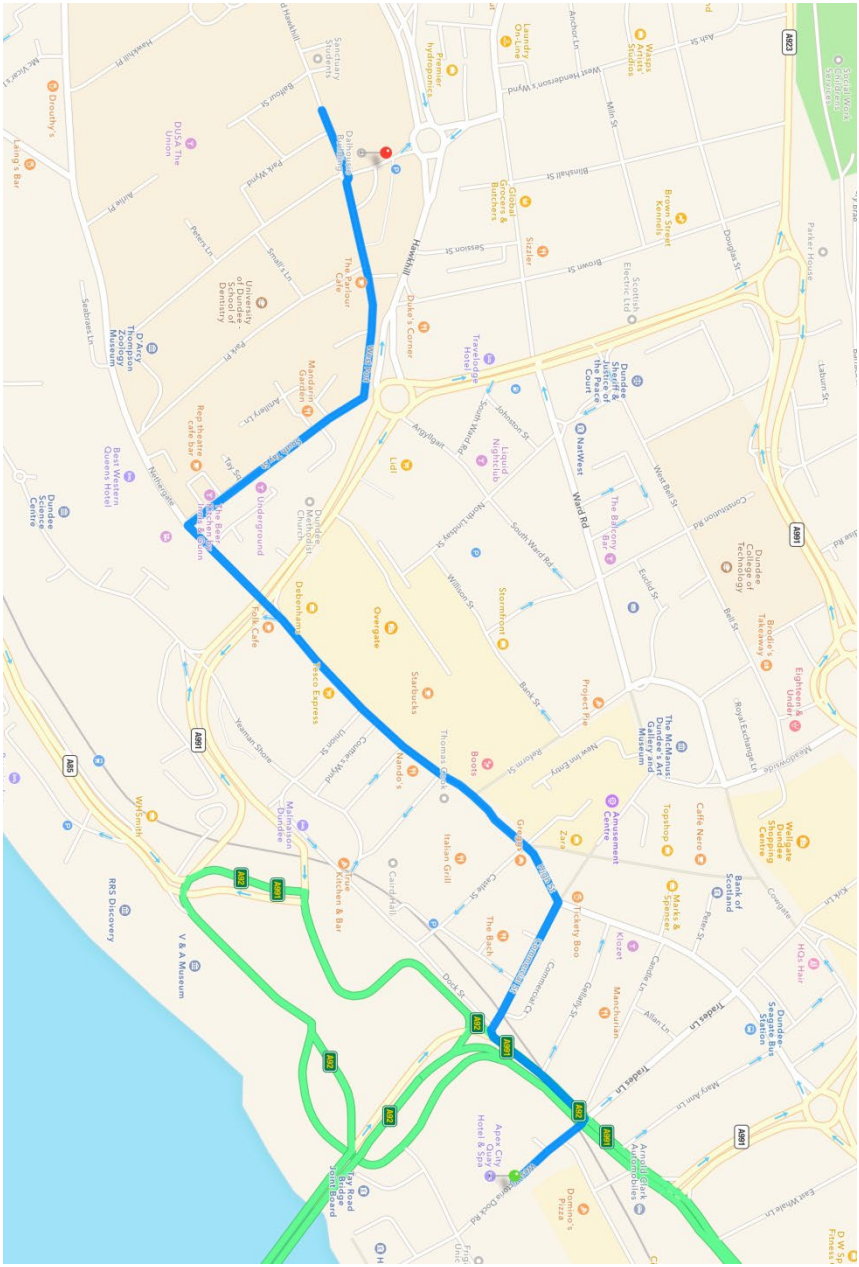
# British Society for Parasitology

## 55th Annual Spring meeting

2nd to 5th April 2017 | University of Dundee


Scientific program and abstracts


Dalhousie Residence
Hawkhill
Dundee Sheriff & Justice of the Peace Court
Dundee Contemporary Arts
Dundee Science Centre
RRS Discovery
V & A Museum
Dundee Railway Station
Dundee Bus Station
Wellgate Shopping Centre
Overgate
Tesco Express
Tesco Kitchen & Bar
Underground
Mandarin Garden
The Parlour Cafe
Sanctuary Students
Premier Hydrotherapy
Laundry On Line
Coles Grocers & Butchers
Sizzler
Travelodge Hotel
Liquid Nightclub
Lidl
Starbucks
Nando's
Italian Grill
Boots
Greggs
Zara
Tickety Boo
The Bach
Kiezet
Manchurian
Topshop
Caffe Nero
Marks & Spencer
Bank of Scotland
Amusement Centre
The McManus: Dundee's Art Gallery and Museum
Broadie's Takeaway
Eighteen & Under
Dundee College of Technology
Best Western Queens Hotel
D'Arcy Thompson Museum
University of Dundee - School of Dentistry
Rep theatre cafe bar
The Bank Kitchen & Bar
Dundee Methodist Church
Dundee Mission
Dundee Cathedral
Premier Inn
Apex City Quay Hotel & Spa
Armoury Park Automobiles
Dominos Pizza
Drouthy's
Laing's Bar
Dundee Parker House
Scottish Electric Ltd
Brown Street Kennels
Wasps Wasps Sicilios
Dundee Cathedral
Dundee Cathedral

## Fáilte!

It is our great pleasure to extend a warm Scottish welcome to all delegates to the 55th Spring Meeting of the British Society for Parasitology, at the University of Dundee. This is the first BSP Spring Meeting to be held here, and we hope that this is a successful, productive and enjoyable meeting for you all. Dundee is a young University, only 50 years old, but has an enviable reputation in the life sciences and fine arts, and for contributions to parasitology in particular. The city of Dundee offers a near unique venue, and we also hope that delegates can enjoy the special atmosphere coming from echoes of Dundee's historical roles in the three Js; "Jute, Journalism and Jam". It is well worth visiting the Discovery and Jute museums, both of which offer excellent insights into the history of the city, the region and the great contributions to exploration and commerce that has marked out Dundee as special. The fair city of St Andrews, the home of golf, is only 25 minutes away and is also a must see, whilst the highlands and the cultural centre of Edinburgh are close by.

Our meeting is based at the Apex Hotel and the Dalhousie Building at the University, both excellent locations for scientific meetings; these venues are only ten minutes apart and embedded within central Dundee. Please check carefully that you are in the correct place for your session.

We hope that the 2017 meeting will be another one to remember, and we have an exceptionally packed and varied timetable with, we hope, something for everyone. The scientific sessions cover the full range of interests of parasitologists, and also extend into special sessions beyond these core disciplines, including diversity, drugs, veterinary parasitology and more. We are incredibly indebted to our session organisers, helpers and many others who have made this meeting a possibility.

We are sure that new collaborations and friendships will emerge from the meeting. We also hope that the City itself will play a starring role, with a traditional Ceilidh at the Apex on Tuesday evening. The Wright medal lecture and the AGM help to round out our program. We thank you for attending the BSP Spring meeting, and hope that you find it stimulating, enjoyable and fun.

**Mark C. Field and David Horn, University of Dundee**

**Session coordinators**

Drugs, diagnostics – **Kevin Read** K.Read@dundee.ac.uk
Epidemiology, vectors - **George** Christophides g.christophides@imperial.ac.uk
Molecular biology - **David Horn** d.horn@dundee.ac.uk
Veterinary/Eco - **Damer Blake** dblake@rvc.ac.uk, **Jo Cable** CableJ@cardiff.ac.uk
Malaria – **Mike Blackman** mike.blackman@crick.ac.uk
Worms - **Karl Hoffmann** krh@aber.ac.uk
Diversity - **Mark Field** mfield@mac.com
Public understanding - **Tansy Hammarton** Tansy.Hammarton@glasgow.ac.uk
In the field – **Jeremy Sternberg** jsternberg@abdn.ac.uk

# The BSP Council 2017

**Professor Mark Taylor**-Council President 2016-2018

Professor of Parasitology at Liverpool School of Tropical Medicine

**Professor Paul Horrocks** – Honorary General Secretary (2016-2019)

Professor in Molecular Parasitology at Keele University

**Dr Paul Denny** - Honorary Treasurer (2016-2019)

Director of Postgrad Research at Durham University

**Prof Maria-Gloria Basanez** - Vice-President (2016-2018)

Professor of Neglected Tropical Diseases at Imperial College London

**Professor Damer Blake** - Honorary Meetings Secretary (2016-2019)

Professor of Parasite Genetics at the Royal Veterinary College

**Dr Catherine Merrick** - Honorary Communications Secretary (2015-2018)

Senior Lecturer in Biology at Keele University

**Dr Alvaro Acosta-Serrano** - Ordinary Council Member (2016-2018)

Senior Lecturer in Parasite and Vector Biology, Liverpool School of Tropical Medicine

**Dr Martha Betson** - Ordinary council member (2014-2017)

Lecturer in Veterinary Parasitology at the University of Surrey

**Professor Jo Cable** - Ordinary Council member (2015-2018)

Professor of Parasitology at Cardiff University

**Dr Jonathan Dalzell** - Ordinary Council member (2015-2018)

Lecturer in molecular parasitology and Leverhulme early career fellow at Queen's University Belfast

**Dr Poppy Lamberton** - Ordinary council member (2014-2017)

Senior Lecturer at the University of Glasgow

**Dr Paul McVeigh** - Ordinary council member (2016-2019)

Research fellow at Queen's University, Belfast

**Dr Justin Pachebat** - Ordinary council member (2016-2019)

Senior Lecturer in Microbial Genomics at Aberystwyth

**Dr Helen Price** - Ordinary council member (2016-2019)

Lecturer in the Centre for Applied Entomology and Parasitology (CAEP) at Keele University

**Dr Bonnie Webster** - Ordinary Council member (2014-2017)

Natural History Museum, London

**Ms Alison Mbekeani** - Student representative

PhD student at Durham University

**Mr Tom Pennance** - Student representative

PhD student at the Natural History Museum and Cardiff University

**Want to become more involved with the BSP?**

The BSP is seeking new members to sit on council when present members rotate. The usual term is three years, and is an opportunity to contribute to the running of a society that seeks to promote parasitology in all its forms. The BSP council meet about four times a year, at various locations around the UK, and is primarily responsible for the smooth running of the Spring and Autumn meetings, together with outreach and other aspects. If you are interested, please talk to any of the present council members listed above or contact the BSP Secretariat at info@bsp.uk.net.

It is highly important for BSP members to have the opportunity to discuss how the BSP proceeds, and the AGM provides the forum for this. The council would encourage you to attend and make a contribution; it is only through having your opinions heard that the Society can adapt and change in the manner you wish it to. The AGM remains the major mechanism by which members can meet and contribute to the running of the Society, and we hope to see you there.

**We politely request that, out of respect for all speakers, debaters and other presenters that you switch your mobile/cellular phone to silent/vibrate whenever you are in an auditorium with an active session in progress.**

# Conference venues

**Reception and registration**

Registration for the meeting will be from 3.00pm to 6.00 pm on Sunday 2nd of April at the Apex hotel. The reception desk will re-open at 9:00am on Monday the 3rd of April (Maps pages 10-12).

Other facilities that will be made available at the reception desk will include:

- Urgent message pickup
- Conference organising committee contact details
- Internet access codes
- An information board
- Tourist Information

**Safety**

**On the continuous sounding of a fire alarm, evacuate by the nearest safe route to the assembly areas. For the Apex this will be on the walkway opposite the main entrance and for Dalhousie in the area immediately outside of the main entrance. Emergency exits are clearly identified with illuminated green signs.**

Please note that the University has a very strict non-smoking policy.

In the event of an emergency, dial 1-999 from any internal phone to contact emergency services.

**Identification**

We would like to remind all delegates that it is important to wear name badges at all times, in order to identify yourselves to the organizers, volunteer helpers and university staff. The conference committee can be identified by name badges which display the BSP 2017 logo and student volunteers who will be wearing BSP 2017 T-shirts. All of these people are here to help you, so please do not hesitate to ask for assistance.

**Internet Facilities**

Delegates can access the internet via several different wireless networks. The Apex has guest Wi-Fi passes valid for the duration of the conference *via* the Lapwing network. Users who have an Eduroam account can also use this to log in direct to the system at the University venue, and will likely find this to be the most efficient option. If there are any problems, please contact the Conference Registration desk who can provide details of IT Services.

## Information for oral presentations

Oral presentations will be given in the Apex and in Dalhousie, and please check when and where your session will be. Loading of oral presentations will take place in the lecture theatre appropriate to the session, and there is either a desktop or laptop provided. Speakers may use their own laptops if required, but please ensure you bring the appropriate video adaptor.

**Please ensure that your presentation is loaded by 8:45 am at the latest if you are presenting in the morning sessions or by 1:45 pm if you are presenting in the afternoon sessions.**

There will be a student volunteer in each room who will help you load your presentation and help you if any problems arise with the equipment.The scientific program is very full and speakers are respectfully requested to keep to their time slot so that delegates who wish to move between sessions can do so.

## Information for Poster Presentations

Posters may be put up from 4:00 pm on Sunday 2nd April in the Apex, and the boards (6ft tall x 3ft wide) are located in the lobby area. As we have two session these mist be removed immediately following the first session and second session posters may then be mounted. Posters must be removed by 12:00 noon on Wednesday 5th April. You will be provided with a number for your poster that will correspond to a particular poster board. Please note that the use of bluetac or drawing pins is prohibited and only the Velcro tabs provided may be used to secure your poster to the boards. These will be made available at the Conference Reception desk. All posters must be displayed in time for the poster sessions on Monday and Tuesday afternoons.

## Food and Refreshments

Breakfast is available in the restaurant until 9.00 am. This is a staff-assisted buffet style meal. A full range of cooked items and cereals is available as well as continental breakfast.
All coffee breaks will be provided in either the lobby area of the Apex or the lobby of Dalhousie. Lunch will be served in the Apex hotel.

Delegates are reminded to ensure that their name badges are easily seen by staff serving food and refreshments.

In addition to the refreshments and meals provided by the conference, the staff at the Apex, are able to provide you with items on request. There are hot and cold beverage and confectionery vending machines situated in the lobby area of the Dalhousie building

## Restaurants and Public Houses

Scotland is famous for its cuisine, its friendliness and its pubs, and these are available in fair abundance close to the Apex. The area immediately adjacent to the hotel, and upwards towards the centre of Dundee has a very good selection

of restaurants, covering a great range of styles and cuisines. Other venues outwith the city centre are also worth considering.

A good website to visit for excellent venues is:

https://theculturetrip.com/europe/united-kingdom/scotland/articles/dundee-s-10-best-restaurants-local-eats/

However, as usual Google Maps, Tripadvisor and others can also provide information, some of it even quite accurate. Lists of pubs in Dundee, whoich are constantly changing, can be found here:

http://www.pubsgalore.co.uk/areas/dundee-central/tayside/

http://foodanddrink.scotsman.com/drink/six-of-the-best-bars-to-check-out-in-dundee/

## Taxi

If things get too much or too late or you are lost, Dundee has several taxi companies, including;

Tay Taxis 01382 450450

Dundee Taxis 01382 500555

Teletaxis 01382 825825

# The Full Programme

## Sunday April 2nd Apex Hotel

Registration 15:00 -18:00

## Monday April 3rd Apex Hotel & University of Dundee (Dalhousie)

### Plenary I – (Apex Hotel)

Chair - David Horn

09:00 (40 mins) A12723 - Being a tapeworm and growing like cancer – how does it work (Klaus Brehm) Invited Speaker

09:40 (40 mins) A12966 - *The evolutionary history of structure and function of the African trypanosome haptoglobin haemoglobin receptor* (Mark Carrington) Invited Speaker

### Tea and Coffee Break

10:20 – 11:00 (Note: assistance available for transfer to Dalhousie)

### Drugs I - (Room 1 Apex)

Chair – Dr M De Rycker

11:00 (30 mins) A12849 - *DNDi – bringing new treatments to neglected* (Charles Mowbray) Invited Speaker

11:30 (30 mins) A13031 - *Optimising Treatment for Human Filariasis: The importance of translational models and human dose predictions.* (Stephen Ward)

12:00 (15 mins) A12959 - *Profiling putative flukicide targets uncovers flatworm-expanded GPCR clusters in Fasciola hepatica* (McVeigh Paul)

12:15 (15 mins) A12992 - *Multi-strain investigations of the Copper/Zinc superoxide dismutase 1 gene as a marker for resistance/susceptibility in Biomphalaria glabrata snails.* (Kehinde Sowunmi)

### Tropical Parasitology I- (Room 2 Apex)

Chair – Dr Poppy Lamberton

11:00 (30 mins) A12722 - *Sulphadoxine-Pyrimethamine and Amodiaquine resistance markers in sub Saharan Africa* (Khalid Beshir) Invited Speaker

11:30 (15 mins) A12973 - *Inhibiting ATG8-ATG3 Protein-Protein interactions in Plasmodium falciparum: targeting autophagy for drug development.* (Ibrahim Ali)

11:45 (15 mins) A12870 - *Understanding the relationship between egg and antigen based diagnostics of Schistosoma mansoni infection post treatment* (Joaquin Prada)

12:00 (15 mins) A12896 - *Genetic diversity of Schistosoma japonicum and its intermediate host Oncomelania hupensis in China* (Pin Nie)

12:15 (15 mins) A13012 - *Have some African countries already reached the World Health Organization targets for the control or elimination of schistosomiasis?* (Arminder Deol)

## Public Understanding of Science I - (Room 3 Dalhousie)

### Chair – Prof T Hammarton

11:00 (30 mins) A12725 - *From Blantyre to Blantyre* (Paul Garside) Invited Speaker

11:30 (15 mins) A13001 - *Partnerships for achieving health and education sector goals through school based platforms* (Laura Appleby)

11:45 (15 mins) A13116 - *Engaging students to enhance the parasitology curriculum in schools* (Tansy Hammarton) Invited Speaker

12:00 (15 mins) *The BSP and public engagement: future plans* (Helen Price)

## In the field I- (Room 4 Dalhousie)

### Chair - Dr Annette MacLeod

11:00 (30 mins) A12869 - *Human trypanotolerance, asymptomatic carriage and animal reservoirs in the context of gambiense HAT elimination* (Bruno Bucheton) Invited Speaker

11:30 (15 mins) A12908 - *Identifying seasonal changes in gastrointestinal nematode communities in feral sheep using next generation sequencing* (Alexandra Chambers)

11:45 (15 mins) A12848 - *Variations in VL burden, mortality and the pathway to care within Bihar, India: Hotspots and the role of socio-economic differences* (Sarah Jervis)

12:00 (15 mins) A12864 - *Giardia duodenalis and Cryptosporidium parvum infection status among migrant workers in Peninsular Malaysia* (Siti Nursheena Mohd Zain)

## Lunch Break (Apex Hotel)

12:30 -14:00

## Drugs II- (Room 1 Apex)

Chair – Dr Susan Wyllie

14:15 (30 mins) A12852 - *The Development of DDD853651; a preclinical candidate for the treatment of Visceral Leishmaniasis* (Michael Thomas) Invited Speaker

14:45 (15 mins) A12867 - *Metabolomics analysis of ozonide-treated Plasmodium falciparum reveals disruption of haemoglobin catabolism* (Carlo Giannangelo)

15:00 (15 mins) A12961 - *CalcuSyn-based drug interactivity studies to define synergistic anti-malarial combinatorial regimes for Emetine dihydrochloride* (Muna Abubaker)

15:15 (15 mins) A13011 - *Antimalarial Drug Discovery: Exploring the MEP Pathway* (Neil Berry)

15:30 (15 mins) A12906 - *Highly sensitive rapid affinity sensor for malaria detection of PfHRP 2 and LDH* (Aver Hemben)

## Malaria I- (Room 2 Apex)

Chair - Prof Matthias Marti

14:15 (30 mins) A12727 - *Expansion of repetitive sequences and generation of protein targeting modules in exported Plasmodium proteins.* (Andrew Osborne) Invited Speaker

14:45 (15 mins) A12977 - *Stress, sirtuins and severe malaria* (Linda Anagu)

15:00 (15 mins) A12975 - *Molecular and functional characterization of a new regulator of Ser/Thr Protein Phosphatase type 1 in Plasmodium falciparum* (Thomas Hollin)

15:15 (15 mins) A12965 - *Charting the transcriptional profile of gametocytogenesis in Plasmodium by AP2-G overexpression.* (Katarzyna Modrzynska)

15:30 (15 mins) A12898 - *Identification of candidate transmission-blocking antigen genes in Theileria annulata and related vector-borne apicomplexan parasites* (Stephen Larcombe)

## Diversity I- (Room 3 Dalhousie)

Chair - Prof Mark C. Field

14:15 (30 mins) A12728 - *Advances in understanding variant antigen diversity in natural African trypanosome populations.* (Andrew Jackson) Invited Speaker

14:45 (30 mins) A12729 - *Ageing and Susceptibility to Parasites* (Tom Little) Invited Speaker

15:15 (15 mins) A13060 - *Population genomics of Leishmania donovani: from macroevolution to direct sequencing of clinical samples* (James Cotton)

15:30 (15 mins) A12901 - *Comparative analysis of Stramenopile genomes reveals patterns of functional streamlining in Blastocystis hominis* (Ross Low)

## In the field II- (Room 4 Dalhousie)

### Chair - Jerry Sternberg

14:15 (30 mins) A12730 - *Immuno-epidemiological investigations into immunity to schistosomes.* (Shona Wilson) Invited Speaker

14:45 (15 mins) A12835 - *Which diagnostic to use and why? New insights into intestinal schistosomiasis along the shoreline of Lake Albert, Uganda* (Hajri Alshehri)

15:00 (15 mins) A12939 - *Epidemiology of gastrointestinal helminth parasites in Scottish red deer* (Greg Albery)

15:15 (15 mins) A12860 - *Variation in parasite burden and immune function during reproduction in wild Soay sheep* (Adam Hayward)

15:30 (15 mins) A12958 - *Predictive value of Ov16 antibody prevalence in different sub-populations for elimination of African onchocerciasis* (Luc Coffeng)

## Tea and Coffee Break

15:45 – 16:15 (Note: assistance available for transfer between Dalhousie and Apex)

## Drugs III- (Room 1 Apex)

### Chair – Prof Mark Taylor

16:15 (30 mins) A12851 - *A Multi-Stage Preclinical Candidate for the Potential Treatment of Malaria* (B Baragana) Invited Speaker

16:45 (15 mins) A12836 - *Local production of a liquid direct agglutination test as a sustainable measure for control of Visceral Leishmaniasis in Sudan.* (Hussam Osman)

17:00 (15 mins) A12932 - *Activation of bicyclic nitro-drugs by a novel nitroreductase (NTR2) in Leishmania* (Susan Wyllie)

17:15 (15 mins) A12700 - *CNS Infection with African trypanosomes: mixed messages from the CSF* (Jerry Sternberg)

17:30 (15 mins) A12971 - *The Odyssey of pro-trypanocides: the oxidative activation of the aminomethyl benzoxaboroles* (Ning Zhang)

## Malaria II- (Room 2 Apex)

### Chair - Prof George Christophides

16:15 (30 mins) A12731 - *Host cell and parasite determinants of Plasmodium sporozoite entry into hepatocytes.* (Olivier Silvie) Invited Speaker

16:45 (15 mins) A12926 - *From force generation to substrate attachment: new functions for the acto-myosin A motor complex in Toxoplasma gondii* (Maria Fernanda Latorre-Barragan)

17:00 (15 mins) A12940 - *Exploring the invasion-blocking activity of chemically-modified and low molecular weight heparins and plant-derived polysaccharides against the human malaria parasite Plasmodium falciparum* (Muqdad Hmoud)

17:15 (15 mins) A12927 - *Alterations in the neurovascular unit of the blood brain barrier in cerebral malaria using an in vitro HBEC-astrocyte tandem model* (Nana Efua Andoh)

## Diversity II- (Room 3 Dalhousie)

### Chair - Dr Andrew Jackson

16:15 (30 mins) A12732 - *Mastigamoeba balamuthi and Entamoeba histolytica: So similar yet so different.* (Jan Tachezy) Invited Speaker

16:45 (15 mins) A12894 - *2b-RAD genotyping for population genomic studies of Chagas disease vectors: Rhodnius ecuadoriensis in Southern Ecuador* (Luis Hernandez)

17:00 (15 mins) A12895 - *Endosymbiosis, origins and gene expression in the photosynthetic protist Euglena gracilis* (ThankGod Ebenezer)

17:15 (15 mins) A13014 - *Genetic variation in potential Giardia vaccine candidates cyst wall protein 2 and a1-giardin* (Matej Radunovic)

17:30 (15 mins) A13013 - *VSGs: 'you'll never express alone'. MISP, a family of metacyclic invariant surface proteins in trypanosomes* (Aitor Casas-Sanchez)

## Worms I- (Room 4 Dalhousie)

### Chair - Prof Jacqui Matthews & Iain Chalmers

16:15 (30 mins) A12850 - *A systems biology approach linking genetic, epigenetic and holobiont inheritance to understand rapid adaptation of parasitic flatworms* (Christoph Grunau) Invited Speaker

16:45 (15 mins) A12931 - *Host-helminth-microbiota interactions in Veterinary species* (Laura Peachey)

17:00 (15 mins) A12583 - *RNA-Protein complexes involved in spliced leader trans-splicing in Nematodes could serve as a target for novel anthelmintic drugs.* (Rotimi Fasimoye)

17:15 (15 mins) A12950 - *Developmental regulation of miRNA secretion in the filarial nematode Litomosoides sigmodontis* (Juan Quintana)

17:30 (15 mins) A12962 - *Neoblast-like cell dynamics and growth in the liver fluke Fasciola hepatica* (Erica Gardiner)

### Poster Session (EVEN Poster Numbers)

18:00 (90 mins)

### Young Parasitologists Party

20:00

## Tuesday April 4th Apex Hotel & University of Dundee (Dalhousie)

### Plenary II

Chair - Prof Mark C. Field

09:00 (40 mins) A12734 - *Immunology informing malaria prevention, treatment and control* (Eleanor Riley) Invited Speaker

09:40 (40 mins) - *The complexity and the simplicity of host-Plasmodium interactions* (Maria Mota) Invited Speaker

### Tea and Coffee Break

10:20 – 11:00 (Note: assistance available for transfer to Dalhousie)

### Molecular Cell biology I- (Room 1 Apex)

Chair - Prof Matthias Marti

11:00 (30 mins) A12738 - *Trypanosoma brucei metabolism is under circadian control* (Luisa Figueiredo) Invited Speaker

11:30 (15 mins) A12995 - *Glycosomal hypertrophy and the response to suramin in African trypanosomes* (Martin Zoltner)

11:45 (15 mins) A12873 - *Defining exosome function in Theileria annulata infection: a parasite which drives host cell metastasis* (Victoria Gillan)

12:00 (15 mins) A12897 - *A putative ATP/GTPase influences virulence of Leishmania mexicana* (Vyacheslav Yurchenko)

### Epidemiology I- (Room 2 Apex)

Chair - Prof George Christophides

11:00 (30 mins) A13171 - *The importance of parasite density in malaria transmission* (Thomas Churcher) Invited Speaker

11:30 (15 mins) A12865 - *Cross-border malaria and new challenges to Thai national malaria control programme* (Wirichada Pan-ngum)

11:45 (15 mins) A13009 - *Contribution of Plasmodium knowlesi to multi-species human malaria infections in North Sumatera, Indonesia.* (Colin Sutherland)

12:00 (15 mins) A12968 - *Assessing the impact of intervention strategies against Taenia solium cysticercosis using the EPICYST transmission model* (Matthew Dixon)

12:15 (15 mins) A12956 - Identifying priority areas for sleeping sickness control: Spatial modelling in the Democratic Republic of Congo (Kat Rock)

## Veterinary & Ecology I- (Room 3 Dalhousie)

### Chair – R Wall

11:00 (30 mins) A12741 - *Progress with understanding the trout-PKD interaction: host immunity and parasite gene expression.* (Christopher Secombes)

11:30 (30 mins) A12742 - *Mapping triclabendazole resistance in Fasciola hepatica: what do we know so far?* (Jane Hodgkinson)

12:00 (15 mins) A12942 - *Upsetting the protease/anti-protease balance could be a novel vaccine strategy against Fasciola hepatica infection* (Orla Drysdale)

12:15 (15 mins) A12698 - *Innate immune response in Intracellular parasitic (Neospora caninum) infection of Cattle* (Parul Sharma)

## Worms II- (Room 4 Dalhousie)

### Chair - Prof John Dalton & Emmanuel Pila

11:00 (30 mins) A12745 - *Trials and tribulations: the highs and lows of nematode sub-unit vaccine development* (Jacqui Matthews)

11:30 (15 mins) A12970 - *Profiling the surface-exposed proteins of Fasciola hepatica extracellular vesicles* (Eduardo de la Torre Escudero)

11:45 (15 mins) A12946 - *Probing the pathways of extracellular vesicle biogenesis in helminth parasites* (Adam Bennett)

12:00 (15 mins) A12910 - *Genetic variation associated with parasite-specific immune responses in a wild mammal population* (Alexandra Sparks)

12:15 (15 mins) A12979 - *A Host ration affects plerocercoid growth in three-spined sticklebacks infected with Schistocephalus solidus (Cestoda: Diphyllobothriidae)* (Awad Hosan)

## Lunch Break (Apex Hotel)

12:30 -14:00

## Workshop (Apex Hotel)

12:30 (105 mins) A12883 - WormBase Session

## Molecular Cell biology II- (Room 1 Apex)

### Chair - Dr Nicolai Siegel

14:15 (30 mins) A12739 - *Biology of malaria transmission in an era of elimination* (Matthias Marti)

14:45 (15 mins) A12997 - *The putative structure of Trypanosoma congolense strain IL3000 mini-chromosomes* (Ali Abbas)

15:00 (15 mins) A12934 - *Single-molecule analysis reveals that DNA replication dynamics vary across the course of schizogony in the malaria parasite Plasmodium falciparum.* (Catherine Merrick)

15:15 (15 mins) A12606 - *Role of a cytosolic and a membrane-bound carbonic anhydrase of Leishmania major in combating acid stress* (Mazharul Abbasi)

15:30 (15 mins) A12953 - *Control of allelic exclusion by a trypanosome 'Vex Histone Chaperone' complex* (Joana Faria)

## Epidemiology II- (Room 2 Apex)

### Chair - Dr Kat Rock

14:15 (30 mins) A12740 - *TBA* (George Christophides)

14:45 (15 mins) A12863 - *Disease spread in age structured populations with maternal age effects* (Jessica Clark)

15:00 (15 mins) A13058 - *Risk factors for giardiasis in south western Sydney: A case-control study* (John Ellis)

15:15 (15 mins) A13018 - *Marine Pomphorhynchus laevis: analysis and appraisal of UK status.* (Alastair Lyndon)

15:30 (15 mins) A12969 - *Epidemiology and evolution of zoonotic schistosomiasis in West Africa* (Elsa Leger)

## Veterinary & Ecology II- (Room 3 Dalhousie)

### Chair – Prof Damer Blake

14:15 (30 mins) A12744 - *Host-parasite interactions in the era of next-generation sequencing technologies* (Cinzia Cantacessi)

14:45 (30 mins) A12743 - *Zoonotic disease epidemiology in multi-host systems* (Sandra Telfer)

15:15 (15 mins) A13000 - *Genomics of sex, drugs, and recombination in the gastrointestinal nematode, Haemonchus contortus* (Stephen Doyle)

15:30 (15 mins) A12862 - *Markers of anthelmintic resistance in gastrointestinal parasites of ruminants* (Jennifer McIntyre)

## Worms III- (Room 4 Dalhousie)

### Chair - Prof Christoph Grunau & Alexander Sparks

14:15 (30 mins) A12746 - *Trematode-designed immunomodulatory molecules with therapeutic potential.* (John Dalton)

14:45 (15 mins) A12839 - *Growth factor-induced gain-of-resistance against Schistosoma mansoni infection in the snail host.* (Emmanuel Pila)

15:00 (15 mins) A12905 - *Early lymphatic remodelling following filarial infection is promoted by host Th2 adaptive immune responses* (Julio Furlong-Silva)

15:15 (15 mins) A13005 - *Into the unknown: exploring proteins of unknown function in Schistosoma mansoni* (Iain Chalmers)

15:30 (15 mins) A12871 - *Effects of host sex and body size on Schistocephalus infection susceptibility and plerocercoid growth in three-spined sticklebacks* (Rana Shalal)

### Tea and Coffee Break

15:45 – 16:15 (Note: assistance available for transfer between Dalhousie and Apex)

### Poster Session (ODD Poster Numbers)

16:15 (90 mins)

### BSP Gala event and Ceilidh (Apex Hotel)

19:00 – Late

## Wednesday April 4th (Apex Hotel):

### Wright Medal Lecture (Apex Hotel)

Chair –Paul Horrocks

09:30 (55 mins) A13191 - *Comparisons of parasite genomes to find genes associated with parasitism and exploitable vulnerabilities* (Matt Berriman)

### A11634 - BSP AGM (Apex Hotel)

10:30 (30 mins)

### Tea and Coffee Break

11:00 – 11:30

### Molecular Cell biology III- (Room 1 Apex)

Chair - Luisa Figueiredo

11:30 (30 mins) A12747 - *Deciphering the 3D architecture of the Trypanosoma brucei genome* (Nicolai Siegel)

12:00 (15 mins) A12998 - *Exploring the connectivity between Leishmania mexicana amastigotes and their host cell through 3D electron microscopy* (Valli Jessica)

12:15 (15 mins) A12945 - *The ZC3H39/40 RNA-binding complex and control of an electron transport chain regulome in African trypanosomes* (Anna Trenaman)

12:30 (15 mins) A12990 - *Structural and functional studies of Trypanosoma brucei MORN1 protein* (Sara Sajko)

12:45 (15 mins) A13030 - *A decrease in mitochondrial membrane potential may be associated with diminazene resistance in Trypanosoma congolense.* (L V Carruthers)

## Veterinary & Ecology III- (Room 2 Apex)

### Chair - Prof Jane Hodgkinson

11:30 (30 mins) A12748 - *Parasitic diseases and their cost to aquaculture* (Giuseppe Paladini)

12:00 (30 mins) A12749 - *Tick and tick-borne disease risk for dogs in the UK* (Richard Wall)

12:30 (15 mins) A12978 - *Eigenanalysis provides insights into the innate immune response induced in commercial broilers following Eimeria tenella provoked coccidiosis* (Matthew Nolan)

12:45 (15 mins) A12933 - *Sea Lice effect on wild Atlantic salmon fecundity* (Roman Susdorf)

## Lunch & Conference close.

13:00

# Oral Abstracts

## Monday April 3rd Apex Hotel & University of Dundee (Dalhousie)

### Plenary I – (Apex Hotel)

Chair - David Horn

09:40 (40 mins)

Being a tapeworm and growing like cancer – how does it work? - *A12723*

Presenter: **Prof Klaus Brehm**, *Associate Professor, University of Wuerzbrg*

**K Brehm**[1];

[1] University of Wuerzbrg, Germany

Larval development of the fox-tapeworm *Echinococcus multilocularis* is unusual in so far as its invading oncosphere does not directly develop into a head-like structure (scolex), as in most tapeworms, but into a continuously growing, cancer-like mass of vesicles (the metacestode) which infiltrates host tissue. We are studying *Echinococcus* development by using sophisticated *in vitro* cultivation systems for parasite larvae and cells. We showed that parasite development is essentially driven by a population of totipotent somatic stem cells, the germinative cells, which are the only mitotically active cells of the parasite and which give rise to all differentiated cells. Interestingly, the germinative cells are resistant to the currently used drugs against echinococcosis which can explain why echinococcosis chemotherapy is so inefficient. Contrasting to the oncosphere and the scolex, the cyst-like metacestode does not display clear body axes, so we hypothesized that modifications of the anterior-posterior (AP) axis might be an underlying principle for metacestode evolution. In free-living planarians, the AP axis is specified by the canonical Wnt pathway, where Wnt signaling defines the posterior and expression of Wnt antagonists (e.g. sFRP) the anterior pole. Using the Hymenolepis model, we show that this also applies to tapeworm oncospheres where Wnt orthologs are expressed posteriorly (close to the hooks) and sFRP orthologs anteriorly. In the *E. multilocularis* metacestode, we found ubiquitous expression of posterior Wnt factors and only in later stages of the infection, Wnt antagonists were locally expressed in metacestode tissue, which preceded the formation of protoscoleces. This indicates that *E. multilocularis* larvae temporarily give up their anterior pole to exclusively proliferate as posterior tissue, followed by local expression of sFRP to achieve protoscolex production (asexual multiplication). According to our data, canonical Wnt signaling plays a crucial role in metacestode development and, accordingly, RNA-interference against the central Wnt component beta-catenin resulted in metacestode tissue disorganization and prevented the formation of vesicles from parasite stem cells. Interestingly, aberrant regulation of Wnt signaling is also observed in many human cancers, pointing to similarities of malignant transformation of human tissue and metacestode formation.

09:40 (40 mins)

### The evolutionary history of structure and function of the African trypanosome haptoglobin haemoglobin receptor - *A12966*

Presenter: **Prof Mark Carrington**, *Professor, University of Cambridge*

**M Carrington**[1]; P MacGregor[1]; H Lane-Serff[2]; O J Macleod[2]; M Higgins[2]; L Peacock[3]; W Gibson[3];
[1] University of Cambridge, Department of Biochemistry, UK; [2] University of Oxford, Department of Biochemistry, UK; [3] University of Bristol, UK;

African trypanosomes are always extracellular and have evolved intricate surface coats that allow them to obtain nutrients while also protecting them from the immune defences of either insects or mammals. The acquisition of macromolecular nutrients requires receptors that function within the context of these surface coats. The best understood of these is the haptoglobin-haemoglobin receptor (HpHbR) of *Trypanosoma brucei*, which is used by the mammalian bloodstream form of the parasite, allowing haem acquisition. However, in some primates it also provides an uptake route for trypanolytic factor-1, a mediator of innate immunity against trypanosome infection. Recent studies have shown that during the evolution of African trypanosome species the receptor has diversified in function from a haemoglobin receptor predominantly expressed in the tsetse fly to a haptoglobin-haemoglobin receptor predominantly expressed in the mammalian bloodstream. Structural and functional studies of homologous receptors from different trypanosome species have allowed us to propose an evolutionary history for how one receptor has adapted to different roles in different trypanosome species.

## Drugs I - (Room 1 Apex)

Chair - Manu De Rycker

11:00 (30 mins)

### DNDi – bringing new treatments to neglected patients - *A12849*

Presenter: **Dr Charles Mowbray**, *Head of Drug Discovery, DNDi*

**C Mowbray**[1];
[1] DNDi, UK

The Drugs for Neglected Diseases initiative (DNDi) is a patients' needs driven, not for profit drug discovery and development organisation. In addition, DNDi harnesses and strengthens R&D capacity in disease endemic regions to enable progression of its pipeline of new drug candidates, and also advocates for policy change to make treatments available to all patients. DNDi adopts a range of innovative and flexible models with a wide range of partner organisations to tackle the challenges of developing safe, effective and field adapted treatments for patients suffering from neglected diseases including sleeping sickness, leishmaniasis, Chagas disease, filarial infections, mycetoma, paediatric HIV infection, hepatitis C virus (HCV) infection, and is also developing the Global Antibiotic Research and Development Partnership (GARDP) to contribute to tackling issues of antimicrobial resistance. DNDi's approach to R&D can be illustrated using the R&D pipelines for sleeping sickness and leishmaniasis as examples. In the case of

sleeping sickness, DNDi helped replace the toxic antimonial drug melarsoprol with a safer and more efficacious combination therapy called NECT (nifurtimox eflornithine combination therapy) but this requires lengthy infusions and is far from ideal for use in remote, resource-limited locations. We aim to provide a major step forward with the simple oral therapies fexinidazole and SCXY-7158 which are in late Phase III and early Phase II clinical trials respectively. Current drugs used for treating leishmaniasis suffer from limitations in efficacy and safety and are not well adapted to the needs of patients. Combining these drugs has led to improvements in efficacy and safety in some geographical regions, but many patients are still in need of more effective, safer and convenient treatments. The current drugs for leishmaniasis were re-purposed from other therapeutic indications and are far from optimal, relying largely on painful intravenous and intramuscular injections. In recent years, new orally acting chemical entities have been designed and selected for development for treating visceral leishmaniasis, and perhaps also the cutaneous form of the disease. These new drug classes have been discovered using phenotypic drug discovery methods and offer great promise for developing new treatments, but their mechanisms of action are often not well understood. Efforts to de-convolute the mechanisms of action of these candidates and newer target based drug discovery approaches should open the door for discovery of further drug classes and candidate molecules. This presentation will highlight the discovery of the NCEs now advancing in the clinic for sleeping sickness, and describe the evolution of drug discovery approaches for leishmaniasis, explore the properties of the emerging drug candidates, and highlight the role of DNDi in leading and catalysing further R&D for neglected diseases.

11:30 (30 mins)

Optimising Treatment for Human Filariasis: The importance of translational models and human dose predictions. - *A13031*

Presenter: **Prof. Stephen Ward**, *Deputy Director, LSTM, Liverpool School of Tropical Medicine*

**S A Ward**[1]; P O'Neil[2]; J D Turner[1]; M J Taylor[1];
[1] Liverpool School of Tropical Medicine, UK; [2] University of Liverpool, UK

Onchocerciasis and lymphatic filariasis (LF) are priority neglected tropical diseases targeted for elimination. In both cases the filarial parasites harbor a symbiotic endobacterium, *Wolbachia*. Targeting *Wolbachia* with an antibiotic such as doxycycline results in a macrofilaricidal effect. The A.WOL consortia was established to seek new anti-*Wolbachia* based treatments that could reduce treatment timeframes and that could be deployed in children and pregnant women. The consortia has screened over 1.8 million compounds for *in vitro* anti-*Wolbachia* activity the hits of which have been progressed through standard pipelines to deliver the next generation of marofilaricide. The outputs of this endeavor include three new repurposing opportunities, two new drug candidates in formal development and dozens of novel lead series ready for development. The establishment of a validated translational path for macrofilaricides has highlighted the critical importance of PK/PD relationships, model selection and model to human bridging studies in de-risking the drug discovery process. These key determinants of success will be described with appropriate examples.

12:00 (15 mins)

Profiling putative flukicide targets uncovers flatworm-expanded GPCR clusters in *Fasciola hepatica* - *A12959*

Presenter: **Dr McVeigh Paul**, *Research Fellow, Queen's University Belfast*

**P McVeigh**P McCusker[2]; N J Marks[2]; A Mousley[2]; R M Morphew[1]; P M Brophy[1]; S Paterson[3]; J E Hodgkinson[3]; A G Maule[2];
[1] Aberystwyth University; [2] Queen's University Belfast; [3] University of Liverpool

As targets for a large proportion of licensed human pharmaceuticals, G protein coupled receptors (GPCRs) could be key targets for the development of new anthelmintics. Using hidden Markov model (HMM)-driven computational methods, we have identified 148 high confidence GPCRs from the *Fasciola hepatica* genome comprising glutamate, rhodopsin, adhesion, frizzled and smoothened receptor families; we did not identify any secretin-like receptors. Pairwise comparisons using a sequence-clustering algorithm (CLANS) compared fluke GPCRs with those of flatworms and non-flatworm phyla. Amongst rhodopsins, this approach identified many evolutionarily conserved amine and peptide receptors, and also verified the presence of the previously described PROF1 (Platyhelminth Rhodopsin Orphan Family #1) family, containing GPCRs that appear uniquely expanded in the platyhelminth lineage. Our data describe up to an additional seven such groupings (PROF2-PROF8) in *F. hepatica* and other trematodes, suggesting considerable expansion of GPCR diversity within phylum Platyhelminthes. This work provides the first GPCR profile from *F. hepatica*, and the first description of several classes of trematode-specific GPCRs, and will facilitate the first functional genomic explorations of these important potential anthelmintic targets.

