BSP

BRISTOL 2013

PROGRAMME OVERVIEW

Monday 8th April	2.00–8.00	Registration			
	5.30–6.30	Wright Medal lecture – Mark Viney			
	6.30–8.00	Drinks reception			

Tuesday 9th April	9.00-10.30	1A Leishmania & Tryps I	1B Helminth biology I	1C Malaria I	1D Ecology I
	11.10-12.40	2A Leishmania & Tryps II	2B Helminth immunology I	2C Malaria II	2D Ecology II
	2.00-3.30	3A Metabolomics	3B Helminth biology II	3C General parasitology	3D Ecology III
	4.10-5.40	4A Fish parasitology	4B Helminth immunology II	4C Parasite – vector I	4D Ecology IV
	5.40-8.00	Poster session and drinks reception			
	8.00-	Younger(er) Parasitologists' Party			

Wednesday 10th April	9.00-10.30	5A Veterinary (BAVP)	5B Apicomplexan genomics	5C Parasite – vector II	5D Ecology V (BES)
	11.10-12.40	Plenary debate			
		AGM			
	2.00-3.30	6A Aquatic parasitology	6B Helminth biology III	6C Public Engagement	6D Malaria IV
	4.10-5.40	7A Veterinary parasitology I	7B Helminth immunology III	7C Malaria V	7D Ecology VI
	6.30 – 00.00	Conference dinner			

Thursday 11th April	9.00-10.30	8A Veterinary parasitology II	8B Target identification / gene silencing I	8C Schistosomes I	8D Ecology VII
	11.10-12.40		9B Target identification / gene silencing II	9C Schistosomes II	9D Ecology VIII

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WELCOME

I am delighted to welcome you to Bristol, and to the University, for the 51st Spring meeting of the Society. There is, as ever, a wide-ranging parasitological programme of talks, posters and plenary events. This year we maintain, and develop, our link with the British Ecological Society and welcome too a British Association of Veterinary Parasitology-sponsored session

We are meeting in the University's Wills Memorial Building, one of the City's landmarks, in the Clifton district of the City. Beyond the meeting and the science, I hope that you enjoy all that the City and the region has to offer, and information to help you in this endeavour is available at bsp2013.info

Very many people have worked hard to put this meeting together. I would particularly like to thank all the session organisers, Claire Nicoll and Jordan Morgan (School of Biological Sciences), Julian Fuller, Catherine Lawrence and Owain Millington for their help.

Mark Viney

VENUE

Everything except the Plenary session and AGM (Wednesday 10th April) will be in the Wills Memorial Building.

Poster sessions, tea, coffee and lunch and other refreshments are in the Great Hall, Wills Memorial Building.

The 4 parallel science sessions are in the Reception Room (same level as the Great Hall) and three lecture theatres on the third floor of the building.

The Wright Medal lecture is in the Reception Room.

The Plenary session and AGM is in lecture theatre 1 in the School of Chemistry.

There is a map of the University precinct inside the back cover of this booklet.

REGISTRATION

Monday 8th April, 2pm – 6pm in the Wills Memorial Building
Tuesday 9th April 8.30 – 12.30 in the Wills Memorial Building
Tuesday 9th April after 12.30pm, BSP office, adjacent to the Great Hall

CONFERENCE OFFICE AND BSP SECRETARIAT

Adjacent to Great Hall, for

- information
- expense claims
- maps
- internet access codes
- anything else

INTERNET ACCESS

There are two options:

- eduroam is available throughout the Wills Memorial Building, and the University precinct.

- For Wi-Fi in the Great Hall, select the wireless connection 'Bristol Visitors Net', then in the dialogue box enter the network key 'welcome.bris1' and then the username and password that you have been given. You can get replacement usernames and passwords from the BSP office

TOILETS

On the ground floor of the Wills Memorial building, as you enter the building, left hand side past the Porters' lodge.

STAIRS AND LIFTS

There is lift access to all floors. To find the lift, enter the building and walk between the two large staircases, the lift is then on your left. The Porters will also direct you.

CITY INFORMATION, DRINKING AND EATING

See bsp2013.info

INFORMATION FOR TALKS

The meetings' four sessions will be in the Reception Room (first floor, the same level as the Great Hall) and lecture theatres 3.30, 3.31 and 3.32 (third floor) all in the Wills Memorial Building.

Please load your talks in the lecture theatre appropriate to your session. There will be student helpers on-hand to help you do this.

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.

INFORMATION FOR POSTER PRESENTATIONS

All posters are in the Great Hall of the Wills Memorial Building. Put your poster on the board with your poster number anytime from 2pm on Monday 8th April, but please remove it by 2pm on Thursday 11th April.

Please only use Velcro (supplied) to attach your posters to the boards.

Your poster board number is indicated at the end of your abstract title. To find this, use the index to find your poster title ; the number in brackets is your poster board number.

STUDENT PRIZES

Cambridge University Press is presenting two *Parasitology* Centenary Prizes for the best student poster and for the best student oral presentation, each worth £200.

Trends in Parasitology is presenting two prizes, for the best student poster and for the best student oral presentation, each of a subscription to the journal.

The British Ecological Society is presenting one prize for the best student oral presentation of an ecological parasitology nature, worth £200

Entrants for these competitions are marked with an asterisk (*) in the programme. You can vote (once only) for the best poster and the best oral presentation using the voting slip at the end of this book. Please hand your completed votes to the conference office.

SPONSORS

We gratefully acknowledge the support of the following sponsors:

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WRIGHT MEDAL LECTURE

The BSP awards an annual medal to commemorate the life of Dr Chris Wright, Natural History Museum, by formal recognition of an individual's research excellence and expertise in parasitology.

The BSP 2013 Wright Medallist is Professor Mark Viney, University of Bristol.

PLENARY SESSION

The Plenary session will be a three-way debate between on the relationship between the shorter term benefits of anti-parasite treatment and the longer-term consequences.

Alan Fenwick (Imperial College) *In defence of unsustainable treatment of parasitic infections using MDA*

Andrew Read (Pennsylvania State University) *In defence of the future: anti-parasite treatments and the case for evolution-proofing*

James Wilson (UCL) *Ethics and the eradication of parasitic disease*

The Plenary session will be held in the School of Chemistry immediately after Wednesday's coffee break. It is a 7 minute walk, and our student helpers will direct you

AGM

The Society's AGM will immediately follow the Plenary session.

Lunch will be served back in the Great Hall, only once the AGM has finished.

PUBLIC ENGAGEMENT : HOW TO DO IT (Tansy Hammarton)

Session 6C, 14.00 Wednesday 10th April.

Engaging with the public is becoming increasingly important, not only to disseminate our research goals and findings, but also to obtain research funding, and it is desirable that all research students gain experience in it. Public engagement can be highly rewarding but is not without its challenges and pitfalls. This session will showcase several very different ways of successfully engaging the public, from working with schools, to events and exhibitions at science fairs and festivals, SciArt and Citizen Science, where the public actually take part in the research. The speakers will provide insights into how to get public engagement activities off the ground as well as the problems that might be encountered along the way. The session will end with a general discussion of how best to share public engagement

experience, expertise and resources amongst BSP members in the future, so all delegates with an interest in public engagement are encouraged to attend.

GENE DB CLINIC

Gene DB will run a “help clinic” at a stand in the Great Hall during the poster session. The clinic is being run by Magdalena Zarowiecki and colleagues of the Wellcome Trust Sanger Institute.

GeneDB currently provides access to more than 40 high quality reference genomes of parasites, several with extensive and on-going manual curation. So whether you are working on apicomlexans, kinetoplastids, bacteria or helminths, GeneDB contains high quality reference genomes that may benefit your research. If you are using this resource, or are thinking of using it, please come to the GeneDB drop-in clinic to talk to scientists from the Parasite Genomics Group at the Wellcome Trust Sanger Institute. Whether you are interested in a particular gene, or want to download very large datasets, we can show you useful functions for getting access to these huge datasets in GeneDB. We can also point you to several other resources provided by the Parasite Genomics Group for accessing and analysing transcriptomic and genomic data.

SOCIAL PROGRAMME

Monday 8th April - a welcome drinks reception in the Great Hall from 6.30

Monday 8th April - British Ecological Society Parasite Ecology Group free social event, with hot food, on a boat in the City harbour (*Under the Stars Bar*, Narrow Quay, Harbourside) from 8pm. All parasite ecologists welcome.

This venue is walking distance from the meeting. To get there, walk down Park Street to the Bristol "Centre" where there are fountains, and steps and a waterfall down to the harbour. Facing the water, the ship on the left is the *Under the Stars Bar*. Alternatively, if you're at the Watershed (see bsp2013.info) the ship is pretty much opposite.

Tuesday 9th April - there will be a guided tour of the Wills Memorial building tower, including access to the bell chamber and to the tower's roof. Up to 40 people, in two groups can be accommodated. You can sign-up for these tours at the registration desk or in the BSP office. First come, first served.

The tour starts promptly at 12.45, to be in the bell chamber to see and hear the bell (Great George – the sixth largest bell in England) strike at 1pm, to be back on *terra firma* by 13.20. Please assemble at the Porters' lodge for the start of the tour.

These tours are made possible by the generous efforts of Dave Skelhorne and Gary Nott, and a donation will be made to the Bristol Children's Hospital Appeal in recognition of this.

Tuesday 9th April - drinks from 6pm during the poster session.

Tuesday 9th April - The Young(er) parasitologists party will be held from 8pm at *Zerodegrees*. All registered students have tickets in their delegate packs. Additional tickets can be purchased (£10, no age limit) from the BSP office.

The venue is walking distance from the meeting. To get there turn left out of the Wills Memorial building and walk along Park Row (which is flat; if you're going downhill, then you're on Park Street, and lost). *Zerodegrees* is on your right as Park Row turns into Perry Road. Also see bsp2013.info

Wednesday 10th April - conference dinner and dancing at *At-Bristol* Bristol Harbourside. *At-Bristol* is a science discovery centre. During the drinks reception you'll have free access to the galleries and exhibits. Dinner is on the top floor of the building

This venue is walking distance from the meeting. To get there walk down Park Street, across College Green (muddy grass, a statue of Queen Victoria and many skateboarders) towards the East end of Bristol Cathedral. Follow the downward path, with steps, between the Cathedral and the neighbouring office building, go across the Zebra crossing and the large glass building slightly to your right is *At-Bristol*.

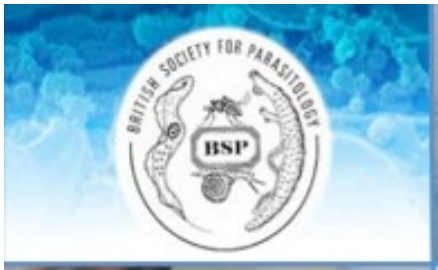
Other eating, drinking and socialising opportunities – see bsp2013.info

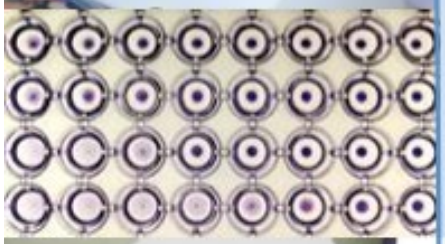
BAGGAGE STORAGE

On Thursday morning you can store your luggage in the BSP office.

YOUR STUDENT HELPERS ARE

Nor Abdul Aziz
Kit Cornall
Lauren Ellse
Olivia Godber
Owen Gethings
Becca Grainger-Wood
Verity Miles
Luke Lazarou
Dan Jue Lan
Hannah Rose
Jess Stokes
Barney Wharam
Rebecca Weka





Advances in diagnostics for infectious diseases

25th and 26th September 2013
BSP Autumn Symposium

Keynote speaker:
Prof. Rosanna Peeling (*UK*)

Speakers include:
Prof. Peter Chiodini (*UK*)
Dr. Mark Perkins (*Switzerland*)
Prof. Giuseppe Gringoli (*Italy*)
Prof. Santiago Mas-Coma (*Spain*)
Prof. Jozef Vercruysse (*Belgium*)

This 2-day symposium, with poster sessions, will cover all aspects of diagnostics for infectious diseases in humans and animals.

We aim to bring together international leaders from industry and academia and discuss diagnostic development, impact evaluation, resistance monitoring and the future of the international diagnostic landscape.

www.bspuk.org/events

Venue: Ness Gardens, Liverpool University

Organised by
Prof. Russell Stothard & Dr. Emily Adams (LSTM)
in collaboration with **RSTMH** and **ISNTD**

ORAL ABSTRACTS

Wright Medal Lecture - Mark Viney

What matters in a worm's world

Mark Viney, Mark Viney

University of Bristol

Nematodes make developmental decisions based on their surrounding environment. For parasites, this environment includes the host, particularly its immune response. Understanding the sensory world of these parasites, and their decision making, is necessary to truly understand what matters in a worm's world.

08/04/2013 Welcome evening 5:30 PM - 6:30 PM (60 mins)

Leishmania and trypanosomes : in the field and in the clinic - Chair Ingrid Muller

Dysregulated arginase mediated L-arginine metabolism contributes to disease severity in patients with cutaneous and visceral leishmaniasis in Ethiopia

Pascale Kropf, Pascale Kropf

London School of Hygeine and Tropical Medicine

The leishmaniases are a complex of vector-borne diseases caused by the parasite Leishmania. They are neglected tropical diseases that affect the poorest population and cause major morbidity and mortality, estimated to 2.4 million disability-adjusted life-years. Leishmaniases can present with a wide range of clinical syndromes that may be cutaneous (CL) or visceral (VL). Leishmaniasis is worsened by co-infections with HIV. The catabolism of L-arginine by arginase is emerging as a critical mechanism of immune regulation. We have recently shown that in an experimental model of leishmaniasis, arginase activity is significantly increased and that this results in local depletion of L-arginine, an amino acid that is essential for efficient T cell responses. This reduction in L-arginine in the microenvironment coincides with impaired T cells activation. To determine whether our experimental data translate to human disease, we tested whether arginase activity is increased in patients with cutaneous and visceral leishmaniasis and whether this coincides with T cell suppression. Our results show that arginase is significantly increased in patients with leishmaniasis and that this might play a role in the pathogenesis of the disease by impairing T cell effector functions.

09/04/2013 Session 1A - Leishmania and trypanosomes : in the field and in the clinic - Chair Ingrid Muller 9:00 AM - 9:30 AM (30 mins)

Extant cryptic sexuality in Trypanosoma cruzi drives the emergence of novel strains with

epidemiologically important phenotypes

Louisa Alexandra Messenger, Louisa A. Messenger-1, Martin S. Llewellyn-1, Michael D. Lewis-1, Juan-David Ramírez-2, Maikell Segovia-3, André Guilherme Costa Martins-4, Valdirene dos Santos-5,Felipe Guhl-2, Marta M.Teixeira-4, Ana M. Jansen-5, Lineth Garcia-6, Hernan J. Carrasco3 and Michael A. Miles-1

1.London School of Hygiene and Tropical Medicine, London, United Kingdom 2.Universidad de los Andes, Bogotá, Colombia 3.Universidad Central de Venezuela, Caracas, Venezuela 4.Universidade de São Paulo, Brazil 5.Fundação Oswaldo Cruz, Rio de Janeiro, Brazil 6.Universidad Mayor de San Simón, Cochabamba, Bolivia

Clonal propagation is considered to be the predominant mode of reproduction among many parasitic protozoa. However, this assumption may overlook unorthodox, infrequent or cryptic sexuality. Trypanosoma cruzi, the causative agent of Chagas disease, is known to recombine in vitro using a mechanism analogous to fungal parasexual reproduction, while two of the six major circulating genetic lineages (TcV and TcVI) resemble meiotic F1 progeny. Despite the existence of natural hybrids, a pervasive view is that recombination was an evolutionarily ancient phenomenon and contemporary genetic exchange is of little epidemiological relevance. We undertook high resolution molecular genotyping (48 nuclear and 10 mitochondrial loci) of field isolates belonging to two of the oldest and most widely occurring lineages (TcI n = 300 and TcIV n = 80). Gross nuclear-mitochondrial phylogenetic incongruence was observed at multiple levels, including among different populations as well as major lineages. In all cases, hybrids had undergone mitochondrial introgression without evidence of reciprocal nuclear recombination, implying additional, as yet uncharacterized, cellular mechanisms can facilitate genetic exchange in T. cruzi. In parallel, we performed in vitro phenotyping of recombinant strains to demonstrate that hybridization is associated with altered axenic growth rates, mammalian cell infectivity, insect vector permissibility and drug susceptibility. Together these observations indicate that genetic exchange is geographically widespread and continues to influence natural parasite population structures, driving the emergence of novel strains with epidemiologically important virulence traits, and challenging the traditional paradigm of clonality in T. cruzi.

