm epidemiology (level of aggregation and intensity of worm infections) and resources. To bridge the gap between this mathematical framework and the end-users we developed ParaDesign, an online interface that guides the user in designing an appropriate survey without the need of prior mathematical or statistical knowledge. At the meeting we will briefly outline the underlying mathematical framework. Subsequently, we will demonstrate selective features of the online tool. Finally, we will highlight features that will be covered by ParaDesign in the near future.

17/04/2015 Session E4 - (Room 14) - Parasites - Co-infections - Chair: D Blake 9:30 AM - 9:45 AM (15 mins)

Do geohelminth co-infections affect outcomes of treatment for *Trichuris trichuria*?

Mark Booth

Durham University School of Medicine, Pharmacy and Health University Boulevard Thornaby TS17 6BH

Geohelminth infections represent a significant threat to public health in countries of the tropics and sub-tropics. Mass Drug Administration programmes based on the principle of 'preventive chemotherapy' with broad-spectrum anthelmintics such as albendazole are widely used to reduce the burden of disease. It has been known for some time that albendazole, does not effectivley treat cases of *Trichuris trichiura*. The underlying factors have not been comprehensively described. One issue that may play a role is co-infections with other species that are susceptible to albendazole. In this analysis, data from 3 studies were re-analysed to assess the potential role of *Ascaris lumbricoides* - a parasite species often associated with *T. trichiura* - in the outcome of treatment for *T. trichiura*. The results indicate a consistent pattern of association between these two species of infections that correlate with the idea of predisposition to multi-species of infection and offers insights into future treatment protocols for *T. trichiura.*

17/04/2015 Session E4 - (Room 14) - Parasites - Co-infections - Chair: D Blake 9:45 AM - 10:00 AM (15 mins)

Age-distribution of soil-transmitted helminth infection after repeated annual school-based deworming: a community-wide cross sectional study in Western Kenya – (SP)

Rita Oliveira[1], Alice Easton[1], Stella Kepha[2&3], Jimmy H. Kihara[4], Sammy M. Njenga[4], Charles S. Mwandawiro[4], Poppy H. L. Lamberton[1], Simon Brooker[3], & Roy M. Anderson[1]

[1]Imperial College London, UK; [2]Makerere University, Kampala, Uganda; [3]London School of Hygiene &

Tropical Medicine, UK; [4]Kenya Medical Research Institute, Nairobi, Kenya

School-age children generally carry the highest infection burden of two of the most prevalent soil-transmitted helminths (STH), *Ascaris lumbricoides* and *Trichuris trichiura*, in endemic communities. However, preschool-age children and adults are also affected, in particular adults in hookworm endemic communities, and may need to be targeted in order to successfully control transmission of infection in the community. This study aimed to determine whether a school-based deworming (SBD) strategy alone can effectively control STH infections in communities with low to moderate transmission of STH infection and past treatment exposure. Over 3000 individuals, aged 2 to 88 years, were recruited in Bungoma, Western Kenya, where SBD is on-going since 2012. Stool samples were collected before and three months following community-wide albendazole treatment, and analysed using Kato-Katz thick smears. Prevalence of *A. lumbricoides* and hookworm across the four villages was 7.3% and 6.2%, respectively, at study baseline; at follow-up, prevalences were 2.6% and 2.0% respectively. The age-distribution of infection in the community showed a positive effect of SBD on *A. lumbricoides* infection, with school-age children having lower prevalence and intensity levels than preschool-age children. Hookworm infection was more prevalent in adults, and additional community-based deworming was effective in reducing prevalence and intensity of hookworm in the whole community. Overall, this study has identified the benefits of SBD treatment, but also the need to target preschool-age children and adults in order to effectively reduce transmission of STH infection in the community and thus maximise the benefits from the recent scale-up of anthelminthic drug donations.

17/04/2015 Session E4 - (Room 14) - Parasites - Co-infections - Chair: D Blake 10:00 AM - 10:15 AM (15 mins)

Global research on eight neglected zoonoses 1950 to 2014

Mahmoud Abo-Shehada

Faculty of Epidemiology and Population Health, London School of Hygiene & Tropical Medicine, Keppel Street, London, WC1E 7HT, England.

Systematic search for research output produced globally for the periods 1950-1994, 1995-2004, and 2005-2014 on eight neglected zoonotic diseases (NZDs), namely; leishmaniasis, rabies, brucellosis, hydatid, anthrax, cysticercosis, zoonotic trypanosomiasis and tuberculosis was carried out using the Web of Science of Thomson Scientific's Essential Science Indicators database. Global research output on the NZDs were compared and ranked based on the number of articles and Hirsh-Index for the 3 studied periods. During the period 1950 to 2014, 181029 research articles were produced, on the eight NZDs, of which 32% were published between 1950-1994, 24% during 1995-2004 and 44% during the last decade. During the periods 1950-1994, 1995-2004 and 2005-2014, the proportions of research papers numbers produced on the eight NZDs were; leishmaniasis 28%, 30% and 45%, rabies 27%, 25% and 19%, brucellosis 21%, 18% and 13%, hydatid 15%, 13% and 8%, anthrax 3%, 7% and 12%, cysticercosis 6%, 7% and 3%, respectively. The share of research output on zoonotic trypanosomiasis and tuberculosis was less than 1% for the 3 periods. For periods 1995- 2004 and 2005-2014, the Hirsh-Indices of the eight diseases were; leishmainasis 132 and >100, rabies 127 and 55, anthrax 112 and 90, brucellosis 100 and 70, hydatid 68 and 38, cysticercosis 65 and 43, zoonotic trypanosomiasis 11 and 20 and tuberculosis 2 and 4 respectively. During the last decade, improvement in research output was evident in 8 NZDS with higher share (57%) for leishmaniasis and Anthrax.

17/04/2015 Session E4 - (Room 14) - Parasites - Co-infections - Chair: D Blake 10:15 AM - 10:30 AM (15 mins)

Session A5 - (Room 11A) - Malaria - Drugs II

Chair: Prof G Biagini, Liverpool School of Tropical Medicine

DDD107498: A novel preclinical candidate for malaria

Beatriz Baragaña[1], Irene Hallyburton[1], Marcus C. S. Lee[2], Neil R. Norcross[1], Raffaella Grimaldi[1], Thomas D. Otto[3], William R. Proto[3], Andrew M. Blagborough[4], Stephan Meister[5], Grennady Wirjanata[6], Andrea Ruecker[4], Leanna M. Upton[4], Tara S. Abraham[2], Mariana J. Almeida[2], Anupam Pradhan[7], Achim Porzelle[1], María Santos Martínez[8], Judith M. Bolscher[9], Andrew Woodland[1], Suzanne Norval[1], Fabio Zuccotto[1], John Thomas[1], Frederick Simeons[1], Laste Stojanovski[1], Maria Osuna-Cabello[1], Paddy M. Brock[4], Tom S. Churcher[4], Katarzyna A. Sala[4], Sara Zakutansky[4], María Belén Jiménez-Díaz[8], Laura Maria Sanz[8], Jennifer Riley[1], Rajshekhar Basak[2], Michael Campbell[10], Vicky M. Avery[11], Robert W Sauerwein[9], Koen J. Dechering[9], Rintis Noviyanti[12], Brice Campo[13], Julie A. Frearson[1], Iñigo Angulo-Barturen[8], Santiago Ferrer-Bazaga[8], Francisco Javier Gamo[8], Paul G. Wyatt[1], Didier Leroy[13], Peter Siegl[13], Michael J. Delves[4], Dennis E. Kyle[7], Sergio Wittlin[14], Jutta Marfurt[6], Ric N. Price[6,15], Robert E. Sinden[4], Elizabeth Winzeler[5], Susan A. Charman[10], Lidiya Bebrevska[12], David W. Gray[1], Simon Campbell[12], Alan H. Fairlamb[1], Paul Willis[12], Julian C. Rayner[3], David A. Fidock[2,16], Kevin D. Read[1], Ian H. Gilbert[1].

[1.] Drug Discovery Unit, Division of Biological Chemistry and Drug Discovery, College of Life Sciences, University of Dundee, Dundee, DD1 5EH, UK. [2.] Department of Microbiology and Immunology, Columbia University College of Physicians and Surgeons, New York, NY 10032, USA. [3.] Malaria Programme, Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Cambridge CB10 1SA, UK. [4.] Cell and Molecular Biology, Department of Life Sciences, Imperial College, London, SW7 2AZ, UK. [5.] University of California, San Diego, School of Medicine, 9500 Gilman Drive 0760, La Jolla, CA 92093, USA. [6.] Global Health and Tropical Medicine Division, Menzies School of Health Research, Charles Darwin University, Darwin, Northern Territory, Australia. [7.] Department of Global Health, College of Public Health. University of South Florida, 3720 Spectrum Blvd, Suite 304, Tampa, FL 33612, USA. [8.] GlaxoSmithKline, Tres Cantos Medicines Development Campus-Diseases of the Developing World, Severo Ochoa 2, Tres Cantos 28760, Madrid, Spain. [9.] TropIQ Health Sciences, Geert Grooteplein 28, Huispost 268, 6525 GA Nijmegen, The Netherlands. [10.] Centre for Drug Candidate Optimisation, Monash Institute of Pharmaceutical Sciences, 391 Royal Parade, Parkville, Victoria 3052 Australia. [11.] Eskitis Institute, Brisbane Innovation Park, Nathan Campus, Griffith University, QLD, Australia 4111 [12.] Eijkman Institute for Molecular Biology, Jakarta, Indonesia. [13.] Medicines for Malaria Venture, PO Box 1826, 20 route de Pre-Bois, 1215 Geneva 15, Switzerland. [14.] Swiss Tropical and Public Health Institute, Socinstrasse 57, 4051 Basel, Switzerland. [15.] Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford, UK [16.] Division of Infectious Diseases, Department of Medicine, Columbia University College of Physicians and Surgeons, New York, NY 10032, USA

Malaria is a devastating disease, leading to several hundred million clinical cases and over 600,000 deaths each year. There is an urgent need to develop new drugs to treat this disease, to counter resistance to current drugs and to expand the range of clinical indications which can be tackled. This

includes the need for single-dose treatment, transmission blocking, chemoprevention and treatment for relapsing malaria. Here we report the discovery and development of a potential new antimalarial agent. The starting point for this project was a phenotypic screen carried out against *Plasmodium falciparum* at the University of Dundee, UK. Several series were identified and one of these was optimized to a compound which fulfilled the Medicines for Malaria Venture criteria for a late lead compound. This compound was extensively profiled in a large number of assays and has now been progressed into preclinical development with the aim of entering human clinical trials. This pre-clinical candidate shows promise as a possible single-dose treatment in combination with another antimalarial and demonstrates both transmission blocking and chemoprevention potential.

17/04/2015 Session A5 - (Room 11A) - Malaria - Drugs II - Chair: G Biagini 11:00 AM - 11:15 AM (15 mins)

Malaria transmission blocking drugs: new assays and new hits.

Sarah D'Alessandro[1], Nicoletta Basilico[2], Silvia Parapini[1], Yolanda Corbett[1], Paola Misiano[1], Grazia Camarda[3,4], Giulia Siciliano[4], Francesco Silvestrini[4], Elisa Michelini[5], Luca Cevenini[5], Aldo Roda[5], Sandra Gemma[6], Giuseppe Campiani[6], Pietro Alano[4], Donatella Taramelli[1]

[1]Dipartimento di Scienze Farmacologiche e Biomolecolari, Università di Milano, Italy; [2]Dipartimento di Scienze Biomediche, Chirurgiche ed Odontoiatriche, Università di Milano, Milano, Italy; [3]Department of Parasitology, LSTM, Liverpool, UK; [4]Dipartimento di Malattie Infettive, Parassitarie, Immunomediate, Istituto Superiore di Sanità, Roma, Italy; [5]Dipartimento di Chimica "G. Ciamician", Università di Bologna, Bologna, Italy; [6] Dipartimento di Biotecnologie, Chimica e Farmacia -Universita' degli Studi di Siena, Italy

Drugs able to inhibit *P.falciparum* gametocytes (GCT) and thus malaria transmission are strongly needed to achieve malaria elimination/eradication. Two new methods to measure GCT drug sensitivity were recently developed by our group. The pLDH spectrophotometric assay is fast, simple, cheap and can be applied to field isolates since transgenesis is not needed (D'Alessandro et al 2013, JAC,68,2048). The luminescent LUC assay is based on the use of a 3D7 *P. falciparum* line which expresses a novel luciferase enzyme (LUC1-G) under the control of a GCT specific promoter (Cevenini L et al ,2014, Anal Chem.86:8814).The LUC assay is rapid, simple and with higher signal to background ratio. The pLDH and LUC assay have been successfully applied to screen the 400 compounds of the MMV- Malaria Box. The primary screening at the dose of 3.7 µM was performed with the pLDH assay: only 7 compounds inhibited GCT viability by more than 50% already after 72h incubation; whereas 29 required a longer time (72+72 h) to reach the same effect. These 36 compounds were then assayed in dose-response experiments to determine the IC50 using both the pLDH and the LUC assays: the results were quite comparable and indicated that 7 compounds had an IC50 lower than 1 µM. By comparing the results obtained by different groups, two of these active hits were chosen for further studies. Chemical modification were introduced to improve efficacy and drugability. The preliminary results will be discussed. Acknowledges: MMV for the malaria box and BMGF for funding.

17/04/2015 Session A5 - (Room 11A) - Malaria - Drugs II - Chair: G Biagini 11:15 AM - 11:30 AM (15 mins)

Assessment of the haematological profile of children with malaria parasitaemia treated with three different artemisinin-based combination therapies

Uchechukwu Chukwuocha, Onyirioha Misherk Chimezie, Nwakwuo Geoffrey Chima, Dozie Ikechukwu Nosike Simplicius

Department of Public Health Technology, School of Health Technology, Federal University of Technology, Owerri, Imo State, Nigeria.

This study was undertaken to assess the haematological profile of children with malaria, treated with three different Antemisinin-based Combination Therapies (ACTs) in South Eastern Nigeria. Using a multistage sampling technique, blood samples were collected from 105 randomly selected malaria positive primary school children aged 6-13 years. Pre and post assessment of their haematological profiles were respectively done on intervention of three different ACTs. Result shows a strong difference (0.4g/dl±0.31) in haemoglobin levels with the Artesunnate/Amodiaquine (AA) (t=7.30, p=0.00). DihydroArtemisinin/Piperaquine (DP) and Arthemether/Lumefantrine (AL) showed haemoglobin (t=4.49, p=0.000) with mean difference (0.6g/dl±0.85) and (t=6.09, p=0.000) with mean difference (0.8g/dl±0.78) respectively. The mean difference of WBC was found to be negative but significant with AA (-1.07±3.12) at 95%CI (-2.14, 0.00) and AL (-0.36±0.28) at 95%CI (-0.45, -0.26) interventions respectively. Significant mean difference of neutrophils was only found for the DP interventions (4.54±8.30) at 95% CI (1.69, 7.40) while lymphocytes indicated a significant mean difference between the pre/post-interventions (-3.60±9.34) at 95%CI (-6.81, -0.39) with DP only. Even though our result does not indicate any life threatening events, it may have some useful implications for investigating future non-infectious diseases of blood origin. Further studies to determine the extent of involvement of malaria parasite and drug interactions in haematological alterations vis-a-vis its implications for non-communicable disease is important.

17/04/2015 Session A5 - (Room 11A) - Malaria - Drugs II - Chair: G Biagini 11:30 AM - 11:45 AM (15 mins)

Screening the malaria box using a rapid in vitro Bioluminescence-Rate-of-Kill (BRoK) assay – (SP)

Imran Ullah, Raman Sharma, Giancarlo Biagini and Paul Horrocks

Institute for Science and Technology in Medicine, Keele University, Staffordshire ST5 5BG,UK Research Centre for Drugs and Diagnostics, Liverpool School of Tropical Medicine, Liverpool L3 5QA, UK

Massive screens of chemical libraries for antimalarial activity have identified thousands of compounds that exhibit sub-micromolar potency against the blood stage of the malarial parasite *Plasmodium falciparum*. Triaging these compounds to establish priorities to take forward for development requires additional information regarding their activity. Key amongst their pharmacodynamics (PD) properties is the rate-of kill (RoK) – with a rapid RoK specifically identified as a key requirement for a Single Exposure Radical Cure and Prophylaxis (SERCaP) product. Compounds that kill quickly (fast RoK) rapidly reduce parasite burden to ameliorate the morbidity and mortality of disease. With the overall aim to accelerate drug screening by validating a rapid RoK, we describe here the validation of a novel, rapid (6hr) and a scalable BRoK assay that demonstrates a good correlation with in vitro recrudescence-based RoK data and available in vivo clinical findings. Further, BRoK data for the 400 compounds in the Malaria Box is

presented here – highlighting leads with initial RoK as good as, and better, than artemisinin. The BRoK assay rapidly provides a second key aspect of the potency of drug development leads that can be exploited in future medicinal chemistry projects – a profound advantage to work that previously only considered the potency of a drug based on its 50% inhibitory concentration.

17/04/2015 Session A5 - (Room 11A) - Malaria - Drugs II - Chair: G Biagini 11:45 AM - 12:00 PM (15 mins)

Multiple approaches towards understanding artemisinin pharmacodynamics – (SP)

Matthew Phanchana[1], Hanafy Ismail[2], Simon Wagstaff[1], Mathirut Mungthin[3], Giancarlo A Biagini[1], and Stephen A Ward[1]

[1]Parasitology Department, and [2]Vector Biology, Liverpool School of Tropical Medicine, Liverpool, UK
[3]Department of Parasitology, Phramongkutklao College of Medicine, Bangkok, Thailand

Artemisinins is a group of antimalarial drugs and also the last effective drug against uncomplicated malaria. Increasing of artemisinin resistance reports raises concern in the need of new class of antimalarial. Although artemisinins have been in use for many years , their mechanism of action and resistance are still uncertain. Recent studies reveal that treatment failure and delayed parasite clearance half-life are associated with mutations in K-13 propeller gene, which is considered a useful artemisinin resistance marker. In the present study we have used a multiple approaches including (i) targeted proteomics with artemisinin clickable probes, (ii) artemisinin (activation) turnover, and (iii) time-dependent parasite phenotyping, to investigate artemisinin mechanism of action and resistance. Parasites with clinical fast and delayed parasite clearance half-life were used in the study. Data will be discussed in the context of current hypotheses of mechanism of action and resistance.

17/04/2015 Session A5 - (Room 11A) - Malaria - Drugs II - Chair: G Biagini 12:00 PM - 12:15 PM (15 mins)

Session B5 - (Room 11B) - NTDs - Molecular Biology II

Chair: DR A Acosta-Serrano, Liverpool School of Tropical Medicine

Proteomic analysis of trypanosome-infected tsetse saliva unravels a novel family of invariable GPI-anchored surface glycoproteins from *Trypanosoma brucei* – (SP)

Aitor Casas-Sanchez[1], Boulanger, Martin J.[2] & Acosta-Serrano, Alvaro[3]

[1.]Liverpool School of Tropical Medicine. Pembroke Place, L3 5QA, Liverpool, United Kingdom. [2.]University of Victoria, Dept. Biochemistry & Microbiology, V8W 2Y2, Victoria BC, Canada.

Development of *Trypanosoma brucei* within the tsetse vector is accompanied by the expression of stage-specific families of glycosylphosphatidyl inositol (GPI)-anchored surface glycoproteins. While (midgut) procyclics sequentially express GPEET- and EP-procyclins, brucei alanine-rich proteins (BARP) and variant surface glycoproteins (VSG) are so far the only surface markers described for the epimastigote and metacyclic stages, respectively. In a recent proteomic analysis of saliva from T.

brucei-infected tsetse flies (Perally S. et al., in preparation), we found that it is particularly enriched with several trypanosome surface molecules, including the BARP, VSG and a novel family of hypothetical GPI-anchored surface glycoproteins previously designated as Clade 'iv'. Clade 'iv' belongs to the large family (Fam50) of trypanosome surface glycoproteins that includes BARP and T. congolense glutamic acid/alanine-rich protein (GARP). Clade 'iv' proteins are encoded by a small family of genes, which are exclusively expressed in the metacyclic stage and have products with 90% identity. In order to gain insights into the function of Clade 'iv' glycoproteins, we expressed one of the paralogs (Tb427.7.360) in Sf9 cells and determined its crystal structure at 1.9 Å resolution, which overall shape highly resembles that of VSG and GARP despite their high degree of sequence divergence. We postulate that one function of Clade 'iv' proteins may be to maintain the tight intramolecular packing with VSG molecules on the metacyclic surface, which may be essential to transition into the vertebrate host. We are currently determining the essentiality and exact localisation of Clade 'iv' proteins.

17/04/2015 Session B5 - (Room 11B) - NTDs - Molecular Biology II - Chair: A Acosta-Serrano 11:00 AM - 11:15 AM (15 mins)

Development of an in silico pipeline for prioritizing novel *Schistosoma mansoni* drug targets. – (SP)

Kezia Whatley[1], Umar Niazi[2], Narcis Fernandez-Fuentes[3], Karl Hoffmann[1]

[1]Edward Llywd Building Penglais Campus Aberystwyth University Dyfed SY23 3DA; [2.]Research Associate National Heart & Lung Institute (NHLI) Imperial College London, UK. [3.]IBERS Penglais Campus Aberystwyth University Dyfed SY23 3DA

Praziquantel (PZQ) is a key pharmaceutical used to treat schistosomiasis, a NTD affecting ~249 million people, across 78 countries. Despite PZQ's high efficacy against all *Schistosoma* sp. and durability in mass drug administration (MDA), concerns over resistance shadow the sustainability of MDA with PZQ alone. Therefore, a novel and rapid chemotherapeutic strategy is needed for identifying next generation anti-schistosomals. To shortlist "druggable" S*. mansoni* proteins (Smps), an in silico approach was developed, utilising freely accessible databases including CHEMBL and DrugBank- (both containing proteins with associated drug-like compounds), Protein Data Base (PDB) and GeneDB. We first used PSI-BLAST (sequence identity of >40%, alignment of >70%, and an E-value cut-off of 0.0001) to identify 1999 *S. mansoni* proteome orthologues that were present in either CHEMBL or DrugBank databases. Transcriptome data was then used to select 1678 of these 1999 Smps expressed in both schistosomula and adult worms. Finally, the 1678 Smps were filtered for targets (same criteria as the initial PSI-BLAST search) demonstrating sequence similarity in both Schistosoma japonicum and PDB databases. A final list of 467 Smp drug targets was produced, each having an orthologue in CHEMBL, DrugBank, PDB and the S. japonicum genome assembly. This in silico workflow has isolated 467 anti-schistosomal targets and their respective drug-like compounds, in an efficient and low-cost manner. These drug-like compounds are now being further scrutinised as starting points for high-throughput screens of schistosomula phenotype.

17/04/2015 Session B5 - (Room 11B) - NTDs - Molecular Biology II - Chair: A Acosta-Serrano 11:15 AM - 11:30 AM (15 mins)

Schistosoma mansoni excretes/secretes extracellular vesicles containing definable populations of small non-coding RNAs (sncRNA) and proteins - (SP)

Fanny Nowacki[1], Martin T. Swain[1], Alastair Ivens[2], Amy H. Buck[2], Oleg I. Klychnikov[3], Paul J. Hensbergen[3], Cornelis H. Hokke[3] and Karl F. Hoffmann[1]

[1] Institute of Biological, Environmental and Rural Sciences, Aberystwyth University; [2]Centre for Immunity, Infection and Evolution, Ashworth Laboratories, University of Edinburgh; [3]Department of Parasitology, Leiden University Medical Center P.O.Box 9600, 2300 RC Leiden, The Netherlands

Upon skin penetration, schistosomes release excretory/secretory (E/S) products in a directed attempt to simultaneously manipulate the host extracellular matrix, to modulate host defensive barriers and to protect itself from oxidative stress. Collectively, these E/S-driven biological processes ultimately enable a large proportion of infectious parasites to successfully continue their complex migration throughout the human host, develop into blood-dwelling dioecious adults and establish an infection that can last for years. As these E/S products need to operate over short distances in the presence of harsh environmental stresses within tissue/blood, their packaging into protective transferable units would be advantageous. An evolutionarily conserved packaging system that, as of yet, has not been investigated in this aspect of schistosome biology is the role coordinated by extracellular vesicles (EVs). Here, utilizing a combination of biophysical processing, Illumina next generation sequencing (NGS) of small noncoding RNA (sncRNA) libraries and MS/MS proteomics, we characterize the biology of schistosomula EVs. Our findings demonstrate the presence of diverse classes of sncRNAs within as well as outside EVs. Among these sncRNAs, we describe 35 known and 172 novel miRNAs as well as tRNA derived fragments . Along with these sncRNAs, we additionally identify 108 proteins reproducibly found in schistosomula EVs including SmTSP2, SmCSS-1 and Sm29. These poly-omics findings open the door for characterising the host modulating potential of these important intercellular communicators

17/04/2015 Session B5 - (Room 11B) - NTDs - Molecular Biology II - Chair: A Acosta-Serrano 11:30 AM - 11:45 AM (15 mins)

G protein coupled receptors in the _Fasciola hepatica_ genome - new opportunities for flukicide discovery?

Paul McVeigh[1], Nikki Marks[1], Angela Mousley[1], Brenda Bondesen[2], Jane Hodgkinson[3], Steve Paterson[4], Aaron Maule[1]

[1]Institute of Global Food Security, School of Biological Sciences, Queen's University Belfast, UK; [2]Merial Limited, 3239 Satellite Blvd., Duluth, GA 30096, USA; [3]Department of Infection Biology, Institute of Infection and Global Health, University of Liverpool, UK; [4]Department of Evolution, Ecology and Behaviour, Institute of Integrative Biology, University of Liverpool, UK

G protein coupled receptors (GPCRs) are recognised as effective drug targets. In helminths, GPCRs are responsible for signalling by both classical and peptidergic neurotransmitters, and are proposed as targets for new anthelmintics. Most flatworm GPCR data are derived from *Schistosoma* spp. blood fluke, while GPCRs have also been mined from cestode and planarian genomes. Several GPCRs have also been deorphanised, primarily in schistosomes. No GPCRs have yet been described in the liver fluke *Fasciola*

hepatica. This study employs class-specific Hidden Markov Models (HMMs) to annotate at least 81 GPCRs from a draft *F. hepatica* genome. These comprise frizzled-, glutamate-, rhodopsin-, and secretin-like sequences; notably, adhesion-like GPCRs appear absent. Homology analyses divide the rhodopsin family into 15 aminergic GPCRs (including putative adrenergic, cholinergic, dopaminergic and serotonergic receptors), 15 peptidergic GPCRs (including receptors for allatostatin-, angiotensin-, capa-, neuropeptide F/Y-, and tachykinin-like peptides), and 29 orphan receptors including putative representatives of the flatworm-specific PROF1 family, previously described in schistosomes, cestodes and planaria. Notably, the Fasciola PROF1 complement appears contracted relative to schistosomes. Our dataset also includes 11 putative flatworm-specific receptors without homologues in other genera. These liver fluke GPCRs represent a source of druggable targets for discovery screens, and will also contribute to the functional genomic analysis of fluke neuromuscular function. We are currently engaged in efforts to map the temporal and spatial expression patterns of these receptors, alongside functional/validation experiments using gene-silencing methods. Funded by BBSRC grant BB/K009583/1.

17/04/2015 Session B5 - (Room 11B) - NTDs - Molecular Biology II - Chair: A Acosta-Serrano 11:45 AM - 12:00 PM (15 mins)

Circulating microRNAs represent species-specific biomarkers of *Dirofilaria immitis* infection

Anna O'Connor[1], Erin M. McCammick[1], Erica Burkman[2], Andy Moorhead[2], Timothy G. Geary[3], Brenda Bondesen[4], Angela Mousley[1], Nikki J. Marks[1], Aaron G. Maule[1], Paul McVeigh[1]

[1.]Parasitology, Institute for Global Food Security, School of Biological Sciences, Queen's University Belfast, UK; [2]Filariasis Reagent Resource Centre, University of Georgia, USA; [3.]Institute of Parasitology, McGill University, Quebec, Canada; 4Merial Ltd, Duluth, GA, USA.

The mosquito-borne filarial nematode *Dirofilaria immitis* is an important parasite of domestic dogs and wild canids. Heartworm infections of companion animals are endemic in regions of North America and Southern Europe, with potential to be zoonotic. Available diagnostics permit the detection of adult female-derived antigens, while microfilariae, can be detected microscopically: a method for the detection of pre-patent heartworm infections is not available. Here, we focus on host- and parasite-derived micro (mi)RNAs as markers of heartworm infection. In addition to their intracellular roles in transcriptional regulation, extracellular miRNAs have been demonstrated in blood and other bio-fluids and they are validated biomarkers for several human diseases. This study aimed to establish if parasite-specific 'miRNA fingerprints' occur in sera from parasitized hosts. We found that: (1) D. immitis-derived miRNAs are exquisitely diagnostic of heartworm infection and can differentiate heartworm-infected sera from hosts carrying other filarial infections; (2) Host-derived miRNAs, possibly linked to parasite-induced tissue damage, are elevated in infected vs uninfected sera; and, (3) Small RNA sequencing demonstrates, for the first time, the presence of miRNAs in heartworm L3-derived exosomes. The relative abundances of individual miRNAs in these exosomes are similar to those of L3 tissue extracts, suggesting that miRNA loading into exosomes may not be a specific process as proposed by studies on exosomal miRNAs from other parasites. This work has direct applications in the development of helminth parasite diagnostics, and in developing understanding of the host-parasite interface. This work was supported by a Gates Foundation grant OPP1083083 to PM.

17/04/2015 Session B5 - (Room 11B) - NTDs - Molecular Biology II - Chair: A Acosta-Serrano 12:00 PM - 12:15 PM (15 mins)

Session C5 - (Room 11C) - Vectors - Zoonosis

Chair: Prof S Torr, Liverpool School of Tropical Medicine

Ticks are knocking at our door - changes in agriculture and density of ticks

Anna Bajer[1], Mohammed Alsarraf[1], Jerzy M. Behnke[2], Ewa J. Mierzejewska[1]

[1]Department of Parasitology, Institute of Zoology, Faculty of Biology, University of Warsaw, 1 Miecznikowa Street, 02-096, Warsaw, Poland. [2]School of Life Sciences, University Park, University of Nottingham, Nottingham NG7 2RD, UK

The effect of agricultural practices has been decreasing in many areas of Europe due to the widespread exodus of inhabitants from rural areas. The aim of the present study was to compare tick densities in different habitats (pasture, meadow, fallow land, post-fire areas) to assess the impact of different agricultural practices on tick densities in vicinities close to human habitation. Between September 2011 and June 2014, 3102 ticks were collected by dragging in Central Poland (Mazovia) and in Mazury lake district (Masuria). In each region, 3 study sites were selected. At each site, three neighboring habitats of surface area 150-600 m^2 were dragged each spring and autumn: permanently grazed cattle or horse pasture; cultivated meadow (grass cut and removed once or twice a year); fallow land (abandoned field/ meadow). Four post-fire areas were identified and dragged in Mazovia in spring and autumn, including in each case a 'control area' comprising intact unburned fallow land situated close to the burned areas. Tick densities were calculated per 100m^2 and compared by mutifactorial ANOVA. The highest tick abundance was recorded on the fallow lands, and the lowest– on the grazed pastures. Tick densities were up to 10x times higher on the control sites compared to neighboring post-fire areas. Conclusion. Some agricultural practices helped to reduce tick densities. Abandonment of agricultural lands has caused a significant increase in tick densities and the risk of tick-borne diseases for local human communities. The study was funded by the National Science Center (NCN), Poland, grant OPUS 2011/03/B/NZ8/02212

17/04/2015 Session C5 - (Room 11C) - Vectors - Zoonosis - Chair: S Torr 11:00 AM - 11:15 AM (15 mins)

What do tsetse and trypanosomes tell modellers about the elimination of human African trypanosomiasis?

Kat Rock[1], Steve Torr[3], Matt Keeling[1,2]

[1.]School of Life Sciences, University of Warwick, Gibbet Hill Road, Coventry, CV4 9HW, UK; [2.] Mathematics Institute, University of Warwick, Gibbet Hill Road, Coventry, CV4 9HW, UK; [3.]Department of Vector Biology, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, L3 5QA, UK

The WHO has declared Gambian human African trypanosomiasis (HAT) as a target for elimination as a public health problem by 2020, however it is possible that in some regions current intervention

strategies alone may not be sufficient to attain this goal. It is crucial that predictive models of HAT are developed and utilised to answer this policy question and to better assess the impact and effectiveness of alternative strategies. The implications of biological and parameter uncertainty within models for HAT are discussed in context of the WHO's 2020 targets and the likely implications for control. A new methodology shows how key features of tsetse life history and vector-parasite interaction can be incorporated in HAT modelling and we discuss the impact that including this type of higher-level biological detail has on model results. We stress the importance of predictive modelling as a tool for optimising and directing control measures to ensure efficient elimination of HAT.

17/04/2015 Session C5 - (Room 11C) - Vectors - Zoonosis - Chair: S Torr 11:15 AM - 11:30 AM (15 mins)

Recombinant salivary proteins as a host exposure marker to sand fly bites

Tatiana Košťálová[1], Michal Šíma[1], Tereza Leštinová[1], Petra Sumová[1], Iva Kolářová[1], Luigi Gradoni[2], Gad Baneth[3], Alon Warburg[4], Petr Volf[1]

[1] Department of Parasitology, Faculty of Science, Charles University in Prague, Czech Republic; [2] MIPI Department, Istituto Superiore di Sanità, Rome, Italy; [3] School of Veterinary Medicine, Hebrew University, Israel; [4] Department of Parasitology, Hadassah Medical School, The Hebrew University of Jerusalem, Israel.

During blood feeding, sand flies deposit into the host skin immunogenic salivary proteins which elicit a specific antibody response. The anti-saliva IgG, measured by ELISA, could be used as markers of host exposure to sand flies. The use of whole salivary glands has several limitations and therefore the recombinant salivary proteins have been produced and compared with whole salivary gland lysates by ELISA. In the Mediterranean area, dogs serve as the main reservoir host of *Leishmania infantum*, the causative agent of zoonotic visceral leishmaniasis (VL). In East Africa, the role of animals in the epidemiology of VL caused by *L. donovani* is not clear. In both areas, however, the disease is transmitted by sand flies of the subgenus Larroussius; *Phlebotomus perniciosus* and *P. orientalis*, respectively. Recombinant yellow-related protein of *P. perniciosus* was found as the best antigen using canine sera collected in an area endemic for VL in Italy. For *P. orientalis*, the best correlations of whole salivary lysate – recombinant proteins were achieved with yellow-related protein, ParSP25 and apyrase tested on domestic animal sera (dogs, sheep and goats) from Ethiopia. In conclusion, these results suggest that recombinant sand fly salivary proteins represent a valid alternative to whole salivary lysates and could be used in large-scale serological studies. This novel method seems to be a practical and economically-sound tool to detect host exposure to sand flies and to estimate the risk of *Leishmania* infection.

17/04/2015 Session C5 - (Room 11C) - Vectors - Zoonosis - Chair: S Torr 11:30 AM - 11:45 AM (15 mins)

Development of a xenomonitoring tool to monitor sleeping sickness – (SP)

Lucas. J. Cunningham, J. K. Lingley, E. R. Adams, L. R. Haines and S. J. Torr

Liverpool School of Tropical Medicine

Loop-mediated isothermal amplification (LoopAMP) kits have been designed for the detection of human pathogenic strains of trypanosomes (sub-species of *Trypanosoma brucei*). We investigated the possibility of using LoopAMP for detecting T. brucei infection in tsetse (*Glossina*) as a tool for xenomonitoring. We tested the efficacy of LAMP kits on colony-reared tsetse (*Glossina morsitans* morsitans) that were either fed or 'spiked' with trypanosomes. Heat killed and live parasites were fed to flies to determine how well the kits could detect *Trypanosoma brucei* s.l. DNA, in mono and mixed infections with non-human pathogenic strains (*T. congolense*). We assessed detection of T. brucei at a range of DNA concentrations to determine the limit of detection and the feasibility of detecting infected flies in pooled samples of infected and uninfected tsetse. Results showed that trypanosome DNA starts to degrade in the fly after 48 h, but can be detected in some flies after six days. LAMP was able to identify infected flies in mixed infections; there were no false positives due to the presence of T. congolense. LoopAMP kits were able to detect trypanosomes at concentrations as low as 1 trypanosome per mL. Field friendly DNA extractions were investigated resulting in a greatly simplified version of the current lab method. Using this method it was possible to detect 1 infected midgut when pooled with 19 un-infected midguts. LoopAMP offers the prospect of being a high throughput and highly sensitive xenomonitoring tool. The next step is to carry out field trials of the methods to test their practicability.

17/04/2015 Session C5 - (Room 11C) - Vectors - Zoonesis - Chair: S Torr 11:45 AM - 12:00 PM (15 mins)

Admixture in humans of two divergent *Plasmodium knowlesi* populations associated with different macaque host species – (SP)

Paul CS Divis[1,2], Balbir Singh[2], Fread Anderios[3], Shamilah Hisam[4], Asmad Matusop[2,5], Clemens H Kocken[6], Samuel A Assefa[1], Craig W Duffy[1], David J Conway[1,2]

[1] Pathogen Molecular Biology Department, London School of Hygiene and Tropical Medicine, Keppel St, London WC1E 7HT, United Kingdom, [2] Malaria Research Centre, Faculty of Medicine and Health Sciences, University Malaysia Sarawak, Kuching, Sarawak, Malaysia, [3] Sabah State Public Health Laboratory, Kota Kinabalu, Sabah, Malaysia, [4] Institute for Medical Research, Kuala Lumpur, Malaysia, [5] Sarawak State Health Department, Kuching, Sarawak, Malaysia, 6 Biomedical Primate Research Centre, Rijswijk, The Netherlands.

Human malaria parasite species were originally acquired from other primate hosts and subsequently became endemic, then spread throughout large parts of the world. A major zoonosis is now occurring with *Plasmodium knowlesi* from macaques in Southeast Asia, with a recent acceleration in numbers of reported cases particularly in Malaysia. To investigate the parasite population genetics, we developed

sensitive and species-specific microsatellite genotyping protocols and applied these to analysis of samples from 10 sites covering a range of >1,600 km within which most cases have occurred. Genotypic analyses of 599 P. knowlesi infections (552 in humans and 47 in wild macaques) at 10 highly polymorphic loci provide radical new insights on the emergence. Parasites from sympatric long-tailed macaques (*Macaca fascicularis*) and pig-tailed macaques (*M. nemestrina*) were very highly differentiated (FST = 0.22, and K-means clustering confirmed two host-associated subpopulations). Approximately two thirds of human *P. knowlesi* infections were of the long- tailed macaque type (Cluster 1), and one third were of the pig-tailed-macaque type (Cluster 2), with relative proportions varying across the different sites. Among the samples from humans, there was significant indication of genetic isolation by geographical distance overall and within Cluster 1 alone. Across the different sites, the level of multi-locus linkage disequilibrium correlated with the degree of local admixture of the two different clusters. Genotype profiles that had a relatively intermediate cluster assignment were seen in some human infections but not in macaque infections, which may indicate enhanced potential for novel parasite adaptation.

17/04/2015 Session C5 - (Room 11C) - Vectors - Zoonesis - Chair: S Torr 12:00 PM - 12:15 PM (15 mins)

Session D5 - (Room 13) - Parasites - Geospatial Ecology II-

Chair: Prof L Rinaldi, Univeristy of Naples

Sheep and *Fasciola hepatica* in Europe: the GLOWORM experience

Laura Rinaldi[1], Annibale Biggeri[2], Vincenzo Musella[3], Theo de Waal[4], Hubertus Hertzberg[5], Antonio Bosco[1], Giuseppe Cringoli[1]

[1]*Department of Veterinary Medicine and Animal Productions, University of Naples Federico II, Naples, Italy, CREMOPAR Campania Region, Naples, Italy;* [2]*Department of Statistics, Informatics and Applications "G. Parenti", University of Florence, Florence, Italy;* [3]*Department of Health Sciences, University "Magna Græcia" of Catanzaro, Catanzaro, Italy;* [4]*UCD School of Veterinary Medicine, University College Dublin, Dublin, Ireland;* [5]*Institute of Parasitology, Vetsuisse Faculty, University of Zurich, Zurich, Switzerland*

Fasciola hepatica infection challenges health, welfare and productivity of small ruminants throughout the world. In order to elucidate the current scenario in terms of prevalence and intensity of *F. hepatica* infection in sheep farms across Europe, a standardized cross-sectional survey was conducted in three pilot areas in Ireland, Switzerland and Italy, all part of the EU funded GLOWORM project. Two consecutive field surveys (in 2012 and 2013) were conducted in the three countries in the same period (August-October) in 361 sheep farms in total. Harmonized procedures (from farm to laboratory) based on pooled samples and FLOTAC were used. The georeferenced parasitological results were modelled (at the pilot area level) following a Bayesian geostatistical approach with correction for preferential sampling and accounting for climatic and environmental covariates. The observed *F. hepatica* prevalence rates did not differ between the two study years in any of the three pilot areas, but they did

vary between the countries showing high values in Ireland (61.6%) compared to Italy (7.9%) and Switzerland (4.0%). Spatial patterns of *F. hepatica* distribution were detected by the Bayesian geostatistical approach in Ireland with a high risk of infection in the south-western part of the pilot area. The latent factor analysis highlighted the importance of year-to-year variation of mean temperature, rainfall and seasonality within a country, while long-term trends of temperature and rainfall dominated between countries with respect to prevalence of infection.

17/04/2015 Session D5 - (Room 13) - Parasites - Geospatial Ecology II - Chair: L Rinaldi 11:00 AM - 11:15 AM (15 mins)

Geographical information systems to plan cross sectional surveys of helminths in sheep farms: an example from southern Italy – (SP)

Antonio Bosco[1], Laura Rinaldi[1], Vincenzo Musella[3], Maria Paola Maurelli[1], Giuseppe Prestera[2], Giuseppe Cringoli[1]

[1]Department of Veterinary Medicine and Animal Productions, University of Naples Federico II, Regional Center for Monitoring Parasitic Infections (CREMOPAR, Regione Campania), Naples, Italy; [2]Regional Association of Farmers, Basilicata; [3]Department of Health Science, University of Catanzaro Magna Graecia, Catanzaro, Italy Via della Veterinaria, 1 - 80137 Naples (Italy)

Sheep farming is an important reality for the rural economy of several regions. Concerning health aspects, particular those related to parasitic infections, the information on the distribution of helminths in sheep farms are usually scant. Therefore, the aim of the present study was to show how geographical information systems can be used as a valid tool to plan cross-sectional surveys and obtain up-to-date information on the presence and distribution of helminths in grazing sheep from the Basilicata region (southern Italy). A cross sectional coprological survey was conducted in 98 sheep farms and the FLOTAC dual technique on pooled samples was used to detect and count parasitic elements. The most frequent nematodes were gastrointestinal strongyles (91.8%), in particular *Haemonchus* (76.9%), *Trichostrongylus* (91.8%), *Teladorsagia* (88.8%), *Cooperia* (77.6%) and *Oesophagostomum* (72.5%). They were followed by lungworms (50.0%), *Trichuris* (39.8%), *Nematodirus* (24.5%), *Strongyloides* (4.1%) and *Skrjabinema* (2.0%). As regard to trematoda, the following prevalence were found: *Calicophoron daubneyi* (10.2%), *Dicrocoelium dendriticum* (61.2%) and *Fasciola hepatica* (1.0%). Cestoda of the genus *Moniezia* was found in the 35.7% of the farms. Interestingly, the spatial analysis showed clusters for *C. daubneyi* and *D.dendriticum*. The findings of the present study showed high level of helminth infections in sheep and some zoonotic parasites were also found reinforcing the One Health concept.

17/04/2015 Session D5 - (Room 13) - Parasites - Geospatial Ecology II - Chair: L Rinaldi 11:15 AM - 11:30 AM (15 mins)

A spatially explicit mathematical model of *Plasmodium knowlesi* malaria transmission in Southeast Asia – (SP)

Mary Parmiter[1], Heather M. Ferguson[2], Rowland R. Kao[1]

[1.] *Boyd Orr Centre, Institute of Biodiversity, Animal Health and Comparative Medicine, Jarrett Building, 464 Bearsden Road, University of Glasgow, G61 1QH* [2.] *Boyd Orr Centre, Institute of Biodiversity, Animal Health and Comparative Medicine, Graham Kerr Building Rm 302, Glasgow, G12 8QQ*

Plasmodium knowlesi, a simian malaria able to infect humans, is still thought to be primarily zoonotic and as such is spatially dependent on the forest which harbours the monkey reservoir. The vertebrate host populations (monkeys and humans near the forest edge) are typically small, numerous and fragmented, which challenges the classic assumption of large, homogenously mixed populations in the Ross MacDonald framework normally used to model malaria. Here we have developed a spatial adaptation of the Ross-MacDonald framework, to explicitly take into account the low host-density typical of the forest-fringe areas where transmission has been reported. We used this spatially explicit simulation model to assess the impact of limited local host density and spatial heterogeneity on transmission (as measured by secondary cases from an initial case), the effect of clustering of vertebrate host types on the likelihood of zoonotic spill-over and whether parameter sensitivity differs from the classic Ross MacDonald model. Local host density influences expected transmission, with the spatially explicit model resulting in lower numbers of secondary cases than predicted by the classic model; although at higher densities, the number of secondary cases becomes more similar to the classical Ross-MacDonald model, unless super-spreading is allowed to occur. In addition, clustering of hosts into small populations can affect the type of transmission event in terms of zoonotic spill-over. These results suggest that spatial heterogeneity may mean that less control effort should be required to interrupt transmission, which could facilitate local-scale control.

17/04/2015 Session D5 - (Room 13) - Parasites - Geospatial Ecology II - Chair: L Rinaldi 11:30 AM - 11:45 AM (15 mins)

Investigation of a new focus of cutaneous leishmaniasis in Ghana- (SP)

Godwin Kwakye-Nuako and Paul A Bates

Division of Biomedical and Life Sciences, Faculty of Health and Medicine, Lancaster University, LA1 4YG

Although known to occur in certain places in the West Africa sub-region, leishmaniasis has never been associated with Ghana until recent times. An outbreak of suspected cutaneous leishmaniasis (CL) was observed for the first time in the Ho District in the Volta Region of southeastern Ghana in 1999. Despite the presence of continued infections in the affected communities, the identity of the species responsible this disease focus has remained uncertain. Elsewhere in Africa cutaneous leishmaniasis is caused by *Leishmania aethiopica*, *L. major* or *L. tropica*. Aim: To identify the species of *Leishmania* responsible for leishmaniasis infections in the Volta region of Ghana. Methods: House to house case search was used, which identified 50 subjects with active cutaneous leishmaniasis. Dermal scraping samples on FTA cards

were analysed by PCR and PCR-RFLP. Parasites were isolated into culture from five aspirate samples, selected genes sequenced and phylogenetically analysed. Results and Conclusions: Leishmaniasis in the Volta region is confirmed. The parasite responsible is a new *Leishmania* species, which is responsible for the majority or even all of the CL cases in the Ho region of Ghana. Future: the vector and potential reservoir hosts remain unknown but are the subject of ongoing investigations.