12:15 (15 mins)

Multi-strain investigations of the Copper/Zinc superoxide dismutase 1 gene as a marker for resistance/susceptibility in *Biomphalaria glabrata* snails. - *A12992*

Presenter: **Kehinde Sowunmi**, *PhD Student, University of Nottingham*

**K O Sowunmi**[1]; C Wade[1]; M Doenhoff[1];
[1] University of Nottingham, UK

Development of either a resistant or a susceptible phenotype in *Biomphalaria glabrata* snails interacting with the parasitic trematode, *Schistosoma mansoni* is partially determined by various genes. Immune response genes including those related to stress responses initiated by parasite invasion in *B. glabrata-Schistosoma mansoni* interactions offer viable options in therapeutic research for sustainable strategies in schistosomiasis prevention and control. An allele of a stress-related gene, the Cu/Zn superoxide dismutase 1 (*SOD1*) has been reported to be correlated with resistance in a predominantly resistant laboratory population. Here we investigate this gene locus in three different laboratory populations of *B. glabrata* and show the presence of new alleles. The possible relationships between these alleles are examined phylogenetically and possible involvement of this gene locus in determining susceptibility or resistance in the snail is discussed.

## Tropical Parasitology I- (Room 2 Apex)

Chair – Dr Poppy Lamberton

11:00 (30 mins)

Sulphadoxine-Pyrimethamine and Amodiaquine resistance markers in sub-Saharan Africa - *A12722*

Presenter: **Dr Khalid Beshir**, *Research Fellow, London School of Hygiene and Tropical Medicine*

**K Beshir** [1]
[1] London School of Hygiene and Tropical Medicine

A continuous fight against malaria requires a variety of specific interventions suitable to local needs. Amodiaquine (AQ) in combination with artemisinin (ASAQ) has been used in a number of West African countries as first line treatment in addition to artemither-lumefantrine (AL). Sulphadoxine-pyrimethamine (SP) has also been used in intermittent prevention treatment (IPTp) in pregnant women and as seasonal malaria chemoprevention (SMC) together with AQ. SMC has been shown to be an effective tool to prevent malaria in children under five years in areas where incidence of clinical cases is strictly seasonal. Implementation of this strategy during the rainy season has been shown to reduce cases of malaria in this age group by 65-80%, depending on setting. Monitoring the development and spread of drug resistance is particularly crucial for large-scale interventions such as SMC and IPTp. This is also needed where ASAQ is in use as a first line of treatment. The scaling up interventions in order to reduce malaria cases and deaths will require monitoring of the development of resistance to SP+AQ. In the Access-SMC programme, more than 30,000 samples have been collected before the scale-up of SP+AQ administration in seven countries in the Sahel: Burkina Faso, Chad, Guinea-Conakry, Niger, Nigeria, Mali and The Gambia. A large cross-section of these baseline samples from each country are being genotyped to identify mutations at pfcrt, pfmdr1, pfdhfr and pfdhps known to impact on the efficacy of AQ or SP. A summary of PCR-determined prevalence of *Plasmodium falciparum* and baseline resistance genotyping data from each country will be presented.

11:30 (15 mins)

Inhibiting ATG8-ATG3 Protein-Protein interactions in *Plasmodium falciparum*: targeting autophagy for drug development. - *A12973*

Presenter: **Mr Ibrahim Ali**, *PhD, Keele University*

**I Ali**[3]; A Siriwardana[2]; P Roepe[2]; A Mete[4]; J Reynisson[1]; P Horrocks[3];
[1] Auckland University, New Zealand; [2] Georgetown University, United States; [3] Keele University; [4]MedSynDesign Ltd

Growth inhibition assays of 135 putative ATG8-ATG3 protein-protein inhibitors (PPI) identified compounds SK1.47 and SK1.49 with $IC_{50}$ of 2.12 and 1.07 µM, respectively. Structure activity relationship data, coupled with molecular docking of interactions with the W and L hydrophobic pockets on the surface of PfATG8, suggest that hydrophobic moieties linked with a spacer chain that contains an amine (to hydrogen bond to Lys48 in PfATG8) are preferred. These compounds are relatively non-toxic against HepG2 cell lines ($CC_{50}$ > 100µM) and share a fast to moderate rate of kill (between chloroquine and quinine) suggesting a common mode of action. Both compounds inhibited the formation of ATG8 labelled vesicles (autophagosomes) in intraeythrocytic parasites induced into autophagy using starvation conditions. Unlike chloroquine, however, neither compound induces the formation of ATG8 labelled vesicles. Transmission electron microscopy of parasites treated with these compounds both showed swelling of digestive vacuoles and a relative depletion in hemozoin formation. These putative ATG8-ATG3 PPI offer chemical probes of autophagy in *Plasmodium falciparum* and potential discovery leads against a novel target in the parasite.

11:45 (15 mins)

Understanding the relationship between egg and antigen based diagnostics of *Schistosoma mansoni* infection post treatment - *A12870*

Presenter: **Dr. Joaquin Prada**, *Research Associate, University of Warwick*

**J M Prada**[3]; P H L Lamberton[2]; M Adriko[1]; M Arinaitwe[1]; D W Oguttu[1]; P Touloupou[3]; T D Hollingsworth[3];
[1] Ministry of Health, Uganda; [2] University of Glasgow; [3] University of Warwick

Schistosomiasis is a major socio-economic and public-health problem in many sub-Saharan African countries. After large mass drug administration (MDA) campaigns, prevalence of infection rapidly returns to pre-treatment levels. The traditional egg based diagnostic for schistosome infections, Kato-Katz, is being substituted in many settings by circulating antigen recognition based diagnostics, such as the point-of-care circulating cathodic antigen test (POCCCA). The relationship between these two diagnostics, particularly after treatment in drug-efficacy studies, is poorly understood. We created an inference model of schistosome infections to better understand and quantify the relationship between these two egg and adult worm antigen based diagnostics. Due to the semi-quantitative nature of CCA, we focused on the current major challenges of interpreting “trace” CCA results. Our analyses suggest that CCA is generally a better predictor of prevalence, particularly after treatment, and that trace CCA results are typically associated with truly infected individuals. Even though prevalence rises to pre-treatment levels only a few months after MDAs, our model suggests that the average infection level is much lower, and is probably due to a smaller burden of surviving juveniles from when the treatment occurred. This work helps to better understand CCA diagnostics and the interpretation of post-treatment prevalence estimations.

12:00 (15 mins)

Genetic diversity of *Schistosoma japonicum* and its intermediate host *Oncomelania hupensis* in China - *A12896*

Presenter: **Prof Pin Nie**, *Professor, Institute of Hydrobiology, CAS*

**P Nie**[1];
[1] Institute of Hydrobiology, CAS, China

The intermediate host snail *Oncomelania* was collected widely in China, and schistosomes were recovered by infecting mice with cercariae released from snails. Initially, ITS sequences, and several fragments of mitochondrial regions were employed for investigating the genetic diversity of the snail and the parasite. No shared haplotypes were found for snails distributed in the upper reaches and in the middle and lower (ML) reaches, nor for the parasites in these two regions. The genetic diversity of 66 populations of *O. hupensis* was further examined using microsatellite markers. The average number of alleles was 10, and 40 populations and 3 loci were significantly deviated from Hardy-Weinberg equilibrium. The pair-wise $F_{ST}$ value ranged from 0.061 to 0.759 among populations, indicating great differentiation in populations. Populations from Yunnan Province were the most distant from others; populations from Sichuan province were clustered together as a separate branch. Populations from Fujian and Taiwan were genetically distinct from those collected in Guangxi and ML reaches. Furthermore, 66 populations were divided into five groups, as revealed through the analysis of molecular variance (AMOVA), including Yunnan, Sichuan, Fujian, Taiwan, ML and Guangxi groups. The Mantel test revealed a significant positive correlation between genetic distance $F_{ST}$ and geographical distance, indicating an isolation-by-distance effect on the differentiation of *O. hupensis*in, with some populations undergone bottle-neck effect. Mitochondrial genomes were

sequenced from nine geographic strains of *S. japonicum* in China, and the constructed phylogenetic relationship showed that the Taiwan strain and strains from Yunnan and Sichuan Provinces and those in the ML reaches were grouped separately.

12:15 (15 mins)

Have some African countries already reached the World Health Organization targets for the control or elimination of schistosomiasis? - *A13012*

Presenter: **Ms Arminder Deol**, *PhD student/Research Assistant, Schistosomiasis Control Initiative*

**A K Deol**[4]; B Calvo-Urbano[4]; M D French[3]; M Walker[2]; J P Webster[2]; F M Fleming[4]; W E Harrison[4]; A Fenwick[4]; SCI Team[4]; M G Basáñez[1];

[1] Imperial College London; [2] Royal Veterinary College; [3] RTI International; [4]Schistosomiasis Control Initiative

Schistosomiasis control programmes map the distribution of infection prior to commencing treatment. This enables each district, or so-called 'implementation unit', to be categorised according to World Health Organization (WHO) prevalence thresholds which in turn determine the appropriate treatment strategy (by mass drug administration, MDA) to control schistosomiasis-related morbidity. With the vision of "a world free of schistosomiasis", the WHO and its partners have pledged to meet the ambitious goals of controlling morbidity of schistosomiasis (<5% heavy infection prevalence) by 2020 and achieving elimination as a public health problem (<1% heavy infection prevalence) and interruption of transmission in selected regions by 2025. The guidelines for progressing through these stages are predominantly based on expert opinion. This study aims to redress this by providing empirical evidence to assist programmes in achieving the 2020 and 2025 goals by answering two key questions: 1) how long will it takes countries to reach the WHO 2020/2025 targets, and 2) how should countries best use sentinel site monitoring and evaluation data? Our analysis of the large datasets available at the Schistosomiasis Control Initiative demonstrate that countries transition from controlling morbidity to eliminating schistosomiasis as a public health problem at different rates depending on the predominant schistosome species and baseline endemicity. These results provide the first empirical comparison with WHO threshold criteria on morbidity control and elimination and question whether a one-size-fits-all approach is optimal for guiding schistosomiasis treatment strategies.

## Public Understanding of Science I - (Room 3 Dalhousie)

Chair – Prof T Hammerton

11:00 (30 mins)

From Blantyre to Blantyre - *A12725*

Presenter: **Prof Paul Garside**, *Director of Centre for Immunobiology, University of Glasgow*

**P Garside**[1]

[1]University of Glasgow

In 2013 I spent six months living in Kenya and Malawi with the aim of developing some new collaborations making people aware of the work we do. As the initial interactions have developed I have learned lots of new ways of interacting with different sectors of the public and scientific communities and seen the impact this can have. I will share some of the approaches we have developed, own up to what has and hasn't worked and show why it can be important and where it can lead.

11:30 (15 mins)

Partnerships for achieving health and education sector goals through school based platforms - *A13001*

Presenter: **Dr Laura Appleby**, *Research Associate, Imperial College London*

**L J Appleby**[2]; G Tadesse[1]; N Dejene[3]; I A Gardiner[2]; E Yard[3]; J E Grimes[2]; L J Drake[2];
[1] Ethiopian Public Health Institute, Ethiopia; [2] Imperial College London, UK; [3] Partnership for Child Development, Ethiopia

Schools provide an effective platform from which simple and safe control and treatment interventions can be distributed, and health messages can be disseminated for the benefit of many children. Coordinating programmes to deliver health through school platforms inherently requires strong partnerships and coordination across and between sectors. In Ethiopia, a costed, integrated school based pilot programme has been implemented over the past four years, in partnership with the Ethiopian Government and implementing partners. The programme, known as the Enhanced School Health Initiative (ESHI), addresses the key needs of school age-children in the area, and was developed following baseline surveys which indicated a high prevalence of soil-transmitted helminths (STH), poor nutritional indicators and inadequate WASH infrastructure in schools. ESHI focused on strengthening multi-sectoral coordination of SHN while collecting operational data on efficacy, effectiveness, and costs. Key coordinating structures include the small-holder farmer cooperatives as well as multi-sectoral coordination committees, headed by the Bureau of Education and attended by bureaus of health, finance and water as well as relevant stakeholders. This regional SHN task force structure is now being scaled up to national level, in accordance with the National School Health and Nutrition Strategy. Operational evidence of the cost-effectiveness and synergistic benefits of and integrated SHN programme provide the Federal Ministry of Education with tangible budget lines for mainstreaming the programme into national sector plans.

11:45 (15 mins)

Engaging students to enhance the parasitology curriculum in schools - *A13116*

Presenter: **Dr Tansy Hammarton**, *Senior Lecturer, University of Glasgow*

**T Hammarton**[1];
[1] University of Glasgow , UK

Until recently, little parasitology has been taught in schools. However, with the introduction of the Curriculum for Excellence, and more recently, the introduction of a new Advanced Higher Biology syllabus in Scotland, there have been increasing opportunities to engage pupils and teachers and to enhance the school curriculum with parasitology-related activities. For over a decade, I have coordinated and run an extensive school public engagement (PE) programme in infection biology, which has reached thousands of children aged 2-17 and their teachers, and has involved hundreds of University of Glasgow volunteers, including many PhD students. More recently, I have incorporated various aspects of PE into my undergraduate teaching, which has led to a number of undergraduates also

volunteering in our PE programme and enhancing their communication skills. Here, I will give an overview of the hands-on parasitology-related activities and experiments I have developed for schools, the resources we have available to share with any interested parties, and my recent work to involve more students in PE.

12:00 (15 mins)

The BSP and public engagement: future plans - *A13121*

Presenter: **Dr Helen Price**, Lecturer in Bioscience, Keele University, BSP

**H Price**[1];

[1] School of Life Sciences, Keele University

Part of the BSP's mission is to promote wider dissemination of advances in the field of parasitology. The BSP Council are currently looking at ways in which we can increase our support of members who are involved with public engagement. We recently ran a survey to collect views from Society members on what they would like from the BSP in this area. In this presentation, I will describe the main findings from the survey and the ideas put forward by the Council to date. There will also be opportunity for discussion.

## In the field I- (Room 4 Dalhousie)

Chair - Dr Annette MacLeod

11:00 (30 mins)

Human trypanotolerance, asymptomatic carriage and animal reservoirs in the context of gambiense HAT elimination - *A12869*

Presenter: **Dr Bruno Bucheton**, *Researcher, Institut de Recherche pour le Développement (IRD)*

**Bruno Bucheton**[1]

[1]Institut de Recherche pour le Développement

Human African Trypanosomiasis or sleeping sickness, transmitted by tsetse flies, is a neglected tropical disease for which elimination as a public health problem has been targeted by WHO in 2020. Whereas the number of annual reported cases has shown a steady decline in the last 10 years, major challenges are still ahead to reach the 2020 goal and later the interruption of transmission. Among those is the existence of overlooked reservoirs of *Trypanosoma brucei gambiense*, i.e. human asymptomatic carriers or wild or domestic animals. Recent progress concerning their identification and potential role in transmission maintenance in West Africa will be presented as well as the results of immunological and genetic association studies aimed at unravelling the biological mechanisms involved in determining the infection resistance/susceptibility status. Awaiting for new diagnostic tools to improve the detection of latent infections in human or animals, these results argue for a greater integration of vector control in designing tomorrow's elimination

strategies. The example of the Boffa focus in Guinea, where a pilot study combining medical screening and control of tsetse flies with small insecticide impregnated target while be presented.

11:30 (15 mins)

Identifying seasonal changes in gastrointestinal nematode communities in feral sheep using next generation sequencing - *A12908*

Presenter: **Miss Alexandra Chambers**, *PhD student, The University of Edinburgh*

**A K Chambers**[2]; F Kenyon[1]; D Nussey[4]; R Avramenko[3]; E Redman[3]; J Gilleard[3]; J Pilkington[4]; N D Sargison[2];
[1] Moredun Research institute; [2] The Royal (Dick) School of Veterinary Studies and the Roslin Institute, The University of Edinburgh; [3] University of Calgary; [4] University of Edinburgh, Institute of Evolutionary Biology

Host fitness is heavily influenced by the presence of co-infecting parasites, and understanding intraspecific dynamics is important in gaining an insight into host health. Previous methods of nematode burden assessment are low-throughput and have limited sensitivity, which prevents fine-scale partitioning of species. Researching the nematode biome structure in the absence of control measures is required to recognise the impact of management decisions on sustainable control. The unmanaged Soay sheep on St Kilda provides an ideal study population. ~ 1000 faecal samples were collected over eight sampling months, from nine different sex-age groups. These were used for faecal egg counting using a cuvette salt floatation method, and were incubated to grow 3rd stage larvae for molecular analyses. The development of a deep sequencing assay of the ITS-2 region of the rDNA cistron has enabled the accurate identification and quantification of clade V species, with this being the first field application of this method. Preliminary analyses of the sequencing data recovered all five species previously identified on St Kilda, with seasonal, age and sex differences in species composition. Additionally, cyclic trends have been observed, with key strongyle species sequentially peaking throughout the year. These seasonal differences appear to correspond with the sheep's dynamic life-history. Correcting for species-specific sequencing biases, amplicon repeatability and species detection threshold, ensures this method is repeatable.

11:45 (15 mins)

Variations in VL burden, mortality and the pathway to care within Bihar, India: Hotspots and the role of socio-economic differences - *A12848*

Presenter: **Dr Sarah Jervis**, *Research Associate, University of Warwick*

**S Jervis**[4]; L A Chapman[4]; S Dwivedi[1]; M Karthick[1]; A Das[1]; E Le Rutte[2]; O Courtenay[4]; G F Medley[3]; I Banerjee[1]; T Mahapatra[1]; I Chaudhuri[1]; T D Hollingsworth[4];
[1] CARE India Solutions for Sustainable Development, India; [2] Erasmus MC, Netherlands; [3] London School of Hygiene & Tropical Medicine; [4] University of Warwick

Visceral leishmaniasis (VL) has been targeted by the WHO for elimination as a public health problem (<1 case/10,000 people/year) in the Indian sub-continent (ISC) by 2020. Bihar state in India, which accounts for the majority of cases in the ISC, remains a major target for this elimination effort. However, there is considerable spatial, temporal and sub-population variation in occurrence of the disease and the pathway to care, which is largely unexplored and a threat to achieving the target. Data from 6,081 VL patients clinically diagnosed during 2012-2013 across eight districts in Bihar were analysed. Graphical comparisons and Chi-squared tests were used to determine differences in the burden of identified cases by season, district, age and sex. Log-linear regressions were fitted to onset (of symptoms)-to-diagnosis and onset-to-treatment waiting times to estimate their associations with age, sex, district and various socio-economic factors (SEFs). Logistic regression models were used to identify factors associated with mortality. Comparisons of VL caseloads suggested an annual cycle peaking in January-March. A 17-fold variation in the burden of identified cases across districts and under-representation of young children (0-5 years) relative to age-specific populations in Bihar were observed. Women accounted for a significantly lower proportion of the reported cases than men (41% vs. 59%, p-value <0.0001). Age, district of residence, house wall materials, caste, treatment cost, travelling for diagnosis and the number of treatments for symptoms prior to diagnosis were identified as correlates of waiting times. Mortality was associated with age, district of residence, onset-to-treatment waiting time, treatment duration, cattle ownership.

12:00 (15 mins)

*Giardia duodenalis* and *Cryptosporidium parvum* infection status among migrant workers in Peninsular Malaysia - *A12864*

Presenter: **Siti Nursheena Mohd Zain**, *University of Malaya*

N Sahamin[1]; B Douadi[1]; Y Lim Ai Lian[1]; **S N Mohd Zain**[1];

[1] University of Malaya, Malaysia

A cross sectional study among 388 migrant workers from five working sectors was conducted to determine the protozoan infection status in Peninsular Malaysia. Microscopy examination showed 42 (10.8%) positive with *Giardia* spp. and 12 (3.1%) samples with *Cryptosporidium* spp. PCR amplicons at the triosephosphate isomerase (*tpi*) gene were successfully obtained for *Giardia duodenalis* from 30 (30/42; 71.4%) samples with assemblages AII and B in 13 (13/30; 43.3%) and 17 (17/30; 56.7%) samples, respectively. While nine samples were identified as *Cryptosporidium parvum* using PCR-RFLP analysis. The presence of pathogenic *G. duodenalis* and *C. parvum* in the study population highlights potential risks of foodborne and waterborne infection to the general public and calls for implementation of control strategies through treatment and health education.

12:15 (15 mins)

Cancelled

## Drugs II- (Room 1 Apex)

Chair – Dr Susan Wyllie

14:15 (30 mins)

The development of DDD853651; a preclinical candidate for the treatment of Visceral Leishmaniasis - *A12852*

Presenter: **Dr Michael Thomas**, *Medicinal Chemist, University of Dundee*

**M Thomas**[2]; I Gilbert[2]; T Miles[1]; M De Rycker[2]; P Wyatt[2]; J M Fiandor-Roman[1]; K D Read[2];

[1] GSK, Spain; [2] University of Dundee - Drug Discovery Unit, UK

Visceral Leishmaniasis (VL) is a poverty associated parasitic infection responsible for around 40,000 deaths worldwide every year. Currently available treatments are hampered by issues such as toxicity, teratogenicity, cost and increasingly, resistance. There is therefore an urgent need for new treatments. The Drug Discovery Unit, University of Dundee, and the GlaxoSmithKline Kinetoplastid Discovery Performance Unit, Tres Cantos, with support from the Wellcome Trust, have formed a partnership to conduct drug discovery within kinetoplastid diseases, with a particular focus on VL. Within this collaboration, a novel chemical series was identified with *in vitro* activity in an intra-cellular *Leishmania* assay. This presentation will concentrate on the lead optimisation and progression of this series, focusing on the identification of compounds with *in vivo* efficacy, utilizing X-ray crystallography for optimization of solubility, and finally, progress towards candidate selection.

14:45 (15 mins)

Metabolomics analysis of ozonide-treated *Plasmodium falciparum* reveals disruption of haemoglobin catabolism - *A12867*

Presenter: **Mr Carlo Giannangelo**, *PhD Candidate, Monash University*

**C Giannangelo**[1]; S A Charman[1]; D J Creek[1];

[1] Monash University, Australia

Artemisinin (ART)-based combination therapies are the current first line treatment for uncomplicated malaria caused by *Plasmodium falciparum*. However, the emergence and spread of ART resistant parasites threatens their ongoing use. Identifying new antimalarial drugs is therefore vital for effective control and to minimise the burden of disease caused by *Plasmodium* infection. The potent and fully synthetic peroxide-based ozonide (OZ) antimalarials, OZ277 and OZ439, are active against all blood stages of the parasite and could

be promising replacements for the ART antimalarials. However, despite being approved for clinical use (OZ277) and in advanced stages of development (OZ439), detailed information on the biochemical mechanisms underlying the activity of these compounds is lacking. We employed an untargeted metabolomics approach to monitor metabolic perturbations induced by the OZs on *P. falciparum* asexual blood stage cultures. Liquid chromatography-mass spectrometry allowed observation of drug-dependent changes in metabolite levels over time, enabling the identification of early effects on parasite metabolism to be distinguished from a non-specific death phenotype. We showed that treatment of trophozoite-stage cultures with OZ277 and OZ439 resulted in depletion of short chain peptides, most likely derived from haemoglobin, within 1.5h. Further untargeted peptidomic studies confirmed haemoglobin-derived peptides were perturbed after OZ treatment. Together these data show that haemoglobin catabolic processes are the most significant initial metabolic perturbations induced by OZ antimalarial treatment, which is consistent with the hypothesis that these drugs are activated by Fe(II) to produce reactive intermediates in the digestive vacuole. Further investigations aim to characterise the parasite response to OZ treatment during the ring-stage of asexual development in ART-sensitive and -resistant parasite lines.

15:00 (15 mins)

### CalcuSyn-based drug interactivity studies to define synergistic anti-malarial combinatorial regimes for Emetine dihydrochloride - *A12961*

Presenter: **Mrs Muna Abubaker**, *PhD student, University of Salford*

**M Abubaker**[1];

[1] University of Salford

The emergence and spread of artemisinin resistance to *Plasmodium falciparum* in Southeast Asia poses a serious threat to ongoing malaria control efforts. Unless new approaches are deployed rapidly, the health and economic burden related to the disease in tropical countries is certain to worsen. The development of treatments through drug repositioning may offer novel candidates permitting new combinatorial regimes with existing anti-malarials. The approach could present a much needed viable, accelerated route to expand the dwindling antimalarial therapeutic repertoire. Drug repositioning screens previously carried out in our laboratory reported the potent antimalarial efficacy ($IC_{50}$ 47 nM for KI) of the anti-amoebic drug Emetine dihydrochloride hydrate. We present here the preliminary data from a study designed to define the combinatorial therapeutic potential of emetine with a panel of antimalarial drugs, in a bid to minimise non-target effects previously experienced with the use of the drug in amoebiasis. The rational discovery of novel synergistic drug combinations can be accelerated by predictions of combination effects through experimental studies. All combinations were analysed using the optimised CalcuSyn fixed-ratio method validated using the atovoquone-proguanil combination. Following a screen of current antimalarial compounds, our preliminary data identified AN16 as the combinatorial partner drug displaying maximum synergistic interactivity with emetine dihydrochloride. The isobologram plot and the combination index (CI) generated by the CalcuSyn software demonstrated that the interaction between emetine and AN16 is synergistic at $IC_{50}$, $IC_{75}$ and $IC_{90}$ levels. The MTT cytotoxicity

results indicated that the emetine-AN16 combination has a better selectivity index in comparison to emetine alone. The results strongly support further *in vivo* investigation of the utility of emetine-AN16 combination as an alternative antimalarial treatment for drug resistance malaria.

15:15 (15 mins)

### Antimalarial Drug Discovery: Exploring the MEP Pathway - *A13011*

Presenter: **Neil Berry**, *Senior Lecturer, University of Liverpool*

**N G Berry**[1]; K E Price[1]; M Pye[1]; C Armstrong[2]; L Imlay[2]; D Hodge[2]; C Pidathala[1]; A S Lawrenson[1]; R Sharma[1]; J Park[2]; M Mikati[2]; N Tolia[2]; A R Odom[2]; P M O'Neill[1];

[1] University of Liverpool, UK; [2] Washington University, St Louis, United States

The development of effective antimalarial chemotherapeutics remains one of the major challenges within drug discovery. Malaria remains a major threat to global health, with ~198 million cases per year and 584,000 deaths annually, primarily in children under the age of five. The non-mevalonate (or MEP) pathway has been validated as a target for treatment of malaria and has the added advantage that it is absent in humans. Our objective is to deliver a lead candidate molecule suitable for clinical development, targeting *Plasmodium falciparum* IspD (*Pf*IspD). Following a chemoinformatics-led high throughput screen, the 1,2-benzoisothiazolone (BITZ) chemotype was identified as a promising PfIspD inhibitor. Further inhibitors have been used to develop structure-activity relationship (SAR) around the PfIspD active site. We have identified some of the most potent PfIspD inhibitors to date which also possess impressive whole cell activity. We have confirmed an essential covalent interaction between the BITZ core and cysteine residue in the *Pf*IspD active site. We are also exploring a second chemical series of non-covalent *Pf*IspD inhibitors, based around the tetrahydro-β-carboline chemotype. This series displays low nM activity at *Pf*IspD and provides a contrasting SAR and mechanism of inhibition.

15:30 (15 mins)

### Highly sensitive rapid affinity sensor for malaria detection of PfHRP2 and LDH - *A12906*

Presenter: **Ms Aver Hemben**, *PhD student, Cranfiled University*

**A Hemben**[1]; J Ashley[1]; I E Tothill[1];

[1] Cranfield University

Malaria is a prominent disease in sub-Saharan Africa that is caused by apicomplexan *Plasmodium* parasites and transmitted by adult female *Anopheles* mosquitoes. Malaria affects approximately 50% of the world's population causing millions of deaths every year mostly in pregnant women and children under five years of age. Despite control efforts the disease continues to affect productivity. Methods available for malaria detection include blood film microscopy, immunochromatographic and serological tests. Blood film

microscopy shows the highest sensitivity and specificity when used by trained personnel with reliable instruments. It is however time consuming and cannot be applied as a point of care diagnostic method. This study aims to develop a malaria biosensing technique that is rapid, portable, of low cost and easy to use. Malaria biomarkers *Plasmodium falciparum* histidine rich protein 2 (*Pf*HRP2) and parasite lactate dehydrogenase (LDH) have been investigated in this work. An immunosensor platform based on an enzyme linked immunosorbent assay was first constructed on a gold sensor surface. The developed sensor was able to detect malarial antigen with a detection limit of 0.3 ng $mL^{-1}$ in buffer and 0.03 ng $mL^{-1}$ in serum. The developed immunosensor is more sensitive, specific and lower in cost than ELISA and dipstick assays and is recommended for field trial.

## Malaria I- (Room 2 Apex)

Chair - Prof Matthias Marti

14:15 (30 mins)

Expansion of repetitive sequences and generation of protein targeting modules in exported *Plasmodium* proteins. - *A12727*

Presenter: **Dr Andrew Osborne**, *Lecturer, University College London*

**A Osborne**[1];

[1] University College London, UK

Repetitive low complexity sequences are common in proteins that are exported by the malaria parasite into its host erythrocyte. We identify a group of exported proteins containing short lysine-rich tandemly repeated sequences that are sufficient to localise to the erythrocyte periphery where key virulence-related modifications to the plasma membrane and the underlying cytoskeleton are known to occur. Efficiency of targeting is dependent on repeat number, indicating that repeat expansion over evolutionary time can shift a protein from the erythrocyte cytoplasm to the periphery of the infected cell. Comparison of proteins from different parasite species shows that targeting sequences can evolve de novo by repeat expansion. Several proteins known to be involved in cyto-adhesion contain lysine-rich repetitive targeting sequences highlighting the importance to disease pathogenesis.

14:45 (15 mins)

Stress, sirtuins and severe malaria - *A12977*

Presenter: **Mrs Linda Anagu**, *PhD Student, Keele University*

**L Anagu** [1]; C Merrick[1];

[1] Keele University

Sirtuin deacetylase enzymes are major players in the mutually exclusive expression of *var* genes in blood-stage *Plasmodium falciparum* parasites. This has been shown by mutagenesis studies in cultured parasites, and a field study of direct patient isolates has also shown that high expression of sirtuins correlates with high expression of severe-disease-associated *var* genes. Furthermore, this in turn correlates with stress factors in the human host: high fever and hyperlactatemia. In this work, we seek to determine cause-and-effect in this relationship: can host stress factors actually cause increased sirtuin expression – and hence potential changes in virulence gene expression? Cultured parasites were exposed to heat shock and/or lactate, and sirtuin expression was assessed by RT-PCR. In a second line of experiment, a luciferase reporter gene under a sirtuin promoter was generated and characterised, providing independent protein-level readout. We show that heat shock and prolonged exposure of schizonts to lactate can lead to increased expression of sirtuin RNA, and we discuss potential disparities between the RNA and protein readouts. This work will ultimately improve our understanding of how *P. falciparum* can respond to variable conditions in its human host.

15:00 (15 mins)

Molecular and functional characterization of a new regulator of Ser/Thr Protein Phosphatase type 1 in *Plasmodium falciparum - A12975*

Presenter: **Mr Thomas Hollin**, *Student, Centre for Infection and Immunity of Lille*

**T Hollin**[1];

[1] Centre for Infection and Immunity of Lille, France

Protein-protein interactions are essential in a broad range of biological processes including the post-translational modifications. Substrate-kinase or phosphatase interactions are considered as transient binding and play a central and essential role in *Plasmodium* cell cycle. The Ser/Thr Protein Phosphatase Type 1 (PP1) is essential to cell viability in *Plasmodium falciparum* and is regulated by the binding of regulatory subunits, up to 200 in humans, but only 4 have been reported for the parasite. To explore the *P. falciparum* PP1 (PfPP1) regulatory network, we carry out three strategies to characterize its interactome. Co-affinity purification followed by MS analysis identified six PfPP1 interacting proteins of which three contained the RVxF consensus binding, two with a Fxx[RK]x[RK] motif, also shown to be interact with PP1 and one with both binding motifs. The Yeast Two-Hybrid screens identified 134 proteins of which 30 present the RVxF motif and 20 have the Fxx[RK]x[RK] motif. The *in silico* screen using a consensus RVxF motif as template revealed the presence of 55 potential PfPP1 interacting proteins. As further demonstration, 35 candidate partners were validated in an ELISA-based assay. The data reports several conserved PP1 interacting proteins as well as a high number of specific interactors to PfPP1 and indicates a high diversity of biological functions for PP1 in *Plasmodium*. Among these candidates, the Gametocyte Exported Protein 15 has been confirmed as true interactor of PfPP1 by different approaches. GEXP15 is over-expressed during gametocyte stage, responsible for the transmission of the parasite in the mosquito. These results as well as functional studies will be presented.

15:15 (15 mins)

Charting the transcriptional profile of gametocytogenesis in *Plasmodium* by AP2-G overexpression. - *A12965*

Presenter: **Dr Katarzyna Modrzynska**, *Research Fellow, Wellcome Trust Centre for Molecular Parasitology, University of Glasgow*

**K K Modrzynska**[1]; R S Kent[1]; R Cameron[1]; A P Waters[1]; O B Billker[2];

[1] Wellcome Trust Centre for Molecular Parasitology,University of Glasgow; [2] Wellcome Trust Sanger Institute

The transmission of malaria between the mammalian host and the mosquito vector relies on the subset of parasites which differentiate into male and female gametocytes. The earliest stages of this process, however, remain poorly understood, as the young gametocytes are morphologically indistinguishable from the asexual parasites and present at very low abundance within the infection. Recently, we described AP2-G - a transcription factor acting as a key regulator of gametocytogenesis across different *Plasmodium* species. AP2-G expression is well correlated with the percentage of gametocytes in the population and its deletion completely abolishes the gametocytogenesis. Here we present the results of inducible overexpression of AP2-G in rodent malaria parasite *Plasmodium berghei*. Upon induction, the vast majority of parasites underwent synchronous differentiation into morphologically normal gametocytes with a normal male to female ratio. RNA-seq was used to generate a detailed timecourse of transcriptome changes throughout the gametocytogenesis. It revealed a small group of genes induced as early as 4h after the initiation of commitment, followed by subsequent waves of transcriptome modifications leading to a mature gametocyte RNA profile. Further analysis of these groups of genes provided new insights into the molecular mechanisms of gametocytogenesis, highlighting the relevance of additional apiAP2 transcription factors and RNA binding proteins in this process.

15:30 (15 mins)

Identification of candidate transmission-blocking antigen genes in *Theileria annulata* and related vector-borne apicomplexan parasites - *A12898*

Presenter: **Dr Stephen Larcombe**, *Postdoctoral Researcher, University of Glasgow*

**S Larcombe**[3]; L Lempereur[4]; Z Durrani[5]; T Karagenc[1]; H Bilgic[1]; S Bakirci[1]; S Hacilarlioglud[1]; J Kinnaird[3]; J Thompson[2]; W Weir[3]; B Shiels[3];

[1] Adnan Menderes University, UK; [2] University of Edinburgh, UK; [3] University of Glasgow , UK; [4]University of Liege, Belgium; [5] University of Liverpool, UK

Strategies for control of vector-borne apicomplexan parasites often target parasite stages in the mammalian host that cause disease, but this can result in reservoir infections that promote pathogen transmission and generate economic loss. Optimal control strategies

should protect against clinical disease, block transmission and be applicable across related genera of parasites. We have used bioinformatics and transcriptomics to screen for transmission-blocking candidate antigens in *Theileria annulata*. A number of candidate antigen encoding genes were identified including domains that are conserved across vector-borne Apicomplexa (*Babesia*, *Plasmodium* and *Theileria*), including the Pfs48/45 6-cys domain and a novel cysteine-rich domain. Expression profiling confirmed candidate genes are expressed by life cycle stages within infected ticks. Candidate genes were identified that encode proteins with similarity to known transmission blocking candidates in related parasites, while one is a novel candidate conserved across vector-borne apicomplexans and has a potential role in the sexual phase of the life cycle. The results indicate that a 'One Health' approach could be utilised to develop a transmission-blocking strategy effective against vector-borne apicomplexan parasites of animals and humans.

## Diversity I- (Room 3 Dalhousie)

Chair - Prof Mark C. Field

14:15 (30 mins)

Advances in understanding variant antigen diversity in natural African trypanosome populations. - *A12728*

Presenter: **Dr Andrew Jackson**, *Senior Lecturer, University of Liverpool*

**A Jackson** [1];

[1] University of Liverpool, UK

Antigenic variation of the Variant Surface Glycoprotein (VSG) is the mechanism by which African trypanosomes (*Trypanosoma brucei*, *T. congolense* and *T. vivax*) survive the humoral immune response of their vertebrate host during the bloodstream stage. The VSG is encoded by a multi-copy gene family, with many hundreds of variants available to the parasite. Understanding the origins of this antigenic diversity, which is so crucial to parasite survival, and analysing it from genome or transcriptome sequence data are major challenges that we are addressing. I will present data describing the scale of variation in VSG genomic repertoire across natural populations of *T. congolense* and *T. vivax*. By defining the limits of antigenic diversity in *T. congolense* and *T. vivax*, it is possible to compare VSG repertoires on a population scale using conserved VSG phylotypes in an approach we call 'Variant Antigen Profiling'. Quantifying population variation also provides an opportunity to examine the molecular evolution of antigenic diversity, and test the hypothesis that differences in recombination rate between species result in different levels of sequence variation. By multiple tests of sequence contiguity, I will show how sequence mosaicism is predicted to be extremely frequent among *T. brucei* VSG, less so among *T. congolense* (though still considerable) and rare among *T. vivax* VSG. Progress is being made towards delimiting what might be called the 'VSG universe', with respect to structural diversity, analytical methods and the mechanisms responsible for generating novel antigens.

14:45 (30 mins)

### Ageing and Susceptibility to Parasites - *A12729*

Presenter: **Prof Tom Little**, *University of Edinburgh*

**T Little**[1];

[1] University of Edinburgh, UK

We conducted a series of experiments to determine how the age of an individual will influence susceptibility. Our work uses the crustacean *Daphnia magna* and the bacterial parasite *Pasteuria ramosa*. Older mothers tended to be more resistant. Offspring born to older mothers were also more resistant. Infection also reduces host longevity, and the expected lifespan-extending effects of dietary restriction are not apparent when individuals are infected. Thus, age structure has considerable potential to alter the rate of disease spread, and infection may in turn alter age structure.

15:15 (15 mins)

### Population genomics of *Leishmania donovani*: from macroevolution to direct sequencing of clinical samples - *A13060*

Presenter: **James Cotton**, *Senior Staff Scientist, Wellcome Trust Sanger Institute*

**J A Cotton**[4]; M Domagalska[3]; H Imamura[3]; S Franssen[4]; F Van den Broeck[3]; C Durrant[4]; T Downing[2]; M J Sanders[4]; O Stark[1]; B Moser[1]; G Schönian[1]; M Berriman[4]; J C Dujardin[3];

[1] Charité Universitätsmedizin, Germany; [2] Dublin City University, Ireland; [3] Institute of Tropical Medicine, Antwerp, Belgium; [4] Wellcome Trust Sanger Institute

Genomic data is starting to provide unprecedented resolution of the genetics of *Leishmania* populations. We show that whole-genome sequence data clarifies the evolution of the *Leishmania donovani* complex, and shows that different populations of visceral leishmaniasis pathogens have strikingly different population genetics, differing in genetic diversity and in the amount of recombination occurring. In our most detailed study, focusing on the Indian subcontinent (ISC), we show that genome data can resolve population structure associated with changes in drug sensitivity that is invisible to traditional molecular markers and can identify molecular variants potentially associated with reduced efficacy of antimonial drugs in that setting. These data should set the scene for genetic surveillance of the *Leishmania* population in the ISC, providing valuable support for disease control efforts. To-date, our data have all been generated from isolates in culture, but to make surveillance possible, we need to be able to generate genomic data for parasites directly from patient clinical samples. We show that an enrichment strategy using oligonucleotide baits allows us to sequence essentially the entire *Leishmania* genome from patient bone marrow samples. Taken together, our database of *L. donovani* genome variation and this technical advance moves *Leishmania* genomics close to being a clinically useful tool.

15:30 (15 mins)

Comparative analysis of Stramenopile genomes reveals patterns of functional streamlining in *Blastocystis hominis - A12901*

Presenter: **Ross Low**, *PhD Student, Mr R LOW*

**R S Low**[1]; A P Jackson[1];

[1] University of Liverpool

*Blastocystis hominis* is an intestinal pathogen of humans associated with Irritable Bowel Syndrome, with the smallest known Stramenopile genome. To understand the evolutionary causes for its size and to examine potential adaptations for pathogenicity, we conducted a comparative analysis of Stramenopile genomes. In the absence of effective out-groups for comparison, we produced a genome for *Proteromonas lacertae*, the closest known relative of *Blastocystis*, and a transcriptome for *Cafeteria roenbergensis*, a free-living Stramenopile, which allowed us to establish character states in the ancestor of *Blastocystis* spp. Our analyses show that *B. hominis* has lost all flagellum components otherwise conserved in Stramenopiles including dyneins and kinesins. Besides motility, we observed no other losses of major cell function. Rather, we show reduced diversity of genes associated with adhesion (EGF domains), protein interactions (WD domains) and gene regulation (ankyrin domains). Overall, evolution of the *B. hominis* genome has evolved with streamlining of genomic complexity. We analysed the phylodiversity of conserved gene families of diverse functions and found that *B. hominis* routinely retains fewer ancestral gene lineages than other Stramenopiles. We suggest that this gene loss, combined with an expansion of IG domain-based cell-surface proteins, reflects a history of increasing dependency on the gut mucosa.

## In the field II- (Room 4 Dalhousie)

Chair - Jerry Sternberg

14:15 (30 mins)

Immuno-epidemiological investigations into immunity to schistosomes. - *A12730*

Presenter: **Dr Shona Wilson**, *Lecturer in Parasitology, University of Cambridge*

**S Wilson**[1];

[1] University of Cambridge

The design of control programmes for schistosomiasis are based upon reproducible epidemiological patterns, in which children carry the major burden of infection, regardless of level of exposure to the parasite, with development of partial immunity being apparent in older adolescents and adults. The rate at which this immunity develops within populations is proposed to increase with force of

transmission. The current models of schistosome infection dynamics on which the long-term success of control programmes is predicted, often lack relevant immunity parameters, highlighting the continuing need for good quality immuno-epidemiological data. The targets of anti-schistosome immunity, and how these relate to the slow development of immunity will be discussed in the context of force of transmission, along with the potential implications for control programme success.