09/04/2013 Session 1A - Leishmania and trypanosomes : in the field and in the clinic - Chair Ingrid Muller 9:30 AM - 9:45 AM (15 mins)

Human Immune Response to Sand Fly Salivary Proteins in Leishmania Endemic and Non Endemic Areas in Jordan.

Rami Mukbel, Rami M. Mukbel 1, Reahab Khasharmeh 2, Nawal S. Hijawi 2, Marry Ann McDwell 3.

1. Department of Basic Veterinary Sciences, Faculty of Veterinary Medicine, Jordan University of Science and Technology, Irbid, Jordan. 2. Department of Medical Laboratory Sciences, Faculty of Allied Health Sciences, Hashemite University, Zarka, Jordan. 3. Eck Institute for Global Health, Department of Biological Sciences, University of Notre Dame, IN, USA.

The role of sand fly saliva in the Leishmania transmission is well established. Recent studies on mice have shown that immunity to sand fly saliva would enhance the immune response against the transmission of Leishmania infection when co-injected with salivary gland homogenate. New

approaches are investigated to study the possibility of integrating sand fly salivary protein to Leishmania vaccine that would post the immune response and protect against the transmission of the infection. In this study, we are investigating the role of sand fly salivary content on immune response of human in Leishmania endemic area and being exposed to sand fly bite compared to unexposed naïve. In this study,blood samples were collected from donors living in endemic area with leishmania and sandfly as exposed infected (Swaymeh), donors living in areas with sandflies as exposed (Mafraq) and donors living in sandfly free areas as unexposed (Amman). The serum was probed for antibodies specific to sand fly salivary proteins (Isolated from field collected Phlebotomus papatasi) using western blot. Also, peripheral blood monocytes (PBMC) were separated and used to determine the effect of sand fly salivary lysate to induce lymphocyte proliferation.

09/04/2013 Session 1A - Leishmania and trypanosomes : in the field and in the clinic - Chair Ingrid Muller 9:45 AM - 10:00 AM (15 mins)

High resolution multilocus microsatellite typing (MLMT) and multilocus sequence typing (MLST) of natural Ethiopan Leishmania donovani isolates reveal parental donors and genetic hybrids, originating from at least three independent hybridisation events.

Matthew Yeo, Tesfaye Gelanew1,3*, Asrat Hailu2, Gabrile Schonian3, Michael A. Miles3 and Matthew Yeo3* Author affiliation(s): 1. Serology Diagnostics and Research Laboratory, Centers for Disease Control and Prevention Division of Vector-Borne Diseases Dengue Branch, San Juan, PR, 2. Faculty of Medicine, Addis Ababa University, Addis Ababa, Ethiopia, 3. London School of Hygiene and Tropical Medicine, London, United Kingdom.

London School of Hygiene & Tropical Medicine

Protozoan parasites of the genus Leishmania (Kinetoplastida:Trypanosomatidae) cause widespread and devastating human diseases. Visceral leishmaniasis is endemic in Ethiopia where it has also been responsible for fatal epidemics. It is postulated that genetic exchange in Leishmania has implications for heterosis, spread of virulent strains, resistance to chemotherapeutics, and exploitation of different hosts and vectors. In the current work over 90 biological clones of Leishmania donovani derived from human isolates from Ethiopia were characterised by high resolution Multilocus Microsatellite typing (MLMT) and Multilocus Sequence typing (MLST). Results showed that four isolates (and associated biological clones) are clearly genetic hybrids, each possessing allelic heterozygous profiles from two parental donors in the Ethiopian panel. Outputs from both MLMT and MLST were largely congruent. Parental alleles situated on different chromosomes were inherited by the hybrid progeny. Differential allelic profiles of the hybrids suggest that three separate recombination may have occurred among the panel of strains studied. FACS analysis demonstrated that all hybrids and associated clones were minimally diploid. Mitochondrial sequences show uniparental inheritance for all hybrids, each possessing a single mitochondrial sequence type. Two of the four hybrid isolates were from patients co-infected with HIV. Together the data suggest a meiotic mode of hybridisation with substantial phyloepidemiological implications.

09/04/2013 Session 1A - Leishmania and trypanosomes : in the field and in the clinic - Chair Ingrid Muller 10:00 AM - 10:15 AM (15 mins)

Trypanosome genetic diversity, polyparasitism and the conservation of Australian marsupials

RC Andrew Thompson, Adriana Botero1, Craig Thompson1, Christopher Peacock2, Peta Clode3, Philip Nicholls1, Adrian Wayne4, Alan Lymbery1, RC Andrew Thompson1

1. School of Veterinary and Life Sciences, Murdoch University, Murdoch, WA 6150, Australia. 2. School of Pathology and Laboratory Medicine, University of Western Australia, Crawley, WA 6009, Australia. 3. Centre for Microscopy, Characterisation and Analysis, University of Western Australia, Crawley, WA 6009, Australia. 4. Department of Environment and Conservation, Science Division, Manjimup, WA, Australia.

The genetic diversity, tissue tropism and potential pathogenicity of trypanosomes naturally infecting Western Australian marsupials will be described. High rates of infection were found in both blood and tissues. Phylogenetic analysis using 18S rDNA and glycosomal glyceraldehyde phosphate dehydrogenase (gGAPDH) sequences showed the presence of eight genotypes that clustered into three clades, one of which included Trypanosoma cruzi. Trypanosome infections were compared in a declining and in a stable population of the endangered Australian marsupial, the brush tailed bettong or woylie (Bettongia penicillata). Differences in the distribution of the genotypes were found between the two woylie populations, with mixed infections common in woylies from the declining but not from the stable population. Histopathological findings associated with either mixed or single infections showed a strong inflammatory process and tissue degeneration predominantly in heart, oesophagus and tongue. The results provide evidence for the potential role of trypanosomes in the decline of a formerly abundant marsupial that is now critically endangered.

09/04/2013 Session 1A - Leishmania and trypanosomes : in the field and in the clinic - Chair Ingrid Muller 10:15 AM - 10:30 AM (15 mins)

Trypanosome and Leishmania-Host Interactions - Chair Ingrid Muller

The dynamic nature of experimental chronic Chagas disease revealed by highly sensitive in vivo imaging

Michael Lewis, Michael D. Lewis, Amanda Fortes Francisco, Martin C. Taylor, Hollie Burrell-Saward, Alex McLatchie, Michael A. Miles and John M. Kelly

London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT, United Kingdom

Chronic Trypanosoma cruzi infections either remain asymptomatic or result in cardiac and/or digestive pathologies. During the chronic stage of Chagas disease parasites are thought to be sequestered in diverse tissues, but links between parasite tissue tropism and disease pathogenesis have been poorly defined. To address this we developed a real-time bioluminescence imaging infection model based on a transgenic T. cruzi cell line, constitutively expressing the 'red-shifted' firefly luciferase variant Ppy RE9. Luciferase expression levels were tightly correlated with parasite number and significant reduction of bioluminescence was observed after oral treatment of acute and chronic infections with benznidazole. The in vivo limit of detection was <1000 parasites per

animal and therefore vastly more sensitive than peripheral blood parasitaemia counts. In a model of acute fulminating disease in an immunuocompromised host (SCID mouse) ex vivo imaging of tissues showed the highest parasite burden to be harboured by visceral fat depots. Parasite burdens in immunocompetent BALB/c mice peaked at 14 dpi and could be visualised for >250 days. Chronic parasite foci were highly dynamic with a high degree of spatial variation and parasite burden intensity fluctuating over 2 logs of magnitude. Ex vivo imaging revealed that the large intestine was the primary site of chronic (153 dpi) parasite persistence with 5 to 12-fold higher burdens compared to the heart. Nevertheless, mice developed myocarditis and progressive heart fibrosis. These data imply that chagasic cardiac pathology may not result exclusively from local parasitism and the specific immune response directed against it.

09/04/2013 Session 2A - Trypanosome and Leishmania-Host Interactions - Chair Ingrid Muller
11:10 AM - 11:40 AM (30 mins)

Virulence loss and amastigote transformation failure determines host cell responses to L. mexicana

Khdija Ali, Khdija Suleman Ali*; Robert C. Rees **; Christopher Terrell-Nield* and Selman A. Ali*
*Interdisciplinary Biomedical Research Centre, School of Science and Technology Nottingham Trent University, Clifton lane, Nottingham, NG11 8NS, UK. ** The John van Geest Cancer Research Centre School of Science and Technology Nottingham Trent University Clifton Lane Nottingham, NG11 8NS, UK

yes

The aim of the present study was to assess the effect of alterations in virulence and transformation by long term in vitro culture of L. mexicana promastigotes on infectivity and immune responses. Fresh cultures of L. mexicana harvested from Balb/c mice lesions were passaged 20 times in vitro. Infectivity was decreased and was completely avirulent after 20 passages. The qPCR results showed a significant (P>0.05) down regulation of virulence associated genes (GP63, LPG2, CPC, CPB2, CPB2.8, CHT1, LACK and LDCEN3) after passage 7 concomitant with a reduced and absence of infectivity by passages 7 and 20, respectively: hence, parasites at passages 1 and 20 are referred to as virulent and avirulent, respectively. The growth of avirulent, but not virulent L. mexicana, was significantly inhibited by conditioned media derived from macrophages or monocytes infected with parasites for 2 hours, irrespective of their virulency. Giemsa staining clearly showed a significant difference in virulent versus avirulent L. mexicana infectivity of host human U937 macrophages. In addition, avirulent but not virulent parasites failed to transform to the amastigote stage in infected host cells, with both virulent and avirulent L. mexicana modulating the expression of CCL-22, Tgad51, Cox2, IL-1, IL-10, TGF-β, TNF-α, Rab7, Rab9 and A2 genes within 2 hours after infection; virulent but not avirulent L. mexicana significantly up regulated Th2 associated cytokines, but down regulated Rab7and Rab9 gene expression. In conclusion, an in vitro model for L. mexicana is reported, which is of potential value in studying host- parasite interaction and vaccination.

09/04/2013 Session 2A - Trypanosome and Leishmania-Host Interactions - Chair Ingrid Muller
11:40 AM - 11:55 AM (15 mins)

The impact of malnutrition on arginase metabolism in experimental visceral leishmaniasis.

Karina Duarte Corware, Karina D Corware, Vanessa Yardley, Ingrid Muller, Pascale Kropf

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Malnutrition is a major health problem in resource-poor countries and is characterised by inadequate dietary intake of energy and micronutrients. Malnutrition has been clearly identified as a causal factor in increasing the severity of diseases. Leishmaniasis is a parasitic disease caused by intracellular flagellate protozoa that infects mammalian hosts via the bite of infected female sand flies. There are over 20 species of Leishmania spp. that are pathogenic to humans. Manifestation of disease is dependent on factors such as the strain that infects and the immune response of the host. The disease Leishmaniaisis can be broadly categorised into cutaneous and visceral leishmaniasis; the latter is a systemic disease that is fatal if left untreated. Visceral leishmaniasis presents with fever, weight loss and characteristically with hepatosplenomegaly due to the preferential targeting of the strains L. donovani or L. Infantum to the spleen and liver. The mechanisms by which malnutrition increases disease susceptibility are unclear and therefore our aim was to investigate whether malnutrition impacts on the phenotype of macrophages and parasite survival. To test the impact of malnutrition on the development of visceral leishmaniasis we used L. infantum infected mice fed on a protein deficient diet. Our results show that protein-energy malnourished mice have increased parasite load and increased arginase activity. This effect is reversed by re-feeding with a normal protein diet.

09/04/2013 Session 2A - Trypanosome and Leishmania-Host Interactions - Chair Ingrid Muller 11:55 AM - 12:10 PM (15 mins)

Understanding differential regional sensitivity of rapid diagnosis for visceral leishmaniasis: antigenic diversity of East African Leishmania donovani, and comparatively higher IgG levels among Indian patients.

Tapan Bhattacharyya, Tapan Bhattacharyya, Duncan E. Bowes, Om Prakash Singh, Rajiv Srivastava, Osman Osman, Sayda El-Safi, Shyam Sundar, Marleen Boelaert, Michael A. Miles.

London School of Hygiene & Tropical Medicine, London, UK; Banaras Hindu University, Varanasi, India; National University of Khartoum, Sudan; Institute of Tropical Medicine, Antwerp, Belgium.

Visceral leishmaniasis (VL) remains an important public health problem in the endemic regions of South Asia, East Africa, and Brazil. A point-of-care rapid diagnostic test (RDT) for anti-Leishmania donvani antibodies, based on the rK39 kinesin antigen, has given high sensitivity in South Asia but is less effective in East Africa. This may be explained by regional diversity of the L. donovani kinesin antigen or by differential levels of IgG production among Indian and East African VL patients. To investigate antigenic diversity, we amplified and sequenced the section of the kinesin gene corresponding to the rK39 diagnostic antigen from a panel of East African L. donovani and compared the sequences to those of South Asian L. donovani. We observed regional specific polymorphisms, with substantial non-conservative changes in the N terminal half of each antigen repeat, and small stretches of conserved residues towards the C terminus. We also compared anti-L. donovani IgG titres among Indian and Sudanese VL patients by ELISA. We showed a clear

difference between the two groups, namely that Indian patients had a significantly higher level of anti-Leishmania antibodies compared to those from Sudan. These observations remained consistent when further analysed by age, gender or geographical source of the lysate antigen used in the ELISA. Thus both diversity of the rK39 diagnostic antigen and the distinct anti-Leishmania IgG response levels between Indian and Sudanese VL patients are likely to contribute to the differential regional efficacy of the rK39 RDT.

09/04/2013 Session 2A - Trypanosome and Leishmania-Host Interactions - Chair Ingrid Muller
12:10 PM - 12:25 PM (15 mins)

Atenolol reduces Leishmania Major induced hyperagesia and the levels of TNF-alpha with no effects on the levels of Interleuken-1beta ï€©ï€ or Keratinocyte Derived Chemokine

Marc Karam, Marc C. Karam (presenting author) Rana Merckbawi Samer Bazzi

University Of Balamand - Lebanon

The infection with a high dose of the intracellular parasitic protozoan L.major induces a sustained hyperalgesia in susceptible BALB/c mice accompanied by the up-regulation of the pro-inflammatory cytokines IL-1□ and IL-6. On the other hand, Interleukin-13 (IL-13) was shown to reduce this hyperalgesia during the period of treatment when the levels of IL-6 were increased and to reduce the levels of IL-1□ during and after the treatment period. Those results favor the cytokine cascade leading to the production of sympathetic amines (involving TNF-α and KC) and not to prostaglandins (involving IL-1□ and IL-6) as the final mediators of hyperalgesia. In this study, we investigated the effect of daily treatment with the □-blockers atenolol on the L. major-induced inflammation in mice with respect to hyperalgesia as well as the levels of TNF-α and KC (the analogue of IL-8 in mice). We demonstrate here that atenolol is able to reduce the L. major induced hyperalgesia which seems to involve no direct role for neither IL-1beta nor KC. More importantly, our results show that TNF-alpha may play a pivotal and direct role in sensitizing the peripheral nerve endings (nociceptors) since its level was reduced during the period of atenolol treatment which correlates well with the reduction of hyperalgesia. Those findings pave the road not only to unravel the cytokine cascade leading to hyperalgesia but also to develop new and more efficient medications for many types of pain.

09/04/2013 Session 2A - Trypanosome and Leishmania-Host Interactions - Chair Ingrid Muller
12:25 PM - 12:40 PM (15 mins)

Metabolomics and proteomics - Chair Jonathan Wastling

Immune-metabolic co-development in murine Leishmania major infection.

Jasmina Saric, Saric, Jasmina

Imperial College London

Metabolic profiling has offered a novel way to extract information on parasite-host interaction in the last decade. More than 10 single parasite-rodent models have been established so far by us

and other groups and have allowed a successive further development of the metabolic profiling core approach. Whilst early models have focused on discovery of diagnostic/prognostic biomarkers in biological fluids, such as urine and plasma, later experiments have addresses the global metabolic effect that a parasite induces in the host, by characterisation and cross-integration of the metabolic information from multiple tissues. More recently we have introduces the concept of immune metabolic profiling which we have applied for the first time extensively in our current work on Leishmania major-infection in dichotomous mouse models. The main aim hereby was to identify metabolites or metabolite patterns that are representative of a successful immune response and may represent candidate metabolic supplements for alternative treatment of cutaneous leishmaniasis based on immune adjustment. Since human and gut microbial metabolism is interdependent and given the important role of gut bacterial species in educating the immune-system we have furthermore characterised the faecal bacteria composition and co-analysed with immune and metabolic measures. Results so far indicate (i) an infection-specific fingerprint for L. major infection in both strains in multiple tissues and biofluids, (ii) different immune-metabolic correlation structures in susceptible and self-healing mice, and (iii) that cage effects supersede infection and immune status of the mice in the gut microbial analysis but not in the metabolic or cytokine analysis.