17/04/2015 Session D5 - (Room 13) - Parasites - Geospatial Ecology II - Chair: L Rinaldi 11:45 AM - 12:00 PM (15 mins)

Cryptosporidiosis in Gaza Strip

Adnan I. Al-Hindi & Ahmed M. Tabash

Medical Laboratory Sciences Department, Faculty of Health Sciences, Islamic University of Gaza, P.O.Box 108, Gaza strip, Palestine

Objectives: The present study aimed to search for the presence of *Cryptosporidium* and determination the prevalence among patients in Gaza strip. Methods: Three hundred stool samples were collected from children less than five years old who attended Al- Nasser hospital and European hospital. The study was done in the period from June to August 2007 and January to March 2008. Stool samples were inspected by wet mount saline, concentration techniques by formalin after that acid-fast stain and ELISA. Results: The results of the present study indicated that the prevalence of Cryptosporidium was 18% by modified acid-fast stain and (16.7%) by ELISA where this parasite is uneasy to be detected by direct smear microscopy. It was found that 12-24 month age groups are more susceptible to infection by *Cryptosporidium* and significant relationship was found between age, sex and the infection. A strong association between C*ryptosporidium* and abdominal pain, nausea and vomiting were found with statistical significance p= (0.001). Significant association between children who live in camps and a village and cryptosporidiosis with statistical significance p= (0.03). There was a relationship between Cryptosporidium infection and the children who live close to open swage or have septic tank, statistical significance (p=.001). Conclusion: It was concluded that cryptosporidiosis still exist among children in Gaza strip and the prevalence of *Cryptosporidium* is high when compared to that in developed countries. It is recommended that cryptosporidiosis should be considered and attention should to be given to such neglected and missed diagnosed parasites.

17/04/2015 Session D5 - (Room 13) - Parasites - Geospatial Ecology II - Chair: L Rinaldi 12:00 PM - 12:15 PM (15 mins)

Session E5 - (Room 14) - Parasites - One Health & Zoonosis

Chair: Prof R Stothard, Liverpool School of Tropical Medicine

Travel medicine allows advances on the knowledge of neglected meat & fish borne parasitic diseases

Jean Dupouy-Camet

Paris Descartes University, Cochin Hospital, Paris, France

If the primary goal of travel medicine is to inform travelers about the risk of major preventable diseases, it is also a good observation point to monitor returning travelers who might have acquired meat or fish borne parasitosis, illustrating quite well the One Health concept and leading to advances in epidemiological knowledge and diagnostic methods. Toxoplasmosis is a travel hazard and severe cases, due to unusual genotypes are reported. Muscular sarcocystosis has recently emerged amongst travelers to Malaysia. The genotyping of a *Diphyllobothrium* isolate acquired after consumption of imported Pacific salmon carpaccio, led us to develop molecular techniques to identify *Taenia solium* DNA in CSF of patients suspected of cerebral cysticercosis. Imported cases of trichinellosis showed that the infection could be contracted either in Laos, or in Inuit countries. Following a lecture given in the Laotian capital, local physicians reported that they regularly saw patients with the pathognomonic symptoms, but were unable to identify the disease. Since then, several outbreaks were identified and Laos is now a hot spot for trichinellosis. Similarly, other cases acquired by French hunters or sailors returning from Northern Canada indicate that trichinellosis is still a concern for Inuit populations. The emergence of unusual cases of meat or fish borne parasitic diseases should be urgently reported via different forms of media (ProMed mail, Eurosurveillance…). The Parasitic Disease Quick Response Committee of the European Federation of Parasitologists can also be alerted as its primary aim is to respond to any emerging parasitic problem in Europe.

17/04/2015 Session E5 - (Room 14) - Parasites - One Health & Zoonosis - Chair: R Stothard 11:00 AM - 11:30 AM (30 mins)

Understanding the mechanisms of a zoonotic reservoir: leptospire infection in *Rattus norvegicus* in urban slums Brazil – (SP)

Amanda Minter[1], Mike Begon[1], Jamie Childs[2], Federico Costa[3], Peter Diggle[4], Albert Ko[2].

[1.] University of Liverpool, [2.] Yale University, [3.] Fundação Oswaldo Cruz, [4.] Lancaster University.

In urban slums, residents often live in close proximity to reservoirs of zoonotic pathogens. The recent population increase in Salvador, a coastal city in North East Brazil led to the creation of slums, which are overcrowded and lack basic sanitation. Leptospirosis is a zoonosis that humans can contract via contact with animal reservoirs directly or with water contaminated with their urine. The Norway rat (*Rattus norvegicus*) is asymptomatic and can transmit the infection for the entirety of its life. There is biological evidence for potentially three different transmission routes of leptospire infection occurring in the rodent population. Using newly obtained prevalence data from the field, we wish to find which transmission routes actually occur in the wild. These analyses will be used to parametrise a simple mechanistic model for leptospire infection in the rodent population. By identifying and quantifying the ecological factors driving leptospire dynamics in its reservoir host in tropical slums, patterns of human infection can be predicted. This work is part of the first study to examine leptospire dynamics in its reservoir host in an urban slum setting.

17/04/2015 Session E5 - (Room 14) - Parasites - One Health & Zoonosis - Chair: R Stothard 11:30 AM - 11:45 AM (15 mins)

Insights into the molecular epidemiology and phylogeography of *Echinostoma revolutum* (Frölich, 1802): a zoonotic agent of human echinostomiasis – (SP)

Egie E. Enabulele[1,2], Scott P. Lawton[1], Anthony J. Walker[1] and Ruth S. Kirk[1]

[1.] School of Life Sciences, Kingston University, Kingston upon Thames, UK; [2.] Department of Animal and Environmental Biology, University of Benin, Nigeria

Echinostoma revolutum is one of 20 echinostome species that cause human echinostomiasis, a zoonosis transmitted by ingestion of metacercariae in raw/undercooked molluscs, fish, crustaceans and amphibians. Accurate morphological identification of *E. revolutum* is problematic and molecular studies have revealed a number of cryptic species within the 'revolutum' species complex comprising echinostomes with 37 collar spines. In this study, lymnaeid snails collected from seven UK freshwater sites were screened for cercariae. Partial mitochondrial nad1 genes of echinostome cercariae were amplified and sequenced resulting in the identification of *E. revolutum* from 26 snails; *Lymnaea stagnalis* (n=13), *Stagnicola palustris* (n=2), *Radix balthica* (n=6) and *R. auricularia* (n=5). Phylogenetic analysis showed that UK isolates clustered within a discrete clade composed of haplotypes representing E. revolutum isolates from six other European countries. A strongly supported USA specific clade also emerged, which formed a sister lineage to the "European" E. revolutum clade. Haplotype network analysis similarly illustrated a lack of association between the USA and European populations and application of the K/θ formula suggested that the USA isolates represent a different species. Molecular diversity analysis of the UK and European populations identified 27 haplotypes, which were not geographically structured, indicating the potential of gene flow between mainland Europe and the UK. Migratory birds, as definitive hosts of E. revolutum, are probably disseminating the parasites throughout Europe.

17/04/2015 Session E5 - (Room 14) - Parasites - One Health & Zoonosis - Chair: R Stothard 11:45 AM - 12:00 PM (15 mins)

***Schistosoma haematobium* and urogenital schistosomiasis; genetics, epidemiology and biological complexities**

Bonnie Webster and David Rollinson

Natural History Museum, London

Schistosomiasis is caused by infection with parasitic worms within the *Schistosoma* genus and remains one of the world's most important neglected tropical diseases (NTD). *Schistosoma haematobium* is one of the most widespread species causing urogenital schistosomiasis in humans. More people are infected with *S. haematobium* than with all the other schistosome species combined. Of the >110 million cases of

S. haematobium infection in sub-Saharan Africa, 70 million are associated with hematuria, 18 million with bladder wall pathology, 10 million with hydronephrosis leading to severe kidney disease and even bladder cancer, and an estimated 16 million women suffer from Female Genital Schistosomiasis (FGS) which causes added complications in relation to fertility and HIV transmission. *S. haematobium* has a large geographical distribution being endemic throughout Africa, parts of the Middle East, Madagascar and the Indian Ocean Islands and is transmitted by various intermediate snail hosts within the genus *Bulinus*. Several efforts are underway to control morbidity and/or eliminate *S. haematobium*, including that of the Schistosomiasis Control Initiative (SCI), and/or perform operational research such as the Schistosomiasis Consortium for Operational Research and Evaluation (SCORE) program. Advances in the molecular tools available to study this parasite are revealing several intricacies surrounding the biology of this parasite and its vectors. Here I will bring together current research and molecular epidemiological findings surround *S. haematobium* and also its closely related species, discuss on going questions and how these findings may have an impact on the distribution, transmission, control, epidemiology and evolution of this devastating parasite.

17/04/2015 Session E5 - (Room 14) - Parasites - One Health & Zoonosis - Chair: R Stothard 12:00 PM - 12:15 PM (15 mins)

Leishmaniasis in Suriname - outcomes of an integrated research programme

Henk Schallig[1], Ricardo Hu[1,2], Alida Kent[1,3], Sahienshadebie Ramdas[1,4], Dennis Mans[3], Sjaak van der Geest[4], Henry de Vries[5], Rudy Lai a Fat[6]

[1]KIT Biomedical Research, Parasitology Unit, Meibergdreef 39, 1105 AZ Amsterdam, The Netherlands; [2]Dermatological Service, Paramaribo, Suriname; [3]Anton de Kom University, Paramaribo, Suriname; [4]University of Amsterdam, The Netherlands; [5]AMC, Tropical Dermatology, Amsterdam, The Netherlands; [6]Academic Hospital, Paramaribo, Suriname

According to text books, leishmaniasis in Suriname is cutaneous leishmaniasis caused by *Leishmania guyanensis*, is treated with pentamidine, but vectors and reservoirs are not well known. A Suriname – Netherlands consortium is currently studying several aspects of the disease in order to gain more in depth knowledge on the disease in the country and to contribute to a control programme for leishmaniasis in Suriname. The research programme comprises three projects: 1) Biology of parasite and vector; 2) Clinical aspects of disease and 3) Medical Anthropology. Biological research has revealed that next to L. guyanensis, at least three other species are present in Suriname, including the muco-cutaneous leishmaniasis (MCL) causing *L. braziliensis*. This finding has therapeutic implications since the first line recommended treatment for *L. braziliensis* infections is not standard in Suriname. At least three, for Suriname new, sand fly species have been identified and molecular analysis revealed that these sand flies can be infected. Reservoir studies are on-going. Clinical research has demonstrated that pentamidine may not be efficacious for all cases of CL found and alternative treatment regimens are being explored. Effect of drugs can be well monitored over time by using a recently developed RT PCR that may even be able to predict treatment outcomes. Medical anthropology has revealed that

stigmatization of infected individuals may not be a major problem in the social acceptability of the disease. Many non-conventional methods, including use of dangerous harmful chemicals, are being practised.

17/04/2015 Session E5 - (Room 14) - Parasites - One Health & Zoonosis - Chair: R Stothard 12:15 PM - 12:30 PM (15 mins)

Session A6 - (Room 11A) - Malaria - Molecular Biology

Chair: Prof A Craig, Liverpool School of Tropical Medicine

Imaging malaria parasite cell biology from whole cells down to single atom: towards achieving superb resolution

Jake Baum

Imperial College London

Of all the inventions that have driven biological research few come close in impact to the microscope. With advances in technology over the last few decades, imaging approaches now extended their application to every level of biology from whole animal centimeter scales through micron tissue and cellular levels right down to nano single molecule and even atomic imaging at the Ångstrom scale – and all using machines that even van Leeuwenhoek would likely recognize as microscopes. The study of malaria parasite cell biology has been no less driven by microscopy innovation right from the first descriptions of the *Plasmodium* parasite by Charles Laveran up to present day utilization of electron tomography and single molecule super-resolution microscopy. Here I will review some of the applications of microscopy that our group has utilized over the last few years at ever diminishing scales of parasite biology towards dissecting the fundamental processes behind parasite biology from cell movement and host-cell invasion right down to protein translation.

17/04/2015 Session A6 - (Room 11A) - Malaria - Molecular Biology - Chair: A Craig 2:00 PM - 2:30 PM (30 mins)

Parasite genes involved in establishing chronic infection using the rodent parasite *P. chabaudi*.

Adam Reid[1], Thibaut Brugat[2], Sarah McLaughlin[2], Garikai Kushinga[2], Irene Tumwine[2], Philip Spence[2,3], Ulrike Boehme[1], Mandy Sanders[1], Chris Newbold[1,4], Matthew Berriman[1] & Jean Langhorne[2]

[1.]Parasite Genomics, Wellcome Trust Sanger Institute, Hinxton, Cambridge CB10 1SA, UK [2.]The Francis Crick Institute, Mill Hill, London NW7 1AA, UK [3.]Current Address: Institute of Immunology and Infection Research (IIIR), School of Biological Sciences, The University of Edinburgh, United Kingdom [4.]Weatherall Institute of Molecular Medicine, University of Oxford, John Radcliffe Hospital, Oxford OX3 9DS, UK

Malaria parasites are temporarily able to evade their host's immune system, persist and increase their chance of being transmitted to the mosquito vector by establishing a chronic infection. While the important role of var genes in these processes in *Plasmodium falciparum* has been the subject of intensive research, the way in which other malaria species that lack var genes achieve the same results is poorly understood. We therefore set out to identify other parasite genes involved in establishing chronic infection using the rodent parasite *P. chabaudi*. This model induces a prolonged chronic infection in laboratory mice, is capable of expressing serologically distinct surface antigens and sequestering in organs despite lacking the var genes which function in all three of these processes in *P. falciparum*. We show that chronic infection is associated with an increase in virulence and increased expression of particular clusters of parasite pir genes whose expression varies in different mice. Our results demonstrate an association between variantly expressed pir gene clusters, the host immune system and establishment of chronic infection. Importantly the pir gene family is present in all *Plasmodium* species, including *P. falciparum* and therefore highlights a mechanism, which might be relevant for malaria in general. A model of chronic infection based on this and previous work establishes a template for future research into how malaria is able to evade the host immune system.

17/04/2015 Session A6 - (Room 11A) - Malaria - Molecular Biology - Chair: A Craig 2:30 PM - 2:45 PM (15 mins)

Effect of malaria infection on lipid profile and oxidative stress in children – (SP)

Olusegun Matthew Akanbi.

Department of Environmental Biology and Fisheries Adekunle Ajasin University, Akungba-Akoko, Ondo state, Nigeria

Malaria is a common disease among pregnant women and children. The pathological effect of malaria has been attributed to changes in the lipid profile and oxidative stress.This work studied the role of malaria infection on the lipid profile and oxidative stress in children. Two hundred and forty children within the age range 0-5 years were enrolled for this study; 170 were malaria positive while 70 were malaria negative (Control). Those who were malaria positive were grouped into two based on the level of parasitaemia. Those who had more than 100,000 parasitaemia were grouped as severe infection, while those who had less than 100,000 parasitaemia were grouped under mild infection. The high density lipoprotein (HDL) level was significantly higher ($P<0.05$) in the control than in the severe and mild groups, while the HDL level was not significantly higher in the mild group than in the severe group. There was a significant increase ($P< 0.05$) in the total protein in the control and mild group than in the severe group. The low density lipoprotein, total cholesterol and triglyceride levels were not significantly reduced in the control and mild group when compared with the severe group. This study also showed that there was a significant increase ($P<0.05$) in MDA and decrease in SOD and GSPX levels in the severe and mild groups when compared with the control group. This study shows that children who belong to severe group may likely to have serious complication and cardiovascular problem during the infection

17/04/2015 Session A6 - (Room 11A) - Malaria - Molecular Biology - Chair: A Craig 2:45 PM - 3:00 PM (15 mins)

Rapid and inducible protein degradation system reveals calcineurin phosphatase function at multiple stages during *Plasmodium* life-cycle

Nisha Philip and Andrew P. Waters

Wellcome Trust Centre for Molecular Parasitology, Institute of Infection, Immunity and Inflammation, University of Glasgow

A major barrier for functional analysis of essential genes in *Plasmodium* is that they cannot be deleted. Since proteins targeted by the best therapeutic compounds will always fall under this category, there is a pressing need for robust conditional knock out technologies. Here we report the development of a rapid, specific and inducible chemical-genetic tool to deplete endogenous *P. berghei* proteins by targeted degradation based upon the plant Auxin Inducible Degron (AID). This small molecule strategy can completely deplete a protein of interest in < 30 minutes making it particularly valuable to delineate rapid signalling cascades. Applying the degron system we could examine the role of protein phosphatase, Calcineurin during both host and vector stages of malaria parasite's life cycle. We uncovered new roles for Calcineurin which include erythrocyte invasion by the merozoite, gamete to ookinete development, ookinete-to-oocyst and sporozoite-to-liver stage transitions. The technology has been further optimized to enable generation of multiple transgenic lines in a single transfection experiment followed by isolation of resultant lines by flow cytometry. The technology not only allows medium-throughput and concurrent generation of transgenic lines, cutting down on animal use but can also be exploited to provide robust internal controls in phenotypic analysis. Here we discuss the development and application of this novel technology to examine protein function in both mammalian and vector stages of the malaria parasite.

17/04/2015 Session A6 - (Room 11A) - Malaria - Molecular Biology - Chair: A Craig 3:00 PM - 3:15 PM (15 mins)

PfPKG - a signalling hub that regulates egress and invasion of the malaria parasite from erythrocytes

Mohammad Mahmood Alam[1], Lev Solyakov[1], Andrew R. Bottrill[3], Christian Flueck[2], Faiza A. Siddiqui[4], Sharad Mistry[3], Maria Viskaduraki[7], Chetan E. Chitnis[4], Christian Doerig[5], Robert W.Moon[6], Judith L. Green[6], David A. Baker[2], Andrew B. Tobin[1]

[1]MRC Toxicology Unit, University of Leicester, Hodgkin Building, Lancaster Road, Leicester, LE1 9HN, UK. [2]London School of Hygiene & Tropical Medicine, Keppel Street, London, WC1E 7HT, UK. [3]PNACL, University of Leicester, Hodgkin Building, Lancaster Road, Leicester, LE1 9HN, UK [4]International Centre for Genetic Engineering and Biotechnology, Aruna Asaf Ali Marg, New Delhi, INDIA. [5]Department of

Microbiology, Monash University, Victoria 3800, Australia. [6]MRC National Institute for Medical Research, Mill Hill, London, NW7 1AA, UK. [7]Bioinformatics and Biostatistics Support Hub (B/BASH), University of Leicester, Leicester, LE1 9HN, UK

Here we describe a chemical genetic approach together with quantitative global phospho-proteomics that is able to define the on and off target activity of a "pro-drug" inhibitor of the essential protein kinase PfPKG (cGMP dependent protein kinase). In so doing, we not only define the potential off target activity of a drug-like protein kinase inhibitor but importantly we are able to dissect the downstream cellular targets of PfPKG. PfPKG is known to play important role in ookinete motility, gametogenesis and egress (release of merozoites from infected erythrocytes). Compound-2 is an inhibitor of PfPKG. A gatekeeper mutation in PfPKG (T618Q) makes it resistant to inhibition by compound-2. A mutant parasite line (PfPKG-T618Q) has been developed and used previously to study the function of PfPKG. Here global phospho-proteomic analysis identified 159 phosphorylation sites that decreased in response to compound-2 treatment. Using the PfPKG-T618Q mutant we were able to determine that of these 159 sites, 107 were downstream of PfPKG activity (representing on-target action of compound 2) and 52 sites were not related to PfPKG activity and therefore constituted off-target actions of the inhibitor. Importantly, serine-64 (S-64) phosphorylation of calcium dependent protein kinase-1 (CDPK1) is one of the on-target phosphorylation sites. By use of phospho-specific antibody, we show that S-64 phosphorylated form of CDPK1 is localized to apical pole of merozoites. We also show that PfPKG regulates the invasion of erythrocytes by merozoites. Altogether we show that PfPKG acts as signalling-hub to control the egress and invasion of erythrocytes.

17/04/2015 Session A6 - (Room 11A) - Malaria - Molecular Biology - Chair: A Craig 3:15 PM - 3:30 PM (15 mins)

Session B6 - (Room 11B) - NTDs - Modelling

Chair: Dr P Lamberton, Imperial College London

Using mathematical models to inform the design of effective control of neglected tropical diseases

Déirdre Hollingsworth

University of Warwick, UK

Mathematical models and statistical analyses are important tools in improving our understanding of the evolution and transmission dynamics of infectious diseases. Neglected tropical diseases (NTDs) fall into two main groups, each of which pose different types of questions which mathematical modelling has the potential to address. For the diseases in which mass drug administration (MDA) is the main control policy, (e.g. soil-transmitted helminths) the timing, frequency, targeting and coverage of the campaigns depend on the epidemiology and transmission patterns. For intensified disease management (IDM)

diseases (e.g. visceral leishmaniasis) the interpretation of case data in terms underlying incidence of infection depends on a good understanding of the relationship between rates of passive or active case finding, case definition and diagnosis and transmission. I will present insights from modelling of these diseases on the design of NTD control programmes and discuss factors which affect the quality and usefulness of the results. These include a close relationship between modellers and experts in the field, the quality and availability of the underlying data and communication of the results and their underlying uncertainties. I will also include a brief discussion of the research activities of the NTD Modelling Consortium.

17/04/2015 Session B6 - (Room 11B) - NTDs - Modelling - Chair: P Lamberton 2:00 PM - 2:30 PM (30 mins)

Development of a Markov transition probability model to predict changes in schistosomiasis infection following treatment

Arminder Deol[1], Webster J[1], Hollingsworth T.D[3], Harrison W[1], Fernandes J[1], Montresor A[4], French, M[1]

[1] Schistosomiasis Control Initiative, School Of Public Health, Imperial College London, London, W2 1PG [2]Department of Mathematics, University of Warwick, Coventry, CV4 7AL [3]Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, L3 5QA [4]Neglected Tropical Disease Department, World Health Organization, Avenue Appia, 20, Geneva,

An STH Markov model developed at the World Health Organization (WHO) used data from Vietnam to predict changes in STH prevalence following successive rounds of deworming treatment. In addition, a user-friendly interface was also developed to help ensure the model is used as widely as possible by programme managers. Data collected by the Schistosomiasis Control Initiative and its country partners from several countries in sub-Saharan Africa have enabled the validation of this model for STH infection, its extension to include schistosomiasis infection, and the addition of robust confidence intervals around the predicted changes in prevalence. It is hoped that the output of this model could potentially provide an early warning of where treatment campaigns are not achieving their aims (for example due to poor coverage, adherence, or putative resistance) and enable programme managers to make the necessary changes to meet the expected targets. The performance of the model will be discussed, with particular reference to the utility of stratifying the model outputs by parasite species, location, underlying endemicity, and host age. In addition, we will discuss the results of a model comparison exercise between the predictive capacity of the Markov model and other models currently available.

17/04/2015 Session B6 - (Room 11B) - NTDs - Modelling - Chair: P Lamberton 2:30 PM - 2:45 PM (15 mins)

How effective is school-based deworming on impacting the burden and prevalence of soil-transmitted helminths and schistosomes?

Jie Yang, James Truscott, Roy M. Anderson

London Centre for Neglected Tropical Diseases, Department of Infectious Disease Epidemiology, School of Public Health, Imperial College London, London, UK

Soil-transmitted helminths, including hookworms and *Ascaris lumbricoides*, and schistosomiasis, which results from being infected by schistosomes, are classified by the World Health Organisation as neglected tropical diseases. They can cause serious morbidity in communities, and are particularly detrimental to the health and development of school-aged children. However, periodic administration of drugs such as albendazole and mebendazole for treating soil-transmitted helminths, and praziquantel for treating schistosomiasis, can be a cost-effective means of reducing disease morbidity. The key is determining what the frequency of treatment should be and identifying exactly which age group(s) should be targeted to reach the most effective treatment strategy that combines the lowest economical cost possible with the method that has the greatest impact over the control or even eradication of the parasites. The World Health Assembly has set a benchmark of deworming 75% of all school-aged children in national school-based chemotherapy programmes by 2020. The paper describes a stochastic individual-based model that takes into account age structure (infants, pre-school children, school-aged children and adults), which is employed to determine how effective various treatment strategies are when annual chemotherapy is applied in different transmission settings, defined by the magnitude of the basic reproductive number, R0.

17/04/2015 Session B6 - (Room 11B) - NTDs - Modelling - Chair: P Lamberton 2:45 PM - 3:00 PM (15 mins)

Multiple ivermectin doses are macrofilaricidal: implications for the elimination of onchocerciasis

Martin Walker, Sébastien DS Pion, Hanwei Fang, Thomas S Churcher, Jacques Gardon, Joseph Kamgno, Maria-Gloria Basáñez, Michel Boussinesq

Department of Infectious Disease Epidemiology, Imperial College London, Norfolk Place, London, UK, W2 1PG

The predominant strategy for achieving the World Health Organization's control and elimination goals for human onchocerciasis is based on mass drug administration (MDA) with ivermectin. The feasibility of achieving these goals crucially depends on the long-term effects of multiple doses of ivermectin on the long-lived Onchocerca volvulus filarial nematode, which causes onchocerciasis. A single dose of ivermectin rapidly kills the microfilariae while also exerting a temporary sterilization (embryostatic) effect on the female adult worms (macrofilariae). Multiple doses of ivermectin are thought to cause a cumulative effect on macrofilariae manifesting either as permanent reductions in fecundity or a

shortened life-span. These assumptions have been incorporated into mathematical models to support elimination efforts. Yet, for decades the nature of this presumed cumulative action has avoided rigorous investigation because scarce longitudinal data on macrofilariae have not been interrogated with suitably powerful analytical techniques. Here, we analyse data on the fecundity and vitality of female worms from the most comprehensive clinical trial of multiple doses of ivermectin treatment (comparing 3-monthly with annual treatment rounds administered during three years in Cameroon) using a recently developed state-of-the-art modelling framework. We demonstrate that multiple doses of ivermectin treatment have a substantial macrofilaricidal effect, even at the doses and frequencies used for routine MDA. We find no evidence that the anti-fecundity activity of ivermectin is enhanced by multiple treatments. We discuss our results in the context of the feasibility to eliminate onchocerciasis in the timeframes set by the global health community.

17/04/2015 Session B6 - (Room 11B) - NTDs - Modelling - Chair: P Lamberton 3:00 PM - 3:15 PM (15 mins)

Longitudinal investigation of trends in *Echinococcus* coproantigen and PCR positivity during a control scheme

Alexander Mastin, Freya van Kesteren & Philip Craig

University of Salford, UK

Human echinococcosis is an increasing public health issue in Kyrgyzstan, where *Echinococcus granulosus* and *E. multilocularis* are coendemic. As domestic dogs are considered the primary source of human echinococcosis, a control scheme based upon dosing dogs with the cestocidal drug praziquantel was commenced in Kyrgyzstan in 2012. The current study describes the household-level *Echinococcus* coproantigen and coproPCR prevalence during this control scheme, over three years. Mixed effects binomial logistic regression models were developed to investigate temporal and seasonal trends for each of the four tests conducted, and associations with other variables such as recent praziquantel dosing, village of study and dog ownership were also investigated. Rather than selecting a single model to approximate these associations, parameter coefficients were estimated from the outputs of a number of models using model averaging techniques. For all outcomes, an apparent decrease in the estimated prevalence over time was observed, which was most apparent for coproantigen and E. multilocularis positivity. Seasonal trends were also apparent – with a higher coproantigen and E. multilocularis PCR prevalence and a lower *E. canadensis* PCR prevalence in the autumn compared to the spring. Reported recent praziquantel dosing did not appear to be strongly associated with the coproantigen or coproPCR prevalence in the household, but generally appeared to be associated with a lower coproantigen prevalence (with the exception of *E. granulosus* PCR results). These results suggest that the praziquantel-based control scheme is effective and that the seasonal patterns of canine exposure to *E. canadensis* and *E. multilocularis* differ.

17/04/2015 Session B6 - (Room 11B) - NTDs - Modelling - Chair: P Lamberton 3:15 PM - 3:30 PM (15 mins)

Session C6 - (Room 11C) - Vectors - Host/Parasite Interactions I

Chair: Dr L Reimer, Liverpool School of Tropical Medicine

Wolbachia-mosquito interactions and pathogen transmission

Steven Sinkins

Lancaster University, UK

Wolbachia are maternally inherited bacterial endosymbionts that have multiple effects on their invertebrate hosts, including some mosquitoes. Many strains manipulate host reproduction using cytoplasmic incompatibility (CI), the imposition of crossing sterilities that enable them to spread to high frequency in host populations. Certain strains of *Wolbachia* can also protect the host from pathogens, and inhibit the development / transmission of various important human arboviruses and parasites including filarial nematodes and *Plasmodium*. By creating stable transinfections with various strains of *Wolbachia* in mosquitoes and in mosquito cell lines, the molecular basis of the pathogen inhibition phenotype is being explored. In some cases such as *Aedes aegypti* and *Anopheles gambiae* upregulation of a number of immune genes occurs, and a contribution of immune effectors to pathogen inhibition has been demonstrated. In Aedes albopictus, however, a transinfection with the wMel strain from Drosophila blocked the transmission of dengue and chikungunya viruses, and generated bidirectional CI, but immune gene transcription was not significantly elevated. This suggests that other mechanisms of inhibition operate independently of immune pathways. Higher *Wolbachia* strain density has been found to correlate with pathogen inhibition, and *Wolbachia* is shown to influence several mosquito metabolic pathways that could directly affect parasite and virus transmission. The implications of these studies for the use of *Wolbachia* to control neglected tropical diseases will be discussed.

17/04/2015 Session C6 - (Room 11C) - Vectors - Host/Parasite Interactions I - Chair: L Reimer 2:00 PM - 2:30 PM (30 mins)

Unravelling the sandfly salivary glycome – (SP)

Karina Mondragon-Shem[1], Katherine Wongtrakul-Kish[2], Daniel Spencer[2], Matthew E. Rogers[3], Alvaro Acosta-Serrano[1]

[1.] Liverpool School of Tropical Medicine. Liverpool, UK. [2.] Ludger Ltd. Abingdon, UK. [3.] London School of Hygiene and Tropical Medicine. London, UK.

Sandfly saliva is crucial in *Leishmania* transmission, as it modulates the immune responses of vertebrate hosts. Although the sialome of several sandflies has been extensively studied, the salivary glycans remain notably overlooked. Sugars play important roles in protein function and immunogenicity, and so they are likely to influence parasite transmission. Furthermore, they may also determine the half-life in blood of anti-hemostatic insect salivary proteins. Here we studied glycoproteins in the saliva of Lutzomyia longipalpis, the vector responsible for the transmission of *Leishmania infantum* in the Americas. In silico predictions suggest ~50% of the *Lu. longipalpis* sialome is glycosylated. SDS-PAGE

coupled to LC-MS analysis of salivary glycoproteins from *Lu. longipalpis* females, before and after deglycosylation with N-glycanase, yielded a list of potential glycoproteins. To determine the diversity of N-glycan structures, enzymatically released sugars from salivary glycoproteins were fluorescently tagged and analysed by HPLC in combination with highly sensitive LC-MS/MS before and after glycosidases. Our results revealed the N-glycan composition of *Lu. longipalpis* mostly consists of high mannose-type sugars, with Man5GlcNAc2 being the most abundant species. MS also revealed the presence of a novel negatively charged glycan structure with a fucose modification in an unusual position. Further work will include determining the function and antigenicity of this novel glycan. The high mannose-type sugars are also found in tsetse saliva (in preparation), which hints at a conserved pathway among haematophagous insects.

17/04/2015 Session C6 - (Room 11C) - Vectors - Host/Parasite Interactions I - Chair: L Reimer 2:30 PM - 2:45 PM (15 mins)

A review of the Importance of the vertical transmission of dengue viruses by mosquitoes – (SP)

Martin Grunnill

Centre for Ecology and Conservation University of Exeter Cornwall Campus Penryn Cornwall TR10 9EZ

Vertical transmission of dengue viruses by mosquitoes was discovered at the end of the late 1970s and has been suggested to be a key disease persistence mechanism, but its importance in the epidemiology of this disease remains controversial. Here I present the findings of a literature review on vertical transmission, discussing its role in dengue's epidemiology and control. Concluding that given the number of studies that failed to find evidence of vertical transmission, mathematical models and its mechanistic basis it is unlikely that vertical transmission is important for the epidemiological persistence of dengue viruses. A combination of asymptomatic infection in humans and movement of people are likely to be more important determinants of dengue's persistence. However there may be a need for further research into the prevalence of dengue viruses in diapausing eggs, the role of horizontal transmission through larval cannibalism and the possibility of using viral detection in larval stages as a dengue epidemic warning/risk assessment system.

17/04/2015 Session C6 - (Room 11C) - Vectors - Host/Parasite Interactions I - Chair: L Reimer 2:45 PM - 3:00 PM (15 mins)

Studies on common ectoparasites of one humped camels (*Camelus dromedarius*) in cholistan desert

Muhammad Fiaz Qamar

Department of Parasitology, University College of Veterinary & Animal Sciences, The Islamia University of Bahawalpur-Pakistan.

Four hundred and fifty camels from 30 herds ranging from 5 months to 17 years old were subjected to examination of ectoparasites (ticks, mange mites and flies) during November 2010 to July 2011 at cholistan, Bahawalpur Pakistan. The ticks in different stages of their life cycle were collected from

infested animals without damage to their mouth parts with forceps and were identified accordingly by the parasitological Keys. An overall prevalence of 55.55% was recorded. Ticks were the most frequent ectoparasites. The ticks in order of their preference were as: *Rhipicephalus* spp (28.95%) *Hyalomma dromedarii* (26.48%), *Dermacentor* sp (18.29%) *H. anatolicum* (12.47%), *H. marginatum* (6.69%), *Ornithodoros* spp. (4.89%) and *Amblyomma variegatum* (2.20%). The mange mite; *Sarcoptes scabiei* var. cameli (42.22%) was identified. One hundred and eighty four (40.88%) camels were infested with two species of flies i.e; *Chrysomyia* spp. (10%) and *Wohlfahrtia magnifica* (16.67%) that cause vaginal and preputial myiasis. Cephalopina titilator fly (11.11%) was found to cause nasal myiasis in camel. The district wise prevalence revealed highest incidence at Rahim Yar Khan (60.87%), followed by Bahawalnagar (49.75%) and Bahawalpur (41.05%). The tick load per animal was higher during summer months than during winter months. The lowest ticks load was observed during December (25.58%), whereas the highest was recorded in July (64.52%). The prevalence was higher (69.53%) in animals between 5 to 7 year of age however the lowest was noted in less than one year of age (23.08%).

17/04/2015 Session C6 - (Room 11C) - Vectors - Host/Parasite Interactions I - Chair: L Reimer 3:00 PM - 3:15 PM (15 mins)

Innate immunity as a structuring mechanism of parasite communities within and between within-host infection sites

Evelyn Rynkiewicz[1], Melanie Clerc[1], Simon Babayan[2], Amy Pedersen[1]

[1]University of Edinburgh, [2]University of Glasgow

In nature, hosts are usually co-infected with multiple parasites and pathogens, which can interact directly or indirectly to influence their transmission, host health or host susceptibility. Therefore, intensity of host immune response and the degree of parasite immunomodulation could determine if one infection is likely to influence another. Also, an individual host is a diverse environment with many habitats for different parasites. In turn, the host immune system can respond locally at a specific infection site or systemically, with immunological changes 'spilling over' and affecting responses to immune stimuli throughout the body. These multiple scales of interaction within an individual host may partially underly within-population variation in co-infection and severity of effects on host health. To investigate how local and systemic immune responses influence parasite co-infection patterns we performed an experimental removal of nematode parasites from wild wood mice (*Apodemus sylvaticus*). We treated, marked and recaptured animals, extracted their spleen and mesenteric lymph nodes, and stimulated leucocytes with a panel of innate immune stimuli to measure in vitro cytokine production by ELISA. We predicted a systemic effect of nematode removal would result in systemic changes reflected in cytokine levels in both lymph nodes and spleen. Alternately, we predicted that removal would result in local effects seen in lymph nodes only. Our approach compartmentalizes the interactions between parasites and host to better understand underlying mechanisms and the scale at which they are important, which may improve predictions of how parasites interact and their impacts on host health.

17/04/2015 Session C6 - (Room 11C) - Vectors - Host/Parasite Interactions I - Chair: L Reimer 3:15 PM - 3:30 PM (15 mins)

Session D6 - (Room 13) - Parasites - Wildlife & Aquatic -

Chair: Dr M Betson, University of Surrey

Worms, MHC and fish speciation: lessons from Lake Tanganyika

Pascal I. Hablützel, Grégoir, Arnout F. Vanhove, Maarten P.M. Volckaert, Filip A.M. Raeymaekers, Joost A.M.

Laboratory of Biodiversity and Evolutionary Genomics, University of Leuven, Ch. Deberiotstraat 32, 3000 Leuven, Belgium Laboratory of Aquatic Ecology, Evolution and Conservation, University of Leuven, Ch. Deberiotstraat 32, 3000 Leuven, Belgium Biology Department, Museum for Central Africa, Leuvensesteenweg 13, 3080 Tervuren, Belgium

The Major Histocompatibility Complex (MHC) of vertebrates plays a central role in the recognition of antigens and is coded by some of the most polymorphic genes. Cichlids of the Great African Lakes are known to carry highly polymorphic MHC genes and are famous to speciate at a rapid pace. In our studies we investigated the influence of adaptive divergence on MHC diversity and how this immunogenetic divergence might have stimulated or accelerated speciation. For this we studied parasite communities and MHC diversity in two cichlid species from Lake Tanganyika. Whereas the phylopatric Tropheus moorii diverged in many genetically divers colour morphs, the dispersing monomorphic Simochromis diagramma shows no signs of population structure at neutral loci. However, populations of both species are infected by differentiated parasite communities and exhibit immunogenetic divergence. We conclude that parasites have possibly played a pivotal role in shaping the contemporary species flocks of the Great African Lakes.

17/04/2015 Session D6 - (Room 13) - Parasites - Wildlife & Aquatic - Chair: M Betson 2:00 PM - 2:15 PM (15 mins)

Parasites and invasive species: transmission during inter-specific interactions and potential effects on invasion dynamics

Jo James[1], Davidson K[1], Mackie ASY[2], Petrusek A[3], Mrugala A[3], Ellis A[4], Young KA[5], Richardson G[1] and Cable J[1]

[1] School of Biosciences, Cardiff University, Cardiff, CF10 3AX, UK; [2]Department of Natural Sciences, National Museum Wales, Cathays Park, Cardiff CF10 3NP, UK; [3]Department of Ecology, Charles University, Viničná 7, Prague 2, CZ-12844, Czech Republic; [4]Ahern Ecology, Unit 13 Hurricane Close,

Salisbury, Wiltshire, SP4 6LG, UK; [5]Institute of Biological, Environmental and Rural Sciences (IBERS), Aberystwyth University, Aberystwyth, SY23 3DA, UK

A key threat to global biodiversity are biological invasions, which act as pathways for disease transmission. Once introduced, non-native parasites may transmit to immunologically naïve native hosts with potentially lethal consequences. Additionally non-native parasites may transfer to other invasive species, possibly mitigating their ecological impacts, providing that they are susceptible to the parasite. Therefore parasite presence may facilitate the displacement of an established invasive species by a newly introduced one with potential ecosystem level impacts. Here we assess the transmission of a common pathogen, Aphanomyces astaci and a less well known symbiont *Xironogiton victoriensis* (Annelida: Clitellata) between two invasive crayfish species currently co-existing in the UK: the established signal crayfish, *Pacifastacus leniusculus* and the recently introduced virile crayfish, *Orconectes rusticus*. Being native to North American signal and virile crayfish are both largely resistant to *A. astaci* but facilitate its transmission to native European crayfish species in which infection is reportedly always lethal. Therefore if the pathogen is able to transmit inter-specifically between alien crayfish species the threat to native crayfish may be intensified. At present *X. victoriensis* is not known from virile crayfish but previous studies on signal crayfish show that infected individuals are less aggressive and have a lower competitive ability. Therefore, if *X. victoriensis* is capable of transmitting to virile crayfish, infection may be detrimental towards their invasion success. Potential impacts of *A. astaci* and *X. victoriensis* infestation on the invasion dynamics of both crayfish species, and concomitantly their impacts on the wider ecological community are discussed.

17/04/2015 Session D6 - (Room 13) - Parasites - Wildlife & Aquatic - Chair: M Betson 2:15 PM - 2:30 PM (15 mins)

Predation by crabs facilitates castrating trematodes in snails

Anieke van Leeuwen, Kevin D. Lafferty[1], Ryan Hechinger[2], Andy P. Dobson[3]

[1]Marine Science Institute, University of California Santa Barbara; [2]Scripps Institution of Oceanography, University of California, San Diego; [3]Ecology and Evolutionary Biology, Princeton University

The realization of the role parasites play in ecosystems has shed an entirely new light on much of what is known about food web structure and food web dynamics. In terms of numbers of interactions, parasitic species dominate over free-living species. In terms of biomass, the component present in parasites can exceed that of top predators, as is observed in several Californian salt marsh systems. Snails as host species, interacting with parasites, were highlighted in food web studies and provide an example of the ecological interconnectedness of trophically transmitted parasite life stages and intra- and interspecific interactions. We ask the question how the size-specific population dynamics of a common host species (*Cerithidea californica*) is affected by the interplay of castrating parasitism, intraspecific resource competition and interspecific predation and competition by crabs (*Pachygrapsus crassipes*). Extensive field surveys and data from previous studies show a characteristic pattern concerning the size-specific pattern of parasite prevalence within the snail population. The signature in this data is of high parasite

prevalence in large individuals (>25mm) and extremely high parasite prevalence in the largest individuals (>35mm) in the population. The current study seeks to address the question what causes this prevalence pattern and to what extent non-parasitic trophic interactions contribute to the snail population size-distribution and the size-specific parasite prevalence pattern. We find that size-specific predation and in particular size-specific intra-guild predation exerted by crabs are essential elements to explain the size-specific prevalence pattern in snails and overall snail population structure.

17/04/2015 Session D6 - (Room 13) - Parasites - Wildlife & Aquatic - Chair: M Betson 2:30 PM - 2:45 PM (15 mins)

Eco-Immunology: the effects of thermal variation on fish hosts of *Saprolegnia parasitica* – (SP)

Alexander Stewart[1], Joe Jackson[2], Martha Brown[2], Chris Williams[3], Jo Cable[1]

[1.]School of Biosciences, Cardiff University, Cardiff, CF10 3AX, United Kingdom [2.]IBERS, Aberystwyth University, Aberystwyth, SY23 3DA, United Kingdom [3.]Environment Agency, Brampton, Cambridgeshire, PE28 4NE, United Kingdom

Temperatures, still within the physiological range of ectotherms, have been shown to alter immune function. The activity of the teleost immune response, particularly the adaptive response, is highly dependent on the ambient temperature of the host. As such changes in temperature can alter the outcome of infection in terms of both prevalence and intensity. Of particular interest to aquaculture is the pathogenic oomycete, *Saprolegnia parasitica*, which can affect >10% of farmed salmonids and causes losses of £25million per annum to the US catfish industry. Previous research on *S. parasitica* infections suggested that changes in the ambient temperature of teleosts were the major cause of infection; leading to 'winter kill syndrome'. Evidence now suggests that stress, caused by rapid temperature change, overcrowding or poor water quality, rather than ambient temperature is the major cause of *Saprolegnia* infections. Here we use the three-spined stickleback (*Gasterosteus aculeatus*), guppy (*Poecilia reticulata*) and red tilapia (*Oreochromis* sp.) to study the effect of temperature on this parasite system to better understand the role of stress and immunity in the development of infection. Our aim is to inform fish stock managers on the potential problems associated with climate change, parasitism and immunity and how best to manage infection in response to climate change and stress.

17/04/2015 Session D6 - (Room 13) - Parasites - Wildlife & Aquatic - Chair: M Betson 2:45 PM - 3:00 PM (15 mins)

The effects of inbreeding on disease susceptibility: *Gyrodactylus turnbulli* infection of guppies, Poecilia reticulate – (SP)

Willow Smallbone, Cock van Oosterhout, Jo Cable

School of Biosciences, Cardiff University, Cardiff CF10 3TL, U.K.

Inbreeding can threaten population persistence by reducing disease resistance through the accelerated loss of gene diversity (i.e. heterozygosity). Such inbreeding depression can affect many different fitness-related traits, including survival, reproductive success, and parasite susceptibility. Prevalence of parasites within a population and disease susceptibility of an individual may be increased with increased homozygosity, and quantifying the effects of inbreeding on parasite resistance is important for ex-situ conservation of vertebrates. Many experimental inbred mating regimes use levels of inbreeding that exceed those existing in natural populations. The present study, therefore, used three different breeding regimes (inbred, crossed with full siblings; control, randomly crossed mating; and fully outbred) to examine the relationship between inbreeding coefficient (F-coefficient) and susceptibility to *Gyrodactylus turnbulli* infection in a live bearing vertebrate, the guppy *Poecilia reticulata*. Gyrodactylids are the most common group of guppy parasites in Trinidad and Tobago, and these infections can lead to marked effects on host behaviour, including courtship and feeding. Breeding regime significantly affected the maximum parasite intensity; inbred fish had a significantly higher number of parasites than fish from the control. *G. turnbulli* extinction was ~50% lower among individual hosts of the inbred regime compared to all other regimes. Control regime individuals had significantly lower maximum parasite number than all other breeding regimes. This is one of the first studies to quantify the effects of inbreeding on disease susceptibility in a captive bred fish, and it highlights the risks faced by small (captive-bred) populations when exposed to their native parasites.