14:45 (15 mins)

### Which diagnostic to use and why? New insights into intestinal schistosomiasis along the shoreline of Lake Albert, Uganda - *A12835*

Presenter: **Mr Hajri Alshehri**, *PhD student, Liverpool School of Tropical Medicine*

**H Alshehri**[1];

[1] Liverpool School of Tropical Medicine

Infection with intestinal schistosomiasis is typically common in children, particularly within regions of sub-Saharan Africa where environmental water contact is high and access to adequate sanitation is poor. Traditional parasitological methods of diagnosis that visualise parasite ova underestimate true prevalence and as control programmes progress, infection egg-tallies may also decline. Consequently, there is a need to develop better methods for detection of schistosomiasis, especially in countries such as Uganda where ongoing school-based control has taken place for over a decade. Against this country-backdrop, we investigate the application of novel diagnostics to shed light on current levels of infection across 5 primary schools within Buliisa District, Lake Albert. We evaluated parasitological- and serological-based methods alongside real-time PCR and focused upon examination of children of school-age (i.e. 5-10 years). PCR-based methods explored the use of *Taqman®* assays on urine and faecal samples. We assessed the diagnostic congruence between methods and report that intestinal schistosomiasis is still pervasive within this lakeshore environment.

15:00 (15 mins)

### Epidemiology of gastrointestinal helminth parasites in Scottish red deer - *A12939*

Presenter: **Mr Greg Albery**, *PhD Student, University of Edinburgh*

**G F Albery**[1]; J M Pemberton[1];

[1] University of Edinburgh

The red deer (*Cervus elaphus*) is one of Europe's most abundant large mammals, sharing much of its range with other wild and domestic ruminants, and like other ruminants it has a characteristic array of helminth parasites. However, there is surprisingly little published work on the epidemiology of red deer parasites, and what is known is mostly based on cross-sectional analysis of culled deer and therefore restricted to statutory culling seasons and deer of unknown life history. In January, April, August and November 2016

colleagues and I collected 1038 non-invasive faecal samples from 339 known individuals living in the individually-monitored red deer population in the North block of the Isle of Rum. I counted strongyle eggs, *Fasciola hepatica* eggs and larvae of the tissue worm *Elaphostrongylus cervi* at high precision. I will present analyses demonstrating high repeatability of counts within and between sampling periods and how they vary with sex, age and season and between the different parasite taxa. This study paves the way for investigation of a wider variety of factors that may affect individual counts including reproductive status, space use, genetics and immunity.

15:15 (15 mins)

### Variation in parasite burden and immune function during reproduction in wild Soay sheep - *A12860*

Presenter: **Dr Adam Hayward**, *Research Fellow, University of Stirling*

**A Hayward**[1];

[1] University of Stirling

A cornerstone of life-history theory is that phenotypic variation may be created and maintained by trade-offs. Experimental studies show that increased investment in reproduction is traded-off with increased parasite burden. Such observations have been ascribed to hormonal changes during reproduction and their interactions with immunity, but collecting data on reproduction, parasite-specific immunity and hormones in wild animals is challenging. Wild St Kilda Soay sheep have been intensively studied for over 30 years and face infection with gastrointestinal strongyle nematodes. Recent work has shown that females reproducing in spring have reduced antibody concentrations in the summer. To further investigate this reproduction-immunity trade-off, I repeatedly collected faecal samples from female Soay sheep during pregnancy and lactation. Samples were analysed for strongyle faecal egg counts (FEC), strongyle-specific antibody concentrations, and hormone concentrations. I will show that between-individual differences explain a large proportion of the variation in these traits and that faecal antibodies represent an effective marker of strongyle resistance. I will examine changes in FEC and antibody concentrations across the lambing season, and identify the role of reproductive investment and between-individual variation in governing these changes. Finally, I will show how changes in hormone concentrations are linked to reproductive traits and antibody production.

15:30 (15 mins)

### Predictive value of Ov16 antibody prevalence in different sub-populations for elimination of African onchocerciasis - *A12958*

Presenter: **Dr Luc Coffeng**, *Assistant Professor, Erasmus MC University Medical Center*

**L E Coffeng**[1]; W A Stolk[1]; S J de Vlas[1]; A Golden[2]; T de los Santos[2]; G J Domingo[2];

[1] Erasmus MC University Medical Center Rotterdam, Netherlands; [2] PATH, United States

One of the currently recommended methods to evaluate elimination of onchocerciasis is to test whether Ov16-antibody prevalence in children of age 0-9 is <0.1%. The predictive accuracy of this decision threshold should be reviewed in context of the geographical variation in pre-control epidemiology of onchocerciasis and the history of mass drug administration (MDA). We use the ONCHOSIM model to investigate the predictive value of Ov16 antibody prevalence in various age groups for elimination of onchocerciasis in a variety of endemic settings and MDA scenarios. Sensitivity and specificity of Ov16 antibody prevalence for predicting elimination highly depends on the pre-control epidemiological situation, history of MDA, the age group that is sampled, and the chosen Ov16 antibody prevalence threshold. Still, threshold values can be defined such that positive predictive values for elimination are close to 100% regardless of the history of MDA. Importantly, we predict that Ov16 antibody prevalence in school-aged children (age 5-14) provides the most information about prospects of elimination. The findings from this study suggest that 1) broadening the sampled population to school-age children instead of children under ten increases the accuracy of anti-Ov16 prevalence as a predictor for elimination; 2) the current threshold of 0.1% may be too stringent except for the most highly endemic settings; and 3) a tiered approach to defining thresholds based on pre-control endemicity is pertinent.

## Drugs III- (Room 1 Apex)

Chair – Prof Mark Taylor

16:15 (30 mins)

A Multi-Stage Preclinical Candidate for the Potential Treatment of Malaria - *A12851*

Presenter: **Dr B Baragana**, *DDU Malaria Team Leader, University of Dundee*

**B Baragana**[1];

[1] University of Dundee, UK

Malaria is a devastating disease with over 214 million clinical cases every year. The World Health Organization (WHO) estimated 438,000 deaths in 2015, predominantly amongst children and pregnant women in sub-Saharan Africa. Malaria in humans is caused by five *Plasmodium* species. The most pathogenic is *Plasmodium falciparum* which accounts for the majority of cases and deaths in Sub-Saharan Africa. *Plasmodium vivax* is the next most prevalent species, particularly in Southeast Asia and Central and South America. The malaria parasite has developed resistance to many of the current drugs available for treatment. To reduce the rate of development of resistance, World Health Organisation recommends an artemsisinin-based combination therapy (ACT) as first-line treatment for the majority of malaria cases. Worryingly there are now reported cases of clinical resistance to artemisinins. To support the current malaria eradication agenda, there are a number of needs for new anti-malarials: compounds with novel modes of action that are not cross-resistant to current drugs; single-dose treatments; compounds that kill gametocytes preventing transmission of the disease and

treatments for relapsing malaria. In my talk I will present the discovery and development of DDD107498, a potential new anti-malarial agent. The starting point for this project was a phenotypic screen carried out against *P. falciparum* at the University of Dundee, UK. One of the identified series was optimized to a compound which fulfilled the Medicines for Malaria Venture criteria for a late lead compound. DDD107498 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.

16:45 (15 mins)

Local production of a liquid direct agglutination test as a sustainable measure for control of visceral leishmaniasis in Sudan. - *A12836*

Presenter: **Hussam Osman**, *Lecturer & Research Officer, Ahfad university for Women*

**H Osman**[1];

[1] Ahfad University for Women, Sudan

A prerequisite for the control of visceral leishmaniasis (VL) is the accessibility to reference diagnostics. The high price of the freeze-dried direct agglutination test (FD-DAT) and the short shelf-life time of the rK39 strip test (rK39) have limited the application of these tests in Sudan. An original liquid DAT (LQ-DAT) with high reproducibility compared with the FD-DAT and rK39 has been routinely produced in our laboratory since 1999. In this study, a 3.4-year-old batch (of more than 90 test batches produced to date) was chosen to validate the diagnostic performance of this test against microscopy, FD-DAT, and rK39 in 96 VL and 42 non-VL serum samples. Relatively higher sensitivity (95/96, 99.0%) was recorded for the LQ-DAT than for the FD-DAT (92/96, 95.8%) and rK39 (76/96, 79.2%), probably because of the use of the endemic autochthonous *Leishmania donovani* isolate as the antigen. Experience with the LQ-DAT, its low cost of production, ease of providing this test, and diagnostic reliability compared with the FD-DAT suggest that wide-scale implementation of the LQ-DAT can contribute to sustainable VL control in Sudan.

17:00 (15 mins)

Activation of bicyclic nitro-drugs by a novel nitroreductase (NTR2) in *Leishmania* - *A12932*

Presenter: **Dr Susan Wyllie**, *Team leader, University of Dundee*

**S Wyllie**[1]; S Norval[1]; S Patterson[1]; A Roberts[1]; A H Fairlamb[1];

[1] University of Dundee

Recently, the bicyclic nitro-compounds (R)-PA-824, DNDI-VL-2098 and delamanid have been identified as potential candidates for the treatment of visceral leishmaniasis. Using a combination of quantitative proteomics and whole genome sequencing of susceptible and

drug-resistant parasites we identified a putative NAD(P)H oxidase as the activating nitroreductase (NTR2). Whole genome sequencing revealed that deletion of a single cytosine in the gene for NTR2 resulted in expression of a non-functional truncated protein. Susceptibility of *Leishmania* was restored by reintroduction of the WT gene into the resistant line, which was accompanied by the ability to metabolise these compounds. Overexpression of NTR2 in WT parasites rendered cells hyper-sensitive to bicyclic nitro-compounds, but only marginally to the monocyclic nitro-drugs, nifurtimox and fexinidazole, known to be activated by a mitochondrial oxygen-insensitive nitroreductase (NTR1). Conversely, a double knockout NTR2 null cell line was completely resistant to bicyclic nitro-compounds. Recombinant NTR2 was capable of reducing bicyclic nitro-compounds in the same rank order as drug sensitivity *in vitro*. Thus, NTR2 is necessary and sufficient for activation of these bicyclic nitro-drugs. These findings may aid the future development of better, novel anti-leishmanial drugs.

17:15 (15 mins)

CNS Infection with African trypanosomes: mixed messages from the CSF - *A12700*

Presenter: **Jerry Sternberg**, *University of Aberdeen*

**J M Sternberg**[2]; S Lamour[1]; P G Kennedy[3]

[1] Imperial College; [2] University of Aberdeen; [3] University of Glasgow

African trypanosome infections progress from an early haemolymphatic stage to a late meningoencephalitic stage. So much is well known. The transition between these stages may be seen from a biological perspective (e.g. anatomical compartments and kinetics of brain invasion) and from a therapeutic imperative (as the late stage requires drug treatment with serious toxicity and/or logistic issues). In the clinic, stage determination is based on the analysis of cerebrospinal fluid (CSF), with the main diagnostic criterion being pleiocytosis. However, it is now becoming apparent that current clinical staging criteria may not be consistent either with biological aspects of stage progression, nor therapeutic cut-offs. We describe the analysis of CSF samples from HAT patients using metabolomic approaches, to discover whether small metabolites may be diagnostic for CNS invasion by trypanosomes and the relationship of metabolomics profile to current staging criteria. Metabolites of tryptophan oxidation indicate the onset of parasite-inducted inflammatory processes in the brain already in conventionally diagnosed early stage patients. Meanwhile, 3-hydroxybutyrate, alanine, mannose and urea were discriminatory for the presentation of daytime somnolence and gait ataxia, two characteristic neurological symptoms of HAT. So while small metabolites discriminate cases with and without neuroinflammation and neurological sequelae, they do not discriminate disease stage as determined by conventional diagnostic methods. These findings call for a re-evaluation of clinical staging criteria and also demonstrate the potential for metabolomic approaches to unravel the pathogenesis of this and other neuro-parasitisms.

17:30 (15 mins)

The Odyssey of pro-trypanocides: Oxidative activation of the aminomethyl benzoxaboroles - *A12971*

Presenter: **Dr Ning Zhang**, *Postdoctoral researcher, University of Dundee*

**N Zhang**[1]; M Zoltner[1]; P Scullion[1]; D Horn[1]; M C. Field[1];

[1] Division of Biological Chemistry and Drug Development, School of Life Sciences, University of Dundee

Despite being targeted for eradication by WHO, African trypanosomiasis is still devastating local communities and remains a threat to global public health. One of the crucial aspects in securing future disease control is to develop new medicines chemically distinct from the ones suffering declined effectiveness in the frontline. Benzoxaboroles are a group of promising candidates in the pipeline. Rational drug design and prevention of potential resistance in the field requires further insights into both the mode of action (MoA), and the uptake and metabolisms of these compounds. Here, we reveal a contextual oxidative enzymatic cascade responsible for the activation of a series of benzoxaborole derivatives. Through this cascade, the methylamine group in the compounds is first converted by an amine oxidase in the host into an aldehyde, which is then transformed by a pathogen-derived aldehyde dehydrogenase, TbALDH3, into a carboxylic acid, generating potent trypanocidal activity. We also provide a molecular insight into how the aldehyde metabolites match the specificity of TbALDH3 as incidental substrates. Overall, this work highlights the importance of understanding the complex and dynamic interaction between the host and pathogen, especially in the context of metabolism.

## Malaria II- (Room 2 Apex)

Chair - Prof George Christophides

16:15 (30 mins)

Host cell and parasite determinants of *Plasmodium* sporozoite entry into hepatocytes. - *A12731*

Presenter: **Dr Olivier Silvie**, *Researcher, Université Pierre et Marie Curie*

**O Silvie**[1];

[1] Université Pierre et Marie Curie, France

*Plasmodium* sporozoites are deposited in the host skin by a female *Anopheles* mosquito and migrate from the dermis to the liver parenchyma in order to infect hepatocytes, where they develop into replicative liver stages inside a parasitophorous vacuole. Sporozoites represent attractive targets for antimalarial preventive strategies, yet the mechanisms of parasite entry into hepatocytes remain poorly understood. We discovered that the two main species causing malaria in humans, *P. falciparum* and *P. vivax*, rely on two distinct host cell surface proteins to infect hepatocytes. Similarly, rodent-infecting *P. yoelii* and *P. berghei* sporozoites rely on distinct host factors for invasion. Using a genetic approach, we have now identified a key sporozoite protein that determines the host cell entry pathway used by the parasite to invade hepatocytes. Our data establish a functional link between sporozoite and host cell entry factors

potentially involved in ligand-receptor interactions. These exciting results open novel perspectives to elucidate the molecular mechanisms involved in sporozoite host cell entry during malaria liver infection.

16:45 (15 mins)

### From force generation to substrate attachment: new functions for the acto-myosin A motor complex in *Toxoplasma gondii* - *A12926*

Presenter: **Miss Maria Fernanda Latorre-Barragan**, *PhD student, University of Glasgow*

**F Latorre-Barragan**[1]; J Whitelaw[1]; S Gras[1]; G Pall[1]; J Leung[2]; G Ward[2]; M Meissner[1];
[1] WTCMP University of Glasgow; [2] University of Vermont, United States

In *Toxoplasma gondii* motility and invasion is thought to rely on the actomyosin- system. The main motor complex, consisting of myosin A, its light chain (MLC1) and gliding associated proteins (GAPs), is anchored to the inner membrane complex (IMC), and is thought to produce the force on short actin filaments (ACT1) for gliding and invasion. This mechanical force is transmitted to transmembrane proteins, which are translocated in a directional manner to the basal end of the parasite, resulting in forward motion on the substrate. Interestingly, using reverse genetics, it has been demonstrated that MyoA, MLC1 or ACT1 are not essential for gliding and invasion, necessitating a reassessment of the individual functions of the key molecules of the complex. One plausible explanation of this surprising finding is the presence of compensatory myosin motors that can take over the role of MyoA. Due to its structural similarity with MyoA, we studied the possibility of myosin C (MyoC) taking over MyoA function. We generated three different complementation constructs, and compared their expression in the *myoA* KO. Our results suggest that IMC-localised MyoC can partially complement for MyoA in terms of invasion and gliding rates, but not average speed or gliding distance, indicating that MyoC cannot compensate the motor function of MyoA *per se*. Moreover, depletion of MLC1 in a *mlc1* cKO demonstrated that MyoA and MyoC cannot be anchored to the IMC. However, parasites were still able to move and invade albeit at reduced levels.
To further investigate the functions of the proteins of the motor complex, we studied attachment capacity under shear stress and retrograde flow using mutant parasites. Our results indicate that attachment capacity was altered but retrograde membrane flow does not depend on the actomyosin-system.

17:00 (15 mins)

### Exploring the invasion-blocking activity of chemically-modified and low molecular weight heparins and plant-derived polysaccharides against the human malaria parasite *Plasmodium falciparum* - *A12940*

Presenter: **Mr Muqdad Hmoud**, *PhD student, Keele University*

**M Hmoud**[1]; L Hadfield[1]; M Skidmore[1]; P Horrocks[1];
[1] Keele University;

Heparin, a sulphated glycosaminoglycan, inhibits blood stage growth of *Plasmodium falciparum*. This inhibitory effect appears to be mediated through interference with merozoite surface proteins, resulting in a block of erythrocyte invasion. Use of heparins as an adjuvant therapy for severe malaria, however, is not possible due to its anticoagulant property. Here we report on the use of a novel bioluminescence assay of invasion-blocking activity using Dd2 and NF54 clones genetically modified to express a luciferase reporter. The invasion-blocking activity of chemically modified heparins, low molecular weight heparins and plant-derived complex saccharides are evaluated and compared between these two parasite clones. A correlation of invasion-blocking effect and anticoagulant activity will be used to identify candidates which block invasion but also have low anticoagulant activity.

17:15 (15 mins)

### Alterations in the neurovascular unit of the blood brain barrier in cerebral malaria using an *in vitro* HBEC-astrocyte tandem model - *A12927*

Presenter: **Nana Efua Andoh**, *PhD student, Keele University*

**N E Andoh**[1]; M F Stins[2]; S J Chakravorty[1];

[1] School of Life Sciences, Keele University; [2] Johns Hopkins Medical School, Baltimore, USA

*Plasmodium falciparum*-infected red blood cells (PRBC) sequestered in brain microvasculature, disruption of the blood brain barrier (BBB) and long term neurological symptoms are associated with cerebral malaria (CM). This study investigates the impact of PRBC on the cellular components of the BBB in CM, using an *in vitro* tandem model comprising human brain endothelial cell (HBEC) (luminal side) and human astrocytes (basolateral side), in a trans-well system. This model mimics the endothelial cells and astrocyte end feet, the main components of the BBB neurovascular unit (NVU) and the interface between the blood and the neuronal cells of the brain. Supernatants and lysates harvested from the co-culture of PRBC and HBEC (*in vitro* model of sequestration), induced a significant increase in the permeability of the endothelial barrier and demonstrated the presence of inflammatory mediators including proteases, MCP-1 and ICAM-1. Endothelial activation and astrogliosis in the NVU was evaluated in this study, represented by release of ADAMTS4 and glial fibrillary acidic protein (GFAP), respectively. Our studies showed that endothelial-derived factors, produced during sequestration mediated a marked increase in the release of ADAMTS4, both luminal and basolateral in the NVU. Interestingly, astrocyte-derived GFAP showed a marked increase only on the luminal side of the NVU, most likely from damage to the astrocyte end feet. We propose that endothelial-derived inflammatory mediators, produced by the BBB in response to PRBC, can induce astrocyte injury in the NVU, during episodes of CM. This astrocyte damage is a key event in the development of neuronal and synaptic dysfunction that leads to the neurological symptoms in CM.

## Diversity II- (Room 3 Dalhousie)

Chair - Dr Andrew Jackson

16:15 (30 mins)

*Mastigamoeba balamuthi* and *Entamoeba histolytica*: So similar yet so different. - *A12732*

Presenter: **Prof Jan Tachezy**, *Professor of Parasitology, Charles University in Prague*

**J Tachezy**[1]; V Žárský[1]; E Nývltová[1]; I Hrdý[1];

[1] Charles University in Prague, Czech Republic

Conoza are an intriguing group of free living and parasitic protists that includes both aerobic (*Eumycetozoa*) and anaerobic (*Archamoebae*) members. Phylogenetic analysis suggested that *Archamoebae* evolved from an aerobic ancestor, which makes amoebozoans very attractive for tracing evolutionary history of cell adaptation to anaerobic niches and parasitic style of life. The adaptation to anaerobiosis included the loss most of canonical mitochondrial and peroxisomal pathways and the acquisition of enzymes required for anaerobic energy metabolism. Comparative analysis of genomes of Amoebozoa group members including free-living *Mastigamoeba balamuthi* and parasitic *Entamoeba histolytica* with selected opisthokont genomes revealed a major loss of genes related to mitochondrial metabolic functions during the transition to anaerobic lifestyle. This loss was probably compensated by acquisition of variety of bacterial genes by lateral gene transfer. Next we specifically focused on metabolism of *M. balamuthi* and *E. histolytica*. The common features for both organisms include (i) acquisition of anaerobic energy metabolism including PFO, hydrogenase, acetyl CoA synthetase (ii) iron-sulfur cluster assembly machinery of bacterial type (NifS, NifU), and (iii) sulfate activation pathway. However, while in *M. balamuthi*, the enzymes of energetic metabolism and NIF pathway have a dual localization in the cytosol and hydrogenosomes (anaerobic mitochondria producing hydrogen), these pathways are not present in mitosomes (reduced mitochondria that don't generate energy) of *E. histolytica*. Unlike mitosomes, the hydrogenosomes of *M. balamuthi* retain several canonical mitochondrial components including TCA enzyme malate dehydrogenase, respiratory complex II, and the glycine cleavage system. We propose that the more complex hydrogenosome in free living *M. balamuthi* represents the intermediate step between the ancestral aerobic organelle and highly reduced mitosomes in parasitic *Entamoeba histolytica*.

16:45 (15 mins)

2b-RAD genotyping for population genomic studies of Chagas disease vectors: *Rhodnius ecuadoriensis* in Southern Ecuador - *A12894*

Presenter: **Mr Luis Hernandez**, *PhD student, University of Glasgow*

**L Hernandez**[5]; **M Paterno**[6]; A G Villacís[3]; B Andersson[1]; J A Costales[3]; M De Noia[4]; S Ocaña-Mayorga[3]; C A Yumiseva[3]; **M J Grijalva**[2]; **M S Llewellyn**[5];

[1] Karolinska Institutet, Sweden; [2] Ohio University, United States; [3] Pontifical Catholic University of Ecuador, Ecuador; [4] Universität Bielefeld, Germany; [5] University of Glasgow; [6]University of Padua, Italy

*Rhodnius ecuadoriensis* is the main triatomine vector of Chagas disease, American trypanosomiasis, in Southern Ecuador and Northern Peru. Genomic approaches and next generation sequencing technologies have become a powerful tool for investigating population diversity and structure which is a key consideration for vector control. Here we assess the effectiveness of three different 2b-RAD genotyping strategies in *R. ecuadoriensis* to provide sufficient genomic resolution to tease apart microevolutionary processes and undertake some pilot population genomic analyses. The 2b-RAD protocol was carried out in-house at a non-specialised laboratory using 20 *R. ecuadoriensis* adults collected from the Central coast and Southern Andean region of Ecuador, from June 2006 to July 2013. 2b-RAD sequencing data was performed on an Illumina MiSeq instrument and analysed with the STACKS *de novo* pipeline for loci assembly and Single Nucleotide Polymorphisms (SNPs) discovery. Preliminary genomic analyses (AMOVA, pairwise $F_{ST}$, principal components and coordinates and Bayesian clustering) were implemented. Our results showed that the 2b-RAD genotyping protocol is effective for *R. ecuadoriensis* and likely for other triatomine species. However only *Bcg*I and *CspC*I Restriction Enzymes provided a number of markers suitable for population genomic analysis at the read depth we generated. Our preliminary genomic analyses highlighted a strong signal of fine and coarse scale genetic structuring across the study area. Our findings suggest that 2b-RAD genotyping is both a cost effective and methodologically simple approach for generating high resolution genomic data for Chagas disease vectors with the power to distinguish between different vector populations at local, epidemiologically relevant, scales. As such, 2b-RAD represents a powerful tool in the hands of medical entomologists with limited access to specialized molecular biological equipment.

17:00 (15 mins)

### Endosymbiosis, origins and gene expression in the photosynthetic protist *Euglena gracilis* - *A12895*

Presenter: **Mr ThankGod Ebenezer**, *PhD Student, University of Cambridge*

**T E Ebenezer**[1,2]; A Vanclova[3]; A Nenarokova[4]; M Zoltner[7]; S O Obado[5]; C Santana[6]; V Hampl[3]; J Lukes[4]; J Dacks[7]; M Carrington[1]; S Kelly[8]; M C Field[2];

[1] University of Cambridge, UK; [2] University of Dundee, UK; [3] Charles University in Prague, Czech Republic; [4] Institute of Parasitology, Biology Centre, ASCR, Czech Republic; [5] The Rockefeller University, United States; [6] Universidad Pablo de Olavide, Spain; [7] University of Alberta, Canada; [8] University of Oxford, UK

The photosynthetic flagellate *Euglena gracilis* harbours a secondary endosymbiotic plastid and is a distant relative of the pathogenic trypanosomatids, a major component of global aquatic ecosystems and also of considerable biotechnological potential with resistance to harsh conditions. Here we report genome, transcriptome and proteome drafts for *E. gracilis*. The genome is over 2Gb and has a coding potential of 36,526 predicted ORFs. Less than 25% of the genome is single copy sequence, indicating extensive repeat

elements. Several gene families likely associated with the cell surface and signal transduction possess very large numbers of lineage-specific paralogs, suggesting great flexibility in environmental monitoring and, together with divergent mechanisms for metabolic control, novel solutions to adaptation to extreme environments. There are clear contributions from photosynthetic eukaryotes to the nuclear genome with red, green and brown algal genes evident, together with orthogroups shared with only trypanosomes and also with other excavates. Furthermore, we demonstrate that the majority of control of protein expression level is post-transcriptional despite the presence of conventional introns, that mRNA metabolism is highly unusual in transcriptional and nuclear export mechanisms and which differentiate Euglenids from the trypanosomatids and higher eukaryotes. These data are a major advance in the understanding of the nuclear genome of Euglenids and provide a platform for investigation of the contributions of *Euglena gracilis* and relatives to the biosphere.

17:15 (15 mins)

Genetic variation in potential *Giardia* vaccine candidates cyst wall protein 2 and a1-giardin - *A13014*

Presenter: **Mr Matej Radunovic**, *Medical student, Univeristy of Bergen*

**M Radunovic**[2]; C Klotz[1]; C S Saghaug[2]; H R Brattbakk[2]; T Aebisher[1]; N Langeland[2]; K Hanevik[2];
[1] Robert Koch-Institute, Germany; [2] University of Bergen, Norway

*Giardia* is a prevalent intestinal parasitic infection seen in children in developing countries, and in travellers returning from endemic areas. The trophozoite structural protein a1-giardin (a1-g) and the cyst protein Cyst wall protein 2 (CWP2), have shown promise as *Giardia* vaccine antigen candidates in murine models. The present study assesses the genetic diversity of a1-g and CWP2 between and within assemblages A and B in human clinical isolates. a1-g and CWP2 sequences were acquired from 15 Norwegian isolates by PCR amplification and 20 sequences from German cultured isolates by whole genome sequencing. Sequences were aligned to reference genomes from assemblage A2 and B to identify genetic variance. Genetic diversity was found between assemblage A and B reference sequences for both a1-g (90.8% nucleotide identity) and CWP2 (82.5% nucleotide identity). However, for a1-g this translates into only three amino acid (aa) substitutions, while for CWP2 there were 41 aa substitutions, and also one aa deletion. Genetic diversity within assemblage B was larger; nucleotide identity 92% for a1-g and 94.3% for CWP2, than within assemblage A (nucleotide identity 99% for a1-g and 99.7% for CWP2). For CWP2 the diversity on both nucleotide and protein level was higher in the C-terminal end. Predicted antigenic epitopes were not affected for a1-g, but partially for CWP2. Despite genetic diversity in a1-g, we found aa sequence, characteristics and antigenicity to be well preserved. CWP2 showed more aa variance and potential antigenic differences. Several CWP2 antigens might be necessary in a future *Giardia* vaccine to provide cross protection against both *Giardia* assemblages infecting humans.

17:30 (15 mins)

VSGs: 'you'll never express alone'. MISP, a family of metacyclic invariant surface proteins in trypanosomes - *A13013*

Presenter: **Mr Aitor Casas-Sanchez**, *PhD student, Liverpool School of Tropical Medicine*

**A Casas-Sanchez**[1]; S Perally[1]; M Boulanger[2]; A Acosta-Serrano[1];

[1] Liverpool School of Tropical Medicine, UK; [2] University of Victoria, Canada

The development of *Trypanosoma brucei* within the tsetse vector is accompanied by the expression of several stage-specific families of GPI-anchored surface glycoproteins. We recently discovered that saliva from *T. brucei*-infected tsetse flies is enriched with Brucei Alanine-Rich Proteins (BARP), VSG and a novel family of GPI-anchored surface glycoproteins. The latter are phylogenetically grouped within the Clade IV of family 50 of trypanosome surface proteins and are encoded by five paralogs, whose products are over 90% identical in sequence. Immunofluorescence and transcript analysis showed that Clade IV proteins are expressed on the surface of metacyclic trypanosomes and also on epimastigotes and pre-metacyclic forms although in lower abundance. This expression pattern opposes that of BARP, which is highly expressed in the epimastigote stage and diminishes during differentiation to metacyclics. Because Clade IV proteins are almost identical in sequence and are heavily expressed in the metacyclic stage, we named them Metacyclic Invariant Surface Proteins (MISPs). In order to gain insights into the function of MISP proteins, we expressed isoform MISP.360 and determined its crystal structure at 1.8 Ã resolution. MISP.360 adopts an extended helical bundle structure with an overall shape that highly resembles that of VSG and BARP despite their high degree of sequence divergence. Furthermore, molecular modelling studies suggest that MISP proteins are projected on top of the metacyclic VSG coat. We postulate that MISP might be important 1) to maintain the tight intermolecular packing with VSG molecules on the metacyclic surface, and 2) for parasite development in the tsetse salivary glands.

## Worms I- (Room 4 Dalhousie)

Chair - Prof Jacqui Matthews

16:15 (30 mins)

A systems biology approach linking genetic, epigenetic and holobiont inheritance to understand rapid adaptation of parasitic flatworms - *A12850*

Presenter: **Prof Christoph Grunau**, *University of Perpignan via Domitia*

**C Grunau**[1]; E Toulza[1]; C Cosseau[1];

[1] University of Perpignan via Domitia, France

The GxE concept, meaning that genoytpe x environment interactions bring about the phenotype is widely used to describe adaptation phenomena. We propose to extend the initial notion of the GxE concept, and to replace G by “Inheritance system”. This system is composed of several elements: the genotype, the epigenotype, cytoplasmic components but also microorganisms. They interact as an inheritance system with the environment, leading to the development of a phenotype. The elements of this system can be defined using their molecular composition, for instance the DNA as genetic information carrier and then the bearers of epigenetic information such as the chromatin marking system. However, it is not the system itself that generates the phenotype but the developmental process that produces over time and in interaction with the environment a phenotypic trait. In each of these processes, genetic, epigenetic and holobiont diversity can change and result in ephemeral, fluctuating or stable, i.e. heritable phenotypic variations that are important for adaptation. To understand how parasitic worms can sometimes rapidly adapt to changing environments the parasitologist must ‘simply’ define (i) the units or elements of interactions i.e. the boundaries of these elements, and (ii) the types of interactions that interrelates them. When the GxE=>P concept was introduced originally, one of the immediate practical consequences was that breeding programs should be carried out in a range of different environments. Equally, the major consequence of our systems approach to inheritance is that if one wishes to understand the heritability of a trait, all elements of the inheritance system must be analysed comprehensively using a range of different genotypes, epigenotypes and holotypes of the Inheritance System. This is, however, almost never feasible. To cope with the caveat, one should remember that the elements of the Inheritance system are operationally defined and depends on the experimenter. We believe it is legitimate to exclude (operationally) some of the elements from the experiment as long as one does not exclude them from the conclusions and generalizations, e.g. the finding that genetic variants have a strong association with a phenotype does not exclude similar or even stronger epiallelic associations and vice-versa.

16:45 (15 mins)

### Host-helminth-microbiota interactions in veterinary species - *A12931*

Presenter: **Laura Peachey**, *Postdoctoral Research Fellow, University of Cambridge*

**L E Peachey**[1]; T P Jenkins[1]; J E Hodgkinson[2]; C Cantacessi[1];

[1] University of Cambridge; [2] University of Liverpool

Gastrointestinal helminth parasites share their habitat with the commensal microbial flora. Increasing evidence, particularly in humans and rodent models of parasite infection, points towards a multitude of interactions occurring between parasites and the gut microbiota, with a profound impact on both host immunity and metabolic potential. Despite this information, the exploration of the effects that parasite infections exert on the commensal gut microbes of veterinary species is a field of research in its infancy. Given the production losses and the considerable morbidity and mortality associated with a range of helminth diseases in veterinary species, as well as the global threat of emerging anthelmintic resistance, further exploration of the complexities of their host-helminth-microbiota interactions is

indicated. In this presentation, the composition of the gut microbiota of two cohorts of thoroughbred horses with high- and low-levels of helminth infection (by cyathostomin nematodes), pre- and post-anthelmintic treatment, will be described. The data presented here will assist the identification of bacterial species that are affected by helminth infection. The implications of this newly acquired knowledge will be multiple, from a better understanding of the systems biology of parasites, to the collection of information that could prove pivotal to the development of novel intervention strategies against gastrointestinal helminths.

17:00 (15 mins)

RNA-Protein complexes involved in spliced leader trans-splicing in Nematodes could serve as a target for novel anthelmintic drugs. - *A12583*

Presenter: **Mr Rotimi Fasimoye**, *Student, University of Aberdeen*

**R Fasimoye**[1]; B Connolly[1]; J Pettitt[1]; B Muller[1]; L Philippe[3]; N Harrison[2];

[1] Institute of Medical Science, University of Aberdeen; [2] University of Birmingham; [3] Yale University, United States

_Worldwide more than two billion people are infected with parasitic nematodes and there are a limited number of drugs available to treat these debilitating diseases. This is becoming a pressing issue since many of the drugs available are losing their efficacy due to the development of resistance in the target nematode populations. There is thus a need to develop new drugs to treat nematode infections. In addition, resistance is always likely to be an issue until the nematode parasites are completely eradicated (an unlikely event for most species), so any new drugs should be designed to limit the development of this resistance. This is most easily achieved by targeting an essential biological process, rather than a specific molecule. In addition, this process should be essential for the viability and/or reproduction of all parasitic nematodes, and not present in the human hosts. Spliced leader (SL) trans-splicing, an essential process in nematodes that is absent in the vertebrate host, has been identified has a possible target for new anthelmintics. The precise molecular mechanism of SL trans-splicing as well as all its molecular components is not yet understood. To further characterise the process we have developed an *in vivo*, GFP-based reporter assay that is able to monitor SL trans-splicing *in vivo* in *Caenorhabditis elegans*. Using this assay we demonstrate that SNA-1, SNA-2 and SUT-1, proteins known to associate with SL RNA and related SmY RNAs, are required for efficient SL trans-splicing. It has been shown by others that SL RNA is part of an snRNP, and associates with Sm proteins. We were able to demonstrate that pICln, SMN and Gemin5 involved in snRNP assembly contribute to SL trans-splicing. We believe that a compound that can act as antagonist to two or more of these SL trans-splicing components will effectively shut down the process and such compound may be a good anthelmintic candidate.

17:15 (15 mins)

Developmental regulation of miRNA secretion in the filarial nematode *Litomosoides sigmodontis* - *A12950*

Presenter: **Mr Juan Quintana**, *The University of Edinburgh*

**J Quintana**[1]; S A Babayan[2]; P Dickinson[1]; A Ivens[1]; A H Buck[1];
[1] The University of Edinburgh; [2] University of Glasgow

The secretion of extracellular RNAs (exRNAs) by parasitic nematodes has opened new avenues for the development of novel biomarkers for helminthiasis, including filariasis. These are catalogued as some of the major neglected tropical diseases, which together account for more than 120 million infections in tropical and subtropical regions. One outstanding question is whether the secretion of small RNAs is developmentally regulated in parasitic nematodes. Here, we present *in vivo* and *in vitro* data that show the presence of ubiquitous, as well as sex- and potentially stage-specific miRNA markers in Excretion/Secretion (ES) products from larval and adult stages from the rodent filarial nematode *Litomosoides sigmodontis*. Moreover, a subset of these miRNAs, including female-specific miRNA markers, are found in biofluids from infected vertebrate hosts, including gerbils, mice, cattle and humans. Using infected BALB/c mice as a model for filarial infection, we tested the performance of a subset of parasite-derived miRNAs as biomarkers, and significantly discriminated between infected animals and naive controls with high sensitivity (~80%) and specificity (100%). Taken together, our data constitute the first report of a comprehensive and detailed characterisation of the miRNA secretion throughout filarial development *in vitro* and *in vivo*, and provide strong evidence to support the development of biomarkers to detect ongoing infections, including the presence of reproductively active female worms.

17:30 (15 mins)

## Neoblast-like cell dynamics and growth in the liver fluke *Fasciola hepatica - A12962*

Presenter: **Miss Erica Gardiner**, *PhD student, Queens University Belfast*

**E Gardiner**[1]; P McVeigh[1]; P McCusker[1]; A Mousley[1]; N J Marks[1]; A G Maule[1];
[1]Queen's University Belfast,, UK

*Fasciola hepatica* (liver fluke) infections of livestock challenge food production systems globally. Control relies heavily upon the drug triclabendazole, but this over reliance has led to widespread issues of resistance. Key players involved in fluke growth appear to be proliferative cells that are neoblast-like. Neoblasts play a major role within free living planarian flatworms where they facilitate their remarkable regenerative abilities, however their roles in parasitic flatworms are less well established. We have identified proliferative 'neoblast like' cells within both juvenile and adult *Fasciola hepatica*. This project sets out to characterise these cells and their regulators to develop an understanding of their role and significance to fluke biology. Here these proliferative cells have been localised in juvenile fluke at various stages of development and under distinct nutritional environments to examine their dynamics. Two day old juveniles maintained in nutrient-rich media had ~2x more proliferative cells than juveniles in unsupplemented media. By seven days of age juveniles in nutrient rich media had >90% more proliferative cells than juveniles maintained in standard media, exposing the dramatic impact of serum on cell proliferation in growing juveniles. Profound differences were observed in the dynamics of neoblast-like cells in juveniles at different stages of development and in *in vivo* compared to *in vitro* maintained juveniles, consistent with the notable

differences in the growth rates of these two groups. An underpinning hypothesis is that these cells are somatic stem cells which fulfil similar roles to those reported in the related blood fluke, *Schistosoma mansoni*. These cells could be valuable as a source for new control targets due to their integral role in parasite growth, development and virulence.

# Tuesday April 4th Apex Hotel & University of Dundee(Dalhousie)

## Plenary II

Chair - Prof Mark C. Field

09:00 (40 mins)

### Immunology informing malaria prevention, treatment and control - *A12734*

Presenter: **Prof Eleanor Riley**, *Professor of Immunology, LSHTM*

**E Riley**[1]

[1]London School of Hygiene and Tropical Medicine

A fundamental understanding of the nature of the immune response to infection, the target antigens and the most protective effector mechanisms, is essential for rational vaccine design. But the insights gained from this immunological understanding can contribute so much more. Immunology contributes to our understanding of disease pathogenesis, resistance and resilience to infection, and the epidemiology of both infection and disease. In this presentation, I will illustrate the ways in which our gradually increasing understanding of malaria immunology over the last 30 years is now helping to inform not just the design and implementation of vaccines, but also helping to identify new treatment and prevention options and to monitor the progress of malaria control interventions.

09:40 (40 mins)

### The complexity and the simplicity of host-Plasmodium interactions - *A12733*

Presenter: **Prof Maria M Mota**, *Instituto de Medicina Molecular, Portugal*

**M Mota**;

[1] Instituto de Medicina Molecular, Portugal

Despite renewed eradication efforts from the international community, malaria still exerts an enormous disease burden, with nearly half the planet's population at risk of infection. Within the human host, the disease-causing Plasmodium parasites pass through two distinct lifecycle stages, each in a different cellular environment. During the liver stage, a single Plasmodium sporozoite will invade a hepatocyte, and while sheltered there, supposedly undetected by the host, gives rise to thousands of new parasites, which will go on to initiate the subsequent blood stage of infection. While only 10-20 new parasites will be generated inside an erythrocyte, consecutive cycles of cell lysis and reinfection causing a potent host response, as well as the symptoms of malaria. The host contribution to

infection outcome, on both the cellular and organismal levels has recently moved to center stage. We have identified hepatocyte molecules that modulate the success of liver stage infection, and showed that distinct host factors, not just the parasite itself, drive the onset and severity of diverse malaria syndromes. Our ongoing work indicates that the web of host-Plasmodium interactions is densely woven, with liver stage-mediated innate immune system activation, host nutritional status, and an antagonistic relationship between the two parasite stages themselves all working to modulate the balance between parasite replication and human health.

## Molecular Cell biology I- (Room 1 Apex)

Chair - Prof Matthias Marti

11:00 (30 mins)

### Trypanosoma brucei metabolism is under circadian control- *A12738*

Presenter: **Luisa Figueiredo**, *Group Leader, Instituto de Medicina Molecular Lisboa*

**L Figueiredo**[1]

[1]Instituto de Medicina Molecular Lisboa

The Earth's rotation forced life to evolve under cyclic day and night environmental changes. To anticipate such daily cycles, prokaryote and eukaryote free-living organisms evolved intrinsic clocks that regulate physiological and behavioural processes. Daily rhythms have been observed in organisms living within hosts, such as parasites. Whether parasites have intrinsic molecular clocks or whether they simply respond to host rhythmic physiological cues remains unknown. Here, we show that Trypanosoma brucei, the causative agent of human sleeping sickness, has an intrinsic circadian clock that regulates its metabolism in two different stages of the life cycle. We found that, in vitro, ~10% of genes in T. brucei are expressed with a circadian rhythm. The maximum expression of these genes occurs at two different phases of the day and may depend on a post-transcriptional mechanism. Circadian genes are enriched in cellular metabolic pathways and coincide with two peaks of intracellular adenosine triphosphate concentration. Moreover, daily changes in the parasite population lead to differences in suramin sensitivity, a drug commonly used to treat this infection. These results demonstrate that parasites have an intrinsic circadian clock that is independent of the host, and which regulates parasite biology throughout the day

11:30 (15 mins)

### Glycosomal hypertrophy and the response to suramin in African trypanosomes - *A12995*

Presenter: **Martin Zoltner**, *Senior Research Associate, University of Dundee*

**M Zoltner**[1]; S Vaughan[2]; C Gadelha[3]; K F Leung[4]; L S Guther[4]1 A Burrell[2]; L Ali[1]; M A Ferguson[1]; M C Field[1];

[1] Wellcome Trust Centre for Anti-Infectives Research, School of Life Sciences, University of Dundee, UK; [2] Department of Biological and Medical Sciences, Oxford Brookes University, Oxford, UK; [3] Queen's Medical Centre, University of Nottingham, Nottingham, UK; [4] Department of Pathology, University of Cambridge, UK;

Suramin, a key trypanosomiasis drug developed over a century ago, remains in the clinic for treatment of early stage disease, while its mode of action is elusive. Recent studies suggest a prominent role of endocytosis for suramin uptake and we investigated the effect of

suramin on *Trypanosoma brucei* at the ultrastructural level using transmission and serial-block-phase scanning electron microscopy. After two days of suramin treatment, cells begin to exhibit morphological abnormalities, which included enlargement of the flagellar pocket. However, the most striking alteration was a significant increase in the volume of glycosomes. Surprisingly, suramin did not lead to a corresponding increase of glycosomal proteins, but a decrease in the glycosomal UDP-glucose 4'-isomerase TbGalE and homologs of peroxisome biogenesis factors 2 and 12. The most prominent protein abundance changes were upregulation of the plasma membrane glucose transporter THT1 and a protein cohort involved in differentiation to stumpy form, including PAD isoforms and the receptor-type adenylyl cyclase GRESAG4. Analysis of sugar nucleotide pools revealed reduced levels of UDP-α-D-N-acetylglucosamine upon suramin treatment, while the four remaining sugar nucleotides were not significantly perturbed. Our data identify for the first time a specific metabolic process impacted by suramin.