09/04/2013 Session 3A - Metabolomics and proteomics - Chair Jonathan Wastling 2:00 PM - 2:30 PM (30 mins)

The interactome of Trypanosoma brucei: Novel trafficking components point to adaptive pathways supporting antigenic variation and immune evasion.

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Intracellular trafficking is of prime importance to all eukaryotic organisms, but in trypanosomes the pathway takes on special significance as part of both immune evasion and host-parasite interaction mechanisms. Based on detailed functional dissection and in silico analysis, it has become clear that, despite a well conserved core of proteins, the trafficking systems of trypanosomes are divergent from their hosts at the molecular level,. There is now unequivocal evidence for loss of many components, suggesting simplification, divergent mechanisms or both. We have applied a cryogenic milling method, coupled to immunoaffinity isolation and LCMSMS to probe the interactomes of clathrin (the major endocytic and post-Golgi vesicle coat protein), the exocyst (a complex required for exocytosis) and retromer (a complex essential for late endosomal trafficking). We report the identification and functional validation of multiple trypanosome-specific interaction partners for each of these entities, indicating that rather than being simplified, that trypanosomes exploit distinct proteins to serve their trafficking requirements. These data also indicate that, despite an apparent level of conservation of many mechanisms, the underlying molecular machinery in trypanosomes is significantly more divergent that perviously appreciated.

09/04/2013 Session 3A - Metabolomics and proteomics - Chair Jonathan Wastling 2:30 PM - 2:45 PM (15 mins)

Application of LCâ€“MS-based absolute metabolite quantification to trypanosomes: Metabolic flux measurement

Dong-Hyun Kim, Dong-Hyun Kim(1)*, Darren J. Creek(2), Fiona Achcar(1), Achuthaunni Chokkathukalam(1), Karl Burgess(3), Rainer Breitling(4), Michael Barrett(1)

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Human African Trypanosomiasis (HAT) is a parasitic disease in sub-Saharan Africa caused by the protozoan parasite, Trypanosoma brucei, and transmitted by tsetse flies. It is fatal if untreated, so effective drug treatment is necessary. In the face of emerging resistance and unacceptable side effects of existing treatments, new drugs are urgently required and the discovery of new targets for chemotherapy is of great importance. LC–MS-based metabolomic studies enable simultaneous measurement of many of the small molecules (metabolites) in a biological system and can give comprehensive information on how drugs perturb metabolism. However, a full understanding of cellular responses requires absolute metabolite concentrations, which can feed into quantitative computational models of metabolism. Quantitative modelling will play a critical role in developing optimised anti-parasite drugs. In order to obtain absolute concentrations of individual metabolites in trypanosomes, uniformly (U)-13C-labelled E. coli metabolite extracts can be used as an internal standard; absolute intracellular concentrations of metabolites can then be estimated by adding known amounts of U-13C-labelled extract to the trypanosome sample prior to the extraction procedure. In addition, we show that U-13C-labelled transgenic E. coli producing 13C-labelled trypanothione can be used for quantification of bio-thiols including trypanothione. T. brucei at different stages of cell growth in culture were analysed using LC-MS for metabolite profiling and absolute quantitative analysis. A total of 57 intra- and 22 extra-cellular metabolites were quantified. We then employed this approach to dissect metabolic responses to oxidative stress and for the calculation of metabolic fluxes as input for computational modelling.

09/04/2013 Session 3A - Metabolomics and proteomics - Chair Jonathan Wastling 2:45 PM - 3:00 PM (15 mins)

Use of Polyomics Approaches to Understanding Drug Resistance in Kinetoplastid Protozoa

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Kinetoplastid protozoa cause some of the most debilitating diseases in humans and animals. These diseases are controlled mainly by chemotherapy with no known vaccines. Amphotericin B (AmB) is an antifungal polyene antibiotic used increasingly in the treatment of visceral leishmaniasis. Isometamidium (ISMM) is a phenanthridinium veterinary drug that is used mostly for prophylactic

purposes and treatment of African animal trypanosomiasis. Development of resistance poses a threat to the use of these drugs. The tools of polyomics, studying genome, transcriptome, proteome and metabolome, offer the means to determine mechanisms of resistance to drugs. We undertook to study the mechanisms of resistance to AmB and ISMM using the tools of polyomics. Resistance to AmB and ISMM was induced in vitro in L. mexicana promastigote and bloodstream forms (BSF) of T. brucei, respectively. The derived AmB resistant cells revealed a multitude of mutations when subject to next generation sequencing. Metabolomics revealed a significant accumulation of 4,4-dimethyl-cholesta-8,14,24-trienol, a sterol biosynthetic pathway intermediate product of this enzyme and a corresponding decrease in ST(3ergosta-5,7,22E-trien-3beta-ol. Combining the metabolomics and genomic observations allowed us to focus specifically on genes involved in the sterol pathway. Proteomics revealed these cells have variation in expression levels of farnesyl diphosphate synthase. For ISMM resistance, few differences in the measured metabolome were found in resistant trypanosomes, although a reduction in the mitochondrial membrane potential and loss of the kinetoplast accompanied resistance in BSF T. brucei. Cross-resistance to ethidium bromide and diminazene aceturate was observed with 10 and 3 fold increases of IC50, respectively.

09/04/2013 Session 3A - Metabolomics and proteomics - Chair Jonathan Wastling 3:00 PM - 3:15 PM (15 mins)

Metabolic Characterisation Studies in in vitro Leishmania major Infection

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Leishmania spp. are intra-cellular protozoan parasites and causative agents for a collection of human diseases called the Leishmaniases. Comprehensive research on experimental in vivo Leishmania infection models revealed that pathology is highly dependent on the host's underlying immune response, particularly the activation state of macrophages – the major target cells of Leishmania spp. Classically activated macrophages (caMΦ) are able to effectively kill the parasite, largely mediated through their generation of nitric oxide (NO) from L-arginine, whilst in alternatively activated macrophages (aaMΦ), L-arginine is converted into L-ornithine and polyamines, allowing sustained infection. Our aim was to use a metabolic profiling approach to investigate the differences between the macrophage activation states and to determine infection-related-changes. Cell extracts and culture media from caMΦ, aaMΦ and non-activated macrophages (naMΦ) that were grown in the presence or absence of L. major were analysed using 1H nuclear magnetic resonance (NMR) spectroscopy. Results revealed differences in metabolic phenotypes between activation and infection states. The highest glucose consumption and lactate production were observed in media from caMΦ, reflecting the high energy demand in these cells, presumably required for successful parasitic elimination. Significantly higher levels of potential parasitic end products were determined in infected samples, including succinate and acetate. In an additional proof of concept study, we demonstrated that parasitic burden of macrophages can be reduced through in vitro supplementation of picolinic acid, a metabolite known to enhance

arginase-based NO production. We plan to expand in vitro experiments using candidate metabolic supplements, to discover potential immune-enhancing and/or anti-parasitic effects.

09/04/2013 Session 3A - Metabolomics and proteomics - Chair Jonathan Wastling 3:15 PM - 3:30 PM (15 mins)

Fish parasitology: ecology & evolution - Chair Nick Taylor

Sticklebacks as model hosts in ecological and evolutionary parasitology: past perspectives, current trends and future directions

Iain Barber, Iain Barber

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Threespine sticklebacks exhibit a number of characteristics that have made them popular model hosts for parasitological studies. First, their wide geographic distribution, ecological diversity and position in trophic position in food webs means the species has a rich, and increasingly well characterized, parasite fauna. Second, the suitability of sticklebacks as models for lab and field studies of behaviour, and their rich ethological history, has prompted a large number of studies examining the behavioural effects of parasites, and sticklebacks have emerged as major models in experimental tests of the parasite manipulation hypothesis. Third, the ease with which sticklebacks can be bred and maintained in the laboratory, coupled with the development of a range of experimentally amenable parasite infection models, has allowed detailed investigation of the consequences of infection for host phenotype at the cellular, physiological, behavioural and ecological level. The ability to expose fish to controlled challenges has also fuelled a substantial number of studies into the mechanisms underpinning individual variability to infection, including tests of the 'good genes' and 'genetic complementarity' hypotheses of females mate choice. Finally, the publication of the stickleback draft genome and the development of high-throughput sequencing technologies provide considerable – though as yet largely untapped – potential for detailed examination of the role played by parasites in the evolutionary biology of hosts. In this talk I will review the key advances in our understanding of host-parasite interactions that have arisen from studies involving stickleback hosts, highlight areas of current research activity, and identify likely areas for future research.

09/04/2013 Session 4A - Fish parasitology: ecology & evolution - Chair Nick Taylor 4:10 PM - 4:40 PM (30 mins)

Dispersal pattern determines spatial structure of parasite communities and immunogenetic adaptation in two sympatric cichlid fish species from Lake Tanganiyka

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Parasites might be among the most important selective agents in natural host populations. When the dispersal ability of a host species is low, local host-parasite co-evolutionary dynamics might allow divergent adaption of isolated host populations in function of their contrasting local parasite community. Among the vertebrate immunogenes, the highly polymorphic Mhc (major histocompatibility complex) represents an ideal candidate to study this aspect of evolutionary

host-parasite interactions. Here, we tested the hypothesis whether infection by multiple parasite species drive polymorphism of the host's Mhc class IIB genes in function of the degree of philopatric behaviour of the host. We compared parasite communities and Mhc allele frequencies in two sympatric cichlid fish species with contrasting dispersal patterns in Lake Tanganyika. We found that allopatric and genetically diverged colour morphs of philopatric blunt-headed cichlids (Tropheus spp.) are infected by contrasting parasite communities and are immunogenetically adapted to them. We could not detect such a pattern in the closely related, but non-philopatric cichlid fish species Simochromis diagramma. This suggests that the presence of migrants among isolated host populations homogenises their respective parasite communities in Lake Tanganyika. The proposed pleiotropic role of the Mhc in parasite defense and assortative mating lets us speculate, whether local parasite communities could drive speciation of their host by by-product reproductive isolation.

09/04/2013 Session 4A - Fish parasitology: ecology & evolution - Chair Nick Taylor 4:40 PM - 4:55 PM (15 mins)

Chemical communication in sea lice, Lepeophtheirus salmonis, controls movement between host Atlantic salmon, Salmo salar

Jessica Stephenson, Jessica F. Stephenson

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Securing mating opportunities must often be balanced by the avoidance of competition for resources. This trade-off is well-studied in habitat selection by free-living animals, but data are lacking from equivalent studies of host selection by dispersing parasites. There is indirect evidence that motile sea lice may distribute themselves among hosts according to this trade-off; at low infection intensities and low resource competition, lice are aggregated among the host population with a few fish carrying the majority of the louse population and most fish carrying few or no lice. As infection intensity and resource competition increase, louse distribution in the host population becomes more normal. A behavioural experiment tested the hypothesis that male sea lice (Lepeophtheirus salmonis) assess the infection load and the presence of potential mates on their host fish through the detection of chemical cues, and that this informs their movement between host fish. Adult male lice are more likely to leave a host if they detect cues of other adult male lice than if they detect the cues of female lice. In the presence of both male and female cues, an intermediate number of males moves between hosts. These results suggest that male sea lice use chemical cues to balance competition for resources and mate acquisition, which highlights the need for further studies on the chemical ecology of this important parasite.

09/04/2013 Session 4A - Fish parasitology: ecology & evolution - Chair Nick Taylor 4:55 PM - 5:10 PM (15 mins)

Helminth biology I - Chair Mark Viney

Transgenesis as a tool for functional genomic study of Strongyloides spp.

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Descriptive genomics of parasitic nematodes has advanced rapidly in the last decade, but lack of robust methods for transgenesis and gene disruption or silencing has hampered functional studies arising from these efforts. Nevertheless, work toward surmounting these obstacles is underway in numerous laboratories, and recent advances in transgenesis hold distinct promise for the future. The existence of free-living adults in the life cycles of Strongyloides spp. and related genera gives these parasites a distinct advantage as subjects for transgenesis, and robust methods for transient promoter-regulated expression of transgenes have been in place for members of this group since 2006. Refinements promoting chromosomal integration of transgenes have allowed us to derive lines of S. ratti that stably inherit and express transgenes over multiple generations. We apply transgenesis to studies of dauer-like signal transduction in S. stercoralis. Reporter constructs fusing promoters for genes of interest to sequence encoding green fluorescent protein allow us to investigate anatomical patterns of gene expression. A G-protein coupled receptor and insulin-like signaling elements in S. stercoralis, Ss-gpa-3, Ss-daf-2, Ss-age-1 and Ss-daf-16, are expressed in similar anatomical patterns to their Caenorhabditis elegans orthologs. In more direct interrogation of gene function, expression of a construct with mutations designed to confer dominant loss in Ss-daf-16 function interferes with morphogenesis in infective third-stage larvae of S. stercoralis. Beyond these, we envision applications for transgenesis in studies of immunity to parasitic nematodes, in mutagenesis, in specific gene knockouts and possibly in boosting RNAi sensitivity of these pathogens.

09/04/2013 Session 1B - Helminth biology I - Chair Mark Viney 9:00 AM - 9:30 AM (30 mins)

Proteomic analysis of parasitism in the nematode Strongyloides ratti

Vicky Hunt, Vicky Hunt, Nadine Randle, Jonathan Wastling & Mark Viney

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The Strongyloides life cycle includes a parasitic female-only stage, which inhabits the small intestine of its host, and a facultative, dioecious free-living adult generation. These adult life-cycle stages are genetically identical and so comparing parasitic and free-living stages offers an almost unique opportunity to investigate and address questions about the molecular adaptations required to be a successful parasitic nematode. We have used quantitative mass spectrometry to compare the proteomes of parasitic and free-living females of S. ratti. This has identified proteins either unique to, or differentially modulated, in the parasitic stage. By analyses of these data we can identify pathways and processes specific to parasitic females, therefore putatively key to parasitism among nematodes.

09/04/2013 Session 1B - Helminth biology I - Chair Mark Viney 9:30 AM - 9:45 AM (15 mins)

Four tapeworm genomes reveal adaptations to parasitism

Magdalena Zarowiecki, Isheng J. Tsai, Nancy Holroyd, Matthew Berriman

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Here we present genome sequences from four tapeworms; the human-infective species Echinococcus multilocularis, E. granulosus, Taenia solium and the laboratory model Hymenolepis microstoma. The genomes are around 115-141 megabases long, and contain some 11.000 genes each. Tapeworms exhibit several instances of micro-exon genes (MEGs), evidence of a high frequency of trans-spliced genes, and polycistrons. There are in tapeworms extreme losses of genes and pathways ubiquitous in other animals, including the loss of 34 homeobox families, and several other determinants of stem cell fate. Tapeworms have species-specific expansions of non-canonical heat shock proteins and families of known antigens. We find that tapeworms have specialised detoxification pathways, and a metabolism adapted to scavenge nutrients from their hosts. We rank all proteins according to their usefulness as drug targets, and identify several new potential drug targets, including those on which existing pharmaceuticals may act. All genomes are available for download at http://www.sanger.ac.uk/resources/downloads/helminths/ and genes can be browsed on http://www.genedb.org.

09/04/2013 Session 1B - Helminth biology I - Chair Mark Viney 9:45 AM - 10:00 AM (15 mins)

The Haemonchus contortus draft genome

Roz Laing, Roz Laing(1), Taisei Kikuchi(2,3), Axel Martinelli(2), Isheng J. Tsai(2,3), Robin Beech(4), Elizabeth Redman(5), Nancy Holroyd(2), David J. Bartley(6), Helen Beasley(2), Collette Britton(1), David Curran(8), Eileen Devaney(1), Aude Gilabert(5), Martin Hunt(2), Stephanie Johnston(1), Ivan Kryukov(8), Keyu Li(8), Alison Morrison(6), Adam Reid(2), Neil Sargison(6), Gary Saunders(1,2), James D. Wasmuth(8), Adrian Wolstenholme(7), Matthew Berriman(2), John S. Gilleard(5), James A. Cotton(2)

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Anthelmintic resistance in strongylid worms threatens the viability of the sheep industry worldwide and provides a cautionary model of mass drug administration to control parasitic disease. The draft genome of Haemonchus contortus, a gastrointestinal nematode of small ruminants, is the first strongylid genome to be published. Its close phylogenetic relationship to the free-living nematode Caenorhabditis elegans enables powerful comparative and functional genetics, and its close relationship to other parasitic nematodes of devastating medical and veterinary importance, underpin its proven value as a parasitic model for this group. The 370 Mb genome consists of 26,044 scaffolds with a N50 of 83,287 bp. Around 93% of conserved eukaryotic genes (CEGs) can be identified, suggesting our draft assembly represents at least that fraction of the H. contortus genome. Genome structure and synteny with C. elegans will be described and genes involved in core nematode pathways and parasite specific pathways are identified. Transcriptome (RNA-seq) libraries of eggs, L1, L3, L4, male adults, female adults and the female adult gut are compared to investigate differential expression of genes throughout the parasite lifecycle to identify key differences between free-living and parasitic life-stages. The parasite gut library is of particular interest as a rich source of potential vaccine and drug targets. The draft genome is expected to provide a wealth of new information for the extensive research effort already focused on H. contortus and for other important parasites in the strongylid group.