17/04/2015 Session D6 - (Room 13) - Parasites - Wildlife & Aquatic - Chair: M Betson 3:00 PM - 3:15 PM (15 mins)

Session E6 - (Room 14) - Parasites - Evolution I

Chair: Prof R Post, John Moores Univeristy Liverpool

Untangling the molecular phylogeny of tapeworms

Andrea Waeschenbach[1], Janine N Caira[2], Kirsten Jensen[3], Jean Mariaux[4], Boyko B Georgiev[5], Tomas Scholz[6], Roman Kuchta[6], Jan Brabec[6], Vasyl Tkach, D Tim J Littlewood[1], PBI Consortium

[1]Department of Life Sciences, Natural History Museum [2]Department of Ecology and Evolutionary Biology, University of Connecticut [3]Department of Ecology & Evolutionary Biology and the Biodiversity Institute, University of Kansas [4]Department of Genetics and Evolution, The Natural History Museum of Geneva [5]Institute of Biodiversity and Ecosystem Research, Bulgarian Academy of Sciences [6]Biology Centre of the Academy of Sciences of the Czech Republic, Institute of Parasitology

The diversity of tapeworms reaches far beyond of what is typically known about this group from the few representatives of biomedical and veterinary importance (e.g. *Taenia* spp., *Diphyllobothrium* spp.). The large diversity of life cycles (typically involving crustacean intermediate hosts and vertebrate definitive hosts) means they have successfully established themselves throughout aquatic (both marine and freshwater) and terrestrial habitats, where the majority of the ~6000 known species are found

parasitising elasmobranch and tetrapod hosts. Over the past two decades, molecular data have produced an ever more stable and well-resolved backbone phylogeny, whilst increasing the number of orders from 12 to 19. In this talk, the recent contributions to the construction of the tapeworm backbone phylogeny will be recapped. Additionally, new molecular phylogenetic results will be presented that have been accumulated over the last 5 years from the NSF-funded Planetary Biodiversity Inventory project 'A survey of the tapeworms from vertebrate bowels of the earth'. This international collaborative project targeted previously unexplored hosts and/or geographic regions to increase the sampled diversity of tapeworms. The resultant phylogeny, based on two nuclear (18S and 28S rDNA) and two mitochondrial genes (16S rDNA and cox1), is composed of ~850 taxa, which represents the most significant contribution to tapeworm phylogeny, to date, allowing us to investigate the effects of host-use and phylogeography on the diversification patterns in this group.

17/04/2015 Session E6 - (Room 14) - Parasites - Evolution I - Chair: R Post 2:00 PM - 2:30 PM (30 mins)

Diversity and divergence of immune genes in wild rodents

Andrew Turner[1]. Mike Begon[1], Amy B. Pedersen[2], Steve Paterson[1]

[1.] *Institute of Integrative Biology, University of Liverpool.* [2.] *Institute of Evolutionary Biology/Institute of Immunology and Infection Research, University of Edinburgh*

Individuals vary substantially in their resistance to infectious disease and experiments on laboratory rodents, such as the house mouse (*Mus musculus*), have proved invaluable in elucidating the mechanistic basis of this resistance. However, controlled laboratory studies provide few insights into the causes and consequences of genetic variation in the natural environment, where increased genetic diversity, multiple infections and fluctuating environmental conditions are the norm. The study of wild rodents represents an excellent opportunity to link the functional genetic knowledge gained from laboratory rodents with the variation in disease susceptibility observed in natural populations, including humans. Here we examined diversity in >800 immune genes and ~500 size-matched, non-immune genes in four wild rodent species: house mice, wood mice (*Apodemus sylvaticus*), field voles (*Microtus agrestis*) and bank voles (*Myodes glareolus*). In all species, genetic diversity was significantly higher in immune genes. Through examination and comparison of diversity within and between individuals, populations and species, we investigate which genes have been subject to natural selection, and whether the same genes have been repeatedly targeted by selection across different populations and species. For example, positive selection appears to have driven divergence between species at multiple pathogen-recognition sites within Toll-like receptor (TLR) genes.

17/04/2015 Session E6 - (Room 14) - Parasites - Evolution I - Chair: R Post 2:30 PM - 2:45 PM (15 mins)

Extensive nucleotide diversity within the mitochondrial genome of *Schistosoma mansoni*

Andrew Briscoe, Andrea Waeschenbach, David Rollinson, Tim Littlewood, Bonnie Webster

Department of Life Sciences, Parasites and Vectors Division, Natural History Museum, Cromwell Road, London, SW7 5BD, UK

Schistosomiasis is one of the most prevalent neglected tropical diseases, affecting an estimated 207 million people in developing countries. Amongst the human-infective species, *Schistosoma mansoni*, the causative agent of intestinal schistosomiasis, is widespread and a major health problem particularly in sub-Saharan Africa. Its distribution is reliant on the presence of specific species of freshwater pulmonate snails of the genus *Biomphalaria*, which act as the intermediate host. Within *S. mansoni*, recent studies have highlighted the potential of utilising short mitochondrial DNA markers to show distinct population structure across its geographical range. Here, 24 complete mitochondrial genomes (~15,000bp) have been sequenced from isolates from the Schistosomiasis Collection at the Natural History Museum (SCAN) spanning the entire geographical range of *S. mansoni*, with representatives collected over the last 30 years from sub-Saharan Africa, the Arabian Peninsula and the neotropics. The data indicate nucleotide variation of over 5% between populations of *S. mansoni*, showing clear relationships between lineages. We explore how within-species mitogenomic studies might provide a route towards improved population markers, in order to identify different geographic isolates and track gene flow amongst them in response to disease control interventions and also spread/migration of *S. mansoni* within and between countries.

17/04/2015 Session E6 - (Room 14) - Parasites - Evolution I - Chair: R Post 2:45 PM - 3:00 PM (15 mins)

South African tortoise haemogregarines: with special focus on *Haemogregarina parvula* Dias, 1953

Courtney Cook, Edward C. Netherlands, Nico J. Smit

Unit for Environmental Sciences and Management, North-West University, Potchefstroom, South Africa.

So far, only a single species of *Hemolivia*, *Hemolivia mauritanica* (Sergent and Sergent, 1904), had been described from African terrestrial tortoises. Although various haemogregarines have been described from southern African terrapins and tortoises including species from the genera Haemogregarina and one from the genus Hepatozoon, no species of Hemolivia have been identified as of yet. Since its morphological redescription, the taxonomic placement of one of these species, Haemogregarina parvula Dias, 1953, was questionable. Hence, research was undertaken to resolve the true taxonomic position of this haemogregarine. Blood smears from nine wild tortoises of two species, *Stigmochelys pardalis* and *Kinixys belliana zombensis*, from South Africa were screened, with the focus on *H. parvula*. Parasite DNA was extracted from ethanol-preserved blood samples, and PCR was undertaken using two primer sets HepF300/HepR900 and 4558/2733 amplifying fragments of the 18S rDNA gene. The 18S rDNA sequences of Haemogregarina parvula fell with species of *Hemolivia* and not with those of Haemogregarina or Hepatozoon. It is thus recommended that this haemogregarine be re-assigned to the

genus Hemolivia, making *Hemolivia parvula* (Dias, 1953) the first species of this genus recorded from southern African tortoises.

17/04/2015 Session E6 - (Room 14) - Parasites - Evolution I - Chair: R Post 3:00 PM - 3:15 PM (15 mins)

Babesia behnkei sp. nov., a novel rodent Babesia species from the Sinai Mountains, Egypt

Anna Bajer[1], Mohammed Alsarraf[1], Małgorzata Bednarska[1], Eman M. E. Mohallal[2], Ewa J. Mierzejewska[1], Jolanta Behnke-Borowczyk[3], Sammy Zalat[4], Francis Gilbert[5], Renata Welc-Falęciak[1]

[1]Department of Parasitology, Institute of Zoology, Faculty of Biology, University of Warsaw,1 Miecznikowa Street, 02-096, Warsaw, Poland; [2]Desert Research Center, Cairo, Egypt; [3]Department of Forest Phytopathology, Faculty of Forestry, Poznań University of Life Sciences, Poland; [4]Department of Zoology, Suez Canal University, Ismailia, Egypt; [5]Faculty of Medicine & Health Sciences, School of Biology, University of Nottingham, UK

Based on morphology and phylogenetic relationships we describe a novel species of Babesia from Wagner's gerbil, which we have named *Babesia behnkei* sp. nov. Rodents (n=1021) were sampled in 2000- 2013 in four wadies in the Sinai Mountains, Egypt. Prevalence of Babesia was the highest in Wagner's gerbil (38.7%) in comparison to spiny mice *Acomys* spp. Trophozoites morphology was compared with the B. microti King's 67 reference strain. Thirty two isolates derived from *D. dasyurus* over a 9 year period (2004-2012) from two wadies were investigated by microscopic, molecular and phylogenetic analysis. A near-full-length sequence of the 18S rRNA gene and the second internal transcribed spacer (ITS2) region were amplified, sequenced and used for the construction of phylogenetic trees. A novel *Babesia* species was identified in two isolated populations of D. dasyurus. Phylogenetic analysis of 18S rDNA and ITS2 sequences revealed that *B. behnkei* spec. nov. is most closely related to B. lengau from cheetahs (South Africa) and to Nearctic species found only in N. America (pathogenic *B. duncani* and *B. conradae*) and that it is more distant to the cosmopolitan rodent species *B. microti* and *B. rhodaini*. Trophozoites of novel Babesia were smaller and less polymorphic than trophozoites of B. microti. Conclusion: *Babesia behnkei* spec. nov. is a novel species from the 'Duncani group' maintained in isolated populations of *Dipodillus dasyurus* living in Egypt. The ability of this species to infect humans shall be considered. This study was funded by the National Science Center (NCN), Poland, grant OPUS 2011/03/B/NZ6/02090

17/04/2015 Session E6 - (Room 14) - Parasites - Evolution I - Chair: R Post 3:15 PM - 3:30 PM (15 mins)

Session A7 - (Room 11A) - Malaria - Epidemiology

Chair: Dr P Horrocks, University of Keele

Going in under the radar: Cryptic populations of infectious *Plasmodium falciparum* clones

Lynn Grignard[1], Bronner Goncalves[1], Sophie Jones[1], Teun Bousema[2] and Chris Drakeley[1]

[1.] London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, United Kingdom. [2.] Institute for Molecular Life Sciences, Radboud UMC, Medical Microbiology, Geert Grooteplein 28, Nijmegen, 6525 GA, The Netherlands

The transmission dynamics of *Plasmodium falciparum* from the human host to the mosquito vector remain poorly understood. The contribution of low density parasitaemia to transmission and to the reservoir of infection is still under debate. In addition, the detection of low density minority clones is hampered by the stochastic effects of PCR and the volume of human blood analysed in genotyping assays. Here, we present data from MSP2 capillary electrophoresis genotyping in conjunction with direct membrane feeding assays from 4 studies in Burkina Faso and the Gambia. We show that low density clones are very effective in transmitting from human to mosquito and we are able to track transmissible clones from the human host to the mosquito. Furthermore, mosquitoes are better at estimating the multiplicity of infection (MOI) than PCR on human blood samples and hence are important in determining the number of circulating clones making up the reservoir of infection.

17/04/2015 Session A7 - (Room 11A) - Malaria - Epidemiology - Chair: P Horrocks 4:00 PM - 4:15 PM (15 mins)

Development of a novel malaria antibody assay utilizing antigens from all 5 human pathogenic *Plasmodium* species

Andreas Latz, A. Latz*1, J. Völger1, Kesara Na-Bangchang3, A. Longhod2, T. Kwenti2

1NovaTec Immundiagnostica GmbH, R+D, Dietzenbach, Germany 2University of Buea, Department of Medical Laboratory Sciences, Buea,Cameroon 3Thammasat University (Rangsit Campus), Thailand

The proper diagnosis of Malaria disease is essential to provide early treatment and improve the prognosis of patients. Transfusion-transmitted Malaria is rare, but it may produce severe problems in the safety of blood transfusion and blood related products due to the lack of reliable procedure to evaluate donors potentially exposed to malaria. ELISAs are known to be ideal for high throughput screening with high sensitivity and specificity, but it also requires trained personal and an equipped laboratory. Line Blots are often used as confirmatory tests since they provide high sensitivity and specificity. There is nearly no lab equipment needed to perform this kind of assay. In addition, blots can also be used in automated processes for high throughput screening. Here we show an improved

diagnostic performance of the new antibody detection Systems (ELISA and Lineblot) utilizing early and late antigens of all 5 human pathogenic *Plasmodium* species (*P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae*, *P. knowlesi*) compared to test systems only relying on antigens derived from one or two *Plasmodium* species. The novel Lineblot is able to discriminate between all 5 parasite species. Assays with a limited number of antigens often fail to detect antibodies from certain regions of the world. For evaluation purpose, we collected samples from all over the world, including samples from newborns. We evaluated the performance of ELISA and Lineblot directly in endemic countries with samples of patients who presented symptoms akin to malaria infection in local hospitals.

17/04/2015 Session A7 - (Room 11A) - Malaria - Epidemiology - Chair: P Horrocks 4:15 PM - 4:30 PM (15 mins)

Revealing a chronic high burden of non-*Plasmodium falciparum* infection in Uganda: a longitudinal survey in Bukoba village, Mayuge District

J.R. Stothard, M. Betson, S. Clifford, C. Sutherland

Liverpool School of Tropical Medicine & London School of Hygiene & Tropical Medicine, UK

Following from previous observations of a substantive number of non-*Plasmodium falciparum* infection in young children on the shoreline of Lake Victoria, analysis of dried blots spots by qPCR was undertaken in 145 children from Bukoba village over an 18 month period. Results obtained from a longitudinal cohort demonstrated that despite access to regular treatment, prevalence of infections increased through time. The overall prevalence of malaria ranged from 82-96%; infections with *P. malariae* and *P. ovale* exhibited a greater percentage increase than *P. falciparum*. However, *P. falciparum* remained the most prevalent species (81-94%), followed by *P. malariae* (12-48%) and finally *P. ovale* (7-22%), with both sub-species of the later also found. An increasing age was significantly associated with *P. malariae* infections (OR 1.7 95% CI 1.3-2.2 p=0.000) and a positive association between *P. falciparum* and *P. malariae* infection was found at baseline and then subsequently at follow-ups. In addition infection with *Schistosoma mansoni* was found to have a significant association with *P. falciparum* (OR 4.7 95% CI 1.8-12.3) and *P. malariae* infections (OR 3.819 95% CI 1.1-13.1). These observations point to high levels of chronic malaria infections masquerading under the radar more obvious falciparum malaria.

17/04/2015 Session A7 - (Room 11A) - Malaria - Epidemiology - Chair: P Horrocks 4:30 PM - 4:45 PM (15 mins)

Performance of rapid diagnostic test for malaria diagnosis at the different specialized hospitals in Wad Medani, Gezira State, Sudan

Bakri Nour, Magid A. A. Almobark, Albadawi A. Talha, Elgaili M. Elgaili, Dafallah Abuidris , Ali B. Habour, Kamal Osman , Yassir M. Elhassan , and Ahmed Bolad

Blue Nile National Institute for Communicable Diseases, University of Gezira

Malaria is overestimated if the diagnosis is based solely on clinical signs. Therefore, laboratory confirmation is essential. Rapid diagnostic tests (RDTs) have become an essential tool in malaria control and management programmes in the world. RDTs can offer a good alternative with the advantage that it is an easy and rapid method, and may assist in diagnosis and improving the practices prescription. This study aims to evaluate the performance of RDTs for malaria diagnosis. In Wad Medani, Central Sudan. 931 patients with symptoms of malaria attended the outpatient clinics at the different specialized hospitals were enrolled in this study, RDT and blood smears methods were performed to diagnose malaria and blood drop spot were collected in filter paper for nested PCR technique as a confirmative diagnostic tool. The results obtained by this study revealed that, 131/931 (14.1%) and 63/931(6.7%) were positive when performed by microscopy and RDT respectively. Also the finding showed that 68 of 131 positive by microscopy were negative by RDT. The nested PCR confirmed that, 125/925(13.5%) were positive while 6 samples gave an insufficient amount of DNA after extraction, indicating that there is a significant difference between the rates of malaria cases diagnosed by microscopy and RDT (P = 0.001). This study concluded that the implementation of RDT as a diagnostic tool could not be an alternative method to diagnose malaria, and it does not replace malaria microscopy.

17/04/2015 Session A7 - (Room 11A) - Malaria - Epidemiology - Chair: P Horrocks 4:45 PM - 5:00 PM (15 mins)

A simplified molecular diagnostic platform for malaria: the direct on blood PCR-NALFIA system.

Henk Schallig, Johanna Roth and Pètra F. Mens

Royal Tropical Institute, Parasitology Unit, Meibergdreef 39, 1105 AZ Amsterdam, The Netherlands

Molecular tools allow for specific and sensitive malaria diagnosis, but current formats, like PCR with gel-electrophoresis, are difficult to implement in resource poor settings. Therefore, a simple, fast, sensitive and specific molecular diagnostic platform, the direct on blood (db)PCR combined with nucleic acid lateral flow immunoassay (NALFIA) to detect amplified PCR products of *Plasmodium*, including species differentiation, and human GAPDH (internal amplification control) was developed. This test format circumvents need of DNA extraction and complex read-out systems. The platform was evaluated under laboratory conditions, a multi country ring trial and in two malaria endemic countries (Burkina Faso and Thailand). Analytical sensitivity and specificity of the dbPCR-NALFIA in a single laboratory evaluation was >95% and the test was able to detect less than 1 parasite/µl blood. All four laboratories in the ring trial reported ease of use of the system and could successfully perform the protocol. Overall laboratory inter-variability was low and the agreement of reported results was high. Field evaluations by local staff without prior training in performing the dbPCR-NALFIA in malaria endemic countries, Thailand and Burkina Faso, were performed and will be reported. The prototype dbPCR-NALFIA test will now be moved forward in diagnostic test development (supported by EU funding: www.diagmal.eu) to provide a molecular diagnostic test to detect malaria in for example near elimination settings. The final format will include a closed transfer unit to reduce possible workspace contamination with amplicons. The further use as a diagnostic platform for undifferentiated fevers is being explored.

17/04/2015 Session A7 - (Room 11A) - Malaria - Epidemiology - Chair: P Horrocks 5:00 PM - 5:15 PM (15 mins)

Session B7 - (Room 11B) - NTDs - Drugs

Chair: Dr O Millington, University of Strathclyde

Towards better drugs for trematode infections: field successes from pharmacokinetics to clinical trials
Jennifer Keiser

Swiss Tropical and Public Health Institute, Basel

Infections with helminths are responsible for a main part of the global health burden associated with neglected tropical diseases. Large scale administration of anthelminthics is the front-line intervention to control morbidity ("preventive chemotherapy") of helminth infections. However, few drugs are available, which have limitations and the drug discovery and development pipeline is empty. New broad spectrum therapeutics should therefore be discovered and developed. In addition, a better use of existing treatments should be explored. In this presentation I will share two examples of our work in anthelminthic R&D. First, tribendimidine is a broad-spectrum anthelminthic drug that was recently approved for the Chinese market for the treatment of hookworm and *Ascaris lumbricoides* infections. Our laboratory in-vitro and in-vivo studies showed that tribendimidine has considerable activity against *Opisthorchis viverrini*. Following our bench to field approach we pursued different clinical trials with tribendimidine in the treatment of *O. viverrini* infected humans in Laos, ranging from Phase 2a dose-finding trial in children and adults, pharmacokinetic (PK) studies and a Phase 2b clinical trial. The second example will focus on schistosomiasis. At present, praziquantel is widely used off label at a standard dose of 40 mg/kg to treat preschool-aged children, as this is the dose used for school-aged children and adults. However, the effective dose for children below the age of 4 years is not known and PK)data are sparse. We developed and validated a liquid chromatography-mass spectrometry (LC-MS/MS) technique for the determination of praziquantel using dried blood spots. In central Côte d'Ivoire we conducted a dose-finding and PK trial in *Schistosoma mansoni* infected pre-school and school-aged children and first results will be presented.

17/04/2015 Session B7 - (Room 11B) - NTDs - Drugs - Chair: O Millington 4:00 PM - 4:30 PM (30 mins)

On the way to new drugs against schistosomiasis – (SP)
Noemi Cowan[1,2], Philipp Dätwyler[2,3], Beat Ernst[2,3], Thomas Spangenberg[3], Chunkai Wang[4], Jonathan Vennerstrom[4], Ivan Yaremenko[4], Igor Krylov[4], Alexander Terent'ev[4], and Jennifer Keiser[1,2]

[1.]Department of Medical Parasitology and Infection Biology, Swiss Tropical and Public Health Institute, P.O. Box, CH-4002 Basel, Switzerland; [2.]University of Basel, P.O. Box, CH-4003 Basel, Switzerland;

[3.] *Institute of Molecular Pharmacy, University of Basel, Klingelbergstrasse 50, CH-4056 Basel, Switzerland;* [4.] *College of Pharmacy, University of Nebraska Medical Center, 986025 Nebraska Medical Center, Omaha, NE, USA*

Schistosomiasis (bilharzia) is a neglected tropical disease, affecting hundreds of millions of people living in poor conditions, impairing their life quality for decades. The mainstay of control is preventive chemotherapy with exclusive use of praziquantel, a safe and cost-effective drug. Nevertheless, research for new drugs with different modes of actions are required to lower drug pressure and anticipated drug resistance. Over the last years, we tested numerous compounds for antischistosomal activity, including artemisinin inspired peroxidic anologes, N,N'-diarylurea derivatives and marketed anticancer drugs. Trioxolanes, demonstrated high activities against larval and adult stage of *Schistosoma mansoni* in vitro, inhibiting parasite activity to 50% at concentrations (IC50) of 2.2 µM and 4.2 µM, respectively, and revealed a worm burden reduction (WBR) of up to 44% in the mouse model. The selectivity index (SI) of 1.6 indicated slight selective activity against schistosomes as opposed to toxicity against a mammalian cell line. N-phenyl benzamide, a N,N'-diaryluea derivative, indicated potential for a moderate to good pharmacokinetic profile, high in vitro activity against *S. mansoni* larvae (IC50=0.2 µM), and adult flukes (IC50=0.6 µM) and an SI of 4.9. The drug achieved a WBR of 66%. Of the anticancer drugs, trametinib, a kinase inhibitor with a long half-life showed the best results against *S. mansoni* larvae (IC50<33.3µM) and adult flukes (IC50=4.1 µM), and a WBR of 84%. Our research for new drugs against schistosomiasis revealed different chemical classes with great potential, which should be researched further.

17/04/2015 Session B7 - (Room 11B) - NTDs - Drugs - Chair: O Millington 4:30 PM - 4:45 PM (15 mins)

A lack of adaptive mutations in the gene coding for the multi-drug transporter SMDR2 suggests that it does not directly confer resistance to praziquantel in the human blood fluke *Schistosoma mansoni* – (SP)

Billie Francesca Norman[1], Ruth S. Kirk[1], Anthony J. Walker[1], Poppy H. Lamberton[2], Joanne P. Webster[3], Scott P. Lawton[1]

[1.] *School of Life Sciences, Kingston University London;* [2.] *Dept. of Infectious Disease Epidemiology, Imperial College London;* [3.] *Dept. of Pathology and Pathogen Biology, Royal Veterinary College*

Schistosomiasis is of considerable concern to global health, with more than 200 million people infected in the tropics and subtropics. Praziquantel (PZQ) is the current drug of choice for treatment but resistance or reduced susceptibility to PZQ has been reported in various isolates of *Schistosoma mansoni*, a major cause of hepatointestinal schistosomiasis throughout Africa. PZQ resistance is genetically inherited but the genes that confer the resistance remain to be identified, primarily due to a lack of understanding of the mode of action of PZQ and a clear phenotypic measure of reduced susceptibility. In other helminths, single nucleotide polymorphisms (SNPs) are associated with drug resistance and it has previously been suggested that SMDR2 (a multi-drug transporter) could be involved in PZQ resistance. Therefore, it was hypothesised that SNPs in SMDR2 may be present in PZQ resistant laboratory isolates of *S. mansoni*. The exons of SMDR2 were sequenced from a resistant isolate and

compared to PZQ susceptible isolates from different geographical locations. This showed a lack of non-synonymous mutations, although allelic variants were identified. The SMDR2 protein was also modelled in silico and interactions with PZQ were measured; suggesting that although SMDR2 does interact with PZQ, it is not the specific drug target. Therefore, it was concluded that although SMDR2 may not be responsible for PZQ resistance, it is likely to be involved in a more complicated detoxification physiological response to PZQ.

17/04/2015 Session B7 - (Room 11B) - NTDs - Drugs - Chair: O Millington 4:45 PM - 5:00 PM (15 mins)

The benefits of collaboration between pharma and academia: the anti-*Wolbachia* drug discovery story – (SP)

Rachel Clare[1], Roger Clark[2], Catherine Bardelle[2], Paul Harper[2], Matthew Collier[2], Kelly L. Johnston[1], Laura Myhill[1], Andrew Cassidy[1], Kevin Cross[2], Helen Plant[2], Eileen McCall[2], Louise Ford[1], David Murray[2], Kirsty Rich[2], Mark Wigglesworth[2], Stephen A. Ward[1] and Mark J. Taylor[1]

[1]Department of Parasitology, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, L3 5QA, UK; [2]AstraZeneca, Discovery Sciences, Alderley Park, Cheshire, SK10 4TG, UK

The Anti-*Wolbachia* consortium (A·WOL) at the Liverpool School of Tropical Medicine (LSTM) has partnered with the Global High Throughput Screening (HTS) Centre at AstraZeneca (AZ) in the first open access HTS project for the World Intellectual Property Organization's (WIPO) Re:Search program against Neglected Tropical Diseases. The A·WOL consortium aims to identify novel macrofilaricidal drugs targeting the essential bacterial symbiont (*Wolbachia*) of the filarial nematodes causing onchocerciasis and lymphatic filariasis. The current in vitro assay carried out at LSTM was the basis for the development and validation of a new screen utilizing antibody based techniques, compatible with a BioCel system (Agilent) for automated staining as well as TTP Acumen® (Laser scanning cytometer) and Perkin Elmer EnVision® (whole well fluorescence) plate readers, to aid an increased throughput. This assay enabled screening of 1.3 million compounds from AstraZeneca's chemical library in just a 3 month single screening activity. Additionally we were able to organize and complete the screening of a ½ million compound library from Medicines for Malaria Venture (MMV) in just 6 weeks. This assay has dramatically decreased our screening timelines from years to months and has resulted in greater than 20,000 anti-*Wolbachia* hits. Hits were classed as compounds with greater than 80% *Wolbachia* depletion at 10µM, with no greater than 60% reduction in cell number. We are currently triaging this large number of hits to identify those to progress for potential new macrofilaricides as part of the A·WOL drug discovery program.

17/04/2015 Session B7 - (Room 11B) - NTDs - Drugs - Chair: O Millington 5:00 PM - 5:15 PM (15 mins)

PK/PD Modelling Predicts High Dose Rifampicin Can Achieve Rapid Elimination of *Wolbachia* from filarial nematodes

Ghaith Aljayyoussi, Hayley Tyrer, David Waterhouse, Jill Davies, Achim Hoerauf, Sabine Specht, Ute Klarmann, Louise Ford, Joseph Turner, Mark Taylor, Steve Ward

Liverpool School of Tropical Medicine, Liverpool, UK

The Anti-*Wolbachia* (A•WOL) programme aims to find safe macrofilaricides for lymphatic filariasis and onchocerciasis through targeting the *Wolbachia* bacterial endosymbiont. Doxycycline demonstrates proof of concept to achieve depletion of *Wolbachia* leading to macrofilaricidal activity when administered for a period of 4-6 weeks. The prolonged period of treatment and exclusion of key target groups (pregnancy and children <8) restricts the widespread scale-up of doxycycline for use in elimination programmes. The A•WOL programme aims to identify new drugs and regimens that can reduce the treatment period to 7 days or less and be used in currently restricted groups. In this study we show that clinically relevant high doses of rifampicin can lead to *Wolbachia* elimination rates from adult worms that are several times faster than elimination rates achieved by doxycycline. Using systemic dose escalation studies in the A•WOL mouse screening model we show that Rifampicin can achieve >90% *Wolbachia* elimination in time periods of 7 days or less resulting in marked macrofilaricidal activity at later stages. Using pharmacokinetic/pharmacodynamic (PK/PD) modelling and mouse-human bridging analysis, we show that high doses of rifampicin, which could be safely administered to eligible populations should reduce treatment times to 7 days or less. Clinical trials are planned to test these findings in human lymphatic filariasis and onchocerciasis.

17/04/2015 Session B7 - (Room 11B) - NTDs - Drugs - Chair: O Millington 5:15 PM - 5:30 PM (15 mins)

Session C7 - (Room 11C) - Vectors - Host/Parasite Interactions II

Chair: Dr L Reimer, Liverpool school of Tropical Medicine

Multihost pollinator pathogens: old and new – (SP)

David Pascall[1], Lena Wilfert[1], Darren Obbard[2], Sam Braine[1]

[1.] Daphne du Maurier Building Centre for Ecology and Conservation College of Life and Environmental Sciences University of Exeter, Penryn Campus, TR10 9FE, UK; [2.] Institute of Evolutionary Biology, University of Edinburgh, The Kings Buildings, Ashworth Laboratories, Charlotte Auerbach Road Edinburgh,EH9 3FL, UK

Many, perhaps even most, pathogens can survive in multiple hosts. Despite this, the study of the ecology and evolution of pathogens in the context of their entire host range is in its infancy. In this study we examined whether and how pathogens differ in their host choice across space. UK bumblebees provide a tractable system with which to study this. Across the temperate regions, bumblebees form multispecies assemblages with significant niche overlap, providing ample opportunities for

between-species transmission. As a group, they were previously known to habour 6 multihost RNA viruses, as well as several unicellular multihost pathogens. On top of these known pathogens, we identified 4 novel multihost RNA viruses in wild bumblebees. We tested for a subset of the known viruses and all of the novel viruses in multiple species at multiple sites across the UK. This data showed that these viruses are multihost pathogens, but that they vary in their degree of generalism. The distribution and prevalence of viruses correlates with host ecology across habitats.

17/04/2015 Session C7 - (Room 11C) - Vectors - Host/Parasite Interactions II - Chair: L Reimer 4:00 PM - 4:15 PM (15 mins)

Onchocerciasis transmission in Ghana: effect of vector species on biting rates, transmission potentials and the human blood index

Poppy Lamberton[1], Robert A Cheke[1,2], Rory J Post[3,4], Peter Winskill[1], J Lee Crainey[4,5], Martin Walker[1], Daniel A Boakye[6], Mike Y Osei-Atweneboana[7], Nana-Kwadwo Biritwum[8], Iñaki Tirados[2,9], Michael D Wilson[5], Anthony Tetteh-Kumah[8], Sampson Otoo[5], María-Gloria Basañez[1]

[1.]Department of Infectious Disease Epidemiology, School of Public Health, Imperial College London, St Mary's Campus, London, W2 1PG, UK; [2.]Natural Resources Institute, University of Greenwich at Medway, Central Avenue, Chatham Maritime, Kent, ME4 4TB, UK; [3.]School of Natural Sciences and Psychology, Liverpool John Moores University, Byrom Street, Liverpool L3 3AH, UK; [4.]Disease Control Department, London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT, UK; [5.]Fiocruz Amazônia, Manaus, Brazil; [6.]Noguchi Memorial Institute for Medical Research, University of Ghana, Legon, Accra, PO Box LG581, Ghana; [7.]Water Research Institute, Council for Scientific and Industrial Research, Accra, PO Box M32, Ghana; [8.]Ghana Health Service, Private Mail Bag, Ministries, Accra, Ghana; [9.]Liverpool School for Tropical Medicine Pembroke Place, Liverpool, Merseyside L3 5QA

The World Health Organization has set goals for the elimination of human onchocerciasis by 2025 in selected African countries. The feasibility of achieving elimination depends on the level of initial endemicity, geographical and therapeutic coverage, treatment compliance, and patterns (intensity and seasonality) of transmission, including species composition of the simuliid vectors and their vectorial capacity. Ghana has a great diversity of *Simulium damnosum* complex species, which are the vectors of Onchocerca volvulus. We present spatial and temporal patterns in biting rates, Onchocerca spp. transmission and bloodmeal host choice of ovipositing and host-seeking blackflies in seven Ghanaian communities with different vector control and ivermectin treatment histories. Monthly biting rates ranged from 714 bites/person/month at Agborlekame (100% S*. damnosum* s.str./*S. sirbanum*, in the savannah region) to 8,586 bites/person/month at Pillar 83/Djodji (98.5% S. squamosum, in the forest mosaic). Parous rates were higher in the dry (41.8%) than in the wet (18.4%) season. Monthly transmission potentials ranged from zero to 422 infective larvae/person/month. Onchocerca spp. larvae were molecularly identified as *O. volvulus*. The human blood index ranged from 0.65 for S. yahense, 0.73 for S. sanctipauli, and 0.74 for S. damnosum s.str./sirbanum to 0.88 for *S. squamosum* and 0.92 for S.

soubrense Beffa form. Our results show that host choice varies between vector species, and may be affected by vector and/or host density with epidemiological relevance for vector-borne disease models.

17/04/2015 Session C7 - (Room 11C) - Vectors - Host/Parasite Interactions II - Chair: L Reimer 4:15 PM - 4:30 PM (15 mins)

A cross-sectional survey of fly populations and latrine condition in trachoma-hyperendemic communities of the Bijagos Archipelago of Guinea-Bissau – (SP)

Lucy Stubbs

University of Birmingham,Edgbaston, Birmingham, West Midlands B15 2TT

Background The eye-seeking fly *Musca sorbens* is a known trachoma vector. The presence of flies around latrines has been associated with trachoma infection in Guinea-Bissau, however these flies have not been speciated. Methods This was a cross-sectional observational study. 84 households were selected using cluster randomised sampling and data were collected on latrine condition using a standardised questionnaire and survey. Fly papers were hung for three days at 52 latrines and control locations. Univariable and multivariable regression modeling were used to identify associations between latrine condition variables and number of flies caught. Results *M. sorbens* accounted for 2.2% of flies at latrines and 0% of flies at controls. There was a strong association between both full latrines and latrines that were collapsing and finding more flies present when compared with less full or intact latrines. Conversely there was a strong association between the presence of a surrounding fence and finding fewer flies. Conclusions Evidence for the role of flies as a trachoma vector in Guinea-Bissau is lacking. *M. sorbens* are present here, although in small numbers. Other fly species should not be discounted as vectors. The total number of flies caught was associated with elements of latrine condition, which may provide targets for latrine maintenance.

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Development of a new generation vaccine against *Dermanyssus gallinae*, the poultry red mite

Tatiana Kuster, James Pritchard, Fiona Tomley

Royal Veterinary College Hawkshead Lane, North Mymms, AL9 7TA

Dermanyssus gallinae is currently the most important ectoparasite to affect egg-laying chickens. Currently, control is limited to the use of acaricides; however, use of pesticides raises important questions about public health and drug resistance, which in turn promotes the development of alternative approaches to control. Here, we build on the successful development of a tick vaccine based on the gut antigen Bm86 by mining next-generation sequence data to select mite membrane proteins: a functional genomics approach will then be utilised to express and localise these employing

immunohistochemistry. The candidates, aquaporin, excitatory aminoacid transporter and lysophospholipid acyltransferase were selected based on their respective predicted transmembrane domains and low homology with host proteins. Following recombinant expression of candidates, we will test their efficacy as potential vaccines using an animal model, in this case a mouse model. Despite being an ectoparasite of chickens, *D. gallinae* shows remarkable low host specificity. The validation of an animal model in mice rather than in chicken would be preferable due to the absence of feathers and more suitable husbandry for the recovery of the mites. Part of this project consists on developing and optimizing an animal model for red mite infestation. The development of a vaccine has the potential to decrease or eliminate red mite infestation without the use of acaricides and thus reduces risk for the development of drug resistant parasite populations. Additionally, a vaccine has the potential to alleviate the financial impact caused by red mite infestations and to increase the general welfare of chickens.

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The importance of freshwater snails in local transmission of urogenital schistosomiasis and the identification and characterization of transmission hot-spots in Zanzibar

Tom Pennance, Alipo N. Khamis, Mtumweni Ali Muhsin, Khalfan A. Mohammed, David Rollinson, Stefanie Knopp

Natural History Museum, London, UK

Urogenital schistosomiasis has been successfully controlled in Zanzibar over the past years and achieving elimination now seems feasible. Despite of large-scale control interventions for multiple years, *Schistosoma haematobium* infection prevalence remains high in certain communities. We aimed to characterize selected “hot-spot” communities in terms of accessibility to natural freshwater bodies (FWBs) and safe water sources (SWSs) to better target future control interventions. In June/July 2014, surveys were conducted in five hot-spot study areas with a *S. haematobium* prevalence >15% and two control areas with a prevalence <5%. Natural FWBs and SWSs were identified and mapped. The transmission potential of FWBs was determined by assessing the presence of *S. haematobium* cercariae shedding *Bulinus globosus* intermediate host snails. Hot-spot communities had considerably more (average=12) FWBs than control areas (average=2), and on average five times as many FWBs containing B. globosus (7.8 versus 1.5). Only *B. globosus* from hot-spot areas shedded cercariae. Distances from schools to the closest FWB containing *B. globosus* were significantly shorter in hot-spot (0.26km 95%confidence Interval (CI)) than control areas (0.72km 95%CI). On average, control communities had fewer SWSs than hotspot areas (38 versus 45). Urogenital schistosomiasis transmission is very focal. The presence of FWBs in close proximity to schools seems to increase the risk for infection / transmission of *S. haematobium*. A higher availability of SWSs seems not to reduce the risk of transmission. Control measures in hot-spot communities should focus on intensified snail control and behavior change interventions to reduce human contact with infested FWBs and hence transmission.

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Session E7 - (Room 14) - Parasites - Evolution II

Chair: Prof R Post, John Moores University Liverpool

Host range of RNA viruses predicts transmission and virulence of human infections – (SP)
Liam Brierley, Amy B. Pedersen, Mark E.J. Woolhouse

Centre for Immunity, Infection and Evolution, Institute of Evolutionary Biology, Ashworth Laboratories, University of Edinburgh King's Buildings, Charlotte Auerbach Road, Edinburgh EH9 3FL, UK

Most human pathogens, particularly newly emerging pathogens, have zoonotic origins. Comparative analyses show that non-human host ranges of pathogens affects risk of human infection, e.g. host shifts are more likely to be successful if the novel and new host are closely related. However, recently observed trends in emerging diseases suggest transmission dynamics and virulence may also depend on host range, though there have been few attempts to explore this systematically. Using mammalian RNA viruses as a study system, we aim to quantify how host type (taxonomic order) and breadth (taxonomic and phylogenetic range) predict virus traits, specifically transmission route, human-to-human transmissibility and virulence in humans. Data on virus traits and non-human mammalian host ranges were collected by extensive, systematic literature searches, and spanned 331 RNA virus species, 180 of which are known to infect humans. Correcting for sampling effort of both hosts and viruses, and within-virus species diversity, we modelled virus traits using mixed regression models.
Vector-transmitted viruses exhibited greater diversity of host taxonomic orders, whereas viruses causing severe clinical disease exhibited greater diversity of host species, but not orders. We also observed higher risk of human-to-human transmission among viruses shared with primates, suggesting viruses infecting closely related hosts are more likely to adapt to humans. We show empirically that non-human host ranges are associated with characteristics of human infections, supporting the recently advocated 'One Health' perspective. These models contribute to a growing set of 'ecological' predictive models surrounding infectious disease emergence, which could ultimately inform public health and surveillance strategies.

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The Hepatozoon species (Adeleorina: Hepatozoidae) of African bufonids – (SP)
Edward Netherlands, Courtney A. Cook, Nico J. Smit

Unit for Environmental Sciences and Management, North-West University, Potchefstroom, South Africa

Haemogregarines include a large group of apicomplexan blood parasites, many of these found parasitizing ectothermic vertebrates such as anurans. All anuran haemogregarines within the genus *Haemogregarina* Danilewsky, 1885 were reassigned in 1996 to the genus *Hepatozoon* Miller, 1908. Most (11/15, 73%) African anuran Hepatozoon species have been recorded from the family Bufonidae, however, all these were until now from only two host species, *Amietophrynus mauritanicus* (Schlegel, 1841) and *Amietophrynus regularis* (Reuss, 1833) from Northern and central Africa. The only description of an anuran haemogregarine from South Africa was *Hepatozoon theileri* (Laveran, 1905), parasitizing *Amietia quecketti* (Boulenger, 1895). Thin blood smears and whole blood were collected from 32 *Amietophrynus garmani* (Meek, 1897), 12 *Amietophrynus gutturalis* (Power, 1927), and nine *Amietophrynus maculatus* (Hallowell, 1854), in Ndumo Game Reserve and Kwa Nyamazane Conservancy, KwaZulu-Natal, South Africa. Morphometrics (light microscopy and TEM) and molecular work (using fragment 18S rDNA) was used to characterize haemogregarine isolates from the above three anuran species. Resulting morphometrics and sequences were compared to each other as well as to comparative haemogregarine sequences from GenBank. Both morphological characteristics and molecular findings supported that all haemogregarine isolates from all three Amietophrynus species were one of the same, a species of Hepatozoon. Furthermore, this species was found to be morphologically distinct from other previously recorded Hepatozoon, supporting its description as *Hepatozoon ixoxo* sp. nov.

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Host barriers to cross-species emergence of rabies virus

Nardus Mollentze[1], Katie Hampson[1], Daniel G. Streicker[1,2], Mafalda Viana[1], Pablo Murcia[2], Roman Biek[1]

[1.] *Institute of Biodiversity, Animal Health & Comparative Medicine, University of Glasgow, Glasgow, G12 8QQ;* [2.] *MRC-University of Glasgow Centre for Virus Research, Glasgow, G61 1QH*

Although most emerging diseases are caused by multi-host pathogens, the determinants of host range and of the pathogen's ability to emerge in a new host are poorly understood. Previous work across many different pathogens has shown that host relatedness positively predicts successful cross-species transmission, but the mechanisms underlying this effect are often unclear. We have been investigating the host barriers to viral host shifts using rabies virus as our model. Rabies virus is capable of infecting all mammals, but is maintained in epizootics by only a small number of species. Through a meta-analysis of 31 cross-species infection experiments involving 42 unique combinations of donor and recipient species, we have found that rabies virus virulence scales with host phylogenetic distance, with more distantly related hosts being killed faster. Furthermore, differences in body-temperature between hosts had a strong effect on virulence, with viruses killing their host faster if they originated in a donor species with lower body temperature than the recipient. These effects come into play only during the short morbidity period when the host is infectious, and can therefore be expected to have a big impact on the probability of successful onward transmission in the new host species. Our work shows a virulence-transmission tradeoff for cross-species transmission in rabies virus and identifies host body temperature

as a potential barrier to successful host invasion. These mechanisms are likely to be relevant to a much broader range of multi-host pathogens.

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The molecular basis of parasitism in the nematode *Strongyloides ratti*

Vicky Hunt[1], Avril Coghlan[2], Bernardo Foth[2], Nancy Holroyd[2], Taisei Kikuchi[3], Nadine Randle[4], Adam Reid[2], Diogo Ribeiro[2], Jason Tsai[5], James Lok[6], Jonathan Wastling[4], Matt Berriman[2] & Mark Viney[1]

[1] School of Biological Sciences, University of Bristol, Bristol BS8 1UG, UK; [2] Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, CB10 1SA, UK; [3] Division of Parasitology, Department of Infectious Diseases, Faculty of Medicine, University of Miyazaki, Miyazaki 889-1692, Japan; [4] Institute of Infection and Global Health, University of Liverpool, Liverpool, L3 5RF, UK; [5] Institute of Molecular Biology, Academia Sinica, Taiwan, R.O.C.; [6] Department of Pathobiology, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA 19104

The *Strongyloides* lifecycle includes a parasitic female-only stage, which inhabits the small intestine of its host, and a facultative, dioecious free-living adult generation. These adult life-cycle stages are genetically identical, so that comparing parasitic and free-living stages offers an almost unique opportunity to discover the molecular adaptations required to be a successful parasitic nematode. We have used quantitative mass spectrometry and RNAseq analyses to compare the proteome and transcriptome of parasitic and free-living females of *S. ratti*, a parasite of rats. We have also analysed RNAseq data for S. stercoralis, a parasite of humans. We find that ~18% of genes are differentially expressed between parasitic and free-living stages in both species. Two key gene families dominate the transcriptome of the parasitic female: astacins of the zinc-metallopeptidase family and SCP/TAPS. Many of the genes with upregulated expression in the parasitic stage, including astacins and SCP/TAPS, are physically clustered in the genome. Clusters comprise 2-18 adjacent genes, mostly from the same gene families and therefore with likely similar functions. These gene families are therefore likely to be key to parasitism in Strongyloides. A genome-wide study of four *Strongyloides* spp., two closely related species from the same evolutionary clade, *Parastrongyloides trichosuri* and *Rhabditophanes* sp., and eight outgroup nematode species spanning four further clades has identified an expansion of the astacins and SCP/TAPS gene families coinciding with the evolution of the Strongyloides genus.

17/04/2015 Session E7 - (Room 14) - Parasites - Evolution II - Chair: R Post 4:45 PM - 5:00 PM (15 mins)

The evolution of life history traits in response to drug selection – (SP)

Alan Reynolds, Jan Lindström, Paul Johnson, and Barbara Mable

University of Glasgow, Institute of Biodiversity, Animal Health and Comparative Medicine. Graham Kerr Building, Glasgow, G12 8QQ.

Resistance management is a key concern in human and veterinary medicine and in agricultural production systems. Although theoretical population genetics models predict factors that might influence resistance evolution in pathogens, potential interactions between life history and specific control measures remain unclear. Previously, we found that population density played a role in the evolution of resistance in selected lines of free-living *Caenorhabditis remanei*. An evolved response in survivorship to drug application was observed in lines selected under drug-treated conditions, as well as in lines where mortality was simulated randomly, at the same rate as caused by drug treatment. In order to assess whether there were changes in life history that could explain the apparent density-dependent effects, we measured size at maturity, life-span and reproductive output in both drug-treated and drug-free environments. Size at maturity increased in response both to drug treatment and random mortality. Interestingly, drug treatment selected for longer life span and increased reproductive output whereas the random mortality treatment showed no such response. Therefore, though both drug and random mortality treatments induced higher survival in drug treated environments, life-history traits of nematodes from the two treatments did not respond in the same way. This differing response to alternative sources of extrinsic mortality suggests that the evolution of life-history traits may result in unexpected outcomes when control measures are applied. Failing to take into account such responses in parasitic species could result in adverse outcomes, such as larger more fecund parasites.

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Plenary Sessions 4, 5, 6, 7 - (Room 1A) –

Chairs - Prof J Smith, BSP President/Univeristy of Salford &

Prof M Taylor, BSP Vice-President/Liverpool School of Tropical Medicne

2015 C A Wright Lecture

J Rayner

The Sanger Centre , UK

NTD research priorities at the Bill & Melinda Gates Foundation

Julie Jacobson

BMGF, USA

For over 15 years the Bill & Melinda Gates Foundation has been supporting biomedical research on a variety of tropical diseases, from malaria to schistosomiasis. In this talk I briefly review past progress and go on to highlight new our research agenda with looking forward to 2030 targets of the sustainable development goals.