11:45 (15 mins)

Defining exosome function in *Theileria annulata* infection: a parasite which drives host cell metastasis - *A12873*

Presenter: **Victoria Gillan**, *Research Associate, University of Glasgow*

**V Gillan**[1]; B Shiels[1]; J Kinnaird[1]; E Devaney[1];
[1] University of Glasgow , UK

The protozoan parasite, *Theileria annulata* is the causative agent of tropical theileriosis, a disease of cattle that is often severe and can be fatal. One of the most interesting features of the *T. annulata* infection cycle is its phase of neoplastic growth with similarity to cancer progression. *In vivo,* infected leukocytes become highly metastatic, and subsequent disorganisation and destruction of the lymphoid system occurs. As evidence from cancer biology has shown, metastasis is a highly complex process and although the pathogenic events have been defined, the mechanisms that initiate and drive metastasis are still largely unresolved. The study of extracellular vesicles (EV) has revealed that intercellular communication is critical for metastatic progression, and that the release of exosomes from tumour cells into the micro-environment induces pre-metastatic niche formation. It is intriguing to consider that exosomes derived from *T. annulata* infected cells may transfer proteins, soluble factors, mRNA, and microRNAs (miRNAs) to recipient cells and therefore may be involved in altering adaptive immune responses or have a role in migration and invasion of infected cells. To investigate the role of EV in this system we carried out mass spectrometry and miRNA profiling on EV from a bovine lymphosarcoma cell line (BL20) and the same cells infected with *T. annulata* (TBL20). The results demonstrate a very different protein profile in EV from TBL20 cells. Differentially regulated proteins were analysed using Ingenuity Pathway Analysis, revealing that many infection associated proteins and molecules shown to be essential for migration and extracellular matrix digestion in other systems are also up-regulated in TBL20 cells. miRNA sequencing of EV revealed a dysregulated repertoire of six miRNA, each with a known role in tumour biology. EV transfer experiments are underway to define the role EV transfer experiments are underway to define the role of TBL20 EV in reprogramming events within a recipient control cell. These results will give insight into the role of EV in the development of this unique infection process.

12:00 (15 mins)

A putative ATP/GTPase influences virulence of *Leishmania mexicana - A12897*

Presenter: **Dr Vyacheslav Yurchenko**, *Assoc Professor, University of Ostrava*

**V Yurchenko**[3]; A Ishemgulova[3]; N Kraeva[3]; J Hlavá ová[1]; A Butenko[3]; T Leštinová[1]; J Lukeš[2]; A Kostygov[3]; J Votýpka[1]; P Volf[1];
[1] Charles University, Czech Republic; [2] Institute of Parasitology, Biology Centre, Czech Republic; [3]University of Ostrava, Czech Republic

In this work we investigated ALV1, a putative factor governing virulence in *Leishmania mexicana*. The gene encoding this protein, *LmxM.30.2090* is located on chromosome 30, previously shown to be enriched in amastigote-specific genes. We demonstrated that ALV1 is involved in virulence in both mouse and insect models. It appears to be deeply wired into the metabolic networks of *Leishmania* as seen from changes in the expression of other genes upon its ablation. The acquisition of this gene by the common ancestor of Leishmaniinae suggests a primary role in the infection of insects.

12:15 (15 mins)

**New Class of Nucleotide Sugar Transporter inTrypanosome Peroxisome**

Presenter**: Lucia Guther.** *University of Dundee*

**L S Guther**[1]; A Prescott[2]; D Wu[3]; L Ali[1]; M Tinti[1]; M A Ferguson[1];
[1] Biological Chemistry and Drug Discovery, School of Life Sciences, University of Dundee; [2] School of Life Sciences University of Dundee; [3] University of Oxford

Trypanosoma brucei expresses essential N--glycosylated and GPI anchored glycoproteins, eg. the variant surface glycoprotein (VSG) and the transferrin receptor (TfR). Glycosylation pathways require nucleotide sugars (NS). NS biosynthesis in T. brucei, uniquely, takes place inside of peroxisomes, which in these organisms are called glycosomes. We are characterizing new class of nucleotide sugar transporters (gNST) present on the membrane of these organelles, which were discovered by High confidence SILAC glycosome proteome and RNAi knock--down followed by VSG glycosylation phenotyping and nucleotide sugars quantitation by mass spectrometry. These glycosome NST allow NS to reach cytosol and ultimately to be taken up by traditional NST present on ER and Golgi.

## Epidemiology I- (Room 2 Apex)

Chair - Prof George Christophides

11:00 (30 mins)

The importance of parasite density in malaria transmission - *A13171*

Presenter: **Dr Thomas Churcher**, *Lecturer in Infectious Disease Dynamics, Imperial College London*

**T S Churcher**[1];
[1] MRC Centre for Outbreak Analysis and Modelling, Imperial College London, UK

It has traditionally been assumed that malaria transmission depends on the on the presence/absence of infectious parasite in hosts or vectors and not the number of parasites harboured. This talk outlines the growing body of evidence which suggests parasite density is important in both human-to-mosquito and mosquito-to-human transmission and that density-dependent processes increase the resilience of the disease to control interventions. Using data from experimental infectious of human and mice it will investigate how parasite density influences the effectiveness of pre-erythrocytic and transmission blocking malaria vaccines currently under development. The epidemiological importance of parasite density shall be assessed to see how it will change the way we measure transmission and target malaria elimination.

11:30 (15 mins)

Cross-border malaria and new challenges to Thai national malaria control programme - *A12865*

Presenter: **Dr. Wirichada Pan-ngum**, *Mathematical Modeller, Mahidol University*

**W Pan-ngum**[3];**S Saita**[3]; J Boondam[1]; L J White[2]; D M Parker[4];
[1] Chulalongkorn University, Thailand; [2] Mahidol - Oxford Tropical Medicine Research Unit, Thailand; [3]Mahidol University, Thailand; [4] Shoklo Malaria Research Unit, Thailand

In order to achieve the target to completely eliminate *Plasmodium falciparum* malaria from the world by 2030, global financing for malaria control has been increased from an estimated US$ 960 million in 2005 to US$ 2.5 billion in 2014. The success was evident when global malaria incidence and mortality have significantly decreased in the past decade and many countries are now moving toward malaria elimination. In Thailand, malaria cases are highly seasonal and mostly clustered along international borders. Malaria case numbers along the Thai-Myanmar border are consistently high, accounting for almost half of all cases. To study the malaria situation in the region, we focus on three main questions i) What are the levels of malaria transmission in Mae Hong Son and Tak, two provinces with different cross-border settings between Thai and Myanmar. ii) How are they different in term of population demographics and movement, vector characteristics, environment and existing malaria control programmes. iii) How population movement influences malaria transmission or malaria re-emergence in these settings and what are potential recommendations to maintain free-malaria status during the post-elimination phase. We plan to take up a multidisciplinary approach using field surveys to collect population movement data and effectiveness of current interventions and retrieve secondary data of malaria, populations and environmental determinants. Statistical and mathematical modelling will be applied to identify geographically varying predictors, assess impacts of population movement on malaria incidence and work out optimal strategies for preventing the resurgence of indigenous cases after elimination. As an ongoing project, the study plan and some primary observations will be presented.

11:45 (15 mins)

Contribution of *Plasmodium knowlesi* to multi-species human malaria infections in North Sumatera, Indonesia. - *A13009*

Presenter: **Colin Sutherland**, *Reader in Parasitology, London School of Hygiene & Tropical Medicine*

**C J Sutherland**[1]; I N Lubis[1];
[1] London School of Hygiene & Tropical Medicine, UK

As Indonesia works towards the goal of malaria elimination, information is lacking on malaria epidemiology from some western regions. As a basis for studies of antimalarial efficacy, we set out to survey parasite carriage in three communities in North Sumatera Province. Methods. A combination of active and passive detection of infection was carried out among communities in Batubara, Langkat and South Nias regencies. Finger-prick blood samples from consenting individuals of all ages provided blood films for microscopic examination and blood spots on filter paper. *Plasmodium* species were identified by nested PCR of rRNA genes, and a novel assay which amplifies a conserved sequence specific for the sicavar gene family of *P. knowlesi.* 614 of 3,731 study participants (16.5%) were positive for malaria parasites by microscopy. PCR detected parasite DNA in samples from 1,169 individuals (31.3%). In total, 377 participants (11.8%) harboured *P. knowlesi.* Also present were *P. vivax* (14.3%), *P. falciparum* (10.5%) and *P. malariae* (3.4%). we conclude that amplification of sicavar is a specific and sensitive test for the presence of *P. knowlesi* DNA in humans. Subpatent and asymptomatic multi-species parasitaemia is relatively common in North Sumatera, and so PCR-based surveillance is required to support control and elimination activities. Our results will be discussed in the general context of persistent complex parasitaemia in asymptomatic primate hosts.

12:00 (15 mins)

Assessing the impact of intervention strategies against *Taenia solium* cysticercosis using the EPICYST transmission model - *A12968*

Presenter: **Mr Matthew Dixon**, *PhD Student, Imperial College London*

**M A Dixon**[1]; P Winskill[1]; W E Harrison[1]; M D French[1]; B Abela-Ridder[2]; M G Basáñez[1];
[1] Imperial College London; [2] World Health Organisation, Switzerland

The cestode parasite**,** *Taenia solium* is the causative agent of taeniasis, cysticercosis and neurocysticerosis in humans, which cause a significant public health burden in low and middle -income countries. Under the World Health Organization 2012 roadmap on Neglected Tropical Diseases (NTDs), *T. solium* taeniasis/cysticercosis has been prioritised as one of 17 key NTDs, targeted with the aim of achieving control and elimination in selected countries by 2020. We have developed a deterministic, compartmental transmission model (EPICYST) to capture the dynamics of the taeniasis/cysticercosis disease system in both the human and pig hosts alongside parasite transmission stages in the environment. EPICYST was used to compare the effectiveness of a range of human-, porcine-, and environment-targeted interventions. Model outputs indicate that annual chemotherapeutic intervention targeted at humans or pigs would be highly effective at reducing taeniasis and cysticercosis prevalence. Improved sanitation, meat inspection, and animal husbandry are less effective but are still able to reduce prevalence singly or in combination. We will also discuss ongoing refinements of EPICYST, including model fitting to longitudinal epidemiological data in distinct epidemiological settings.

12:15 (15 mins)

Identifying priority areas for sleeping sickness control: Spatial modelling in the Democratic Republic of Congo - *A12956*

Presenter: **Dr Kat Rock**, *Postdoc researcher, Warwick University*

**K S Rock**[1]; M J Keeling[1];
[1] University of Warwick

Human African trypanosomiasis (HAT, sleeping sickness) is a virulent vector-borne disease that has experienced a global decline in cases in recent years, but pockets of infection still persist, particularly within the Democratic of Congo (DRC), which had over 80% of all cases in 2014. In order to achieve the 2020 WHO goal of elimination as a public health problem, it is important to quantitatively estimate how intervention strategies could impact HAT in these regions. Using spatial mathematical modelling, the past impact of medical-only interventions in two previously high-burden provinces was assessed. Model predictions of intervention strategies, including different screening coverages and new vector control, were simulated. The results indicate that there are many areas within the provinces which may require no additional interventions to locally achieve the 2020 elimination target, particularly in former Equateur province which is largely on track. However, some crucial areas are identified as potentially missing this target without an improved strategy. In regions with persistent disease, vector control was found to be a promising method to reduce transmission quickly.

## Veterinary & Ecology I- (Room 3 Dalhousie)

Chair – R Wall

11:00 (30 mins)

### Progress with understanding the trout-PKD interaction: host immunity and parasite gene expression. - *A12741*

Presenter: **Prof Christopher Secombes**, *Regius Professor of Natural History, University of Aberdeen*

**C Secombes**[1]
[1]University of Aberdeen

Proliferative kidney disease, caused by the myxozoan parasite *Tetracapsuloides bryosalmonae*, is a major disease issue for farmed rainbow trout in the UK. The parasite is now recognised as a Cnidarian, and so the host-parasite interaction is relatively unique. Fish can become immune to the disease if they survive a first infection, and we have studied the immune responses elicited in both naive and re-exposed fish to shed light on this phenomenon. In addition, we have used transcriptomic approaches to study the parasite genes expressed in trout with a view to identify vaccine candidates. This talk will outline the results to date, indicating that a dysregulation of immunity occurs post-infection, and that host specific gene expression can be identified in the parasite.

11:30 (30 mins)

### Mapping triclabendazole resistance in *Fasciola hepatica*: what do we know so far? - *A12742*

Presenter: **Prof Jane Hodgkinson**, *University of Liverpool*

**J Hodgkinson**[1]
[1]University of Liverpool

The liver fluke, *Fasciola hepatica* is an economically important trematode parasite pathogen of livestock that frequently impacts on the health and welfare of cattle and sheep worldwide and is regarded by the WHO as a re-emerging zoonosis. With predictions for further increases in the prevalence of infection due to a changing climate, increased animal movement and changes in land management *F. hepatica* infection is likely to have a substantial impact on livestock production and human health in future. Control of *F. hepatica* relies heavily on drug treatment, in particular the drug triclabendazole (TCBZ), which targets the highly pathogenic juvenile fluke migrating through the liver. However, as with many helminth parasites drug resistance has emerged and is now considered a substantial threat to sustainable liver fluke control. By studying naturally infected sheep and cattle in the UK we have identified high levels of genetic diversity in populations of liver fluke; genetic variation that poses a challenge to identifying the underlying genetic and molecular basis of drug resistance. Similarly, the fact that liver fluke are hermaphrodites capable of self-fertilization and that a clonal expansion occurs in the snail intermediate host, raises questions about how parasite biology influences the spread of drug resistance genes. This paper will report a series of studies we have taken to better understand the genetic basis of TCBZ resistance in *F. hepatica*. We have used single miracidial:snail infections of *F. hepatica* to generate and characterise clonal parental lines of TCBZ-resistant (TCBZ-R) and TCBZ-susceptible (TCBZ-S) liver fluke. In order to identify areas of the genome with signatures of drug selection we have taken an experimental approach by crossing TCBZ-S and TCBZ-R clones and whole-genome mapping of TCBZ-R genes through subsequent F1 and F2 populations. These parental clones have been used to derive F1 progeny using a panel of neutral microsatellite markers to track those parasites that had undergone cross fertilization between -R and -S parasites and to allow subsequent identification of F2 recombinants. By comparing the frequency of SNP alleles derived from the resistant parental clone and linked to the TCBZ resistance loci in pooled, phenotyped F2 recombinants we have localised regions of the genome under selection. Our concurrent population genetic studies have provided insights into how, once drug resistance is present, it may disperse through parasite populations infecting sheep and cattle in the UK.

12:00 (15 mins)

Upsetting the protease/anti-protease balance could be a novel vaccine strategy against *Fasciola hepatica* infection - *A12942*

Presenter: **Orla Drysdale**, *PhD Student, Queen's University Belfast*

**O C Drysdale**[1]; D Smith[1]; H Jewhurst[1]; K Cwiklinski[1]; J P Dalton[1];
[1] Queen's University Belfast

The liver fluke, *Fasciola hepatica* is a pathogen of economic significance in ruminants, such as sheep and cattle worldwide and is now recognised as an important zoonosis. Due to over-reliance on anthelmintics, drug-resistant parasites have emerged, meaning that new control strategies are required. Vaccine development is becoming a greater focus of current research. *Fasciola hepatica*-expressed molecules that act at the host-parasite interface, modify host cell function and aid parasite development and survival are therefore of major interest as vaccine targets. Based on recent genome and associated stage specific transcriptome/proteome analysis, we have identified a number of molecules as potential vaccine candidates including cystatin and kunitz-type protease inhibitors. We have

successfully expressed these inhibitors in *Pichia pastoris*, achieving a high purity and yield. Extensive characterisation of these inhibitors revealed that the cystatins are broad range inhibitors of both host and parasite cysteine proteases compared with the kunitz-type inhibitor that shows specific inhibition of cathepsin L type proteases. The protease/anti-protease balance may be critical in the regulation of parasite processes including penetration, feeding, development and immune evasion, as well as modulation of host innate cell proteases involved in antigen processing and presentation. The potential of upsetting this balance is currently being assessed in sheep vaccine trials.

12:15 (15 mins)

### Innate immune response in intracellular parasitic (*Neospora caninum*) infection of cattle - *A12698*

Presenter: **Parul Sharma**, *PhD Student, University of Nottingham*

**P Sharma**[1,2]; S Egon[2]; R Flynn[1];
[1] University of Liverpool; [2] University of Nottingham;

*Neospora caninum* is an intracellular protozoan parasite which causes abortion in cattle and neuromuscular disease in dogs. Bovine infection can be initiated *in utero* or after birth through ingestion of infectious material. Our previous studies have shown differences in young monocytes compared to adult cells in terms of cytokine responses and expression of CD80. In this study we investigated if there was an age dependent effect on invasion of monocytes and their subsequent interaction with NK cells during *N. caninum* infection. NCLiv-1 isolate of *N. caninum* was maintained in a VERO cell line. Naive $CD14^+$ and NK-cells were isolated from peripheral blood mononuclear cells (PBMCs) from young and adult cattle by magnetic cell separation. Monocytes were sequentially infected with *N. caninum* CFSE labelled tachyzoites before co-culture with NK cells. The number of infected cells was determined post-culture and CD80 expression, as a marker of cellular activation, was determined by flow cytometry. There was an age-related variation in infection of monocytes with cells derived from old animals more likely to harbour greater numbers of parasites. A reduction in parasite numbers post culture with NK cells was noticed in both young and adult cattle with increased CD80 expression also observed. The greater uptake of parasites into monocytes in combination with NK-cell interaction inhibits parasite multiplication and may be one mechanism to explain the age-related differences in innate immune response to intracellular parasitic (*N. canium*) infection.

## Worms II- (Room 4 Dalhousie)

Chair - Prof John Dalton

11:00 (30 mins)

### Trials and tribulations: the highs and lows of nematode sub-unit vaccine development - *A12745*

Presenter: **Prof Jacqui Matthews**, *Moredun Research Institute*

**J Matthews**[1];
[1] Moredun Research institute, UK

In spite of years of research, commercially viable recombinant sub-unit vaccines against parasitic nematodes have yet to be realised. This talk details progress in development of a recombinant vaccine for control of *Teladorsagia circumcincta*, the major parasitic nematode of small ruminants in temperate regions. The vaccine is based on antigens selected using both immune-proteomic and functional analysis of worm excreted/secreted molecules. An eight-protein cocktail has now been tested in sheep on several occasions and parasitological and immunological parameters compared in immunised versus control sheep subjected to repeated infections designed to mimic field conditions. Varying levels of protection have been observed in the different trials, with variation within and between groups identified. This presentation will cover the antigen selection strategy, the immunisation trials and the recent immunological and transcriptomic analyses that have been undertaken to try identify sources of variation in vaccine responsiveness. Steps being taking to optimise the prototype to mitigate variation in responsiveness and to improve the vaccine's commercial viability will also be described.

11:30 (15 mins)

Profiling the surface-exposed proteins of *Fasciola hepatica* extracellular vesicles - *A12970*

Presenter: **Dr Eduardo de la Torre Escudero**, *Research Fellow, Queen's University Belfast*

**E de la Torre-Escudero**[1]; A Bennett[1]; M Robinson[1];
[1] Queen's University Belfast

Helminth parasites release extracellular vesicles (EVs) that can transfer a range of effector molecules to host cells. Several studies have described the contribution of parasite-derived EVs to the modulation of the host immune system or the pathological effects on host cells. However, the mechanisms of interaction/internalisation between parasite-derived EVs and host cells remain elusive and a better understanding of these processes may open new avenues for parasite control. We recently showed that *Fasciola hepatica* releases an EV population loaded with various internal cargo proteins, including several known immunomodulators. Here, we have used a membrane-impermeable biotin to label proteins specifically exposed on the outer surface of the parasite vesicles. Following streptavidin pulldown and mass spectrometry we identified a number of protein functional groups, including membrane pumps, tetraspanins, integrins as well as trematode-specific antigens that detail EV surface architecture but may also provide insight into how parasite-derived EVs interact with host cells. Experiments are currently underway to investigate the role of the surface-exposed proteins and whether these could be targeted by novel anti-parasite therapies.

11:45 (15 mins)

Probing the pathways of extracellular vesicle biogenesis in helminth parasites - *A12946*

Presenter: **Mr Adam Bennett**, *PhD student, School of Biology, Queen's University Belfast*

**A Bennett**[1]; E de la Torre-Escudero[1]; M W Robinson[1];
[1] Queen's University Belfast

Extracellular vesicles (EVs) released by helminths are now recognised as major players at the host-parasite interface. However, there is a limited understanding of the molecular machinery controlling their production. Here, we address this using a comparative genomics approach. From an extensive search of the literature, corroborated with helminth EV proteomic data, we identified 104 putative EV

biogenesis proteins and used these to interrogate a variety of helminth genomes. We have found that whilst subunits of the Endosomal Complex Required for Transport (ESCRT) pathway are broadly conserved across most helminths, sequence analysis reveals significant differences in the domains required for interactions between pathway members. As part of our genomic analysis we have identified a trematode-specific EV marker (tetraspanin) that is localised to a vesicle population associated with the gastrodermal cells of *Fasciola hepatica*. Further localisation studies demonstrate differing spatial expression patterns of two classic exosomal markers involved in the ESCRT pathway, supporting the notion that a non-canonical ESCRT pathway could exist in helminths. From this work, we infer that ESCRT-dependent pathways have the potential to operate in helminths, including species in which the release of EVs has yet to be described, and reveal putative sites of EV biogenesis in *F. hepatica*. In doing so, we provide a platform to investigate EV production in helminths using functional studies.

12:00 (15 mins)

Genetic variation associated with parasite-specific immune responses in a wild mammal population - *A12910*

Presenter: **Miss Alexandra Sparks**, *PhD student, University of Edinburgh*

**A M Sparks**[2]; K A Watt[2]; R Sinclair[2]; J G Pilkington[2]; J M Pemberton[2]; T N McNeilly[1]; S E Johnston[2]; D H Nussey[2];
[1] Moredun Research institute; [2] University of Edinburgh

An individual's immune response to parasite challenge is key to determining susceptibility to infection, but the genetic and environmental sources of variation underlying immune responses have rarely been examined under natural infection conditions in the wild. The wild Soay sheep population on St Kilda have been the focus of an individual based study for over 30 years and are heavily infected with strongyle gut nematodes. This population offers an excellent opportunity to investigate the causes of variation in parasite-specific immune responses in the wild. We assayed a total of 6,543 plasma samples from 3,190 sheep caught in August between 1990-2015 for levels of IgA, IgE and IgG antibodies against the prevalent nematode *Teladorsagia circumcincta*. A quantitative genetic approach was used to partition the phenotypic variance in parasite-specific antibody levels. All three antibody levels were highly repeatable across an individual's lifetime and significantly heritable ($h^2$: IgA: 0.36±0.03; IgE: 0.19±0.02 and IgG: 0.17±0.02). In addition, a genome wide association study found that IgA levels were associated with single nucleotide polymorphisms on a region of chromosome 24. Our results suggest that immune responses are fairly stable across time within individuals, and this stability is determined in part by genes. We have also identified a rare example of a particular genomic region explaining variation in an immune measure in the wild.

12:15 (15 mins)

The host ration affects plerocercoid growth in three-spined sticklebacks infected with *Schistocephalus solidus* (Cestoda: Diphyllobothriidae) - *A12979*

Presenter: **Mr Awad Hosan**, *Phd student,Uuniversity of Leicester*

**A Hosan**[1]; I Barber[1];
[1] University of Leicester

Host dietary factors, including the quantity and quality of food ingested, have considerable potential to influence the outcome of host-parasite interactions. For example, increased food intake may improve resistance to parasite infections if it improves host immune responses; however, it could alternatively increase the supply of nutrients available to parasites, benefiting parasite growth and development. The aim of this study was to investigate the effects of host ration on the growth of *Schistocephalus solidus* plerocercoids in experimentally infected three-spined sticklebacks *Gasterosteus aculeatus*. Lab-bred sticklebacks were either exposed to infective stages of *S. solidus* by feeding them copepods containing infective parasites, or were sham-exposed. Experimental fish were subsequently fed either a high ration or a reduced ration (6% or 3% body weight per day respectively) for a period of 12 weeks. At the termination of the study, fish were dissected and a range of indices of fish growth, energetic status, health and infection status were quantified. Our results indicate that the level of host ration plays an important role in the value of the indices and suggest that host ration had a significant effect on the performance of both infected and non-infected fish in the study.

## Molecular Cell biology II- (Room 1 Apex)

Chair - Dr Nicolai Siegel

14:15 (30 mins)

### Biology of malaria transmission in an era of elimination - *A12739*

Presenter: **Prof Matthias Marti**, *University of Glasgow*

**M Marti**[1]
[1]University of Glasgow

Targeting malaria transmission is key to elimination, yet the underlying biology of these gametocyte stages is poorly understood. We are focusing our efforts towards investigating how the malaria parasite regulates the rate of gametocyte formation to ensure transmission, and how these stages sequester during their long development before being released into the blood stream for subsequent mosquito transmission. For these studies we are performing comparative investigations in infected humans and animal models of malaria.

14:45 (15 mins)

### The putative structure of *Trypanosoma congolense* strain IL3000 mini-chromosomes - *A12997*

Presenter: **Mr Ali Abbas**, *PhD student, Institute of integrative biology/Department of functional and comparative genomics*

**A H Abbas**[1]; N Hall[2]; C Hertz-Fowler[1]; A C Darby[1];
[1] University of Liverpool; [2] Earlham Institute;

_Trypanosome Mini-chromosomes (MCs) are important genomic regions as these chromosomes carry genes that help the parasite to avoid the host immune system. MCs of *Trypanosoma brucei* range in their size from (30 to 100 kbp). However, the sequence of *T. congolense* MCs is presently not known. To unravel the nucleotide sequence of these regions, we used PACBIO single-molecule real-

time sequencing to sequence *T. congolense IL3000* gDNA. We generated 1.7 Gb of PACBIO reads with an average read length of 8kb, and assembled with HGAP v3 into 1541 contigs, with a total assembly size of ~39Mbp, contig $N_{50}$ 156kb, max contig length 1.4Mb. Seven putative complete *T. congolense* MCs (TcMCs) were identified and 60 partial TcMCs. The structure of the TcMCs can be simplified and subdivide into four regions: 1. A central palindromic repeat with a ~369bp repeating unit, which represents 32% - 65% of the total length of the TcMC, 2. A conserved GC rich sequence of 1.5 - 2kbp, 3. Variable subtelomeric region stretched of ~5Kbp which can contain a number of features which include variant surface glycoprotein (VSG) genes and 4. Telomeric repeats. The results suggest that the subtelomeric region 3 are highly variable and carrying expression site association genes (ESAG), VSG or DEAH/D box RNA helicase genes. Our findings also suggest that the length of the TcMCs depends on the length of the central palindromic repeat region.

15:00 (15 mins)

Single-molecule analysis reveals that DNA replication dynamics vary across the course of schizogony in the malaria parasite *Plasmodium falciparum*. *- A12934*

Presenter: **Dr Catherine Merrick**, *Senior Lecturer, Keele University, Keele University*

**C J Merrick**[1]; S Stanojcic[2]; N Kuk[2]; I Ullah[1]; Y Sterkers[2];
[1] Keele University, UK; [2] University of Montpellier and Centre Hospitalier Universitaire, France

The mechanics of DNA replication and the cell cycle have been well characterized in model organisms, but less is known about these basic aspects of cell biology in apicomplexan parasites, which do not divide by canonical binary fission but undergo unconventional cell cycles. Schizogony in *Plasmodium* generates ~16-24 new nuclei *via* independent, asynchronous rounds of genome replication prior to cytokinesis, and little is known about the control of DNA replication facilitating this mode. We have characterised DNA replication dynamics in *P. falciparum* throughout schizogony, using DNA fibre labelling and combing to visualise replication forks at a single-molecule level. We show that replication origins are very closely spaced in *Plasmodium* compared to most model systems, and that replication dynamics vary across schizogony, with faster synthesis rates and more widely-spaced origins in early trophozoites, versus slower synthesis and closer-spaced origins later on. This is the opposite of the pattern usually seen across S-phase in human cells, when a single genome is replicated. Replication forks also stall at an unusually high rate throughout schizogony. Our work explores DNA replication in *Plasmodium* in unprecedented detail and opens up tremendous scope for analysing cell cycle dynamics and developing interventions that target this unique aspect of malaria biology.

15:15 (15 mins)

Role of a cytosolic and a membrane-bound carbonic anhydrase of *Leishmania major* in combating acid stress *- A12606*

Presenter: **Mr Mazharul Abbasi**, *Research Scholar, IISER Kolkata*

**M Abbasi**[1]; D S Pal[1]; D K Mondal[1]; R Datta*[1];
[1] IISER Kolkata, India

The intracellular parasite *Leishmania* efficiently proliferates within acidic phagolysosomes of human macrophages. The underlying mechanism by which *Leishmania* survive within the phagolysosomal acidic environment is largely unknown. We have shown earlier, pharmacological inhibition of carbonic anhydrase (CA) activity resulted in faulty growth due to intracellular acidosis and cell death. Here we report the presence of two CAs, LmCA1 and LmCA2, involved in acid acclimation of the parasite. Immunolocalization studies confirmed LmCA1 as cytosolic whereas LmCA2 as a plasma membrane-bound enzyme. For functional analysis targeted replacement of both genes with antibiotic selectable markers was attempted, but we failed to generate null mutants for any of these genes after repeated attempts, indicating functional importance of these genes. However we were able to generate LmCA1$^{+/-}$, LmCA2$^{+/-}$ heterozygous and LmCA1$^{+/-}$: LmCA2$^{+/-}$ double heterozygous strain. Comprehensive analysis of these mutant strains along with genetic complementation studies clearly shows that both the genes are crucial for parasite growth in acidic environment. The mutant strains also exhibited a marked decrease in virulence upon infection in J774A.1 macrophages which was reversed by lysosomal alkalization using chloroquine. Collectively, these data provide strong evidence that LmCAs play a determining role in parasite multiplication within acidic phagolysosomes of macrophages.

15:30 (15 mins)

Control of allelic exclusion by a trypanosome 'Vex Histone Chaperone' complex - *A12953*

Presenter: **Dr Joana Faria**, *Dundee, School of Life Sciences University of Dundee*

**J Faria**[2]; L Glover[1]; S Hutchinson[1]; C Boehm[2]; M C Field[2]; D Horn[2];

[1] Institut Pasteur, Paris, France; [2] University of Dundee

Specialised metazoan cells and pathogenic protozoa can activate a single gene from a family of closely related genes, but the underlying mechanisms have remained mysterious. In parasitic trypanosomes, association of one telomeric variant surface glycoprotein (VSG) gene with an RNA-polymerase-I (pol-I) transcription factory known as the expression-site body (ESB), and with VSG exclusion 1 (VEX1), facilitates monotelomeric VSG expression and antigenic variation. We isolated and identified VEX1-interactors: a Vex Histone Chaperone or 'VHC' complex incorporates a putative RNA helicase (VEX2) and the conserved replication-associated histone chaperone, chromatin assembly factor 1 (CAF-1). VEX2 forms a single sub-nuclear focus that colocalises with VEX1, immediately adjacent to the ESB, and CAF-1 displays enrichment in the same nuclear compartment, particularly in S-phase. VEX1 displays the properties of a limiting transcription factor, specifically, all known pol-I transcribed genes are activated when VEX1 is overexpressed or when VEX2 is knocked down, which causes VEX1 redistribution. In addition, transcription inhibition leads to redistribution of VEX1 and VEX2 to multiple sub-nuclear foci. VEX2 mediates post-transcriptional suppression of other Expression Site Associated Genes (ESAGs), boosting the proportional output from the VSG, while CAF-1 blocks transcription at other telomeres. In summary, a VHC complex activates one telomeric VSG, excluding others through a mechanism involving locus-specific sequestration of a transcription factor and histone-chaperone dependent silencing of other alleles. Our results provide a new paradigm for the establishment and inheritance of allele-specific epigenetic states.

## Epidemiology II- (Room 2 Apex)

Chair - Dr Kat Rock

14:15 (30 mins)

TBA - *A12740*

Presenter: **Prof George Christophides**, *Imperial College London*

**G Christophides**[1]

[1]Imperial College London

14:45 (15 mins)

Disease spread in age structured populations with maternal age effects - *A12863*

Presenter: **Miss Jessica Clark**, *Ph.D Researcher, University of Edinburgh*

**J Clark**[1]; J S Garbutt[1]; L McNally[1]; T Little[1];

[1] University of Edinburgh

Extrinsic mortality will determine population age structure, which in turn will influence disease spread when individuals of different ages differ in susceptibility, or when maternal age determines offspring susceptibility. Our experiments show that *Daphnia magna* offspring born to young mothers are more susceptible to the specialized parasite *Pasteuria ramosa*, than those born to older mothers. Previous observations show that susceptibility declines with age in this system. We used a Susceptible-Infected compartmental model to investigate how age specific susceptibility and maternal age effects on offspring susceptibility interact with demographic factors to affect disease spread. Our results show a scenario where an increase in extrinsic mortality drives an increase in transmission potential and so we identify a realistic context, in which age effects and maternal effects produce conditions favouring disease transmission. Ongoing experiments are investigating genotypic variation in age effects on parasite fitness.

15:00 (15 mins)

Risk factors for giardiasis in south western Sydney: A case-control study - *A13058*

Presenter: **John Ellis**, *Professor of Molecular Biology, University of Technology Sydney*

**J T Ellis**[3];P Zajackowski[2]; S Mazumdar[1]; S Conaty[2]; S Fletcher-Lartey[2];

[1] South Western Sydney Local Health District, Liverpool Hospital, NSW, Australia; [2] South Western Sydney Local Health District, NSW, Australia; [3] University of Technology Sydney, NSW, Australia

It is unclear why developed countries are still at risk of giardiasis despite their high health standards. In this study, we describe the epidemiology of giardiasis and identify modifiable risk factors associated with giardiasis in south western Sydney, Australia. A retrospective 1:3 unmatched case-control study of confirmed giardiasis cases notified to the South Western Local Health District Public Health Unit between January 2011 and August 2016 was used to investigate giardiasis. Three groups of controls, neighbourhood, friend and pertussis controls selected from the same health district were included to increase response rate and reduce selection bias. Demographic, clinical and potential risk factor data was collected from both cases and controls through contact with mail and

telephone. This study revealed that giardiasis is significantly associated with swimming in pools, contact with domestic animals, wildlife or livestock and with those who visited their country of birth (or their parent's country of birth). Males, younger children and working adults were the most at-risk groups and the vast majority of these giardiasis cases were acquired locally rather than imported from overseas countries. Unexpectedly, residents living in urban settings were associated with an increased giardiasis risk. This study emphasised the need to identify risk factors for giardiasis and the importance of surveillance and control strategies.

15:15 (15 mins)

### Marine *Pomphorhynchus laevis*: analysis and appraisal of UK status. - *A13018*

Presenter: **Alastair Lyndon**, *Senior Lecturer, Heriot-Watt University*

**A R Lyndon**[1]; S J Paterson[1]; E L Strong[1];
[1] Heriot-Watt Univeristy

The distribution of *Pomphorhynchus laevis* marine strain in the UK has historically been fragmentary. New data from Scottish populations where freshwater *P. laevis* is absent allows a clearer analysis of the marine strain's host specificity and a more comprehensive description of its Scottish distribution. This further allows a reappraisal of previous English records, and suggests an hypothesis regarding its probable distribution across the UK and Ireland, with implications for threatened sea trout populations.

15:30 (15 mins)

### Epidemiology and evolution of zoonotic schistosomiasis in West Africa - *A12969*

Presenter: **Dr Elsa Leger**, *Postdoctoral researcher, Royal Veterinary College, University of London*

**E Leger**[4]; C B Fall[5]; A A Hamidou[3]; A M Borlase[4]; S Catalano[4]; D Rollinson[2]; A M Emery[2]; M Sene-Wade[6]; N D Diouf[1]; A Garba[3]; J P Webster[4];
[1] IFSAR Bambey, Universite de Thies, Senegal; [2] Natural History Museum, UK; [3] RISEAL (Reseau International Schistosomoses Environnements Amenagements et Lutte), Niger; [4] Royal Veterinary College, University of London, UK; [5] Universite Cheikh Anta Diop de Dakar, Senegal; [6] Universite Gaston Berger de Saint Louis, Senegal

Schistosomiasis is a Neglected Tropical Disease (NTD) of profound medical and veterinary importance across many parts of the world, with the greatest burden within sub-Saharan Africa (SSA). It has attracted increased focus and funding for control for the past years however, challenges remain and novel challenges have emerged. Anthropogenic changes in selective pressures following, for instance, new dam constructions, altered agricultural practices, together with mass drug administration (MDA) programs, may all be predicted to further impact the availability of suitable definitive and intermediate hosts for schistosomes. Our molecular studies on schistosomes obtained from both human and animal definitive hosts and snail intermediate hosts in Senegal and Niger have shown evidence of viable hybridization within and between human and livestock schistosome species. Moreover, these zoonotic hybrid schistosomes appear to be occurring at extremely high prevalence and intensity levels in continued 'hot spots' despite high coverage MDA. We discuss our results in terms of distribution and role of such novel zoonotic hybrid schistosomes on host range, drug efficacy, and hence ultimately transmission potential and implications for successful and sustainable control.

## Veterinary & Ecology II- (Room 3 Dalhousie)

Chair – Prof Damer Blake

14:15 (30 mins)

### Host-parasite interactions in the era of next-generation sequencing technologies - *A12744*

Presenter: **Dr Cinzia Cantacessi**, *University of Cambridge*

**C Cantacessi**[1]
[1]University of Cambridge

High-throughput molecular and bioinformatics technologies have become instrumental for systems biological explorations of gastrointestinal (GI) helminth parasites of major socio-economic importance and their interactions with the vertebrate hosts. The exploration of the genomes, transcriptomes and proteomes of helminth parasites, and the characterization of global host responses to infection, is assisting the elucidation of a number of key molecular processes linked to parasite development and host invasion, as well as the pathobiology of disease and the development of anthelmintic resistance. High-throughput sequencing technologies are also increasingly being applied to studies aimed to investigate the complex relationships between GI helminths and the resident commensal microbial flora. These studies are mainly driven by the need to better understand the relative contribution of parasite-associated changes in the composition of microbial populations to host malnutrition and immune-modulation. This presentation will provide an overview of recent applications of high-throughput 'omics technologies to large scale studies of the genomes, transcriptomes and/or proteomes of socioeconomically important GI helminths as well as of parasite-microbiota interactions and emphasize the prospects of fundamental explorations of these pathogens using these technologies for the development of new intervention strategies.

14:45 (30 mins)

### Zoonotic disease epidemiology in multi-host systems - *A12743*

Presenter: **Dr Sandra Telfer**, *Senior Research Fellow, University of Aberdeen*

**S Telfer**[1];
[1] University of Aberdeen, UK

The epidemiology of zoonotic diseases may involve both wild animals and livestock. The burden of zoonotic disease falls disproportionately on those from resource-poor countries. Identifying key reservoir hosts is crucial for control efforts, and understanding disease dynamics within those hosts can also make significant contributions to our understanding of the processes driving transmission and epidemiology in natural populations. Focussing on two diseases that involve small mammals as reservoirs, plague and leptospirosis, I will use ecological, epidemiological and genetic data from Madagascar to examine the potential complexities of epidemiological cycles that involve multiple host species, the challenges posed in researching such systems and some of the key drivers of transmission rates.

15:15 (15 mins)

Genomics of sex, drugs, and recombination in the gastrointestinal nematode, *Haemonchus contortus* - *A13000*

Presenter: **Dr Stephen Doyle**, *Postdoctoral Fellow, Wellcome Trust Sanger Institute*

**S R Doyle**[4]; J Cotton[4]; U Chaudhry[2]; N D Sargison[2]; D Bartley[1]; K Maitland[3]; L Matthews[3]; M Berriman[4]; B Mable[3]; C Britton[3]; R Laing[3]; E Devaney[3];

[1] Moredun Research institute, UK; [2] The Royal (Dick) School of Veterinary Studies and the Roslin Institute, The University of Edinburgh, UK; [3] University of Glasgow , UK; [4] Wellcome Trust Sanger Institute, UK

Gastrointestinal nematodes are responsible for significant health and economic burdens in human and animal hosts worldwide. *Haemonchus contortus* is a major pathogen of ruminants, and is the focus of significant anthelmintic control to minimise parasite burden and reduce disease, which includes anemia, lethargy, weight loss, and death. Perhaps not surprisingly, drug resistance is widespread, and isolates resistant to all major classes of anthelmintics (including multi-drug resistant strains) have been described. We have exploited and built upon the available genomics resources for *H. contortus* by undertaking a genome-wide approach toward understanding the mechanisms of anthelmintic resistance, and aim to identify genetic markers to diagnose drug resistance in the field. A genetic cross between the drug-susceptible ISE (used in WTSI genome assembly) and the multi-drug (benzimidazole, levamisole, & ivermectin) resistant UGA/2004 strains was performed, from which a F1 genetic linkage map was constructed. The F2 progeny of the cross were subsequently used to disconnect and dissect the genetic basis for each of the individual drug classes via a bulk segregant analysis of pre- and post-drug treatment. We will discuss the expected (and some unexpected) outcomes of the genetic cross, provide evidence for drug selection throughout the genome, and outline how we propose to use this information to monitor the evolution and spread of drug resistance in the field.

15:30 (15 mins)

Markers of anthelmintic resistance in gastrointestinal parasites of ruminants - *A12862*

Presenter: **Jennifer McIntyre**, *PhD Student, University of Glasgow*

**J McIntyre**[3]; K Maitland; D Bartley[1]; A Morrison[1]; K Hamer[2]; N D Sargison[2]; F Sargison[1]; P Johnson; R Laing; E Devaney;

[1] Moredun Research institute; [2] University of Edinburgh; [3] University of Glasgow

Parasitic gastroenteritis (PGE) is the primary production limiting disease of lambs in the UK, estimated to cost the industry £84 million pounds per annum. The primary pathogen in the UK is *Teladorsagia circumcincta*, an abomasal nematode which has rapidly developed resistance to the anthelmintics used in its treatment and control. The most commonly used anthelmintic is ivermectin, and once significant ivermectin resistance develops on a holding, future sheep production may no longer be economically viable. The long-term aim of this project is to find markers of ivermectin resistance in *T. circumcincta* isolated from UK farms, using genome-wide approaches. Firstly, in order to characterise and phenotype the parasite population on farm, faecal egg counts, resistance bioassays and speciation PCRs were performed throughout the season, culminating in a faecal egg count reduction test (FECRT) using three groups of lambs treated with a benzimidazole, levamisole or ivermectin. Next, pyrosequencing at the β-tubulin isotype-1 locus was undertaken to correlate the benzimidazole resistance phenotype from the egg hatch assay and FECRT, with the benzimidazole resistance genotype and assess the influence of counter selection with ivermectin. Data gathered from these assays show the

complexity of species present on a farm and demonstrates that the strongyle species composition has a significant impact on both the 'resistance' status of the parasite population and the clinical relevance of this. As such, the importance of speciating a strongyle faecal egg count cannot be ignored in clinical practice when diagnosing PGE and/or anthelmintic resistance.