09/04/2013 Session 1B - Helminth biology I - Chair Mark Viney 10:00 AM - 10:15 AM (15 mins)

Conservation across the nematode phyla of an astacin metalloprotease essential to cuticle formation

Gillian Stepek, Gillian Stepek, Gillian McCormack & Antony Page

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Parasitic nematodes cause chronic, debilitating infections in both livestock and humans worldwide. Animal, human and free-living nematodes are classed together into five phylogenetic clades. Haemonchus contortus and Teladorsagia circumcincta, the major gastrointestinal nematodes infecting sheep, belong to Clade V, as does the free-living nematode, Caenorhabditis elegans. Brugia malayi, a filarial nematode infecting the lymphatic system of humans, is a Clade III nematode. Despite this phylogenetic difference, all nematodes have a protective cuticle, which has a key role in nematode survival. Cuticle synthesis is a conserved multi-step process, involving numerous enzymes, including Nematode AStacin (NAS) metalloproteases, and these proteases are crucial to the development of C. elegans, with specific roles in hatching, cuticle formation and moulting. Genome searches have found homologues of DPY-31 (NAS-35) in the genomes of H. contortus, T. circumcincta and B. malayi showing high homology to the C. elegans enzyme. Functional conservation was shown when the parasitic dpy-31 orthologues fully rescued a C. elegans dpy-31 mutant. Further bioinformatic searches have indicated homologues to SQT-3 in these three nematode species. SQT-3 is an essential C. elegans cuticle collagen, which DPY-31 cleaves at the C-terminal procollagen processing site for correct cuticle formation. Early results suggest that recombinant parasitic DPY-31 also performs this cleavage, further demonstrating interspecies conservation. Thus, DPY-31 would appear to be crucial for correct cuticle formation amongst nematode species across the nematode phyla.

09/04/2013 Session 1B - Helminth biology I - Chair Mark Viney 10:15 AM - 10:30 AM (15 mins)

Helminth immunology I - Chair Judi Allen

Macrophage Dynamics in Helminth Infection

Judith Allen

University of Edinburgh

Awaiting content

09/04/2013 Session 2B - Helminth immunology I - Chair Judi Allen 11:10 AM - 11:40 AM (30 mins)

Lung immune responses mediate developmental arrest of hookworms

Tiffany Bouchery, Tiffany Bouchery, Elizabeth Blom-Forbes, Mali Camberis, Graham LeGros

Malaghan Institute of Medical Research, Wellington, New Zealand

Establishing sterilizing immunity to helminth nematodes through vaccination is currently a major global health objective. Amongst the helminths infecting humans, the hookworm is currently estimated to infect 1 billion of people and is considered to be the leading cause of anemia worldwide. To date, the gut immune response has been considered as the principal source of protection against geohelminths but data is emerging that other tissue sites including skin and lung could also be important. Little information is currently available concerning the specific components of the immune response that can confer resistance or immunity to hookworm, principally because of the absence of an adequate model. We use the closely related rodent parasite Nippostrongylus brasiliensis to model the early stages of hookworm infection that may confer subsequent immunity. Using gene deficient mice, truncated infection studies and fluorescent labeling of the worms, we show that the lung is both the priming site and the protection site against Nippostrongylus brasiliensis infection. Furthermore we have identified a novel developmental defect in the worms occurring during the molt 3 process which is strongly dependent on Il-4 mediated immune pathways and is associated with the acquisition of protective immunity in the lung. The implications of these findings in the development of a vaccine against hookworm will be discussed.

09/04/2013 Session 2B - Helminth immunology I - Chair Judi Allen 11:40 AM - 11:55 AM (15 mins)

Granule-exocytosis of granulysin and granzyme B as a potential key mechanism in vaccine-induced immunity in cattle against the nematode Ostertagia ostertagi

Frederik Van Meulder, Van Meulder F. , Van Coppernolle S. , Borloo J. , Rinaldi M. , Li R.W. , Chiers K. , Van den Broeck W. , Vercruysse J. , Claerebout E. , Geldhof P.

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Ostertagia ostertagi is considered one of the most economically important bovine parasites. As an alternative for anthelmintic treatment, an experimental host-protective vaccine was previously developed based on ASP-proteins derived from the adult worms. Intramuscular injection of this vaccine, combined with QuilA as adjuvant, significantly reduced the faecal egg counts by 59 %. However, the immunological mechanisms triggered by the vaccine are still unclear. Therefore, in this study, the differences in immune responses at the site of infection, i.e. the abomasal mucosa, between ASP/QuilA-vaccinated animals and QuilA-vaccinated control animals were investigated on a transcriptomic level, using a whole genome bovine micro-array, combined with histological analysis. Sixty nine genes were significantly impacted in animals protected by the vaccine, 48 of which were upregulated. A correlation study between the parasitological parameters and gene transcription levels showed that the transcription levels of two of the upregulated genes, granulysin (GNLY) and granzyme B (GZMB) negatively correlated to cumulative faecal egg counts and total worm counts, respectively. Both genes also positively correlated to each other, and to another upregulated gene, the IgE receptor subunit FCER1A. Surprisingly, these three genes also correlated significantly to CMA1, a mast cell marker, and to cell counts for mast cells and cells previously described as globule leukocytes. Furthermore, immunohistochemical data showed that GNLY was present in the granules of globule leukocytes and that it was secreted in the mucus. Overall, the results suggest a potential role of granule exocytosis by globule leucocytes, potentially IgE-mediated, in the vaccine induced protection against Ostertagia.

09/04/2013 Session 2B - Helminth immunology I - Chair Judi Allen 11:55 AM - 12:10 PM (15 mins)

A role for eosinophils in the intestinal immunity against infective Ascaris suum larvae

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The aim of this study was to explore the mechanisms of resistance against invading Ascaris suum larvae in pigs. Pigs received a low dose of 100 A. suum eggs daily for 14 weeks. This resulted in a >99% reduction in the number of larvae that could migrate through the host after a challenge infection of 5000 A. suum eggs, compared to naïve pigs. Histological analysis at the site of parasite entry, i.e. the caecum, identified eosinophilia, mastocytosis and goblet cell hyperplasia. Increased local transcription levels of genes for IL5, IL13, eosinophil peroxidase and eotaxin further supported the observed eosinophil influx. Further analysis showed that eosinophils degranulated in vitro in response to contact with infective Ascaris larvae in the presence of serum from both immune and naïve animals. This effect was diminished with heat-inactivated serum, indicating a complement dependent mechanism. Furthermore, eosinophils were efficient in killing the larvae in vitro when incubated together with serum from immune animals, suggesting that A. suum specific antibodies are required for efficient elimination of the larvae. Together, these results indicate an important role for eosinophils in the intestinal defense against invading A. suum larvae.

09/04/2013 Session 2B - Helminth immunology I - Chair Judi Allen 12:10 PM - 12:25 PM (15 mins)

A low-tech vaccine preparation method eliciting protection against Haemonchus contortus and Mecistocirrus digitatus.

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Mecistocirrus digitatus is a blood-feeding abomasal nematode infecting cattle and buffalo in areas of the world, such as India, Asia and the Philippines, where Haemonchus species also infect livestock. The feasibility of a vaccine approach to control both species was investigated. A low-tech method to produce native antigens from M. digitatus and H. contortus, suitable for local production in developing countries, was refined and tested against H. contortus challenge in a vaccine trial. Reductions in cumulative mean faecal egg counts of 99% and 28%, respectively, were achieved with the H. contortus and M. digitatus extracts. A corresponding reduction in total worm burden of 87% was achieved using the H. contortus extract, although no reduction in total worm burden was observed with the M. digitatus extract. This work shows the potential for low-tech local vaccine production against both nematode species, potentially leading towards the development of a bivalent vaccine.

09/04/2013 Session 2B - Helminth immunology I - Chair Judi Allen 12:25 PM - 12:40 PM (15 mins)

Helminth biology II - Chair James Lok

Schistosoma mansoni DNA methylation: characterising the machinery and identifying the marks.

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The recent elucidation of Schistosoma mansoni's draft genome has provided an important step in our further understanding of these pathogenic trematodes and the collection of pathologies that they cause. When coupled to the rapid advances made in functional genomics, we are now poised to make great progress in identifying when and where the approximately 12,000 protein coding genes are expressed during the schistosome's complex lifecycle. While this genetic information is critical for developing future control strategies (i.e. identifying new drug and vaccine targets), we are still just beginning to understand how schistosome gene expression is regulated and what role epigenetics have in this and other processes. In this lecture, I will describe our work on one particular epigenetic modification in schistosomes, DNA methylation. Utilizing a range of technologies, I will specifically show how DNA methylation was unambiguously identified, what genome elements are targeted by it and how this epigenetic mark changes throughout the schistosome lifecycle. Exploiting functional genomics tools as well as DNA methyltransferase inhibitors, I will additionally illustrate how we identified the schistosome gene product responsible for this epigenetic modification and demonstrate the functional significance of an intact DNA methylation machinery during oviposition. These findings collectively show that DNA methylation

exists in the Platyhelminthes and is an important regulator of schistosome development. The role of DNA methylation in shaping future studies of platyhelminth biology will be discussed.

09/04/2013 Session 3B - Helminth biology II - Chair James Lok 2:00 PM - 2:30 PM (30 mins)

Receptor tyrosine kinases of Schistosoma mansoni as new potential drug targets: the example of Venus Kinase Receptors

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Receptor tyrosine kinases (RTK) are transmembrane molecules involved in a wide variety of cellular mechanisms such as proliferation, migration or differentiation. In humans, deregulation of RTK activities is often associated with cancer, and some of these receptors are already validated targets in chemotherapy. Recent studies have shown that Schistosoma mansoni was sensitive to cancer drugs that target protein kinases (reviewed in Dissous and Grevelding, 2011). This was in accordance with the functional studies that have demonstrated the importance of several RTKs in the biology of S. mansoni and S. japonicum. Among them, Venus Kinase Receptors (VKR) could represent attractive targets. VKRs form a family of atypical RTKs that are found in many phyla but interestingly, not in vertebrates (Vanderstraete et al. (1), accepted). In S. mansoni, two VKR genes have been found, Smvkr1 and Smvkr2. Quantitative RT-PCR as well as in situ hybridization indicated a large expression of both genes in larval stages and in the ovary of adult females. RNA interference experiments further confirmed the implication of SmVKRs in oogenesis and egg formation and led us to consider these receptors as potential anti-fecundity targets (Vanderstraete et al., in prep). By using commercial RTK inhibitors, we demonstrated that a single chemical compound was able to inhibit both Insulin Receptor and VKR kinase activities (Vanderstraete et al. (2), accepted). This dual-hit targeting led to death of schistosomula and adult worms in vitro and thus constitutes the first proof of principle that RTKs represent novel and attractive chemotherapeutic targets to fight schistosomes.

09/04/2013 Session 3B - Helminth biology II - Chair James Lok 2:30 PM - 2:45 PM (15 mins)

The Fasciola hepatica cathepsin B4 conundrum: Does the Cys/Ser active site substitution create an inactive protease?

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Fasciola spp. liver flukes cause fasciolosis, a global disease of domestic animals and a neglected tropical disease which infects up to 17 million people. Infection with liver fluke occurs following ingestion of dormant metacercarial larvae which occur encysted on vegetation. Metacercariae are activated and larval parasites excyst in the host duodenum, penetrate the duodenal wall, and migrate to the bile ducts via the hepatic parenchyma. During this invasion phase, juvenile fluke secrete a battery of proteolytic enzymes dominated by multiple cathepsin B and cathepsin L cysteine proteases. Fasciola hepatica expresses at least ten distinct cathepsin B (FhCB) transcripts; we have profiled the expression of these cathepsins in metacercariae, newly-excysted juvenile (NEJ) and adult F. hepatica and Fasciola gigantica using qPCR. We identified expression of FhCB1, 2, 3, 4, 6, 7, 9 and 10 and FgCB1, 2, 3, 4, 6, 7 and 9, with some variation across the life stages; as expected, expression of FhCB1, 2 and 3 predominates in NEJs and then diminishes comparatively in adult stage worms. FhCB4, which is expressed in metacercariae, NEJs and adult parasites, represents an unusual cysteine protease, in that its active site cysteine residue appears to be replaced by serine. To determine the impact of this Cys-Ser exchange on proteolytic activity, we have expressed recombinant FhCB4, alongside S29C and A27G/A28S/S29C variants, in the pPink alpha Pichia pastoris system. Analyses of proteolytic activity in these variants are underway, with the aim of understanding the unusual cathepsin's biological function.

09/04/2013 Session 3B - Helminth biology II - Chair James Lok 2:45 PM - 3:00 PM (15 mins)

Biochemical characterization of metabolic enzymes from the liver fluke, Fasciola hepatica

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The World Health Organization has estimated that ~2.4 million people have fasciolosis and another 180 million are at risk of being infected. It is considered to be the most economically damaging trematode disease of livestock, with annual costs estimated at US$2000 million per annum worldwide . An important evolutionary pressure on Fasciola hepatica is its changing environment throughout its life cycle, requiring its metabolism to move from aerobic to anaerobic as it matures. The fluke's metabolic adaptations include an adaptation of the tricarboxylic acid cycle (TCA), allowing it to maintain energy production in anaerobic conditions. We are currently working on five enzymes concerned with energy production - triose-phosphate isomerase (TPI), citrate synthase, galactokinase, glyceraldehyde 3 phosphate dehydrogenase (G3PDH), and UDP-galactose 4-epimerase. TPI from F. hepatica has been successfully cloned, sequenced, expressed, purified and biochemically characterized. The protein shows remarkable thermal stability. Citrate synthase has been cloned and sequenced; however, expression and purification have proven difficult. Nevertheless, extracts from bacterial cells expressing the protein showed additional citrate synthase activity. Galactokinase has been been successfully cloned, sequenced, expressed and purified; characterisation is still in the early stages. G3PDH has been successfully cloned, sequenced, expressed and purified. The expressed enzyme is active; and a full kinetic analysis is underway. UDP- glucose 4-epimerase has been successfully cloned, sequenced, expressed and purified. Biochemical characterisation is underway. These biochemical studies, combined with molecular modelling, will enable us to assess whether catabolic enzymes from F. hepatica make plausible targets for the development of novel anthelmintics.

09/04/2013 Session 3B - Helminth biology II - Chair James Lok 3:00 PM - 3:15 PM (15 mins)

Functional assessment of calmodulin-like proteins in Fasciola hepatica newly excysted juveniles

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Fasciola hepatica is a zoonotic pathogen with global veterinary and medical importance. The WHO has designated Fasciolosis as a neglected tropical disease with an estimated 17 million people infected; in addition fluke-related costs to the global agri-food industry are estimated to be ~$20 billion per annum. Deficiencies associated with current flukicides highlight the need to identify and validate novel drug-targets. Calmodulins are small calcium-sensing proteins with ubiquitous expression in all eukaryotic organisms. They act by transducing fluctuations of intracellular calcium levels into cell signalling events and are involved in mediating processes such as the phosphorylation status of protein kinases, gene transcription and calcium transport. In Schistosoma mansoni, calmodulins have been implicated in egg hatching, miracidial transformation and larval development. Three calmodulin-like proteins have previously been identified and biochemically characterised in adult F. hepatica. We aim to investigate the roles of FhCaM1, FhCaM2 and FhCaM3 through the application of RNAi methodologies, protein localisation techniques, and behavioural phenotype assays, in newly excysted juveniles (NEJs), and assess their potential as drug target candidates. Results reveal that (i) FhCaMs are expressed in NEJs (FhCaM2 and FhCaM3 localise to myocyton-like cells and processes); (ii) FhCaMs are amenable to RNAi (dsRNA directed against FhCaM1, FhCaM2 and FhCaM3 triggered transcript knockdown of 68%, 94% and 97%, respectively); (iii) FhCaM-RNAi results in protein knockdown in NEJs maintained in vitro for up to 3 weeks. Functional analyses post-RNAi are on-going.