Developing drugs for neglected tropical diseases

Robert Don

DNDi, Switzerland

DNDi acts in the public interest to address the needs of patients suffering from the most neglected communicable diseases. Bridging existing R&D gaps, DNDi has become a solid platform to collaborate with the international research community, the public sector, the pharmaceutical industry as well as other relevant stakeholders and has developed new formulations of existing drugs as well as new identifying new drug targets. Current research activities concerning leishmaniasis, human African trypanosomiasis and filarial disease will be discussed.

Drugs for malaria for today and tomorrow

Jeremy Burrows,

Medicines for Malaria Venture

Malaria is a devastating disease affecting millions of people each year yet, surprisingly, apart from Artemisinin Combination Therapies (ACTs) there are relatively few effective treatments for *Plasmodium falciparum* and only one complete treatment for *Plasmodium vivax*. This presentation will detail Medicines for Malaria Venture's (MMV's) mission to reduce the burden of malaria in disease-endemic countries by discovering, developing and facilitating delivery of new, effective and affordable antimalarial drugs in collaboration with international partners. Our challenging vision to ultimately eradicate the disease requires drugs that will not only cure patients of all human relevant blood stage malaria, but will also disrupt the life-cycle through blocking transmission, preventing infection or relapses (in *Plasmodium vivax*). MMV manages a significant antimalarial pipeline and this has been strengthened in recent years with the delivery of new artemisinin combination therapies, promising new clinical candidates and early stage discovery projects. The talk will explain both the challenges that need to be overcome and the strategy adopted to eradicate the disease, including definitions of target product and candidate profiles necessary for asexual blood stage cures (including single dose combination treatment), transmission blocking, vivax and chemoprotection. In addition, MMV's progress towards our vision and learnings from the malaria drug discovery experience to other neglected diseases, particularly in the context of the MMV Malaria and Pathogen box projects, will be shared.

18/04/2015 Plenary Sessions 4,5,6,7 - (Room 1A) - Chairs - Prof J Smith - Salford & Prof M Taylor - Liverpool School of Tropical Medicne 10:30 AM - 11:00 AM (30 mins)

Poster Abstracts

P## indicates the poster board this is on and (SP) indicates that they are eligible for the student prize completion.

Discovery of an Akt-like protein kinase in the human parasite Schistosoma mansoni - P13 (SP)

Maxine Mckenzie, Ruth S. Kirk, Anthony J. Walker

School of Life Sciences, Kingston University, KT1 2EE, UK

Protein kinases are intracellular signalling enzymes, fundamental to the co-ordination of cellular function. We know little about the mechanisms of activation and downstream functional responses of the 252 protein kinases in *Schistosoma mansoni*. Our research focuses on the Akt signalling pathway in S. *mansoni*, which in humans is regulated by phosphoinositide 3-kinase (PI3K) and plays a role in insulin signalling, glucose metabolism and transcriptional regulation. Western blotting demonstrated that three anti-phospho Akt (mThr-308, pThr-308, pTyr-315) antibodies recognise a conserved phosphorylated motif, and an antibody against total Akt detects an Akt-like protein kinase in insulin treated S. *mansoni* schistosomules. This Akt phosphorylation (activation) was blocked by incubating schistosomules in Akt inhibitor X. Immunoprecipitation of phosphorylated Akt from protein extracts of insulin treated adult worms and schistosomules with anti-phospho Akt (mThr-308) antibodies, demonstrated that the immunoreactive Akt-like protein possessed kinase activity towards the downstream substrate glycogen synthase kinase 3 (GSK-3) in both life stages. Immunohistochemistry of schistosomules, using the validated anti-phospho Akt antibodies, revealed that phosphorylated (activated) Akt was primarily located in the tegument. In adult worms, activated Akt localised throughout the worm tegument, particularly in the tubules, and along the edge of the gynacophoric tract of the male worms, indicating that Akt may play a role in the signalling that occurs between male and female schistosomes.

Neoblast proliferation supports growth and longevity of in vitro maintained *Fasciola hepatica* juveniles - P69

Paul McCusker, Paul McVeigh[1], Vignesh Rathinasamy[2], Hayley Toet[2], Erin McCammick[1], Anna O'Connor[1], Nikki J. Marks[1], Angela Mousley[1], Gerard P. Brennan[1], Terry W. Spithill[2], Aaron G. Maule[1]

1 Institute for Global Food Security, School of Biological Sciences, Queen's University Belfast, UK;
2 Department of Animal, Plant and Soil Sciences, and Centre for AgriBioscience, La Trobe University, Bundoora, Australia

The liver fluke *Fasciola hepatica* is the cause of considerable economic and health burdens around the world with an estimated global cost to the agriculture industry of $3.2 billion and 17 million humans infected. The infective juvenile stage of this neglected tropical disease causing parasite has long been the focus for research into novel drug and vaccine targets. However, with rapidly improving genomic/transcriptomic data for fluke there is a pressing need for new functional genomics tools that facilitate research on liver fluke biology. A hurdle to gene function studies is the inability to maintain developing liver fluke in vitro. Here, we report the development of a culture system that stimulates

juvenile fluke growth and development; supporting 80% survival for more than 200 days (more than two fold longer than in any previous study). These juveniles display developmental changes in the tegument, reproductive system and gut that are consistent with those reported in vivo. We have found that juvenile fluke growth and development is supported by the proliferation of neoblast-like cells (putative totipotent stem cells), which originate throughout the parenchyma. Once formed, these cells migrate, differentiating into mature cells in distinct tissues. In summary, we present enhanced methods for the maintenance of juvenile fluke in vitro that will enable the study of developmental biology in juvenile fluke. This work was supported by a Glover Memorial Scholarship grant to PMcC and BBSRC grant BB/K009583/1.

Hight Throughput Drug Sensitivity **Testing Methods for Human Parasite *Trichomonas vaginalis* - P80**

Manal J. Natto, Anthonius A. Eze and Harry P. de Koning

University of Glasgow

Trichomonas vaginalis is a protozoan parasite of humans responsible for the sexually transmitted disease, trichomoniasis. Nearly 250 million new cases of the disease occur worldwide every year. The disease is often associated with increased susceptibility to other infections such as HIV, low birth rates and preterm delivery. Metronidazole has been the standard treatment of trichomoniasis since the early 1960s, however an increasing number of cases with metronidazole-resistant strains is being reported. This situation calls for drug-screening in order to identify potential new treatments for trichomoniasis. To date, drug-screening have proved to be unviable for high throughput testing, as the standard procedure still remains the microscopic evaluation of drug-exposed in vitro cultures of *T. vaginalis*. To speed up this process, we developed two separate in vitro protocols that use fluorescent dyes and allow for standardized drug sensitivity testing on the required scale. The first assay is a modification of the resazurin method, in which further reduction of the indicator dye to the colourless compound, dihydroresorufin, is produced only by live parasites, fulfilling the requirements for a genuine viability indicator. The second assay is based on the dye propidium iodide, which becomes highly fluorescent upon binding with parasite DNA in cells permeabilised using digitonin. This approach has the advantage that it does not require incubation with live cells. Both assays have been fully validated for 96-well plate formats and should be adaptable to 384-well formats. Keywords: *Trichomonas vaginalis*; drug screening; metrodinazole; drug resistances; resazurin; resorufin; propidium iodide.

RNA interference: A novel method for the control of African Trypanosomiasis - P37 (SP)

Natasha Aghtarafi, Lee Rafuse Haines [2], Alvaro F. Acosta-Serrano [2], Paul J. Dyson [1] and Miranda M. A. Whitten [1]

1 Institute of Life Science, College of Medicine, Swansea University, Singleton Park, Swansea, SA2 8PP, U.K.
2 Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, Merseyside L3 5QA. U.K.

African trypanosomiasis is an infectious protozoan parasitic disease causing sleeping sickness in humans and nagana in animals. The current methods of prevention and control of trypanosomiasis are unsatisfactory, as are the available treatments. Control of trypanosomiasis includes insect repellents,

pesticides, traps and the sterile insect technique (SIT). However the problem of resistance is a reoccurring issue so a molecular approach to control the parasite has the potential to be an effective method of control. In the tsetse fly, the infectivity of trypanosomes depends on their ability to transform from procyclics to epimastigotes and then metacylics. In order to disable this transformation in vivo, genes that express components of the cytoskeleton and flagellum will be targeted for RNA interference (RNAi): FLA-1, PFR and Tubulin alpha -1 chain. By incubating different strains and species of *Trypanosoma b. brucei* and *T. congolense* in vitro with dsRNA (as opposed to electroporation), we demonstrate that RNAi can be achieved via uptake of dsRNA by endocytosis at the flagellar pocket, resulting in knockdown phenotypes that cause parasite death or disable them from completing their life cycle. This sets the scene for RNAi-mediated interruption of the parasite life cycle in the tsetse fly gut. We demonstrated this effect using Cy3-labelled dsRNA and visualizing the uptake of dsRNA by confocal microscopy. This work has been optimized in vitro as a proof-of-concept, and we aim to use this method in the tsetse fly.

Uncovering the genetic diversity of parasites infecting freshwater fish from the Kinabatangan River, Malaysia - P92

Michael Reynolds[1], Jo Cable[1], Benoit Goossens[1,2] and Raquel Xavier[1,3]

1 School of Biosciences, Cardiff University, Cardiff, CF10 3AX, UK
2 Danau Girang Field Centre, Sabah, Malaysia
3 Centro de Investigação em Biodiversidade e Recursos Genéticos, Universidade do Porto, Campus Agrário de Vairão, Rua Padre Armando Quintas, nº 7, 4485-661 Vairão, Portugal

Whilst little is understood about the effects of habitat degradation on the freshwater fish stocks within Sabah, Malaysia, nothing is known about parasite fauna infecting these fish. Parasites play integral roles in all biological systems, and understanding their ecology provides valuable information regarding host population dynamics, life history traits and host-parasite co-evolutionary mechanisms. Habitat pollution affects parasite communities, altering pathogenicity and leading to the emergence of diseases, thus having tremendous impacts on riverine ecosystems by reducing the diversity of fish species and altering food web dynamics. It is therefore essential to understand parasite ecology as this information is invaluable when looking at sustainable aquaculture, in particular subsistence of local families who rely heavily on healthy fish stocks. Here we utilize nuclear and mitochondrial markers to identify monogenean and digenean parasites infecting two common freshwater food fish species; Cyclocheilichthys repasson and Ompok bimaculatus from the Kinabatangan River, Sabah. Genetic diversity and phylogenetic relations of these parasites have been investigated and compared between sites along the river, its surrounding tributaries and oxbow lakes. Preliminary analysis identifies 4 new monogenean and 5 new digenean genetic lineages infecting host species. Additionally, these new parasite lineages exhibit host but not site specificity. This study is an important contribution to understanding the diversity of parasites infecting freshwater fish within the Kinabatangan River.

The distribution of Blastocystis subtypes in isolates from Qatar - P71

Marawan Abu-Madi[1], Aarti Sharma[1], Mahmoud Aly[2], Hanan Balkhy[2,3], Jerzy M. Behnke

1 Department of Health Sciences, College of Arts and Science, Qatar University, P.O. Box 2713, Qatar.

2 King Abdullah International Medical Research Center National Guard Health Affairs PO Box 22490, Riyadh 11426, KSA Mail Code: 2216
3 King Saud bin Abdulaziz University for Health Sciences, Riyadh Saudi Arabia.
4 School of Life Sciences, University of Nottingham, University Park, Nottingham, United Kingdom NG7 2RD.

In the past decade Qatar has seen a fast-paced transformation in the standards of living of its citizens. This tremendous growth has spawned building and modernization programs. Large influxes of immigrant workers are drawn to Doha to complete very ambitious and large-scale construction projects.To date, despite Blastocystis being the most isolated protist from diarrheal patients in the developed world, a causal link has not yet been established conclusively. Blastocystis is genetically diverse and based on small subunit rRNA analysis (SSU rRNA), at least 17 subtypes have been identified in humans, other mammals, and birds. From these subtypes, ST1-ST4 collectively account for 90% of human carriage, while the ST5-ST9 account for the remaining 10%. As prevention is far more effective than cure, we can improve the identification of carriers and facilitate the medical management of individuals who shed these pathogens, through the application of sensitive screening methods and thereby minimize the risk of infection spreading to other sectors of the community. Herein, we implement a molecular screening assay (MSA) using real-time PCR to detect and subtype Blastocystis spp. in samples collected from migrant workers newly arriving in Qatar.

An anthropological exploration of self-use technologies and their impact on perceptions of illness and health-seeking behaviours in Blantyre, Malawi - P39 (SP)

Rosemary Gallagher[1], Booth, M.[1], Hampshire, K. R.[1], Desmond, N.[2]

1. Durham University
2 Malawi-Liverpool-Wellcome Trust, Clinical Research Programme

The use of western-derived technologies for the diagnosis of parasitic and infectious diseases in developing countries is rapidly emerging. Some items such as bed-nets are already widely distributed as prevention measures but need to be appropriately used and interpreted by their users. In future, diagnostic technologies such as mHealth apps and self-testing kits for HIV and malaria, which are even more dependent upon correct adherence, may become available to the general population. However, despite their emerging use, it is currently unclear how these self-testing technologies impact on local people's knowledge and health behaviours in resource-poor settings. In this proposal, we aim to ascertain the availability of self-use biomedical technologies in urban Blantyre, Malawi, including HIV and chlamydia testing kits and Rapid Diagnostic Tests for malaria. We then plan to explore how these technologies are changing users' perceptions of illness, well-being and their engagement with health services. By exploring these issues, we plan to develop a method, grounded in anthropological theory, to further our understanding of the complex cultural processes at play as health-related technologies transition into developing contexts. A mixed-method approach will be used, including questioning of suppliers and in-depth semi-structured interviews with purposively selected participants, focusing on their perceptions and interpretations of self-testing technologies. Through this research we hope to gain insight into the potential for future use of biomedical technologies in prevention, self-diagnosis and self-management of diseases in resource-poor settings, laying the foundations for future research in this area.

Mapping of tick Dermacentor reticulatus expansion in Poland in 2012-2014 - P102 (SP)

Ewa Julia Mierzejewska[1], Agustin Estrada- Peña[2], Mohammed Alsarraf[1], Maciej Kowalec[1] and Anna Bajer[1]

1 Department of Parasitology, Institute of Zoology, Faculty of Biology, University of Warsaw, 1 Miecznikowa Street, 02-096, Warsaw, Poland.
2 Department of Animal Health (Parasitology), University of Zaragoza, Zaragoza, Spain

Rapid expansion of the tick Dermacentor reticulatus (Fabricius) has been reported in many European countries. In Poland tick range was limited to the area on the eastern side of the Vistula River up until the 1990's. However, new foci were recently discovered, while the center of the country and mountain regions are believed to be free of this tick and are known as "the gap". Unfavorable weather conditions have previously been reported as possible reasons for the absence of D. reticulatus in this area. Given that D. reticulatus plays an important role for the maintenance and the circulation of tick-borne pathogens, we (1) determined its actual range in Poland, (2) monitored its expansion in 2012-2014 and (3) correlated temperature on its known range. Dragging was conducted in the area between the Vistula River and the western border of Poland in 2012-2014, along the three major Polish rivers and their tributaries. Temperature on the ground was recorded 4 times a day at a total of 32 sites. Dermacentor reticulatus was found in 21 new locations on the western side of the Vistula River and in 22 locations in western Poland. Existence of 'the gap' was confirmed. This gap divides the tick population in Poland into two settled and spreading populations- Western and Eastern. Our study showed the need for the monitoring of the D. reticulatus expansion. Early detection of new foci is crucial for taking proper prevention measures. This study was supported by the National Science Center (NCN) grant OPUS

Intestinal parasitic infections amongst migrant workers in Malaysia - P119

Siti Nursheena Mohd Zain, Sahimin, N.[1], Mohd Zain, S.N.[1], Lim, Y.A. L.[2], Behnke, J.M.[3] and Lewis, J.W.[4]

1. Institute of Biological Sciences, Faculty of Science, University of Malaya, Kuala Lumpur, 50603, Malaysia.
2. Department of Parasitology, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur.
3. School of Biology, University of Nottingham, University Park, Nottingham, NG7 2RD, UnitedKingdom
4. School of Biological Sciences, University of London, Egham, Surrey, TW20 OEX, United Kingdom.

Malaysia imports a high number of migrant workers from several neighboring countries to cope with an expanding workforce especially in the low skills category. It is mandatory that migrant workers entering the country are screened for communicable diseases such as AIDS, STD and TB, but parasitic infections are often neglected, thus posing a high risk of transmission especially under conditions of poor sanitation and hygiene. The present study was therefore undertaken to highlight those parasitic infections occurring in migrant workers from five sectors of the community such as manufacturing, construction, plantation, domestic and services (food and cleaning). Up to 89 faecal samples were microscopically examined for protozoan and helminth parasites from 99 volunteers originating from Indonesia (n=33, 33.3%), Myanmar (n=23, 23.2%), Nepal (n=21, 21.2%), Bangladesh (n=13, 13.1%), India (n=8, 8.1%) and Vietnam (n=1, 1.0%). Samples were processed using potassium dichromate, followed by concentration in formalin ethyl acetate and staining with iodine. A large proportion of workers (65.2%) were positive for at least one parasite species with relatively high prevalences of infection being

recorded for the roundworm Ascaris lumbricoides (36.0%), hookworms (20.2%), the whipworm Trichuris trichiura (14.6%) and two protozoan parasites Entamoeba sp. (12.4%) and Giardia sp. (10.1%). These levels of infection suggest that a thorough diagnosis of parasitic infections in migrant workers entering and residing in Malaysia is required to ensure a more effective public health policy.

Investigating metabolic control in Plasmodium falciparum - P46 (SP)

Eva Caamaño-Gutiérre[1,2], Arturas Grauslys[1,2], Marie M Phelan[3], Simon Wagstaf[1], Hugo van den Berg[2], Lu-Yun Lian[4], Stephen A Ward[1] and Giancarlo A Biagini[1].

1 Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, L3 5QA, UK,
2 Warwick Systems Biology Centre, Senate House, University of Warwick, Coventry, CV4 7AL, UK,
3 NMR Centre for Structural Biology, Shared Research Facility, Technology Directorate, University of Liverpool L69 7ZB UK and
4 Institute of Integrative Biology, University of Liverpool, Crown Street, Liverpool, L69 7ZB UK.

Plasmodium falciparum, the deadliest malaria parasite has the ability to adopt an assortment of forms during its life cycle and to succeed in very different host environments. A 'just-in-time' transcription, ensures that genes are only expressed when needed, allowing the parasite to develop and transit between hosts. However it is not understood how parasites are able to control central metabolism in response to environmental changes. *P. falciparum* presents stage-specific changes in metabolic fluxes. During the intra-erythrocytic asexual stages glucose breakdown in glycolysis does not follow catabolism by the Krebs cycle and subsequent oxidative phosphorylation. Instead, high rates of lactic fermentation are observed. We hypothesise that (a) glycolytic intermediates support rapid proliferation by their redirection into anabolic reactions and (b) flux to lactate could provide an effective strategy to control biomass production. By using Nuclear Magnetic Resonance (NMR) spectroscopy of 13C isotopes, we have been able to identify key glucose-derived catabolic products. The parasitic nature of *Plasmodium* hinders intracellular studies over the whole life cycle, thus we have pursued analysis of extracellular material in order to infer metabolic changes in the fluxes. Using a new and innovative approach combining NMR metabolomics and imaging analysis we have related biomass production to the consumption and excretion of the most abundant metabolites over the entire 48h intra-erythrocytic life cycle of P. *falciparum* both qualitatively and quantitatively. A variety of nutrient conditions have been used to assess the interplay between metabolism and biomass. Here we present current findings in the context of the proposed hypotheses.

Secreted proteins from the intestinal nematode Strongyloides -secreted protein acidic and rich in cysteine (SPARC) and thioredoxin-like protein - affect the intestinal mucosal defense system of the host - P78

Norbert Brattig, Emmanuela M. Anandarajah*[1,2], Dana Ditgen*[1,2], Hanns Soblik[1], Abuelhassan E. Younis[1], Jan Hansmann[3], Klaus D. Erttmann[1], Eva Liebau[3], Norbert W.Brattig[1] * both authors contributed equally to the work

1 Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany
2 Westphalian Wilhelms-University Munster, Germany
3 University Hospital Wuerzburg, Germany

Intestinal nematodes represent multicellular organisms within the gut microbiota which colonise their habitat for years by sustaining tolerance mechanisms and containing inflammatory host responses thereby preventing their expulsion. According to the Old Friends Hypothesis numerous harmless intestinal organisms can induce regulatory immune responses. Secreted helminth products represent first-line molecules affecting the mucosal immunological regulatory network. By proteomic analysis of excretory/secretory products from *Strongyloides ratti* (Sr) developmental stages we had identified 586 secreted proteins (Mol Cell Proteomics 2011). After describing a prolyl serine carboxypeptidase, small heat shock proteins, galectins and calumenin, we here report our preliminary characterization of two S. ratti proteins: the secreted protein acidic and rich-in-cysteine (SPARC) and the thioredoxin family protein (TRX). The genes of Sr-SPARC and Sr-TRX were identified, cloned and recombinantly expressed under optimized conditions. SPARC was found to be primarily expressed in parasitic females while TRX was detected in all stages. The binding capacity of both proteins to mucosa-associated immune cells was determined by flow cytometry. The effect of the parasite proteins on host cells were studied applying a novel in vitro 3D mucosal model that mimics the in vivo natural microenvironment. In the 3D co-cultures - which comprise human intestinal epithelial and dendritic cells growing on a collagen scaffold - an initially pro-inflammatory response (IL-6, TNF-alpha) after 24 h was followed by an increased anti-inflammatory response after 48-72 h with detection of the Th2-type-related cytokines IL-10, IL-22, TSLP and IL-33. Thus, Sr-SPARC and Sr-TRX can contribute to the reported immunoregulatory potential of intestinal Strongyloides.

Clinical and sub-clinical infection by Trichomonas gallinae in a declining population of European Turtle Doves, Streptopelia turtur - P68

Jenny Dunn, Jennifer E. Stockdale[1,2], Rebecca C. Thomas[2], Rosie J. Lennon[2], Jenny C. Dunn[3], Antony J. Morris[3], Simon J. Goodman[3], Keith C. Hamer[3]

1 School of BioSciences, Cardiff University, Sir Martin Evans Building, Museum Avenue, Cardiff CF10 3AX, UK
2 School of Biology, University of Leeds, Irene Manton Building, Leeds, LS2 9JT, UK
3 RSPB Centre for Conservation Science, The Lodge, Sandy, Bedfordshire, SG19 2DL, UK

Trichomonas gallinae, the protozoan parasite that can cause the disease trichomonosis, is globally widespread in populations of wild pigeons and doves. Host susceptibility and parasite virulence vary, although population limitation by *T. gallinae* has been suggested in the endangered Mauritian Pink Pigeon Columba mayeri. The European Turtle Dove Streptopelia turtur is the UK's fastest declining breeding bird (UK trend 1995-2012: -88%) and has shown a dietary switch from arable weed seeds to anthropogenic seed resources (frequently gamebird feeders or seed in farmyards), concurrent with a reduced reproductive effort (up to 4 broods per pair in the 1960s compared with 1-2 broods currently). As part of a wider auto-ecological study of Turtle Doves in farmland habitats, we investigated the prevalence of T. gallinae in UK pigeon and dove species sampled over three years, carrying out gross necropsy on Turtle Dove adults and nestlings found dead in 2012 to determine whether T. gallinae causes direct mortality in this species. We report early results of ongoing research identifying parasite transmission routes in farmland environments.

Functional and genetic evidence that nucleoside transport is highly conserved in *Leishmania* species: implications for nucleoside-based chemotherapy - P11 (SP)

Khalid Jamaan H Alzahrani[1,2], Juma A. M. Ali[1,3] and Harry P. de Koning[1]

1 Institute of Infection, Immunity and Inflammation, University of Glasgow, Glasgow, United Kingdom
2 Faculty of Applied Medical Sciences, Taif University, Taif, Saud Arabia
3 Faculty of Science, Al Jabal Al Gharbi University, Gharyan, Libya

Research has delineated four nucleobase and nucleoside transporters in *Leishmania* promastigotes, designated as NT1-4, with the vast majority of studies on NT1 and NT2 being carried out using L. donovani genes. However, it is not known whether the same genes similarly mediate purine/pyrimidine transport in other *Leishmania* species. In this study, we determined uptake profiles and inhibition patterns for purine and pyrimidine nucleosides in L. mexicana and L. major, and characterized the NT1A, NT1B, and NT2 genes by expressing them in T. b. brucei strain B48, which lacks the aminopurine transporter TbAT1. B48 trypanosomes were unable to transport [3H]-inosine in the presence of adenosine, but introduction of LmaNT2 and LmexNT2 into B48 significantly increased the rate of [3H]-inosine uptake. We also determined that transport of [3H]-uridine was mediated by LmexNT1A and LmexNT1B in L. mexicana, and by LmaNT1A and LmaNT1B in L. major. While [3H]-uridine uptake was undetectable in T. b. brucei B48 in the presence of uracil and inosine, introduction of NT1A and NT1B in T. b. brucei B48 significantly increased the rate of uptake of [3H]-uridine to almost the same level as in L. major and L. mexicana. The results confirmed that the L. major and L. mexicana genes expressed in trypanosomes are orthologues of the previously characterised L. donovani ENT-family nucleoside transporters LdNT1 and LdNT2 with near-identical substrate selectivities. The observation that nucleoside transport is highly conserved in *Leishmania* species is essential information for the development of nucleoside-based anti-leishmanial chemotherapy.

Evaluation of ultrasound as a predictor of macrofilaricidal activity in a pre-clinical drug screening model of lymphatic filariasis - P38

Hanna Sjoberg, H. Tyrer, J. Gamble, L. Hayward, S. Cross, A. Stevens, M. Taylor, J. Turner

Parasitology Department Liverpool School of Tropical Medicine Pembroke Place Liverpool L3 5QA

New drugs effective against adult filariae (macrofilaricides) would accelerate the elimination of lymphatic filariasis and onchocerciasis. Drug development is hindered by the long and unpredictable time frame for adulticidal activities to manifest. We trialled the use of ultrasonography (USG), within a murine model of lymphatic filariasis, to evaluate whether it could predict macrofilaricidal activity of drug candidates. The benzimidazole filaricides flubendazole (10mg/kg, qd 5 days, subcutaneously), albendazole (5mg/kg, bid 7 days, orally) or oral vehicle control, were tested against adult *Brugia malayi* (Bm) following intraperitoneal (ip.) surgical implantation into CB.17 SCID mice (15 filariae/recipient). Adult Bm were sourced form CB.17 SCID donor mice, 6 weeks following infection with 100 infectious stage larvae ip. Worm motility (filarial dance sign; FDS) was evaluated using portable USG with a 13-6 mHz transducer (M-turbo, Sonosite) 6 weeks post-treatment. Imaging took a maximum of 5 minutes, performed under anaesthesia. Animals were culled immediately after USG assessment and motile worms were enumerated. Flubendazole induced a high macrofilaricidal response against adult female

Bm in CB.17 SCID mice (>99%). Albendazole had no effect on worm counts. USG predicted the presence/absence of motile worms in the intraperitoneal cavity at 6 weeks-post treatment with 90% accuracy. USG imaging could also predictively discriminate between low and high worm burdens. We have established that lack of detection of FDS by USG is an accurate prognostic indicator of macrofilaricidal activity. We propose USG could be adopted as a prognostic of total or partial drug effect to accelerate pre-clinical development of candidate macrofilaricides.

G-quadruplexes in pathogenic microbes: a common route to virulence control? - P87

Catherine Merrick & Lynne M. Harris

Centre for Applied Entomology and Parasitology, School of Life Sciences, Keele University, Keele, Staffordshire, United Kingdom

DNA can form several structures besides the double helix: one that has gained attention in recent years is the G-quadruplex (G4). This is a four-stranded structure formed by the stacking of quartets of guanines. Recent work has convincingly shown that G4s can form in vivo, affecting DNA replication, transcription and translation, and playing important roles at G-rich telomeres. Now, several exciting reports have begun to reveal roles for G4s in virulence processes in pathogenic microbes. These come from a range of kingdoms –protozoa, bacteria and viruses – yet all may facilitate immune evasion in different ways. Among prokaryotes, Neisseria shows a well-characterised role for G4s in pilin antigenic variation, while among eukaryotes, G4s are strikingly associated with variantly-expressed var genes in *Plasmodium falciparum*, and fragile sites in the G-rich telomeres of *Trypanosoma* brucei – also potential G4-forming sites – can facilitate switching of VSG genes. Thus, highly disparate pathogens may use G4s to control DNA/RNA dynamics in ways relevant to common virulence phenotypes. G4s also have roles in silencing at least two major viruses, HIV and EBV. Although quite distinct from antigenic variation, this is similarly a route to immune evasion and maintenance of chronic infections. This poster reviews current knowledge of G4 biology in a range of human pathogens and explores the potential for future research on therapeutics involving G4s. We suggest that cross-fertilization of tools and ideas from G4 studies in model systems could inform new work on parasites.

High Throughput Phenotypic Screening against Three Kinetoplastid Parasites: An Open Resource of new chemical starting points for drug discovery - P16

Manuela Berlanga[1], Imanol Peña [1], M. Pilar Manzano [2], Juan Cantizani [2], Albane Kessler [2], Julio Alonso-Padilla [3], Ana I. Bardera [1], Emilio Alvarez [1], Gonzalo Colmenarejo[1], Ana Rodriguez [3], Jose M. Fiandor [2] & J. Julio Martin [1]

1 Molecular Discovery Research, Tres Cantos Medicines Development Campus, GlaxoSmithKline, Tres Cantos, Spain.
2 Diseases of the Developing World (DDW), Tres Cantos Medicines Development Campus, GlaxoSmithKline, Tres Cantos, Spain.
3 Department of Microbiology, Division of Parasitology, New York University School of Medicine, New York, NY, USA

Three of the Neglected Tropical Diseases (NTDs) declared by the WHO, and included in the London

Declaration of 2012, are caused by kinetoplastid parasites. All NTDs have been categorized as "tool ready," yet also "tool deficient" because many of these tools (i.e. drugs and diagnostics) and implementation strategies are inadequate to achieve the desired goals. New effective, safe, and affordable drugs are needed. We present in this poster an integral approach to the early drug discovery for the three major diseases caused by kinetoplastids: visceral leishmaniasis, Chagas disease and sleeping sickness. The GSK 1.8 million compounds diverse collection has been phenotypically screened against their causative parasites, Leishmania donovani, *Trypanosoma* cruzi and Trypanosma brucei, using the current state-of-the-art methodologies available in high throughput screening, including genetically modified parasites for screening of intracellular forms of the parasites. Secondary confirmatory and orthogonal assays have been applied in order to confirm anti-parasitic activity and to identify potential cytotoxic activity. Hit compounds have been chemically-clustered and triaged for suitable physicochemical properties. As a result of this effort, three anti-kinetoplastidal boxes of approximately 200 compounds each have been assembled, which represent all the chemical and biological diversity identified and are intended to serve as an open source of starting points for further lead discovery programs, as well as to address important research questions.

Evaluation of Parasitological Methodologies and Development a Multiplex PCR Technique for Detection of Intestinal Parasites in Clinical Samples - P120 (SP)

Hajri Alshehri[1], James LaCourse[1], Narcis Kabatereine & Russell Stothard[1]

1Department of Parasitology, LSTM; 2Vector Control Division, MoH, Uganda

Infection with schistosomes and soil-transmitted helminths are typically common in children, particularly within regions of sub-Saharan Africa where environmental water contact is high and access to adequate sanitation is poor. Typically, traditional parasitological methods of diagnosis that visualise parasite ova underestimate true prevalence. Consequently, there is a need to develop better methods for detection of schistosomiasis and soil-transmitted helminthiasis (STH), especially in countries such as Uganda where school-based control of these infections with de-worming drugs has taken place. Against this country-backdrop, we intend to shed light on current levels of infection across a landscape where disease control is ongoing in Buliisa District, Lake Albert. We will evaluate parasitological- and serological-based methods alongside real-time PCR and focus upon examination of children of school-age (i.e. 5-12 years). PCR-based methods will explore the use of Taqman assays on various biological samples (blood, urine and stool), assessing diagnostic congruence between methods. Preliminary results from laboratory development of multiplex PCR assays will be presented.

Loop-mediated isothermal amplification (LAMP) for the detection of Clonorchis sinensis DNA in human fecal samples - P83

Min-Ho Choi[1], S.M. Mazidur Rahman[1], Jin-Kyoung Oh[2], Min Kyung Lim[2], Sung-Tae Hong[1]

1 Department of Parasitology and Tropical Medicine, Seoul National University College of Medicine, and Institute of Endemic Diseases, Seoul National University Medical Research Center, Seoul, Korea
2 National Cancer Center, National Cancer Control Research Institute, Goyang, Gyonggi, Korea

The loop-mediated isothermal amplification (LAMP) assay has been developed for the detection of *Clonorchis sinensis* DNA in human fecal samples. Six primers targeting eight locations on the cytochrome c oxidase subunit 1 (COI) gene of *C. sinensis* were designed for species-specific amplification using the LAMP assay. The LAMP assay was sensitive enough to detect as little as 0.1 pg of *C. sinensis* genomic DNA and the minimum number of eggs in stool samples detectable by this assay was one. The assay was highly specific because no cross-reactivity was observed with the DNA of other helminths, protozoa or Escherichia coli. Compared with the results from the Kato-Katz method and real-time PCR, the sensitivity and specificity of the LAMP assay was 97.1% (68/70) and 100% (50/50), respectively. Moreover, the assay detected the *C. sinensis* DNA in all stool samples with more than 100 eggs per gram of feces (EPG). Due to the rapid, simple, sensitive and specific detection of *C. sinensis* DNA in fecal samples, the LAMP assay can be applied as a point-of-care diagnostic tool in low resource clinical settings.

Studies on expression of gamma glutamylcystein synthetase in *leishmania* tarentolae - P25 (SP)

Muattaz Hussain, G. Westrop, M. Wiese and K.C. Carter.

Strathclyde Institute of Pharmacy and Biomedical, University of Strathclyde, 161 Cathedral Street, Glasgow, G4 0RE, UK.

Leishmaniasis is a disease that causes significant mortality and morbidity. In the last five years, 1 million cases of cutaneous leishmaniasis (CL) have been reported and 300,000 cases of visceral leishmaniasis (VL). There have been 20,000 deaths/year and 310 million people are at risk of infection. At present there is no clinical vaccine for this disease. We have shown that vaccination with recombinant (γGCS) produced in *Eschericheria coli* can protect against CL and VL in murine models. However in this expression vector truncated recombinant protein was produced. Therefore, we carried out studies to determine if we could produce better quality γGCS in *L. tarentoloe*, which is phylogenetically more related to Leishmania. We successfully produced a construct that allowed transfection of *L. tarnetoloe* with the gene sequence of γGCS from three different *Leishmania* species. Western blot studies showed that full length protein was produced indicating that L. tarentolae, may be a better expression vector than E. coli.

Awareness of parasitic infections and deworming practices in plantation sector adult community, Sri Lanka - P1 (SP)

Lahiru Galgamuwa[1], W.M.D.R.Iddawela[1] and S.D. Dharmarathne[2]

1. Department of Parasitology, Faculty of Medicine, University of Peradeniya, Sri Lanka
2. Department of Community Medicine, Faculty of Medicine, University of Peradeniya, Sri Lanka& Institute for Health Metrics and Evaluation, University of Washington, USA

Parasitic infections are one of the commonest and neglected diseases in the world. Parent's knowledge and hygiene habits affect children due to the close contact between parents and children. The aim of this study was to describe the awareness and deworming practices for parasitic infections and hygiene behavior of parents with children in 1 – 12 years age group in the plantation sector in Sri Lanka. This cross-sectional study was carried out in the Tea plantation areas in the Central province, Sri Lanka from January to April 2013. Information were obtained by an interviewer administrated srtuctured

questionnaire. The data was analyzed with SPSS version 17 statistical software. 431 fathers and 427 mothers (mean age 31±6.1 years) participated for this study. 26% fathers and 32% mothers had adequate knowledge of parasite transmission and preventive methods of parasitic infections. Many parents (> 85%) were aware of common symptoms of parasitic infections such as abdominal pain and anaroxia. 22% parents mentioned that they got antihelminth drugs from public dispensaries while 14% from government hospitals and 64% from private pharmacies without any medical prescriptions. 55% of parents have encouraged their children to use antihelminth drugs in regular pattern while only 15% parents used regularly. This study identified that awareness of parental education regarding parasitic infection and proper deworming practices in this community are very low. This study emphasizes the importance and need of health education programs among the study population.

Laboratory Diagnosis and Risk Factors of Gastrointestinal Parasites among Basic School Children in Greater Wad Madani locality, Gezira State ,Sudan (2011 - 2014) - P99

Nshwa El Emam, Nour, B.Y.M and Abakar, A.D

Blue Nile National Institute for Communicable Diseases, University of Gezira, Sudan

Infection by intestinal parasites and soil transmitted helminths are widely distributed among children, particularly school children. This is across sectional study conducted in Great Wad Madani locality, Gezira state among basic school children, to know the distribution of gastrointestinal parasites and soil transmitted helminths (STH) by using different diagnostic methods and to investigate the risk factors of some of the sources of infection. Ten basic schools were selected randomly, five school for males and five ones for females. A questionnaire designed of 15 questions, about the demographic data, behavioural risks environmental sanitation and living condition characteristics and health conditions with history of symptoms was administered .Check list about the school environment was filled. Stool samples (400) were collected. Stool samples were immediately wet mounted using physiological normal saline and iodine. To know the intensity of the ova, a Kato – kat technique was performed for some samples. Formol ether concentration technique was performed for all samples. Soil samples (112) from areas suspected to be source of STH (red bricks working areas and the main vegetables and fruits importing markets in the study area) were cultured. The results showed that formol ether concentration technique is the superior method to detect gastrointestinal parasites and STH than wet prepration. The infection rate was higher in males than females especially in the age group (9-12) years .The highest infection by worms was caused by H.nana whereas *G. Lamblia* was the dominant protozoa. The check list demonstrated that there is a strong relation between the school environment and the prevalence of parasitic infection. According to the statistical analysis, there was relationship between behavioural risks, environmental sanitation and living condition characteristics and the rate of infection. Semi quantative Kato – kat technique showed that the intensity of ova was not high, the highly intensity recorded from basic school for males. Of the 112 soil cultured samples, 53 samples showed the presence of larvae after 15 days .The study concluded that the prevalence of gastrointestinal protozoa is higher than STH. Due to the lack of health education and poor schools environment, the infection was higher in those with poor hygnic practice with prevalence in males rather than females. Areas that suspected to be the source of infection record high positivity rate of infection. The study recommended the combination of wet prepration and formol ether concentration technique in the diagnosis of gastrointestinal parasites and STH. Health education in schools should improve to reduce the rate of infection. Routine examination for gastrointestinal parasite and STH is recommended for school children for early discover and treatment. The school and home water supply and the sanitation system should

be improved to eliminate risk factors of gastrointestinal parasites and STH. *H.nana* recorded high rate, therefore further study should be done to determine whether *H. nana* represent public health problem among school children, this study is the first study in the study area, therefore further study should be done.

Screening of *Toxoplasma gondii* antibodies in pregnant and aborted women attending Wad Medani Maternity Teaching hospital and Um Algura hospital using Latex Agglutination and Electro-chemiluminescence immunoassay (ECLIA) - P119

Adam Dawoud Abakar Salim, Mohamed M.Y [1], Abakar A.D [1] and Nour B.Y [2]

1 Department of Medical Parasitology, Faculty of Medical Laboratory Sciences, University of Gezira
2 Blue Nile National Institute for Communicable Diseases, University of Gezira

Toxoplasmosis is an infection caused by an obligate intracellular parasite *Toxoplasma gondii* in final and intermediate host. *Toxoplasma gondii* is commonly associated with congenital infections that are not clinically apparent. The infection in the first trimester pregnancy may cause severe congenital anomalies or even foetal loss. In congenitally infected children can cause devastating effects including eye blindness, neurological impairment and mental retardation. The parasite distributed world-wide, in Sudan the prevalence was reported to be 34.1% and in Gezira state it was 41.7%. This study aimed to diagnose *T. gondii* infection in pregnant and aborted women by latex agglutination test and Electro-chemiluminescence immunoassay for IgG and IgM antibodies. Out of Total 100 samples of venous blood collected from pregnant and aborted women, 37 and 63 samples were from participants in Wad Medani and Um Algura, respectively. These samples were diagnosed using latex agglutination test for IgG antibodies and Electro-chemiluminescence immunoassay for both IgG and IgM. The results showed that a seropositivity of Toxoplasma IgG antibodies by latex agglutination test was 69% while was represented as 52.6% by Electro-chemiluminescence immunoassay. The Toxoplasma IgM seropositivity was (5.1%). There was significant difference between two methods (P <0.0001). The sensitivity and specificity of latex agglutination test was (94%) and (57.8%) respectively with positive predictive value (71.2%) and negative predictive value (89.6%). The seroprevalence of Toxoplasma IgG antibodies showed (67.6%) in Wad Medan and (69.8%) in Um Algura by latex agglutination test while by Electro-chemiluminescence immunoassay was 43.2% and 54% in Wad Medani and Um Algura respectively. The seroprevalence of Toxoplasma IgM antibodies was (7.9%) and this present in Um Algura. The high prevalence noted among age group 26-35. There is relation between the positive results with clinical symptoms; strong correlation with risk factors specially eating undercooked meat (71%), consumption of raw meat (68.1%), and contact with cats (52.1%). There was negative correlation between the seropositivity and parity number. The Electro-chemiluminescence immunoassay remain high specific and sensitive method for diagnosis of Toxoplasmosis, but a high cost of both apparatus and test reagents may prevent applicability in rural area, so the latex agglutination test may be useful in screening for disease due to simple applicability. The study recommended that the screening of *Toxoplasma gondii* should be done to all pregnant women to prevent disease progression, control cats, avoiding eating raw and undercooked meat and drinking filtrated water.

Second phase lead optimisation of Emetine dihydrochloride for repositioning as an antimalarial drug - P60 (SP)

Muna Abubaker, Holly Matthews, May Rajab, James Wilkinson and Niroshini Nirmalan

University of Salford,School of Environment and Life Sciences, Manchester, M5 4WT.

The emergence and spread of drug resistance has prompted further initiatives to develop new antimalarial drugs to aid the control of malaria. Even with the sustained commitments of scientists and pharmaceutical companies, several challenges persist. It is crucial that the drug development timeline is expedited and a wider repertoire of candidates identified to ensure drug resistance is combated efficiently. One of the strategies to discover new drugs is to reposition or repurpose existing drugs. The singular advantage of adopting a repositioning strategy which screens patent-expired drug libraries is that the compounds screened are already known to be bioactive and safe for use in humans. This significantly reduces the time and cost involved in drug development. Repositioning strategies are aptly placed to yield not only novel potent mono-therapy options, but also synergistic partners for combination therapy to prolong the shelf life of the current frontline antimalarial drugs. The Malaria research group at the University of Salford has already screened 700 current drugs, yielding ~ 50 potential leads exhibiting strong-moderate antimalarial potency. Preliminary screens have identified the anti-amoebic drug Emetine dihydrochloride as a potent antimalarial option. This study focuses on the second-phase optimisation of this compound to define its cytotoxicity profile. HepG2 cytotoxicity data profiles in relation to single and combinatorial use will be presented

Anthelminthic Drug Target Identification and Validation - P122 (SP)

Pilaslak Akrachalanont, Catherine Lawrence and Katharine Carter

Strathclyde Institute of Pharmacy and Biomedical Sciences University of Strathclyde SIPBS Building, 161 Cathedral Street, Glasgow G4 0RE

There are over 300 species of helminths associated with humans and more than half of these species inhabit the GI tract. Children are the most at risk of these infections and prevalence rate is very high and gets close to 100% in some endemic areas. Although there are the number of anthelminthics available the developments of resistance means we need new drugs urgently. The objective of this study is to develop assay for screening for activity of compound against helminthic parasites (*Trichinella spiralis*). We evaluated the colorimetric Alamar Blue method for screening for anthelminthic activity of novel compounds. Alamar Blue assay was performed in 96-well culture plates and different concentrations of *T. spiralis* muscle larvae were used in triplicate and incubated at 37ºC in 5% CO2 in presence of Alamar Blue (10% v/v). Levamisole (LEV) and nitazoxanide (NIT) were used as positive controls for this assay. The results showed that Alamar Blue assay is non-toxic, fast and provide quantitative data for screening of compounds active for *T. spiralis*. We have identified 11 novel compounds which displayed activity against the parasite in vitro. We will next evaluate these compounds for activities against other helminth parasites in vitro (*Heligmosomoides polygyrus*) as well as their in vivo efficacy.

Intestinal helminth infections and the impact of physical growth among school children in tea plantation sector, Sri Lanka - P2 (SP)

Lahiru Galgamuwa[1], W.M.D.R.Iddawela[1] and S.D. Dharmarathne[2]

1. Department of Parasitology, Faculty of Medicine, University of Peradeniya, Sri Lanka
2. Department of Community Medicine, Faculty of Medicine, University of Peradeniya, Sri Lanka & Institute forHealth Metrics and Evaluation, University of Washington, USA

Intestinal helminth infections and low physical growth constitute a major health problem in plantation sector communities in Sri Lanka. A cross sectional study was conducted in children aged between 6-12 years old in plantation sector in Kandy, Sri Lanka. Anthropometric measurements were collected and height-for-age (HAZ), weight-for-age (WAZ) and weight-for-height (WHZ) were analyzed using WHO AnthroPlus version 1.0.4 and SPSS version 17. Stool samples were subjected to direct smear stained with Lugol's iodine and formaldehyde-ether concentration technique to determine the prevalence of intestinal helminths. 298 children with a mean age of 9.0 (SD±2.1) years were assessed from June to September 2013. 44.3% of the children had intestinal helminth infections. Out of total children, 24.2% were stunted, 21.5% were wasted, and 45.0% were underweight. Prevalence of underweight, stunting and wasting was higher in children with helminth infections (48.5%, 27.3% and 22.7% respectively) than in the uninfected (42.2%, 21.7% and 20.4% respectively) and no statistically difference between these groups. And also prevalence of stunting and underweight increase significantly with age (p=0.009 and 0.042 respectively) while wasting decrease with age (p>0.05). Multivariate analysis showed that underweight is significantly associated with stunting (OR = 42.93, 95% CI: 8.95-205.38) and wasting (OR = 6.43, 95% CI: 2.12-19.63) in helminth infected children. Intestinal helminth infections and low physical growth were highly prevalent in the studied community. Future research providing more insight on the nutritional impact of intestinal helminth infections are required to determine the association between intestinal helminth infections and physical growth in this community.