## Worms III- (Room 4 Dalhousie)

Chair - Prof Christoph Grunau

14:15 (30 mins)

### Trematode-designed immunomodulatory molecules with therapeutic potential. - *A12746*

Presenter: **Prof John Dalton**, *Professor in Infectious Diseases, Queen's University Belfast*

**J Dalton**[1];
[1] Queen's University Belfast, UK; Helmedix Ltd, Sydney, Australia, UK

Various helminth parasites secrete molecules that modulate the immune responses of their hosts to benefit their survival. These molecules may not only be relevant targets for anti-parasite vaccine development, but could also have potential for the treatment of immune-mediated human disorders e.g. autoimmune diseases. During our on-going analysis of the secretory proteome of the *Fasciola hepatica* we identified a novel and abundant 8 kDa protein (68 amino acids). Immunohistochemical studies have shown that parasites secrete the molecule into host tissues as it migrates. Structural studies revealed that the 37 amino acid C-terminal region of the protein adopted a secondary structure (amphipathic α-helix) similar to a number of peptides with known antimicrobial and/or immunomodulatory functions, in particularly mammalian LL-37, and thus may act as a molecular mimic. Because of its ability to block the proinflammatory effect of endotoxin on macrophages we described this molecule as a helminth defence molecule, and termed it FhHDM-1. When added to macrophages *in vitro*, FhHDM-1 prevents acidification of the endolysosome. This prevents maturation of lysosomal cathepsin B protease and impairs the activation of NLRP3 inflammasome and the downstream production of IL 1β (which *in vivo* could block the development of protective Th1 type immune responses that are detrimental to parasite survival). This peptide ameliorated disease in two different *in vivo* murine models of autoimmunity, type 1 diabetes and relapsing-remitting immune-mediated demyelination. Phylogenetic studies have revealed that, so far, HDMs are expressed by trematodes but not by nematodes or cestodes. We have discovered a number of new HDMs in trematodes, which we expect will help us design more potent and effective immunomodulatory peptides for future vaccine/therapeutic applications.

14:45 (15 mins)

### Growth factor-induced gain-of-resistance against *Schistosoma mansoni* infection in the snail host. - *A12839*

Presenter: **Mr Emmanuel Pila**, *PhD Candidate, Univeristy of Alberta*

**E A Pila**[1]; M A Gordy[1]; V K Phillips[1]; A L Kabore[1]; S P Rudko[1]; P C Hanington[1];
[1] University of Alberta, Canada;

The digenean trematode *Schistosoma mansoni* is one of the causative agents of human schistosomiasis, a chronic and devastating disease that affects over 260 million people worldwide. To complete their life cycle, schistosomes must undergo their larval development within specific species of snail intermediate hosts. The specificity in host requirement presents an opportunity for utilizing the snail as a possible target for schistosomiasis control efforts. Compatibility between the snail host and *S. mansoni* is determined in part by the snail immune response, mediated primarily by the haemocytes as well as soluble immune factors. However, very little is known about endogenous control of haemocyte development in any gastropod model. Here, we present the functional report of a snail endogenous growth factor, granulin (BgGRN). This granulin was identified as part of a peptide screen of snail plasma proteins that differed in abundance between the *S. mansoni*-resistant (BS-90) and susceptible (M-line) strains of *Biomphalaria glabrata*. BgGRN transcript expression was found to be responsive in both BS-90 and M-line snails when challenged with *S. mansoni* increasing 39 and 16 folds respectively relative to β-actin (non-immune control gene). Injection of recombinant BgGRN induced haemocyte proliferation in the snails, particularly of the adherent haemocyte subset that is known to participate in the anti-digenean response. BgGRN-induced proliferation of this haemocyte subset in M-line snails prior to parasite challenge resulted in significant reversal of the highly susceptible phenotype, yielding a 54 % reduction in infection success. This represents the first functional characterization of an endogenous growth factor of any gastropod mollusc, and is also the first gain-of-resistance study in a snail-digenean infection model using a defined factor to induce snail resistance to infection.

15:00 (15 mins)

## Early lymphatic remodelling following filarial infection is promoted by host Th2 adaptive immune responses - *A12905*

Presenter: **Julio Furlong-Silva**, *PhD Student, Liverpool School of Tropical Medicine*

**J Furlong-Silva**[1]; S D Cross[1]; N Pionnier[1]; A Steven[1]; J Archer[1]; M Taylor[1]; J Turner[1];
[1] Liverpool School of Tropical Medicine

Lymphatic Filariasis (LF) related morbidity (lymphoedema and elephantiasis) affects 40 million patients globally, making it the third leading cause of global disability by the WHO. Current treatment is limited to symptom management, suggesting novel therapies to prevent, or reverse pathology are urgently required. LF is associated with significant lymphatic remodelling and dysfunction, however the underlying mechanisms that mediate these changes, and how they relate to LF pathology is poorly understood. An LF leg pathology model was developed were 100 *B. malayi* L3 larvae were subcutaneously injected into the feet of mice (BALB/c and C57BL/6). An intravital imaging system was utilised to analyse lymphatic flow 2-5 weeks post infection (P.I). Intracellular cytokine staining was undertaken on lymph nodes (LNs) proximal to infection and plasma taken for luminex analysis. Early, significant lymphatic remodelling with dilation, collateral tortuous lymphatics and dermal back flow was observed 2 weeks P.I. and was concomitant with significant expansion of IL-4/IL-13 expressing CD4 T-cells in draining LNs. Deficiencies in T/B cells or IL-4/IL13 responses- using SCID and IL-4rα KO mice- resulted in amelioration of remodelling, with a reduced incidence and magnitude in SCID vs WT mice and no significant differences between sham vs infected IL-4rα KO mice. Plasma analysis indicated significant increases in several circulating

lymphangiogenic markers following infection including: VEGF-C, β-cellulin, prolactin and sALK-1. The data suggests a key role for a Th2 adaptive immune response in early lymphatic remodelling following filarial infection, with early pathological alterations associated with elevated multifactorial lymphangiogenic mediators. Together, these data reveal a Th2 lymphangiogenic pathway in the initiation of filarial lymphatic disease. Targeting this pathway may yield novel therapeutic strategies against LF pathology.

15:15 (15 mins)

### Into the unknown: exploring proteins of unknown function in *Schistosoma mansoni* - *A13005*

Presenter: **Iain Chalmers**, *Aberystwyth University*

**I W Chalmers**[1]; K F Hoffmann[1]; T A Gasan[1]; C L Dunham[1]; N Fernandez-Fuentes[1]; E Tukahebwa[3]; J M Wawrzyniak[2]; D Dunne[2]; S Wilson[2];
[1] Aberystwyth University; [2] University of Cambridge; [3] Vector Control Division, Ugandan Ministry of Health

In genomic, transcriptomic and proteomic studies throughout parasitology, proteins of unknown function are common. Further, these sequences with no clear sequence similarity to characterised proteins also frequently exhibit highly restricted species range limited to parasites. In *Schistosoma mansoni*, the unique nature of these proteins make them intriguing and attractive targets for potential control methods due to lack of cross-reactivity with human proteins. By their nature, progress in investigating these unusual (but likely crucial) proteins is slow. In a previous study, we revealed by motif and structure prediction studies that several proteins listed as having no known homolog (such as the vaccine candidate Sm29) are actually members of the Ly6 protein family, present on the surface of the parasite and immunologically recognised during human infections. Here, utilising extensive genomic searches, phylogenetics and a range of techniques we describe current progress in characterising two other proteins of unknown function released by the parasite during infection. In addition to sequence-based analysis and transcriptional profiling, we have used recombinant expression to produce, purify and examine the serological responses in endemic communities pre- and post-treatment, finding specific antibody recognition to these unique proteins. Future studies aim to continue sequence-based, functional and immunological characterisation of these proteins.

15:30 (15 mins)

### Effects of host sex and body size on *Schistocephalus* infection susceptibility and plerocercoid growth in three-spined sticklebacks - *A12871*

Presenter: **Mrs Rana Shalal**, *PhD student, University of Leicester*

**R Shalal**[1]; I Barber[1];
[1] University of Leicester

Parasites do not affect all individuals equally, and both the level of infection and the severity of the effects that parasites have on hosts can be influenced by pre-existing host variation within populations. Host sex and body size are two potentially important factors that potentially influence the interactions of hosts with parasites, affecting the susceptibility to infection, as well as influencing the subsequent growth and development of parasites. Plerocercoid larvae of the cestode *Schistocephalus solidus* often impact the health,

growth and development of three-spined sticklebacks *Gasterosteus aculeatus* in natural populations. We used experimental infection techniques to examine how pre-existing variation between individual stickleback hosts influences the outcome of *S. solidus* infections. Sticklebacks that varied in body size and sex were determined non-invasively by PCR analysis of a sex-linked marker and were exposed experimentally to controlled doses of infective *S. solidus* parasites, and the consequences of each host factor for infection susceptibility and parasite growth, as well as a range of indicators of host health and development, were quantified to determine their influence the emerging infection phenotype. Here we report the findings of this study, and also investigate the implications of host size and sex for the fecundity of adult parasites derived from plerocercoids growing in hosts of different sizes and sex. Our results provide support for the hypothesis that pre-existing host differences can influence the progression of disease, and have implications for host-parasite interactions in the face of systematic changes in host biology that may occur under altered ecological conditions, for example under changing climates.

# Wednesday April 4th (Apex Hotel)

## Wright Medal Lecture (Apex Hotel)

Chair –Paul Horrocks

09:30 (55 mins)

Wright Medal Lecture

**Matt Berriman,** *Wellcome Trust Sanger Institute*

**M Berriman**[1];

[1] Wellcome Trust Sanger Institute, UK

Parasitology has been transformed by genome sequencing. Comparisons across genomes have addressed questions at different levels and identified candidate genes for detailed follow-up. Sets of genes have been defined that are conserved over different evolutionary distances as well as extremely divergent genes with restricted distributions. The *Plasmodium* genus is the best example of where a comparative approach has been applied. Comparisons have encompassed all human-infective species, plus selected relatives from rodents, non-human primates, and birds, and have revealed the strikingly differences in the composition and organisation of highly divergent multigene families. Fine-grained comparisons within a single sub-genus have given us the clearest picture yet of how a parasite of humans has arisen. In contrast, the large and complex genomes of helminths have presented technical and economic challenges that in most cases have limited the availability and accuracy of genome assemblies. Nevertheless, genomes have now been individually described for 40 helminth species and in a few clades, with higher-accuracy genomes, comparative genomics approaches have revealed genes associated with parasitism. We have used published, as well as new, genome data to create a large comparative genomics dataset that samples the diversity across platyhelminths and nematodes. By covering multiple species, potential problems of fragmentary data have been avoided to reveal patterns of metabolic differences across multiple lineages, possible new drug targets, and lineage-specific multigene families. As with protozoan studies, changes to sequencing technologies are opening new opportunities to delve deeper and reveal genes associated with the evolution of individual parasite species.

## Molecular Cell biology III- (Room 1 Apex)

Chair - Luisa Figueiredo

11:30 (30 mins)

### Deciphering the 3D architecture of the *Trypanosoma brucei* genome - *A12747*

Presenter: **Dr Nicolai Siegel**, *Young Investigator, University of Wuerzburg*

**N Siegel**[1]

[1]University of Wuerzburg

Antigenic variation is a widely employed strategy used by pathogens to evade the host immune response. It requires controlled recombination and gene expression to ensure diversification and mutually exclusive expression of antigens. Both gene expression and recombination are strongly affected by genome architecture. Yet the repetitive nature of antigen arrays has complicated their assembly. Thus, the causal links between genome architecture and mutually exclusive antigen expression remain unknown. To be able to better study the mechanism underlying antigenic variation, we have developed a strategy for de novo genome assembly and scaffolding of complex genomes. Taking advantage of Pacbio long-read sequencing technology and conserved features of chromosome folding, we assembled the genome of the protozoan parasite *Trypanosoma brucei*, one of the most important model organisms in antigenic variation research. We found *T. brucei* chromosomes to contain homozygous cores and long heterozygous sub-telomeric regions, which code for the extensive variant surface glycoprotein (VSG) repertoire. Using genome-wide chromosome conformation capture (Hi-C) analyses we determined the 3D genome architecture of bloodstream form parasites. Our data revealed folding of the transcriptionally repressed sub-telomeric VSG arrays into distinct, highly compacted compartments, characterized by very little interaction with other regions of the same chromosome. We suspect that the observed folding of sub-telomeric VSG arrays may represent a means to maintain them in a transcriptionally repressed state, ensuring the expression of a single VSG.

12:00 (15 mins)

### Exploring the connectivity between *Leishmania mexicana* amastigotes and their host cell through 3D electron microscopy - *A12998*

Presenter: **Ms Valli Jessica**, *PhD Student, University of Oxford*

**J Valli**[1]; E Johnson[1]; E Gluenz[1];

[1] University of Oxford, Sir William Dunn School of Pathology

Parasites of the *Leishmania mexicana* complex reside within large, communal parasitophorous vacuoles (PVs), with parasites typically aligned along the PV membrane. Ultrastructural studies have reported close contact between amastigotes and the PV, either involving the posterior pole or flagellar tip, but how parasite positioning changes over time remains unexplored. We used 3D electron microscopy techniques to follow orientation of *L. mexicana* amastigotes within the PV at different time points after infection, and to explore the connectivity at contact sites. Models produced from serial block face scanning electron microscopy data suggest a progression in amastigote orientation over an infection time-course. Amastigote-PV contact was initially maintained at both the posterior end and flagellar tip, with the main vacuole volume bulging laterally away from the amastigote. Electron tomography showed infiltration of

flagellar membrane tubules into invaginations of the PV membrane, and provided evidence of vesicular activity at the flagellar tip and PV membranes at contact sites. As PV size increased, flagellar contact was lost, leaving amastigotes with only their posterior ends embedded. PV enlargement has been shown to facilitate amastigote survival. Further work will be required to determine whether the membrane activity observed at regions of initial PV-flagellum contact could be involved in regulation of PV enlargement or modulation of other host cell functions.

12:15 (15 mins)

### The ZC3H39/40 RNA-binding complex and control of an electron transport chain regulome in African trypanosomes - *A12945*

Presenter: **Dr Anna Trenaman**, *Postdoctoral Research Assistant, University of Dundee*

**A Trenaman**[2]; S Hutchinson[1]; L Glover[1]; D Horn[2];
[1] Institut Pasteur, France; [2] University of Dundee

We ran an RNAi screen in bloodstream form *Trypansoma brucei* that implicated the RNA-binding proteins, ZC3H39 and ZC3H40 in variant surface glycoprotein (VSG) gene silencing. Knockdown of either protein disrupted VSG silencing as determined by western blotting, flow-cytometry and RNA-seq. The presence of a cytoplasmic ZC3H39/40 complex in *T. brucei* was supported by immunofluorescence co-localisation, co-destabilisation and co-immunoprecipitation. A CLIP-seq experiment, surprisingly, identified transcripts encoding multiple components of the electron transport chain, including those for cytochrome oxidase and the F-ATPase. Consistent with this association, these same transcripts were down-regulated in ZC3H39/40 knockdowns as determined by RNA-seq and by stable isotope labelling in cell culture followed by mass-spectrometry and proteomic profiling. Notably, this regulation was only observed in bloodstream form parasites following ZC3H40 knockdown. Thus, we report an RNA-binding complex that controls the expression of electron transport chain components in *T. brucei*. Our findings also establish an intriguing link between an electron transport chain regulome and VSG expression control.

12:30 (15 mins)

### Structural and functional studies of *Trypanosoma brucei* MORN1 protein - *A12990*

Presenter: **Miss Sara Sajko**, *Structural and functional studies of Trypanosoma brucei MORN1 protein, Max F. Perutz Laboratories, University of Vienna*

**S Sajko**[2]; I Grishkovskaya[2]; M Puchinger[2]; J Kostan[2]; B Morriswood[1]; K Djinovic-Carugo[2];
[1] Department of Cell & Developmental Biology, Biocentre, University of Würzburg, Germany; [2] Department of Structural and Computational Biology, Max F. Perutz Laboratories, University of Vienna, Austria

Membrane occupation and recognition nexus repeat (MORN)-containing proteins are found in organisms throughout the tree of life. The MORN1 protein in *Trypanosoma brucei* is composed of 15 MORN repeats and is essential for the viability of the parasite`s bloodstream form. It localizes to a hook-shaped complex that wraps around the neck of the flagellar pocket membrane. Our biophysical characterization of TbMORN1 including circular dichroism, electron microscopy, and solution small angle X-ray scattering (SAXS) suggest that it is an all-beta protein, existing as a rod-shaped dimer. These data are consistent with a recently solved crystal structure

for TbMORN1 homologue from *Plasmodium falciparum*, the construct missing the first six MORN repeats. Mutational, chemical cross-linking, and SAXS data indicate that TbMORN1 dimerizes via its C-terminal repeats. Lipid blots, native electrophoresis, and fluorescence anisotropy assays showed that TbMORN1 binds to the lipid phosphatidylinositol 4,5-bisphosphate ($PI(4,5)P_2$) with low micromolar affinity. Based on a computational model, putative $PI(4,5)P_2$ binding sites were predicted and $PI(4,5)P_2$ binding mutants have been generated and assayed. With the ongoing structural and *in vivo* studies we are trying to understand whether $PI(4,5)P_2$-binding is essential for correct protein assembly and/or localization in the parasite.

12:45 (15 mins)

A decrease in mitochondrial membrane potential may be associated with diminazene resistance in *Trypanosoma congolense*. - *A13030*

Presenter: **L V Carruthers** *Institute of Infection, Immunity and Inflammation, University of Glasgow*

**L V Carruthers**[2]; J Munday[2]; G D Campagnaro[2]; G Ebiloma[2]; F Giordani[2]; L Morrison[3]; R Peter[1]; M Witty[1]; M P Barret[2]; H P de Koning[2];
[1] Global Alliance for Livestock Veterinary Medicine, UK; [2] Institute of Infection, Immunity and Inflammation, University of Glasgow, UK; [3] Roslin Institute, UK

Animal trypanosomiasis is a parasitic disease of livestock and *Trypanosoma congolense* is a major cause. It causes economic hardship in many developing regions due to illness and death of infected domestic animals. Although treatment is available, there are field reports of *Trypanosoma congolense* resistant to diminazene. This project therefore aimed to determine the mechanism by which *T. congolense* can develop resistance to diminazene to aid future drug administration, drug discovery and improve resistance reporting. Wild type *T. congolense* cell lines were exposed to increasing concentrations of diminazene in culture. Uptake of radiolabelled diminazene, fluorescence activated cell sorting (FACS), DAPI staining, DNA and RNA sequencing, and drug sensitivity assays were used to assess the mechanism/s of resistance. Previous studies on *Trypanosoma brucei* strains have shown loss of drug uptake to be the key drug resistance mechanism for many drugs, including diminazene; however, here we show that diminazene uptake in *T. congolense* did not differ between resistant and sensitive lines. A shift in mitochondrial membrane potential, however, was evident in resistant lines, indicating that this is linked to diminazene resistance in *T. congolense*. The implications of this mechanism with respect to limiting the development and/or spread of drug resistance will be discussed.

## Veterinary & Ecology III- (Room 2 Apex)

Chair - Prof Jane Hodgkinson

11:30 (30 mins)

Parasitic diseases and their cost to aquaculture - *A12748*

Presenter: **Dr Giuseppe Paladini**, *Lecturer in Aquatic Parasitology, University of Stirling*

**G Paladini**[2]; J E Bron[2]; A P Shinn[1];
[1] Fish Vet Group Asia Limited, UK; [2] University of Stirling, UK

Productivity, sustainability and economic viability of the global finfish and shellfish aquaculture industry are threatened by obligate and opportunistic parasites. The impact of these pathogens can often be significant if appropriate control measures are not taken promptly. Calculating the impact of parasitic diseases in aquaculture is challenging and most of the time the result is an underestimation, since costs may be affected by a range of environmental and management factors. The current study attempts to estimate the potential global economic costs attributable to a range of key parasite pathogens using a number of specific parasite-associated events recorded for the world's major marine, brackish and freshwater aquaculture production industries. This provides a baseline resource for risk assessment and the development of more robust biosecurity practices. Such developments can, in turn, help to mitigate against and / or minimise the potential impacts of parasite-mediated disease in aquaculture.

12:00 (30 mins)

Tick and tick-borne disease risk for dogs in the UK - *A12749*

Presenter: **Prof Richard Wall**, *Professor of Zoology, University of Bristol*

**R Wall**[1]; F Smith[1]; S Abdullah[1];
[1] University of Bristol, UK

Ticks are abundant, clinically-important, blood-feeding ectoparasites that damage their hosts both directly as they feed and indirectly through the transmission of an extensive range of bacterial, viral and protozoal pathogens. Recent changes in the distribution of tick vectors and the incidence of tick-borne disease, driven variously by factors such as climate change, habitat modification, increasing host abundance and the increased movement of people and animals, highlight the importance of active surveillance. As part of an on-going analysis of the tick-borne disease risk for dogs, large-scale national surveys were undertaken by asking veterinarians to collect ticks on dogs presented to veterinary practices in the UK. This participatory approach allows relatively cost- and time-effective extensive data collection. Participating practices were asked to select five dogs at random each week and undertake a thorough, standardized examination of each dog for ticks. The clinical history and any ticks found were then sent to the investigators. In two surveys, more than 15,000 dogs have been examined and 7,000 tick samples collected, identified and subjected to pathogen analysis by PCR and sequence analysis following DNA extraction. The results of these surveys provide a comprehensive spatial understanding of tick distribution, species abundance and tick-borne pathogen prevalence in the UK, contributing to our understanding of disease risk in dogs.

12:30 (15 mins)

Eigenanalysis provides insights into the innate immune response induced in commercial broilers following *Eimeria tenella* provoked coccidiosis - *A12978*

Presenter: **Dr Matthew Nolan**, *PDRA in Vaccine Development, Royal Veterinary College*

**M Nolan**[1]; K Boulton[2]; F Tomley[1]; D Hume[2]; D P Blake[1];
[1] Royal Veterinary College; [2] The Royal (Dick) School of Veterinary Studies and the Roslin Institute, The University of Edinburgh

*Eimeria* are parasites of major importance to the poultry industry. A reduced portfolio of control options has stimulated research seeking alternate solutions, including breeding birds with greater resistance/tolerance to disease. Here, 1,200 broilers were subject to *Eimeria*

*tenella* challenge. A genome-wide association study (GWAS) assessed genetic variance in response to infection for percentage body weight gain (%BWG), caecal lesion score (CLS), and serum interleukin 10 (IL10). *Eimeria tenella* challenge resulted in significant phenotypic variation in response to infection in all traits. Eigenanalysis defined the relationships among the different components of the response. The first Eigenvector classified correlations to reflect differential susceptibility to the pathology associated with infection. The second revealed resistance is not the inverse of susceptibility. A third identified a subpopulation of birds that were tolerant in the face of severe inflammation with little or no IL10 response to severe caecal injury, and good maintenance of %BWG. GWAS identified suggestive genome-wide significant SNPs associated with CLS and IL10, while a chromosome-wide SNP was located for %BWG. Pathway analysis identified candidate genes putatively responsible for each trait. Visualisation of Eigenvectors provides a valuable insight into variation in the immune responses of animals to diseases and, in conjunction with GWAS, may identify biomarkers to support breeding programs.

12:45 (15 mins)

Sea Lice effect on wild Atlantic salmon fecundity - *A12933*

Presenter: **Roman Susdorf**, *PhD candidate, University of Aberdeen / Marine Scotland Science*

**R Susdorf**[4]; N Salama[2]; D Lusseau[3]; E de Eyto[1];

[1] Marine Institute, Ireland; [2] Marine Scotland Science; [3] University of Aberdeen; [4] University of Aberdeen / Marine Scotland Science

Parasitic sea lice are ectoparasites infesting Atlantic salmon. In Scotland, the species of interest are the salmonid specialist *Lepeophtheirus salmonis* and the generalist *Caligus elongatus*. Mobile stages move across host surface feeding on its skin and blood. In recent decades, wild Atlantic salmon populations have declined globally, corresponding with an increase in salmon cultivation since 1960s which has escalated host and parasite densities. This led to the interest in sea lice and wild salmonid interactions due to their potential impact on wild returns. Laboratory experiments show that sea lice elicit sub-lethal effects causing stress, a reduction in growth and condition. We evaluated the influence of sea lice on body condition of returning salmon using data from Strathy Point (North Scotland). We show that sea lice reduce condition by 4 % (1-11). Applying this condition effect to female salmon indicates an ova reduction by 3 % (0-11). Being more likely to die at sea, fish in poor condition (potentially highly infested) are underrepresented. Thus, it is crucial to note, that the described effect from sea lice on condition (and thus fecundity) is likely underrated. This is the first study revealing a non-lethal impact from sea lice in wild Atlantic salmon. Furthermore, we also derive a useful proxy (i.e. condition) for fecundity incorporating both fish weight and length, which can improve current management practise. We show that a sea lice-mediated condition-effect has the potential to diminish Atlantic salmon stock components and thus can influence population dynamics.

# Posters

### Posters

Poster 1 : Intestinal parasites - *A12837*

Presenter: **Dr Victoria Pam**, *Lecturer, Federal University Lafia, Nassarawa State, Nigeria*

**V Pam**[1]; P N James[2]; D D Pam
[1] Federal University Lafia, Nassarawa State, Nigeria, Nigeria; [2] Plateau State University, Bokkos, Plateau State Nigeria, Nigeria; [3] University of Jos, Nigeria

Intestinal parasitic infections are the most common parasitic infections affecting man and can result to important morbility or mortality in infected individuals. Intestinal parasites are common in resource-poor communities where they are also associated with considerable economic loss. From the 100 patients examined in Plateau State Specialist Hospital (PSSH), 22.0% tested positive to intestinal parasites while 6.0% WAS reported for Vom Christian Hospital (VCH). The prevalence of intestinal parasites in PSSH revealed a high prevalence with *Ascaris lumbricoides* (31.82%) followed by *Taenia spp* (31.82%), Hookworm (18.18%), *S. starcoralis* (9.09%), the least prevalence was observed with *B. Coli* and *Entamoeba histolytica* with (4.55%) respectively, on the contrary Vom Christian hospital had a higher prevalence of Hookworm (50.0%), and *Ascaris lumbricoides* (33.33%) but lower of *Taenia spp* (16.67%). Our results in relation to sex in plateau state specialist hospital (PSSH) shows that the female 12 (54.54%) recorded higher prevalence than the male 10 (45.45%) on the other hand we observed high prevalence in the female 4 (66.67%) than the male 2 (33.33%) in Vom Christain hospital. The prevalence of intestinal parasite in relation to age in PSSH shows high level among age group 11-20 years 9 (36%) and the least among age group 21-30 years 7 (19.44). On the contrary VCH shows high level among age group 31-40 years with 2 (9.09%) and the least among 11-20 years with 1 (4%). exposure among that particular age group. The result in relation to water source in patients attending PSSH shows that the boreholes sources 66.67% had high prevalence followed by dug well 17.5% the least prevalence was observed with the source from the tap 7.89%, while VCH shows that streams/rivers 16.67% revealed high prevalence followed by borehole 13.64%. This prevalence is directly related to the sanitary condition, socio-economic status, educational level, the age and hygienic habits of the patients. Thus, necessary sanitary policies, awareness, screening and de-worming exercises and occasional check of intestinal parasites are recommended.

Poster 3 : Protein complexes in *T. brucei* and changes in the proteome across the cell cycle. - - A12*882*

Presenter: **Dr Michele Tinti**, *Bioinformatician, School of Life Sciences, University of Dundee*

**W M Crozier**[1]; **M Tinti**[1]; A I Lamond[2]; M A Ferguson[1];
[1] Biological Chemistry and Drug Discovery, School of Life Sciences, University of Dundee; [2] Centre for Gene Regulation and Expression, School of Life Sciences, University of Dundee

*Trypanosoma brucei* is a highly divergent organism in comparison to commonly studied model organisms and its genome is poorly annotated for protein function. Therefore, we have applied global proteomic analyses to gain further insight into cell cycle protein regulation and protein-protein interactions. Here we report the regulation of 5,033 proteins across the cell-division-cycle of the procyclic form (insect stage) of the parasite. Furthermore, we have analysed the elution profiles of 5,845 proteins across three forms of chromatography, building a high-confidence interaction network of 234 complexes comprising 805 proteins.

Poster 4 : Redesigning the BRRoK assay: a high throughput tool to determine rate of kill for discovery anti-malarials. - - *A12974*
Presenter: **Mr Ibrahim Ali**, *PhD, Keele University*

**M Famodimu**[1]; P Horrocks[1];
[1] Keele University

The bioluminescence relative rate of kill assay (BRRoK) offers a rapid, 6 hours, assay format to determine a compound immediate cytocidal effect (1). An important limitation in scaling the BRRoK assay is the requirement to measure $IC_{50,}$ a process that takes longer than determining initial rate of kill. Using fixed concentrations of discovery compounds would greatly assist in scaling the assay format such that large compounds sets, e.g. TCAMS (2), can be tested. We hypothesized that the loss of bioluminescence signal following fixed dose drug perturbation would combine the effect of both the $IC_{50}$ (multiples achieved with the fixed concentration employed, 10 µM and 2 µM) and immediate rate of kill. Exploring this effect using 10 antimalarial drugs and 100 compounds from the MMV Malaria Box for which $IC_{50}$ and immediate rate of kill are known, we were able to derive cut offs based on the specificity and sensitivity of the assay that enable potent and rapidly cytocidal drugs to be identified using this simpler assay format. Validation of this approach is demonstrated by screening all 400 compounds in the MMV Pathogen Box, with hits identified within nano-molar potency range and immediate rate of kill greater than that of chloroquine. We propose this revised BRRoK assay offers an important *in vitro* tool for lead discovery of antimalarial compounds.

Poster 5 : A genome-scale screen for cell cycle defects in the African trypanosome - - *A12989*
Presenter: **Dr Catarina A. Marques**, *Post-Doc, University of Dundee*

**C A Marques**[1]; L Glover[2]; A Cassidy[3]; D Horn[1];
[1] Division of Biological Chemistry and Drug Discovery, School of Life Sciences, University of Dundee; [2]Institut Pasteur, Paris, France; [3] Tayside Centre for Genomic Analysis, School of Medicine, University of Dundee, UK

RNA interference (RNAi) library screening in *Trypanosoma brucei* has proven to be a powerful approach for determining which proteins are, for example, required for the parasite's viability. Proteins that are essential for viability can then be considered genetically validated as potential drug-targets. Major challenges remain however, in terms of developing a deeper understanding of how these proteins impact trypanosome biology and viability. To gain further insight into protein function at a genomic scale, we have now carried out a screen for cell cycle defects. A genome-wide bloodstream form RNAi library was induced for 24 h and ~$10^8$ cells, stained with propidium iodide, were isolated by fluorescence-activated cell sorting (FACS) according to DNA content. Sub-G1, G1, S, G2/M and >G2/M populations were recovered and subjected to RNAi Target sequencing (RIT-seq). In this approach, each read serves as a barcode to report the relative representation of each gene-knockdown in each of the five isolated populations. As expected, we find that cell-cycle perturbations are enriched for gene-knockdowns previously associated with a fitness-cost. One particularly prominent feature

is a >G2 enrichment profile that emerges for cohorts of genes associated with the cytoskeleton and motility. Another notable feature is the association of proteasome components knockdowns with an accumulation at G2/M. We are currently analysing the datasets and will present findings in relation to factors involved in DNA-replication, chromosome segregation, phosphorylation and RNA-binding, among others.

Poster 6 : Report on the phylogenetic studies of diplostomatids parasites - - *A12605*
Presenter: **Mr Ami Mitonga**, *Technical officer and student , Sefako Makgatho Health Sciences University*

**M Mitonga;** E Moema; P King
[1] Sefako Makgatho Health Sciences University , South Africa

Diplostomid metacercariae inhabit freshwater fish species as the second intermediate hosts. These parasites have been found in the eye lens, the retina, vitreous humour and the nervous system of freshwater fish. The classification of these parasitic stages to the species level using only morphology is often difficult and ambiguous. The use of molecular techniques has allowed links to be elucidated using various developmental stages of these parasites. The aim of this study was to provide a summative report on the phylogenetic tree by applying molecular biology techniques to the investigation of larval diplostomid parasites. *Diplostomid metacercariae* were preserved in 70% ethanol prior to DNA extractions using a Qiagen kit. Standard techniques for amplification of rRNA region were followed. The DNA amplicons were sent to inqaba Biotech laboratory for sequencing and phylogenetic trees generated using software programs. RESULTS: The amplicons of these diplostomids had band sizes of 500 base pairs. The amplicons contained only partial regions (ITS-2). The parasitic species 28S rDNA genomic region was successfully amplified. The application of molecular techniques on digenetic trematodes seems very promising and may yield great potential in future descriptions of morphologically similar parasitic species.

Poster 7 : Insecticide susceptibility status of *Anopheles gambiae* complex in Osun state, southwestern Nigeria - - *A12614*
Presenter: **Dr Monsuru Adeleke**, *Lecturing/Research, Osun State University*

**M ADELEKE**[3]; J Adeyemi[1]; K Fasasi[3]; L Oforka[4]; A Adeogun[2]; G Olatunde[3];
[1] Federal University of Technology, Akure, Nigeria; [2] Nigerian Instituite of Medical Research, Nigeria; [3]Osun State University, Nigeria; [4] University of Lagos, Nigeria

One of the major challenges facing malaria control today is the high spate of insecticide resistance in mosquito populations. The present study is therefore designed to investigate (i) the sibling composition of *A. gambiae* complex using molecular techniques (ii) the susceptibility status of *A. gambiae* complex to DDT and Deltamethrin at selected locations in Osun State, Nigeria. The larvae of *A. gambiae* complex were collected from six selected towns, representing the three Senatorial geopolitical zones in Osun State. Two to three day old unfed female mosquitoes were subjected to bioassays using papers impregnated with 0.05% Deltametrin (pyrethroid) and

4% DDT (organochlorine) in accordance with WHO protocol. The mosquitoes were thereafter subjected to Polymerase Chain Reaction assay for molecular characterization of the sibling species. The results of the knockdown effects of the insecticides within 60 min of exposure ranged from 40-70% in mosquitoes exposed to Deltamethrin and 15-45% for the mosquitoes exposed to DDT across the locations. The post-exposure mortality caused by the two insecticides varied significantly; and mortality recorded in mosquitoes exposed to Deltamethrin was significantly higher than DDT (P>0.05) in all the study locations. The mortality recorded in mosquitoes exposed to DDT was less than 80% in all the locations. All the mosquitoes exposed to Deltamethrin also had less than 98% mortality except at a site where 100% mortality was recorded. Molecular identification showed that *n. gambiae* s.s and *n. arabiensis* occurred at the study area. Therefore, the use of the two insecticides (Deltamethrin and DDT) for vector control and management in Osun State may not yield any appreciable results as the local populations of *A. gambiae* complex are virtually resistant to the two insecticides.

Poster 8 : The influence of the branched chain amino acids degradation pathway on the differentiation in T*rypanosoma cruzi* - - *A12923*

Presenter: **Miss Nubia Carolina Manchola Varon**, *Trypanosoma cruzi BCAA metabolism, Biomedical Science Institute - USP*

**N Manchola Varon**[1]; N L Rapado[1]; A M Silber[1];
[1] Biomedical Science Institute - USP, Brazil

Chagas disease (CD) is a zoonosis caused by the flagellate protozoan *Trypanosoma cruzi*, which is transmitted by insects of the Reduviidae family. The branched chain amino acids (BCAA) (valine (Val), leucine (Leu) and isoleucine (Ile)), are efficiently taken up by epimastigotes though an ATP-dependent single system. As there is no BCAA biosynthesis in the parasite, their intracellular availability depends on the balance between their incorporation and consumption. We demonstrated that parasites incubated with $^{14}$C-U-Leu are able to oxidize it to $CO_2$. Additionally, it was early suggested that Leu behaved as a negative modulator of the metacyclogenesis, when we submitted epimastigotes to metacyclogenesis assays in the presence of BCAA differentiation was diminished more than 95% for all BCAA. We explored the ability of BCAAs to interfere with the parasite intracellular infection. In the presence of 5 mM Leu, trypomastigote bursting was 67% diminished. As differentiation and intracellular infection are proline (Pro) dependent, we explored the ability of Leu to inhibit the pyrroline-5-carboxylate dehydrogenase. Leu behaved as a non-competitive inhibitor of TcP5CDH (Ki: 3.5 mM). Thus, essential processes in the biology of *T. cruzi* are dependent on the ability of the parasite to accumulate BCAAs. To better understand the dynamic between uptake and consumption of BCAAs we investigated the first steps in their degradation pathway, which is expected to be catalyzed by specific BCAA transaminase, but according to *T. cruzi* genome databases this enzyme is absent, we explored if, aspartate and tyrosine aminotransferases could be responsible for a non-canonical BCAA aminotransferase activity. Both were able to transfer the amino group from BCAA to a-ketoglutarate. In conclusion, we have demonstrated a connection between BCAA availability, their metabolism (which comprises unique biochemical activities of ASAT and TAT),

Poster 9 : Study on the feasibility of using magneto-archimedes levitation to fractionate schistosome eggs from faecal samples - - *A12885*

Presenter: **Dr Renata Candido**, *Research Fellow, University of Western Australia*

**R Candido**[3]; T D Acker[1]; C Mandy[3]; R C Woodward[3]; A L Morassutti[1]; C Graeff-Teixeira[1]; T St Pierre[3]; M K Jones[2];
[1] Pontificia Universidade Catolica do Rio Grande do Sul, Brazil; [2] The University of Queensland, Australia; [3] The University of Western Australia, Australia

Schistosomiasis is prevalent in rural areas of approximately 70 nations, where it is persistently associated with poverty. In many endemic areas, diagnosis is often neglected because of associated costs, giving rise to an urgent need for affordable and reliable diagnostic services. The feasibility of using magneto-Archimedes levitation for schistosome egg detection in faecal matter was explored in this study. A prototype device that uses magneto-Archimedes levitation was used to separate *Schistosoma* eggs in faecal suspensions. *Schistosoma japonicum* and *S. mansoni* eggs were placed into a 2.55 M MnCl2 solution in a 4.5 mL cuvette placed between two permanent NdFeB magnets positioned coaxially in an anti-Helmholtz configuration. The eggs migrated to highly reproducible positions in the device. The range of densities of *S. japonicum* eggs was observed to lie between 1.31 and 1.46 g/mL while *S. mansoni* eggs were between 1.30 and 1.46 g/mL. When 100 *S. mansoni* eggs were seeded into 200 mL of human formalin-fixed faeces, 30% could be retrieved. Our data indicate that schistosome eggs can be fractionated from faecal matter using the MAL device. Furthermore, the separation technology could potentially be used for separation of eggs of other helminths and protozoan cysts.

Poster 10 : Towards validation of an immune suppressor protein from liver fluke : Prostaglandin D Synthase as a drug target - - *A12891*
Presenter: **Mr David Cutress**, *PhD student, Aberystwyth University – IBERS*

**D Cutress**[1];
[1] Aberystwyth University - IBERS

The Liver flukes, *Fasciola hepatica* and *F. gigantica* are zoonotic parasitic flatworms of significant health and economic interest. Predictions on livestock production estimates losses at over $3 billion annually in reduction in meat, milk and other agriculturally significant yields. The WHO has also designated fascioliasis, liver fluke disease, as a neglected food borne human disease with up to 17 million infections and up to 200 million people living in areas at risk. In absence of vaccines, the current mainstay treatment is Triclabendazole (TCBZ); the only drug effective against both juvenile and adult flukes. However, evidence of TCBZ resistance is now confirmed worldwide and new chemical compounds are being discovered or designed and synthesised to novel protein targets in liver flukes to combat increasing TCBZ resistance. Sigma class glutathione transferases aka prostaglandin D synthases offers a key target, due to well characterised role in immune modulation and limited relationship to host orthologues and potential roles specific life cycle stages. Using structure - activity response studies and computer assisted modelling, drug structures are being designed and synthesised to screen for activity and specificity. Enzyme kinetic studies are being used to elucidate compound inhibitory profiles in

comparison between native and recombinant enzymes, prior to lead compounds being measured for toxicity in cell lines and ultimately animal tolerance testing.

Poster 11 : Transcriptome analysis of malaria parasite and endothelial cell responses to co-adhesion interactions - - *A12888*
Presenter: **Mr Basim Othman**, *PhD student, Liverpool School of Tropical Medicine*

**B Othman**[2]; S Wagstaff[2]; A Pain[1]; A Craig[2];
[1] Biological and Environmental Sciences and Engineering Division, Saudi Arabia; [2] Liverpool School of Tropical Medicine

The interaction between *Plasmodium falciparum* infected erythrocytes and endothelial cells is thought to play a key role in the pathogenesis of cerebral malaria (CM). This interaction between different repertoires of receptors/ ligands could mediate downstream effects on both the host and the parasite and can also influence protection and susceptibility to disease. The purpose of the present study was to understand how the malaria parasite can alter the behaviour of human microvascular endothelial cells responses via co-adhesion interactions. To investigate this phenomenon, Illumina next generation sequencing was used to profile the transcriptional changes of HBMEC and HDMEC in response to IT4var14 parasite isolate in the presence of tumour necrosis factor cytokine (TNF) at 6h and 20h. The most highly significant gene of interacting IT4var14 parasite with HBMEC at 6h was C3, whereas; the ID2 gene was the lowly expressed gene. At 20h of interaction malaria parasite with brain cells, PRND was highly up-regulated gene, however; NOG gene was the most down-regulated gene. The gene functional annotation analysis illustrated that adhesion of the malaria parasite with HBMEC at 6h induced the expression of genes involved in inflammation and apoptosis, such as PLA2G4A. However, it reduced expression of other genes involved in NOTCH signalling, for example HES1. Adhesion of malaria parasite with brain cells at 20h leaded to reduction in cells proliferation. Overall, the outcomes from the study facilitate a greater understanding about changes in host responses after cytoadherence with the malaria parasite, identifying pathways with potential pathogenic or protective roles.