09/04/2013 Session 3B - Helminth biology II - Chair James Lok 3:15 PM - 3:30 PM (15 mins)

Helminth immunology II - Chair Richard Grencis

Dendritic cells: central players in orchestration of Type 2 inflammation

Andrew MacDonald, Andrew MacDonald

University of Edinburgh

Dendritic cells (DCs) are specialised innate immune cells that play a key role in initiation and direction of adaptive immunity against diverse immune challenges. However, relatively little is known about precisely how DCs become activated and function in Type 2 settings, either during parasitic helminth infection or following exposure to allergens. Using a combination of in vitro and in vivo model systems, we have shown that DCs responding to helminths display an unusual, low level, activation phenotype distinct from that ordinarily seen during viral or bacterial infection. Irrespective of this, we have demonstrated that DCs are both sufficient and necessary for

induction of Type 2 immunity against several helminth species. More surprisingly, we have found that DCs can also be critical for maintenance of the Type 2 response and for survival during chronic infection with the medically important helminth Schistosoma mansoni. Although DCs are clearly centrally involved in coordination of the immune response during Type 2 inflammation, the specific mechanism(s) by which they direct Th2 polarisation remain poorly understood. We have recently discovered that epigenetic regulation of DCs, via the action of the methyl-binding protein Mbd2, is vital for optimal induction and development of Type 2 inflammation against either helminths or allergens. This reveals that epigenetic mechanisms can play an essential role in controlling DC activation and function, and identifies methyl-binding proteins and/or the genes that they regulate as exciting new targets for therapeutic modulation of Type 2 immunity.

09/04/2013 Session 4B - Helminth immunology II - Chair Richard Grencis 4:10 PM - 4:40 PM (30 mins)

Differential Genetic Regulation of Peripheral Blood Monocytes in a Schistosoma haematobium Exposed Population

Amir Kirolos, Amir Kirolos, Norman Nausch, Laura Appleby, Francisca Mutapi

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Introduction: 200 million people in the developing world are chronically infected with the water-borne parasite Schistosoma haematobium. Infection results in monocytes producing a forceful immune response in the urinary tract system, often causing haematuria, hydronephrosis, bladder fibrosis and bladder cancer. Genes implicated in this response include macrophage complement receptors, C5AR1 and C3AR1, and Th2 associated proteins, IL-10 and LOX-15. Methods: 86 participants from a Zimbabwean village endemic with S.haematobium had venous blood collected. CD14+ peripheral blood monocyte cDNA were separated from the blood samples and underwent real-time PCR. Expression of the genes above were compared between each other and with infection intensity (eggs/10ml urine) in participants, as well as gender and age from census data. Results: C3AR1 was expressed significantly more in monocytes of individuals with higher infection intensities ($p=0.016$), particularly in those aged over 14($p=0.002$). IL-10 was expressed significantly more with higher infection intensities, particularly those aged 10-14($p=0.021$). In those aged 5-9, C5AR1 was expressed significantly more in those infected compared to those who were not($p=0.048$). LOX-15 expression was not related to any characteristics but correlated with C5AR1($p<0.001$) and IL-10($p=0.033$), while C3AR1 and IL-10 were also correlated($p=0.018$). Conclusions: This study indentifies monocyte genes differentially regulated based on age and S.haematobium infection intensity. This implicates these genes as potential players in the aetiology of complications arising from S.haematobium infection. This adds to the emerging picture of immune responses in infection and has implications for further research into potential treatment and vaccination of this disease.

09/04/2013 Session 4B - Helminth immunology II - Chair Richard Grencis 4:40 PM - 4:55 PM (15 mins)

Schistosoma mansoni Ly6 family members are immunogenic in both experimental models and

endemic communities.

Iain Chalmers, Iain W. Chalmers1, Martha Truscott1, Christine Pierrot2, Frances Jones3, Colin M. Fitzsimmons3, Edridah M. Tukahebwa4, David Dunne3, Jamal Khalife2, Karl F. Hoffmann1

1. Institute of Biological, Environmental & Rural Sciences, Aberystwyth University, Edward Llwyd Building, Aberystwyth, SY23 3FG, UK 2. Centre d'Infection et d'Immunité de Lille, Inserm U1019-UMR CNRS 8204, Institut Pasteur de Lille, Lille, France 3. Department of Pathology, University of Cambridge, Tennis Court Road, Cambridge, CB2 1QP, UK 4. Vector Control Division, Ugandan Ministry of Health, Kampala, Uganda

As the schistosome tegument is the major interface between host and parasite, investigation of the proteins present in this surface layer is crucial to our understanding of host/parasite interactions and to the discovery of novel drug targets and vaccine candidates. Applying a suite of bioinformatics tools to the S. mansoni genome, transcriptome and proteome, we have identified a set of predicted surface proteins, including several with weak homology to the Ly6 family. Ly6 proteins are cell surface molecules present across metazoans sharing similar three-dimensional structures despite low sequence similarity. In humans, Ly6 domain-containing proteins perform important functions such as inhibition of complement activity (CD59) or binding/regulation of serine protease activity (uPAR). Here, we present data on the identification, protein features and transcriptional profiles of the eleven S. mansoni Ly6 proteins (SmLy6A-K). Presence of the diagnostic set of cysteine residues, signal peptides and GPI-anchor sites strongly suggest SmLy6 proteins are cell surface-bound Ly6 members. Further, we present evidence of Th2-associated antibody responses directed against rSmLy6A and B in both S. mansoni-infected mouse (IgG1>IgG2b response) and rat models (IgG2a response). Finally, we report antibody responses to rSmLy6A and B from a cohort of S. mansoni-infected Ugandan males. Analysis of antibody titers/isotypes to these proteins pre- and post- praziquantel treatment reveals few individuals responding to SmLy6A, while ~25% of individuals produce anti-SmLy6B IgG1 antibodies. Collectively, these results point to SmLy6 proteins as being an important new class of S. mansoni surface proteins, which elicit immunological responses during infection in experimental models and endemic communities.

09/04/2013 Session 4B - Helminth immunology II - Chair Richard Grencis 4:55 PM - 5:10 PM (15 mins)

Using known allergen structures to predict IgE binding antigens in the metazoan parasite Schistosoma mansoni; a link between evolved protective immune responses and allergy?

Edward Farnell, Edward Farnell(a), Angela Pinot de Moira(a), Frances Jones(a), Edridah Tukahebwa(b) and David Dunne(a)

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It has long been known that IgE mediated immune responses are at the heart of many allergic diseases and there is a growing body of evidence that suggests IgE mediated immune responses evolved to protect against metazoan parasite infections. We hypothesise that allergy to environmental and food allergens is the by-product of structural homology between allergens and

metazoan parasite antigens that react with IgE. We expect that major families of clinically significant environmental and food allergens should have worm or arthropod pathogen structural homologues. Allergen associated molecular patterns deposited in the Allfam allergen family database were used to predict IgE binding to antigens from a group of previously identified S. mansoni proteins known to abundant in human life cycle stages of S. mansoni infection. A subset of these proteins, including both proteins that were either expected or not expected to bind IgE were cloned and screened against human sera from an infected population for both prevalence and magnitude of IgG and IgE antibody responses. Our findings not only indicate that this methodology is effective in predicting IgE binding antigens in natural S. mansoni infections but also show a broad range of antibody mediated responses that describe a complex interplay between IgE and IgG4 dependent on antigen type, life cycle stage abundance and levels of exposure during infection. This is a collaborative work funded by a Wellcome Trust Project Grant to Cambridge University (Edward Farnell and David Dunne), Edinburgh University (Stephanie Ryan and Rick Maizels) and EBI (Nidhi Tyagi and Nicholas Furnham).

09/04/2013 Session 4B - Helminth immunology II - Chair Richard Grencis 5:10 PM - 5:25 PM (15 mins)

Malaria : Molecular biology & genomics - Chair Catherine Merrick

Proteolytic maturation of the major malaria merozoite surface protein MSP1: new insights and functional significance

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The malaria parasite replicates and matures within an intraerythrocytic membrane-bound parasitophorous vacuole (PV). Eventually, in a process collectively called egress, several major surface proteins of the developing intracellular merozoites undergo dramatic proteolytic modification whilst the enclosing PV and residual host erythrocyte membranes rupture, releasing merozoites which rapidly invade fresh erythrocytes to perpetuate the cycle. A single parasite protease called SUB1 plays a key role in both proteolytic maturation of merozoite surface proteins, required for subsequent invasion of fresh host cells, and rupture of the PV and host membranes to allow merozoite release. Egress is a potential drug target as compounds that selectively inhibit SUB1 activity, or that block its discharge, potently block egress. However, nothing is known about precisely how SUB1-mediated modifications to merozoite surface proteins modulate parasite invasiveness, nor how the two barriers surrounding the merozoites (the PV and host red cell membranes) are disrupted. In this presentation I will describe unpublished results from our investigations into the role of SUB1 in modifying the major merozoite surface protein MSP1. Our findings shed intriguing new light on the importance of MSP1 processing and confirm the SUB1 pathway as a target for new chemotherapeutic approaches to interfering with malaria parasite replication.

09/04/2013 Session 1C - Malaria : Molecular biology & genomics - Chair Catherine Merrick 9:00 AM - 9:30 AM (30 mins)

Modelling the spatial and temporal arrangement of transcripts over intergenic regions in the human malarial parasite Plasmodium falciparum

Paul Horrocks, Karen Russell, Sandra Hasenkamp and Paul Horrocks

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Plasmodium falciparum invasion, colonisation and multiplication within diverse host environments, as well as its ability to manifest its virulence within the human host, are activities all tightly linked to the temporal and spatial control of gene expression. Yet, despite the wealth of high throughput transcriptomic data available for this organism there is very little information regarding the location of key transcriptional landmarks or their associated cis-acting regulatory elements within the intergenic regions. Here we describe a modelling approach to explore questions relating to the organisation of the untranscribed regions of transcripts within intergenic regions. Specifically here, we propose to discuss how transcriptional units are spatially and temporally organised over these intergenic regions. This study provides a theoretical framework that challenges our current understanding of the transcriptional landscape across the P. falciparum genome.

09/04/2013 Session 1C - Malaria : Molecular biology & genomics - Chair Catherine Merrick 9:30 AM - 9:45 AM (15 mins)

A putative formate transporter of Plasmodium falciparum is located in the plasma membrane and digestive vacuole membrane

Amy Clarke, Sylke Müller, Shiela E Unkles

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The PF3D7_0316600 gene of Plasmodium falciparum is annotated as a putative formate-nitrite transporter, and is a potential new drug target as it is absent from humans. Algae, fungi and bacteria possess orthologues, which confer the transport small anions such as formate, nitrite, pyruvate and the hydrosulphide ion. To assess the biological function of the protein, a synthetic version of the PF3D7_0316600 gene was generated and expressed in E. coli lacking the endogenous formate and nitrite transporters. This revealed that when PF3D7_0316600 was expressed in E. coli, it was able to transport formate but not nitrite. To investigate the localisation of the PF3D7_0316600 protein in P. falciparum, the synthetic gene was C-terminally tagged with a GFP or (HA)3 tag and transfected into P. falciparum. Fluorescent light microscopy using either live cell imaging or immunofluorescence analysis indicated that the transporter is located in the parasite plasma membrane and digestive vacuole of intraerythrocytic parasites, suggesting a role of the protein in uptake or excretion of metabolites or metabolic end-products, respectively. It was impossible to delete the gene, while the endogenous gene locus could be targeted by addition of a 3' (HA)3 tag, suggesting the gene is essential for blood stage parasite survival.

09/04/2013 Session 1C - Malaria : Molecular biology & genomics - Chair Catherine Merrick 9:45 AM - 10:00 AM (15 mins)

Intracellular stages of Plasmodium falciparum catabolize glucose and glutamine via a canonical tricarboxylic cycle.

James MacRae, James I. MacRae, Matthew W. A. Dixon, Megan K. Dearnley, Hwa H. Chua, Jennifer M. Chambers, Shannon Kenny, Iveta Bottova, Leann Tilley & Malcolm J. McConville

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The bloodstream stages of the malaria parasite Plasmodium falciparum are thought to have a highly streamlined energy metabolism and to primarily depend on glucose uptake and glycolysis for ATP synthesis. These parasite stages express all of the enzymes needed for a canonical mitochondrial tricarboxylic acid (TCA) cycle, although the function of the mitochondrion in energy metabolism remains unresolved. Here we show that rapidly dividing P. falciparum asexual red blood stages, as well as non-dividing gametocyte stages, catabolize both 13C-glucose and 13C-glutamine via a canonical TCA cycle, linking glucose and amino acid metabolism and providing a source of reducing equivalents and precursors for the respiratory chain and anabolic pathways, respectively. The differentiation of asexual red blood cell stages to gametocytes was associated with a marked increase in catabolism of glucose-derived pyruvate in the TCA cycle, indicating a switch to a more efficient form of energy generation. While chemical inhibition of the TCA cycle had little effect on the growth of asexual stages, gametocyte development was strongly arrested potentially offering a new way to target parasite transmission.

09/04/2013 Session 1C - Malaria : Molecular biology & genomics - Chair Catherine Merrick 10:00 AM - 10:15 AM (15 mins)

Mannose activation as a drug target in Plasmodium falciparum

Chris Williams, Chris Williams1, AM Tomlins2, EHWong2, S Müller2 and TK Smith1

1Biomedical Sciences Research Complex, University of St Andrews 2Wellcome Trust Centre for Molecular Parasitology, University of Glasgow

The major surface proteins of Plasmodium merozoites and sporozoites known to be critical for host cell invasion are attached to the parasite membrane via glycosylphosphatidylinositol (GPI) anchors. The parasites ability to synthesize these GPI anchors is totally dependent upon the enzymes that form activated mannose. Thus, the enzymes involved in the generation of mannosylated GPI-anchors are likely to have fundamental roles in both proliferation and invasion. Two P.falciparum enzymes, guanidine diphosphomannose pyrophosphorylase (GDP-Man PP) and dolichol phosphate mannose synthase (DPMS) function in tandem to provide dolichol-phosphate mannose for GPI-anchor biosynthesis. Here we show the sub-cellular localisation of these two proteins (via the use of transgenic parasites), in addition to this various other genetically altered cell lines (including double knock out and over expression lines) have been produced to elucidate

their essentiality. A cell free system and recombinant assays for DPMS have also been developed which have allowed the DPMS activity of various cell lines to be analysed as well as for the screening of small molecule inhibitors.

09/04/2013 Session 1C - Malaria : Molecular biology & genomics - Chair Catherine Merrick 10:15 AM - 10:30 AM (15 mins)

General Parasitology - Chair Judith Smith

Malaria parasite population genomics identifies targets of immunity among other causes of selection

David Conway, David Conway

London School of Hygiene and Tropical Medicine, UK

Genes with alleles causing phenotypic differences which affect survival or reproduction often show patterns of polymorphism that depart statistically from those expected under neutrality. Information contained in the nucleotide site frequency spectrum or haplotype structure is particularly useful to prospectively identify loci most likely to be under balancing selection or recent positive directional selection. Parasite genomic data generated from paired end short-read sequencing of samples of 50-100 clinical isolates from an endemic area enables a reasonable scan for evidence of such selection in within-population analyses. Furthermore, replication and comparison of analyses across different endemic populations helps to confirm and refine the inferences of probable causes of selection. Our current studies on West African P. falciparum populations illustrate how such analyses identify previously-known targets of immunity as well as revealing interesting new hypothetical targets, a number of which exhibit variation in expression as well as antigenic structure. New candidate targets are thereby identified, particularly at the merozoite stage, including those with limited numbers of alleles that can be considered as potential components of a polyvalent multiple serotype vaccine. A similar approach would be applicable to identifying targets of naturally-acquired immunity in P. vivax and other endemic parasite species.