Protein kinase A signalling in cercariae and schistosomules of Schistosoma mansoni - P5 (SP)

Natasha Hirst, Scott P. Lawton and Anthony J Walker

Kingston University

Schistosomes are parasitic blood flukes that cause the devastating disease human schistosomiasis. Protein kinase A is a cell signalling enzyme that regulates critical eukaryotic cellular functions. This study focused on the localisation and regulation of protein kinase A (PKA) in the cercariae and schistosomules of *Schistosoma mansoni*. Western blotting using 'smart' anti-phospho PKA antibodies revealed that cercariae and schistosomules possessed an immunoreactive band of ~40 kDa confirming the presence of phosphorylated (activated) PKA in both these life stages. Confocal microscopy revealed the presence of activated PKA in the tegument, nervous system and sensory structures in the cercariae; PKA activation was also seen in the rudimentary oesophagus of schistosomules. Furthermore, considerable activation of PKA could be seen in specific areas of the cercariae nervous system using PKA substrate antibodies. Exposure of schistosomules to serotonin or dopamine resulted in increased activation of PKA, an effect also shown by the PKA activator forskolin, which in turn stimulated schistosomule movement. Comparative bioinformatics revealed that *S. mansoni* possess a putative receptor for neuropeptide Y (NPY). However, in contrast to serotonin or dopamine, human NPY reduced schistosomule PKA activity. Experiments are currently being carried out to further investigate the role NPY plays in locomotion of schistosomules. Collectively, the data from this study indicates the potential effects host signalling molecules may have on parasite physiology via PKA signalling.

Haemozoin a potential diagnostic biomarker at different stages in the lifecycle of Plasmodium falciparum - P63

Henk Schallig, D M Newman[1], R J Matelon[1], C Price[1], L de Bes[2], P F Mens[2]

1 College of Engineering, Mathematics & Physics., University of Exeter, United Kingdom;
2 Royal Tropical Institute/ Koninklijk Insituut voor de Tropen, KIT Biomedical Research, Parasitology Unit, Amsterdam, The Netherlands

Several groups are exploring use of haemozoin as a biomarker for malaria as it offers the advantage of being detectable by reagent free techniques not dependent on cold chain availability. Under laboratory conditions our magneto-optic technique is sensitive to the presence of mature crystals (1000nm x 200nm) of haemozoin or its artificial analogue β-haematin at concentrations ≈ 1ng/ml. However during clinical evaluation in Thailand when the blood samples of all patients presenting were found by microscopy to display only early ring stage parasites the performance of our rugged, miniaturised magneto-optic device was significantly suppressed in comparison with earlier trials in Kenya. Theory indicates that both the response of crystals to a magnetic field and their interaction with polarised optical radiation decrease with crystal size. To understand the impact of this on instrument sensitivity in early stage infection and the prospect of hemozoin as a diagnostic biomarker we studied the development of haemozoin crystals throughout the lifecycle of P. *falciparum*. Synchronized *falciparum* in vitro cultures were grown and sampled every 2-3hrs over a 48hrs period. Intra- erythrocytic hemozoin was isolated at each time point and the purified crystals were examined via electron microscopy, enabling an accurate account of crystal shape and size distributions throughout the life cycle of the parasite with approximately 20,000 crystals analysed. Like many optical techniques reliant on haemozoin assay, the detection sensitivity possible via magneto-optics is shown to be highly dependent on parasite development. Direct hemozoin detection may be insightful in drug discovery

Variant antigen profiling: a novel approach to population genomics of Variant Surface Glycoproteins in *Trypanosoma congolense* - P89 (SP)

Sara Silva Pereira, [1] Harry Noyes [2] Matthew Berriman [3] Andrew Jackson [1]

1 Dept of Infection Biology, Institute of Infection and Global Health, University of Liverpool, IC2 Liverpool Science Park, 146 Brownlow Hill, Liverpool L3 5RF
2 Dept of Infection Biology, Institute of Integrative Biology, Biosciences Building, University of Liverpool, Crown Street Liverpool L69 7ZB
3 Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge. CB10 1SA

Animal African Trypanosomiasis (AAT) is endemic in East Africa, where is it primarily caused by *Trypanosoma* congolense. AAT causes considerable animal morbidity and losses of livestock, having a detrimental effect on economic development. Effective control of AAT, which would improve animal welfare while increasing productivity and economic prosperity across Africa, requires a precise assessment of disease risk, for the effective application of vector control, drug therapy and animal stocking. However, while the epidemiology of human trypanosomiasis is relatively advanced, our knowledge of the distribution and diversity of animal trypanosomes is poor, and this limits our ability to assess risk or prioritize resource use. We introduce the 'variant antigen profile' (VAP) as a novel means

of dissecting pathogen variation and understanding its impact on disease. AAT is a particular challenge due to antigenic variation of the variable surface glycoprotein (VSG) coat surrounding the parasite. At any time, a single VSG gene is expressed from hundreds of alternatives and sequential expression of different VSG enables the parasite to evade the immune response. Previously, we have shown that T. congolense VSGs segregate into defined phylotypes according to genetic proximity, between which recombination does not occur. We wish to exploit this predictable repertoire to produce a VAP for any T. congolense strain. In this project, we are estimating VAPs for an historical collection of 35 strains to quantify population variation in VSG repertoire and confirm the universality of VSG phylotypes, as well as understand their link to population structure and geography.

DNA vaccination with Onchocerca volvulus Glyceraldehyde-3-Phosphate Dehydrogenase leads to protection in a mouse model of human filariasis - P7

Norbert Brattig, Vera Steisslinger[1], Simone Korten[1,2], Alfons Renz[3,4], Daniel Achukwi[4], Klaus D. Erttmann[1]

1 Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany
2 Department of Microbiology, MVZ Laboratory Lademannbogen, Germany
3 Institute of Evolution and Ecology, University of Tübingen, Germany
4 Institute of Agricultural Research for Development, Wakwa Regional Centre, Cameroon

The filaria *Onchocerca volvulus* is the causative agent of river blindness (onchocerciasis). Over the last decades control programs successfully prevented tens of millions of onchocerciasis cases worldwide, mostly by mass drug administration of ivermectin. This strategy, however, has its limitations, which might be overcome by the additional use of a vaccine. Previously our group cloned and characterized *Onchocerca volvulus* (Ov)-Glyceraldehyde-3-phosphate Dehydrogenase (GAPDH) and conducted a small scale DNA vaccination study with OvGAPDH.DNApl in cattle as compatibility test [1]. The infection of the susceptible Balb/c mouse with the rodent filaria Litomosoides sigmodontis serves as a model of human filariasis, in which we tested the protective potential of OvGAPDH. Three different vaccine formulations were used to immunize BALB/c mice: (i) the DNA-construct OvGAPDH.DNApl, (ii) a combination of the DNA-construct plus recombinant OvGAPDH protein, and (iii) OvGAPDH peptides in alum. After challenge infection of immunized and control mice with L. sigmodontis, the formulations including the DNA-plasmid, led to significant reduction of adult worm load (up to 57% reduction) and microfilaraemia (up to 94% reduction) in the immunized animals. Our results indicate that vaccination with OvGAPDH has protective potential against filarial challenge infection in the mouse model thus allowing to proceed to the Onchocerca ochengi /cattle model. This natural host-parasite system has previously provided evidence for natural cross-protection in a co-endemic system [2,4] and for the protective effect of vaccination against O. ochengi under field conditions [3,4]. [1] BBA 2005;6:85; [2] Parasitology 1998;116:349; [3] Parasite Immunol 2007;29:113; [4] PNAS 2006;103:5971

Drug development assay of in vitro rate of kill of intracellular *Leishmania* species - P9

Rosario Diaz, Fernando Aguilar, Diana Tegazzini, Juan Cantizani, Vanessa Yardley & Simon Croft

London School of Hygiene and Tropical Medicine, London, UK. 1ITN ParaMet, GSK. 2GSK, Tres Cantos, Spain.

One of the main challenges in drug discovery research of neglected diseases, such as Leishmaniasis, is the development of new biological tools and assay methodologies for better evaluation of new, promising compounds which are also able to predict success in compound progression. One of the most interesting biological tools to develop is a biological assay that allows evaluation of the effect of novel hits during the treatment. A multiplex qPCR has been developed to determine time and concentration dependent compound evaluation for in vitro infection models. We have been able to estimate parasite load and dose response effect in real time along with effect on the host cell in a single well, single reaction. This methodology is fast and reproducible, and suitable to evaluate different host and parasite strains.

"You'll have had your tea": Blood meal timing influences life history of Anopheles stephensi - P107

Aidan O'Donnell & Sarah Reece

University of Edinburgh Kings Buildings Charlotte Auerbach Rd Edinburgh EH9 3FL

A summary of three projects that aim to disentangle how circadian rhythms in mosquitoes, and in the properties of mammalian blood, influence mosquito life history and how these interact with malaria parasites. If mosquito rhythms play a role, this would provide explicit evidence that circadian clocks provide an evolutionary advantage to their owners and that changes in these mosquito rhythms may influence transmission success of the parasites.

The influence of *Brugia malayi* infection on the behaviour and longevity of Aedes aegypti - P12 (SP)

Katherine Gleave

Liverpool School of Tropical Medicine

Preliminary short range host assay designed to determine whether the prevention of oviposition effected mosquitoes initiating the search for hosts. *Aedes aegypti* mosquitoes then exposed to *Brugia malayi* at low (5,450 – 7,750 mf/ml), moderate (10,550 – 15, 400 mf/ml) and high (15,900 – 17,900 mf/ml) microfilaremia, control mosquitoes remained unexposed. Mosquito mortality was observed and dissections performed to observe any parasites present. Alterations in host-seeking behaviour were examined at different time periods in the parasite life cycle. Mosquito responsiveness was recorded and a subset dissected to determine parasite prevalence, mean intensity and yield. A mean estimate to the volume of blood ingested per mosquito was gathered to establish any effects on blood feeding. Changes in successful oviposition at different microfilariae densities was determined by using individual oviposition containers and observing how many mature eggs were laid, or retained within the body cavity. Prevention of oviposition was found to significantly reduce mosquito-host responsiveness ($P< 0.0001$, n= 800). Mosquitoes allowed to lay eggs were 11 times more likely to initiate a host search. Stage specific manipulation of mosquito host seeking behaviour was determined, with a 5 fold increase in receptivity when infective stage larvae were present as opposed to developing stages. Density dependent changes in mortality, and fecundity were observed, but not in feeding behaviour. Suggests higher microfilarial densities do not necessarily lead to greater transmission, mosquitoes exposed to low density infections were able to survive for longer, produce higher yields of L3 and were equally as aggressive about host seeking.

Defining the host protective antigens of the mouse whipworm, Trichuris muris: Pathway to vaccination - P14 (SP)

Rebecca Shears, Allison J. Bancroft, David R. Knight, Richard K. Grencis and David J. Thornton

Faculty of Life Sciences, AV Building, University of Manchester, Manchester, M13 9PT

Gastrointestinal nematodes are large multicellular pathogens that are a major cause of morbidity in humans and their livestock. Ideally, this morbidity would be reduced by the widespread use of prophylactic vaccines. Laboratory studies using *Trichuris muris* indicate that the mouse host can expel gastrointestinal nematodes by mounting a strong Th2 response, which protects the host from subsequent infections. The first step in designing effective vaccines against these parasites is the isolation and identification of antigens that stimulate host protective immunity (ie a strong Th2 response). We have used a two-step size exclusion chromatography approach to isolate a group of proteins secreted by the *T. muris* adult and larval stages, which induce a strong Th2 response in vitro. The next step will be to synthesise recombinant versions of these proteins and investigate whether they induce protective immunity both in vitro and in vivo. *T. muris* is antigenically similar to the human whipworm, *T. trichiura*, so this work is likely to be highly translational, bringing us one step closer to a vaccine for this globally important parasite.

Evaluation of GENEDIA® Malaria P.f/pan Ag Rapid Test relative to microscopy in a malaria endemic area Ethiopia. - P123 (SP)

Abeba Gebretsadik Reda, Ashenafi Assefa,Gemechu Tadesse,Dr. Adunga woyesa Ethiopian public Health institute

1. Abeba Gebretsadik Reda, Malaria and other vector born parasitic research team, Ethiopian public Health Institute,P.o.box 1242,Addiss Ababa, Ethiopia

Antimicrobial drug action determined using metabolomics - P20

Isabel Vincent (1,2), David E Ehmann 2, Scott Mills 2, Manos Perros 2, Michael P Barrett 1

1, University of Glasgow, Glasgow UK.
2, AstraZeneca, Waltham, MA, USA.

Antimicrobial drugs are often old yet their modes of action (MOAs) are unknown. For new hits emerging through phenotypic screens, the MOA of compounds can be elusive. A knowledge of the MOA of a drug is useful, allowing drugs to be more efficiently targeted, reducing toxicity, predicting resistance mechanisms and helping with licencing regulations. Current methods to determine the MOA of a drug can be time consuming and are often low resolution. At Glasgow Polyomics, we have developed a liquid chromatography mass spectrometry (LC-MS) based method that is able to capture the metabolome (substrates and products of enzymatic reactions) of a cell population during drug perturbation. Analyses of the changes to the metabolome reveal a great degree of insight into how drugs work at a molecular

level in *Trypanosoma brucei* and *Escherichia coli*. Eflornithine, fosmidomycin, TK-666 and nifurtimox are used to show that our untargeted LC-MS metabolomics approach can identify specific drug targets. As well as revealing drug modes of action, our platform has also been used to analyse drug resistance mechanisms, drug modifications and drug synergy. These experiments can be performed in a relatively high throughput, non-hypothesis driven manner.

Tocopherol biosynthesis in *Leishmania* (L) amazonensis - P24

Jose Mario de Freitas Balanco; [1]Sussmann, R.A.C.; [2]Cebrián-Torrejón, G.; [1]Gabriel, H.B.; [1]Kimura, E.A. and [1]Katzin, A.M.

1 Department of Parasitology, Institute of Biomedical Sciences, University of São Paulo, Av. Prof. Lineu Prestes, 1374, São Paulo, SP 05508-000, Brazil.
2 Research Support Center in Molecular Diversity of Natural Products, Institute of Chemistry, University of São Paulo, Av. Prof. Lineu Prestes, 748, São Paulo, SP 05508-000, Brazil.

Leishmaniasis, a neglected tropical disease, is caused by a protozoan of the genus *Leishmania* and is transmitted by the bite of sandflies. It affects either the skin or the internal organs and is estimated 2 million of new cases occur annually, with about 12 million people currently infected. Isoprenoid biosynthesis in *Leishmania spp* has not been studied yet and this pathway could be a possible therapeutic target. Using metabolic labeling with 1-(n)-3H GGPP or 1(-n)-3H FPP, two different methods of RP-HPLC purification and scintillation counting we detected in *Leishmania* (L) amazonensis promastigotes extracts, radiolabeled fractions with a coincident retention time of α and γ-tocopherol standards, which we confirmed the presence of their chemical structures by GCMS in non-radiolabeled parasites extracts. The treatment of usnic acid (UA), an inhibitor of HPPD enzyme that catalyzes the conversion of p-hydroxyphenylpyruvic acid to homogentisic acid, a precursor of tocopherol biosynthesis, inhibited the growth of parasite in a concentration-dependent manner. Parasite growth inhibition by UA was reversed by the addition of α-tocopherol (the viability of parasites was measured by MTT and Sybrgreen DNA incorporation). In conclusion, this study shows for the first time evidences for tocopherols biosynthesis in *L. (L) amazonensis* promastigotes and antileishmanial activity of UA. This pathway could serve as an antiprotozoan target, once it is absent in mammal. This research was supported by FAPESP and CNPq.

The Grand Challenge of Developing a Filarial Nematode Cell-line - P29

Vera Unwin, Mark J. Taylor, Kelly L. Johnston

Department of Parasitology, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, L3 5QA, UK

The development of a macrofilaricidal drug that can target the long-lived adult filarial nematodes, *Brugia malayi, Wuchereria bancrofti* and *Onchocerca volvulus* is a research priority. Typically, screening chemical libraries directly against parasitic nematodes is cumbersome, low throughput and relies on animal reservoirs. This has prevented access to a critical mass of hits that can be investigated further, unlike in other fields, which often have access to cell-based screens as the primary step in the drug discovery pipeline. With a Bill and Melinda Gates Foundation Grand Challenge Exploration award, we

have investigated the potential to develop a robust filarial nematode cell line that can be used in a high-throughput screening (HTS) assay. Through the use of the automated Operetta High Content Imaging platform, we have maximised the ability to monitor multiple cultures at any one time, with the aim of defining the optimum culture conditions for cells retrieved from various life-cycle stages of B. malayi and define the culture requirements that can promote continuous culture. We are currently evaluating immortalisation strategies to prolong longevity and induce proliferation in the cell line. Specifically, we aim to investigate techniques including transfections with oncogene-encoded plasmid/ viral vectors and using small molecule agonists to stimulate cell cycle pathways.

Turning the Worm Against its Symbiont: Activating autophagy as a novel anti-*Wolbachia* mode of action for macrofilaricidal drug discovery - P30

Amber Fanthome, Denis Voronin and Mark J. Taylor

Department of Parasitology, Liverpool School of Tropical Medicine, UK

River blindness (*Onchocerca volvulus*) and elephantiasis (*Wuchereria bancrofti and Brugia malayi*) affect over 150 million people in more than 80 countries, with a further 1 billion at risk of infection. Each of these nematode parasites has evolved a mutualistic association with the bacterial endosymbiont *Wolbachia*, and depletion of *Wolbachia* with the antibiotic doxycycline delivers potent macrofilaricidal activity in clinical trials. In order to identify alternative anti-*Wolbachia* drugs with a more rapid activity we have exploited the host nematodes immune regulation of *Wolbachia* populations through autophagy to discover drugs with a wolbachiacidal mode of action. Libraries of autophagy-inducing drugs and compounds were screened for anti-*Wolbachia* activity in B. malayi. Selected 'hits' were then screened against transgenic *C. elegans* and human embryonic kidney (HEK) cells expressing a fluorescent autophagy marker, ATG8, to identify drugs that were selectively more potent at activating autophagy in nematode versus human cells. Finally, a combined treatment regime for autophagy inducing drugs and antibiotics was established. Hits will be progressed through the A·WOL drug discovery and development screening pipeline to identify pre-clinical lead candidates and optimized combinations of anti-*Wolbachia* drugs to reduce treatment timeframes.

Biomarker discovery of novel and dynamic plasma proteins indicative of active adult Onchocerca volvulus infection - P32 (SP)

Cara Macfarlane, Gemma Molyneux, Simon Wagstaff, Mark Taylor

Parasitology Department Liverpoool School of Tropical Medicine Pembroke Place Liverpool L3 5QA

Onchocerciasis is a debilitating eye and skin disease primarily affecting people in Sub-Saharan Africa. The filarial worm *Onchocerca volvulus* causes progressive disease in the host when the microfilarial stage die and invoke immune responses. As ongoing control efforts are advancing to elimination programmes, a diagnostic test capable of identifying live adult worm infections is crucial for test and treat strategies and to define and monitor the stopping criteria for elimination programmes. Based on the hypothesis that biomarker signatures can be identified and quantified in the human plasma proteome and/or the sub-proteome of *O. volvulus* from human patients, a unique plasma sample set collected sequentially over a two year period from doxycycline-treated patients will be exploited to

identify protein biomarkers that show a rapid dynamic reduction or loss over the course of treatment. Plasma proteome studies are limited by the vast dynamic range (over 10 orders of magnitude) of protein abundance, which obscures potential biomarkers. Biomarker discovery utilizes extensive pre-fractionation of the plasma proteome to deplete high abundance proteins, followed by a discovery-based MS-approach to identify differences in plasma protein profiles over time. Potential biomarker candidates of live adult female infection will then be progressed to a targeted high-throughput selected reaction monitoring validation stage to provide a biomarker with the necessary sensitivity, specificity and robustness for development as a diagnostic test of use in ongoing clinical trials endpoint evaluation.

Development of *Leishmania* mexicana lines expressing novel variants of luciferase - P35

Helen Price & Anna Thomason

Centre for Applied Entomology and Parasitology, Faculty of Natural Sciences, Keele University, Newcastle-under-Lyme, Staffordshire. ST5 5BG. United Kingdom

There is an urgent need to develop new safe drugs to treat kinetoplastid infections. Transgenic parasites expressing luciferase can be valuable tools for compound library screens and in vivo drug efficacy studies. The most commonly used luciferase originates from the Common Eastern firefly, *Photinus pyralis* but new variant forms of the enzyme have been isolated which may have better properties for these applications.The aims of this study were to engineer *Leishmania mexicana* parasites to express one of two variant forms of luciferases: a red-shifted firefly enzyme and NanoLuc from the deep sea shrimp *Oplophorus gracilirostris*. Red-shifted luciferase has been used in *Trypanosoma brucei* and *T. cruzi* to improve in vivo imaging. NanoLuc is a very small protein and has been reported to have extremely high enzyme activity in other eukaryotic systems. These two luciferases were successfully expressed in an active form in *L. mexicana*. While red-shifted luciferase resulted in moderate luminescence comparable with other studies, the luciferase activity in NanoLuc-expressing cells was exceptionally high, enabling less than 10 cells to be detected in vitro. The half-life of each protein was determined by measuring luminescence following treatment with cyclohexamine and actinomycin D. While red-shifted luciferase had a half-life of 2 hours in promastigotes, the NanoLuc enzyme was found to be extremely stable with a half-life greater than 7 hours. We conclude that NanoLuc is suitable for detecting very low numbers of transgenic parasites but may not be suitable for drug screening applications

Malaria parasite population structure on the edge of endemic distribution in West Africa - P41

Craig Duffy, Hampate B[2], Ambroise D. Ahouidi[3], Boubou Deh Yacine[2], Abderahmane Tandia[2], Freja Kirsebom[1], David J. Conway[1]

1 London School of Hygiene and Tropical Medicine, London, UK
2 Institut National de Recherche en Santé Publique, Nouakchott, Mauritania
3 Le Dantec Hospital, Cheikh Anta Diop University, Dakar, Senegal

Malaria is a major cause of mortality throughout most of Africa with the highest regions of endemicity located across West Africa. Within West Africa there has been a substantial decline in the incidence of

malaria in The Gambia and Senegal over the last decade, raising the possibility of eventual elimination in these countries. The large country of Mauritania, dominated by the Sahara desert, lies to the north of Senegal at the northern edge of the *P. falciparum* transmission zone while the high frequency of Duffy positive individuals allows for the continued transmission of *P. vivax*. With a limited transmission season driven by highly variable seasonal rainfall there is little information regarding the distribution of these two species and whether the extremely low transmission has given rise to a genetically isolated and fragmented population structure. Sampling at 13 health clinics and hospitals spread across a ~900km region of the country during two transmission seasons identified 447 PCR positive cases, with P. *falciparum* present in 62.7%. *P. falciparum* dominated in the south and east of the country, with *P. vivax* largely restricted to the north and coastal regions. Using 10 highly polymorphic P. *falciparum* specific microsatellite loci to analyse the population structure we observe a high proportion of single clone infections, in sharp contrast to the majority of West Africa, and examine the impact of a highly restricted transmission season on gene flow between the geographically isolated sites.

Activation of astrocytes of the blood brain barrier in cerebral malaria: an in vitro study - P43 (SP)

Nana Efua Andoh, Mohd Hamzah Mohd Nasir [2] Ignacio A Romero [3] Monique F Stins [1] Srabasti J Chakravorty

1 School of Life Sciences, Keele University, Keele, Staffordshire, ST5 5BG, UK
2 Biomedical Research Network, The Open University, Walton Hall, Milton Keynes, MK7 6AA, UK
3 John Hopkins University, Baltimore, USA

Cerebral malaria (CM) is the most severe form of *Plasmodium falciparum* malaria infection, mostly affecting children under 5 years of age. Sequestration of *Plasmodium falciparum*-infected red blood cells (PRBCs) in brain microvasculature is believed to cause damage to the blood brain barrier (BBB). Endothelial cells, astrocytes and pericytes form an integral part of the BBB and are referred to as the neurovascular unit (NVU). Astrocytes are involved in BBB function, tightness and protein expression. However, little is known about the role of astrocytes in BBB damage during CM. Thus the aim of this project is to investigate alterations in astrocytes during CM. Firstly, Human brain endothelial cells (HBEC) were co-cultured with PRBC (to mimic sequestration), and the supernatants harvested. Loss of BBB integrity was induced when HBEC were treated with these co-culture supernatants (Nasir BSP2013). The current study investigates whether the co-culture supernatant containing endothelial cell – derived soluble factors could activate astrocytes. In preliminary studies, immunofluorescence assays showed increased expression of glial fibrillary acidic protein (GFAP), an astrocyte activation marker, in astrocytes treated with the PRBC-HBEC co-culture supernatant as compared to astrocytes treated with control co-culture (uninfected RBC-HBEC) supernatant. These results suggest that soluble factors released when PRBC sequester on the EC of the BBB, may contribute to activation of the astrocytes. This suggests that PRBC sequestration on the EC has deleterious effects not only on the EC but also on the underlying components of the NVU, in CM.

Malaria elimination in the kingdom of Saudi Arabia - P50 (SP)

Amal Sultan & Mohammed H Alzahrani

King Fahad Hospital, PO Box 8488, 21196, Saudi Arabia

Malaria is an acute parasitic disease caused by a single cell parasite that lives both in mosquitoes and humans. It is caused by parasitic protozoa of genius plasmodia, human infection can be contracted by 5-species. Malaria infection is considered as one of the most serious & fatal diseases in tropical and subtropical countries. Around 1.8 billion people in the Southeast Asian region and 870 million people in the Western Pacific region remain at risk of contracting malaria. The Middle East will soon have a Research Centre directly responsible for monitoring and evaluation of insect-borne infectious diseases such as malaria and dengue. Saudi Arabia Ministry of Health has allocated US$ 5.5 million as a seed for funding of a joint Research Centre to develop innovative ways to monitor, evaluate and control major diseases transmitted by vectors, in collaboration with Liverpool School of Tropical Medicine (UK) to form an Innovative Vector Control Consortium. It could but a foreword step towards elimination of malaria in Saudi Arabia, where just over half of the population live in areas where they are at risk of contracting the disease, (WHO -2013).

Molecular identification and functional characterisation of a new partner of the phosphatase protein type I in Plasmodium falciparum - P51

Astrid Lenne, Caroline De Witte, Christine Pierrot, Jamal Khalife

Center for Infection and Immunity of Lille, Inserm U1019, CNRS, Institut Pasteur de Lille, Univ Lille Nord de France, 1 rue du Professeur Calmette, Lille cedex 59019, France astrid.lenne@pasteur-lille.fr, caroline.de-witte@pasteur-lille.fr, christine.pierrot@pasteur-lille.fr, jamal.khalife@pasteur-lille.fr

Malaria is a major problem of public health because of its high mortality rate, the lack of vaccine, and the increase in drug resistance. Hence, the search of new therapeutic targets, through a better understanding of parasite biology, is necessary. In our laboratory, we study the regulatome of *Plasmodium falciparum*'s Protein Phosphatase type I (PfPP1), a major enzyme involved in the progression of the cell cycle of the parasite. To this end, we performed an in-depth approach using high-throughput yeast two-hybrid system with PfPP1 as bait. Among the 36 identified partners we focused on a protein called RCC (Regulator of Chromosome Condensation) -containing protein. This protein was found 8 times and is specific for *Plasmodium.* The objective of this work is to characterize this RCC-containing protein at molecular and functional levels in *Plasmodium falciparum*. Bioinformatics studies revealed the presence of 2 RVXF motifs which is known to be present in 80% of PP1 regulators, and 2 motifs RCC which could be involved in protein-protein interactions. The first analyses of the interaction between the prey (a part of the RCC-containing protein which has one RVXF motif) and PfPP1 seemed to indicate that the RVXF motif is required for the binding. Functional studies of the prey on PfPP1 phosphatase activity suggest that this protein is an activator of the enzyme. Then we would like to make a yeast two-hybrid screening with RCC motifs as bait to discover its interactome. Finally, localization and function experiments in blood-stage parasite are underway.

A Study of Incidence of Malaria in Rural Hospital in Upper West Region of Ghana - P61 (SP)

Marilena Ioannou, Azra Khan, Lisa Brown

Upper West Region Ghana

Marilena Ioannou Senior Lecturer Faculty of Health and Life Sciences De Montfort University The Newarke Leicester LE1 9BH Dr Azra Khan Nuffield Health Microbiology Laboratory Milverton Road Leamington Spa Lisa Brown Alexandra Hospital Pathology Department (Biochemistry) Woodrow Drive Redditch B98 7UB

Comparative analysis of the fauna of molluscs as intermediate hosts of the protostrongylidae larvae in Â«Losiniy ostrovÂ» national park, Moscow, Russia - P74

Nina Samoylovskaya, A. Uspenskiy, L. Maklakova, V. Gorohov, E. Malahova, K. Kurochkina, A. Moskvin, V. Berejko,V. Kiseleva

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The population of mollusks may vary depending on the season. Optimum conditions in biotopes for their development appear in May and/or June. In early July mollusks finish their transition from anabiosis to the active state. From this time they start leading an active mode of life: they feed, breed, lay eggs. In mid-July youngsters appear, and because of this fact the population grows. The greatest density of mollusks takes place in August and/or September – from 20 to 80 and more specimens per square meter. In October their numbers either does not change, or reduces a little, due to deterioration of weather conditions METHODS: To study the species composition and the dynamics of mollusks infestation with Protostrongylidae larvae samples were taken in May, June, July, August, September and October. RESULTS: Endogenous intoxication with protostrongylidae of the elks at Losiny Ostrov National Park constituted from 30 to 60 per cent, so it became necessary to study the dispersal, population and infestation of intermediate hosts (terrestrial mollusks) with protostrongylidae larvae in the biotopes of woodland area and determine the areas of invasion. CONCLUSION: 22 species of terrestrial and freshwater mollusks were found in Losiniy Ostrov National Park: *Agriolimax reticulatus; Agriolimax agrestis; Bradybaena fruticum; Cochlicopa lubrica; Euomphalia strigella; Helicolimax pellucidus; Perforatella bidens; Pupilla sp.; Succinea putris; Succinea oblonga; Trichia hispida; Vallonia pulchella; Vallonia costata; Zenobiella rubiginosa; Zonitoides nitidus; Zonitoides sp.; Anisus spirorbis; Aplexa hypnorum; Planorbis planorbis; Planorbaris corneus; Lymnaea stagnalis; Lymnaea truncatula.*

Using transcriptomics and metabolomics to assign functions to hypothetical genes associated with metabolism in Plasmodium - P52

Anubhav Srivastava, Nick Dickens, Oliver Billker, Andy Waters

Wellcome Trust Centre for Molecular Parasitology, University of Glasgow, UK Wellcome Trust Sanger Institute, UK

Increased drug resistance and difficulties in vector control have made the need to discover novel drug and vaccine targets against malaria causing parasite *Plasmodium* more important than ever. Even though the *Plasmodium* genome was sequenced almost a decade ago, almost 50% of the genome still comprises of orphan genes and filling this gap in the knowledge about *Plasmodium* biology can facilitate this. We aim to use transcriptomics and metabolomics to annotate metabolism associated hypothetical

genes in *Plasmodium*. From PlasmoDB, we have identified 480 genes associated with metabolism and have combined published data (e.g Winzeler et al. 2008) and RNA seq data generated in our laboratory to generate a list of metabolism associated hypothetical genes owing to co-expression (guilt by association). We plan to use the PlasmoGem technology in *P.berghei* (Gomes, Ana Rita et al. 2015) to generate gene deletion mutants of these hypothetical genes. Essential genes will be explored as possible drug targets and studied by using conditional knock-down systems. All mutants will undergo untargeted metabolomics by LC-MS and GC-MS and the data will be processed for multivariate statistical analysis to pinpoint differences in metabolism between wt and mutants. Missing metabolites will be identified by comparing the mass spectra between the genotypes and further verified by biochemical assays, isotopically labelled standards and MS/MS. This study will provide us with information to fill in the existing gaps in metabolism of *Plasmodium* and very likely, lead to the discovery of novel biochemical pathways which will be amenable to targeting for malaria intervention.

Back-scattering interferometry: A new tool for the quantification of Plasmodium-host interactions - P124

Abigail Perrin, Phoonthawee Saetear, S Josefin Bartholdson, Madushi Wanaguru, Amanda Kussrow, Darryl J Bornhop and Gavin J Wright

Wellcome Trust Sanger Institute, Genome Campus, Hinxton, Cambridgeshire CB10 1SA

Invasion of host erythrocytes by *Plasmodium falciparum* is central to the pathogenesis of malaria and involves key recognition events between erythrocyte receptors and merozoite ligands. Identification and characterisation of these host-parasite interactions is often impeded by the biochemical challenges of working with isolated or recombinant membrane glycoprotein receptors, such that it is desirable to perform binding assays with receptors embedded within the membranes of intact human erythrocytes. Here we introduce backscatting interferometry (BSI) as a novel platform for the detection and measurement of protein interactions at the erythrocyte surface. BSI is a unique optical detection method that can be used to infer binding events in tiny volumes of solution based on changes in refractive index. We have used BSI to obtain equilibrium binding measurements for known host-parasite interactions involved in erythrocyte invasion. Purified recombinant proteins constituting the entire ectodomains of *P. falciparum* merozoite ligands PfRH5 and PfEBA175 bound to the erythrocyte surface with KDs of 1.1µM and 50nM respectively, in good agreement with previous biophysical measurements of the PfRH5/BSG and PfEBA175/GYPA interactions. These results demonstrate that BSI can be used to detect and quantify the interactions of free-solution merozoite invasion ligands with their receptors on intact human erythrocytes with a very high sensitivity, without the need for labelling and requiring only nanomoles of recombinant *Plasmodium* protein. Hence BSI can be used to investigate host-parasite protein interactions without the limitations of other assay platforms, and represents a valuable new method to investigate the molecular mechanisms underlying erythrocyte invasion by *P. falciparum*.

Genome sequence of the ape malaria parasite Plasmodium gaboni from naturally infected chimpanzee blood samples - P53

Lindsey Plenderleith[1], Sesh Sundararaman[2], Weimin Liu[2], Elizabeth Loy[2], Jerry Learn[2], Yingying Li[2], Katharina Shaw[2], Beatrice Hahn[2], Paul Sharp[1]

1 Institute of Evolutionary Biology, University of Edinburgh, UK;
2 Department of Medicine, University of Pennsylvania, USA

Wild apes harbour several *Plasmodium* species closely related to human malaria parasite *Plasmodium falciparum*, which are of considerable interest for comparative genomics. Obtaining samples from gorillas is problematic, so efforts to date have focused on chimpanzee parasites. Species of particular interest are *P. reichenowi*, the chimpanzee parasite most closely related to *P. falciparum*, and *P. gaboni,* which can be used as an outgroup to provide context for *P. falciparum-P. reichenowi* comparisons, but is close enough for confident identification of orthologous genes. A complete genome of *P. reichenowi* was recently published, but only a partial, fragmentary genome is available for *P. gaboni.* We used selective whole-genome amplification to sequence genomes of two *P. gaboni* strains and an additional *P. reichenowi* strain, directly from naturally infected blood samples – the first time this approach has been applied to eukaryotes. Genome comparisons revealed evidence that the present sequences of vaccine candidate PfRH5 and neighbouring genes are likely the result of recent horizontal gene transfer (HGT) into the ancestor of *P. falciparum*, from a close relative of *P. gaboni.* RH5 appears essential for erythrocyte invasion by *P. falciparum*, and we speculate that sequence change resulting from HGT may have been an important step in *P. falciparum* acquiring the ability to infect humans. More generally, comparative studies of inter- and intra-species diversity have identified genes that appear to be evolving differently along the phylogenetic tree branch leading to *P. falciparum*, and are thus candidates for genes with roles in *P. falciparum* host tropism and pathogenesis.

Identifying dominantly expressed var genes of Plasmodium falciparum: A Tale of Two Samples - P54

Eilidh Carrington [1], Szestak, Tadge [1], Otto, Thomas D. [2], Craig, Alister G. [1]

1 Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, L3 5QA,
2 Wellcome Trust Sanger Institute, Hinxton, Cambridge, CB10 1SA

The large gene family var encode *Plasmodium falciparum* erythrocyte membrane protein 1 (PfEMP1) proteins responsible for antigenic variation in the malaria- causing parasite *Plasmodium falciparum*. Of the ~60 var genes per genome, only one is dominantly expressed and translated into PfEMP1 on the surface of infected erythrocytes, where it mediates sequestration capabilities linked to disease pathogenesis. Identifying the dominantly expressed var genes in a parasite population can be challenging, not least because there may be multiple genotypes per patient. Here, I describe and contrast attempts to identify the dominant var genes from two very different sample types. The first are laboratory adapted patient isolates selected for ICAM-1 binding. The second are genomic DNA samples extracted from tissue biopsies taken at autopsy from patients who died of cerebral malaria, for which a dominantly expressed sequence was previously partially identified. The first can be grown in culture and are amenable to RNA and DNA extraction, whereas the second are finite and upon analysis are of poor quality and consist mainly of human DNA. These contrasting sample types proved challenging in different ways and produced markedly different outcomes.

Validation of decontamination procedures for *P. falciparum* infected erythrocytes in CatIII facilities - P55

Pauil Horrocks, Farhana Chowdhury, Imran Ullah

Institute for Science and Technology in Medicine, Keele University, Staffordshire ST5 5BG,UK

Culturing of *Plasmodium falciparum* infected erythrocytes in the United Kingdom requires Health and Safety Executive approval of CatIII cell culture facilities and the procedures for the use of this facility as laid out in associated Code of Practice. A key aspect of the Code of Practice is a description of the decontamination procedures for materials that come into contact with *P. falciparum* infected erythrocytes as well as any spills. These procedures typically describe the application of a disinfectant followed by autoclave to ensure effective kill of the parasite prior to disposal. These protocols, however, typical rely on empirical evidence for the procedures used. Here we describe the use of a sensitive bioluminescence assay of parasite viability to validate the conditions for the effective use of Virkon and Trigene disinfectants, commonly used in the United Kingdom, as well as a validation of parasite kill following a standard autoclave cycle (121 °C for 15 minutes). Our evidence also indicates that dried *P. falciparum* infected erythrocytes (eg. thin smear slides prior to fixation or droplets on the hood surface) should be still considered to contain viable parasites.

Long-term storage and real time PCR detection of Cryptosporidium from in vitro cultures - P65

Henk Schallig, Anna Paziewska-Harris, Gerard Schoone, Martin Singer

Royal Tropical Institute / Koninklijk Instituut voor de Tropen (KIT), KIT Biomedical Research, Parasitology Unit, Meibergdreef 39, 1105 AZ Amsterdam, The Netherlands

In vitro culture represents an important tool for diagnosis and characterisation of *Cryptosporidium* strains, allowing amplification of samples from relatively small amounts of starting material. The *in vitro* methodology developed by Hijjawi et al. (2001) allowing culture of *Cryptosporidium* in monolayers of host cells, has great potential, but remains a research tool rather than a diagnostic method. Here we present methodological improvements in two areas allowing in vitro culture to be more widely adopted for diagnostic purposes. The first concerns storage of infected mammalian cells in liquid nitrogen and subsequent successful recovery of living *Cryptosporidium*; this allows long-term storage of the non-resistant thin walled oocysts which are predominantly formed when *Cryptosporidium* is cultured on monolayers. The second innovation concerns demonstration of *Cryptosporidium* in monolayers using real time PCR; this avoids uncertainty over the success of inoculation and sub-culturing, and reduces the time needed between isolation of oocysts from a sample and first characterization of the infection. Together these methodological developments improve the utility of the Hijjawi method for *Cryptosporidium* diagnosis and epidemiological research.

Secondary Peritoneal Hydatidosis, the challenges of Echinococcal disease in South Sudan: A case report - P72

Richard Thomas, Daniel Winson & Rwth Ellis-Owen

Juba Teaching Hospital, South Sudan

A 28 year old male presented to the Juba Teaching Hospital with progressive shortness of breath. 18 months prior to admission, he presented to a rural hospital with severe abdominal pain. An emergency

laparotomy was performed, and a large hepatic cyst was removed. Examination at the Juba Teaching hospital revealed a grossly distended abdomen with multiple palpable masses per abdomen. An Abdominal Ultrasound revealed multiple loculated cysts throughout the abdomen. A diagnosis of Secondary Peritoneal Hydatidosis resulting from incorrectly performed surgery was made. The patient was conservatively treated and at 14 weeks, the cysts showed a moderate reduction in size. Cystic Echinococcusc(CE)is common in South Sudan and has a considerable disease burden throughout the developing world. Greater governmental and international support is required to develop effective control measures for these diseases.

Functional analyses of sphingolipid biosynthesis in an apicomplexan parasite - P73

Amjed Ibrahim, Hosam Shams-Eldin; Ralph T Schwarz and Paul W. Denny

School of Biological and Biomedical sciences/Durham University Philipps-University Marburg, 35043 Marburg, Germany Biology Department / College of Science / Baghdad University

The phylum *Apicomplexa* includes many parasites that cause serious human and animal disease, for example *Plasmodium* (malaria), *Eimeria* (coccidiosis) and *Toxoplasma* (toxoplasmosis). Treatments against these parasites are limited and novel solutions are urgently required. Recently, research has focused on parasite specific features of lipid biosynthesis as potential drug targets. In particular the biosynthesis of sphingolipids, which have essential roles in many processes, has been highlighted as a potential target. Using the model apicomplexan *Toxoplasma gondii* we are studying the role of parasite and host sphingolipid biosynthesis in invasion and proliferation. To do this we are functionally characterizing the *Toxoplasma* sphingolipid biosynthetic pathway. In parallel, the response of the host sphingolipid biosynthetic pathway to parasite infection is being investigated. Results so far demonstrate that host cell SPT is up-regulated on *T. gondii* infection, indicating that sphingolipid biosynthesis is increased. However, metabolic labelling shows that several distinct complex sphingolipids, including inositol phosphorylceramide (IPC), are synthesized independently by the parasite. The fungal IPC synthase inhibitor aureobasidin A (AbA) has been reported to target Toxoplasma IPC synthesis. Our results show that AbA and an orthologue are active against the parasite; however their effect on *Toxoplasma de novo* sphingolipid biosynthesis is unclear. Together these approaches will lead to further understanding of the roles of sphingolipid biosynthesis in parasitism and also demonstrate the possibilities of targeting the parasite pathway for therapeutic intervention.

A new species of Pleistophora (Microsporida: Pleistophoridae) parasitic in the shrimp scad (Alepes djedaba), ultrastructure and molecular study - P75 (SP)

Lamjed Mansour [1,2] and Suliman Y. Al Omar[1]

1 Department of Zoology, College of Science, King Saud University PO. Box: 2455, Riyadh, 11451, Saudi Arabia
2 Unité de Recherche de Biologie intégrative et Ecologie évolutive et Fonctionnelle des Milieux Aquatiques, Département de Biologie, Faculté des Sciences de Tunis, Université de Tunis El-Manar, Tunisia

Specimens of the shrimp scad, *Alepes djedaba (Forsskhl)* collected from the Arabian Gulf were found

infected with a microsporidia parasite forming a whitish large cyst or xenoma in the abdominal cavity of the fish. Some cysts could reach 1.5 cm and are filled with mature spores. Spores develop in sporophorous vesicules in the cytoplasm of the infected cell. Fresh mature spores are pyriform and measured 5.4-5.8 x 2.5-2.7 µm. The polar filament is isolfilar and arranged in three raw with 27-30 coils. The parasite occurs in 24% of examined fish. Merogony and sporogony are multinucleated and divide by fragmentation in direct contact with the cytoplasm of the host cell. Characterization of different development stages allowed the identification of the genus as *Pleistophora.* Molecular analysis based on the small subunit rRNA gene shows highest similarity with *Glugea* and *Pleistophora* species. However the percentages of identity are lower with *Pleistophora* species (88-92%) then with some *Glugea* species (92-98%). Sequencing of the large subunit rRNA gene will be undertaken for a best identification of this microsporidia species.

Molecular Characterization of the Trichomonas gallinae in British birds - P76 (SP)

Abdulwahed Alrefaei[1], Diana Bell[1], Becki Lawson[3] and Kevin Tyler[2]

1 University of East Anglia, School of Biological Sciences, Norwich NR4 7TJ, UK
2 Norwich Medical School at the University of East Anglia, Norwich NR4 7TJ, UK
3 Institute of Zoology, Zoological Society of London, Regents Park, London NW1 4RY, UK

Trichomonas gallinae is a single cell protozoan parasite, is the causative agent of the trichomonosis disease, which commonly infects many species of birds worldwide, although previously it was mainly restricted to pigeons and their avian predators. *Columba livia* (Rock Dove) is considered the primary host of *T. gallinae*. Trichomonosis has a world-wide distribution, and has recently been highlighted as a pandemic threat to finches in Europe and North America. Since 2005, when trichomonosis was first found in wild finches in UK, it has caused unprecedented population declines in European Greenfinches (*Chloris chloris*) and Common Chaffinches (*Fringilla coelebs*) via a clonal epidemic strain. To understand the potential origin of this epidemic and to further investigate its host range, we have extracted DNA of *T. gallinae* from a range of avian species in Britain to identify the genotype of the strains using polymerase chain reaction (PCR). Sequence analyses of the Fe-hydrogenase gene and ITS1/5.8S rRNA/ITS2 region indicate variation in these parasite strains found in samples collected. This study demonstrates for the first time the presence of *T. gallinae* strain diversity in British columbids and Black Naped Fruit Dove, but the finch epidemic strain was predominant amongst in British birds.