Poster 12 : Development of novel DNA minor groove binders for the treatment of animal African trypanosomiasis - - *A12889*
Presenter: **Dr Federica Giordani**, *Research Assistant, University of Glasgow*

**F Giordani**[6]; K Gillingwater[3]; A I Khalaf[5]; F J Scott[5]; C J Suckling[5]; L J Morrison[2]; H P De Koning[4]; R Peter[1]; M Witty[1]; M P Barrett[6];
[1] GALVmed; [2] Roslin Institute; [3] Swiss Tropical and Public Health Institute, Switzerland; [4] University of Glasgow; [5] University of Strathclyde; [6] WTCMP University of Glasgow

Animal African trypanosomiasis (or nagana) is a wasting disease caused by protozoan trypanosomes *Trypanosoma congolense*, *T. vivax* and *T. brucei*. Transmitted by haematophagous flies, these parasites cause high morbidity, mortality and infertility in livestock, with disastrous effects on Africa's rural economy. As resistance to the few compounds licensed to treat and prevent infection soars, the quest for efficacious alternatives becomes a critical research priority. Following evidence of good activity against the three aetiological agents of nagana, we are currently progressing a series of DNA minor groove binders (S-MGBs). *In vivo* activity was demonstrated for

selected S-MGBs in a standard *T. congolense* mouse model. No indications of cross-resistance to the currently used drug diminazene aceturate have emerged, and the S-MGBs also retained their activity against parasites resistant to the other veterinary trypanocides isometamidium chloride and homidium bromide. Although the S-MGBs are believed to target the parasite's DNA, their specific MOA is still unclear. After treatment with high doses, partial inhibition of DNA synthesis and changes in the nucleotide pool were observed, along with an accumulation of parasites with multiple nuclei and kinetoplasts, indicative of a cytokinesis block. Whether these are direct or indirect effects of the S-MGBs is under investigation.

Poster 13 : Water resource, hygienic practice, and soil-transmitted Helminthiasis in some rural communities of Osun State, Nigeria - - *A12893*

Presenter: **Prof Uwemedimo Ekpo**, *Postgraduate student, Federal University of Agriculture Abeokuta*

T S Fafunwa[3]; H Mogaji[4]; A S Oluwole[1]; A A Adeniran[1]; M T Fagbenro[1]; S O Sam-Wobo[1]; B S Bada[2]; **U F Ekpo**[1];
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A study to investigate the burden of Soil Transmitted Helminthiasis (STH) and status of WASH resources was conducted in eight rural communities in Osun State, Nigeria. Four of the communities were supported with improved water and hygiene resources (Category A), and another four supported only with improved water resources (Category B). Two hundred and sixteen fresh stool samples were collected from consenting community members and screened for *Ascaris lumbricoides*, Hookworm and *Trichuris trichiura* infections. The status and condition of WASH resources were determined using questionnaire and physical observation. An overall prevalence of 35.2% was observed for any STH infection. Species' prevalence of *A. lumbricoides* , Hookworm and *T. trichiura* prevalence was 33.8%, 22.7%, and 0.5% respectively. Intensity of STH infection was significantly higher in Category A communities than in Category B communities. The prevalence of STH in Category A communities was higher (42.0%) than that in Category B communities (30.1%). There were significant differences (p = 0.000) in STH infections between the two categories. The status of improved water supply was not significantly different (p =0.3153) in the two categories. Knowledge, attitude, and practices about STH, its transmission and control were low in both categories of communities. These results imply that current WASH provision which tends to focus on resource distribution, equity, and coverage, is unlikely to impact on STH transmission and control.

~~Poster 14 : Quantifying the physical, social and economic impact of chronic lymphatic filariasis in Nigeria - - *A12899*~~

~~Presenter: **Mr Obiora Eneanya**, *PhD Candidate , Imperial College London*~~

~~**O Eneanya**[1]; **T Garske**[1]; C Donnelly[1];~~
~~[1] Imperial College London~~

~~Lymphatic filariasis (LF) is a mosquito-borne parasitic disease and a leading cause of disability worldwide. To better understand requirements for morbidity management, it is important to evaluate the needs of sufferers. This study aimed to quantify the physical, social and economic impact of LF in two endemic rural communities in Nigeria. We used a matched case-control study strategy. Cases~~

~~were identified with the help of district health officers and community-directed distributors (CDDs) of mass drug administration (MDA) programmes. Seemingly disease-free Controls were selected from similar population as Cases, matched by age and sex. Logistic regression was performed in R. 52 Cases and 52 controls participated in this study. Among Cases, 48 presented with various stages of lower limb lymphedema, and 4 with scrotal elephantiasis. 40% of all Cases reported to feel stigma and were 10 times (95% CI: [1.7, 55.7]) more likely to avoid forms of social participation. Cases were 7 times (95% CI: [0.3, 135.5]) more likely to be divorced and 20 times (95% CI: [2.9 to 142.5]) more likely to remain unmarried. Cases were 68% (95% CI: [0.06, 1.6]) less likely to have skilled employment and spent significantly less time engaging in income generating activities. The economic effect of lower income was exacerbated by health expenditure as Cases were 55 times (OR 55.7, 95% CI 16.8 to 184.3) more likely to spend over $100 on their last healthcare payment. As the push for elimination of LF as a public health problem intensifies, morbidity management requirements needs to be better understood so that most essential support is provided to sufferers.~~

Poster 15 : Practices of cattle keepers of southwest Nigeria in relation to bovine trypanosomosis - - *A12900*
Presenter: **Dr Paul Odeniran**, *PhD student, University of Edinburgh*

**P Odeniran**[1]; I Ademola[2]; E MacLeod[1]; **S Welburn**[1];
[1] University of Edinburgh; [2] University of Ibadan, Nigeria

The rainforest zone of Nigeria has become settlement for pastoralists because of its market advantage despite fly abundance. This study aimed at evaluating the impact of bovine trypanosomosis and its vectors from livestock owners sense of proportion. Participatory rural appraisal was conducted with 209 livestock owners (households) in 10 locations to determine the practices of animal husbandry, knowledge and attitude to bovine trypanosomosis. Disease peaks were reported to be between March – August. A total of 70.8% (CI: 64.32 – 76.56%) owners perceived trypanosomosis as a major disease, 13.4% (CI: 9.43 – 18.68%) practised transhumance in wet season, 93.9% (CI: 88.58 – 96.92%) use trypanocides and approximately US$ 8.4 million is spent annually on trypanocides in the zone. About 60.5% (CI: 51.84 – 68.48) make use of insecticides against transmitting vectors and only 1.9% (CI: 0.75 – 4.82%) have ever heard of any form of government intervention scheme (which existed three decades previously). Estimated losses US$ 426 (80 – 100% loss) can be incurred on a single animal depending on the size and market value. There is significant increase (16.2%, CI: 11.15 – 23.00%, $P < 0.05$) in the mortality rate of bovine trypanosomosis when compared to other livestock diseases. It is therefore necessary to strategically consider integrated measures of combating the disease with modifications since the livestock keepers have the wrong approach in managing the disease.

Poster 16 : Expression and characterisation of *Plasmodium falciparum* NADPH-cytochrome $P_{450}$ reductase - - *A12903*
Presenter: **Piyaporn Jirawatcharadech**, *Liverpool School of Tropical Medicine*

**P Jirawatcharadech**[1]; G Camarda[1]; C Yunta-Yanes[1]; M J Paine[1]; G Biagini[1]; S A Ward[1];
[1] Liverpool School of Tropical Medicine

NADPH-cytochrome P450 reductase is a membrane-bound protein required for electron transfer from NADPH to cytochrome p450 (CYPs). In humans, CYPs are essential for biotransformation of potentially toxic compounds. A homologous of human CPR has been identified in *Plasmodium falciparum,* however; a sequence-conserved CYP has not been reported in the genome. The absence of a CYP in *P. falciparum* raises the question of what alternative role and function of the PfCPR. We report here the expression of a functional truncated PfCPR in *Escherichia coli*. The soluble protein was successfully purified by Ni-NTA affinity followed by SP sepharose chromatography. A spectral characterisation of purified PfCPR was recorded in both oxidised and reduced forms. Initial steady-state enzyme kinetics of cytochrome *c* reduction in PfCPR were performed. The inhibitory effects of adenosine analogs (e.g. NAD, NADH, NADP, and 2',5'-ADP) and the flavoprotein inhibitor (e.g. diphenyliodonium chloride) on PfCPR activity were studied and are described herein.

Poster 17 : Large-scale screening effort to identify new chemical starting points for visceral *Leishmaniasis* using a novel *in vitro* screening cascade - *- A12904*
Presenter: **Mrs Lalitha Sastry**, *Biologist, University of Dundee*

**L Sastry**[1];
[1] University of Dundee

A key issue in visceral *Leishmaniasis* (VL) drug discovery is the difficulty finding new chemical starting points. Poor translation between the developed insect stage promastigote or axenic amastigote assays and the "gold-standard" intracellular assays has often been observed. The work presented here shows how some of these issues can be overcome by redeveloping existing assays and combining assays in screening cascades. The screening cascade presented was used to screen a large number of compounds from various pharma and commercial sources. We reconfigured our existing axenic amastigote assay to only detect compounds that are cytocidal. This was achieved by improving the detection limit of the assay and increasing the starting cell density. A screening cascade was developed using the "cidal" axenic amastigote assay as a primary screening platform, followed by potency and selectivity determination and a human counter-screen assay, and finally by assessment in a high-content intracellular amastigote assay. This cascade was used for the screening of >700,000 compounds. Our results show that the cidal axenic amastigote assay is a better predictor of intracellular amastigote activity compared to its non-cidal format. It provides a valuable primary screening platform for large scale screens, especially since throughput limitations do not allow the use of the intracellular assay. The screening cascade used here was successful in identifying several new hit series for VL drug discovery. Results from a single screening campaign will be presented. This work shows that there is value in using axenic *Leishmania* screening assays, and that the way these are configured, in particular with respect to the detection limit, has a major impact on the hits identified, and their translation to intracellular amastigote activity. Through the use of a rational and pragmatic screening cascade we have been able to identify much needed new chemical starting points for VL drug discovery.

Poster 18 : The behaviour and ecology of highly insecticide resistant malaria vectors in south-western Burkina Faso. - *- A12911*
Presenter: **Mr Antoine Sanou**, *PhD candidate , University of Glasgow*

**A S Sanou**[1];
[1] University of Glasgow

Long lasting impregnated nets (LLINs) are the most common and successful method of malaria vector control in Africa. However, the continued success of this approach is being threatened by the emergence of insecticide resistance and/or behavioural changes in vector populations that reduce their contact with LLINs. Insecticide resistance has now been detected in malaria vectors throughout Africa, with exceptionally high levels occurring in Burkina Faso. Understanding the consequences of resistance for malaria control requires a detailed understanding of the ecology, behaviour and transmission potential of insecticide resistant vectors. Here we describe the establishment and initial results from a new surveillance study in Burkina Faso, designed to investigate the ecology of insecticide resistance vectors. A 3-year longitudinal study was initiated in October 2016 to study the population dynamics, behaviour and ecology of malaria vector populations within 12 villages in south-western Burkina Faso where insecticide resistance levels are high. This study began just one month later deltamethrin based LLINs (Permanet® 2.0) were distributed to the population. Resting mosquitoes and host seeking mosquitoes are being sampled monthly in each village using respectively resting Bucket and human landing catch both indoor and outdoor the houses. A new exposure-free Mosquito Electrocuting Trap (MET) is being evaluated as an alternative to the gold standard Human Landing Catch for measuring vector biting activity. Mosquito abundancy, time and location of biting, and location of resting (in/outside houses) were recorded. Results: Results from the first three months of study indicate malaria vector abundance is high (an average 52 mosquitoes per night, SEM 9.50), and varies between sites (between 4 and 240 mosquitoes per night with respectively SEM between 1.54 and 66.36). Most malaria vectors were from the *A. gambiae* complex (~ 90%) and importantly *A. coluzzii* and *A. gambiae*. Whilst these species are typically considered to be indoor biters, high levels of outdoor biting were recorded at all sites (56.82%). The MET collected proportionately fewer mosquitoes than the HLC, but provided a similar representation of vector biting behaviour. Preliminary results indicate that insecticide resistant vectors can also exhibit behavioural avoidance strategies (outdoor biting) that limit their contact with LLINs. Longer term investigation is required to evaluate the net effect of these strategies to malaria control.

Poster 19 : Profiling of transposase accessible chromatin reveals general features of the regulator chromatin landscape in malaria parasites - *- A12916*
Presenter: **Dr Sebastian Kirchner**, *Research Fellow, University of Glasgow*

**S Kirchner**[1]; M Van Wyngaarden[1]; H Vaikkinen[1]; A P Waters[1];
[1] WTCMP University of Glasgow

Malaria represents one of the major global threats to human health. It is caused by unicellular parasites of the *Plasmodium* genus, which alternate between their mosquito vector and mammalian host. The complex life cycle requires the parasite to transition through many phases each with its own gene expression profile. Within the confined nuclear space of eukaryotic cells DNA is usually wrapped around histone octamers to form so-called nucleosomes, which are further organized into densely packed chromatin. Despite its

compact organisation, key molecular players of fundamental biological processes associated with developmental transitions such as transcription, DNA replication, and DNA repair require access to the genetic code. This accessibility is tightly regulated through chromatin remodelling processes, facilitating dynamic conversion of chromatin regions between an accessible and inaccessible state. We have adapted the recently developed Assay of Transposase-Accessible Chromatin using sequencing (ATAC-seq) to the extreme AT-rich genome of the rodent malaria species *Plasmodium berghei*. ATAC-seq is based on the integration of next-generation sequencing compatible adaptors into regions of accessible chromatin using a hyperactive transposase. By profiling accessible chromatin regions throughout the *P. berghei* intra-erythrocytic development cycle we uncovered general features of the regulatory chromatin landscape in malaria parasites. These include the identification of transposase accessible chromatin sites, correlation between open chromatin in promoter regions and transcription of their downstream genes, and positioning of nucleosomes along key transcriptional features. This will set the scene for an expanded study to understand the impact of the histone code on chromatin structure and accessibility

Poster 20 : Biochemical and structural characterization of selective allosteric inhibitors of the *Plasmodium falciparum* drug target, prolyl-tRNA synthetase - - *A12920*

Presenter: **Ms Irene Hallyburton**, *Biologist, University of Dundee*

**I Hallyburton**[4]; **S N Hewitt**[2]; D M Dranow[2]; B Forte[4]; C Jansen[4]; B Baragaña[4]; C Walpole[3]; W C Van Voorhis[1];
[1] Center for Emerging and Reemerging Infectious Disease (CERID), University of Washington, United States; [2] Seattle Structural Genomics Center for Infectious Disease (SSGCID), United States; [3] Structure-guided Drug Discovery Coalition (SDDC), Canada; [4] University of Dundee, UK

*Plasmodium falciparum* (Pf) prolyl-tRNA synthetase (ProRS) is one of the few chemical-genetically validated drug targets for malaria, yet highly selective inhibitors have not been described. In this poster we describe the screening of approximately 40,000 compounds to identify compounds that selectively inhibit Pf ProRS enzyme activity. X-ray crystallography structures were solved for apo, as well as substrate- and inhibitor-bound forms of Pf ProRS. Two new inhibitors of Pf ProRS that bind outside the active site were identified. These two allosteric inhibitors showed >100 times specificity for Pf ProRS compared to HsProRS, demonstrating that this class of compounds could overcome the toxicity related to HsProRS inhibition by halofuginone and its analogues. Initial medicinal chemistry was performed on one of the two compounds, guided by the co-crystallography of the compound with Pf ProRS, and the results can instruct future medicinal chemistry work to optimize these promising new leads for drug development against malaria.

Poster 21 : Occurrence of *Cryptosporidium* in UK sheep - - *A12941*

Presenter: **Eijelana Salim**, *Student, Salford University*

**E Salim**[1]; R J Birtles[1]; D R Brooks[1];
[1] University of Salford, UK

The protozoan parasite *Cryptosporidium* infects a wide range of animals, including humans, across the world. However, there is a paucity of data on the presence of this parasite in livestock in the United Kingdom. We therefore investigated the occurrence of *Cryptosporidium* spp. in sheep at two farm locations in North West England using a combination of classical parasitological and molecular approaches. Across 2015-16, a total of 552 faecal samples were collected from female sheep (Swaledale and Herdwick breeds) reared at two farms in South Cumbria. DNA extractions have been performed on the faecal samples and the presence of *Cryptosporidium* parasites confirmed by successful PCR amplification targeting either the 18S rRNA gene, or the actin gene. In total, 99 samples (17.9%) were confirmed positive, and 94 of these were typed to species level by sequencing of the PCR products. The most common species was found to be *C. xaio*; other species noted, in decreasing order of prevalence, were: *C. ubiquitum*, *C.* sp. and *C. parvum*. Analysis of the *C. ubiquitum* isolates by PCR amplification of the gene encoding GP60 confirmed that they were all the same subtype (XIIa). Infections in 55 of the 99 PCR-positive samples were also confirmed using staining (cold Kinyoun's ZN stain) and microscopy. A qPCR-based approach targeting the 18S rRNA gene was then utilized to assess parasite infection loads. The maximum and minimum *Cryptosporidium* infection loads (oocysts per $gm^{-1}$ faeces) were confirmed as 43,000 and 1 respectively. Overall, the data confirms that different *Cryptosporidium* species are present in UK sheep, that prevalence levels are relatively high and that these livestock may potentially act as a reservoir of zoonotic disease. We are now investigating potential environmental sources of *Cryptosporidium*.

Poster 22 : Study the therapeutic potential of philokinone in experimental cutaneous *Leishmaniasis - - A12967*

Presenter: **Dr Shahnaz Shirbazou**, *Associate Professor of parasitology, University of Medical Sciences*

**S shirbazou**[1]; S Damghani[2]; N Maspi[3];

[1] Baqiyatallah University of Medical Sciences. Tehran, Iran; [2] Shahid Beheshti University, Tehran, Iran; [3]Tarbiat Modares University, Tehran, Iran

Cutaneous leishmaniasis is the most common form of leishmaniasis affecting humans. The available treatments are not well tolerated, and have side effects. The purpose of this study was to examine the possible useful effect of vitamin K1 (phylloquinone) in the complementary treatment of cutaneous leishmaniasis. In this case-control study, *Leishmania major* amastigote (MRHO/IR/75/ ER), were inoculated in the foot of 24 Balb/c mice. After 25 days, the lesion appeared in Mice feet. The mice were divided into 3 groups and treated with standard doses of phylloquinone (vitamin K1), and Glucantime for 28 days, interperitoneally. The control group received no treatment. Ulcer lesion size was measured in both groups. Based on paired t-test, the mean effect of Glucantime reduced over time from zero week to fifth week. Phylloquinone decreased from zero week to third week, and then took an upward turn so much that in the fifth week has reached the baseline level as in the zero week. Average effect of Glucantime was (0.61 ±-6.33), and phylloquinone (0.39 ±-6.59). Mean difference of drugs was statistically significant (0.001). According to the results, it seems that vitamin K1, due to fibrinopeptide and thrombin, can be used as a substitute treatment in controlling the lesion in the first three weeks of cutaneous leishmaniasis in the absence of other drugs or the prohibited use of Glucantime. Therefore, it is recommended that similar studies be done with vitamin K1, and Glucantime.

Poster 23 : A-lice through the looking glass: monitoring sea louse infection of wild salmonids in the river Tamar, England (UK) - - *A12976*
Presenter: **Dr Jo James**, *Technical Officer, Environment Agency*

**J James**[1]; H Bradley[1]; A J Reading[1]; R Hillman[1]; P Elsmere[1]; C F Williams[1];
[1] Environment Agency

The sea lice, *Lepeophtheirus salmonis* and *Caligus elongatus* are amongst the most damaging parasites of farmed salmonid fish globally. Infections of sea lice may also impact wild fish populations following spill-over from aquaculture production. However, little is known about the interactions between wild and farmed populations, with a paucity of data on 'natural' sea louse levels in wild fish. Here, we screened wild adult sea trout (*Salmo trutta*) and Atlantic salmon (*Salmo salar*) returning to the river Tamar, England, for the presence of sea lice. From 2013 to 2015, the average prevalence of sea lice on these fish was 55% (range: 51-58%) and the mean intensity of 6.19 (range: 1-66). All 2520 lice collected were identified as *L. salmonis.* Mean infection intensity did not differ between fish species or across years. Epidermal erosion and localised haemorrhage were observed more frequently in infected than uninfected fish (28% and 11%, respectively). In addition, within infected fish, infection intensity was positively correlated with the amount of external damage present on both *S. trutta* and *S. salar.* This is the first study to establish infections of sea lice in wild migratory salmonids in England. Whilst the prevalence of *L. salmonis* in salmonid fish returning to the river Tamar was low compared to other regions elsewhere in the UK, there is the potential that future development of marine aquaculture could increase disease risk to wild fish populations, already under pressure from declining marine survival, climate change, habitat loss and barriers to migration.

Poster 24 : Investigating nanoparticle-induced hyperthermia as a novel method for treatment of cutaneous leishmaniasis - - *A12994*
Presenter: **Dr Helen Price**, *Lecturer in Bioscience, Keele University*

S L Berry[2]; C Hoskins[1]; N Telling[1]; **H Price**[2];
[1] Institute for Science and Technology in Medicine, Keele University; [2] School of Life Sciences, Keele University

The use of magnetic nanoparticles to produce heat (magnetic hyperthermia) has gained considerable interest in development of novel cancer therapies due to the increased sensitivity of cancerous cells to heat shock. In the current study, we are taking the first steps to establish whether magnetic hyperthermia could be used as an inducible, controlled and localised form of thermotherapy for cutaneous leishmaniasis. Stable ferrofluids were produced by coating a range of iron oxide nanoparticles with citric acid. Uptake of nanoparticles by the human monocytic cell line THP-1 and *Leishmania mexicana* axenic amastigotes was analysed by FerroZine assays, microscopy and flow cytometry. Magnetic hyperthermia was induced by the application of an alternating magnetic field and the resulting effects on cell viability and morphology were investigated. The magnetic nanoparticles were readily taken up by differentiated THP-1 cells and a controlled increase of temperature of up to 20°C could be achieved by application of an alternating magnetic field. Treatment with nanoparticles alone had a limited effect on viability of macrophages and amastigotes, whereas the subsequent induction of magnetic

hyperthermia was found to be highly effective in killing parasites in vitro. Studies are ongoing to characterise the uptake, localisation and effects of magnetic nanoparticles in THP-1 and *L. mexicana* amastigotes and to determine the effects of magnetic hyperthermia on *L. mexicana* infected macrophages.

Poster 25 : Co-evolutionary analyses of the symbiosis between the sheep tick (*Ixodes ricinus*) and its symbiont '*Midichloria*' by multi-locus sequence typing - *A13024*

Presenter: **Mrs Alaa Al-Khafaji**, *PhD student, University of Liverpool/ Institute of Infection and Global Health/ Department of Infection Biology*

**A AL-Khafaji**[3]; S Clegg[3]; K Hansford[1]; J Medlock[1]; J McGarry[3]; E Feil[2]; D Sassera[4]; B Makepeace[3];
[1] Public Health England, Salisbury, UK, UK; [2] University of Bath, UK; [3] University of Liverpool, UK; [4]University of Pavia, Italy

The sheep tick *Ixodes ricinus* is the most important tick of medical and veterinary importance in Europe. It also harbours a vertically-transmitted bacterial endosymbiont, *Midichloria mitochondrii* (Rickettsiales: Midichloriaceae), which is found in 100% of adult female and ~50% of adult male *I. ricinus* in continental Europe. The nature of the relationship between *M. mitochondrii* and *I. ricinus* is unknown, but the lifecycle of the symbiont involves replication inside mitochondria and the bacterial density increases dramatically following a blood meal. In this study, we sought to estimate the prevalence of *M. mitochondrii* in English *I. ricinus* and the population genetic structure of the symbiont in relation to its host across Europe. We assayed a total of 500 nymphs from five sites across southern England, which revealed a prevalence of *M. mitochondrii* of 80%. However, the density of *M. mitochondrii* in English nymphs was apparently higher than that previously reported from the Czech Republic. A multi-locus sequence typing (MLST) for *M. mitochondrii* was developed and used alongside an established mitochondrial MLST scheme for *I. ricinus*. New data were compared with 318 British and 188 Latvian published *I. ricinus* mitochondrial sequences that exhibited 10% and 14% variability at the DNA and amino-acid level, respectively, allowing some differentiation between British and Latvian samples. Among French, German and Italian ticks, small clusters of Italian and German mitochondrial sequences were observed, while other sequences were distributed throughout the tree. The MLST scheme for *M. mitochondrii* indicated low levels of diversity, with some geographic clustering in continental Western Europe and partial congruence with the phylogeny of the tick host. Further co-evolutionary analyses of *M. mitochondrii* and its host will facilitate the characterisation of this symbiosis (parasitic, mutualist or commensal), as well as its origin and spread.

Poster 26 : Time resolved metabolic foot printing of *Leishmania mexicana* promastigotes in simple defined minimal media. - *A13007*

Presenter: **Mrs Archana Nayak**, *PhD student, University of Glasgow*

**A Nayak**[1]; M P Barrett[2]; R J Burchmore[1];
[1] University of Glasgow; [2] WTCMP University of Glasgow

Metabolic foot printing involves quantification of metabolite uptake and excretion from the culture media. Use of chemically defined media for metabolic foot printing brings new insights into nutrients utilisation, determination of growth dependent changes of cellular metabolism and standardisation of results between laboratories. In our study, time resolved metabolic foot printing was carried out by comparison of culture supernatant of *L. mexicana* promastigotes at various time points and extensive bioinformatics analysis was carried out to derive significant biological information. Of the 205 metabolites putatively identified across replicates in both positive and negative ionisation mode, 68 metabolites matched with authentic standards for individual mass/charge ratio and retention time comparison. Overall, ~25 % metabolites depleted from the medium, ~15% not changed significantly and ~40% of metabolites significantly enriched in the medium. Glucose, adenosine and certain amino acids were amongst the depleted components of the medium compared to vitamins from the defined medium composition. Furthermore, amino acids such as L-tryptophan, L-aspartate, L-glutamate, L-arginine, L-methionine and L-serine were classified under continuous utilisation as more than half the initial abundance were consumed from the medium in nine days growth period. Amino acids such as L-leucine, L-threonine, L-valine, L-phenylalanine, L-tyrosine and L-lysine were taken up moderately. L-Glycine, L-glutamine, L-asparagine, L-proline and L-alanine were significantly enriched in medium over time. Systematic analysis of the 40% excreted small molecules enriched in the culture media allowed new insights about their role in establishment of parasitism, with macrophage cells as *in vitro* experimental model.

Poster 27 : Morphology and molecular diversity of Leishmaniasis and sand fly species in Albaha region, Saudi Arabia. - *A13015*
Presenter: **Mr Ali Alghamdi**, *PhD Student, Institute of Infection Immunity and Inflammation*

**A Alghamdi**[2]; H P De Koning[2]; M Wagih[1];
[1] Albaha University, Albaha, KSA, Saudi Arabia; [2] University of Glasgow , UK

This paper presents a research plan and preliminary data of a PhD project on the genetics of *Leishmania* strains and sand fly species isolated from Albaha province, Saudi Arabia with emphasis on markers for drug resistance and diversity in the sequences and relevant transport proteins to gain insights in the epidemiology and diversity of Leishmaniasis in the region.

Poster 28 : Evaluation of *Trypanosoma cruzi* phosphodiesterases as potential drug targets - *A13016*
Presenter: **Miss Titilola Kalejaiye**, *PhD student, University of Glasgow*

**T Kalejaiye**[3]; J Munday[3]; H de Koning[5]; J Siciliano de Araújo[1]; M de Nazaré Correia Soeiro[1]; L Maes[2]; R Leurs[4];
[1] Instituto Oswaldo Cruz, Brazil; [2] University of Antwerp, Belgium; [3] University of Glasgow , UK; [4] VU University Amsterdam, Netherlands; [5] Wellcome Trust Centre for Molecular Parasitology, University of Glasgow, UK

Chagas disease is primarily a disease of South and Central America, and it is caused by the protozoan parasite *Trypanosoma cruzi*. The available drugs benznidazole and nifurtimox are only effective against the acute stage of the disease and there are different strains

of the parasites that are innately resistant to current treatment. There is therefore need for new, safer, more affordable, easy to administer and effective drugs. In order to avoid cross-resistance with current therapies, these should have a different mode of action from the existing ones. Cyclic nucleotide phosphodiesterases (PDEs) from trypanosomatids appear to be a good target. With success recorded by targeting human PDEs and also PDEs from *T. brucei*, we aim to target and evaluate the PDEs of *T. cruzi* as potential drug targets. Since *T. cruzi* is divided into different groups, we decided to use genomic DNA from two strains of *T. cruzi* (Colombiana and Y strain) that differ in their sensitivity to available chemotherapy and geographical locations. Cloning of the PDE genes from the two strains has been completed and we have started complementation assays to evaluate whether TcrPDEB1 and B2 can complement for the activity of TbrPDEB1/2. This work is part of the PDE4NPD (PhosphoDiEsterases for Neglected Parasitic Diseases) consortium. This consortium pursues target repurposing of phosphodiesterase inhibitors to shorten new drug discovery times for neglected parasitic diseases. Therefore, we rely on this consortium for genetic materials and compounds to be tested on our constructs. We intend to build on success stories from human PDE inhibitors (Maurice et al., 2014) and also from validation of *T. brucei* PDEs as drug targets (De Koning et al., 2012) for the evaluation and characterization of TcrPDEs as drug targets and the development of TcrPDE inhibitors. There is sufficient knowledge of the structure of this enzyme family and this can be exploited to design highly efficient parasite-specific PDE inhibitors.

Poster 29 : Comparative evaluation of molecular methods to detect *Leishmania* DNA in dogs - *- A12752*
Presenter: **Miss Andreia Albuquerque**, *PhD, Medizinische Hochschule Hannover*

**A Albuquerque**[2]; L Cardoso[3]; L Campino[1]; S Cortes[1];
[1] Global Health & Tropical Medicine/IHMT/UNL, Portugal; [2] Medizinische Hochschule Hannover, Germany; [3] University of Tras-os-Montes e Alto Douro, Portugal

Canine leishmaniasis is a zoonotic disease caused by *Leishmania infantum* and transmitted by phlebotomine sand flies. It is considered an important veterinary and public health problem in many countries, namely in the Mediterranean basin and Brazil, where dogs are considered the main reservoir hosts of the parasite. Not only diseased dogs but also those sub-clinically infected play a relevant role in the transmission, therefore, early diagnosis is essential. Currently a wide range of accurate and sensitive molecular tools as approaches for diagnosis are under use. The aim of this work was to compare four PCR-based protocols for the diagnosis of canine leishmaniasis in a cohort of dogs from north-eastern Portugal. 229 bone marrow samples were collected from dogs in Douro region, an endemic area for leishmaniasis. Four PCR protocols were evaluated for *Leishmania* DNA detection in canine samples, three single (ITS1, MC, Uni21/Lmj4 PCRs) and one nested (SSUr RNA-nPCR). The higher percentage of infected dogs was detected with the SSU rRNA-nPCR (37.6%), which also was able to detect the parasite DNA in a higher number of samples from apparently healthy dogs (25.3%). The SSU rRNA-nPCR is an appropriate method to detect *Leishmania* infection in dogs. Accurate and early diagnosis in clinically suspect as well as apparently healthy dogs is essential, in order to treat and protect animals and public health contributing to control and awareness of the disease.

Poster 30 : Addition of a *Leishmania* strain panel to the hit discovery screening cascade for visceral leishmaniasis improves translation to *in vivo* efficacy studies. - - *A12843*

Presenter: **Lorna MacLean**, *Post-doc, Drug Discovery Unit*

**L M MacLean**[1]; M De Rycker[1];
[1] University of Dundee

Visceral Leishmaniasis (VL) is caused by the protozoan parasites *Leishmania donovani* and *L. Infantum* which are transmitted by female phlebotomine sandflies. VL causes >50,000 deaths annually, new drugs are urgently required. Our *in vitro* screening cascade to identify new phenotypic hits against *L. donovani* which could progress to new clinical candidates starts with an axenic amastigote luminescence assay, followed by a high-content image-based intracellular assay (LdBob/THP1). However, to identify compounds that are effective against clinically relevant strains from different geographical locations development of a strain panel was undertaken. Low passage metacyclic parasites were used to infect CD14+ M-CSF differentiated human PBMC which were subsequently dispensed onto compound containing 96 well plates for 96h. These were stained with Sytox green and imaged by the Operetta to generate potency and toxicity data. (Buffy coat was obtained ethically and its research use was in accordance with the terms of donor informed consent). High levels of PBMC infection was observed for all *Leishmania* strains. However, replication rates varied and strain-specific variation in potency profiles was reported for some compounds. In addition, the potency data generated in this assay was a better predictor of pharmacokinetic/ pharmacodynamic relationships reported in our *in vivo* animal model relative to the LdBob/THP1 assay. Incorporation of a *Leishmania* strain panel using primary macrophages and clinically relevant strains has proved essential in building confidence in hits coming through our VL screening cascade and has improved predictability of *in vivo* efficacy results.

Poster 31 : Improved equine faecal egg counting - Validation of a novel method: FECPAKG2 - - *A12866*

Presenter: **Mrs Fiona Tyson**, *PhD student, Aberystwyth University*

**F Tyson**[1]; S Dalesman[1]; P M Brophy[1]; R M Morphew[1];
[1] Aberystwyth University - IBERS

Faecal egg counts (FECs) are the standard method of diagnosing the level of parasitic infection in horses and other grazing animals. Testing before treatment is an important factor in slowing the appearance of anthelmintic resistance in nematode parasites of horses. The FECPAK$^{G2}$ allows owners to perform FECs on their own animals, without the need for a microscope or any specialist knowledge. A comparison of the FECPAK$^{G2}$ (G2) method with an accepted FEC method (FECPAK$^{G1}$) was made, using samples from 17 horses in Wales and 22 horses in New Zealand. There was no significant difference between the FECs obtained using the two methods (rmANOVA: $F_{1,37} = 0.052$, $p = 0.821$, $\eta^2_p = 0.001$), and no effect of the country of origin of the data (rmANOVA: $F_{1,37} = 2.084$ $p = 0.157$, $\eta^2_p = 0.053$). Accuracy of the G2 method was not affected by FEC level ($r = -0.251$ (CI: 0.030, -0.472) $p = 0.124$ $n = 39$) and repeatability was slightly better in the G2 method. It was concluded that the FECPAK$^{G2}$ method is an acceptable method of performing

FECs in horses. It is hoped that the user-friendliness of the method will increase the uptake of FECs amongst horse owners, either by direct use of the technology or through their veterinary practice, hence slowing the development of anthelmintic resistance.

Poster 32 : MFS transporters in African trypanosomes: looking for a function. - *A13040*
Presenter: **Amani Alhejely**, *Glasgow University*

**A Alhejely;** V Delespaux[3]; D Tagoe[1]; M Natto[2]; H de Koning[2];
[1] Institute of Infection Immunity and Inflammation; [2] Institute of Infection, Immunity and Inflammation, University of Glasgow; [3] Institute of Tropical Medicine, Antwerp, Belgium; [4] University of Glasgow

The trypanosomiases cover several parasitic diseases that are found in Africa, South Asia and Latin America. In *Trypanosoma brucei*, drug sensitivity and resistance depends on transporters mediating the uptake and/or efflux of chemotherapeutic agents. For example, in *T. brucei* the TbAT1/P2 aminopurine transporter is involved in the uptake of diamidine and arsenical drugs including pentamidine, diminazene aceturate and melarsoprol whilst a loss of TbAT1/P2 and HAPT1 gives a high pentamidine-melarsoprol cross-resistance phenotype in *T. b. brucei*. The related parasite *T. congolense*, has a major amplification of the ENT family (up to 19 members), but phylogenetically most of these cluster as nucleobase transporters rather than nucleoside transporters (P1-cluster) or nucleoside/nucleobase transporters (P2 cluster). As such, *T. congolense* does not have a counterpart of TbAT1 and as a result it is much less sensitive to diminazene, although this is the main drug for the treatment of *T. congolense* infection. Another important class of transporters in chemotherapy mediates efflux of metabolites. Among the most promising drug targets in trypanosomatids are cAMP Phosphodiesterases (PDEs); inhibitors of these enzymes prevent cAMP degradation, leading to toxic levels of cAMP in the cell. However, the effectiveness is limited by a mechanism exporting excess cAMP from the cell. Thus, the efflux transporter for cAMP is important in the pharmacology of PDE inhibitors, and in understanding cAMP signaling in the trypanosome. The aim of the current project is to find *T. congolense* transporter genes (and their orthologues in *T. brucei*) that drive drug resistance and or cAMP efflux. For this we commenced the first study of Major Facilitator Superfamily (MSF) transporters in trypanosomes. Three *T. congolense* MFS transporter proteins (MF 5.2, 7.1 and 18.8) caused significant increases in resistance to Pentamidine in *T. brucei* clone ISMR1, a clone adapted to high levels of resistance to isometamidium but sensitive to pentamidine suggesting a possible efflux mechanism. Both alleles of the syntenic *T. brucei* genes were knocked out using homologous recombination and functionally characterised. The phenotypes of each of the gene deletion mutants will be presented. The cellular localisation of these MFS transporters is being assessed using fluorescence microscopy. This study constitutes the first attempt to determine functions for some of the MFS transporters expressed by trypanosomes.

Poster 33 : Heterologous expression of *Trichomonas vaginalis* equilibrative nucleoside transporter family members in *Trypanosoma brucei* - *A13042*
Presenter: **Dr Manal Natto**, *Postdoctoral, Glasgow University*

**M Natto**H P de Koning[1];
[1] Institute of Infection, Immunity and Inflammation, University of Glasgow; [2] University of Glasgow

Trichomoniasis is the most common of the non-viral sexually transmitted diseases (STD); it is caused by the amitochondriate protozoan *Trichomonas vaginalis*. Increased resistance of *T. vaginalis* to metronidazole, the drug of choice for the treatment of the disease, necessitates the development of newer chemical entities with different chemotypes. The nucleoside/nucleobase salvage system of the parasite is an attractive target, because the parasite cannot synthesise either purines or pyrimidines *de novo* and has to salvage the nutrients from the host through transporters, whereas their human hosts have both purine salvage and synthesis pathways for purines and pyrimidines. Therefore, depriving the parasites of these essential requirements, through controlled blockage of the salvage transporters or pathways, is certain to cause parasite death, but should not affect the human host. Nucleoside salvage in the parasite was therefore systematically investigated using an array of radiolabelled nucleosides and nucleobases. The results show the existence in *T. vaginalis* of at least four transporters: with high and low affinity for purine and pyrimidine nucleosides, as well for as adenine, similar to that of transport activities previously characterised in other protozoans. In order to match the observed transport activities to specific genes, all 9 *T. vaginalis* Equilibrative Nucleoside Transporter (ENT) genes were cloned from cDNA, sequenced, and expressed in *Trypanosoma brucei*, selecting a strain from which one of the main nucleoside transporters, TbAT1, was already deleted. Each gene was resynthesized in the codon preference of *T. brucei* since *T. vaginalis* DNA. Two identical sets of transfectants have been constructed: one with synthetic but otherwise original open reading frames, and one with the ORFs coupled C-terminally to 6xHA tags to assess cellular localisation of the gene products. Immunofluorescence has demonstrated that the transporters are correctly routed to the cell surface, and qRT-PCR has shown substantial levels of expression.

Poster 34 : Metabolomics analysis of the livestock trypanosomes - *A13021*
Presenter: **Pieter Steketee**, *Research Fellow, The Roslin Institute*

**P C Steketee**[2]; F Achcar[3]; F Giordani[3]; E Paxton[2]; S Jayaraman[2]; A Donachie[3]; M Witty[1]; R Peter[1]; H de Koning[3]; M P Barrett[3]; L J Morrison[2];
[1] GALVmed; [2] Roslin Institute; [3] Wellcome Trust Centre for Molecular Parasitology

The trypanosome species *Trypanosoma congolense* and *T. vivax* are the primary causative agents of animal African trypanosomiasis (AAT). In contrast to *T. brucei*, our biological knowledge of these parasites remains limited. As a result, there is a severe lack of novel therapeutics to counter AAT, which affects tens of millions of livestock annually. Moreover, there have been no new drugs for >50 years and resistance has been reported to the few veterinary trypanocides available. One of the key issues in studying AAT remains our limited ability to culture both *T. congolense* and *T. vivax*. The primary aim of this project is the use of omics-driven approaches to further our understanding of both *T. congolense* and *T. vivax*, with a view to developing optimised in vitro culturing media that will enable the culture of field isolates, as well as high-throughput in vitro drug screens. Using a metabolomics-driven approach, we have identified key differences in the metabolic usage and output of bloodstream forms of a laboratory-adapted *T. congolense* strain (IL3000). We have shown that the parasite consumes significantly less glucose than *T. brucei* and excretes large amounts of succinate

and malate, in contrast to *T. brucei*, for which pyruvate is a primary output. These data suggest bloodstream form *T. congolense* is not solely reliant upon glycolysis, but also utilises other metabolic pathways for central carbon metabolism, highlighting significant metabolic differences between *T. congolense* and *T. brucei* that could have important implications in therapeutic design.

Poster 35 : Nitric oxide, DNA damage and genome integrity in *Trypanosoma brucei*: role of uracil-DNA glycosylase - *A12857*
Presenter: **Miss Miriam Yague Capilla**, *PhD student, Instituto de Parasitologia y Biomedicina "Lopez-Neyra"*

**M Yague-Capilla**[1]; D Garcia-Caballero[1]; M Valente[1]; L M Ruiz-Pérez[1]; A E Vidal[1]; V M Castillo-Acosta[1]; D González-Pacanowska[1];
[1] Instituto de Parasitología y Biomedicina "López-Neyra", CSIC. Granada, Spain

During infection, an essential component of the primary immune response is the production of nitric oxide (NO) by the inducible nitric oxide synthase of activated phagocytes. However, the impact of NO on the progression of African trypanosomiasis is still unclear. The reaction of NO with oxygen radicals gives rise to reactive nitrogen species that generate multiple damage in DNA thus triggering mutagenesis and genome instability, as well as other detrimental effects on proteins and lipids. The base excision repair (BER) pathway plays a pivotal role in counteracting DNA lesions through the removal of defective bases. Uracil-DNA glycosylase (UNG) is the first enzyme of BER responsible for uracil cleavage from DNA. By characterising the formation of strand breaks, the mutation rate and spectra, the uracil and a basic sites content and the number of γH2A repair foci we show that NO exposure has a significant impact on DNA integrity in *Trypanosoma brucei*. Parasites lacking UNG exhibit an increased uracil content as well as a higher number of γH2A repair foci compared to the parental line upon treatment with DETA-NO in vitro. We also report the increased occurrence of uracil and DNA damage in wild-type and UNG knock-out parasites recovered from infections in vivo thus indicating that exposure to the primary immune response has an impact on parasite DNA integrity and that base excision repair has an important role in this process.