09/04/2013 Session 2C - Malaria : Host-Pathogen interface - Chair Mike Blackman 11:10 AM - 11:40 AM (30 mins)

Decreasing the threshold of protective antibody and T cell responses in malaria by combination of antigens

Karolis Bauza, Karolis Bauza Arturo Reyes-Sandoval

The Jenner Institute/University of Oxford

Consistent efficacy in clinical trials has been achieved by two leading malaria vaccine candidates – RTS, S and viral vectors expressing ME.TRAP - that target the pre-erythrocytic antigens circumsporozoite (CS) and thrombospondin-related adhesion proteins (TRAP), respectively. However, protection in humans relies on high antibody titers and frequencies of T cells when

these antigens are used individually. With the aim to enhance protection using malaria pre-erythrocytic antigens, we investigated the effect of combining CS and TRAP expressed individually in the recombinant viruses ChAd63 and MVA and analyzed the mechanisms that are associated with protection. Combination of the two antigens expressed by ChAd63 and MVA prime/boost regimens did not offer any protective advantage over the use of antigens individually as anti-CS responses were sub-optimal with the use of MVA. Therefore, we explored a bifurcated way to maximize both, anti-CS antibodies by Ad/protein prime-boost vaccinations and anti-TRAP T-cell responses using Ad/MVA. Combination of the two approaches stimulated optimal humoral and cellular responses that afforded sterile protection in C57Bl/6 animal model that is highly susceptible to malaria.

09/04/2013 Session 2C - Malaria : Host-Pathogen interface - Chair Mike Blackman 11:40 AM - 11:55 AM (15 mins)

Vector transmission regulates immune control of Plasmodium virulence

Philip Spence, Philip J. Spence, William Jarra, Prisca Lévy, Adam J. Reid, Lia Chappell, Thibaut Brugat, Matthew Berriman & Jean Langhorne

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Serial blood passage of Plasmodium through rodents, primates or humans increases parasite virulence, suggesting that the mosquito vector regulates Plasmodium virulence within the mammalian host. Here we utilise mosquito transmission of serially blood passaged (SBP) Plasmodium chabaudi chabaudi to interrogate vector regulation of parasite virulence. Analysis of SBP P.c. chabaudi before and after mosquito transmission demonstrates that the vector intrinsically modifies the asexual blood-stage parasite, such that it elicits a distinct mammalian immune response that attenuates parasite growth and virulence. Attenuated virulence associates with modified expression of the pir multi-gene family. Vector transmission of Plasmodium thus regulates gene expression of probable variant antigens in the erythrocytic cycle, transforming the elicited mammalian immune response that, in turn, dictates and defines parasite virulence. These results place the mosquito at the centre of our efforts to dissect mechanisms of protective immunity to malaria for the development of an effective vaccine.

09/04/2013 Session 2C - Malaria : Host-Pathogen interface - Chair Mike Blackman 11:55 AM - 12:10 PM (15 mins)

Genotyping of C loop(CAMP) and F loop(FCR-3) Alleles of Erythrocyte Binding Antigen 175 KD (EBA-175) of Plasmodium falciparum in South-East of Iran

adel Ebrahimzadeh, Ebrahimzadeh Adel 1*, Saryazdipour Khadijeh1, Mohammadi Saeed 1

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Abstract Background: The erythrocyte binding antigen-175 (EBA-175) on Plasmodium falciparum merozoites mediates sialic acid dependent binding to glycophorin A on host erythrocytes and,

therefore, plays a crucial role in cell invasion. Dimorphic allele segments have been found in its encoding gene with in FCR-3 strains (F-segment) and CAMP strains (C-segment).This study was designed to determine the distribution of EBA-175 alleles of Plasmodium falciparum in the South-East of Iran. Methods: We used Nested Polymerase Chain Reaction method with specific primers, which improves the two fragments of the EBA-175 gene. Ninety-four microscopically positive blood samples were collected from the infected P.falciparum malaria subjects from four different districts in South-East of Iran. Results: In this study, of the 94 confirmed P. falciparum samples obtained, 88 samples were successfully scored for EBA-175. Genotyping CAMP strains (714 bp) and FCR-3 strains (795 bp) were found in 31(32.97%) and 49(52.12%) cases. Eight cases 8(8.51%) had mix CAMP/FCR-3 infection. Conclusion: The two fragments of dimorphic EBA-175 gene were observed and the FCR-3 allele was more prevalent in South-East of Iran. This distributional pattern should be considered in designing to control P. falciparum malaria in the region. Key words: Plasmodium falciparum, Erythrocyte binding antigen-175, South-East of Iran

09/04/2013 Session 2C - Malaria : Host-Pathogen interface - Chair Mike Blackman 12:10 PM - 12:25 PM (15 mins)

Temporal dynamics of Plasmodium falciparum, P. malariae and P. ovale wallikeri and P. ovale curtisi infections in a high-endemic setting in Uganda

Sarah Clifford, Miss Sarah Clifford, Dr Martha Betson, Professor Russell Stothard

Place of Research; Liverpool School Of Tropical Medicine S Clifford; University of Liverpool, Liverpool L69 3BX M Betson; Royal Veterinary College, Hawkshead Lane, North Mymms, Hatfield, Hertfordshire AL9 7TA R Stothard;Room; Liverpool School of Tropical Medicine, Liverpool L3 5QA

Background: The non-falciparum malaria species in particular P. ovale and P. malariae, have been neglected in terms of research. However the use of molecular techniques have led to the detection of higher levels of co-infections of these species with P. falciparum than previously thought. The prevalence of malaria in Uganda is increasing. Current control and monitoring programmes are focused on the reduction of P. falciparum infections. However knowledge of the prevalence of non-falciparum malaria is essential so that the response of these species to current control methods can be monitored and improved. An 18-month longitudinal cohort study was performed to improve knowledge of the temporal dynamics of non-falciparum malaria in children living in Uganda. Blood spot samples and questionnaires were obtained from 248 children at baseline and every 6 months. The blood spots were analysed using real-time PCR. Results: The overall prevalence of malaria ranged from 82-96%. P. falciparum is the most prevalent species (81-94%), followed by P. malariae (12-48%) and finally P. ovale (7-22%). There was an increase in prevalence of all malaria species over the course of the study but the two non-falciparum species P. malariae and P. ovale showed the greatest percentage increase. Statistical analysis showed a positive association between P. falciparum and P. malariae infections. Conclusions: The prevalence of mixed malaria infections was much higher than anticipated. The species with the greatest percentage increase during the study was Plasmodium malariae. The response of mixed/non-falciparum malaria infections to standard malaria control methods targeting falciparum malaria warrants further investigation.

09/04/2013 Session 2C - Malaria : Host-Pathogen interface - Chair Mike Blackman 12:25 PM - 12:40 PM (15 mins)

General Parasitology - Chair Judith Smith

Planarian regenerative polarity acts as an orthologous phenotype for the discovery of antihelmintic targets

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Over a quarter of the world's population is estimated to be infected with parasitic helminths, the most devastating belonging to the Platyhelminth flatworms. Research into the biology of many parasitic Platyhelminths is limited by various experimental intractabilities in the laboratory setting. As an alternative, we became interested in evaluating the non-parasitic flatworm Dugesia japonica as a model organism to better understand parasitic Platyhelminths. D. japonica is sensitive to antihelmintic compounds and amenable to RNAi knockdown, allowing the function of gene products to be interrogated by pharmacological and genetic screens [1]. We previously reported that the major pharmacotherapeutic for schistosomiasis – the drug praziquantel (PZQ) – caused a surprising effect on regeneration of the planarian D. japonica. Worm fragments exposed to PZQ after amputation regenerated as two-headed animals [2]. Here, we use this phenotype to investigate the mechanism of action for the orphan drug praziquantel (PZQ) and assess whether this phenotype is broadly predictive of antihelmintic activity. We report that PZQ efficacy is attenuated by RNAi of a single neuronal voltage dependant Ca2+ channel (Cav), potentiated by positive regulators of neuronal excitability, and functionally linked to select neurotransmitters. Our findings demonstrate the utility of a free living model organism to dissect flatworm signal transduction, and underscore the merit for future investigation of flatworm neuromodulators in developing antihelmintic therapies. [1] Chan JD and Marchant JS. J Vis Exp. 2011 Aug 31;(54). [2] Nogi T, Zhang D, Chan JD, Marchant JS. PLoS Negl Trop Dis. 2009 June; 3(6): e464.

09/04/2013 Session 3C - General Parasitology - Chair Judith Smith 2:00 PM - 2:15 PM (15 mins)

Probing praziquantel action in the model microturbellarian, Macrostomum lignano

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Praziquantel (PZQ) is the drug of choice for the treatment of schistosomiasis and many cestodiases. In spite of its central role in the control of blood fluke, its mechanism of action has not been fully resolved, undermining the detection and evaluation of resistant isolates. The most compelling data on the action of PZQ implicate a variant β subunit of voltage operated calcium channels (VOCCs) as a key target for the drug. Previous studies have discovered that a variant of this subunit, which lacks two protein kinase C (PKC) phosphorylation sites conserved in other phyla, appears to be necessary for helminth PZQ sensitivity. The microturbellarian Macrostomum lignano is becoming established as a model organism in stem cell biology due to its impressive

regenerative capacity. It is also an attractive model organism for the study of parasitic helminths due to its basal phylogenetic position within phylum Platyhelminthes, the availability of a complete genome sequence, its compatibility with a range of bioimaging and molecular tools and, its ease of laboratory culture. This study revealed that M. lignano is sensitive to treatment with PZQ, displaying concentration-dependent motility and survival phenotypes. Although bioinformatic surveys identified several VOCC β subunits, they all displayed the conventional sequence and lacked the variant signature. These data suggest that PZQ is active at their conventional VOCC β subunits or that it has a distinct target in M. lignano. To examine this further we have probed the impact of VOCC β subunit RNA interference on worm phenotype and sensitivity to praziquantel.

09/04/2013 Session 3C - General Parasitology - Chair Judith Smith 2:15 PM - 2:30 PM (15 mins)

Relationship between Enterobious vermicularis infection and appendicitis among patients in Gaza strip

Adnan Al-Hindi, Dr. Adnan I. Al-Hindi, Dr. Abdel Monem Lubbad, Mrs.Shereen Hamdounah Islamic University of Gaza, Faculty of Science, Department of Biology P.O.Box 108, Gaza strip, Palestine

The place of the work is Gaza Strip, Palestine -Dr.Adnan Al-Hindi, PhD Islamic University of Gaza, Faculty of Science, Department of Biology P.O.Box 108, Gaza strip, Palestine -Dr. Abdel Monem Lubbad, PhD Islamic University of Gaza, Faculty of Medicine P.O.Box 108, Gaza strip, Palestine - Mrs. shereen Hamoudah

Background: Enterobius vermicularis is one of the most prevalent nematodes; the association between E. vermicularis and appendix has been established. Objectives: Is E. vermicularis infection the cause of appendicitis among patients in Gaza Strip. Materials: Two hundred appendices were collected from patients aged 8-54 years old of them 121 (60.5%) were males and 79 (93.5%) were females. They are complained from different symptoms including: itching in the perianal area, abdominal pain, and constipation, loss of weight and loss of appetite. Those patients attended the three hospitals; Al-Shifa, Abu-Yousef Al-Najar and European hospital in Gaza Strip. All appendix tissue was preserved in 10% formalin immediately after surgical operation. Gross examination and histological techniques were applied for each tissue Results: It was found that 30 (15%) of patients with appendix were associated with E. vermicularis. Appendix and E. vermicularis were mostly found in age groups 14-19 years old 17 (23.6%). No significant relationship was found regarding sex, education and residence in association of E. vermicularis with appendix. Patients from south Gaza were found the most infected individuals with E. vermicularis and complained from appendicitis 12 (19.0%). Conclusion: The results of the present study, showed that E. vermicularis was likely to be involved in the etiology of appendicitis in the studied patients. It is recommended: It is recommended to examine patients complains from appendicitis with STP before the surgical operation. Key Words: Enterobius vermicularis, appendicitis, infection, Gaza Strip

09/04/2013 Session 3C - General Parasitology - Chair Judith Smith 2:30 PM - 2:45 PM (15 mins)

Monitoring intermediate snail hosts as indicators of schistosomiasis transmission within control programmes

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Schistosomiasis is a disease with focal transmission centred around water bodies containing susceptible intermediate snail hosts. As prevalence of schistosomiasis in the human population is reduced by mass drug administration (MDA), locating and monitoring transmission at these foci becomes more significant as control progresses towards elimination. SCORE is a consortium programme undertaking operational research on schistosomiasis control. Snail monitoring is on-going in 16 villages participating in different treatment strategies, for Schistosoma mansoni in Tanzania and for Schistosoma haematobium in Niger as part of SCORE "Gaining" and "Sustaining" studies. Bulinus spp. are collected on a monthly basis during the rainy season in Niger, and Biomphalaria spp. on a quarterly basis in Tanzania. Abundance and patent infection prevalence data are recorded. Species of snails and schistosome cercariae are identified by morphology and a subset confirmed by molecular barcoding. In addition, as part of the Zanzibar Elimination of Schistosomiasis Transmission (ZEST) programme, 15 shehias on both Unguja and Pemba islands are targets of snail monitoring and control (with Niclosamide). Approximately 150 transmission sites have been surveyed and treated so far. Data on snail density and parasite prevalence will be linked with parasitological surveys of school age children and used to assess the effectiveness of control interventions.

09/04/2013 Session 3C - General Parasitology - Chair Judith Smith 2:45 PM - 3:00 PM (15 mins)

Schistosoma mansoni egg reduction rates and cure rates in primary school children, Mayuge, Uganda, ten years after the start of praziquantel mass drug administration

Poppy Lamberton, Poppy H. L. Lamberton, Narcis B. Kabatereine, Edridah Tukahebwa Muheki, Alan Fenwick and Joanne P. Webster

Poppy H. L. Lamberton,Alan Fenwick and Joanne P. Webster: Department of Infectious Disease Epidemiology, Imperial College London, UK Narcis B. Kabatereine and Edridah Tukahebwa Muheki: Vector Control Division, Ministry of Health, Kampala, Uganda

The Schistosomiasis Control Initiative (SCI) began annual praziquantel (PZQ) treatment of school-aged children in Uganda in 2003. Monitoring how parasite infections change as a result of PZQ-treatment has important implications for the success of this and other control programmes. Prevalence, intensity of infection, morbidity, host behavioural data and any potential side-effects post-PZQ-treatment were recorded for S. mansoni infections of children (aged 6-12) from three primary schools in Mayuge district, Uganda, on the shores of Lake Victoria, at twelve time points

across three years from baseline. These schools are being revisited in February and March 2013, 10 years after the mass drug administration programme began, and epidemiological and parasitological data collection pre-, one-week-post- and four-weeks-post-PZQ-treatment will be repeated. At the 2003 baseline, 80.6% of children still excreted eggs 1 week post-treatment with 40 mg/kg PZQ, and 39.9% of these had counts >100 eggs per gram. Four weeks post-treatment 23.9% of children were still excreting eggs with 2.9% having counts >100 epg. Prevalence returned to baseline levels at six months, one year, one year six months and three years. Mean infection intensity remained lower than baseline, but was above 100epg at six months, and one, two and three years. Reported side-effects were less in children who had previously reported ill health, whilst anaemia was associated with a reduced egg reduction rate (ERR) in comparison with non-anaemic children. Epidemiological and parasitological data collection from 2013 will be presented here in comparison to the baseline findings.

09/04/2013 Session 3C - General Parasitology - Chair Judith Smith 3:00 PM - 3:15 PM (15 mins)

The exploitable strengths and weaknesses of phospholipid metabolism in Trypanosoma brucei.

Simon A. Young, Terry K. Smith

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Lipids are essential structural components in the membranes of all cellular organisms. However many lipids also have distinct functional roles in metabolic, developmental and signal transduction pathways in the cell. In Trypanosoma brucei, the causative agent of human African trypanosomiasis, the major lipid species phosphatidylcholine (PC) and sphingomyelin (SM) are essential structural and functional membrane components of this protozoan parasite. Unlike humans, T. brucei lack the ability to synthesise PC via methylation of phosphatidylethanolamine, and thus generate PC exclusively de novo via the Kennedy pathway from choline. We have genetically validated the sole choline kinase as a drug target in the bloodstream form, both in culture and in a mouse model, confirming T. brucei is vulnerable to the inhibition of key enzymes in PC metabolism. SM is the primary sphingolipid in T. brucei membranes and we have genetically validated the neutral sphingomyelinase (TbnSMase), catabolising SM to generate ceramide. In the bloodstream form of the parasite, ceramide formation in the ER by the TbnSMase is essential for the post-Golgi sorting and exocytosis of newly synthesised GPI-anchored variant surface glycoprotein (VSG) to the cell-surface. In the non-VSG expressing procyclic insect form T. brucei we show that the TbnSMase has an alternative but essential role in the maintenance of a distinct metabolic pathway, an equally critical function when extrapolated to the physiological situation in the tsetse fly vector.