Genetic diversity of African isolates of Toxoplasma gondii: are local strains identical? - P77 (SP)

Mohammed H Alruhaili[1,2], Judith E Smith[1]
1 School of Environment and Life Science, Biomedical Science Research Centre, University of Salford, UK
2 Department of Microbiology and Medical Parasitology, Faculty of Medicine, King Abdulaziz University, KSA

School of Environment and Life Science, Biomedical Science Research Centre, University of Salford, UK

Toxoplasma gondii is intracellular protozoa parasite and has the ability to infect all warm-blooded animals including humans. While the three clonal lineages predominate in North America and Europe, strains from other regions in the world appear to have more diverse genotypes. Analysis of isolates from

South America, Asia and Africa via PCR-RFLP or microsatellite markers reveals that majority of isolates have type I, II or III alleles, identical to those in the main three lineages. The main aim of this study is to focus on African isolates and investigate their genetic relationship to global strains and the level of variation across multiple loci relative to reference type II and III strains. The study conducted multi-locus nested PCR analysis of *Toxoplasma gondii* samples collected from Africa, which was applied by using eleven different genetic markers distributed across eight chromosomes and the apicoplast genome "SAG1, 5'-SAG2, 3'-SAG2, Alt.SAG2, GRA6, L358, BTUB, SAG3, C22-8, C29-2, PK1 and Apico" to increase the resolution and discriminative power in detecting the genetic diversity between isolates. The analysis across multiple loci revealed high level of sequence homology between the African isolates and the reference strains that originate from North America. However there were some limited genetic variations among these isolates, it is noted that the growth characteristics of the parasites differ despite this limited genetic diversity. The deeper sequencing –whole genome- is applied to understand the impact of local variation on strain diversity and phenotype, noting the significant differences in growth rate among closely related isolates.

Bats and endoparasites: the role of Toll-like receptors - P81 (SP)

Hattan Gattan, Jennifer Lord, Arianne Lovey, Steve Parker, Fiona Parker, Geoff Hide and Darren Brooks

University of Salford

Bats (*Chiroptera*) are one of the most successful and diverse of mammalian orders, with an estimated 1100 species worldwide. They are host to a range of infectious agents including rabies, SARS and ebola viruses, and they also harbour parasites. However, studies of bat parasites are relatively limited when compared with that of other mammalian orders such as the *Rodentia*. As such, there are many fundamental questions concerning parasites of bats that remain unanswered. To this end, we initiated a parasitological analysis of a population of pipistrelle bats (*Pipistrellus pipistrellus* and *P. pygmaeus*) obtained from the South Lancashire/Greater Manchester area of the United Kingdom. These specimens were either dead upon acquisition, or, were euthanized due to extent of injury. Our published findings show that pipistrelles are commonly infected with trematodes and that interestingly, there was a statistically significant difference in the distribution and abundance of these parasites between male and female bats (Lord et al. 2012). We have also recently confirmed that bats may act as a reservoir host for the protozoan parasite *Toxoplasma gondii* (Dodd et al. 2014). We have also utilised molecular screening to detect the presence of trypanosomes, *Babesia vesperuginis* and eimerian parasites. We now wish to address how the bat immune system interacts with this plethora of parasites and hence have initiated an analysis of pipistrelle Toll-like receptor genes. Currently, we are screening pipistrelle TLR4 and TLR2 genes with a view to characterising the genetic variation in these Toll-like receptors and whether,

The Study of Phosphoinositide 3-Kinase Signalling in Giardia intestinalis - P86

Priyvudh Herabutya

Royal Holloway University of London, Egham hill, Egham, Surrey TW20 9BF

Phosphoinositide 3-kinase signalling pathways are critical in the regulation of several cellular mechanisms studied in mammalian and yeast cells. Previous studies have identified and characterised

two putative phosphoinositide 3-kinase (PI3K) genes in *Giardia intestinalis* called GiPI3K1 and GiPI3K2, which have homology to Class I and Class III PI3K isoforms, respectively. *G. intestinalis* is a parasitic protozoan causing diarrhoea and malabsorption throughout the world. It has been hypothesised that Giardia processes such as cell growth, differentiation and vesicle trafficking, all of which are important for parasite proliferation and disease transmission, may be mediated by the PI3K signalling mechanism. This research aims to test this hypothesis using bioinformatics and a range of experimental approaches. We used BLAST and Clustal W analysis to further characterise PI3K genes and identify and characterise additional putative ancillary components of lipid signalling cascades. A limited number of such components was identified in the Giardia genome by homology searching, but two genes with high homology t*o Saccharomyces cerevisae* glycogen synthases kinase-3 (GSK-3) were found with 40% identity to Giardia GSK sequence alignment. To investigate the putative functionality of these lipid signalling kinases in Giardia, we exposed parasite trophozoites to a range of well characterised specific inhibitors of GSK and PI3K and measured their effect on parasite growth. Moreover, scanning and transmission electron microscope were employed to study the effect of PI3K inhibitors on Giardia morphology.

Seroprevalence of Antibodies and Genotype Analysis of *Toxoplasma gondii* in Pet and Stray Types of the Domestic Cat, Felis catus, in Riyadh City - P70 (SP)

Albandra Hamd & Ebtesam Mohammed Salah Al- Olayan King Saud University.

Saudi Arabia in Riyadh City

Toxoplasma gondii is an obligate parasite. The parasite infects warm-blooded animals and humans, causing toxoplasmosis. Cats play an important role in the disease as it the definitive host and intermediate hosts. This study included blood sample collected from 70 stray and 60 pet cat from different districts of the Riyadh city .The detection of antibodies using both IFAT and ELISA techniques the compare between both techniques. Also, PCR was using to identify B1 and SAG2 genes prevalence of antibodies in stray cats was 52.86% compared with 13.33% in pet cats using IFAT-IgG test.And using ELISA- IgG test found that the prevalence the stray cats was 15.71% compared to 8.33% in pets one.and high incidence was recorded in females (37.1% in stray cats and 11.7% pet) then males (15.7% stray and 1.7% pet cat). Also by ELISA technique females (10% stray and 6.7% pets) then males (5.7% stray and 1.7% pet). PCR in which all the samples showed negative results in the PCR technique and this may be due to the need to study more genes to identify the genotyping. In conclusion *Toxoplasma gondii* parasite was more prevalent in stray cats than in pet ones and was correlated with the regions for the presence of the cats and also their sexes and this may be an important cause for spreading of this disease.

***Fasciola hepatica* from naturally infected sheep and cattle in Great Britain are diploid - P88 (SP)**

Nicola Beesley, K. Cwiklinski, D. J. L. Williams, J. E. Hodgkinson

Veterinary Parasitology, Institute of Infection and Global Health, University of Liverpool

Fasciola hepatica is increasingly a cause of parasitic disease of economic and welfare importance in sheep and cattle in the UK. Information on ploidy and spermatic status is key to understanding the

complex reproductive biology of *F. hepatica* as well as for genome assembly and population genetic studies. Although diploid (2n=2x=20) and triploid (2n=3x=30) *F. hepatica* have been reported in the UK, and in Asia diploid, triploid and mixoploid (2x/3x) *Fasciola spp.* exist, there is little information to indicate how commonly triploidy occurs, particularly in UK fluke. Using an aceto-orcein squash technique the stages of spermatogenesis were identified and ploidy was determined for 565 adult *F. hepatica* from 66 naturally infected British sheep and 150 adult *F. hepatica* from 35 naturally infected British cattle. All 715 of these parasites were diploid, based on observation of ten bivalent chromosomes and sperm (n=335) or, since triploids are aspermic, sperm alone (n = 380). The proportion of triploids was 0% (95% CI: 0-0.49%). This constitutes the first extensive analysis of the ploidy of wild British *F. hepatica* and shows that *F. hepatica* isolated from naturally infection sheep and cattle are primarily diploid and, since sperm was seen in all parasites studied, they also have the capacity to undergo sexual reproduction. Triploids, and by extension parthenogenesis, are rare or non-existent in wild British populations.

Liver Fluke Neuropeptide Biology - P90 (SP)

Christopher McFarland[1], P. McVeigh [1], A.G. Maule [1], A. Mousley [2], J. Hodgkinson [2], S. Paterson [2], and N.J. Marks [1].

1 Molecular Bioscience-Parasitology, Institute of Global Food Security, School of Biological Sciences, Queen's University Belfast, Belfast BT9 7BL.
2 Institute of Integrative Biology, University of Liverpool, UK.

Fasciola hepatica infection is estimated to cause $3.2 billion of annual losses in global agriculture through reductions in meat production, liver condemnation, reduced wool and milk output and expenditure upon flukicidal drugs. In addition, current estimates suggest 2.4 million people worldwide are infected with liver fluke, with over 18 million cases potentially undiagnosed and a further 180 million living in areas at risk of infection. Whilst Triclabendazole has remained the drug of choice to treat liver fluke infections, an upsurge in drug resistance in the past two decades has prompted the discovery of novel treatments. The recent completion of a liver fluke genome project has, for the first time, facilitated bioinformatics led approaches to the discovery of new control targets/target systems in fluke. One such system encompasses neuropeptide signalling, known to be central to normal motor and sensory capabilities in helminths. Here we report the identification of a set of 19 predicted neuropeptide genes discovered using bioinformatic search criteria including cleavage sites and conserved motifs. The 19 putative neuropeptide genes span a variety of peptide families including: NPFs, FLPs, L/M/I amides and non-amidated peptides and provide starting points for the functional interrogation of their role in fluke biology.

A Population Study of Schistosomiasis haematobium infection in pre-school children presenting to rural health outposts in Mulanje, Malawi - P3

Andrew Nicolson, Clare Shakespeare, Elizabeth Hennessy

Mulanje Mission Hospital, PO Box 45, Mulanje, Malawi University of Aberdeen, King's College, Aberdeen AB24 3FX

Schistosomiasis haematobium is endemic throughout Malawi, with prevalence rates exceeding 50% in some regions of the country. However the extent of disease nationally in the pre-school population is currently unknown. A deficiency of evidence exists for this age group worldwide, with a small number of studies showing prevalence ranging from 11.2-71.8%. As a result they are not currently included in mass drug administration of preventative therapy. The aim of this population study was to determine the prevalence rate of infection in children under 5 in the Mulanje region of southern Malawi. Methods: In January 2014, the presence of *S. haematobium* in pre-school aged children was assessed across 6 rural health outposts in the Mulanje region of southern Malawi. Urine samples were analysed for the presence of microhaematuria and *Schistosoma* ova. A questionnaire was also implemented to identify the primary water based habits of the children. Results: Prevalence of *S. haematobium* was detected as 10.58% (CI95 4.48-16.68) from 101 sampled children. Microhaematuria was present in 62.5% of these samples. No significant difference in infection rates was noted between sexes (p=0.5). Water habits of the population indicated that 45.12% (CI95 35.95-54.29%)) bathed in local rivers while 34.51% (CI95 25.72-45.3) utilized boreholes. Increased water exposure was noted within individuals bathing in rivers. Conclusion: It would appear that *S. haematobium* infection is prevalent within the preschool population of the Mulanje region. Further research is required with regards to including these children in Malawi's mass drug administration for the treatment of Schistosomiasis.

Epidemiology of *Toxoplasma gondii* in pigs from Yucatan - P91 (SP)

Ana Isabel Cubas Atienzar [1], Smith Judith [1], Jimenez-Coello Matilde[2], Ortega-Pacheco Antonio[2].

1: University of Salford (UK)
2: Autonomous University of Yucatan (Mexico)

Yucatan is considered an endemic area of Toxoplasmosis in Mexico; more than 70% of the population is infected with this highly successful parasite. In the current study, the prevalence of *T. gondii* was assessed in 444 pigs from 12 intensive farms from Yucatan. A stratified study by age was developed and questionnaire information was collected of farm management and characteristics. The aim of this study is to establish the disease levels in the Mexican pig industry and reveal which factors could be important in *T. gondii* transmission at farm level. IgG antibodies were measured with an indirect ELISA kit (Human-GmbH, Wiesbaden, Germany) and all the samples were tested by nested-PCR for the SAG 1 gene. Results of this survey showed 71% overall prevalence of IgG antibodies and a 27% of PCR positives. The seroprevalence increased with the age, reaching the 95.8% in the oldest pigs. PCR positives were found in all ages and production areas. The statistical analysis revealed a significant association between age and seropositivity and the risk factors with stronger association with T. *gondii* transmission were: high density of cats (OR=2.76), lack of rodent control (OR=2.69) and concrete pens in the nursery area (OR=2.17). These results showed high levels of *T. gondii* IgG antibodies in pigs at market age suggesting that pork can be a risk for human consumption. Risk assessment suggested that cats and mice could be associated with higher risks of infection and that improved farm management could have an impact in *T. gondii* transmission dynamics.

Anopheles gambiae redox enzymes: Haem oxygenase and Cytochrome P450 Reductase - P100 (SP)

Christopher Spencer[1], Glauber Pacelli Gomes de Lima[1], Cristina Yunta Yanes[1], Kay Hemmings[1], Lu-Yun Lian[2], Gareth Lycett[1], Mark Paine1

1 Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, L3 5QA
2 Institute of Integrative Biology, Biosciences Building, University of Liverpool, Crown Street, L69 7ZB

Blood sucking insects depend on haematophagy for survival and oogenesis. However, the free haem released by haemoglobin proteolysis is known to be toxic, generating reactive oxygen species, leading to oxidative damage, as well as alterations in cell membrane permeability. To overcome this, bloodsucking insects have evolved a number of systems of haem detoxification including antioxidant enzymes, peritrophic membranes, aggregation and haem oxygenase (HO) directed haem catabolism. In this study, we have examined HO function in the malaria mosquito *Anopheles gambiae*. HO was identified via genome database searches, then amplified, cloned, and expressed in *E. coli*. Spectroscopic assays have been performed to confirm the presence of each of the classical products of haem catabolism, confirming that AgHO is a true haem oxygenase. Preliminary in vivo data suggest that haem oxygenase activity is related to insect fecundity, hinting at a novel target for vector control. Also cloned and expressed were cytochrome P450 reductases (CPRs) from a range of different haematophagous and non-haematophagous insects. As CPR is the necessary redox partner of HO, in vitro experiments were performed to examine whether or not a blood feeding habit has any correlation with differences in CPR activity.

Epidemiological Reports of Leishmaniasis Disease in Saudi Arabia until 2013 - P4

Abdulsalam Abdulhadi Alkhaldi
Department of Biology, College of Science, Aljouf University, Sakaka, Saudi Arabia

Saudi Arabia is a country in which leishmaniasis disease is spreading remarkable. In this paper, the epidemiology of leishmaniasis in Saudi Arabia (up to 2013) was studied. Data were obtained from the Ministry of Health, which show two types of leishmaniasis: cutaneous leishmaniasis (CL) and visceral leishmaniasis (VL). In 2010, 2011, 2012 and 2013, the number of patients with CL was 4131, 1951, 1464 and 1988 respectively, and the percentage of Saudi patients to non-Saudi patients was almost 52% throughout these years. In addition, more than 75% of patients were male throughout these years. The highest number of patients occurred in January 2013, with 250 cases; the lowest number occurred in July, with 77 cases. Al-Madinah al-Munawarah province registered high numbers, with 591 cases. On the other hand, in 2010, 2011, 2012 and 2013, a smaller number of cases were recorded for VL: 8,7,8 and 13 respectively. The highest incidence of VL was observed in Jizan province, with 8cases. It was concluded that the number of cases of CL decreased from 2010 to 2013 but there has been no change in the last three years

Investigating the basis of metabolic resistance to insecticides in Anopheles gambiae from Uganda using whole genome transcriptomics - P104

Alison Isaacs [1] Henry D. Mawejje[2], Martin J. Donnelly1

1 Department of Vector Biology, Liverpool School of Tropical Medicine, Liverpool, United Kingdom
2 Infectious Diseases Research Collaboration, Kampala, Uganda

Insecticide use in Uganda for both malaria control and agricultural purposes has led to the proliferation

of DDT and pyrethroid-resistant mosquitoes. To combat malaria transmission, the Ugandan government has recently embarked on an ambitious program of indoor residual spraying with a carbamate class insecticide, bendiocarb. In anticipation of this campaign, we measured insecticide resistance among An. *gambiae* s.l. from three sites in Uganda using WHO bioassays. Resistance to DDT, permethrin and deltamethrin was detected, while susceptibility to both fenitrothion and malathion was observed. Intermediate levels of bendiocarb resistance were detected in all three sites, with the lowest mortality observed in Kanungu (79%). Bendiocarb-resistant mosquitoes were collected for subsequent whole genome microarray experiments, and expression of candidate genes was validated using qPCR. Elevated expression of CYP6M2, a cytochrome P450 gene, and an epithelial serine protease gene was detected in mosquitoes from Kanungu. In contrast, resistant mosquitoes from Tororo displayed overexpression of a gene encoding a cuticular protein and several genes encoding salivary gland proteins. CYP6M2 overexpression has previously been identified as a component of metabolic resistance to both pyrethroid and carbamate class insecticides in West Africa. Our findings elucidate a mechanism of carbamate resistance that protects mosquitoes lacking a target site mutation. Further studies of mosquitoes from Tororo will allow us to characterize novel mechanisms of resistance.

The depletion of *Wolbachia* from *Brugia malayi* microfilariae blocks transmission in Aedes aegypti - P34

Darren Cook, Gemma R Molyneux, Andrew Steven, Ana Guimaraes, Kelly L Johnston, Hayley E Tyrer, Mark J Taylor

Department of Parasitology, Liverpool School of Tropical Medicine Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5QA

The filarial nematode *Brugia malayi* is a human pathogen that harbours the bacterial endosymbiont, *Wolbachia*. Tetracycline treatment causes the depletion of *Wolbachia* leading to infertility and early death in the adult worm. Here we have investigated the effect of *Wolbachia* depletion from microfilariae (Mf) on their development to the L3 infective stage within the mosquito, *Aedes aegypti*. Following antibiotic treated for 2, 4 and 6 weeks Mf were extracted and fed to mosquitoes and the subsequent development to L3 larvae was compared to untreated mf. Live Mf were directly visualised within the mosquito midgut and also proteomic analysis was conducted of secretory/excretory products from treated and control Mf. The results show the significant effect of *Wolbachia* depletion on the ability of Mf to progress to L3 stage and treated Mf are unable to escape the mosquito midgut. The retardation of Mf development will provide a potent transmission blocking effect soon after *Wolbachia* depletion by antibiotics.

Endemic UK Entomopathogenic Nematodes as Vector and Haematophage Control - P106 (SP)

Sandra Hughes-Crean

Liverpool John Moores University, James Parsons Building, Byrom Street, Liverpool L3 3AF

Entomopathogenic nematodes (EPNs) have been successfully used as a means of controlling insect crop pests since the 1980s and are now used regularly where the use of insecticides are prohibited such as citrus crops. Laboratory experiments have shown that EPNs are capable of parasitizing more than 200

species of insect and that they are naturally occurring parasites of many vector families. The central theme of this research is to ascertain whether naturally occurring EPNs be used to control nuisance biting and vector species such as mosquitoes, blackflies and midges. Preliminary experiments have shown that commercially available preparations of the nematode *Steinernema kraussei* have successfully penetrated and killed Chironmid larvae and 4th instar larvae of the mosquitoes Culex pipiens and *Aedes aegypti*. This research will be expanded to include other heamatophagous species such as *Simulium sp*., *Cimex lectularius* and common Ixodidae species. This research also includes mapping the diversity and distribution of naturally occurring EPN species throughout the whole of the United Kingdom at a genetic level. This collection of isolated EPNs will also be used to test the pathogenicity of naturally occurring species from the U.K. as a potential means of biocontrol for nuisance and vector species.

T. cruzi Strain Panel Development for High Throughput Phenotypic Screening - P33

Lorna MacLean, John Thomas, Manu De Rycker.

Drug Discovery Unit Division of Biological Chemistry and Drug Discovery James Black Centre College of Life Sciences University of Dundee DD1 5EH UK

Chagas disease is caused by the protozoan parasite *Trypanosoma cruzi* which is transmitted in the faeces of infected *Triatomine* bugs. An estimated 8 million people are infected across 21 Latin American countries, however, Chagas disease is also becoming a global problem due to human migration. 30% of cases develop cardiac disorders and/or digestive mega syndromes resulting in ~13,000 deaths annually. The current drugs Benznidazole and Nifurtimox are inadequate as these provide variable efficacy in chronic Chagas disease, cause adverse side effects, and require long treatment duration, therefore, new treatments are urgently required. We have developed a screening cascade using several in vitro high-content image-based intracellular assays for *T. cruzi* hit discovery. These assays use the x10/7-A1 strain/ vero cell model and have successfully identified 3 series with in vivo activity in an acute model of Chagas disease. However, *T. cruzi* is genetically highly diverse and has been assigned discrete typing units (DTU) TcI-VI. Therefore, we have developed a genotype-confirmed *T. cruzi* strain panel isolated from patients to verify that lead-op drug candidates are effective across all DTU. We show varying replication rates between strains and potency profiles between compound series. Nirfurtimox, Benznidazole and series A were active across the panel, while Posaconazole and series B were not active against slowly replicating strain PAH179 Cl5 suggesting a possible replication-dependent mode of action. Our ultimate aim is to correlate *T. cruzi* panel data with in vivo data to improve predictability of our in vitro screening cascade for *T. cruzi* drug development.

Intermediate host snails of Schistosoma on water hyacinth migrating in Lake Victoria - P110

Kyoko Futami, George Sonye, Peter A. Lutiali, Ayub Ofulla, Shinjiro Hamano, Noboru Minakawa

1.Institute of Tropical Medicine, Nagasaki University, Japan (KF, SH, NM)
2.Springs of Hope, Mbita, Kenya (GS)
3.NUITM-KEMRI Project, Nairobi, Kenya (PAL)
4.Maseno University, Kenya (AF)

Water hyacinth is a suitable habitat for the intermediate host snails of *Schistosoma* in Lake Victoria. Because several batches of water hyacinth migrate in the lake, the plant could transfer *Schistosoma* infected snails. This study was designed to confirm the presence of snails on floating water hyacinth, and to reveal on which plant parts likely snails attached. A total of 279 floating water hyacinth plants within 65 batches were examined in the Kenyan part of the lake in 2014, and carefully searched for snails on the plants within a batch (each plat was distinct with presence of roots). Then, the number of stems was recoded for each plant, and the lengths of the longest stem and fibrous root were measured. When a snail was found, the location and distance from the base were measured. Total wet weight and the number of plants of each batch were also recorded. Collected snails were placed under light for shedding cercaria in lab. Most snails were located within 5 cm from the base. Collected snails had various shapes, i.e. discoidal, spirally coiled with dextral or sinistral opening. Only one snail produced cercaria having two tails, but it was not human *Schistosoma*. More snails were collected from larger plants, irrespective of batch size. This study revealed that floating water hyacinth carried various types of snail. As taxa of collected snails are currently being identified, it is still uncertain whether water hyacinth transfers *Schistosoma* snails.

Bloodmeal digestion and peritrophic matrix kinetics in four sand fly species differing in vector competence to *Leishmania* donovani - P112

Jovana Sadlova, Katerina Pruzinova, Miroslav Homola and Petr Volf

Department of Parasitology, Faculty of Science, Charles University, Prague, Czech Republic

The early phase of *Leishmania* development in sand flies is closely connected with bloodmeal digestion. Here we compared various parameters of bloodmeal digestion in four sand fly species that are either susceptible (*Phlebotomus argentipes* and *P. orientalis*) or refractory (*P. papatasi* and *Sergentomyia schwetzi*) to *Leishmania donovani*. The volume of the bloodmeal ingested, time of defecation of bloodmeal remnants, timing of formation and degradation of the peritrophic matrix (PM) and dynamics of proteolytic activities were studied. Interestingly, the two natural *L. donovani* vectors strikingly differed from each other in kinetics of the PM and secretion of midgut proteases. Females of P. argentipes possessed fast bloodmeal digestion with a high peak of chymotrypsin activity, degraded the PM rapidly and defecated on day three PBM. On the other hand, *P. orientalis* females digested slowly, had low peaks of proteolytic activities and defecated around day five PBM. In comparison to *P. papatasi* and *S. schwetzi*, both *L. donovani* vectors had lower trypsin activity and slower formation of the PM. In all tree *Phlebotomus* species studied the period between the breakdown of the PM and defecation of the bloodmeal remnants was significantly longer than in *S. schwetzi.* This period, i.e., the time frame when *Leishmania* escape from intraperitrophic space and attach to the midgut epithelium in order to prevent defecation, seems to be one the crucial parameter acting in the early phase of *Leishmania* development in the sand fly midgut.

Development of amastigote-initiated infections of *Leishmania* donovani in four sand fly species - P113

Jitka Myskova[1], Jovana Sadlova[1], Matthew Yeo[2], Petr Volf[1]

1 Department of Parasitology, Charles University, Vinicna 7, 12844 Prague 2, Czech Republic
2 Department of Pathogen Molecular Biology, London School of Hygiene and Tropical Medicine, London,

UK

In sand flies, the *Leishmania* life cycle proceeds from amastigotes ingested with a bloodmeal to promastigotes which undergo a sequential morphological development, multiply and migrate anteriorly to colonize the stomodeal valve in order to be transmitted to a vertebrate host. This complex parasite-vector interaction is often species-specific. Here we compared development of *Leishmania* donovani in two sand fly species susceptible to *L. donovani (Phlebotomus orientalis, P. argentipes)* and in two refractory ones (*P. papatasi, Sergentomyia schwetzi*). Amastigote-initiated infections were performed using a membrane feeding method; parasite numbers, their location and proportion of morphological forms were examined by microscopy by day 2, 3, 6 and 10 post bloodmeal (PBM). By day 2 PBM, heavy infections prevailed and no differences in infection rates were found in four sand fly species tested. From day 3 PBM, different patterns of *Leishmania* infection was observed. In both *L. donovani* vectors the parasites escaped from the endoperitrophic space, colonized the thoracic midgut and often reached the cardia region; elongated nectomonads were the predominant parasite form by this time. On the other hand, in *P. papatasi* the parasites were limited to abdominal midgut and in *S. schwetzi* remained enclosed in the peritrophic matrix; procyclic promastigotes remained the prevailing morphological form in both refractory species. Late stage infections with massive parasite loads and colonization of the stomodeal valve were found only in *P. orientalis* and *P. argentipes*.

Physiological and behavioural aspects of insecticide resistance in dengue vectors in the kingdom of Saudi Arabia (KSA) - P114 (SP)

Ashwaq Alnazawi, David Weetman., Philip McCall.

Liverpool School of Tropical Medicine, Liverpool

Dengue has become increasingly common since it was first recognised as an endemic disease in (KSA) in 1994. Integrated vector control including the use of insecticides remains the only method for the control and prevention of outbreaks. Successful control of dengue virus is challenging due to the diurnal biting behaviour of the primary vector mosquito *Aedes aegypti*, and widespread physiological resistance to many insecticides. The possibility that behavioural resistance also might compromise control tools is an additional challenge, though the nature of such resistance and its interaction with physiological resistance is poorly understood. This study is investigating physiological and behavioural resistance in wild *Aedes aegypti* populations from dengue endemic areas of Makkah and Jeddah, in comparison with highly resistant and wholly susceptible laboratory reference strains. This preliminary work compared the effect on 5-day old adult female *Aedes aegypti* of deltamethrin delivered as a single 60-minute exposure as multiple daily exposures for 10 days. Experiments also investigated the effect of exposure duration (1,6 and 8 hours) using wild mosquitoes from KSA and the reference strains. The results showed that mosquito age at exposure did not affect mortality rates after a single exposure (P=0.16). Conversely and surprisingly, multiple exposures over 10 days led in higher survival rates (P=0.007); exposure durations of 1, 6 and 8 hours showed no difference in effect on young adult females (P=0.72), but did increase mortality in suggesting there are age-dependent costs of resistance. Future work will investigate resistance in recently collected mosquitoes from KSA.

Avian coccidia: intestinal terrorists but systemic saviours? - P115 (SP)

Sarah Macdonald, Fiona M. Tomley[1], Richard Stabler[2] and Damer P. Blake[1]

1 Pathology and Pathogen Biology, Royal Veterinary College, Hawkshead Lane, North Mymms, AL9 7TA, UK.
2 Department of Pathogen Molecular Biology, London School of Hygiene and Tropical Medicine, Keppel St, London, WC1E 7HT

Eimeria causes the intestinal disease coccidiosis, most notably in poultry. While the impact of coccidiosis on animal health and welfare is clear, its influence on enteric microbiota and knock-on effect on chicken health and production remains largely unexplored, with the possible exception of Clostridium perfringens. *Campylobacter*, is the most common cause of bacterial foodborne illness in humans in the developed world; with raw or undercooked poultry meat identified as major sources of infection. A combination of One Health factors including zoonotic impact, animal welfare and associated economic ramifications elevate interest in *Campylobacter* within the chicken gut. Nonetheless the influence of enteric microbiota on *Campylobacter* colonisation within the avian intestine and deeper tissue remains a neglected area of research. Quantification of early *Campylobacter jejuni* colonisation of the chicken caeca, liver and spleen has revealed significant variation in the presence of concurrent *Eimeria tenella* infection. Intriguingly, parasite co-infection associates with an elevated *C. jejuni* load within the caecal lumen three and ten days post bacterial challenge but reduced colonisation of the liver and spleen. Thus, while faecal shedding of *C. jejuni* is temporarily increased by concomitant *E. tenella* infection, deep tissue bacterial contamination is decreased. The role of various immune modulators including β-defensins, mucins, Th1/Th2 signature molecules and heterophils have been investigated to explain these inversely correlated findings. Building on these studies the influence of eimerian infection on microbiome composition and pathogen colonisation of poultry may impact both the use of live eimerian vaccines and novel development of *Eimeria* as vaccine vectors.

The Current Situation of Cutaneous Leishmaniasis Control in Saudi Arabia - P116 (SP)

Waleed Al-Salem, Mohammed Adnan Aldahan [2] Hisham Altamimi [2] Abdullah Alnsiri [2] Yahya Alwan [2] Abdulltif AlRajh [2] Ali Alsharani [2] Abdulaziz Aljarallah [2] Emad Albather [2] Mohammed Alzahrani [2] Alvaro Acosta-Serrano [1]

1 Liverpool School of Tropical Meidicne
2 Saudi Ministry of Health

Cutaneous leishmaniasis (CL) is one of the most prevalent vector-borne diseases in Saudi Arabia. *Ph.papatasi*, the sandfly species that transmits *Leishmania major*, is widely distributed in arid and semi-arid areas including central, east and northern region of Saudi Arabia. However, in the higher altitude regions, *L. tropica* is transmitted by *Ph.sergenti*. Both environmental and man-made factors (climatic factors, irrigation, migration and urbanization) play very important roles to sustain disease spread. The leishmaniasis control programme strategy is based on an annual plan to control outbreaks of cutaneous leishmaniasis. This annual plan focuses on four themes. First, detect active and passive CL cases in the endemic areas and in areas having a high intensity of active rodent burrows (reservoir species). Second, monitor rodent habitats that are closely situated next to human settlements and then destroy of active burrows. Third, following rodent reservoir control, apply vector control strategies (such as indoor residual spraying with Cyhalothrin, thermal and ultra-low volume fogging (ULV) with Deltamethrin) where sandfly population densities are high. Fourth, establish a robust public health education campaign to improve general awareness of the actions that must be adopted to control CL.

Well-designed and integrated reservoir/vector control strategies have had an enormous impact on reducing CL cases with about 90% disease reduction within the last 30 years.

A Disease Control Strategy to Overcome Old World Cutaneous Leishmaniasis Outbreaks - P117 (SP)

Waleed Al-Salem, David M Pigott[3],Louise Kelly-Hope[1], Karina Mondragon-Shem[1], Ahmed AL-Mehna[2], Salah Balgonaeem[2], Khalid Alsuhaibani[1], Maha Abdeladhim[4], Jesus G. Valenzuela[4], Alvaro Acosta-Serrano[1]

1 Liverpool School of Tropical Medicine, Liverpool , The UK
2 Saudi Ministry of Health, Riyadh, Saudi Arabia
3 University of Oxford, Oxford, United Kingdom
4 Vector Molecular Biology Section, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, United States of America

Cutaneous leishmaniasis (CL) is one of the most prevalent vector-borne diseases in the East Mediterranean Region. Therefore, developing new public health approaches for CL control in endemic areas is required to. A case study was undertaken at a new construction site in a remote area of Al-Ahsa province, KSA, which had not been covered by the local leishmaniasis control team. Immediately prior to the leishmaniasis transmission season started (~April 2012), 150 recently arrived (non-local) construction labourers were hired to work on a new government construction. On January 2013, ~60% of the construction labourers were reported to have acquired CL before. Serum and skin aspiration samples were taken from both infected migrant labourers and local residents from the same area. Exposure to sandfly bite was determined by measuring the levels of anti-SP32 antibodies that found significantly higher among migrant labours at non-controlled areas compared to local at controlled areas. Over the course of 2013, an integrated disease control strategy was carried out by governmental sectors, consisting of rodent (mechanical) and vector control, was applied in (and around) the construction area. Mechanical control was achieved by removal of *Hammada elegans* (rodent food plant) and burrow destruction within a radius of 500 m around the construction area. In addition, vector control was undertaken by insecticide spraying in rodent burrows and wall cracks by deltamethrin. Case study suggest develop a new public health approach for CL control in endemic areas by combination of mechanical and vector control under integration of governmental sector.

Visceral Leishmaniasis in an immunocompromised patient with Myasthenia Gravis - P6

Alex Kew, Pradhib Venkatesan, Elizabeth Hart, Louise Berry

Nottingham City Hospital, Nottingham.

A 75 year old white Caucasian male with myasthenia gravis, treated with azathioprine, presented with ongoing fevers, night sweats, rigors, weight loss, headaches and pancytopenia on blood count monitoring. He reported no other symptoms. Physical examination was remarkable for high grade pyrexia, pale mucous membranes and splenomegaly. Laboratory findings included a pancytopenia thought to be azathioprine associated but with no cause apparent from the blood film, raised C-reactive protein and raised alkaline phosphatase. Blood and urine cultures were negative and chest X ray was clear. A bone marrow aspirate and trephine was performed to investigate his pancytopaenia.

Intracytoplasmic Donovan bodies were seen and he was transferred to our Infectious Diseases Unit. On further questioning he had travelled to southern France and Spain. His *Leishmania* direct agglutination test was positive at a titre of 1 in 102,400. For a diagnosis of visceral leishmaniasis he was commenced on liposomal amphoterin (Ambisome) and after discussions with Neurology, azathioprine was cautiously replaced by oral prednisolone and he was given supportive and symptomatic treatment. There was only a partial improvement in his fevers, pancytopaenia and C-reactive protein levels at the end of 10 doses of ambisome. After finding sparse management literature for non-HIV immunocompromised patients he was then commenced on oral miltefosine for fourteen days with considerable improvement after one week. The patient was HIV negative. This case illustrates serendipity in bone marrow examination, the benefit of a detailed travel history and the added benefit of adding miltefosine to ambisome in a non-HIV immunocompromised patient.

Polylysogeny magnifies competitiveness of a bacterial pathogen in vivo - P118

Ellie Harrison, Nicola Burns [1] Chloe James [2]

1 University of York
2 University of Salford

The rise of next generation sequencing is revealing a hidden diversity of temperate phages within the microbial community. While a handful of these phages have been well characterized, for the vast majority the role of phage carriage, and especially multiple phage carriage (polylysogeny), is poorly understood. The Liverpool Epidemic Strain (LES) of *Pseudomonas aeruginosa* is an aggressive pathogen in Cystic Fibrosis lung infections that has recently been found to contain several unique prophages within its genome. Here we experimentally investigate the role of two of these phages in vivo, using an insect model of infection. We find that while no benefit is conferred by phage carriage in single bacterial infections, phages confer a large fitness advantage during mixed infections by mediating bacteria-bacteria competition. Differences between the two phages appeared to be associated with the rate at which the competitor acquired chromosomal copies of the phage, and consequently phage-resistance. However the advantage was greatest in the polylysogen, suggesting that the carriage of multiple phages may itself be beneficial by hindering the spread of phage-resistance in rival bacterial populations. This study therefore suggests that the LES phages may play a role in the success of this pathogen by enhancing the within-host competitiveness of this aggressive strain.

Overcoming drug-resistant malaria using structure-based drug design - P67 (SP)

Michael Capper, Paul M. O'Neill [2] Neil G. Berry [2] S. Samar Hasnain [1] Giancarlo A. Biagini [3] Svetlana V. Antonyuk [1]

1 Molecular Biophysics Group, Institute of Integrative Biology, Faculty of Health and Life Sciences, University of Liverpool, Liverpool, L69 7ZB, UK.
2 Department of Chemistry, Faculty of Science and Engineering, University of Liverpool, Liverpool, L69 7ZB, UK.
3 Research Centre for Drugs and Diagnostics, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5QA.

Incidence of drug resistance in malaria is increasing. The rise of antimalarial resistant *Plasmodium falciparum* has put an increasing pressure on drug development. By examining existing protein targets it is possible to overcome this resistance through rational drug design. This method can be assisted by structural biology, which allows us to view a three-dimensional model of the protein and examine the site of drug binding and how the compound can be modified. Cytochrome bc1 is a proven drug target and the site of action of atovaquone, a popular antimalarial sold in combination with proguanil as MalaroneTM. Cytochrome bc1 is a membrane protein complex and is essential for maintaining the production of reduced ubiquinol for use in pyrimidine biosynthesis. It functions with two distinct binding sites: the Qo site and the Qi site. Mutations in Qo site of cytochrome bc1 have conferred resistance to atovaquone in P. *falciparum* across much of Africa. By using protein crystallography to explore drug-like compounds that are able to overcome resistance, we have shown how the 4(1H)-quinolone compounds are able to remain effective by binding at the Qi site and inhibiting of cytochrome bc1. By showing that these compounds overcome resistance by binding the Qi site, we have opened up the possibility that other compounds overcome resistance in a similar way. This work has also opened up the Qi site of cytochrome bc1 to further development of antimalarials that may help overcome the rise of resistance.

ExoRNAi, a new tool to probe plant gene function exposes contrasting roles for sugar exudation in host-finding by plant pathogens - P121

Johnathan Dalzell, Neil D. Warnock, Leonie Wilson, Juan V. Canet-Perez, Thomas Fleming, Colin C. Fleming, Aaron G. Maule

Queen's University Belfast, Institute for Global Food Security.

Here we present a simple and rapid new method for RNAi-induced knockdown of genes in tomato seedlings, through treatment with an aqueous solution of double-stranded RNA (exoRNAi). The exoRNAi method is used to assess the involvement of tomato Sugar Transporter Protein genes, stp1 and stp2 on the root exudation of glucose, fructose and xylose; monosaccharide constituents of tomato root exudate. Plant parasitic nematodes (PPNs) are responsible for an estimated 12.3% loss in crop production globally, which equates to financial losses of approximately £100 billion annually. Our data show that infective juveniles of the promiscuous PPN, *Meloidogyne incognita* are attracted to glucose and fructose, but not xylose. Glucose and fructose also agonise serotonergic stylet thrusting in M. incognita infective juveniles; a key parasitic behaviour necessary for invasion and parasitism of host plants. In contrast, infective juveniles of the selective *Solanaceae* PPN, *Globodera pallida* are not attracted to tested monosaccharides, nor do the monosaccharides stimulate stylet thrusting. We demonstrate that knockdown of both SlSTP1 and SlSTP2 in tomato seedlings by the exoRNAi method is robust and specific, and that corresponding reductions of glucose and fructose, but not xylose, in collected exudate, correlate directly with reduced infectivity and stylet thrusting of *M. incognita*. Knockdown of SlSTP1 or SlSTP2 have no impact on the infectivity or stylet thrusting of *G. pallida*. The exoRNAi platform can underpin future efforts to understand the early stages of plant-pathogen interactions in tomato, and potentially other crop plants.

Haem detoxification by haem oxygenase in the human African trypanomiasis vector Glossina morsitans morsitans - P101 (SP)

Glauber Pacelli Gomes de Lima, Chris Spencer [1]; Alvaro Acosta-Serrano [1]; Gareth Lycett [1]; Lu-Yun Lian [2]; Mark Paine [1]

1 Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, L3 5QA, UK
2 Institute of Integrative Biology, University of Liverpool, Crown Street, L69 7ZB, UK

During blood feeding haematophagous insects acquire nutrients needed for survival and successfully generate offspring. During haemoglobin proteolysis a considerable amount of highly oxidant haem is released, potentially causing membrane permeability alterations and oxidative damage through reactive oxygen species generation. Haem degradation, by the haem oxygenase (HO) enzyme, is one of the few mechanisms proposed to deplete haem levels in these organisms, avoiding its deleterious effects. However, differently from mammals, bacteria and plants, little information is known about the kinetics, physiological context and tissue distribution of insect HOs. In this study, we aim to elucidate their physiological role as well as their biophysical and biochemical features, in particular the interaction with its potential electron donor, cytochrome NADPH P450 reductase (CPR). We have cloned and expressed HOs and CPRs from several insect genera. One focus is *Glossina morsitans*, vector of sleeping sickness. Biochemical tests from an N- terminal truncated *G. morsitans* HO (.GmHO) orthologue suggests that the enzyme binds to haem, but no degradation activity has yet been observed. HPLC analysis shows a decrease in haem concentration in the insect's midgut after a blood meal. However, qPCR data suggests that GmHO expression is stimulated by blood feeding in tissues such as testes and head, but not in the midgut. Our early findings suggest that HOs may play a role in haem binding and detoxification in *G. morsitans*, however further assays are needed to confirm and clarify other biochemical and physiological properties of this potential new molecular target for insecticide development.

Reducing Infant Mortality: Success of Malaria Control Programme in Bangladesh - P66 (SP)

Mohammad Moktadir Kabir, Mohammad Harun-Or-Rasid, Shamsun Naher, Shahidul Islam Laskar, Nur-E-Naznin Ferdous, Md. Akramul Islam

Bangladesh

Background: Malaria is endemic in 13 districts of Bangladesh bordering with India and Myanmar and about 13 million people are at risk. BRAC has been working in malaria control since 1998, in partnership with the government, which was scaled up in 2007 with the support from the Global Fund. Methodology: Community-based female service providers have been deployed to deliver services at the doorstep of the people. They provide diagnosis (using RDT) and treatment services (ACT/chloroquine and primaquine) to uncomplicated confirmed cases, and refers severe cases, pregnant women and <5kg child to the government health facility. They also promote LLIN use with special focus on children and pregnant women and mobilize people to improve care-seeking behaviour through regular household visits and group meetings. Result: LLIN use by U-5 children was maintained at >80% since 2008 (92.2% in 2014). Infant morbidity showed significant decline (3.7% of total in 2007 to 0.5% in 2014). There was also a decline in the number of deaths from malaria (252 in 2007 to 45 in 2014) where there was no infant death since 2011. Despite an upsurge of malaria cases in 2014 with threefold death from previous year, the infant mortality continued to be zero. Conclusion: Scaling up of LLIN use, expansion of EDPT and community mobilisation through household visits of the community service providers increased accessibility to malaria diagnosis & treatment services and improved early health care-seeking behaviour. All these contributed reduction of morbidity and mortality of malaria especially among

infants.

A novel and stable method of gene knockdown in the Chagas disease vector Rhodnius prolixus - P126

Miranda Whitten [1], Paul D. Facey [1], Ricardo Del Sol [1], Lorena T. Fernández-Martínez [1,2], Meirwyn C. Evans 1, Jacob J. Mitchell [1,3], Owen G. Bodger [1] and Paul J. Dyson [1].

1 Institute of Life Science, College of Medicine, Swansea University, Singleton Park, Swansea, SA2 8PP, U.K.
2 John Innes Centre, Norwich Research Park, Colney, Norwich, NR4 7UH, U.K.
3 Centre for NanoHealth, ILS2, Swansea University, Singleton Park, Swansea, SA2 8PP, U.K.

RNA interference (RNAi) is a powerful tool for inhibiting insect gene expression, but it can be challenging in many species due to methodological problems associated with double-stranded (ds) RNA delivery. These problems have limited the study of insects and the development of RNAi-based biological control. Here, we demonstrate constitutive, trauma-free RNAi in an insect vector of disease using symbiotic bacteria as the dsRNA delivery vehicle. Systemic knockdown phenotypes were mediated by recombinant symbiotic *Rhodococcus rhodnii* bacteria in the vector of Chagas disease, *Rhodnius prolixus*. When ingested, the manipulated bacteria colonized the gut and successfully competed with the wildtype microflora. As expected, *R. rhodnii*-mediated knockdown of genes encoding salivary nitrophorins resulted in dysfunctional salivary glands. Additionally, exceptional knockdown stability and longevity was demonstrated in a 200-day trial in which vitellogenin synthesis was compromised, resulting in an impaired fecundity phenotype. Additionally, the recombinant bacteria (and hence the phenotype), were horizontally-transferable between individual insects. Symbiont-mediated RNAi offers considerable potential for use both as a research tool and as a means of biocontrol for insect vectors of disease.

Screening of Dengue viruses in human sera and analysis of specific serotypes - P127

Nusrat Jahan and Noreen Aziz

GC University, Lahore 54000 Pakistan

Dengue is a vector borne viral infection which poses a serious threat to public health in most of the tropical and subtropical countries around the world, including Pakistan. Dengue has been occurring as an annual epidemic since 2006 in Pakistan. More than fifteen thousand cases were listed in 2011 from Punjab with about > 250 deaths. Dengue situation is alarming with high risk of epidemics in future. About four antigenically varying DENV serotypes are reported for dengue infection. Current study was designed to detect Dengue viruses with molecular detection of dengue serotype using RT-PCR in infected human sera. Dengue infected human sera (n=100) were collected during the above mentioned period for screening of DENV serotypes using dengue NS1 AG specific ELISA kit. DENV +ve samples (n=40) were used for molecular detection of dengue viruses serotypes by reverse transcriptase PCR (RT-PCR) using universal and type specific primers for dengue viruses nucleotide sequencing targeting the C-prM gene junction. Among forty dengue NSI AG ELISA positive samples, 12 sera (30%) were found +ve with type specific nested PCR. Out of 12 PCR +ve samples, five samples (41.6%) were positive for each DEN-2 and DEN-3. Whereas, two samples (16.6%) revealed the simultaneous presence of DEN-2 and DEN-3 serotypes. In conclusion, current study documented the detection of dengue viruses

serotypes in human sera with DEN-2 and DEN-3 prevailing serotypes during the study period in Lahore, Pakistan.