Poster 36 : Characterisation and validation of Phosphodiesterase-d in trypanosomes - - *A13061*
Presenter: **Miss Charlotte Marsboom**, *Postgraduate student, University of Glasgow*

**C Marsboom**[1]; T Kalejaiye[1]; H de Koning[1];
[1] Institute of Infection, Immunity and Inflammation, University of Glasgow

*Trypanosoma brucei*, which causes human African trypanosomiasis (HAT) or sleeping sickness, belongs to the group of neglected diseases of the world and is a life-threatening disease. There are three different subspecies of *T. brucei*: *T. b. rhodesiense* causing East African trypanosomiasis which is the acute form, *T. b. gambiense,* which causes West African trypanosomiasis, the chronic form, and *T. b. brucei* which is only infectious for animals but is used as an experimental model of human trypanosomiasis. The tsetse fly is responsible for the transmission, this means that the disease is only prevalent in the natural biotope of the tsetse fly, rural sub-Saharan Africa. Due to vector control and surveillance measurements, the incidence of HAT was gradually reduced in the last decade. HAT has two disease stages. The first one is the haemolymphatic stage which is accompanied by non-specific symptoms such as fever,

lymphadenopathy and headache. The Winterbottom's sign is a typical sign of the gambiense form. The second stage or neurological stage has sleep disturbance and coma as major symptoms. HAT is a life-threatening disease when left untreated. The most used diagnostic tool for the gambiense form is card agglutination test for trypanosomiasis/*T. b. gambiense* (CATT) and microscopical conformation of trypanosomes for the rhodesiense form. The current available treatments are old and have toxic side effects. Drug resistance is also seen in the field. There is an urgent need for new, more efficient and safer drugs. Those drugs need to be easy to administer. Cyclic nucleotide phosphodiesterases (PDEs) may present a new group of drug targets. PDEs catalyse the hydrolysis of cyclic adenosine monophosphate (AMP) to AMP. cAMP plays a role in the cell proliferation of the parasites. Adenylyl cyclases are responsible for the production of cAMP from ATP and PDEs are responsible for the degradation of cAMP. The steady state concentration of cellular cAMP is different in the stumpy forms compared to the level in the long slender ones. The catalytic domains of the PDEs are highly conserved between humans and *T. brucei*. This means that the extensive research on human PDEs can be used in the research for PDEs inhibitors against trypanosomiasis. TbrPDEB1/B2 is already validated as drug target. Currently there are no successful experimental models of a double knockout of TbrPDED, this means that TbrPDED is potentially an essential gene for *T. brucei* and is potentially a new drug target. In this project, the aim is to validate TbrPDED as potential drug target by the use of a conditional knockout model. The expression of the enzyme can be turned off by withdrawal of tetracycline. The principal aim is to characterize the conditional construct by the use of drug sensitivity assays, localisation studies and cAMP assays. In addition, a TcrPDED expression construct will be made and tested whether it can complement for TbrPDEB1/2. If it can complement, this will also be characterized in the same way.

Poster 37 : Targeting PKD: DNA vaccine trials based on host specific gene expression - *A13045*
Presenter: **Mr Marc Nicolas Faber**, *PHD, University of Aberdeen*

**M Faber**[1]; C J Secombes[1]; J W Holland[1];
[1] University of Aberdeen

Proliferative kidney disease, caused by the myxozoan parasite *Tetracapsuloides bryosalmonae*, is a major disease issue for farmed rainbow trout in the UK. To combat the infection, rainbow trout farms undertake exposure programs, with surviving fish becoming immune to the disease. To combat this bottleneck in production, we generated DNA-vaccines based on *in silico* selected *T. bryosalmonae* genes that exhibit a fish-specific expression profile relative to the invertebrate host. Fish were vaccinated on a disease free hatchery prior to transfer to a farm enzootic for PKD. Apparent protective efficacy was assessed during the onset of advanced clinical disease. Here we present the first results of *in-silico* based selection, RT-PCR verified host specificity, and field testing of DNA-vaccines against a myxozoan parasite affecting rainbow trout aquaculture.

Poster 38 : ARF-regulating proteins in *Trypanosoma brucei* - *A12996*
Presenter: **Dr Helen Price**, *Lecturer in Bioscience, Keele University*

J P Chandrathas[1]; **H Price**[1];
[1] School of Life Sciences, Keele University

Several members of the ADP-ribosylation factor (ARFs) family of the small GTPases are known to be essential for viability in *T. brucei* bloodstream form cells. However, the molecular interactions of these proteins have not been fully characterised in *T. brucei* and there is a high level of identity shared between *T. brucei* and human ARF protein sequences, thus impacting on their potential as drug targets. An alternative method of targeting the ARFs may be through their regulators, the guanine nucleotide exchange factors (GEFs) and GTPase activating proteins (GAPs). These regulating molecules are responsible for maintaining the active/inactive state ARFs and are highly divergent in *T. brucei*. We have identified seven putative ARF regulators in *T. brucei* by bioinformatic analysis. We are currently using RNAi to determine whether these proteins are essential in the parasite. Further studies will determine which ARFs are regulated by these proteins, towards development of an assay for inhibitor screening.

Poster 39 : Malaria bifunctional DHFR-TS enzyme as a target for drug discovery against asexual stages of *Plasmodium falciparum* - *A13038*
Presenter: **Mrs Sara Palomo Diaz**, *Scientist, GSK*

**S Palomo Díaz**[1]; V Franco[1]; L Mata[1]; M Linares[2]; L De las Heras[1]; M G Gómez-Lorenzo[1]; F J Gamo[1];
[1] GSK, Spain; [2] Hospital 12 de Octubre, Spain

Malaria is a deadly infectious disease which affects millions of people each year in tropical areas. The causative agent is a protozoan parasite that belongs to the genus *Plasmodium*. Resistance to current antimalarial treatments is alarming, being necessary to discover new drugs against the human pathogen displaying a novel mechanism of action able to bypass current resistances. With this aim, the Bill & Melinda Gates Foundation has granted several laboratories to identify new antimalarial targets using chemogenomic methods. A progression cascade from diverse libraries was established in GSK in order to select compounds with good potency and a presumable novel mode of action. Then, *Plasmodium falciparum in vitro* resistant mutants have been selected under drug exposure using standard methodologies. In this work, an example of the successful chemogenomic approach is given using the compound MMV027634. After two weeks, a culture under continuous drug pressure at a dose of 10x IC50-fold rendered parasite growth. Selected mutants displayed a high level of resistance when compared to the wild type strain. Whole genome sequencing of resistant mutants to MMV027634 revealed mutations in the *dihydrofolate reductase-thymidylate synthase* (*dhfr-ts*) gene. Mutations mapped in amino acids of the highly conserved TS domain. The role of this enzyme in *Plasmodium* metabolism, mode of action studies including metabolic bypass, cross-resistance of derivatives as well as combinations with MMV027634 are discussed. Results of these studies highlight the importance of the DHFR-TS enzyme in parasite metabolism and open possibilities to explore thymidylate synthase as a target to discover promising novel drugs with therapeutic efficacy against asexual stages of *P. falciparum*.

Poster 40 : Functional genomics approach to investigate the Giant Panda roundworm *Baylisascaris schroederi*: global proteomics for diagnostics and control. - *A13048*
Presenter: **Miss Sarah Pye**, *PhD Candidate, Aberystwyth University*

**S Pye**[1]; S Girling[2]; P M Brophy[1]; I Valentine[2]; R M Morphew[1];
[1] Aberystwyth University; [2] Edinburgh Zoo

The roundworm *Baylisascaris schroederi* is estimated to infect 50-100% of wild Giant Pandas. *Baylisascaris schroederi* is regularly found among captive individuals, causing clinical and subclinical disease, and thus presents as a threat to both captive and wild populations of Giant Pandas.
Due to the inaccuracy of current techniques for quantitative diagnosis there is, as yet, no research utilising functional genomics approaches to aid development of novel diagnostics and vaccines. Thus, initiating functional genomics approaches in neglected parasites of protected wild and captive species is a priority to help improve our understanding of the parasite biology, allowing an insight into how the species interacts with the host, with the hope of identifying future control methods for *Baylisascariasis* in Giant Pandas. Therefore, we have begun to characterise the proteome of *B. schroederi* from naturally infected Giant Pandas. Global somatic proteins from adult *B. schroederi* were subjected to both 1D GeLC approaches, for whole proteome characterisation, and 2D gel electrophoresis, followed by Western blotting with infection sera, to characterise immune recognised proteins. The application of this initial functional genomics approach will provide important data for future research into *B. schroederi* control methods via improved diagnostics and potential vaccine candidates.

Poster 41 : Development of a point-of-care diagnostic for *Schistosoma* infections to improve drug-efficacy monitoring - *A13008*
Presenter: **Miss Alice Garrett**, *University of Glasgow*

**A Garrett**[1]; J C Cooper[1]; P Lamberton[1];
[1] University of Glasgow

Current diagnosis of *Schistosoma mansoni* uses faecal samples to measure eggs per gram of stool using Kato-Katz thick smears. There is now an opportunity to develop a microfluidic test to analyse genomic information – testing for species and if necessary drug-resistant strains. Such techniques have traditionally been time-consuming, requiring expensive laboratory equipment and power supplies. We have developed a new design for a rapid, point-of-care, highly sensitive stool-based test to detect *S. mansoni* (eggs), and *Schistosoma* hybrids using a low-cost, disposable system to separate the eggs, using flotation in a handheld format. The system integrates with a paper-based multiplexed nucleic acid test for infection detection. The device brings reagents together through an origami style folding with the output read visually with a lateral flow assay. Microfluidic flow will be enabled passively through capillarity within the interstitial space of the paper. Flow control and assay timing will be tuned by using different cellulose matrices. These devices will be tested in the field in Uganda in March 2017.

Poster 42 : Evaluation of phosphodiesterases as potential drug targets in *Trypanosoma cruzi - A13039*
Presenter: **Miss Titilola Kalejaiye**, *Phd student, University of Glasgow*

**T Kalejaiye**[1]; J C Munday[1]; J Siciliano de Araújo[2]; M de Nazaré Correia Soeiro[2]; L Maes[3]; R Leurs[4]; H P de Koning[1];
[1] Institute of Infection, Immunity and Inflammation, University of Glasgow, UK; [2] Instituto Oswaldo Cruz, Rio de Janeiro, Brazil; [3] University of Antwerp, Belgium; [4] VU University Amsterdam, Netherlands

Chagas disease is primarily a disease of South and Central America, and it is caused by the protozoan parasite *Trypanosoma cruzi*. The available drugs benznidazole and nifurtimox are only effective against the acute stage of the disease and there are different strains of the parasites that are innately resistant to current treatment. There is therefore need for new, safer, more affordable, easy to administer and effective drugs. In order to avoid cross-resistance with current therapies, these should have a different mode of action from the existing ones. Cyclic nucleotide phosphodiesterases (PDEs) from trypanosomatids appear to be a good target. With success recorded by targeting human PDEs and also PDEs from *T. brucei*, we aim to target and evaluate the PDEs of *T. cruzi* as potential drug targets. Since *T. cruzi* is divided into different groups, we decided to use genomic DNA from two strains of *T. cruzi* (Colombiana and Y strain) that differ in their sensitivity to available chemotherapy and geographical locations. Cloning of the PDE genes from the two strains has been completed and we have started complementation assays to evaluate whether TcrPDEB1 and B2 can complement for the activity of TbrPDEB1/2. This work is part of the PDE4NPD (PhosphoDiEsterases for Neglected Parasitic Diseases) consortium. This consortium pursues target repurposing of phosphodiesterase inhibitors to shorten new drug discovery times for neglected parasitic diseases. Therefore, we rely on this consortium for genetic materials and compounds to be tested on our constructs. We intend to build on success stories from human PDE inhibitors (Maurice et al., 2014) and also from validation of *T. brucei* PDEs as drug targets (De Koning et al., 2012) for the evaluation and characterization of TcrPDEs as drug targets and the development of TcrPDE inhibitors. There is sufficient knowledge of the structure of this enzyme family and this can be exploited to design highly efficient parasite-specific PDE inhibitors.

Poster 43 : Glutamine is used for glutamylation of proteins, a post-translational modification, that is important for cell proliferation and cytokinesis in *Trypanosoma brucei* bloodstream forms. - *A13063*
Presenter: **Miss Flavia Silva Damasceno**, *Institute of Biomedical Science, University of São Paulo*

**F S Damasceno**[1]; K Figarella[2]; M Duszenko[2]; A M Silber[1];
[1] Biomedical Science Institute - USP, Brazil; [2] University of Tuebingen, Germany

*Trypanosoma brucei* is the causative agent of African Trypanosomiasis. In this work, we investigated the importance of glutamine (Gln) and glutamine synthetase (*Tb*GS) for cell proliferation, cytokinesis and glutamylation of tubulin in *T. brucei* bloodstream forms. For this purpose, SMB cells were cultivated in HMI-9 medium Gln-free or not, with or without *Tb*GS knockdown induction. The uninduced and

induced parasites cultivated in the Gln-free medium were not able to maintain the proper proliferation rate, whereas the induced parasites, cultivated in the control medium, grew properly. The results show that parasites depend on the extracellular supply of Gln. Moreover, parasites synchronized in the G1 cell cycle phase and cultivated in Gln-free medium, were able to proceed from G1 to S and G2 phases and resulted in polyploid cells, but were not able to complete cell division. This finding suggests that Gln participates in cytokinesis, a process that depends on the integrity and dynamic of the cytoskeleton. Interestingly, parasites maintained in Gln-free medium decreased the level of glutamylated tubulin, but recovered when Gln was added back to the medium. In conclusion: Gln is important for tubulin glutamylation that is a prerequisite for cell proliferation and cytokinesis in bloodstream forms of *T. brucei*.

Poster 44 : Towards the pen-side detection of triclabendazole efficacy against liver fluke parasites of livestock - *A13069*
Presenter: **Miss Clare Florence Collett**, *PhD student, Aberystwyth University*

**C Collett**[1]; R M Morphew[1]; J P Dalton[3]; G Parry[2]; P M Brophy[1];
[1] Aberystwyth University; [2] Hybu Cig Cymru Meat Promotion Wales; [3] Queen's University Belfast

The common liver fluke, *Fasciola hepatica*, threatens global food security as it causes huge agricultural losses worldwide. As a zoonotic food borne disease, fascioliasis is recognised by WHO as an emerging global public health concern. Current diagnostics are impeded by low sensitivities of faecal egg counting, influenced by irregular egg passage into faeces, and by the problematic performance in the field of commercial and in-house ELISAs for antigen and antibody detection. In the continued absence of a vaccine, control strategies rely heavily on a novel benzimidazole, triclabendazole (TCBZ), as it is the only commercially available compound active against both juvenile and adult flukes. There is an urgent drive to develop rapid diagnostics that measure both fluke presence and level of drug resistance at the pen-side, especially as disease modelling predicts a dramatic rise in incidence coupled with spreading TCBZ resistance. To this end, we have developed a new approach to biomarker discovery utilising proteomics to identify secreted proteins of the adult fluke TCBZ response. Our control biomarkers for fluke presence are cathepsin L proteases, major components of excretory/secretory products, and biomarkers of TCBZ-SO treatment whereby their presence indicates fluke fitness. We have raised polyclonal antibodies to a recombinant cathepsin L zymogen to confirm protein recovery from animal samples and now report progress on our biomarker validation pipeline.

Poster 45 : Development of a stringent screening cascade for *Trypanosoma cruzi* phenotypic screening - *A13084*
Presenter: **Mr John Thomas**, *Biologist, University of Dundee - Drug Discovery Unit*

**J Thomas**[1]; L MacLean[2]; M De Rycker[2];
[1] University of Dundee; [2] University of Dundee - Drug Discovery Unit

An estimated 6 to 7 million people are infected with the protozoan parasite *Trypanosoma cruzi* (*T. cruzi*), the causative agent of Chagas' disease, mostly in endemic regions of Latin America. Chagas' disease has recently also been reported in the US and Europe

resulting from increased immigration and tourism. Chagas' disease can progress into a chronic phase causing irreversible damage to the heart, nervous and/or digestive systems. The current drugs, benznidazole and nifurtimox, have adverse side-effects and limited efficacy in the chronic phase. There is thus an urgent need for new drugs. High-content phenotypic screening of intracellular amastigotes has proven to be a successful tool to identify new small-molecules with anti-trypanosomal activity. Our original intracellular phenotypic screening assay could not distinguish between cytostatic and cytocidal compounds due to low numbers of parasite per cell at the start of the assay. This assay has a high hit-rate but a low confirmation rate in secondary assays which do differentiate cytostatic from cytocidal compounds. To address this and increase the efficiency of our screening cascade we have developed a "cidal" screening assay by increasing the initial level of infection by 10-fold. This now allows distinction of compounds that kill parasites versus compounds that merely arrest their growth. While our current suite of screening assays is able to prioritise compounds that are cytocida

Poster 46 : Fast tracking antimalarial drug discovery through molecular modelling and repositioning: Lead optimisation of synthetic emetine analogues SALF01/02 - *A13090*

Presenter: **Miss Panwar Priyanka**, *PhD student, University of Salford*

P Panwar[2]; H Matthews[1]; N Nirmalan[2];

[1] Imperial College London; [2] University of Salford

Malaria is a life threatening infectious disease caused by parasitic protozoa belonging to the genus *Plasmodium*. With resistance reported in all categories of anti-malarial drugs, the need for a new class of affordable anti-malarial is an urgent priority. The anti-amoebic drug Emetine dihydrochloride has been identified as a potent antimalarial option (Matthews *et al.*, 2013). Wong et al., reported the target binding site of emetine on 40s subunit of the 80s ribosome. Two synthetic analogues of emetine SALF1 and SALF2 are modelled on the 40S small subunit of 80S Ribosome. Lead optimisation of SALF1 and SALF2 was done to identify parasite reduction rate and stage specificity. The project includes virtual screening of FDA approved library of drugs against the ribosomal binding site of emetine to fast-track drug discovery. The results have identified synergies between SALF1 and two FDA approved drugs. The proposed anti-malarial combination therapies for synthetic analogues of emetine would potentially reduce the side-effects whilst maintaining the efficacy of the treatment.

Poster 47 : Engaging students to enhance the parasitology curriculum in schools - *A13112*

Presenter: **Dr Tansy Hammarton**, *Senior Lecturer, University of Glasgow*

**T C Hammarton**[1];

[1] Institute of Infection, Immunity and Inflammation, University of Glasgow

Until recently, little parasitology has been taught in schools. However, with the introduction of the Curriculum for Excellence, and more recently, the introduction of a new Advanced Higher Biology syllabus in Scotland, there have been increasing opportunities to engage

pupils and teachers and to enhance the school curriculum with parasitology-related activities. For over a decade, I have coordinated and run an extensive schools public engagement (PE) programme in infection biology, which has reached thousands of children aged 2-17 and their teachers, and has involved hundreds of University of Glasgow volunteers, including many PhD students. More recently, I have incorporated various aspects of PE into my undergraduate teaching, which has led to a number of undergraduates also volunteering in our PE programme and enhancing their communication skills. Here, I will give an overview of the hands-on parasitology-related activities and experiments I have developed for schools, the resources we have available to share with any interested parties, and my recent work to involve more students in PE.

Poster 49 : Identification of new chemical starting-points for visceral leishmaniasis drug discovery through primary screening and re-assessment of historic screening campaigns. - *A13075*

Presenter: **Dr Sujatha Manthri**, *Post Doctoral Research Fellow, University of Dundee*

**S Manthri**[1];
[1] University of Dundee

*Leishmania donovani* is the causative agent of visceral leishmaniasis, with an estimated 300,000 cases and 20,000 deaths annually. There is an urgent need for new treatment therapies as the current options involve high cost, lengthy regimes, toxicity and emerging drug resistance The University of Dundee Drug Discovery Unit and GSK have set up a collaboration focused on developing new drugs for visceral leishmaniasis. Free living parasites (promastigotes or axenic amastigotes) have been used by many groups for compound screening. Poor translation between these assays and the more physiologically relevant intracellular assay has often been observed. In our screening cascade we either perform primary screening using a medium-throughput intracellular assay, or for higher throughput we use an axenic amastigote assay that has been optimised to detect only cytocidal compounds.
Here we describe the results of two hit-finding campaigns, one conducted with the intracellular amastigote assay (Global Health Chemical Diversity Library (68,320 compounds)), and a second that focused on re-assessing hits from a large high-throughput screen (2 million compounds) carried out with axenic amastigotes. For this reassessment we put in place a screening cascade comprising of compound prioritisation, cidality profiling and assessment of intracellular activity. Both screening efforts have yielded promising new starting points for visceral leishmaniasis drug discovery programmes.
In conclusion, our work demonstrates the utility of both axenic assays as well as intracellular amastigote assays for compound screening. We show how revisiting previous hit-discovery campaigns using new assays can help rescue hits that may have been overlooked, and we also present the outcome of a large compound screen using the intracellular amastigote assay.

Poster 50 : Delineating the role of stage-specific histone modifications and regulators of histone acetylation in sexual development of the rodent malaria parasite, *Plasmodium berghei - A13082*

Presenter: **Miss Bridget Power**, *PhD student, Wellcome Centre for Molecular Parasitology*

**B J Power**[1]; H J Vaikkinen[1]; R S Kent[1]; N Philip[1]; A P Waters[1];
[1] University of Glasgow, Institute of Infection, Immunity & Inflammation,, UK

According to the World Health Organisation (WHO), 2015 saw 212 million new cases of malaria and 429,000 deaths attributed to malaria worldwide. Five species of the *Plasmodium* genus are responsible for malaria in humans, of which *Plasmodium falciparum* is the most lethal. In *P. falciparum,* it has been shown that the epigenetic regulators, heterochromatin protein 1 (PfHP1) and histone deacetylase 2 (PfHDAC2), are essential for both mitotic proliferation of asexual stage malaria parasites and the transition from asexual to sexual stage parasites (gametocytogenesis) required for transmission to the mosquito vector. In this study, we investigated the epigenetic regulation of commitment to gametocytogenesis, using the rodent malaria model, *Plasmodium berghei.* We employed both gene knockout and conditional auxin-induced knockdown of proteins involved in the acetylation and deacetylation of histones with successful knockout of putative histone deacetylase 1 (HDA1) and histone acetyltransferase 1 (HAT1). Auxin-inducible knockdowns were created for HDA1 and three additional histone deacetylases in *P. berghei.* In addition, we have identified both conserved and stage-specific histone modifications for mature synchronous asexual parasites (schizonts) and sexual-stage parasites (gametocytes). Our current work focusses on the identification of chromatin regions demarcated by the stage-specific histone modifications H4K8Ac, H3K122Ac, and H3K64Ac.

Poster 51 : *Pomphorhynchus*: something old, something new? - *A13085*
Presenter: **H Bradley**, *Environment Agency*

**H A Bradley**[2]; A J Reading[2]; D Andreou[1]; C F Williams[2];
[1] Bournemouth; [2] Environment Agency

**Discussion**

Acanthocephalans are intestinal parasites that use amphipods as their intermediate host. In the UK, greatest attention has been given to *Pomphorhynchus laevis*, which matures in freshwater fish such as chub (*Leuciscus cephalus*) and barbel (*Barbus barbus*), and cycles through *Gammarus pulex*. The larval stage (cystacanth) causes an orange spot to develop within the body of the intermediate shrimp host, increasing visibility to fish. Recent taxonomic studies have suggested two previously synonymised species of *Pomphorhynchus*, *P. laevis* and *P. tereticollis*, are genetically distinct. This has raised uncertainty over the identity, distribution and impact of these parasites in English rivers. This study provides clarity on the status of this parasite in England and Wales through application of citizen science to assist with sampling of infected shrimps. Morphological examinations of archived parasites (previously recorded as *P. laevis*) combined with genetic analysis of recently collected cystacanths have so far revealed only *P. tereticollis*. Work is underway to progress our understanding of the distribution, impact and ecology of this parasite in fisheries in light of these recent taxonomic changes.

Poster 52 : First description of a digenean trematode associated with dusky grouper dermatitis (DGD) lesions in *Epinephelus marginatus* (Lowe) from Libyan waters - *A13080*

Presenter: **Jamila Rizgalla**, *Postdoc, University of Stirling*

**J Rizgalla**[1]; A P Shinn[1]; H W Ferguson[2]; G Paladini[1]; J E Bron[1];
[1] Institute of Aquaculture, University of Stirling, Faculty of Natural Sciences; [2] Marine Medicine Programme, School of Veterinary Medicine, St. George's University, Grenada

Eggs and adults of a digenetic trematode were found in close association with "dusky grouper dermatitis (DGD)" lesions affecting the wild population of dusky grouper *Epinephelus marginatus* in the coastal waters of Libya. Histological evaluation of lesions found gravid hermaphroditic digeneans (ca. 1,500-2,000 µm long), within dermal blood vessels. The digeneans, based on their morphology, were subsequently assigned to the Aporocotylidae Odhner, 1912 (Platyhelminthes: Trematoda). Eggs (ca. 20-37 µm long), with embryos at various stages of development, from homogenous embryos *in utero* to fully developed miracidia, were found located within the dermis and epidermis. Evidence suggests their passage through host tissues is facilitated by the host's inflammatory response - migrating from the dermal blood vessels to the dermis and then the epidermis, whereon the miracidia hatch and are released into the external aquatic environment. Alternatively, eggs are conveyed with the natural turnover of epidermal cells. The host's inflammatory process involves the recruitment of eosinophils to the sites of infection and their degranulation in close proximity to eggs situated within blood vessels. Although blood flukes are recorded from the blood vascular system of serranids (Epinephelinae), this is the first record of a aporocotylid digenean occupying the cutaneous blood vessels of a piscine host.

Poster 53 : The effect of mass drug administration on *Schistosoma mansoni* population genetic diversity and structure - *A13088*
Presenter: **Mr Marco Crotti**, *PhD student, University of Glasgow*

**M Crotti**[1]; C Faust[1]; P Lamberton[1];
[1] University of Glasgow

Schistosomiasis is a neglected tropical disease (NTD) that affects over 240 million people worldwide. Repeated mass drug administration (MDA) is currently the World Health Organization's recommended strategy to control morbidity and transmission of the disease. However, the effect of the drug on the genetic diversity of the parasite has rarely been investigated. In this study, we looked at the effect of multiple MDAs on the genetics of *Schistosoma mansoni* over a period of three years. Three primary schools in separate villages in a high endemicity region of Uganda were sampled at 11 time points over the study period. This represents one of the most complete longitudinal datasets to date in terms of data coverage. A total of 4743 parasites were collected from 207 children and genotyped at seven microsatellite loci. Overall, genetic diversity decreased after drug administration. Analysis of Molecular variance showed a very low, but sometimes significant structure between villages, with most of the genetic structure being within hosts and parasites. This and other analyses will be discussed in terms of the long-term effects of MDA and potential implications for the success of control programmes.

Poster 55 : Communicating our science to our customers: drug discovery in five simple experiments - *A13087*
Presenter: **Lesley-Anne Pearson**, *Biologist, University of Dundee*

**L Pearson**[1];
[1] University of Dundee

The complexities of modern drug discovery–an interdisciplinary process that often takes years and costs billions–can be extremely challenging to explain to a public audience. We present details of a 30 minute demonstrative lecture that uses well-known experiments to illustrate key concepts in drug discovery including synthesis, assay and metabolism.

Poster 57 : Evidence for novel gene duplications associated with pyrethroid resistance in *Anopheles minimus*. - *A13132*
Presenter: **Miss Sinead Mutton**, *MSc student, The Liverpool School of Tropical Medicine*

**S Mutton**[1]; G Weedall[1];
[1] The Liverpool School of Tropical Medicine

Use of insecticides in controlling malaria vectors will remain the cornerstone of control measures for the foreseeable future and the mechanisms of insecticide resistance continue to be important areas of study. Pyrethroid resistance is associated with several resistance mechanisms including metabolic resistance. This occurs through upregulation of one or more relevant genes but may also occur by gene duplication. CYP P450 gene products, associated with detoxification of chemicals, are known to confer resistance to pyrethroid insecticides. *Anopheles funestus* putative ortholog sequences to duplicated genes CYP6P9 (CYP6P9a and CYP6P9b) and CYP6P4 (CYP6P4a and CYP6P4b) from VectorBase were aligned in SeaView v 3.2 using the MUSCLE algorithm and compared across a range of anopheline species. If in a particular species an ortholog existed but was not annotated, to find orthologous exons a BLASTP search was performed against *A. funestus* and *A. gambiae* reference genomes on VectorBase. We found apparent novel duplications of these genes in *A. minimus*, an important vector of malaria in Southeast Asia. Such duplications have been described as conferring pyrethroid resistance in both *A. funestus* and *A.* g*ambiae*.

Poster 58 : Mapping insecticide resistance using spatially explicit statistical models: a simulation approach to investigate pyrethroid resistance in mosquito in Banfora district, Burkina Faso. - *A12957*
Presenter: **Dr Luca Nelli**, *Research Associate, University of Glasgow*

**L Nelli**[1]; H Ferguson; H Ranson[3]; S W Lindsay[2]; S Nfale[1]; A Tiono[1]; A S Sanou; J Matthiopoulos[4]
[1] Centre National de Recherche et de Formation sur le Paludisme, Burkina Faso; [2] Durham University; [3]Liverpool School of Tropical Medicine; [4] University of Glasgow

High levels of insecticide resistance (IR) in the primary mosquito vectors is hypothesized to be a major contributor to persistent levels of malaria transmission. As part of a long-term interdisciplinary programme, we are developing a spatial modelling framework aimed at quantifying the contribution of IR within vector populations on local patterns of malaria incidence. While much of the data required to formulate this model is being collected, we are developing the model framework definition. Initial work has focused on a simulation approach to generate a simulated dataset of malaria infection reported across the whole study area, as a function of environmental factors. A subsequent modelling approach based on Bayesian statistics was used to test whether the model was able to correctly predict a range of hypothetical relationships between IR, environmental variables and local malaria incidence, against a simulated background of realistic levels of uncertainty in the measurements. Preliminary results indicate that our approach seems promising for being able to pick up subtle effects of IR on malaria incidence – if they exist – even within the type of patchy and incomplete surveillance data that is typically collected, and provides a useful framework for a more quantitative analysis of the impacts of IR on malaria control efforts – as is needed to anticipate the potential consequences and how to respond to them.

Poster 59 : Reversing the irreversible: phosphofructokinase activity in Trypanasomatids - *A12984*
Presenter: **James Kinkead**, *Research Technician/PhD Student, The University of Edinburgh*

**J Kinkead**[1];
[1] The University of Edinburgh

Discussion

Poster 60 : Near Infra-Red optical imaging to track fluorescently labelled filarial parasites *in vivo* - *A13089*
Presenter: **Amy Marriott**, *PhD Student, Liverpool School of Tropical Medicine*

**A E Marriott**[1]; A Steven[1]; J Archer[1]; H Poptani[2]; M J Taylor[1]; J D Turner[1];
[1] Liverpool School of Tropical Medicine; [2] University of Liverpool

Filarial drug screening *in vivo* is a time-consuming process. Due to uncertainty of when efficacy may be manifest, screens require large numbers of animals in order to assess multiple time points and to employ extended timeframes (upward of 8 months). Thus far, Ultrasonography (USG) is the only tool to identify loss of parasite motility signal in response to drug therapy. Here we report the optimisation of an in vivo near infra-red imaging technology (IVIS® Perkin Elmer) in order to track fluorescently labelled *Brugia malayi*/*Brugia pahangi* microfilariae in circulation and adult parasites in the peritoneum over a 7-day time-course both *in vitro* and *in vivo*, in immunodeficient mouse strains. Initial optimisation has successfully defined the conditions for optimal, intra-vital, fluorescent labelling of *Brugia* parasite proteins, yielding a persistent, detectable signal over seven days without detrimental effects to parasite viability. Further, we have validated the detection of signal within mouse anatomical locations.We foresee that this platform may be applied to monitor the assessment of drug or vaccine efficacies, whereby change in fluorescent signal, due to parasite death/deterioration in response to therapeutics, can be evaluated by longitudinal imaging. Once validated, this would provide an early prognostic prediction of macrofilaricidal or vaccine efficacy, accelerating preclinical development projects. The successful application of

longitudinal bioimaging will significantly reduce the total number of animals required for the assessment of efficacy. Additionally, such a non-invasive approach will be beneficial in refining the use of animals in drug screens by obviating the necessity for invasive filarial viability sampling.

Poster 61 : Co-culture of schistosomes with mammalian cells to reveal host pathogen interactions - *A13091*
Presenter: **Miss Arporn Wangwiwatsin**, *PhD student, Wellcome Trust Sanger Institute*

**A Wangwiwatsin**[2]; M Lotkowska[2]; A Protasio[1]; G Rinaldi[2]; M Berriman[2];
[1] University of Cambridge; [2] Wellcome Trust Sanger Institute

While residing in the bloodstream of its mammalian hosts, *Schistosoma mansoni*, parasitic blood flukes, are in close proximity to the cells lining blood vessels and, in early stage of infection, development into adults has been associated with localisation in the liver. Little is known about how the parasites interact with specific host tissues, though it generally accepted that the parasites employ multiple strategies during infections to promote their survival and infection success. Understanding how *S. mansoni* and host tissues influence one another could provide insight for the significance of such interactions on overall infection outcome. In this study, we co-cultured mechanically transformed schistosomules with commercially available cells derived from human tissues - endothelial cells, hepatocytes, and embryonic kidney cells - and investigated transcriptional changes in both the schistosomules and the co-cultured cells. Transcriptional changes in the co-cultured parasites suggest influences of site-specific information that may trigger downstream responses in the parasites. Whereas responses in co-cultured mammalian cells demonstrate how parasites might modulate host gene expression to promote their survival. This information provides further insight into *S. mansoni*/host-parasite interactions and the involvement of host cells in determining key aspects of the infection.

Poster 62 : Kingston University mosquito watch - *A13115*
Presenter: **Dr Ruth Kirk**, *Associate Professor, Kingston University*

**R Kirk**[1]; D Corbishley[1]; S Edwards[1]; A Ghafoor[1]; O Jimoh[1];
[1] Kingston University

Increasing concern about mosquito-borne diseases as emerging or re-emerging threats in Europe has emphasised the need for surveillance of UK mosquito species. Early detection of invasive mosquitoes is crucial for understanding the risks of virus transmission, particularly in the context of environmental and climatic changes which may enable movement and increase of vector populations and virus amplification. The Kingston University Mosquito Watch Project was launched in 2016 to engage undergraduate students in the surveillance of mosquitoes in southern England and monitor introduction of invasive species. Mosquitoes from four urban sites in Kingston upon Thames and Egham, Surrey were sampled and morphologically identified. Larvae were collected from water containers and reared to adults. Adults were trapped using a BG Sentinel trap with Sweetscent attractant. The common and widespread native

species *Culex pipiens* and *Culiseta annulata* were found at all sites. The potential of these species as vectors of disease is discussed and the pedagogic value of the project in teaching mosquito identification skills to students is highlighted. Data will be communicated to Public Health England and further surveys at urban and rural sites are planned.

Poster 63 : Long term *in vitro* culture of adult *Brugia malayi* parasites - *A13111*
Presenter: **Amy Marriott**, *PhD Student, Liverpool School of Tropical Medicine*

**A E Marriott**[1]; A Steven[1]; J Archer[1]; M J Taylor[1]; J D Turner[1];
[1] Liverpool School of Tropical Medicine

The preclinical assessment of new macrofilaricides against filarial parasites, which cause lymphatic filariasis and onchocerciasis, necessitates *in vivo* experimentation because currently, adult parasites cannot be generated from infectious stage larvae *in vitro* and adult female reproductively active parasites have a very limited life-span in culture. The current *in vitro* systems are maintained for only short periods (<1 week). Arguably, this period of time is not sufficient to accurately simulate effects of *in vivo* drug exposures and may not accurately inform *in vivo* preclinical testing parameters. We have developed an *in vitro* co-culture system with human lymphatic endothelial and myeloid cell lines which more accurately replicates the environment in which lymphatic parasites inhabit, making it possible to maintain parasite 'fitness' for a period of 2-3 weeks, comparable to those isolated from animal hosts. The longevity of this culture system should facilitate the more accurate *in vitro* assessment of treatment efficacy, thereby reducing dependence upon *in vivo* models. As the *in vitro* co-culture system is more representative of the parasitic niche, it may be used for a first stage drug screen in order to reduce the numbers of animals used. Additionally, our *in vitro* co-culture system allows for interrogations of host-pathogen relationships and parasite biology to be explored in further detail, again reducing the need for animal experiments.

Poster 64 : Functional transcriptomic approaches to understanding anthelmintic metabolism in the liver fluke *Fasciola hepatica* - *A13120*
Presenter: **Miss Rebekah Stuart**, *Researcher , Aberystwyth University*

**R B Stuart**[1]; M Wilamska- Chyrczakowska[1]; P M Brophy[1]; R M Morphew[1];
[1] Aberystwyth University

Fasciolosis of livestock is a global threat to food security and is now an increasing food borne risk to humans. At present, there are no commercial vaccines to underpin control programmes. To help secure future anthelmintic control of fasciolosis, uncovering the parasite's anthelmintic detoxification capacity directed towards anthelmintics such as Triclabendazole (TCBZ) has been deemed of paramount importance. Thus, a functional transcriptome of resistant and susceptible *F. hepatica* isolates following TCBZ-SO exposure *in vitro* culture was produced. Analysis of this transcriptome surprisingly revealed that classic detoxification families did not respond to anthelmintic exposure. However, a number of membrane associated proteins (tegument like antigens and cathepsin Ls)

were up regulated in the presence of TCBZ-SO for the TCBZ susceptible (TCBZ-S) isolates. Perhaps more significantly, alpha tubulins (a binding partner of beta tubulins as a potential target of TCBZ) were also found to be up-regulated in TCBZ-S isolates following *in vitro* culturing. Further *in silico* investigation of the current transcriptome and newly sequenced genome revealed that the *F. hepatica* genome encodes for a greater number of both alpha and beta tubulins than previously identified. This work redirects research into the mode of action of TCBZ back towards microtubules and tubulins.

Poster 66 : Signalling pathway from glucose transporter towards $F_OF_1$-ATPase - *A13123*
Presenter: **Dr Julie Kovarova**, *postdoc, University of Dundee*

**J Kovarova**[1]; D Horn[1];
[1] University of Dundee

Bloodstream *Trypanosoma brucei* lives in its host's blood and its metabolism is reduced, adapted to such a nourishing environment. However, several studies recently found these parasites in additional tissues, such as the adipose tissue or skin. We present here a signalling pathway which would contribute to quick adaptation of metabolism when transferring from blood to a glucose depleted environment. Baker *et al.* (2015) observed that depletion of vacuolar ATPase (vATPase) enables loss of the kinetoplast, hence loss of subunit A6 of $F_OF_1$-ATPase, leading to $F_OF_1$-ATPase uncoupling. In contrast to most other organisms, the canonical function of mitochondrial ATPase ($F_OF_1$-ATPase) in bloodstream *T. brucei* is to sustain mitochondrial membrane potential at the expense of ATP, which is mainly produced in glycolysis. Under specific conditions (or in dyskinetoplastic trypanosomes) $F_O$ and $F_1$ moieties are separated and $F_OF_1$-ATPase becomes uncoupled losing its function. We propose that a signalling pathway is present and dependent upon glucose availability, leading via vATPase towards $F_OF_1$-ATPase; depletion of glucose leads to disassembly of vATPase, which further triggers uncoupling of $F_OF_1$-ATPase. Inhibitors of glucose transport do indeed render the kinetoplast dispensable, as predicted.

Poster 67 : Endonuclease V processes hypoxanthine-containing RNA in *Trypanosoma brucei- A13124*
Presenter: **Mr Daniel García**, *Role and activity of Endonuclease V, CSIC*

**D García-Caballero**[1]; G Pérez-Moreno[1]; L M Ruiz-Pérez[1]; A E Vidal[1]; D González-Pacanowska[1];
[1] Instituto de Parasitologia y Biomedicina "Lopez-Neyra", CSIC. Granada, Spain

Hypoxanthine (Hx) may arise in DNA as a result of oxidative deamination of adenine or misincorporation of dITP during replication. On the other hand, the occurrence of Hx in RNA is considered a normal and essential modification induced by specific adenosine deaminases acting on RNA. Hx is mainly removed from DNA by specific DNA glycosylases through the Base Excision Repair pathway. In prokaryotes, Endonuclease V (EndoV) can recognize and cleave Hx in DNA, and may be initiating Hx removal by an Alternative Excision Repair pathway. In contrast, human EndoV preferentially cleaves Hx-containing RNA substrates, suggesting a role in RNA metabolism. We have purified and characterized the catalytic properties of the EndoV encoded by *Trypanosoma brucei* (TbEndoV). *In*

*vitro*, TbEndoV efficiently processes Hx-containing single-stranded RNA oligonucleotides, including A to Hx-edited tRNA-like substrates. However, a weak activity was observed over Hx-containing DNA, except when a ribonucleotide was placed 3' to the lesion. Analysis by immunofluorescence microscopy indicates that TbEndoV localizes mainly in the cytosol. The enzyme appears to be not essential in bloodstream forms where the two EndoV copies could be knocked out. In contrast, double allele inactivation could not be achieved in procyclic forms while protein depletion by RNA interference led to impaired growth and defects in cell cycle progression, suggesting a specific role for TbEndoV in this life stage.

Poster 68 : Potential antimicrobial activity of parasite EVs - *A13125*
Presenter: **Amber Fanthome**, *PhD Student, Aberystwyth University*

**A Fanthome**[1]; P M Brophy[1]; R M Morphew[1];
[1] Aberystwyth University

Exosomes are membranous extracellular organelles of diameter 30-100nm. Typical exosome cargo includes proteins and mRNA. Exosome like vesicles (EVs) are produced by several platyhelminth and nematode species studied to date, including *Fasciola hepatica*, a master of immune-modulation. EVs from several helminths have been shown to be taken up by host cells and to potentially direct the manipulation of host immune responses, thereby contributing to parasite establishment and long-term survival in the host. The ancestral role of worm EVs is not resolved. For example, molecules resembling antimicrobial peptides have been identified in the EV cargo of the free-living model nematode *Caenorhabditis elegans*. However, exactly how helminth EVs interact with host cells and the environment is not yet fully understood, and it is unclear if EV host interaction is a prerequisite for worm parasitism. We report on an EV discovery and purification pipeline in nematodes and flatworms using an ultracentrifugation strategy. EVs were isolated from the excretory/secretory products of the cestode *Moniezia expansa* and the economically important ruminant nematode *Haemonchus contortus*. To investigate whether antimicrobial activity is conserved in parasitic helminth EVs, isolated *M. expansa* EVs were screened against *Escherichia coli* K12 strain, with the aim of determining minimum inhibitory concentrations for antibiotic activity.

Poster 70 : Spliced-leader pull out for trypanosomatid genomics - *A13134*
Presenter: **Mr Philipp Schwabl**, *PhD student, University of Glasgow*

**P Schwabl**[1]; M Llewellyn[1];
[1] University of Glasgow

The power of whole-genome sequencing for epidemiology remains throttled by parasite sample quality and quantity. Parasite cells are inherently tethered to vector/host tissue, typically swamped by orders of magnitude in contaminating material that challenges direct extraction and cedes too little sample to sequence. Follow-up cell culture often proves ineffective, many costly *ex vivo* systems raising more bias and frustration then parasite. To bypass this laboratory bottleneck in the landscape genomics of Chagas disease, we are

developing a magnetic-capture-hybridization protocol to recover genome-wide information on *Trypanosoma cruzi* directly from its arthropod vector. We target an idiosyncrasy of trypanosomatid gene expression, the 39-nucleotide "spliced leader" sequence that primes each RNA message for translation, to bait the transcriptome all at once for RNAseq without prior parasite extraction or culture. Employing a variety of sample types, we examine our method's performance (sensitivity, reproducibility, bias, etc.) and its ultimate reach…RAD-like reduced representation for landscape genomics – or more?