09/04/2013 Session 3C - General Parasitology - Chair Judith Smith 3:15 PM - 3:30 PM (15 mins)

Parasite-vector interactions I - Chair Paul Bates

Mosquito responses to malaria parasites

Elena Levashina, Elena A. Levashina

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Malaria is the most devastating infectious disease which is exclusively transmitted by mosquitoes of the Anopheles genus. Disease transmission reposes on an intricate interplay between 3 organisms - the human, the Plasmodium parasite and the mosquito. A series of biological features renders a limited number of Anopheles species very efficient vectors of Plasmodium parasites, the causative agents of malaria. These include a genetically determined preference for blood meals on a human host for egg development, a high reproductive rate and a long life span, combined with the ability to support parasite development. On the other hand, malaria parasites have developed sophisticated strategies to evade the mosquito immune system, to cope with a changing environment and to increase the success of infection in both human host and the mosquito vector. Here, we will summarize our recent advances in the unraveling the molecular bases of mosquito responses to Plasmodium, and highlight the mosquito and parasite factors that determine outcome of infection.

09/04/2013 Session 4C - Parasite-vector interactions I - Chair Paul Bates 4:10 PM - 4:40 PM (30 mins)

Temperature during larval development and adult maintenance influences Anopheles gambiae s.s. survival

Céline D. Christiansen-Jucht, Dr. Paul E. Parham Prof. Jacob Koella Mr. Adam Saddler Prof. María-Gloria Basáñez

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Malaria transmission depends on vector population dynamics and life-history parameters, particularly survival. These factors are sensitive to climatic and environmental factors, and temperature is known to be a particularly strong driver. We investigated the effect of environmental temperature during larval and adult stages on the survival of adult Anopheles gambiae s.s.. Six hundred juveniles were reared at different, constant temperatures (23°C, 27°C, 31°C, and 35°C), reflecting those at which malaria transmission typically occurs in endemic and epidemic areas. Upon emergence as adults, mosquitoes were either kept at the same larval

temperature, or placed at a different temperature: 23°C larvae, for example, were kept at 23°C, or moved to 27°C, 31°C, or 35°C as adults. Larval and adult survival data were then subjected to (a) non-parametric analyses (Kaplan-Meier analysis, log-rank testing) and (b) the fitting of parametric functions. This exposure to temperature combinations allowed us to disentangle the effects of larval versus adult temperatures on adult survival. While environmental temperature during the larval stages influenced larval survival, and environmental temperature during the adult stages influenced adult survival, larval development temperature also markedly affected adult survival. This is particularly important as, of all the vector parameters, adult survival influences transmission intensity substantially, yet current estimates of the malaria basic reproduction number do not account for larval environmental conditions on adult survival. Our data also suggest that larval and adult temperatures may also affect other parameters including size, oviposition rate, blood feeding, hatching rate, and developmental rate.

09/04/2013 Session 4C - Parasite-vector interactions I - Chair Paul Bates 4:40 PM - 4:55 PM (15 mins)

Cattle Ticks and Tick-borne Diseases in central Nigeria

Vincenzo Lorusso , Vincenzo Lorusso, Kim Picozzi, Ayodele Majekodunmi, Goni Dogo, Gyang Balak, Charles Dongkum, Augustine Igweh, Sue Welburn

Plateau State (Nigeria) The University of Edinburgh, Edinburgh (UK)

Introduction Ticks and tick-borne diseases (TBDs) undermine cattle fitness and productivity in the whole of sub-Saharan Africa, including Nigeria. This study aimed to assess the occurrence of ticks and TBDs in cattle in an area of central Nigeria where no acaricidal treatment has historically been employed, in order to help the design of area specific targeted control interventions. Methods The study was carried out in 9 villages in the Plateau State. In October 2010, adult ticks were collected from at least 15 indigenous (Bos indicus) cattle in each village (n=228). Collected ticks were kept in 70% ethanol and morphologically identified. In addition, a molecular screening for TBDs by means of polymerase chain reaction and reverse line blot hybridization was carried out on blood samples collected in October 2008 from 712 cattle of the same villages. Results Eleven ixodid species were identified, belonging to genera of great veterinary importance such as Amblyomma, Hyalomma, and Rhipicephalus (sub-genus Boophilus included). No Rhipicephlaus (Boophilus) microplus was retrieved, suggesting that the eastward expansion within West Africa of this tick species has not yet reached central Nigeria. Ten different TBDs were detected, with high frequency of co-infections with two or more microorganisms. Amongst others, the high prevalence (>30%) found for Anaplasma marginale and Theileria mutans poses a threat to the introduction of exotic breeds. Moreover, the lower prevalence recorded for Babesia bigemina (<10%), Anaplasma centrale, Babesia bovis, and Ehrlichia ruminantium (<5%) highlights their involvement in the episodic outbreaks of acute disease in the indigenous cattle population.

09/04/2013 Session 4C - Parasite-vector interactions I - Chair Paul Bates 4:55 PM - 5:10 PM (15 mins)

Tick-borne parasite dynamics in a water vole metapopulation

Claire Davies, Claire Davies Xavier Lambin Sandra Telfer

The University of Aberdeen

Animal populations often exhibit patchy distributions in space as a result of heterogeneous resource distribution or social aggregation. This patchiness can have profound influences on parasite dynamics by changing contact rates and forcing more localised transmission. Metapopulation theory demonstrates that both the within-patch dynamics and between-patch host dispersal can play a role in determining parasite spread and persistence. However, in the case of generalist parasites or vector-borne micro-parasites, parasite dynamics will also be influenced by the distribution, abundance and movement patterns of alternative hosts or vectors. Using a well characterised water vole (Arvicola amphibius) metapopulation in Scotland, I will examine what factors influence the abundance of two tick species (Ixodes ricinus and Ixodes trianguliceps) and the prevalence of a generalist tick-borne protozoan (Babesia microti). Specifically, I will explore the relative importance of host metapopulation structure; including patch population size and between-patch connectivity, the distribution of an alternative host (field vole, Microtus agrestris), and the importance of current and past tick distribution and abundance, on water vole infection.

09/04/2013 Session 4C - Parasite-vector interactions I - Chair Paul Bates 5:10 PM - 5:25 PM (15 mins)

Bridging Scales in Disease Ecology - Chair Jess Metcalf

Linking the ecology and evolution of HIV across multiple scales

Katrina Lythgoe, Katrina Lythgoe

Imperial College London

Pathogens can often face conflicting selection pressures at different ecological scales. For example, traits that maximise the competitive ability of pathogens within hosts might reduce their ability to transmit between hosts, a process commonly referred to as ‘short-sighted’ evolution. Using HIV as an example, I show how disentangling how the virus evolves at different ecological scales can give us important new insights into the biology of pathogens. A fundamental question in HIV biology is why it has evolved an intermediate level of virulence that maximises its between-host fitness, despite ample opportunity for the virus to evolve during the course of an infection. Applying a nested modelling framework to HIV, we have found that if replication rates have limited opportunity to evolve during the course of an infection, as preliminary data suggests, HIV virulence will evolve to a level that is only marginally higher than the level that maximizes the between-host fitness of the virus. An intriguing alternative explanation is that HIV might effectively bypass within-host evolution by preferentially transmitting ‘ancestral’ strains of the virus that kicked off the infection in the first place. This ancestral virus probably persists at a low frequency within hosts due to the cycling of virus through very long-lived memory CD4+ T-Cells. This might not only explain why virulence is heritable from one infection to the next, but might also explain the puzzling observation that HIV evolves much faster within individuals than it does

at the epidemiological level.

09/04/2013 Session 1D - Bridging Scales in Disease Ecology - Chair Jess Metcalf 9:00 AM - 9:30 AM (30 mins)

Parasite induced changes in individual host life-history trait, do they scale to population level changes?

Joanne Lello, Joanne Lello, 1 Jo Cable 1, Joanna Randall2

1. Cardiff University, School of Biosciences, UK 2 Lancaster University, Lancaster Environment Centre, UK

Endemic parasites can influence both individual host survival and fecundity and such effects will then result in population level change. However, environmental influences may alter the individual effects, making estimation of population dynamics from individual based data problematic. Here we use a model host parasite system, the German cockroach, and one of its endemic gut parasites, to assess such scaling issues. We assessed individual level changes in host life-history traits following experimental infection and used these data to parameterise a population dynamic model. We then compare the model predictions to the population dynamics from infected and uninfected colonies. We find that even under these fairly controlled laboratory conditions, scaling is not simple and we discuss potential reasons for the differences observed.

09/04/2013 Session 1D - Bridging Scales in Disease Ecology - Chair Jess Metcalf 9:30 AM - 9:45 AM (15 mins)

The ecology of timing in host-parasite interactions: probing the particulars of periodicity in Plasmodium parasites

Aidan O'Donnell, Aidan J. O'Donnell, Nicole Mideo & Sarah E. Reece 1

Aidan & Sarah: Institutes of Evolution, Immunology and Infection Research, University of Edinburgh, Edinburgh, UK Nicole : Centre for Infectious Disease Dynamics, Pennsylvania State University, USA

Circadian rhythms are thought to have evolved to enable organisms to organise their activities according to the Earth's predictable daily cycles, but data quantifying the benefits of circadian rhythms are scarce. Our previous work has found that perturbation of Plasmodium chabaudi parasite rhythms resulted in a two-fold cost to the production of stages responsible for in-host survival and stages required for between-host transmission, revealing a role for circadian rhythms in the evolution of host-parasite interactions. The coordination of parasite and host rhythms could be controlled by parasites, hosts, or both parties. We experimentally investigated the roles of hosts and parasites by asking if parasites have evolved to time their cell cycle progression to avoid producing the most vulnerable developmental stage at the time of peak immune activity. Specifically, we tested whether rhythms in mammalian innate immune defence play a role in protection from infection, and whether parasite developmental stages differ in their vulnerability to rhythmic host defences. Our data demonstrate that timing matters for parasite success, but this

is not due to rhythms in host barriers to infection or how they interact with parasite developmental stages. We discuss other aspects of host circadian physiology that affect the performance of parasites during infections and may explain the evolution of periodicity in parasites.

09/04/2013 Session 1D - Bridging Scales in Disease Ecology - Chair Jess Metcalf 9:45 AM - 10:00 AM (15 mins)

Contact networks for pathogen transmission in field voles

Mike Begon, Mike Begon, Stephen Davis, Babak Abassi, Shrupah Shah and Sandra Telfer

University of Liverpool; RMIT, Melbourne, Australia; University of Aberdeen

The dynamics of transmission are central to the dynamics of infection. The transmission process operates at the individual level. Its outcomes are played out in whole populations. Contact networks may link the two. Previous work has used population time series data to infer details of the transmission of cowpox virus in field voles in Kielder Forest. Here, new analyses of contact networks for these field voles are presented for comparison with those inferences. The average contact rate is positively correlated with density, independently of season, providing empirical support for the density-dependent contact rate assumption common to many mathematical models for infectious disease dynamics. However, the strength of spatial constraints on contact rates also increases with density. For the pathogens negotiating these contact networks, spatial constraints have a dampening effect on transmission because of local build-up of infected and recovered animals. Furthermore, important heterogeneities in transmission potential between individuals are suggested, the degree of which varies with season. These results suggest that there may be large differences between the contact processes in wildlife populations and the assumptions regularly used in mathematical models for wildlife disease.

09/04/2013 Session 1D - Bridging Scales in Disease Ecology - Chair Jess Metcalf 10:00 AM - 10:30 AM (30 mins)

Life histories of hosts and parasites - Chair Sarah Recce

Ecology of a host-pathogen interaction: African armyworm and its virus

Kenneth Wilson, Kenneth Wilson, Robert I Graham, Wilfred Mushobozi & David Grzywacz.

Lancaster University, U.K., EcoAgriConsult Ltd., Tanzania & University of Greenwich, U.K

African armyworm is a major pest of maize, rice and other cereal crops in sub-Saharan Africa, and SpexNPV (a highly host-specific baculovirus) is being developed as a potential biological control agent against it. SpexNPV may kill >90% of insects in natural virus epizootics, but the prevalence of disease shows considerable spatio-temporal variation. Here, I will present our research aimed at understanding the ecology of this host-pathogen interaction in Tanzania, with a view to gaining a better understanding the natural disease dynamics and how bestter to deploy SpexNPV as a biopesticide. I show that disease dynamics is a complex interaction between the environment

(especially, the seasonal pattern of rainfall), host dynamics (and its interaction with the seasonal rains), virus dynamics (horizontal and vertical transmission, covert low-intensity infections, strain variation), host phenotypic plasticity (including density-dependent prophylaxis), and interactions with other species (including the obligate intra-cellular bacterium, Wolbachia pipientis).

09/04/2013 Session 2D - Life histories of hosts and parasites - Chair Sarah Recce 11:10 AM - 11:40 AM (30 mins)

A microcosm approach to understand the effects of host life-history variation on disease transmission

Anaid Diaz, Olivier Restif

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One key aspect of the evolution of virulence is the rate of transmission between susceptible hosts. In theory, a virulent strain may increase in frequency if selection favours its transmission. However, it is not always know what host traits positively select for transmission and how individual variation and population demography affect its evolution. We are working with an experimental system in which specific aspects of infectious disease dynamics can be measured. We use the nematode Caenorhabditis elegans and fluorescent pathogenic bacteria (Salmonella enterica Typhimurium) to tract the spread of infection. In the soil, C. elegans lives in contact with many microorganisms, including pathogenic bacteria. It is known that similar to the mammalian innate immune response, C. elegans is able to mount a response to Salmonella. Despite this, Salmonella can colonise the worm intestine and increases death. Yet, it is not understood if and how the pathogenic effects of Salmonella can contribute the transmission of the disease in a population. We have characterised in detail C. elegans demography in response to the pathogen and varying conditions (i.e. age of infection, worm population size and genetic background). As reported before we found that Salmonella reduces worm survival. However, we found no decrease in the reproduction as a consequence of the pathogen, but a strong negative population density-dependence feedback on C. elegans. As a consequence of the high bacteria shedding of worms and little effects on its reproduction, Salmonella is very likely to thrive in the population.

09/04/2013 Session 2D - Life histories of hosts and parasites - Chair Sarah Recce 11:40 AM - 11:55 AM (15 mins)

Integrating life-history and host-parasite biology: maternal effects on body size and feeding rate influence susceptibility to a parasite in Daphnia magna.

Jennie Garbutt, Jennie S. Garbutt, Philip J. Wilson and Tom J. Little

Institution of Evolutionary Biology, University of Edinburgh

Variations in life-history can influence the probability that a host becomes infected and therefore the evolutionary ecology of host-parasite interactions. In organisms that encounter parasites whilst they eat, body size and feeding rate may be especially important in determining infection outcome. We studied how body size, as well as age and maternal food treatment (both factors

which affect body size), influenced the probability that the crustacean Daphnia magna will become infected following exposure to Pasteuria ramosa, a bacterial parasite picked up during filter feeding. Older animals and those born of food restricted mothers (both of which were relatively large) were more resistant to the parasite, but within each age class, larger individuals were more likely to become infected. We present a simple mechanistic explanation for the maternal effect of food on parasite resistance: feeding rate experiments revealed that the offspring of low-food mothers consume algae at a reduced rate, and these hosts are therefore likely to consume fewer parasite spores and receive a smaller infective dose. This study demonstrates that quite small maternal-environment-mediated changes in resource acquisition can have marked consequences for parasite resistance, highlighting the link between life-history and host-parasite interactions.

09/04/2013 Session 2D - Life histories of hosts and parasites - Chair Sarah Recce 11:55 AM - 12:10 PM (15 mins)

Immune memory in insect parasite defence

Matt Tinsley, Matt Tinsley, Niki McAllister, Danielle Mackenzie

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Unlike vertebrates, insects lack an acquired immune system, instead relying on classically innate immune mechanisms to defend against parasites. However, recent studies indicate that prior immune challenges can provide insects with some protection against subsequent pathogenic encounters. Nevertheless, the mechanisms underpinning this specific protection have remained relatively unclear. We have studied the Drosophila melanogaster cellular immune response and have found that it displays impressive immune memory. 'Priming' flies with injections of individual microbes considerably enhanced immune cell phagocytic activity. This response was specific to the priming microbe and persisted for at least two weeks. Further, we found that aged flies are less able to form immune memories, providing a clear parallel with senescence of the acquired immune response in vertebrates. Our data show that this specific immune enhancement against one microbe, also impairs phagocytic efficacy against novel immune challenges, creating a potentially costly trade-off to forming immune memories. Our work establishes a clear mechanistic basis for specific immune memory in insects. These findings have clear fundamental implications for the evolutionary ecology of insect disease, and strong applied relevance to the control of insect pests and the parasites they vector.