Co-infections involving TBE virus, Babesia and Rickettsia spp in ticks Dermacentor reticulatus collected in newly inhabited and endemic regions of Poland - P128

Ewa Julia Mierzejewska[1], Agnieszka Pawełczyk[2], Renata Welc-Falęciak[1], Marek Radkowski[2], Anna Bajer[1]

1 Department of Parasitology, Faculty of Biology, University of Warsaw, Miecznikowa 1, 02-096 Warsaw, Poland
2 Department of Immunopathology of Infectious and Parasitic Diseases, Medical University of Warsaw, 3c Pawińskiego Street, 02-106 Warsaw, Poland

Dermacentor reticulatus is the second most abundant species of ticks in Poland. Its range was limited to Eastern Poland and since 1990's expansion in Central and Western Poland has been noted. *D. reticulatus* is the main vector for Babesia canis, the protozoan causing canine babesiosis. It may be involved in the transmission of tick-borne encephalitis virus (TBEV) and intracellular bacteria of the genus Rickettsia - pathogens dangerous to both people and animals. To investigate the differences in the risk of tick-borne diseases, depending on the time of occurrence of D. reticulatus, we determined the prevalence of TBEV in questing ticks from TBE endemic region and concurrent infections with *B. canis and Rickettsia spp*. in old and newly inhabited areas. Ticks (n=2576) were collected in 2012-2014 in North-Eastern, Central and Western Poland. DNA of *B. canis and Rickettsia spp*. was detected using PCR. RNA of TBE virus was detected using RT-PCR. Obtained sequences were compared with sequences stored in Genebank. Depending on regions, significant differences in prevalence of Rickettsia (25-93%) and *B. canis* (0-17.5%) infection were demonstrated. High prevalence of TBEV (7.6%) was detected. Our study confirmed the importance of *D. reticulatus* in the circulation and maintaining of pathogens constituting health hazard either for humans or animals. This study was supported by the National Science Center (NCN) grant OPUS 2011/03/B/NZ8/02212.

Development and performance evaluation of enzyme linked immunosorbent Assay and lineblot for serological diagnosis of leishmaniasis in dogs - P129

Andreas Latz, J. Völger

NovaTec Immundiagnostica GmbH, R+D, Dietzenbach, Germany

Canine leishmaniasis is a zoonotic disease by the protozoan parasite *Leishmania* transmitted by the bite of an infected *phlebotomine* sandfly. *Leishmania infantum* is the most common and important cause of canine leishmaniasis worldwide. Other *Leishmania spp*. reported from dogs include *L. mexicana, L. donovani, and L. braziliensis*. Leishmaniasis can be categorized by two types of diseases in dogs: a cutaneous reaction and a visceral reaction also known as black fever, the most severe form of leishmaniasis. Infection does not invariably lead to illness. In fact, most infected dogs remain asymptomatic and may never develop clinical manifestations. In endemic regions, the prevalence of disease is often less than 10% and only about 1 in 5 infected dogs are considered likely to develop clinical disease. Diagnosis of canine leishmaniasis is based on the presence of clinical signs together with positive specific antibody assay. The aim of this work was to develop a serological ELISA assay to

detect IgG and IgM antibodies against *Leishmania* in serum or plasma samples derived from all mammals. Microtiterplates were coated with antigen preparations of *Leishmania infantum*. The presents of antibodies against *Leishmania* is detected by protein A/G-HRP. A sample collection of about 200 positive samples and 400 negative samples was used for development and evaluation of the assay. Here we show the performance characteristic of the newly developed assay. Due to the improved antigen design, purification method and test setup a superior assay performance was achieved compared to other test methods.

In vivo functional analysis of insecticide resistance in Anopheles gambiae mosquitoes - P108 (SP)

Adriana Adolfi, Amy Lynd, Hilary Ranson, Gareth Lycett

Liverpool School of Tropical Medicine Vector Biology Department Pembroke Place L3 5QA Liverpool United Kingdom

Insecticide resistance in the malaria mosquito *Anopheles gambiae* is spreading fast seriously hindering vector control in Africa. In this scenario, identifying the genetic and molecular basis of resistance is crucial for the development of new active compounds and for re-directing control programs. The monooxygenase-encoding genes cyp6m2 and cyp6p3 are the strongest gene candidates linked to insecticide resistance as supported by in vitro metabolism experiments. Yet, *in vivo* analysis is needed to identify which cyp6 genes and tissues are responsible for the resistant phenotype to manifest in the absence of other adaptations. Here we aim to create transgenic mosquitoes to characterise the resistance phenotype resulting from the Gal4/UAS-driven overexpression of either cyp6m2 or cyp6p3 in both tissue-specific (midgut, oenocytes, Malpighian tubules) and ubiquitous expression patterns. To date, we have generated two independent UAS mosquito lines carrying cyp6m2 and cyp6p3 and successfully crossed them with midgut- and oenocyte-specific Gal4 driver lines. The expected spatio-temporal pattern of expression was confirmed in UAScyp6m2-Gal4 mosquito dissected body parts at RNA and protein level, while validation of cyp6p3 overexpression is in progress. Mosquitoes overexpressing either cyp6m2 or cyp6p3 in the midgut or in the oenocytes do not show increase in resistance to insecticides, thus the creation of a new Gal4 mosquito line for ubiquitous gene expression is the current main focus. So far, the study provides the first in vivo evidence in elucidating the molecular basis of P450-mediated metabolic resistance in *A. gambiae* suggesting a potential involvement of other cyp6-overexpressing tissue/s in driving resistance.

Innovation Program to Larvae Monitoring for Prevent Dengue Fever at Medan City North Sumatera Indonesia - P130 (SP)

Dwi Endah Kurniasih, Villino Melda Sitepu

Medan, North Sumatera, Indonesia

Dengue Haemorhagic Fever (DHF) disease still prevalent in Indonesia. *Aedes aegypti* mosquito vector control, can be done through monitoring larvae. Young cadres *Aedes aegypti* larvae monitoring which is assistance the one form of monitoring and eradication efforts dengue vector. Activity of program young cadres monitoring larvae is monitor the larvae were present throughout the house in a settlement, provide education and increase knowledge, remind to the bathroom tub drain once a week. The

purpose of research to determine the success of young cadres larvae monitoring program. The method used to quantitative approach during November 2014 in Medan Indonesia. The total sample of 72 people. Analysis using descriptive and analytic with chi square. The result is the community has a good level of knowledge (86%) about prevent DHF disease. Public attitudes about DHF disease (99%) have a good attitude. Analytical test shows that there is a correlation between knowledge of DHF with attitude P value = 0.012. So with a good knowledge of it will get a good attitude. Most communities have a good behavior (63%). Behavior regarding the handling of dengue in the community with both categories. 100% of the water drain tank. House Index looks better at 96% in the last program. Since there is a young cadre larva monitoring program, the area not found DHF disease with prevalence (0%). The existence of a cadre of young larvae monitoring has a positive contribution to the prevention of the presence *Aedes aegypti* mosquito vector, improve knowledge and behavior of society.

In vitro and gene expression studies evaluating the role of P-glycoproteins in the emerging resistance to macrocyclic lactones in cyathostomins - P139 (SP)

Laura Peachey, G.L. Pinchbeck[1], J.B. Matthews[2], F.A. Burden[3], J.E. Hodgkinson[1].

1 The Institute of Infection and Global Health, The University of Liverpool, UK
2 Moredun Research Institute, Pentlands Science Park, Penicuik, Scotland, UK
3 The Donkey Sanctuary, Sidmouth, UK

For decades cyathostomins have remained sensitive to the macrocyclic lactones (MLs) in spite of intensive environmental selection. Unfortunately recent studies have reported a reduction in ML efficacy on farms and studs that use / have used interval worming strategies. Studies in other species such as Haemonchus contortus suggest a role for P-glycoproteins (Pgp) in resistance to MLs. Here we compared ivermectin (IVM) efficacy in a population of cyathostomins which are phenotypically resistant to MLs in vivo (R) with an anthelmintic naive population (N), using two in vitro bioassays, the larval migration inhibition test (LMIT) and the larval development test (LDT). We were able to consistently detect differences in IVM efficacy between the two populations using the LMIT but not the LDT. We went on to evaluate the effects of P-glycoprotein inhibitors on IVM efficacy in populations R and N using a general linear mixed model to compare the dose response data. We found that Pgp inhibitors had a significant effect of IVM efficacy in both populations in the LDT but only in population R in the LMIT, suggesting the LMIT is a more sensitive tool for evaluating resistance and it mechanisms in cyathostomins. In addition we demonstrated a significant increase in the expression of Pgp-9 in population R compared with N, which was amplified three fold by exposure to IVM in vitro. Our data strongly suggest Pgps play a role in ML resistance in cyathostomins, this discovery may lead to novel drug combinations to tackle drug resistance in these species.

Prevalence of mutations in the antifolates resistance-associated genes (dhfr and dhps) in Plasmodium vivax parasites from Eastern and Central Sudan - P141

Albadawi Abdelbagi , Sekineh Pirahmadi; Bakri Y.M. Nour; Sedigheh Zakeri

Department of Parasitology: Faculty of Medical Laboratory Sciences, Blue Nile National Institute for Communicable Diseases University of Gezira. P.O. Box 20, Wad Medani, Sudan

Plasmodium vivax is the most geographically widespread species, and its burden has been increasingly documented in Eastern and Central Sudan. *P. vivax* becomes the crucial challenge during elimination programs; thus an effective treatment is necessary to prevent the development and the spread of resistant parasites. Therefore, the main objective of the present study was to provide data on the prevalence of molecular markers in two genes (pvdhfr and pvdhps) associated with SP resistance after nine years of AS + SP deployment among *P. vivax* parasites from Eastern and Central Sudan using PCR-RFLP. During 2012–2013, a number of 66 blood spots were obtained on filter paper. The samples were collected before treatment from febrile patients who were microscopically positive for *P. vivax*, from three states in Eastern and Central Sudan (Gezira, Gedarif, and Kassala). Mutations were detected in three codons of pvdhfr (I13L, S58R, and S117N) and none in pvdhps. The majority of *P. vivax* parasites had double mutations (58R/117N, 58%) in dhfr gene, while all parasites were wild type in dhps gene. In addition, limited distinct haplotypes (n = 4) were detected. In conclusion, the prevalence of mutations associated with SP resistance is low in Eastern and Central Sudan. Such information is necessary for guiding malaria control measures in the frame of Roll Back Malaria strategies for the elimination of malaria in the world.

Characterisation of a novel Schistosoma mansoni cercariae/schistosomula secreted protein (SmCSS-1) exhibiting developmentally regulated alternative splicing - P10 (SP)

Thomas Gasan [1]Fanny C. Nowacki[1], Paul J. Hensbergen[2], Oleg I. Klychnikov[2], Cornelis. H. Hokke[3], Anna V. Protasio[4], Karl F. Hoffmann[1] and Iain W. Chalmers[1]

1. Institute of Biological, Environmental & Rural Sciences (IBERS), Aberystwyth University, Edward Llwyd Building, Aberystwyth, SY23 3FG, United Kingdom
2. Department of Parasitology, Leiden University Medical Center P.O.Box 9600, 2300 RC Leiden, The Netherlands
3. Center for Proteomics and Metabolomics, Leiden University Medical Center P.O.Box 9600, 2300 RC Leiden, The Netherlands
4 Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, United Kingdom.

To establish a successful infection, *Schistosoma mansoni* parasites must migrate through the skin and avoid inducing damaging host immune responses. The biological characterisation of parasite products secreted/excreted during this time is, therefore, important for fully understanding the intricacies of long-term host/parasite interactions. To this end, we initiate characterisation of a novel S. *mansoni* protein of unknown function, SmCSS-1, recently found in cercarial/schistosomula excreted/secreted proteomes and in exosome-like extracellular vesicles. Utilising existing DNA microarray and RNAseq data, we find that SmCSS-1 is differentially expressed across the schistosome lifecycle with peak expression in mixed-sex cercariae larvae and male biased expression in the dioecious adult. Sequencing analysis of SmCSS-1 transcripts cloned from different parasite lifestages reveal that multiple isoforms exist and crucially differ in abundance. These isoform differences are produced by cassette-based alternative splicing and may create antigenic variation leading to immune evasion. Further, we present evidence that SmCSS-1 is only present in schistosome species and is not present in other platyhelminths. Comparative sequence analysis has revealed homologues in other schistosome species (*S. haematobium, S. japonicum and S. magrebowei*) but with significant differences identified in encoded protein sequences. No homologues were present in other related trematode genomes or transcriptomes analysed. Future research aims to discover the location of SmCSS-1 within the parasite, immune responses elicited by this protein and the role of different isoforms during parasite

development. Collectively, these results point to SmCSS-1 being an abundant new class of schistosome secreted protein, capable of developmentally regulated antigenic variation.

Development of novel melamine-based nitroheterocycles as anti-trypanosomal compounds - P21

Federica Giordani, Constance Chollet [2], Annamaria Buschini [1], Michael P Barrett [3], Ian H Gilbert [2]

1 Dipartimento di Bioscienze, Università degli Studi di Parma, Parco Area delle Scienze, 11/A, 43124, Parma, Italy.
2 Division of Biological Chemistry and Drug Discovery, College of Life Sciences, University of Dundee, Sir James Black Centre, Dundee, DD1 5EH, UK.
3 Wellcome Trust Centre for Molecular Parasitology, Institute of Infection, Immunity and Inflammation, College of Medical, Veterinary and Life Sciences, University of Glasgow, 120 University Place, Glasgow G12 8TA.

Nitro compounds possess a broad anti-infective activity, and they include drugs used for the treatment of cryptosporidiosis, trichomoniasis, giardiasis, amoebiasis, Chagas disease and human African trypanosomiasis. Many nitro compounds behave as prodrugs: the enzymatic reduction of the nitro group generates cytotoxic species that lead to cellular damage. This same reactivity can also result in toxic and genotoxic side effects for the host and is the reason why nitro compounds are often excluded from screening collections. Nevertheless, the licensing of various nitro derivatives shows that their activity is not always associated with a genotoxic risk. With the aim of identifying new anti-trypanosomal agents, we synthesised a highly potent melamine-nitroheterocycle, designed in order to be selectively delivered to trypanosomes through specific parasite nutrient transporters. Unfortunately, the compound was positive in both Ames tests and mammalian based-Comet assay. In this poster we describe the modification of the compound in an attempt to separate the trypanocidal effects from the genotoxic liabilities. We describe this process and the discovery of a compound with submicromolar activity against the parasite, *Trypanosoma rhodesiense*, but which is negative in an Ames assay. This suggests that it is possible to separate out the trypanocidal effects from the genotoxic effects of these nitroheterocycles.

Unraveling the MoA of the Malaria Box Set: Identification of inhibitors targeting mitochondrial and folate biosynthesis pathways - P57

Sara Prats, Alameda Fernando Neria Maria Jose Lafuente Francisco Javier Gamo

GlaxoSmithKline, Tres Cantos Medicines Development Campus, Diseases of the Developing World (DDW),Severo Ochoa 2, 28760 Tres Cantos, Spain sara.2.prats@gsk.com maria.j.lafuente-monasterio@gsk.com francisco-javier.b.gamo@gsk.com

The Malaria Box is a set composed of 400 commercially available chemical entities derived from a selection of more than 20000 hits from the screening of corporate and academic libraries. Different approaches including target-based and functional screening strategies are being carried out by several groups to gain insights into the antimalarial MoA of the Malaria Box Set that will be useful for the development of new drugs. Malaria Box set of compounds have been tested against two know antimalarial pathways (electron transport and folate). 1/ Folate metabolism has long been recognized

as an attractive chemotherapeutic target and is essential for the survival of P. *falciparum*. Antifolates have been identified by supplementing the growth medium with folic acid. 2/ Erythrocytic stages of the human malaria parasite *P. falciparum* seem to maintain an active mitochondrial electron transport chain to serve just one metabolic function: regeneration of ubiquinone required as the electron acceptor for dihydroorotate dehydrogenase (DHODH), an essential enzyme for pyrimidine biosynthesis. Mitochondrial electron transport inhibitors have been identified using transgenic *P. falciparum* parasites overexpressing *Saccharomyces cerevisiae* DHODH, which does not require ubiquinone as an electron acceptor, the addition of proguanil restores the inhibitory activity of cytochrome bc1 inhibitors but not DHODH inhibitors against this strain. The compounds identified are currently under evaluation in order to characterize its biochemical target.

Specifically active metabolism in early (post-invasion) *P. falciparum* asexual cycle: analysis of gene expression publicly available data - P40 (SP)

Stephen Schur, Joseph Cole Enrique Salcedo-Sora

School of Health Sciences Liverpool Hope University Liverpool L16 9JD

The metabolism of the initial growing phase of the intra-erythrocytic cycle of *P. falciparum* is largely unknown. In recent years these first hours of *falciparum* malaria in blood cells have been put back in the spotlight due to the apparent slow-down (dormancy) of the cell growth that seems to underlie tolerance/clinical resistance to artemisinins. This a worrisome scenario since drug combinations containing artemisinins have been during the last two decades the first line of treatment against the different forms of *falciparum* malaria. As part of the initial efforts to study the metabolic biochemistry of the first 10 hours of the development of *P. falciparum* in red cells we have analysed data from six different gene expression studies. The final set of genes encompassed those specifically over-expressed in the fist 10 or less hours and under-expressed thereafter (20 or more hours) in the intra-erythrocytic cycle. From at least 80 different enzyme-coding genes, it is very apparent that the metabolic traits of early rings are very specific. Lipid metabolism represented by the biosynthesis of acetyl-CoA driven fatty acids is particularly represented. Strikingly, enzymes involved in haemoglobin degradation are already present in this gene set together with nine different membrane transporters, including at least three active transporters. This initial information is encouraging and supports the validity of the less known metabolism of early forms of *P. falciparum* as a source of specific targets to screen for effective antimalarials. Particularly, if this approach yields strategies to control the emerging and fast increasing tolerance/resistance against artemisinins.

The Healthy Futures Atlas - P98

Mark Booth, Healthy Futures Consortium Michael Hagenlocher Stefan Kienberger

Durham University

The recently concluded EU FP7 funded study 'Healthy Futures' developed and implemented new mathematical models linking downscaled climate change projections with the natural history of *Schistosoma mansoni*, Rift Valley Fever and Malaria in East Africa. The outputs included 'hazard' maps of infection highlighting where new foci may emerge or where infection transmission may intensify or

reduce with changing climate over the next 40 years. Simultaneously, project members designed an interactive online atlas that allows individuals to explore the potential impact of different climate change scenarios on future overall 'risk' of each infection. The atlas is freely available as an online tool and utilises the outputs of mathematical models developed in the project as well as openly available data sources associated with lack of capacity to cope, generic susceptibility, biological susceptibility and lack of capacity to anticipate. By bringing together these diverse data sources covering multiple domains we have increased our understanding of how climate change may impact on hazard, vulnerability and overall risk of infection. The atlas has potential for use as an educational tool across a range of sectors and provides a framework for future efforts to map the future transmission potential of environmentally-sensitive infectious diseases in East Africa and elsewhere.

The metabolome of activated macrophages: implications for disease and inhibitors - P97

Kevin Rattigan, Carl S Goodyear, Michael P Barrett

University of Glasgow

Immune activation requires rapid and sustained changes in the metabolomic profile of the different cells involved. These different profiles require changes in both the uptake of nutrients and the up- or down-regulation of pathways that consume these nutrients. Depending on the stimuli involved, macrophages can be skewed towards different parts of a spectrum that has M1 (pro-inflammatory) or M2 (anti-inflammatory) endpoints. The metabolomic changes associated with these different profiles are required for the specific functions of the macrophage such as phagocytosis, oxidative burst, nitric oxide response, migration and infiltration. These functions are important in the involvement of macrophages in immune response to infectious/auto-immune diseases and whether the outcome is disease resolution or disease progression. We have use an untargeted metabolomics approach and bioinformatic tools to investigate the metabolome of macrophages of M1/M2 phenotypes. We see alterations in pathways in M1 macrophages that have previously been reported such as upregulation of iNOS mediated metabolism of arginine. The alterations that were most pronounced were in the pentose phosphate pathway (PPP) with a large upregulation at multiple stages of the pathway. The PPP is used to cope with the oxidative stress and its upregulation is required for activation to a M1 phenotype. We will be investigating the potential of several different PPP inhibitors to prevent the switch to the M1 phenotype.

Three-dimensional skin equivalents for investigations on percutaneous helminth invasion - P131

Norbert Brattig, Maren Jannasch, Florian Groeber, Clemens Unger, Heike Walles, Jan Hansmann

Chair Tissue Engineering and Regenerative Medicine, University Hospital Wuerzburg, Wuerzburg, Germany: for authors 1,5,6 Department of Cell and Tissue Engineering, Fraunhofer Institute of Interfacial Engineering and Biotechnology (IGB), Stuttgart, Germany: for author 2 Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany: for author 3 Institute of Tropical Medicine, University Hospital Tuebingen, Tuebingen, Germany: for author 4

Chronic helminth infections constitute to the most common infectious diseases in humans and thereby contribute, especially in developing countries, to life's burden of disease and disability. To address one

key target of preventive strategies – the transmission of larvae through the skin – a profound understanding of the infection process is of importance. In this present study the applicability of in vitro tissue-engineered skin equivalents for investigations on percutaneous helminth invasion was evaluated (Exp Parasitol 2015; 150:22). Therefore, a quantitative assay on the larval invasiveness of the intestinal nematode *Strongyloides ratti* (phylum *Nemathelminthes*) and the vein-dwelling fluke *Schistosoma mansoni* (phylum *Platyhelminthes*) to tissue-engineered skin equivalents was accessed. Tissue-engineered skin equivalents generated a physical barrier to larval invasion of *Strongyloides ratti*, while these larvae invaded and permeated a cell-free collagen scaffold and ex vivo epidermis. In contrast, the tissue-engineered skin equivalents exhibited a human host-specific susceptibility to larvae of *S. mansoni*, which invaded the models well. For all experimental conditions the invasion of *S. mansoni* in cell-free collagen scaffold was lowest. Thus, tissue-engineered skin equivalents confirmed a high degree of accordance to native tissue. The present study indicates that, especially for human-pathogenic invading helminths, the limitations in transferability of predictive infection testing to human beings can be overcome by tissue-engineered in vitro skin equivalents. By allowing the analysis of interaction between parasites and their hosts, we hypothesize, that tissue-engineered skin equivalents provide a human-specific screening platform for new preventive drugs.

Effects of Resource Environment on Transmission Strategies of Malaria Parasites - P42

Charlotte Repton, Philip L. G. Birget, Petra Schneider and Sarah E Reece.

Centre for Immunity, Infection & Evolution, Institutes of Evolution, Immunology and Infection Research, School of Biological Sciences, Ashworth Laboratories, University of Edinburgh, Edinburgh EH9 3FL Scotland, UK

Rapid changes in the host environment are a significant selection pressure on parasites. Previous work by our group has shown that malaria parasites can maximise their fitness throughout an infection by plastically adjusting investment into transmission stage production (gametocyte conversion rate) according to a wide range of within-host stresses (including competition and antimalarial drugs). Transmission investment is predicted to vary along a continuum, from favouring asexual reproduction (reproductive restraint) when stressed, to prioritise parasitaemia and maximise in host survival; or a terminal increase in gametocyte investment (terminal investment) to maximise transmission in a lethal, or likely lethal, situation. We have tested whether the reaction norm for plasticity in transmission investment follows the predicted pattern by manipulating the availability of red blood cell resources and quantifying the resulting investment decisions. Our experiment, using the rodent parasite *Plasmodium chabaudi* also investigates the evolutionary potential of plasticity by investigating whether there is genetic variation for the reaction norm. Understanding parasite strategies for growth and transmission over the course of a normal infection or clinical intervention allows more effective management of the spread and severity of disease. In addition, malaria parasites exhibit sophisticated strategies for resource management and trade-offs traditionally studied in multicellular organisms – providing a novel testing ground for evolutionary theory.

Development of a non-invasive, longitudinal Near-infrared (NIR) imaging technique applicable for lymphatic filariasis pathology and drug intervention studies - P8

Stephen Cross, H Tyrer, H Sjoberg, J Gamble, L Hayward, A Stevens, D Cook, M J Taylor, J D Turner

Department of Parasitology, Liverpool School of Tropical Medicine, Liverpool, L3 5QA UK (All Authors)

Peturbations of the lymphatic system during lymphatic filarial infection causes lymphatic insufficiency leading to chronic progressive condition of filarial lymphoedema (LE; elephantiasis). Accurately modelling the development of lymphatic abnormalities in filariasis may allow for testing novel treatments which aim to reduce filarial disease. We developed a long-term, pre-clinical model of filariasis to study development of early onset filarial LE. In this model, BALB/c or CB.17 inbred mice with severe-combined immune deficiency (SCID) were administered a subcutaneous inoculum of 100 *Brugia malayi* infectious stage larvae in the hind limb, with the contralateral limb serving as the internal control. Using NIR imaging we visualised changes in lymphatic structure. Indocyanine green (ICG), a non-toxic near-infrared (NIR) dye used in clinical ophthalmic and cardiac imaging, was injected subcutaneously in each hind foot and dye drainage was tracked through the lymphatic vasculature using a photodynamic eye (PDE) NIR imaging device (Hamamatsu Photonics, Japan). The integrity of the local lymphatics was assessed by; the relative accumulations of ICG in the popliteal and subileac lymph nodes, the development of tortuous collateral lymphatics and incidence of dermal backflow. Of 69 animals inoculated, 33 developed anomalous lymphatic flow (48%). There was no difference in development in pathology when comparing between mouse strains. Using this technique we establish that it is possible to accurately track lymphatic remodelling following lymphatic filarial parasitism. The model may be of use to study basic cellular and molecular mechanisms controlling filarial LE and to test novel anti-morbidity interventions.

Anti-*Wolbachia* macrofilaricidal drug discovery and development - the current A·WOL portfolio - P36

Louise Ford, Gemma L. Nixon[1], Kelly L. Johnston[1], Joseph D. Turner[1], Ghaith Aljayyoussi[1], Neil G. Berry[2], Paul M. O'Neill[2], Stephen A. Ward[1] and Mark J. Taylor[1]

1 Department of Parasitology, Liverpool School of Tropical Medicine, Liverpool, UK
2 Department of Chemistry, University of Liverpool, Liverpool, UK

Lymphatic filariasis and onchocerciasis are debilitating neglected tropical diseases, infecting ~150 million people throughout the tropics. As with other NTDs, classical drug discovery and development is lacking. To date a macrofilaricidal drug for use as a public health tool is yet to be delivered. Targeting *Wolbachia*, essential bacterial symbionts of filariae, provides safe macrofilaricidal activity with superior outcomes compared to standard anti-filarials. The Anti-*Wolbachia* Consortium has established a discovery and development programme with the goal of finding drugs that are suitable where current treatments are compromised by the risk of drug resistance or adverse events. The Go/No-Go criteria applied to the A·WOL pipeline is aligned with the Target Product Profile for an anti-*Wolbachia* macrofilaricide, which includes oral delivery, with ≤7 days treatment. A·WOL Drug Discovery is progressing lead series through a rigorous lead optimisation process, using iterative cycles of medicinal chemistry and biological testing. This approach has led to the selection of one novel preclinical candidate, which meets the TPP in a *Brugia malayi*-mouse efficacy model. In addition, testing of both chemically distinct series and large diversity libraries will expand the structural diversity of anti-*Wolbachia* chemotypes. A·WOL Drug Development is optimising regimens of anti-*Wolbachia* antibiotics, and anti-*Wolbachia* and anti-filarial drug combinations, using in vivo efficacy testing driven by rational PK-PD modelling which supports dosage regimens. By adopting this approach A·WOL has identified high-dose rifampicin as a clinical candidate. Here we discuss the current A·WOL portfolio and both the preclinical and clinical candidates

which have been selected for onward development.

RNAi persistence in liver fluke - an opportunity for both in vitro and in vivo functional genomics? - P95 (SP)

Wasim Hussain, Paul McVeigh, Paul McCusker, Angela Mousley, Nikki Marks, Aaron Maule

Parasitology, The Institute for Global Food Security, School of Biological Sciences, Queen's University Belfast, Belfast BT9 7BL

Fasciola hepatica is a trematode parasite that causes the disease fascioliasis. The parasite commonly infects ruminants but is also a human pathogen with fasciolosis a recognized neglected tropical disease. The drug triclabendazole has been traditionally used to treat fascioliasis but its utility is being undermined by drug-resistance which has been reported worldwide, including in livestock in the UK, highlighting the pressing need for new flukicides and/or alternative control strategies. Difficulties in the genetic manipulation of *F. hepatica* have undermined the discovery and validation of new drug targets although we have demonstrated the ability to silence specific genes in vitro promoting the exploitation of RNA interference (RNAi)-based functional genomics approaches for new target discovery and validation. We have found that RNAi-based gene silencing in *F. hepatica* newly-excysted juveniles (NEJs) maintained in vitro is remarkably persistent and hypothesise that 'RNAi-worms' could be used to infect host animals and probe gene function (target validation) in vivo. As a proof-of-concept we examined the impact of silencing two different targets (cathepsin L and sigma-glutathione transferase (σGST)) on the progression of in vivo infection in rats. We hypothesise that the pathology of fascioliasis will be reduced in rats infected with NEJs that have important genes silenced. This research will not only validate new flukicide targets but could also provide a platform for the in vivo examination of gene function in liver fluke.

***Leishmania infantum* Asparagine Synthetase A is dispensable for parasites in vivo infectivity - P132**

Joana Correia Faria[1], Inês Loureiro[1], Nuno Santarém[1], Sandra Macedo-Ribeiro[2], Joana Tavares[1], Anabela Cordeiro-da-Silva[1,3]

1 Parasite Disease Group, Instituto de Biologia Molecular e Celular (IBMC) da Universidade do Porto, Portugal
2 Protein Crystallography Group, Instituto de Biologia Molecular e Celular (IBMC) da Universidade do Porto, Portugal
3 Departamento de Ciências Biológicas, Faculdade de Farmácia, Universidade do Porto

A growing interest in asparagine (Asn) metabolism has currently been observed in cancer and infection fields. Asparagine synthetase (AS) is a key player responsible for the conversion of aspartate into Asn in an ATP-dependent manner, using ammonia or glutamine as a nitrogen source. There are two structurally distinct AS: the strictly ammonia dependent, type A, and the type B, which uses preferably glutamine. Absent in humans and present in Trypanosomatids, AS-A was worthy of exploring as a potential drug target candidate. Appealingly, it was reported that AS-A was essential in *Leishmania donovani*, making it de facto drug target. In the work herein, we have biochemically characterized *L. infantum* and *L. major* AS-A, that similarly to *Trypanosoma sp* and *L. donovani*, are able to atypically use both ammonia and

glutamine as nitrogen donors. Moreover, we have successfully generated LiAS-A null mutants by targeted gene replacement in *L. infantum*. Although the dKO parasites didn't display any significant defect (in vitro growth or in vivo infectivity), upon Asn deprivation, null mutants presented a severe impairment of in vitro growth, being auxotrophic to Asn. Notwithstanding, sKO mutants, showed no phenotype, as they were able to upregulate AS-A expression to the level of the WT, rescuing the growth. Altogether our results demonstrate that despite the interesting biochemical features of LiAS-A, this enzyme is not essential for parasite survival, growth or infectivity. Therefore we conclude AS-A is not suitable as a drug target against *L. infantum*.

Blockade of the CTLA4 Inhibitory Pathway Augments CD8 T Cell Mediated Protection Against Malaria Pre-erythrocytic Stages - P44 (SP)

Samuel Thorburn, Jan Burgold, Saif U-Rehman Khan, Matthew P. Gibbins, Kai Matuschewski, Julius C. R. Hafalla

Department of Immunology and Infection, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK Max Planck Institute for Infection Biology, Berlin, Germany

Sterile protection from malaria through multiple attenuated sporozoite immunisations has been shown in mouse and human studies to be dependent on T cells and antibodies. Understanding these protective mechanisms is crucial in the future development of novel vaccines. Currently, CD8 T cell regulation mechanisms are not well understood in pre-erythrocytic malaria. This research investigated two co-inhibitory receptors that have been shown to influence CD8 T cell proliferation and activation. C57Bl/6 mice were given one attenuated sporozoite immunisation concurrently with antibody blockade of cytotoxic T lymphocyte antigen 4 (CTLA4) or programmed death ligand 1 (PDL1). CTLA4 blockade increased the likelihood of sterile protection with sporozoite challenge; however PDL1 blockade led to parasitaemia in all mice in these conditions. This is a proof of principle that blockade of specific negative regulators of CD8 T cell activation can augment parasite specific responses after a normally non-protecitve single whole sporozoite immunisation and provide improved vaccine efficacy.

Pharmacokinetic/Pharmacodynamic modelling of anti-*Wolbachia* agents - P27 (SP)

David Waterhouse, Ghaith Aljayyoussi, Raman Sharma, Joseph Turner, Mark Taylor, Stephen Ward

Liverpool School of Tropical Medicine, UK

Doxycycline is currently the gold standard for the targetting of *Wolbachia* in lymphatic filariasis and onchocerciasis chemotherapy. However, the current drug regimen is a 100-200 mg/day doxycycline dose given for 4 to 6 weeks to patients. The AWOL consortium funded by the Bill & Melinda Gates foundation aim to generate new AWOL molecules that can reduce treatment time to 7 days or less and that are compatible with mass drug administration programmes. Preliminary in vitro screening for anti-*Wolbachia* compounds indicated that the tetracycline minocycline was significantly more potent than the gold standard doxycycline. The superiority of minocycline has been evaluated further in in vivo models adopting a rational PK/PD approach to understand relative drug efficacy. Using an infected SCID mouse model of *Brugia malayi*, the pharmacokinetics of both minocycline and doxycycline have been evaluated with concurrent evaluation of their relative anti-*Wolbachia* potencies. A PK/PD model

was generated using population non-parametric modelling (Pmetrics). The PK/PD model outputs confirm the in vitro superiority of minocycline over doxycycline. Furthermore PK predictions and Monte Carlo simulations indicate that this superiority of minocycline will extrapolate to the human infection.

The mutualistic symbiosis of *Wolbachia* and the filarial nematode *Brugia malayi* - Unravelling the proteome and transcriptome - P28

Gemma Molyneux[1], Bronowski, C.[1], Harris, S.[1], Wagstaff, S.[1], Taylor, M.J.[1]

Department of Parasitology, Liverpool School of Tropical Medicine, Liverpool, L3 5QA, UK1

The parasitic nematode *Brugia malayi* is a causative agent of lymphatic filariasis, a disfiguring disease affecting over 120 million people worldwide. *B. malayi* exists in a mutualistic symbiotic relationship with the α-proteobacterium *Wolbachia*. We have applied a global proteomic profiling approach to investigate the molecular basis of this symbiosis. Adult female *B. malayi* in the mammalian host Meriones unguiculatus were sampled at multiple time-points post-antibiotic depletion. Using a combination of extensive peptide pre-fractionation and established proteomic workflows we observed improved proteome coverage by an increase in peptide/protein identification. Such proteomic approaches coupled with reversed phase liquid chromatography and analysis by high-resolution mass spectrometry were used for the comprehensive proteome profiling of *Wolbachia*/worm at these selected time-points. Following basic analysis through established bioinformatics pipelines, transcriptomic, proteomic, and published datasets have been integrated in a systems biology approach with the objective of understanding the molecular basis of the mutualistic *Wolbachia/B. malayi* symbiosis.

Evaluation of the trypanocidal activity of truncated neplanocin fleximers designed as inhibitors of kinetoplastid S-adenosylhomocysteine hydrolase - P22 (SP)

Godwin Ebiloma [1], Sarah C. Zimmermann[2], Elizaveta O'Neill[2], Lynsey J. M.[1] Wallace, Katherine L. Seley-Radtke[2], Harry P. De Koning[1].

1 Institute of Infection, Immunity and Inflammation, College of Medical, Veterinary and Life Sciences, University of Glasgow, 120 University Place, Glasgow G12 8TA, UK.
2 Department of Chemistry & Biochemistry, University of Maryland, Baltimore County, 1000 Hilltop Circle, Baltimore, MD 21250, USA.

S-adenosylhomocysteine hydrolase (SAHase) is an important enzyme responsible for the hydrolysis of S-adenosylhomocysteine (SAH), the by-product of biomethylations that utilize S-adenosylmethionine (SAM). In protozoa, SAM is required as the methyl donor for methylation of the four nucleosides present in the "cap-four" terminal end of mRNA. This cap structure is important for RNA recognition and stability, is highly conserved across almost all protozoan species, and needed for replication. Inhibition of SAHase results in the accumulation of SAH, halting methylations, and disrupting the formation of the cap structure. The resulting effect on mRNA stability ultimately affects protein synthesis and thereby various biochemical pathways and cellular systems. SAHase thus offers a significant target for the development of antiparasitic chemotherapy. Modified nucleosides, especially carbocyclic nucleosides, are known potent inhibitors of SAHase. In an effort to study the effects of increased flexibility on enzyme inhibition, a series of flexible nucleoside analogues ('fleximers') in which the purine base is split

into its respective imidazole and pyrimidine components were used to investigate their potential anti-protozoan activities by inhibition of SAHase. The selectivity index for all fleximers, relative to human embryonic kidney (HEK 293) cells is >1000. Three fleximers tested displayed moderate in vitro anti-trypanocidal activities (EC50 values ~200 µM). Further studies using the corresponding ribosylated fleximers, most closely related to the natural nucleoside substrates, revealed low affinity for the *T. brucei* P1 and P2 nucleoside transporters. We conclude that a lack of high affinity uptake is likely responsible for the reduced trypanocidal activity observed.

Biochemical and metabolic characterization of mutant Plasmodium falciparum lacking apicoplast E3 or LipB - P45

Marco Biddau1, Larissa M. Laine[1], Sonal Sethia[1], Eleanor H. Wong[1], Gavin J. Blackburn[2], Achuthanunni Chokkathukalam[2], Graham H. Coombs[3], Sylke Müller[1].

1. Institute of Infection, Immunity & Inflammation, College of Medical, Veterinary and Life Sciences, University of Glasgow.
2. Glasgow Polyomics, Wolfson Wohl Cancer Research Centre, University of Glasgow.
3. Strathclyde Institute of Pharmacy and Biomedical Sciences; University of Strathclyde, Glasgow.

Apicoplast pyruvate dehydrogenase complex (PDC), a three-enzyme complex with a crucial role in acetyl-CoA and NADH synthesis, relies on the activity of dihydrolipoyl dehydrogenase (aE3) and lipoylation by lipoate protein ligase B (LipB). Although PDC is not essential for intra-erythrocytic growth of *Plasmodium falciparum*, we hypothesised that it plays a role in maintaining apicoplast redox balance and is important for the supply of acetyl-CoA necessary for acetylation reactions and fatty acid elongation. This study applied a focused proteomics and metabolomics analysis of gene-deficient mutants to assess the parts played by aE3 and LipB in the metabolism of the parasite. Both parasite mutants showed an increased flux of glucose into the TCA cycle as demonstrated by targeted metabolomics using 13C-U-D-glucose, suggesting adaptations of their carbon metabolism. In addition, expression of the E2-subunit of branched chain α-ketoacid dehydrogenase, the enzyme responsible to decarboxylate pyruvate in the mitochondrion, was increased in the mutant parasites, corroborating the hypothesis that substantial metabolic changes take place in the mutant parasites to compensate for the loss of apicoplast PDC activity.

Identification of novel promoter regions to optimise the expression of foreign genes in Eimeria species parasites - P93

Elaine Pegg[1], Virginia Marugan-Hernandez[1], Sarah Macdonald[1], Keith Redhead[2], Colin Crouch[2], Ian Tarpey[2], Michael Francis[2], Damer Blake[1] and Fiona Tomley[1]

1 The Royal Veterinary College, University of London, Hawkshead Lane, North Mymms, AL9 7TA, UK;
2 MSD Animal Health, Walton Manor, Milton Keynes, MK7 7AJ

Eimeria tenella is an apicomplexan parasite of great importance to the poultry industry where it is a leading cause of coccidiosis in chickens. The disease costs the industry an estimated US$3 billion globally every year. Stable lines of transgenic *Eimeria* have potential to act as vaccine delivery vectors, as illustrated using candidate vaccine antigens targeting pathogens such as *Campylobacter jejuni* (Clark et

al., 2012 Vaccine). Existing transfection constructs utilise *E. tenella* actin endogenous regulatory sequences to promote expression of foreign coding sequences. However, recent transcriptome data (Reid et al., 2014 Genome Research) have associated the EtActin promoter with a low level of transcription, suggesting suboptimal transgene expression in current constructs. Promoter optimisation may increase transgene expression and induce a more effective immune response following infection in the chicken. Here, we have predicted nine putative promoter regions using *E. tenella* genome and transcriptome datasets which show high or medium levels of transcription and tested their capacity to support fluorescent reporter transgene expression in a transient transfection system. Two of the candidates were found to support equal or superior expression to the EtActin promoter, one at a level comparable with the *E. tenella* Microneme Protein 1 promoter, known to support a high level of gene expression. Furthermore, we have investigated the minimal functional length of the two promoter regions and predict both are functional throughout the lifecycle of the parasite. These findings can be used to improve the *E. tenella* transgene expression system for the production of stably transfected parasites.

Modelling the impact of veterinary medicines upon dung fauna - P111 (SP)

Andrew Cooke[1,2], Morgan, E[2]., Wall, R[2]. and Dungait, J.[2]

1 Bristol University Life Sciences Building, 24 Tyndall Avenue, Bristol, BS8 1TQ
2 Rothamsted Research, Rothamsted Research, North Wyke, Okehampton, Devon, EX20 2SB

Non-target insecticidal effects of veterinary medicine residues in animal dung have been widely reported, especially for anthelmintics. Resulting reductions in dung fauna may inhibit dung degradation and may have implications for parasite transmission and anthelmintic resistance. In addition, dung fauna play a vital role in local ecosystems by recycling nutrients. A novel approach to modelling these insecticidal effects was used in the work described here, removing the need for arbitrary weighting of specific variables. Published data on *Scathophaga stercoraria* (yellow dung fly) was used to model the insect's life cycle in an agricultural system with the facility to alter dung drug residue toxicity (EC) and the proportion of cattle treated (PT). This allowed for various simulations to predict the impact of a drug at varying EC and PT, on the population size of *S. stercoraria*. Variables EC and PT significantly ($P<0.001$) affected predicted *S. stercoraria* population size, with EC accounting for 11.3 % of variation in population size and PT for 48.1 %. Results suggest that anthelmintics with an EC >40 % pose a notable risk to dung fauna and that whole-herd treatments pose the greatest risk. Targeted part-group treatments in grazing livestock could offset effects of dung drug residues and ameliorate ecological impacts of chemical control of parasites.

Hotspots of Schistosoma mansoni transmission ten years into a mass drug administration programme - P134

Poppy Lamberton[1], Charlotte M Gower[1], Moses Adriko[2], Moses Arinaitwe[2], Annet Enzaru[2], Annet Namukuta[2], Thomas Crellen[1], Edridah M. Tukahedwa[2], Narcis B. Kabatereine[3], Alan Fenwick[1] and Joanne P. Webster[1,4]

1 Department of Infectious Disease Epidemiology, School of Public Health, Imperial College Faculty of Medicine, St Mary's Campus, London W2 1PG, UK,

2 Vector Control Division, 15 Bombo Road, Ministry of Health, Kampala, PO BOX 1661, Uganda,
3 Schistosomiasis Control Initiative at Vector Control Division, Ministry of Health, Kampala, PO BOX 1661, Uganda,
4 Department of Pathology and Pathogen Biology, Centre for Emerging, Endemic and Exotic Diseases (CEEED), Royal Veterinary College, University of London, AL9 7TA, UK

The Schistosomiasis Control Initiative began mass drug administration (MDA) with praziquantel in Uganda in 2003 with great reductions in infection prevalence, intensities and associated morbidity. However, possible treatment failures have been recorded. In addition, theoretical models have indicated that cessation of MDA may result in higher egg counts than pre-intervention levels in certain individuals. Prevalence and intensity of infection by Kato-Katz were recorded for *S. mansoni* in children from three primary schools in Mayuge District, Uganda. Data were collected pre-, one-week-post- and four-weeks-post-praziquantel in 2004, 2005 and 2006, and pre-, one-week-post- and three-weeks-post-praziquantel in 2013 and pre-praziquantel in 2014. In 2004 and 2013 point-of-care circulating-cathodic-antigen tests (POC-CCA) were also performed. Mean egg reduction rates by three/four-weeks-post-praziquantel from 2004, 2005, 2006, and 2013 were 94.5%, 97.8%, 97.1%, and 95.0% respectively and cure rates 72.3%, 75.7%, 80.7% and 87.2%. Cure rates by POC-CCA in 2004 and 2013 were however significantly lower at 47.8% and 9.4% respectively. Infection prevalence and intensities in 2013 and 2014 were higher than at baseline. We indicate that drug efficacy measured by Kato-Katz has not reduced with MDA, but that cure rates measured by POC-CCA are lower. Although cure rates are often considered to be a less important criteria for morbidity than a reduction in egg output, it is imperative that the causes for the significant differences between Kato-Katz and POC-CCA results, and the higher infection intensities after ten years MDA, are elucidated so we can understand any risks of MDA strategies as well as measure their benefits.

Transcriptome analysis of Schistosoma mansoni sexual maturation from 18 to 38 days post infection - P31

Florian Sessler & Matthew Berriman

Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge. CB10 1SA UK

An estimated 250 million people are infected with *Schistosoma mansoni* causing 200,000 deaths (WHO, 2012) and an overall disease burden of 1.7 million disability-adjusted life years (DALYs) per year, particularly in sub-Saharan Africa, South America and Southeast Asia. After the infective stage, the cercaria, penetrates the host skin, it becomes a schistosomulum, which spends several weeks developing into an adult worm, with females requiring stimulation from male worms to reach sexual maturity. Since worm eggs are responsible for transmission and most pathology, understanding the processes that lead to female maturation is critical to open up new avenues for interventions. Here, we use RNA sequencing to gain insight into the process of sexual maturation from 18 to 38 days post-infection (d.p.i.) by comparing the transcriptome of female worms without male stimulation, to females with male stimulation that mature sexually. Using edgeR to call differentially expressed genes we found that worms of both genders appear very similar until 18 d.p.i, after which their transcriptomes begin to diverge. Furthermore, differences in stimulated and un-stimulated females become apparent in the transcriptome between 21 and 28 d.p.i. and continue to increase until 38 d.p.i. Our differential expression analysis suggests significant enrichment of pigment biosynthesis and digestion related genes in stimulated females while genes involved in ion transport, signal transduction and neurotransmitter

transport are under represented over that time period.

Vector competence of British mosquitoes to arboviruses - P103

Marcus Blagrove, G Chapman, A Patabendige, D Impoinvil, J Medlock, S Galbraith, H Ranson, P McCall, T Solomon, & M Baylis

University of Liverpool

Despite there being 34 known species of mosquito in Great Britain, there have been no known instances of mosquito-borne virus transmission to either humans or livestock. The reasons for this are currently unknown and whether British mosquitoes are competent to transmit arboviruses has not been established. In order to address whether the UK is at risk from mosquito-borne virus transmission in the future, we are currently collecting wild larvae and pupae of British mosquitoes from field sites across the UK. The immatures are reared to adulthood under laboratory conditions, given blood meals containing West Nile, dengue, chikungunya or Japanese encephalitis virus, and then incubated. The presence of virus in the expectorate is determined at multiple time points to evaluate the competence of the mosquitoes. Furthermore, given the importance of environmental temperature on the extrinsic incubation period of arboviruses, its effect therefore on vector competence, and the ongoing change in the British climate, the competence of these mosquitoes is being tested at multiple temperatures. Such an assessment will provide information on whether the current British climate is suitable for arbovirus transmission, and by how much an increase in mean temperature will increase the risk to the UK.