Poster 71 : Imaging ellipsometry as a novel detection method for protein-protein interactions. - *A13138*
Presenter: **Mr John Tomes**, *Research Student, Aberystwyth University*

**J Tomes**[1]; R M Morphew[1]; P M Brophy[1]; D Langstaff[1]; M Gunn[1]; R Stuart[1];
[1] Aberystwyth University

*Fasciola hepatica*, the common liver fluke, is a global zoonotic parasite that currently infects over 17 million people and costs global farming in excess of $3 billion annually. At present, fluke control is hampered by inadequate diagnosis based primarily on faecal egg counting or problematic antibody based tests. These tests do not detect the juvenile pathogenic liver fluke responsible for the acute disease phase. Therefore, improving diagnostics is likely to enhance both control and sustainability of anthelmintics in absence of vaccines and spreading drug resistance. The over-arching objective is to develop a novel instrumentation system, based on ellipsometry, capable of helminth disease diagnostics utilising protein-protein interactions. Previous studies at Aberystwyth University provided proof of principle and showed that 'Imaging Ellipsometry' could realise a label free, real time method of detecting model protein interaction at a nanometre scale. The research equipment is now being optimised to discover if protein interactions can be measured for key biomarkers from *F. hepatica* a) Sigma GST, a well characterised secreted liver fluke protein. b) Extracellular Vesicles (in conjunction with Atomic Force Microscopy). The wider impact of this research is a novel approach to rapid diagnostic testing and can also offer opportunities for increased understanding of wider protein-protein interactions, protein function analysis and anthelmintic development.

Poster 72 : A 'tick'ing time bomb – a survey of public knowledge of ticks and tick-borne diseases in Northern Ireland - *A13143*
Presenter: **Miss Lesley Haddock**, *PhD Student, QUB*

**L Haddock**[1]; N J Marks[1]; A G Maule[1]; D M Scantlebury[1];
[1] Queen's University Belfast

Public perception of disease risk significantly affects the likelihood of an individual engaging with preventative behaviours, which in turn affects disease spread and success of control efforts. There is limited information around how the Northern Irish populace perceives emerging disease risks, especially in relation to ticks and tick-borne diseases. This survey provides an indication of public knowledge

and awareness of ticks and the risks they pose as well as identifies ways to increase understanding and uptake of preventative behaviours.
A survey of 40 questions was distributed throughout Northern Ireland, receiving 512 responses. Areas covered by the survey included: recognition and experiences with ticks; emerging disease knowledge and awareness of tick-borne disease and disease awareness around travel. 20% of respondents had suffered tick bites however understanding of removal techniques and potential disease risks were both poor. Respondents felt their personal risk was low based on the lack of media coverage and a shortage of reliable information. Better access to clear and accurate materials on risks associated with tick bites and simple preventative behaviours is needed. Increasing knowledge could improve assessment of personal risk and increase the use of precautionary acts in risky environments.

Poster 74 : Proline metabolism in *Trypanosoma cruzi*: a possible mechanism of transhydrogenase - *A13145*
Presenter: **Ms Letícia Marchese**, *LabTryps, Universidade de São Paulo*

**L Marchese**[1]; B S Mantilla[1]; K Olavarría[1]; **A M Silber**[1];
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Mitochondrion of insect trypanosomes are able to oxidize L-proline (Pro) to L-glutamate (Glu) through two enzymatic steps for energy production. However, little is known about Pro biosynthesis in these organisms. Pro could be only produced from Glu by two reductions steps via $\Delta^1$-pyrroline-5-carboxylate (P5C) synthase (P5CS) and P5C reductase (P5CR). Here, we show that the Glu-P5C-Pro pathway is operative in *Trypanosoma cruzi*, and is absent in *Trypanosoma brucei*. After depletion of the intracellular pools of free Pro, epimastigotes of *T. cruzi* were able to restore their Pro levels when supplied with Glu or P5C, while procyclics of *T. brucei* (PCFs) were not. Furthermore, neither P5CS nor P5CR were detected in PCF lysates using antibodies raised against both *T. cruzi* enzymes. Digitonin permeabilization and immunofluorescence of *T. cruzi* epimastigotes showed that P5CS and P5CR are cytosolic. A biochemical characterization of the recombinant TcP5CR was performed. It is a NADPH-dependent enzyme and this cofactor has a substrate-inhibitory effect on TcP5CR ($K_i^{app}$ = 50,5 µM), suggesting that this enzyme is important in the regulation of Pro metabolism. Our results hint that Pro is not an essential metabolite in *T. cruzi*, while seems to be essential in *T. brucei*. Other possible roles for this metabolic pathway in *T. cruzi* are being explored.

Poster 75 : Characterization of a schistosome metalloprotease that facilitates *S. mansoni* infection establishment and maintenance of the snail host. - *A13146*
Presenter: **Patrick Hanington**, *Assistant Professor, University of Alberta*

**P C Hanington**[1]; A L Kabore[1]; E A Pila[1];
[1] Univeristy of Alberta, Canada

A number of metalloproteases (MP) have demonstrated roles in immune modulation. In some cases, these enzymes are produced by parasites to influence host immune responses such that parasite infection is facilitated. One of the best examples of this is the matrixmetalloprotease leishmanolysin (Gp63), which is produced by *Leishmania* in order to evade killing by macrophages. Leishmanolysin-like proteins appear to be quite common in many invertebrates, however our understanding of the functions of these non-*Leishmania* enzymes is limited. Numerous proteomic and transcriptomic screens of schistosomes at all life cycle stages has identified leishmanolysin-like MPs as being present in abundance; with the highest levels being found during the intramolluscan larval stages and being produced by cercariae. This study aimed to functionally characterize a variant of leishmanolysin that most resembled the enzyme produced by *Leishmania*, termed SmLeish. We demonstrate that SmLeish is an important component of *Schistosoma mansoni* excretory/secretory products and is also present on the sporocyst surface. The presence of SmLeish interferes with the migration of *Biomphalaria glabrata* haemocytes, and causes them to present a round, non-adherent phenotype. Knockdown of SmLeish in *S. mansoni* miracidia prior to exposure to *B. glabrata* causes a delay in reaching patent infection, and also reduced miracidia penetration success and ultimate cercaria output from infected snails.

Poster 76 : Parasites, pathogens and the sustainability of Northern Ireland's honey bees - *A13147*
Presenter: **Mr Stephen Bell**, *PhD Student,*

**S H Bell**[2]; A G Maule[2]; A Mousley[2]; R J Paxton[1]; N J Marks[2];
[1] Martin-Luther Universtat, Halle-Wittenburg; [2] Queen's University Belfast

Honey bees (*Apis mellifera*) are pivotal to the sustenance of human and animal populations through their ability to pollinate key agricultural crops throughout the world. Honey bees pollinate 75% of crops which are integral to human and animal life. The amount of land requiring pollination has increased by up to a third between 1961 and 2006. Colony losses are experienced by beekeepers across the world. There are multiple causes of colony loss such as parasites, viruses, microsporidia and environmental factors. This project will assess honey bee health and husbandry techniques employed by beekeepers in relation to the parasitic mite *Varroa destructor* through a questionnaire and disease analysis using molecular screens. *Varroa* is a parasitic mite which impacts honey bee health directly by inflicting physiological damage such as affecting flight. *Varroa* additionally have an indirect impact on honey bee populations as they act as a vector for viruses which have been shown to have adverse impacts on honey bee health, such as Deformed Wing Virus (DWV). Honey bees infected with DWV in their pupal stage can develop crippled wings when they are adults, inhibiting flight. 98% of beekeepers in Northern Ireland stated that their hives have been infested with *Varroa*, the majority of which found *Varroa* to be endemic within their hives. Project results can inform policy decisions and initiatives regarding honey bee health.

Poster 79 : Phenotypic high-throughput screening identified potent *Trypanosoma* inhibitors with ability to cure Human African Trypanosomiasis - *A13141*
Presenter: **Dr Srinivasa P S Rao**, *Investigator, Novartis Institute for Tropical Diseases*

**S Rao**[1]; J Jiricek[1]; P Ng[1]; M Kaiser[2]; E Myburgh[4]; S Lakshminarayana[1]; P Gedeck[1]; P Maeser[2]; M P Barrett[3]; J Mottram[4]; T Diagana[1];
[1] NITD, Singapore; [2] Swiss Tropical and Public Health Institute, Switzerland; [3] University of Glasgow; [4]University of York

The current anti-trypanosomal therapies suffer from problems of toxicity, inadequate efficacy hence there is an urgent need for safer, more efficacious and 'easy to use' oral drugs. Novartis carried out whole cell based high-throughput screening using ~2 million compounds and obtained ~28,000 hits showing > 50 % growth inhibition against *Trypanosoma brucei brucei* at 10 µM concentrations. Further reconfirmation, removing cytotoxic hits and cheminformatics analysis for drug-like properties resulted in ~1,000 tractable hits with *T. b. brucei* $IC_{50}$ < 10 µM. Biological characterization using reversibility and kill kinetic profiling helped to group them in to 'cidal' and 'non-cidal' compounds. Following chemical hit triaging 36 chemical series were identified; further seven chemical series were prioritized on the basis of cidality, broad SAR, metabolic stability and efficacy against clinical isolates. Tool compounds from all the chemical series were subjected to early efficacy testing using blood stage mice model, wherein they significantly reduced parasitemia, followed by either complete or partial cure. One of the series was prioritized for lead optimization to address brain penetration and other pharmacological properties. This led to successful identification of a lead compound which completely cured *Trypanosoma* infection in brain stage mice model. Mechanisms of action studies on this series revealed 20S proteasome as the target for this series. Characterization of hits in disease relevant assays and early animal efficacy studies helped in identification of promising chemical series which had the ability to cure HAT in both blood and brain animal models.

Poster 80 : Investigating Ca2+ channel blockers as antimalarials - *A13157*
Presenter: **May Rajab**, *PhD Student, University of Salford*

**M Rajab**[1];
[1] University of Salford

Calcium, calcium channels along with calmodulin (CaM) play important roles in human RBCs and within *Plasmodium falciparum* parasites. Studies have shown that calcium levels are higher in infected RBCs than non-infected ones and interfering with calcium signalling can lead to degeneration and eventually parasite death. Likewise several antimalarial drugs are reported to have anti-CaM activity. This supports results of a repositioning study carried out at the University of Salford were 700 patent expired drugs were screened against the multidrug resistant K1 *P. falciparum* strain. The results showed several calcium channel blockers and CaM inhibitors to have antimalarial activity. The work presented here covers the synthesis and investigation of the antimalarial efficacy of a calcium channel blocker and CaM inhibitor MR15 and numerous of its synthetic analogues. The initial results from the in vitro phenotypic screens on the multidrug resistant K1 *P. falciparum* strain, HepG2 cytotoxicity assay, hERG safety test, and stage specificity analysis were promising and thus supported further studies. Other work presented here includes CalcuSyn based combination studies of MR15 with current anti-malarial drugs and other calcium channel blockers. Additionally, ongoing optimisation using fluorescent dyes is being carried out to detect fluctuations of calcium levels within *P. falciparum* infected RBCs using flow cytometry.

Poster 81 : Structure and function of the trypanosome nuclear envelope - *A13118*
Presenter: **Norma Padilla-Mejia** , *Postdoctoral Research Assistant, University of Dundee*

**N E Padilla-Mejia**[1]; E R Butterfield[1]; L Koreny[2]; S O Obado[3]; S R Scutts[4]; B T Chait[3]; M P Rout[3]; M C Field[1];
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The nucleus is contained by the nuclear envelope (NE) which associates with multi-protein complexes, these function in structural support (lamina), bidirectional transport of RNA and proteins (nuclear pore complex), nuclear positioning (LINC complex) and signal transduction in higher eukaryotes. The lamina is associated with chromosomal and heterochromatin organisation and transcription and regulation of replication. Proteins with similar functions have been identified in organisms across different evolutionary supergroups. In *Trypanosoma brucei* two lamina proteins have been identified, NUP-1 and NUP-2, involved in the maintenance of the nuclear architecture, organization of the heterochromatin, chromosome positioning and variant surface glycoprotein switching regulation. To further characterise lamina function and identify possible interacting partners in *T. brucei*, we used co-immunoprecipitation, imaging, overexpression analysis and comparative genomics. We conclude NUP-1 has three domains with indications both the N and C-terminus act as nucleation/polymerisation sites. We have also identified proteins which interact with NUPs which we termed NAPs for NUP associated proteins. These proteins are predicted to be localised to the nucleus and contain domains related to nuclear activities. Overall, these advances are leading us to define the manner in which the NE is structured, how it participates within the cell cycle and how its components interact.

Poster 82 : Defining D-arabinose metabolism in *Leishmania major* and *Crithidia fasciculata* - *A13119*
Presenter: **Miss Elda Iljazi**, *PhD student, University of Dundee*

**E Iljazi**[1]; M A Ferguson[1];
[1] University of Dundee

D-arabinopyranose (D-Ara*p*) is found, uniquely, in cell surface glycoconjugate structures of certain trypanosomatid parasites: *Leishmania major* lipophosphoglycan, *Crithidia fasciculata* lipoarabinogalactan and *Endotrypanum schaudinni* glycoinositol phospholipids. The activated donor molecule of D-Ara*p* has been identified in *L. major* as GDP-α-D-Ara*p*. So far it is known that both *L. major* and *C. fasciculata* have a salvage pathway allowing the parasites to internalize D-Ara from the extracellular medium or the lumen of the insect guts and convert it to GDP-α-D-Ara*p* via an arabinose-1-kinase/pyrophosphorylase. A *de novo* pathway, whereby D-Glucose is converted to D-Ara*p* via loss of the Glc C-1 carbon atom has been postulated but many details are missing. Many gram-negative bacteria have an Arabinose-5-phosphate isomerase enzyme. In bacteria API enzymes catalyse the interconversion of D-ribulose-5-phosphate, the product of the oxidative phase of the pentose phosphate pathway, and D-arabinose-5-phosphate. We speculate that trypanosomatids may also convert D-Glc to D-Ara*p* via Ru5P and its isomerisation to A5P followed by dephosphorylation

to D-Ara*p*. Apart from cell surface incorporation it is possible that D-Ara*p* may be used by all the kinetoplastids to make D-erythroascorbate, similar in structure and physicochemical properties to Vitamin C.

Poster 83 : Characterisation of a novel trypanosomatid mitochondrial alternative oxidase as a drug target - *A13135*
Presenter: **Stefanie Menzies**, *PhD Student, University of St Andrews*

**S K Menzies**[1]; G J Florence[1]; T K Smith[1];
[1] University of St Andrews

We report the characterisation of the secondary alternative oxidase (AOX2) as a novel drug target in the trypanosomatids. The trypanosome alternative oxidase (TAO) has been well characterised as a drug target in *T. brucei*, but it is absent from *T. cruzi* and *Leishmania* spp. However, the previously un-investigated AOX2 is present in the three human-infective trypanosomatids and has no mammalian orthologue, thus making it an attractive potential kinetoplastid specific drug target. We report evidence that AOX2 is an essential mitochondrial protein in *Trypanosoma brucei, T. cruzi* and *Leishmania major*, and is involved in mitochondrial respiration. Furthermore, we have successfully purified recombinant AOX2 and confirmed its function as an iron-dependent ubiquinol oxidase. We are screening for selective inhibitors of the AOX2 using our in-house natural product-like library and a fragment library to identify lead compounds.

Poster 84 : *Trypanosoma brucei* TbTAF1 is a transcriptional regulator of VSG expression that negatively regulates differentiation. - *A13137*
Presenter: **Mr Andreu Saura**, *PhD Student, Instituto de Parasitol. y Biomed.*

**A Saura**[3]; D López-Farfán[3]; P Iribarren[2]; V Alvarez[2]; I Vidal[3]; J M Bart[3]; M Field[1]; M Navarro[3];
[1] Biological Chemistry and Drug Discovery, School of Life Sciences, University of Dundee; [2] IIB-INTECH, Argentina; [3] Instituto de Parasitologia y Biomedicina "Lopez-Neyra", CSIC. Granada, Spain

Post transcriptional modification by the Small Ubiquitin MOdifier (SUMO) peptide functions in Variant Surface Glycoprotein (VSG) expression in *Trypanosoma brucei*. SUMO-conjugated nuclear proteins are enriched in the High SUMOylated Focus (HSF) that partially colocalizes with the Expression Site Body (ESB), the nuclear body where *VSG* is transcribed. Proteomic analyses of HA-SUMO-conjugated proteins identified Transcription Activator 1 (TAF1), a SNF2 family member. Functional characterization of TAF1 by RNAi showed a significant reduction (50%) of active *VSG*221 mRNA levels. ChIP analysis showed RNA Polymerase I occupancy decreased on the active VSG221 following TAF1 KD, suggesting this factor is required for VSG transcription. TAF1-ChiP analysis suggested occupancy at sequences upstream of the VSG promoter. DNAs isolated from TAF1 ChIP experiments showed heterogeneity of the VSG promoter sequences suggesting TAF1 is located not only in the active VSG221, but rather in many other inactive ones. Upon TAF1 KD, we also detected an unexpected increase of Procyclin mRNA, normally repressed in the bloodstream form. Thus, we

investigated Protein Associated with Differentiation (PAD1 and PAD2) expression levels. TAF1 KD showed a clear upregulation of PADs, suggesting TAF1 also regulates differentiation. Together these data suggest a dual function of TAF1 that regulates both, VSG transcription and developmentally regulated gene expression.

Poster 85 : CalcuSyn-based drug interactivity studies to define synergistic anti-malarial combinatorial regimes for Emetine dihydrochloride - *A13159*

Presenter: **Mrs Muna Abubaker**, *Full time PhD, University of Salford*

**M Abubaker**[1];

[1] University of Salford

The emergence and spread of artemisinin resistance to *Plasmodium falciparum* in Southeast Asia poses a serious threat to ongoing malaria control efforts. Unless new approaches are deployed rapidly, the health and economic burden related to the disease in tropical countries is certain to worsen. The development of treatments through drug repositioning may offer novel candidates permitting new combinatorial regimes with existing anti-malarials. The approach could present a much needed viable, accelerated route to expand the dwindling antimalarial therapeutic repertoire. Drug repositioning screens previously carried out in our laboratory reported the potent antimalarial efficacy ($IC_{50}$ 47nM for *P. falciparum* K1 strain) of the anti-amoebic drug Emetine dihydrochloride hydrate. We present here the preliminary data from a study designed to define the combinatorial therapeutic potential of emetine with a panel of antimalarial drugs, in a bid to minimise non-target effects previously experienced with the use of the drug in amoebiasis. The rational discovery of novel synergistic drug combinations can be accelerated by predictions of combination effects through experimental studies. All combinations were analysed using the optimised CalcuSyn fixed-ratio method validated using the atovoquone-proguanil combination. Following a screen of current antimalarial compounds, our preliminary data identified AN16 as the combinatorial partner drug displaying maximum synergistic interactivity with emetine dihydrochloride. The isobologram plot and the combination index (CI) generated by the CalcuSyn software demonstrated that the interaction between emetine and AN16 is synergistic at IC50, 1C75 and IC90 levels. The MTT cytotoxicity results indicated that the emetine-AN16 combination has a better selectivity index in comparison to emetine alone. The results strongly support further in vivo investigation of the utility of emetine-AN16 combination as an alternative antimalarial treatment for drug resistance malaria.

Poster 86 : New records of the copepod mesoparasite *Haemobaphes cyclopterina* indicate long-rough dab is a key definitive host - *A13148*

Presenter: **Alastair Lyndon**, *Senior Lecturer, Heriot-Watt University*

G A MacKay[1]; S J Paterson[1]; L Fergusson[1]; **A R Lyndon**[1];

[1] Heriot-Watt University

*Haemobaphes cyclopterina* (Copepoda: Lernaeoceridae) has rarely been recorded from the North Sea area, with only five locations recorded over the last century, three of these being in Norway and Denmark. Of the two records further south, one was from butterfish and the other from dab. Recent sampling of long-rough dab (*Hippoglossoides platessoides*; total N = 76) from three localities off eastern Scotland produced eight individual *H. cyclopterina* over a period of four years, representing only the third to sixth records from this definitive host. Prevalence was between 4 and 20 %, much higher than the next most recent record in the area (1990-92) from dab (*Limanda limanda*) of five individual parasites in more than 18,000 hosts. This indicates that long-rough dab are a previously overlooked definitive host for this parasite in the central North Sea, which furthermore appears to be the most important host for *H. cyclopterina* in this area.

Poster 87 : A tale of two flatties: macroparasite communities in dabs and long-rough dabs. - *A13149*
Presenter: **Alastair Lyndon**, *Senior Lecturer, Heriot-Watt University*

S J Paterson[1]; S B Anderson[1]; G A MacKay[1]; L Regan[1]; **A R Lyndon**[1];
[1] Heriot-Watt University

Few data are available on parasite communities in marine fish, especially for those of limited commercial importance. Dabs (*Limanda limanda*) and long-rough dabs (*Hippoglossoides platessoides*) are abundant non-fishery flatfish species in the North Sea, for which limited or parasite community studies are available. Samples of both species were obtained from prawn-trawl by-catch in the Firth of Forth area (eastern Scotland), enabling characterization and comparison of parasites across both species. Results show a degree of overlap between the communities of both host species, with some generalist parasites, but with distinctive characteristics in each. Dab communities were characterized by having more adult digeneans in the gut and larval acanthocephalans (*Corynosoma strumosum*), whereas long-rough dab communities were dominated by crustacean ectoparasites and in the most recent survey larval cestodes, which were both scarce in dabs. Generalist larval nematodes were moderately abundant in both host species, contributing most to the overlap between parasite communities. In conclusion, despite morphological and habitat similarities between the two hosts, their macroparasite communities were distinct, despite the presence of nominally generalist parasites common to both species.

Poster 88 : A thorny issue? – First record of the genus *Aspersentis* in UK waters: a new acanthocephalan species from the sea scorpion? - *A13150*
Presenter: **Alastair Lyndon**, *Senior Lecturer, Heriot-Watt University*

O Thomas[1]; J Buckman[1]; **A R Lyndon**[1];
[1] Heriot-Watt University

A new location and host record of the acanthocephalan genus *Aspersentis* is presented from long-spined sea scorpion (*Taurulus bubalis*). The specimens were sampled from fish associated with seagrass beds off south Arran in the Firth of Clyde, and represent

only the second record of *Aspersentis* spp. in the northern hemisphere. The possibility that these represent a new species of *Aspersentis* is investigated.

Poster 89 : Parasite communities of deep-sea fishes: the need for a benthic connection? - *A13151*
Presenter: **Alastair Lyndon**, *Senior Lecturer, Heriot-Watt University*

A McCarthy[1]; R Perry[1]; **A R Lyndon**[1];
[1] Heriot-Watt University

Macroparasite communities were examined in three species of bathypelagic fish sampled off the Azores. Only one of the three species (*Coryphaenoides guentheri*) supported any macroparasites, and these were found to become less abundant and diverse with increasing host size. It is suggested that fully bathypelagic species lack significant macroparasite communities and that connection of early life stages with the benthos enables parasite transmission to *C. guentheri.* Parallels with reduced host densities in over-fished shelf communities are explored.

Poster 91 : Identifying highly divergent glycosyltransferases in the African trypanosome - *A13175*
Presenter: **Dr Samuel Duncan**, *Postdoctoral Researcher, The University of Dundee*

**S M Duncan**[1]; M A Ferguson[1];
[1] The University of Dundee

*Trypansoma brucei* is a protozoan parasite that infects humans and cattle via a tsetse fly vector. Key to parasite survival during progression through this complex life cycle is the expression of cell surface and endocytic pathway glycoproteins, modified with glycosylphosphatidylinositol (GPI) membrane anchors and/or N-linked oligosaccharides. We estimate that protein glycosylation in this parasite requires at least 38 distinct glycosyltransferases (GTs), only a few of which can be predicted by bioinformatics. Interestingly, a family of 21 putative trypanosome GTs has been identified that share a single beta 1-3 transferase ancestor but catalyse a diverse array of glycosidic linkages. Inhibition of such highly divergent GTs is therefore a promising therapeutic avenue, yet 17 of these putative TbGTs require characterisation. This project aims to identify their function by utilising reverse genetics and RIT-Seq approaches.

Poster 92 : Elevated temperature increases the growth and development of *Schistocephalus solidus* procercoids in copepod hosts - *A12872*
Presenter: **Mrs Zalina Ismail**, *PhD Student, Department of Neuroscience, Psychology and behavior*

**Z Ismail**[1]; I Barber[1];
[1] University of Leicester

Global climate change has the potential to impact the interactions between aquatic parasites and their hosts both directly, for example by acting on free-swimming infective stages, and indirectly, by affecting their interactions with intermediate hosts. Such effects potentially affect transmission dynamics, parasite development time and ultimately life cycle completion rates. Here, we describe the results of experimental studies designed to examine how elevated temperatures affect the infectivity, growth and development of life cycle stages of the diphyllobothriidean cestode *Schistocephalus solidus*, the plerocercoids of which are ecologically important parasites of stickleback fish. Following the *in vitro* culture of adult worms, individual copepods (*Cyclops strenuus abyssorum*) were exposed to a controlled dose of newly-hatched *S. solidus* coracidia, and held at 10°C, 15°C and 20°C. Infectivity of the parasite under the different temperatures was quantified by screening exposed copepods after 7d, and the subsequent growth rates of procercoids was tracked at 7d intervals over a 6-week post-infection period, by microscopic examination and image analysis. While temperature treatment had no effect on the infectivity of coracidia to copepods, procercoids grew more quickly in copepod hosts at 20°C than at 10°C or 15°C, and procercoids developed cercomers – caudal appendages associated with infectivity to fish hosts – more quickly at the highest temperature. Our results suggest that changing thermal regimes in aquatic environments can influence the growth and development of parasite life cycle stages, with implications for the dynamics of life cycles.

Poster 93 : A high field gradient magnetic probe for detecting parasite eggs in faecal matter processed by the Helmintex method - *A13006*
Presenter: **Dr Renata Candido**, *Research Fellow, University of Western Australia*

**R Russo frasca Candido**[3]; V Favero[1]; C Lindholz[1]; C De Marco Verissimo[1]; R Perotto de Souza[1]; R Charles Woodward[3]; A Loureiro Morassutti[1]; C Graeff-Teixeira[1]; M K Jones[2]; T St Pierre[3];
[1] Pontificia Universidade Católica do Rio Grande do Sul, Brazil; [2] The University of Queensland, Australia; [3] The University of Western Australia, Australia

The aim of this study was to test the sensitivity of a new method for detecting schistosome eggs in faeces. 580 stool samples were collected in an endemic area, Estancia, northeast Brazil and tested using the Kato-Katz (KK) method. A case-control study was then carried out on 20 KK +ve and 20 KK -ve samples (randomly selected). Urine samples were tested with POC CCA. Faecal samples were processed according to the Helmintex method to produce a suspension of solids in a 1.5-mL tube. The suspension was gently stirred for 20 seconds with the tip of a probe that produces a source of high magnetic field gradient at the tip. Two approximately 40-uL droplets were extracted from the sediment by using the probe. Each droplet was deposited on a glass slide during demagnetisation of the probe to enable inspection by optical microscopy. The remainder of the sediment was screened for confirmatory results. For analysis of sensitivity, a composite reference standard was defined as follows: if any of KK, probe, or standard Helmintex screening identified an egg, the case is disease +ve; otherwise -ve. Eggs were detected in all 20 KK positive samples using the probe. In the KK -ve samples, the probe yielded +ve results for three samples. The time needed to read the samples using the probe was approximately

one third of the time required to screen Helmintex processed samples by the standard method. Against the composite reference standard, the following sensitivities (95% CIs) were observed: KK 83% (63-95%), POC CCA 79% (58-93%), probe 92% (73-99%), standard Helmintex 96% (79 -100%). The high field gradient magnetic probe used on Helmintex prepared faecal suspensions can provide rapid and sensitive detection of *Schistosoma* eggs.

Poster 94 : Prevalence, types of carpets mites in Gaza, Palestine - *A13179*
Presenter: **Adnan Al-Hindi**, *Dean, Faculty of Health Sciences, Islamic University-Gaza*

**A Al-Hindi**[2]; D Suhwail[1]; H Tafesh[1];
[1] Islamic University-Gaza, Palestinian Territory; [2] The Islamic University, Gaza, Palestinian Territory

Human Dust Mites are classified as invertebrates, as they do not have an internal skeleton. Most often they are found in habitats intimately associated with man, such as beds, bed linen, couches, sofas, other upholstery furniture's, clothing, curtains, window stills, floors and carpets. These domestic environments are very important locations for forensic investigations, but this richness of mite diversity has not been exploited by forensic investigators. This study aimed to determine the prevalence of carpet mites, isolate and identify the different species in Gaza. A total of 200 dust samples; vacuums machine (98 samples) and manual cleaning (102 samples) were collected in cups from house to house. After that, the cups were transported to the parasitology laboratory. Each dust sample was sieved, sedimented, and examined under microscope for morphological classification. Results:
*Dermatophagoides* sp, *Dermatophagoides pteronyssinus*, and other types were isolated. It was found that mites were more prevalent in carpets with more than 1 cm thickness (60%) compared to carpets with thickness less than 1 cm. It was found that mites were more prevalent in carpets age of 2-4 years (72.6%) compared to other age periods. It was found that house dust mites are prevalent in Gaza. Different types of mites were isolated in the present study. A strong association was found between presences of mites and complains of medical symptoms.

Poster 95 : Global migration and transmission of disease: a Malaysian case study - *A13019*
Presenter: **Siti Nursheena Mohd Zain**, *University of Malaya*

**S N Mohd Zain**[1]; Y Lim Ai Lian[1]; N Sahamin[1];
[1] University of Malaya, Malaysia

Mass migration from less developed to more developed countries have created a shift in the global population. Urbanization and extension in industrialization of developing nations have resulted in millions of migrants migrating to major urban cities around the globe to cope with expanding workforce. This has attracted many to flock to major cities in Malaysia both legal and illegally from South East (Indonesia, Cambodia, Vietnam, the Philippines and Myanmar) and South Asian countries (Nepal, India and Bangladesh) where endemic infections are very much prevalent and most likely to pose public health problems to the local community. Presently, compulsory medical screening for workers prior entering to the workforce does not include parasitic screening. As the number of

migrant workers has grown exponentially over the past decade and the incidents of communicable disease have become more prevalent in the country, therefore, there is an acute need for a more accurate and current information on the parasitic infections in this particular group of workers and factors associated to infections as it impacts the local community significantly.

Poster 96 : A Host ration affects plerocercoid growth in three-spined sticklebacks infected with *Schistocephalus solidus* (Cestoda: Diphyllobothriidae) - *A12979*

Presenter: **Mr Awad Hosan**, *phd student, University of Leicester*

**A Hosan**[1]; I Barber[1];
[1] University of Leicester

Host dietary factors, including the quantity and quality of food ingested, have considerable potential to influence the outcome of host-parasite interactions. For example, increased food intake may improve resistance to parasite infections if it improves host immune responses; however, it could alternatively increase the supply of nutrients available to parasites, benefiting parasite growth and development. The aim of this study was to investigate the effects of host ration on the growth of *Schistocephalus solidus* plerocercoids in experimentally infected three-spined sticklebacks *Gasterosteus aculeatus.* Lab-bred sticklebacks were either exposed to infective stages of *S. solidus* by feeding them copepods containing infective parasites, or were sham-exposed. Experimental fish were subsequently fed either a high ration or a reduced ration (6% or 3% body weight per day respectively) for a period of 12 weeks. At the termination of the study, fish were dissected and a range of indices of fish growth, energetic status, health and infection status were quantified. Our results indicate that the level of host ration play an important role in value of the indices and suggest that host ration had a significant effect on the performance of both infected and non-infected fish in the study.

Poster 97 : Enhanced delivery of a prototype poultry red mite vaccine - *A12981*

Presenter: **Dr Tatiana Kuster**, *PDRA in Parasitology, Royal Veterinary College*

**T Kuester**[3]; D Price[1]; A J Nisbet[1]; O Oines[2]; D P Blake[3]; F Tomley[3];
[1] Moredun Research institute; [2] Norwegian Veterinary Institute, Norway; [3] Royal Veterinary College

*Dermanyssus gallinae* is the most important ectoparasite affecting egg-laying chickens. Infested birds may suffer from anaemia, dermatitis, weight loss and decreased egg production. The scarcity of effective pesticides has contributed to a significant problem for the layer industry. Commercially available acaricides are not effective in the control of poultry red mite infestations due in part to increased parasite resistance. Additionally, acaricide use is gradually being discontinued as a consequence of public awareness and legislation against chemical residues on food products, and chemical release and accumulation in the environment. The development of an effective vaccine can decrease the occurrence and impact of *D. gallinae*, thereby improving the general health and welfare of layers without the use of acaricides. Transfection vectors have been developed for genetic complementation of *Eimeria tenella*,

prompting the notion that live-attenuated coccidial parasites could be used as effective vectors for the oral delivery of heterologous vaccine antigens to poultry. In cooperation with two PARAGONE partners we propose to compare the delivery of a defined antigen (cathepsine D1) in three systems, namely DNA vaccination, recombinant protein formulation in montanide and cytosolic, secreted, or membrane-tethered antigen expressed by the *Eimeria* vector. The immune responses, efficacy, and endurance of the effect of vaccination are being currently investigated.

Poster 101 : Investigation of a possible mitochondrial mechanism of action of naphtoquinone-anacardic acid hybrids compounds against trypanosomiasis - *A13184*

Presenter: **Miss Michaela Cerone**, *Student, University of Glasgow*

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In a search for new effective and low-cost drug-hybrids for Neglected Tropical Diseases, we aimed at designing and synthesizing a focused combinatorial chemical library of 15 naphtoquinone-anacarcic acid hybrids to treat trypanosomiases. By following a merging strategy, the naphthoquinone scaffold derived from an in-house hit anti-trypanosomatid compound, named B6, has been combined to the natural phenols of cardanol derivatives, a renewable food production waste product from Anacardum Occidentale. In particular, B6 has been identified (i) to inhibit trypanosomal glyceraldehyde-3-phpsphate dehydrogenase (GAPDH) (IC50 of 7.25 µM); (ii) to exhibit potent trypanocidal activity (EC50 of 80 nM against *Trypanosoma brucei rhodesiense*); (iii) to possess a promising selectivity index (SI of 74); (iv) to generate oxygen radicals in the trypanosomal mitochondrion.1 Furthermore, the anacardic acid derivatives, extracted from cashew nut shell liquid (CNSL), are endowed of many biological activities. They proved to be micromolar inhibitors (IC50 28.0 µM) of GAPDH of *Trypanosoma cruzi*. 2 Some of the newly synthetized compound have been preliminary tested against *T. brucei* GAPDH, showing an interesting inhibitory activity (micromolar range).3 Given the profile of the starting hit compounds, we decide to evaluate their mechanism of action at the mitochondrial level, as the drug design strategy is inspired to be a synergistic inhibition of energy metabolism. All compounds are designed on

Poster 102 : Cullin-RING complexes in *Trypanosoma brucei*: TbCUL1 complex composition and preliminary functional insighta - *A13182*

Presenter: **Ricardo Canavate del Pino**, *PhD student , University of Dundee*

R Canavate del Pino[1]; M Zoltner[1]; M C Field[1];

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Recent evidence links cullin-RING complex ubiquitin ligases to the regulation of the surface of *Trypanosoma brucei* as well as other functions. The surface iis the interface between the host and the parasite and determinants for the uptake of trypanocidal drugs are present there. In mammalian systems, cullins are key regulators of the cell cycle, control ubiquitination pathways involved in receptor internalisation and have been suggested as drug targets. Despite the broad scope of ubiquitination pathways in the Kinetoplastida and the potential to impact the entirety of trypanosome biology, our current understanding of all classes of ubiquitin ligases including the cullin RING ligases is extremely limited. We have identified and assembled a phylogenetic reconstruction of the cullin family in the Kinetoplastida as well as adaptor proteins and E3 ligases. Using cryo-milling and immuno-isolation we have identified components of the *Tb*CUL1 complex. Proteomic analysis revealed multiple protein abundance changes upon *Tb*CUL1 silencing, including F-box and WD-repeats proteins, which homologues have been described as substrates for cullin RING ligases. These data provide a first systematic assessment of cullin composition and function in trypanosomes.

Poster 103 : Molecular identification and relative abundance of Surra vectors from camels of Cholistan desert, Punjab, Pakistan - *A13180*

Presenter: **Prof Nusrat Jahan**, *Professor, Govt College University*

**S Tehseen[1],** N Jahan[1];
[1] Govt College University, Pakistan

Surra is a vector borne disease of animals and has a worldwide distribution. *Trypanosoma evansi*, the causative agent, principally transmitted by hematophagous flies. It is associated with great economic losses, working capacity, and productivity of animals. Recently reported Surra in Camels of Cholistan desert from our laboratory necessitated to find the vectors in selected areas. In current study field collection of vectors was done directly from the same camel herds investigated for surra. The collection was done twice a month from January 2012 to December 2013. Flies were identified morphologically by using taxonomic keys for *Tabanidae*, *Stomoxys* and *Hematobia*. Random samples (n=100) of flies per species, collected from the field diagnosed camels for Surra were examine for the signs of engorgements. Molecular identification was carried out on whole flies and fly body parts mid-guts and mouthparts following DNA extraction. TBR1/2 PCR and RoTat 1.2 PCR were carried out for the diagnosis of trypanosomes. Cytochrome b PCR was carried out on all samples for the evaluation of DNA quality. Blood meal analyses were also carried out by amplification of Cytochrome b genes and PCR products were purified and sequenced. A total of 4517 flies (tabanids, *Hematobia* and *Stomoxys*) were collected during the study period comprising *T. rubidus* (18.6%), *T. striatus* (37.8%) and *S. calcitrans* (43.6%). The total fly catch of each species was non-significantly different from each other ($p < 0.05$). *Hematobia* sp. were the most common flies found on camels. No significant difference was found between collected males and females of *S. calcitrans* ($p > 0.05$) while 100% collected population of *T. rubidus* and *T. striatus* comprised of females only. Seasonal variations in abundance of different flies was irregularly distributed. The *Tabanus rubidus* population peaked in May and September and decreased after October. *Tabanus striatus* increased in July onwards before disappearing in November, 2013. *Stomoxys* were seen throughout 2012 and 2013 with three peaks in April, July and September 2012 whereas, two peaks were observed in the months of June and August in 2013. A significant difference was observed in *S. calcitrans* populations in summer and spring having higher abundance than autumn and winter ($p < 0.05$). The apparent and relative abundance

of *T. rubidus*, *T. striatus* and *S. calcitrans* on camels is suggestive of their role as a mechanical vector of Surra in Punjab Pakistan. The current study is a first and novel work related with recently reported study in our laboratory on the prevalence of Surra in camels of Cholistan desert, Pakistan.

Poster 104 : Breeding for resistance to nematode infection in sheep - a diagnostic tool. *A12914*
Presenter: **Karen Fairlie-Clarke,** *University of Glasgow*

**K Fairlie-Clarke**[2]; N Brady[2]; L Matthews[2]; M Stear[1];
[1] La Trobe University, Australia; [2] University of Glasgow

In the UK *Teladorsagia circumcincta* is the predominant nematode of sheep. This parasitic infection causes disease and untreated can result in death. Even a mild infection compromises production reducing weight gain by 25%. In the UK sheep industry alone nematode infection is estimated to cost approximately £84 million a year. With the rise in anthelmintic-resistance it is important to identify animals with natural resistance to parasitic disease.
One of the major mechanisms of resistance to *T. circumcincta* is the mucosal IgA antibody response. Importantly the IgA response is not associated with impaired host growth. Thus, there is great potential to include the IgA response in selective breeding programs. However, measuring IgA responses at the site of infection (abomasum) is not feasible in large flocks. Saliva is a readily accessible source of IgA and can be sampled by simply inserting a swab into the cheek pouch of the animal. We have developed an assay to measure salivary IgA activity against *T. circumcincta* third stage infective larvae (L3) in sheep. This simple test provides breeders with a means of identifying animals that are suitable for inclusion in selective breeding programs for nematode control.

Poster 105 : First description of a digenean trematode associated with dusky grouper dermatitis (DGD) lesions in Epinephelus marginatus (Lowe) from Libyan waters. *A13076*
Presenter: **Jamila Rizgalla**, Postdoc, University of Stirling

J Rizgalla[1]; A P Shinn[1]; H W Ferguson[2]; G Paladini[1]; J E Bron[1];
[1] Institute of Aquaculture, University of Stirling, Facultry of Natural Sciences, UK; [2] Marine Medicine Programme, School of Veterinary Medicine, St. George's University, Grenada

Eggs and adults of a digenetic trematode were found in close association with "dusky grouper dermatitis (DGD)" lesions affecting the wild population of dusky grouper Epinephelus marginatus in the coastal waters of Libya. Histological evaluation of lesions found gravid hermaphroditic digeneans (ca. 1,500-2,000 µm long), within dermal blood vessels. The digeneans, based on their morphology, were subsequently assigned to the Aporocotylidae Odhner, 1912 (Platyhelminthes: Trematoda). Eggs (ca. 20-37 µm long), with embryos at various stages of development, from homogenous embryos in utero to fully developed miracidia, were found located within the dermis and epidermis. Evidence suggests their passage through host tissues is facilitated by the host's inflammatory response - migrating from the dermal blood vessels to the dermis and then the epidermis, whereon the miracidia hatch and are released into the external aquatic environment. Alternatively, eggs are conveyed with the natural turnover of epidermal cells. The host's inflammatory process involves

the recruitment of eosinophils to the sites of infection and their degranulation in close proximity to eggs situated within blood vessels. Although blood flukes are recorded from the blood vascular system of serranids (Epinephelinae), this is the first record of a aporocotylid digenean occupying the cutaneous blood vessels of a piscine host.

Poster 106 : The use of microbeads to mimic T.gondii uptake by aquatic invertebrates. A possible reservoir for higher vertebrates?
*A13231*

Presenter: **Mr Anusheel Varshney**, BSP conference , University of Salford

A Varshney[1]; C Benvenuto[1]; G Hide[1]; D Thomason[1];
[1] University of Salford, UK

The parasite Toxoplasma gondii oocysts are considered to be a terrestrial parasite due to the definitive host being the cat. Infection of intermediate hosts has been reported from contamination by oocysts in both fresh and marine waters. Oocysts of this parasite are microscopic (10µm) and easily transported in water. Accidental uptake of oocysts by micro-organisms may aid the distribution of the parasite in aquatic environments and create a reservoir for entry into the aquatic food chain. To determine this role, fluorescent microbeads were used as a model to mimic the properties of oocysts in different concentrations of water. Eight different aquatic micro-organisms were exposed to the beads over different time intervals then observed under confocal microscopy. Five different species were observed to have ingested the beads one species ingested and collected the beads externally. Micro-organisms accidentally ingest oocysts and could be a possible reservoir and source of T. gondii into the aquatic food chain.

Poster 109: New Class of Nucleotide Sugar Transporter inTrypanosome Peroxisome

Presenter**: Lucia Guther.** *University of Dundee*

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Trypanosoma brucei expresses essential N--glycosylated and GPI anchored glycoproteins, eg. the variant surface glycoprotein (VSG) and the transferrin receptor (TfR). Glycosylation pathways require nucleotide sugars (NS). NS biosynthesis in T. brucei, uniquely, takes place inside of peroxisomes, which in these organisms are called glycosomes. We are characterizing new class of nucleotide sugar transporters (gNST) present on the membrane of these organelles, which were discovered by High confidence SILAC glycosome proteome and RNAi knock--down followed by VSG

glycosylation phenotyping and nucleotide sugars quantitation by mass spectrometry. These glycosome NST allow NS to reach cytosol and ultimately to be taken up by traditional NST present on ER and Golgi.

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