Point-of-care detection of haematuria and albuminuria as proxy markers for egg-patent infection and urinary tract morbidity in a low transmission area of urogenital schistosomiasis - P26 (SP)

Andrew Blanshard, Kate McMonnies Amaya Bustinduy Charles King Francis Mutuku Peter Mungai Elizabeth Joekes Russell Stothard

Andrew Blanshard – Liverpool School of Tropical Medicine Kate McMonnies – Liverpool School of Tropical Medicine Amaya Bustinduy – St George's University, London Charles King – Case Western Reserve University Francis Mutuku – Technical University of Mombasa Peter Mungai – Case Western Reserve University Elizabeth Joekes – Royal Liverpool Hospital Russell Stothard – Liverpool School of Tropical Medicine

Background: Haematuria detection, whether by visual inspection or reagent strip, is an accepted method for *Schistosoma haematobium* screening within endemic communities owing to its simplicity, low cost and effectiveness. These methods are sensitive in high-prevalence areas but may be less useful in low-transmission settings. Some studies have suggested that albuminuria measured by new point-of-care machines may be a better measure of infection, and additionally *S. haematobium*-related urinary tract morbidity, though this requires validation. Aim: To test the hypothesis that detection of albuminuria by POC assay could be a more sensitive indicator of infection than haematuria, and additionally of urinary tract pathology (UTP) in a low transmission region endemic for *Schistosoma haematobium*. Method: The present study compared the diagnostic performance of visually-read versus machine-read reagent strips and photometry in two rural villages of Msambweni Sub-county, coastal Kenya. Urine was collected from 275 women and 106 children (aged 3 - 16) and each participant

received an ultrasound scan of the urinary tract to detect UTP. Haematuria was measured visually, by visually-read dipstick and machine-read dipstick. Albuminuria levels were recorded both by photometer and machine-read dipstick. Results were compared to microscopy for schistosome eggs (active infection) and to ultrasonography-detection of UTP. Results: Machine-read dipstick and photometry-measured albuminuria gave receiver-operating areas under the curve (AOC) of 0.76 and 0.81 respectively for detection of egg-patent infection, outperforming measures of haematuria (highest AOC 0.69). No test performed well as a UTP proxy. We conclude that albuminuria may be a better infection marker than haematuria in low-transmission settings.

DNA sequence polymorphism in the inflammasome protein Nlrp1a gene from Apodemus sylvaticus (wood mice) and its relation to *Toxoplasma gondii* infection - P94 (SP)

Abdullah Shater[1,2,] Geoff Hide[1]
1 School of Environment and Life Science, Biomedical Science Research Centre, University of Salford, UK
2 Department of Microbiology and Medical Parasitology, Faculty of Medicine, Tabok University, KSA

University of Salford

Toxoplasma gondii is an intracellular protozoa parasite and is considered to be one of the most successful parasites due to its worldwide distribution and wide range host. It has the ability to infect all warm-blooded animals including humans. *Apodemus sylvaticus* (the woodmouse) is one of the most common mice in UK and Europe and some populations have been shown to have reasonably high prevalences of parasite infection. Recent studies on laboratory rodents have suggested that susceptibility to parasitic infection may be related to the host innate immune response. Specifically, genes such as the Nlrp1a gene may influence resistance to parasite infection by influencing the susceptibility of the macrophage to parasite proliferation. However, nothing is known about the variation of this gene locus on parasite infection in wild populations. Using a well characterised *A. sylvaticus* population in which infection status has been determined for a number of parasites, the aims of this study were to investigate Nlrp1a DNA polymorphism in infected and uninfected individuals. PCR primers for the Nlrp1a gene from *A. sylvaticus* have been successfully designed and analysis of sequences from a limited sample of mice has revealed several Single Nucleotide Polymorphisms (SNPs) within this gene. The future aims of this work will be to further characterise the DNA sequences from the whole population of mice and investigate relationships with parasite infection.

A tale of two cities: differences in the prevalence and distribution of the canid nematode Angiostrongylus vasorum in slugs in Bristol and Swansea - P82

Nor Azlina Abdul Aziz[1,2,] Ebbs Daly[1], Simon Allen[1,3], Ben Rowson[4], Carolyn Greig[3], Dan Forman[3] and Eric R Morgan[1]

1 Veterinary Parasitology and Ecology, School of Biological Sciences, University of Bristol, England
2 School of Animal Sciences, Faculty of Bioresources and Food Industry, Universiti Sultan Zainal Abidin, Malaysia
3 Swansea Ecology Team, Dept. Of Biosciences, Swansea University, Wales
4 Dept. Natural Sciences, National Museum of Wales, Cardiff

Angiostrongylus vasorum has an indirect life cycle with gastropod mollusc intermediate hosts. Infection in dogs (*Canis lupis familiaris*) and foxes (*Vulpes vulpes*) appears to be geographically patchy and factors driving these patterns is ambiguous. This is perhaps as a result of heterogeneous influences on mollusc populations and infection rates. The aim of this study was to investigate the distribution of the parasite in slugs in two nearby cities Swansea in South Wales (a known endemic hotspot for *A. vasorum*) and Bristol in south-west England (where reported cases are rare). In each location, slugs were sampled from nine sites across three broad habitat types (urban, suburban and rural). A total of 180 slugs were collected in Swansea and 338 slugs in Bristol, and tested for the presence of *A. vasorum* by amplification of the second internal transcribed spacer (ITS-2) using a real-time PCR assay. There was a significant difference in the prevalence of *A. vasorum* in slugs between cities ($p < 0.01$): 29.4% in Swansea and 0.3% in Bristol. In Swansea, there was a substantially higher prevalence of *A. vasorum* in suburban areas compared to rural and urban areas ($p = 0.026$) and the most common slug species infected were Arion rufus, Limacus maculatus and Arion flagellus. Results highlight that two urban areas which were close in distance and share similar climate can have substantial differences in the prevalence of this parasite, though the factors behind this pattern remain unknown.

Transcriptomics to identify genes for Ae. aegypti control - P105 (SP)

Elizabeth Sutton, Kelly Matzen, Sebastian Shimeld, Helen White-Cooper and Luke Alphey

ES and SS - Department of Zoology, University of Oxford KM - Oxited Ltd, Milton Park HWC - School of Biosciences, Cardiff University
LA - Vector-borne Viral Diseases, The Pirbright Institute

Ae. aegypti is the primary vector of dengue fever, and transmits a number of other diseases including chikungunya and yellow fever. Oxitec Ltd is developing a strategy for control of *Ae. aegypti* that involves releasing genetically engineered sterile males expressing a transgene that renders sperm non-functional. When these males mate with wild females, no offspring are produced, leading to population suppression. Engineering sterility requires functioning of transgenes specifically in testis. Also, sterility must be conditional to enable rearing. Testis-specific conditional expression can be achieved using testis-specific promoters or introns to control expression of the transgene via the Tet-Off™ system. Due to the transcriptional arrest at the first meiotic division, promoters must be active early in spermatogenesis. In this transcriptomics study, we used RNA-seq data from *Ae. aegypti* staged testis samples to identify testis-specifically expressed genes with expression highest early in spermatogenesis, and to identify genes with testis-specific introns. Candidate genes were identified using the standard TopHat-Cufflinks workflow followed by custom-written Python programs. The testis-specificity of a number of candidates was confirmed by RT-PCR, and expression timing profiles confirmed with quantitative RT-PCR. The use of high-throughput transcriptomics for identifying such genes represents a novel approach in the field, particularly the pipeline we have developed to identify testis-specific spliceforms; previous candidates were identified on an individual basis. Confirmed candidates will be taken forward for functional testing in transgenic constructs, with the ultimate aim of *Ae. aegypti* population suppression. This strategy also has the potential to be used for other vectors in future.

A new software resource for rapid automatic annotation of kinetoplastid genomes - P19

Sascha Steinbiss[1], Fatima Silva, Brian Brunk[2], Bernardo Foth[1], Thomas Dan[1], Otto[1], Gowthaman

Ramasamy[4], Peter Myler[4], David Roos[3], Stephen Beverley[5], Wes Warren[6], Christiane Hertz-Fowler[7], Matt Berriman[1]

1: Wellcome Trust Sanger Institute, Hinxton, Cambridge, UK Fatima Silva, 2: University of Pennsylvania, Computational Biology and Informatics Laboratory, Philadelphia, PA, USA
3: University of Pennsylvania, Department of Biology, Philadelphia, PA, USA
4: Seattle Biomedical Research Institute, Seattle, WA, USA
5: Washington University School of Medicine, Department of Molecular Microbiology, St. Louis, MO, USA
6: Washington University School of Medicine, The Genome Institute, St. Louis, MO, USA
7: University of Liverpool, Institute of Integrative Biology, Liverpool, UK

With many efficient and accurate sequencing technologies at the disposal of researchers today, it is becoming more important to quickly produce structural and functional gene annotations of newly sequenced, draft quality genomes. To make full use of the assembled data, an annotation software should provide a comprehensive, high-quality set of both coding and non-coding gene features, as well as information about orthologs in reference genomes, protein domain structure and basic functional information. While such software solutions are available for prokaryotes, there is still a need for easy-to-use software which specifically takes the requirements of kinetoplastid genomes into account, such as gene structure and genomic organization. We present a full-stack software pipeline to annotate kinetoplastid genomes in various states of assembly, covering all stages from pseudochromosome contiguation, gene model predictions to functional annotation. The pipeline integrates both the transfer of annotations from related species as well as de novo gene finding, with particular support for partial genes likely to be found in highly fragmented assemblies. Gene models are automatically named according to user-provided patterns and annotated with product descriptions, GO terms, orthologs and domain model hits. Special care is taken to produce semantically valid annotation files in standardized formats to reduce the turnaround time to database submission. We demonstrate the use of the pipeline to annotate 22 unpublished *Leishmania* and *Trypanosoma* genomes, produced as part of the NHGRI/NIAID Kinetoplastid White Paper Project (9 already available through TriTrypDB), as well as to extend currently available annotations (e.g. *Trypanosoma congolense*) with additional functional data.

An investigation into the efficacy of calcium channel blockers in malaria - P58 (SP)

May Rajab, Steven Rossington, Holly Matthews, Muna Abubaker, James Wilkinson, Niroshini Nirmalan

School of Environment and Life Sciences, University of Salford, Manchester, M5 4WT

The need to develop new antimalarial drugs due to the low number of drugs emerging and the rising resistance to current drugs is as important now as it has ever been. This is leading many researchers to consider the re-purposing or re-positioning of existing drugs in a bid to fast track the preclinical phase of drug discovery. The proven safety and bioavailability profiles of such lead compounds will impact favourably on the R&D stages of drug development as well as the cost and time of drug development. The malaria research group at the University of Salford has already screened approximately 700 drugs to find potential antimalarial drugs that inhibit the in vitro growth of the multidrug resistant K1 *Plasmodium falciparum* strain. The results of the screening have been positive, with several drugs showing antimalarial potential, one of which includes a calcium channel inhibitor drug (MR15). Further analysis on the efficacy of MR15 and its synthetic derivatives as antimalarials are being carried out.

Preliminary data on in vitro phenotypic screens on the multidrug resistant K1 P. *falciparum* strain and HepG2 cytotoxicity profiles has been promising. The results support the further research into these compounds with the next step being the hERG safety test.

Development of two novel high throughput assays to quantify ubiquitylated proteins in cell lysates: application to screening of new antimalarials - P56

Lydia Mata Cantero [1], Concepción Cid [2], Maria G. Gomez-Lorenzo [1], Wendy Xolalpa [3], Fabienne Aillet [3], J. Julio Martín [2] and Manuel S. Rodriguez [3]

1 Tres Cantos Medicines Development Campus, Diseases of the Developing World. GlaxoSmithKline. Severo Ochoa 2, Tres Cantos 28760, Madrid, Spain.
2 Centro de Investigación Básica, GlaxoSmithKline, Santiago Grisolía, 28760 Tres Cantos, Madrid, Spain.
3 Ubiquitylation and Cancer Molecular Biology. Inbiomed. Mikeletegi 81, 20009, San Sebastian, Spain

The Ubiquitin Proteasome System (UPS) is one of the main proteolytical pathways in eukaryotic cells and plays an essential role in key cellular processes such as cell cycle, stress response, signal transduction and transcriptional regulation. Many components of this pathway have been implicated in diverse pathologies including cancer, neurodegeneration and infectious diseases like malaria. The success of proteasome inhibitors in clinical trials underlines the potential of the UPS in drug discovery. *Plasmodium falciparum*, the malaria causative pathogen, has been used to develop two assays that allow the quantification of the parasite protein ubiquitylation levels in a high throughput format that can be used to find new UPS inhibitors. In both assays Tandem Ubiquitin Binding Entities (TUBES), also known as ubiquitin traps, have been used to capture ubiquitylated proteins from cell lysates. The primary assay is based on Alphalisa technology, and the orthogonal secondary assay relies on a Dissociation-Enhanced Lanthanide Fluorescent Immunoassay (DELFIA) system. A panel of well-known proteasome inhibitors has been used to validate both technologies. An excellent correlation was obtained between these biochemical assays and the standard whole cell assay that measures parasite growth inhibition. Preliminary results of the HTS campaign will be presented.

Direct VEGF-specific anti-angiogenic activities of the anti-*Wolbachia* drugs, doxycycline and minocycline, in an in vitro microvascular blood and lymphatic endothelial cell culture system P23

Hayley Tyrer, Amber Fanthome, Ana F. Guimaraes, Rachel Clare, Mark J. Taylor & Joseph D. Turner

Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, UK

Lymphatic filarial infection (LF) is the cause of elephantiasis and hydrocoele lymphoedemas (LE). LE is initiated as a result of episodic inflammatory damage and remodelling of parasitized lymphatics. Heightened inflammatory responses in LE patients are associated with pro-angiogenic/lymphangiogenic molecules in circulation, such as vascular endothelial growth factors (VEGFs), suggesting inflammatory angiogenesis is relevant in the pathophysiology of LF. Current MDA treatments for LF have mainly microfilaricidal activities and do not alleviate the suffering of current LE patients. There is an un-met need to identify new therapeutics to help reduce LF morbidity. Encouragingly, in two recent trials, 6-week doxycycline therapy was identified to improve LE grade after 12-24 months. The anti-morbidity mode of action (MoA) of doxycycline has not been defined but LE grade is improved both in doxycycline

treated patients with and without active LF infection, suggesting a separate MoA to that of targeting the filarial inflammatory endosymbiont, *Wolbachia*. We developed an in-vitro blood and lymphatic endothelial cell culture system to assess VEGF-specific anti-angiogenic activities of the anti-*Wolbachia* compounds, doxycycline and minocycline. Utilising a 96 well/200 µL based OperettaTM (Perkin Elmer) fluorescent bio-imaging system we have stimulated the proliferation of human adult dermal microvascular blood endothelial cells (HMVECd) and lymphatic endothelial cells (HMVECdLy), using VEGFs targeting VEGF receptors 1-3. Titrations of doxycycline and minocycline toward physiological plasma levels demonstrate a dose-dependent reduction in both VEGF-specific HMVECd and HMVECdLy proliferation. This data supports a direct anti-angiogenic MoA of second-generation tetracyclines that could be used for the treatment of LF.

Localization and alternative splicing the FPPS/GGPPS involved in the isoprenoid pathway during intra-erythrocytic cycle of Plasmodium falciparum - P47

Heloisa Berti Gabriel, João Marcelo P. Alves; Mauro F. de Azevedo; Gerhard Wunderlich; Alejandro M. Katzin; Emília A. Kimura

Department of Parasitology, Institute of Biomedical Sciences, University of Sao Paulo, 05508-900 Sao Paulo, Brazil

Malaria is one of the leading and most widespread of human parasite. The search for new biological targets has also focused in the understanding of metabolic pathways. In *P. falciparum* has been characterized the bifunctional enzyme FPPS/GGPPS. This enzyme catalyzes the condensation of isopentenyl diphosphate (IPP) with geranyl diphosphate (GPP) to form the farnesyl diphosphate (FPP). FPP can be condensed with a further molecule of IPP to form the geranylgeranyl diphosphate (GGPP). FPP and GGPP are essential to biosynthesis of ubiquinone, dolichol, proteins isoprenylation and carotenoids. Through experiments using transfectants parasites by confocal microscopy, amplification of FPPS/GGPPS coding region from cDNA of intra-erythrocytic stages for sequencing and RT-PCR, we have showed that, in the young stages of the intra-erythrocytic cycle the parasite, this enzyme is located in the cytoplasm, but in mature stages is focused in different points. We demonstrated that the enzyme not co-localizes with the mitochondria nor apicoplast. We found the alternative splicing event with the presence of isoforms of this protein. One specific isoform is present in all stages of the parasite cycle, it has a deletion of the important domain by the addition of premature stop codon and it is transcribed about 100 times less when compared to primary protein. Our results suggest that different localization of this protein during intra-erythrocytic cycle of the *P. falciparum* is due to the presence of isoforms that may be interfering in its localization and/or function during the cycle of the parasite. Supported by FAPESP/CNPq

Identification of a Plasmodium falciparum inhibitor 2 motif involved in the binding and regulation activity of protein phosphatase type 1 - P49

Géraldine Tellier, Aline Fréville Christine Pierrot Jamal Khalife

Center for Infection and Immunity of Lille, Inserm U1019, CNRS, Institut Pasteur de Lille, Univ Lille Nord de France, 1 rue du Professeur Calmette, Lille cedex 59019, France geraldine.tellier@pasteur-lille.fr aline.freville@pasteur-lille.fr christine.pierrot@pasteur-lille.fr jamal.khalife@pasteur-lille.fr

Malaria is still the most severe infectious disease in the world because of its high rate of morbidity and mortality. Given the lack of proven vaccine and the increase of resistance against current treatments it is necessary to better understand the biology of *Plasmodium falciparum* to find new means of control. Phosphorylation/dephosphorylation process plays a key role in parasite survival. In our laboratory, we are investigating the regulators of protein phosphatase type I (PfPP1), a main Ser/Thr phosphatase, which is essential for cell growth, differentiation and division. Regulators are known to play diverse roles including the trafficking, the activity and the specificity of PP1. They interact with PfPP1 via several binding motifs such as RVXF, HYNE motifs. We recently identified one of the most ancient PP1 regulators, named PfI2 (Inhibitor 2). Reverse genetic approaches suggested that PfI2 is essential for parasitic growth. In vitro and in blood stage parasites, we demonstrated that I2 interacts with and inhibits PP1 activity, through the implication of RVXF and HYNE binding motifs. Recently, using NMR spectroscopy, a third motif was identified: FxxR/KxR/K. Both RVXF and FxxR/KxR/K motifs act together. Indeed, mutations in both motifs abolished completely the interaction with PfPP1. In addition, using Xenopus oocytes model, we showed that both motifs were necessary for PfI2 to regulate the activity of PP1. Finally the use of a peptide covering the FxxR/KxR/K motif of PfI2 regulator showed an accumulation in infected erythrocytes and an antiplasmodial effect was observed.

The effect of G-Quadruplex stabilising compounds on Plasmodium falciparum - P48 (SP)

Katelyn Monsell & Catherine Merrick

Centre for Applied Entomology & Parasitology, Huxley Building, Keele University, ST5 5BG

DNA can form several non-canonical structures besides the double helix, including the G-quadruplex (G4). This is a four-stranded DNA structure formed by the stacking of quartets of guanines. G4s have been shown to form in vivo in model cell systems and to affect DNA replication, transcription and telomere biology. In the AT-rich genome of the human malaria parasite *Plasmodium falciparum*, potential G4-forming sequences are strikingly rare, and are concentrated in G-rich telomeres and in the upstream regions of sub-telomeric var genes. Here we investigate the effects of G4 stabilising agents that show very different toxicities in *Plasmodium falciparum*. The aim of the research is to characterise how these compounds exert their lethal effects on the parasite, focussing on changes to the parasite cell cycle when exposed to the compounds, and on changes that can be detected in the parasite genome following long term treatment. This research will improve our understanding of G4 biology in *P. falciparum* and begin to define the potential of G4-binding compounds as new anti-malarial drugs.

Development of a high throughput assay for A-WOL macrofilaricide drug discovery through collaboration with Astrazeneca - P18

Laura Myhill[1], Rachel Clare[1], Paul Harper[2], Helen Plant[2], Darren Plant[2], Roger Clark[2], Catherine Bardelle[2], Matthew Collier[2], Kelly L. Johnston[1], Andrew Cassidy[1], Kevin Cross[2], Louise Ford[1], David Murray[2], Kirsty Rich[2], Mark Wigglesworth[2], Stephen A. Ward[1] and Mark J. Taylor[1]

1 Department of Parasitology, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, L3 5QA, UK;
2 AstraZeneca, Discovery Sciences, Alderley Park, Cheshire, SK10 4TG, UK

The aim of the Anti-*Wolbachia* consortium (A•WOL) is to identify novel macrofilaricidal drugs targeting the essential bacterial symbiont (*Wolbachia*) of the filarial nematodes causing onchocerciasis and lymphatic filariasis. Through the extensive use of robotics, the A•WOL cell-based drug screening assay has increased its screening capacity 25 fold from around 25,000 to over 500,000 compounds per month through partnership with the Global High Throughput Screening (HTS) Centre at AstraZeneca. The robotics used included three separate automation platforms; one consisting of a BioCel system (Agilent) incorporating three robotic arms and equipment for washing and handling the assay plates and two HighRes Biosolutions platforms incorporating plate readers (TTP Acumen® and Perkin Elmer EnVision®) for data capture. This new screening assay has been used to screen 1.3 million compounds from AstraZeneca's chemical library, and 500,000 compounds from the Medicines for Malaria Venture (MMV). This screen has delivered more than 20,000 hits, which are undergoing further triage, annotation and prioritization for progression through A•WOL's screening pipeline.

Population and comparative genomics of African Schistosoma mansoni P17 (SP)

Thomas Crellen [1,2], Sophia David [2], Thomas Huckvale [2], Nancy Holroyd [2], Fiona Allen [3], Matthew Berriman [2], Joanne Webster [4], James Cotton [2]

1. Imperial College, London, United Kingdom
2. Wellcome Trust Sanger Institute, Cambridge, United Kingdom,
3. Natural History Museum, London, United Kingdom
4. Royal Veterinary College, London, United Kingdom

Schistosomiasis is among the most important parasitic diseases, with over 200 million people infected and 300,000 deaths annually across Africa, Asia, South America and the Caribbean. Around 90% of cases are in sub-Saharan Africa, where *Schistosoma mansoni* is one of the two most clinically important species, and the principal cause of intestinal schistosomiasis. A draft reference genome is available for S. *mansoni* and is being actively curated and improved. Here, we present genome sequence data and assemblies from seven adult male *S. mansoni* that were recently collected from the field with minimal lab passage, including six diverse African isolates - the first genomic data from the region of greatest public health interest. We confirm that the *S. mansoni* reference sequence is a suitable substrate for genomic analysis of African populations. We use this genomic diversity data to investigate signatures of natural selection on the *S. mansoni* genome, and apply two coalescent-based models to infer the population history of *S. mansoni* on two continents. Our results show that the New World strains have smaller past effective population sizes (Ne) than African strains, suggesting the possible occurrence of a past population bottleneck. We estimate the divergence time between the African and New World populations, finding support for the hypothesis that *S. mansoni* colonised the New World via the 16-19th century West African slave trade. In the light of this potential population bottleneck, we investigate systematic differences between South American populations and African populations in both genome structure and single nucleotide polymorphisms (SNPs).

Lifelong impact of Insecticide Resistance in Anopheles gambiae - P109

Angela Hughes, Philip McCall and Hilary Ranson

Vector Biology Department, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5QA

Lifelong impact of Insecticide Resistance in *Anopheles gambiae* Does insecticide resistance affect the age profile in mosquito populations? Insecticide resistance monitoring techniques such as WHO susceptibility bioassays measure short term (24hr) responses to insecticide exposure and determine the presence of resistance by exposing young adult mosquitoes (3-5 days) to diagnostic doses of insecticides. But do insecticide resistant vectors have a reduced lifespan after exposure to insecticide treated surfaces? Understanding this relationship is key to determining the impact of resistance on malaria transmission. To assess this, insecticide resistant female *Anopheles gambiae* mosquitoes were repeatedly exposed to insecticide treated or untreated bednets, using WHO cone bioassays. Their daily survival was recorded to measure the long term impact of surviving insecticide exposure. Three different exposure regimes were used to mimic different scenarios in which mosquitoes encounter insecticides in the field. Results show a significant reduction in fitness of mosquitoes after insecticide exposure. Current insecticide bioassays also ignore the potential impact of resistance on behaviour which, again, could have important implications for the impact that resistance is having on disease transmission. The second part of this project is therefore contrasting the behaviour of insecticide resistant and susceptible mosquitoes at the net interface. The data from both study areas will be used in mathematical models to predict the impact of resistance on both existing and future malaria interventions

Physiology and Pharmacodynamics of Plasmodium falciparum gametocytes - P59 (SP)

Ahmed Saif, Grazia Camarda, Giancarlo Biagini, Stephen Ward.

Ahmed Saif 1- Parasitology Department, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, United Kingdom. 2- Department of Medical Laboratories Sciences, Faculty of Applied Medical Sciences, Najran University, Najran, Saudi Arabia. Grazia Camarda Parasitology Department, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, United Kingdom. Giancarlo Biagini Parasitology Department, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, United Kingdom. Stephen Ward. Parasitology Department, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, United Kingdom.

The development of interventions to block the malaria transmission are a cornerstone towards efforts of malaria elimination/eradication. The sexual gametocyte stage of *Plasmodium falciparum* is responsible for parasite transmission from the human host to the mosquito, however despite the importance of this developmental stage, the biology and pharmacology of gametocytes are very poorly understood. Using a real-time single-cell confocal imagining platform, gametocyte physiological studies have been undertaken to characterize key cellular bioenergetics processes. A ratiometric pH indicator (BCECF) was used to show that the pHi of gametocytes (stages IV&V) were 7.64±0.14 (7.5-7.73) compared to asexual parasites 7.24±0.02 (7.2-7.38). Gametocytes were also shown to be sensitive to V-type H+-ATPase inhibitors, consistent with this primary active transporter being responsible for H+ in these sexual stages. Gametocytes were also shown to possess a high plasma-membrane potential (pΨm), as indicated by accumulation of tetramethyl rhodamine ethyl ester (TMRE), and this accumulation was again shown to be dependent to the activity of V-type ATPases. Consistent with recent metabolomics data, accumulation of the glucose probe (6-NBDG) was significantly lower compared to asexual intraerythrocytic parasites, indicating either a reduced dependence on glycolysis. Time-dependent killing assays using a newly generated luciferase-reporting transgenic line indicate a

significantly different inhibition profile of gametocytes compared to asexual parasites, and data is presented for new inhibitors in pre-clinical development as well as synthesised metabolites of primaquine. These data are presented and discussed in context of the development of strategies to develop and discover new transmission-reduction antimalarials.

Efficacy and Safety of Artemether-Lumfantrine (Coartem®) for the Treatment of Uncomplicated Plasmodium falciparum Malaria in Pawe, North West Ethiopia - P62 (SP)

Melaku Tamene Asfaw[1], Walelign Dessie [1], Tedla Mindaye [1], Gebru Mullugeta [1], Moges Kassa [2]
1 Addis Ababa University, College of Health Science, School of Medical laboratory Science Addis Ababa, Ethiopia
2 Ethiopian public health Institute (EPHI), Addis Ababa, Ethiopia

Pawe, Benishangul Gumuz regional state, North West Ethiopia

Background: Malaria prevention and management in Ethiopia aims to reduce the overall burden of the disease. The recommended first-line treatment of all uncomplicated *P. falciparum* malaria is an artemisinin-based Combination Therapy (ACT) called artemether-lumefantrine (AL). If AL is not available, oral quinine is recommended. Objective: To assess the efficacy and safety of AL(Coartem®) for the treatment of uncomplicated *P. falciparum* infections in Pwae /Felege Selam Health Center, Benishangul Gumuz regional state (BG-RS). Methods: Antimalarial drug efficacy trials were conducted in Pawe/Felege Selam health center, BG-RS, Ethiopia from October-to-December, 2013. The participants were febrile over 6 months of age with confirmed uncomplicated *P. falciparum* infection. Patients were treated with a 3-day, six-dose regimen of AL combination. To evaluate the drug-efficacy 28-day follow-up period monitored. The data were analyzed by SPSS-and-Kaplan Meier and presented by tables and figures. Result:- The cure rate, adequate clinical and parasitological response(ACPR) was found to be high 96.7%(PCR uncorrected). The parasite and fever clearance time was rapid. AL for the treatment of acute uncomplicated *P. falciparum* malaria in the study area showed PCR corrected cure rate of 97.8% and only 2.2% failure rate. The cure-rate exceeded 95.8% in each body-weight group (P=0.338) with no indication that outcome differed between groups. There were also no clinically relevant differences in safety or tolerability between body weight groups. Conclusion: The result showed that the six-dose regimen of AL is a good choice for managing uncomplicated *P. falciparum* malaria in all body weight groups of ≥5kg, with a high efficacy and a good tolerability.

Associations between the nematode Caenorhabditis elegans and the snail *Helix aspersa maxima* - P85 (SP)

James Cutler, Mark Viney Laura Weldon

Biology Life Sciences Building School of Biological Sciences 24 Tyndall Ave Bristol BS8 1TQ

The free-living nematode *Caenorhabditis elegans* is used widely in biology as a model organism, but relatively little is known about its ecology. In the wild *C.elegans* can be found in rotting vegetation, in anthropogenic habitats, and it has also been found in association with invertebrates. The current idea is that *C. elegans* associates with invertebrates to enhance its dispersal, but that it does not live, or reproduce, on these animals for extended periods of time. The aim of this work was to investigate

whether *C. elegans* can live, and reproduce on the snail *Helix aspersa maxima*. This was tested using controlled *C. elegans* infections of *H.aspersa*, after which the snails were maintained in an environment where *C. elegans* would be unlikely to survive off of the snails. Our results provide evidence suggesting that *C. elegans* can live on *H.aspersa* for up to 15 days, during which time *C. elegans* would have grown, developed and possibly reproduced. Such extended living of one free-living animal upon another is likely to be the evolutionary route to animal parasitism.

Malaria - visceral leishmaniasis co-infections in East Africa - P64

Henk Schallig[1], Erika van den Bogaart[1], Marieke Berkhout[1], Pètra Mens[1], Emily Adams[1], François Chappuis[2], Koert Ritmeier[3], Bakri Nour[4]

1 KIT Biomedical Research, Parasitology Unit, Meibergdreef 39, 1105 AZ Amsterdam, The Netherlands;
2 MSF-Switzerland, Geneva, Switzerland;
3 MSF Holland, Amsterdam, The Netherlands;
4 Blue Nile Institute for Communicable Diseases, University of Gezira, Wad Medani, Sudan

Due to geographic overlap of malaria and visceral leishmaniasis (VL), co-infections exist but have been poorly investigated. Two studies have been undertaken to gather data on malaria-VL co-infections in East Africa. To describe prevalence, features and risk factors for VL-malaria co-infections, a case-control analysis was conducted on data collected at Amudat Hospital, Uganda by Médecins sans Frontières. A second retrospective study was performed using medical records of VL patients admitted to Tabarakallah and Gedarif Teaching Hospitals (Gedarif State) and Al`Azaza kala-azar Clinic (Sennar State), Sudan. In Uganda, of 2414 patients with confirmed VL, 450 (19%) were positively diagnosed with concomitant malaria. Young age was identified as a risk factor, particularly the age groups 0-4 and 5-9 years. Mild and moderate anemia negatively correlated with the co-morbidity. Anorexia was slightly more frequent among co-infected patients. The in-hospital case-fatality rate did not significantly differ between cases and controls, being 2.7% and 3.1% respectively. In Sudan, the prevalence of malaria co-infection among VL patients ranged from 3.8 to 60.8%. Co-infected patients presented at hospital with deteriorated clinical pictures; emaciation, jaundice and moderate anemia were found to be positively associated with the co-infection. Severity of splenomegaly and, to a lesser extent, hepatomegaly (OR: 0.52; 95%CI: 0.27-1.01) appeared to be reduced by concomitant VL and malaria. The in-hospital case-fatality rates did not significantly differ between co- and mono-infected patients. The work indicates that routine screening of VL patients living in malaria endemic-areas and close monitoring of co-infected patients should be implemented.

Octopamine receptors of platyhelminths: drug target validation in a planaria model - P84

Sally Williamson, Calista Dufton-Kelly

School of Natural Sciences and Psychology, Liverpool John Moores University, James Parsons Building, Byrom Street, Liverpool L3 3AF

Parasitic platyhelminths, such as trematodes and cestodes, are a major human and animal health burden, and are the causative agents of many neglected tropical diseases. Drugs for treating these parasites are few, and drug resistance a major issue: validating novel drug targets in the helminth

nervous system is therefore important if new drugs are to be developed. Octopamine receptors, found only in invertebrate and not mammalian nervous systems, are a potential novel drug target. Although well studied in insects, the pharmacology of platyhelminth octopamine receptors, and the role of these receptors in modulating behaviour, has not previously been described. Using the planarian Dugesia tigrina as a model organism for investigating platyhelminth neurobiology, we have tested a spectrum of drugs which target octopamine receptors for their effects on motility and behaviour. Octopamine clearly plays an important role in modulating muscular contraction in planaria, and future work will test similar compounds on trematodes, such as *Fasciola hepatica*, to validate this potential drug target in a helminth parasite.

Assessment of Artesunate/ Sulfadoxine Pyrimethamine Tablets Awareness And Acceptance Among Healthcare-Providers And Patients, Great Wad Medani Locality, Gezira State, Sudan - P135 (SP)

Maha Maatoug, Bakri Yousif [2], Mirghani Abdel Rahman [1]

1. Department of Pharmaceutics , Faculty of Pharmacy , University of Gezira, Sudan
2. Blue Nile Institute for Communicable Diseases , University of Gezira ,Sudan

In Sudan the National Malaria Control Program adopted the use of artesunate + sulphadoxine-pyrimethamine (ASP) as the first line of treatment of uncomplicated malaria since 2004. The aim of this study was to evaluate the awareness and acceptance of ASP among healthcare-providers and patients in Wad Medani locality, Gezira State, Sudan. To investigate the knowledge and practice regarding ASP usage three types of questionnaire were randomly distributed. The first to prescribers (whether doctors or medical assistants) and pharmacists. The second to pharmacy assistants and the third to patients. The respondents were 326 healthcare- providers, 46 pharmacy assistants and 687 patients. The data collected were organized, tabulated and analyzed using SPSS (Statistical Package for Social Sciences, version 14). Regarding the awareness of healthcare - providers 256 (78.5%) of the questioned healthcare-providers were aware about the protocol, while 70(21.5%) were not aware about the protocol. 218(66.9%) adhered to the protocol, 46(14.1%) did not adhere to the protocol and 62(19%) adhered to the protocol sometimes. Two-hundred thirty (70.6%) of healthcare- providers were not trained about the protocol guidelines. Two-hundred fifty eight (79.1%) of them considered ASP as the first line of treatment in their practice. Pharmacy assistants in private pharmacies were neglected in training programs 28(90.3%) were not trained, 3(60%) from revolving drug pharmacies and 6(75%) health- insurance pharmacies were also not trained about the malaria protocol. This was serious because many patients used to go directly to pharmacies with laboratory diagnosis asking for advice. ASP was highly accepted among patients 528(76.9%) and 609 (88.6%) of them obeyed ASP instructions given to them. The study revealed that ASP was accepted by healthcare-providers and patients but low awareness and poor adherence to the protocol were due to lack of training and information, the decreased availability and affordability of the consecutive lines of malaria treatment and the absence of dosage form suitable for children and in case of vomiting.

P-selectin is a host receptor for Plasmodium MSP7 ligands - P125

Abigail Perrin, S Josefin Bartholdson and Gavin J Wright

Wellcome Trust Sanger Institute, Genome Campus, Hinxton, Cambridgeshire CB10 1SA

Plasmodium parasites, the etiological agents of malaria, typically elicit a non-sterile but protective immune response in human host populations. P-selectin is a cell surface receptor expressed in mammals that is a known component of the inflammatory response against pathogens and has been previously identified as a host factor that influences malaria-associated pathology both in human patients and rodent infection models. To better understand the molecular mechanisms underlying the involvement of P-selectin in the pathogenesis of malaria, we used a systematic extracellular protein interaction screen to identify *Plasmodium falciparum* MSP7, best known as a component of the MSP1 complex, as a binding partner of human P-selectin. We showed that the two proteins bound each other directly via the P-selectin C-type lectin and EGF-like domains and N-terminus of MSP7, which is not found on the merozoite surface. We also showed that multiple P. *falciparum* MSP7-related proteins bound to P-selectin and that orthologous proteins in the murine parasite P. *berghei* (PbMSRP1 and PbMSRP2) interacted with mouse P-selectin. P-selectin binding is the first described function of the secreted N-terminus of PfMSP7, and its conservation across the *Plasmodium* MSP7 family implies an important biological function. Finally, we demonstrate that P-selectin, when complexed with MSP7, could no longer bind to its endogenous carbohydrate ligand, Sialyl-LewisX providing a possible mechanism for the known immunomodulatory effects of both MSP7 and P-selectin in malaria infection models.

Macronutrient Ratios in Host Diet Determines Pathogen Success - P138 (SP)

Robert Holdbrook, Catherine Reavey, Yamini Tummala, Joanna Randall, Sheena Cotter, Judith Smith, Ken Wilson

Lancaster University Lancaster LA1 4YW

It is widely accepted that nutrition plays a vital role in disease progression. Pathogens are reliant on their hosts for nutrition, either by extracting nutrients directly from the host or by competing for resources the host ingests. As a result, host diet-choice may play a role in deciding the outcome of infection. Whilst the host is normally the focus of nutritional immunology studies, it is also important to understand how changes in host nutrition impact the pathogen. *Xenorhabdus nematophila*, a gram-negative entomopathogenic bacterium, is ideal for such studies since it does not have an external life-stage, but relies on its symbiont, *Steinernema carpocapsae* to transfer between hosts. Using the Egyptian cottonworm *Spodoptera litorallis* as a model host, we found that the host's time-to-death following bacterial challenge was longer for larvae fed diets that were relatively high in protein and low in carbohydrate, but only when diets were calorie-dense. This extended time to death was also positively correlated with a slower bacterial replication rate. At this stage, it is unclear whether these relationships are driven by the effects of nutrition on the host's resistance mechanisms or the pathogen's growth rate, or a combination of the two. The next step of this study is to quantify the effects of host nutrition on the pathogen through an in vitro examination of bacterial nutrient-use in the absence of immune components.

Plasmodium alveolins possess distinct but structurally and functionally related multi-repeat domains - P140

Fatimah Al-Khattaf, Tremp, A.Z. Al-Khattaf, F.S. Dessens, J.T.

London School of Hygiene and Tropical Medicine Keppel Street, London WC1E 7HT

The invasive and motile life stages of malaria parasites (merozoite, ookinete and sporozoite) possess a distinctive cortical structure termed the pellicle. The pellicle is characterised by a double-layered 'inner membrane complex' (IMC) located underneath the plasma membrane, which is supported by a cytoskeletal structure termed the subpellicular network (SPN). The SPN consists of intermediate filaments, whose major constituents include a family of proteins called alveolins. Here, we re-appraise the alveolins in the genus *Plasmodium* with respect to their repertoire, structure and interrelatedness. Amongst 13 family members identified, we distinguish two domain types that, albeit distinct at the primary structure level, are structurally related and contain tandem repeats with a consensus 12-amino acid periodicity. Analysis in *Plasmodium berghei* of the most divergent alveolin, PbIMC1d, reveals a zoite-specific expression in ookinetes and a subcellular localisation in the pellicle, consistent with its predicted role as a SPN component. Knockout of PbIMC1d gives rise to a wild-type phenotype with respect to ookinete morphogenesis, tensile strength, gliding motility and infectivity, presenting the first example of apparent functional redundancy amongst alveolin family members.

Development and evaluation of a serological Chikungunya antibody detection assay - P128

Andreas Latz[1], P. H. Duchmann[1], J. Völger[1]
1 NovaTec Immundiagnostica GmbH, R+D, Dietzenbach, Germany

Germany, Dominican Republic

Chikungunya is an emerging disease in many tropical settings. Causative agent for this disease is a single-stranded, enveloped RNA-Virus that belongs to the genera *Alphavirus (Togaviridae).* The symptoms of Chikungunya include fever which can reach 39°C (102,2°F) a petechial or maculopapular rash usually involving the limbs and trunk, and arthralgia or arthritis affecting multiple joints which can be debilitating. *Alphaviruses* rarely appear in Europe but can be noticed as import or travel associated infection. The aim of this work was to develop a serological assay to detect IgG and IgM antibodies against Chikungunya and to evaluate in endemic outbreak settings. An IgG-capture and IgM-capture ELISA was developed. Both take advantage of native antigens produced with a proprietary technique, exclusively developed for this serological antibody detection assay. In house measurements as well as external evaluations in many endemic regions of the world conducted by well know tropical institutes revealed excellent clinical sensitivity and specificity as well as high positive and negative predictive values (all above 95%). Data from the current outbreak in the Caribbean will be discussed. Therefore the newly developed ELISA seems to be a superior tool to diagnose past and acute Chikungunya infection in common and outbreak settings all over the world. It will assist diagnosis of travel returners with unknown fever as well as military in endemic operation area. To further improve Chikungunya diagnostic a Lineblot is currently under development as tool for conformation of ELISA results as well as for small labs with limited lab equipment.

The role of rodents circulating pathogenic Leptospira in urban cities in Peninsular Malaysia – P144

Siti Nursheena Mohd Zain, Douadi Benacer, Sim S.Z., Khairul Nizam and Kwai Lin Thong

Douadi Benacer Institute of Biological Sciences, Faculty of Science, University of Malaya, Malaysia Laboratory of Biomedical Science and Molecular Microbiology, Institute of Graduate Studies, University of Malaya, Malaysia; Bacteriology Unit, Institute for Medical Research, Ministry of Health, Malaysia; Sim S.Z. Khairul Nizam Bacteriology Unit, Institute for Medical Research, Ministry of Health, Malaysia; Kwai Lin, Thong Institute of Biological Sciences, Faculty of Science, University of Malaya, Malaysia Laboratory of Biomedical Science and Molecular Microbiology, Institute of Graduate Studies, University of Malaya, Malaysia

Leptospirosis is an emerging infectious disease of global significance, and endemic in tropical countries including Malaysia. Over the last decade, a dramatic increase of human cases were reported however information on the rat and the serovar circulating among the population is limited. Therefore, the present study was undertaken to determine the infection prevalence and serovar circulating in the urban rat populations from selected main cities in Peninsular Malaysia. Five cities represented different geographical locations in Peninsular Malaysia with trapping commencing from October 2011 to February 2014. Microscopic agglutination test (MAT) and PCR was carried out to identify and determine the pathogenic status of the isolates while pulsed-field gel electrophoresis (PFGE) and random amplified polymorphic DNA (RAPD)-PCR to characterize the isolates. Three species were identified from 357 rats captured with Rattus rattus, the dominant rat species (285, 80%) followed by Rattus norvegicus (53, 15%) and Rattus exulans (19, 5%). Only 11.1% were positive through culture and further confirmed as pathogenic Leptospira by PCR with two serogroups distinguished in the population namely; L. borgpetersenii serogroup Javanica and L. interrogans serogroup Bataviae. Host infection was significantly associated with locality, host-age and species with infections higher during the wet season ($p = 0.01$).

Molecular diagnostics development for emerging and re-emerging infectious diseases – P143

Hisham Alharbi, , Thomas Edward, Luis Cuevas, Emily Adams

Liverpool School of Tropical Medicine

The aim of this study is to develop a multiplex molecular diagnostic kit for Malaria, Dengue and Chikungunya as emerging and re-emerging infectious diseases. Malaria, is one of the major causes of the death worldwide with an estimation of 207 million at risk. Dengue virus is one of the most rapidly increasing transmitted vector diseases worldwide with higher morbidity and mortality than all other Arbovirus's. There is an estimated 50-100 million cases of dengue fever. As of January 2015, over 1.1million suspected cases of Chikungunya have been recorded in Latin America and the USA. 176 deaths have also been attributed to this disease during the same period. Molecular diagnostic tests help to aid the identification of the pathogen therefore impacting the clinical diagnoses, treatment of a patient and evade diseases outbreaks. They can identify the acute phase of disease where viral load is high but there are low antibody titres. We will design primers and probes sets for each target disease and explore combining them as multiplex test for qPCR. Further we will perform field assessment of the diagnostic test in two settings. The first is Saudi Arabia, where Dengue is endemic and may overlap with the emergence of Chikungunya and re-emergence of Malaria. The second, Brazil, is endemic with Dengue, Malaria and Chikungunya (although rarely confirmed) which is emerging from Central America and could lead to a new outbreak.

WormBase-ParaSite: a comprehensive, open-access resource for helminth genomic data – P142

Jane Lomax, on behalf of the WormBase Consortium

Wellcome Trust Sanger Institute

WormBase-Parasite (parasite.wormbase.org) is a major new resource for storing, analyzing and exploring the genomes of helminth parasites. The public database, developed jointly by EMBL-EBI and the Wellcome Trust Sanger Institute, contains 97 annotated genomes from a total of 89 helminth species. A large number of the genomes were sequenced as part of the International Helminth Genomes Initiative - the largest collection of helminth genomic data ever assembled. The majority of the genome assemblies in WormBase-ParaSite are as yet unpublished so this resource provides unprecedented access to this high quality genomic data. WormBase-ParaSite is based on the well-established Ensembl infrastructure and provides several tools for exploring and analyzing the helminth data: a BLAST tool for aligning sequence to multiple genomes; a BioMart data-mining tool and Compara gene trees for comparative genomics analysis. We plan to add tools for the exploration of transcriptomic data for the next release of WormBase-ParaSite. This resource will allow researchers to perform critical investigations for example to identify of orthologs for existing drug targets, to discover new 'druggable' candidate genes, or to study the evolution of parasitic traits such as the ability to infect through skin. WormBase-ParaSite is closely integrated with WormBase, the genomic database for C. elegans and related species. Key reference parasitic genomes are incorporated in WormBase, as they become established and stable, where they are more richly curated. We welcome submissions from the helminth research community to gradually improve the phylogenetic coverage and build a robust resource for future research.

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