09/04/2013 Session 2D - Life histories of hosts and parasites - Chair Sarah Recce 12:10 PM - 12:25 PM (15 mins)

Experimental analysis of factors influencing helminth reproduction

Richard Tinsley, Richard Tinsley, Lucy Stott and Matthew Tinsley

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Helminth infection success may be regulated by environmental factors including climate variables, host condition, immune effects and within-host interactions between conspecific parasites. This study investigated the sensitivity of helminth reproduction to specific factors using the monogenean Protopolystoma xenopodis in Xenopus laevis. Experimental laboratory infections, set up with samples from a natural population, were designed to minimize host and environmental variation: recipient hosts were lab-raised from a single sibship and maintained in constant conditions including temperature. Data demonstrated major heterogeneity in reproductive characteristics despite standardised environmental conditions; this heterogeneity (including worm burden, developmental rate, time to patency, egg output) would have a major influence on transmission in the wild. Polystomatid monogeneans occupy a spatially-confined habitat, the urinary bladder, and several published studies have reported strong density-dependent competitive effects. However, our data show no evidence of negative effects of density on reproduction. Instead, highest per capita egg output occurred in larger burdens, where worms had faster development and larger body size. These effects contradict accepted interpretation of competition and are more likely to reflect host x parasite genotype interactions. Controlled infections of different sibships of hosts produced marked differences in worm performance (including growth and egg production) confirming host-parasite genetic interactions. Between-sibship differences were equivalent to the outcome of parallel infections of a single sibship maintained at different temperatures (20 and 25°C). So, the influences on reproduction of genetic differences present within existing host and parasite populations are of similar magnitude to those that

09/04/2013 Session 2D - Life histories of hosts and parasites - Chair Sarah Recce 12:25 PM - 12:40 PM (15 mins)

Parasite and host behaviours - Chair Richard Tinsley

Ecology and Evolution of bodyguard manipulations

Thomas Frederic , Thomas Frederic

University of Lancaster

Among the different strategies used by parasites to usurp the behaviour of their host, one of the most fascinating is the bodyguard manipulation. In certain parasitic wasps, larvae egress from the host to pupate and subsequently induce their hosts to behave as true “bodyguards”: hosts remain close to the parasitoid pupae and display a range of aggressive/defensive behaviours that protect cocoons against natural enemies. In spite of extensive research on manipulative organisms, bodyguard manipulations are among the less explored ones. I will first document a novel case of bodyguard manipulation, and also provide evidence that this manipulation comes with a cost for the parasite. Then, from this specific example, I will discuss two ideas. I will first argue that a potentially large number of host manipulations that are multidimensional possess a ‘bodyguard’ dimension, so that she should extend the current definition of bodyguard manipulation. Secondly, I will discuss the idea that the energy required to accomplish parasite induced behaviours may represent a key energetic constraint for parasites. Depending on the energetic expenditures specific to each type of manipulation, parasites should be selected to secure resources for their host to allow them to perform manipulated behaviours.

09/04/2013 Session 3D - Parasite and host behaviours - Chair Richard Tinsley 2:00 PM - 2:30 PM (30 mins)

The role of Toxoplasma gondii-produced tyrosine hydroxylase (TgTH) in parasite manipulation of host behaviour

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The predilection of Toxoplasma gondii cysts for the brain of its intermediate rodent host places it in a privileged position to manipulate host behaviour through a variety of mechanisms, increasing the chance of successful transmission to its definitive feline host. Using the epidemiologically and clinically applicable rat-T. gondii model, and incorporating a range of both novel and classical non-invasive behavioural and physiological assays, our overall prediction was that the parasite is manipulating its host, at least in part, via T. gondii-produced tyrosine hydroxylase (TgTH), an enzyme involved in the synthesis of various neuromodulators including L-DOPA, dopamine, and noradrenaline. Preliminary results indicate that TgTH may be involved in increasing activity levels within the host, but may not be exclusively involved in the specific response to feline odour observed in infected rats. There may be evidence that TgTH influences the host via elevated noradrenaline levels. Gender-specific effects of T. gondii are seen which involve interactions between infection, gender and potentially testosterone levels. These initial results support the hypothesis that TgTH plays a part in the mechanism involved in behavioural alterations that may facilitate parasite transmission, but that additional mechanisms of action may be involved in the specific 'fatal feline attraction' to the parasite's definitive host. This is further evidence for the complexity of the evolution of parasite manipulation within the mammalian brain, which is likely to involve multiple pathways to maximise transmission success. These results will be discussed in terms of their theoretical and applied implications.

09/04/2013 Session 3D - Parasite and host behaviours - Chair Richard Tinsley 2:30 PM - 2:45 PM (15 mins)

Predation, Parasitism and Parental Care: Factors affecting brooding in amphipod crustaceans

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In amphipods, active brood-care may involve specialised motions by the female, to enhance aeration of the brood pouch. The frequency of these ventilation behaviours has been shown to increase in response to reduced oxygen availability, indicating a phenotypically plastic response. Active brood-care is energetically costly and may increase predation risk for ovigerous females. Therefore, the amount of brood-care performed by females is likely to be the result of a trade-off between maximising reproductive success and avoiding predation. We report the first investigation into the impact of predator cues and parasitism on brooding in amphipod

crustaceans. We found no evidence for any reduction in brooding behaviour or reproductive success in response to microsporidian infection, but this is perhaps to be expected in vertically transmitted parasites, which rely on reproduction for transmission to the next generation. Interestingly, we found some evidence for changes in broodcare behaviour in response to predator cues. Larger C. pseudogracilis females, with higher O2 demands for their broods, seemingly need to trade-off brood care with predator avoidance. Additionally, G. duebeni were found to reduce intermoult duration in response to predator cues, thus reducing brooding duration. We suggest that this is likely to enhance survival of the brood, by spreading the risk of predation on juveniles.

09/04/2013 Session 3D - Parasite and host behaviours - Chair Richard Tinsley 2:45 PM - 3:00 PM (15 mins)

Information use and plasticity in the transmission strategies of malaria parasites

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Parasites live in the bodies of others – with whom they are engaged in a life-and-death struggle – yet, how parasites cope with the challenges of their lifestyle is poorly understood. Malaria parasites face a resource allocation trade off that is common to all sexually reproducing organisms: between investing in sexually reproducing stages (required for between-host transmission) and in asexually replicating stages (required for within-host survival). There is mounting evidence that malaria parasites adjust levels of investment into sexual and asexual stages (reproductive effort) in response to changes in the in-host environment (including resource availability, competition from conspecifics, and drug treatment). This plasticity in reproductive effort appears to be adaptive, in which parasites strategically prioritise investment in sexual or asexual stages according to the impact of in-host factors on parasite proliferation (state). Here, we ask what information parasites use to detect changes in the in-host environment, by experimentally testing how parasites in single clone infections respond to treatments 'mimicking' conditions of resource-limitation, high parasite density, and mixed-clone infections. Our results show that parasites respond to the presence of others and use this as a cue for their 'state', which we define as the integrative effect of all in-host environmental factors on proliferation rate. Understanding how and why parasites adjust their reproductive effort is important because this trait is a key component of disease severity and epidemiology. Likewise, explaining how parasites have evolved to cope with variable conditions experienced during infections is central to making medical interventions as “evolution-proof” as possible.

09/04/2013 Session 3D - Parasite and host behaviours - Chair Richard Tinsley 3:00 PM - 3:15 PM (15 mins)

The evolution of communication and virulence in a pathogen

Roman Popat , Roman Popat

University of Edinburgh

Organisms use signals to coordinate a wide range of behaviours, from feeding offspring to predator avoidance. In particular pathogenic bacteria can use signals to coordinate pathogenesis. This poses an evolutionary problem, because individuals could potentially signal dishonestly to coerce others into behaving in a way that benefits the signaller. Theory suggests that honest signalling is favoured when individuals share a common interest and signals carry reliable information. However, whilst many studies have manipulated signals, to examine how this influences behaviour, it has not been possible to directly test how the behaviour of signallers and receivers evolve in response to manipulation. Here, we exploit the opportunities offered by signalling between bacteria ('quorum sensing') to show that a reduced relatedness, and therefore reduced common interest between interacting individuals, leads to the relative breakdown of signalling. The populations evolved under a lower relatedness caused less mortality and damage to insect hosts, showing how signal evolution leads to strain diversity influencing the evolution of virulence in the opposite direction to that usually predicted by theory. Whilst our results provide clear support for signalling theory, we did not find evidence for the previously predicted coercion at intermediate relatedness, suggesting that mechanistic details can alter even the qualitative nature of specific predictions. We are now investigating the mechanistic constraints to coercive signalling in quorum sensing.

09/04/2013 Session 3D - Parasite and host behaviours - Chair Richard Tinsley 3:15 PM - 3:30 PM (15 mins)

Population Ecology and Evolution - Chair Matt Tinsley

A symbiont-mediated shift in the ecology and evolution of host-parasite interactions

John Jaenike, John Jaenike

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Innumerable insects and other arthropods are infected with maternally-transmitted endosymbionts. Some of these spread and persist by manipulating host reproduction, but many have no such effects, and the means by which they are retained within species is unknown. Drosophila neotestacea carries endosymbiotic Spiroplasma bacteria, which render female flies resistant to the sterilizing effects of nematode parasitism. The prevalence of Spiroplasma infection in D. neotestacea has risen in the eastern US in recent decades, and the infection is now spreading rapidly from east to west across North America. The increase in Spiroplasma has been accompanied by a dramatic decline in the prevalence of nematode parasitism, due, perhaps, to the lower reproductive rate nematodes withinSpiroplasma-infected flies. Experimental infection of other Drosophila species with Spiroplasmaresulted in high levels of maternal transmission, and, in one species, restoration of fertility to nematode-parasitized flies. Finally, infection of D. neotestacea with strains Spiroplasma obtained from otherDrosophila species revealed that only the strain native to D. neotestacea confers any resistance to nematode parasites. Comparative

analysis of these Spiroplasma strains may shed light on the underlying genetic basis for resistance to nematode parasitism.

09/04/2013 Session 4D - Population Ecology and Evolution - Chair Matt Tinsley 4:10 PM - 4:40 PM (30 mins)

Avian Malaria infections reinforce competative asymmetry between two Ficedula Flaycatchers in a recent contact zone.

Katarzyna Kulma , Katarzyna Kulma, Matthew Low, Staffan Bensch, Anna Qvarnstrom

Uppsala University

Parasites may influence the outcome of interspecific competition between closely-related host species through lower parasite virulence in the host with which they share the longest evolutionary history. We tested this idea by comparing the prevalence of avian malaria (Haemosporidia) lineages and their association with survival in pied and collared flycatchers (Ficedula hypoleuca & F. albicollis) breeding in a recent contact zone on the Swedish island of Öland. A nested PCR protocol amplifying haemosporidian fragments of mtDNA was used to screen the presence of malaria lineages in 1048 blood samples collected during 6 years. Competitively inferior pied flycatchers had a higher prevalence of blood parasites, including the lineages that were shared between the two flycatcher species. Multistate mark-recapture models revealed a much lower survival of infected versus uninfected female pied flycatchers, while no such effects were detected in male pied flycatchers or in collared flycatchers of either sex. Our results show that a comparatively new host, the collared flycatcher, appears to be less susceptible to a local northern European malarial lineage where the collared flycatchers have recently expanded their distribution. Pied flycatchers experience strong reproductive interference from collared flycatchers, and the additional impact of species-specific blood parasite effects adds to this competitive exclusion. These results support the idea that parasites can strongly influence the outcome of interspecific competition between closely-related host species, but that the invading species need not necessarily be more susceptible to novel parasites.

09/04/2013 Session 4D - Population Ecology and Evolution - Chair Matt Tinsley 4:40 PM - 4:55 PM (15 mins)

Phylogenetic determinants of host shifts

Ben Longdon, Ben Longdon, Jarrod D Hadfield, Claire L Webster, Darren J Obbard and Francis M Jiggins

University of Cambridge

Pathogens switching to new hosts can result in the emergence of new infectious diseases, and determining which species are likely to be sources of such host shifts is essential to understand disease threats to both humans and wildlife. However, the factors that determine whether a pathogen can infect a novel host are poorly understood. We have examined the ability of three

host-specific RNA-viruses (Drosophila sigma viruses from the family Rhabdoviridae) to persist and replicate in 51 different species of Drosophilidae. Using a novel analytical approach we found that the host phylogeny could explain most of the variation in viral replication and persistence between different host species. This effect is partly driven by viruses reaching a higher titre in those novel hosts most closely related to the original host. However, there is also a strong effect of host phylogeny that is independent of the distance from the original host, with viral titres being similar in groups of related hosts. Most of this effect could be explained by variation in general susceptibility to all three sigma viruses, as there is a strong phylogenetic correlation in the titres of the three viruses. These results suggest that the source of new emerging diseases may often be predictable from the host phylogeny, but that the effect may be more complex than simply causing most host shifts to occur between closely related hosts.

09/04/2013 Session 4D - Population Ecology and Evolution - Chair Matt Tinsley 4:55 PM - 5:10 PM (15 mins)

Investigation into the distribution of Toxoplasma gondii infection in wild mammal populations using microsatellite DNA analysis of hosts

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Toxoplasma gondii is a ubiquitous parasite which affects all warm blooded animals as an intermediate host. The cat is the definitive host and transmission from cats occurs by ingestion of oocysts or by carnivory between secondary hosts. However, these transmission routes do not fully explain the ubiquity of the parasite and there is evidence to suggest that vertical transmission may be more important than previously thought. If this is the case then the expectation would be that the parasite would be associated with family units in natural populations. A total of 126 wood mice (A. sylvaticus) were sampled, using Longworth Traps, from the surrounding area of Malham Tarn Field Centre (Tarn Woods, Tarn Fen, Ha Mire and Spiggot Hill), North Yorkshire over a 2 year period. DNA was successfully isolated from all 126 mice brains and tested for the presence of T gondii (tested by B1, SAG1 SAG2, and SAG3). Positive amplifications in 40 of the 126 samples demonstrated the prevalence of Toxoplasma infection to be 31.74%. The genotyping of the parasite confirmed that only type III was present. The assignment test in STRUCTURE revealed that our four sampling areas represent three populations. The results indicate that the wood mice from all areas are genetically related but fragmentation of the populations is observed. The high prevalence of T. gondii infection and the presence of only one genotype in the area almost free of cats suggested that one possible transmission route that could maintain these relatively high prevalences is congenital

09/04/2013 Session 4D - Population Ecology and Evolution - Chair Matt Tinsley 5:10 PM - 5:25 PM (15 mins)

A perturbation experiment to investigate between-species transmission of Bartonella spp. in woodland rodent communities.

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Many parasites infect multiple host species. This is an important property, relevant to both novel disease emergence and the maintenance of endemic disease in ecological communities. Predicting future disease emergence, and understanding disease maintenance, requires an appreciation of the ecological mechanisms underlying transmission between multiple host species. For example, interactions between hosts and parasites, infection seasonality, and interactions between co-infecting parasites may all be implicated in determining the likelihood, and rate, of between-species transmission. Here I present preliminary results of a perturbation experiment in which we aimed to reduce between-species transmission of flea-borne bacterial blood parasites (Bartonella spp.) within natural woodland communities of bank voles (Myodes glareolus) and wood mice (Apodemus sylvaticus). At least five "species" of Bartonella circulate within these rodent communities, and seasonal prevalence data suggest varying levels of host-specificity and therefore potentially differing levels of between-species transmission. To test this, we administered an insecticide to all voles caught on experimental grids, to prevent fleabites and therefore vector transmission of Bartonella to wood mice. Combined with phylogenetic analysis of co-circulating Bartonella genotypes, the results of this experiment will provide novel insights into the way that transmission processes within and between multiple host populations interact and underlie emergent epidemiological measures such as prevalence, infection intensity and duration of infection.

09/04/2013 Session 4D - Population Ecology and Evolution - Chair Matt Tinsley 5:25 PM - 5:40 PM (15 mins)

Parasites and food security (BAVP) - Chair Eric Morgan

Trematode infections in cattle under different management strata in Meru district

Jahashi Nzalawahe, 1). A.A. Kassuku, 2). J.R. Stothard, 3). G.C. Coles 4). M.C. Eisler and 5). J., Nzalawahe 1&5)Department of Veterinary Microbiology and Parasitology, Sokoine University of Agriculture, Morogoro, Tanzania. (2)Liverpool School of Tropical Medicine, Liverpool, UK. (3&4)School of Veterinary Sciences, University of Bristol, Langford house, Langford, Bristol, UK

Meru District, Arusha Region, northern Tanzania

A study was conducted to determine prevalence of trematode infections in cattle at Meru district Arusha Region, northern Tanzania. Selected villages were grouped into three cattle management strata, (i) all year round zero grazing (ZZ) (ii) zero grazing during the rainy season and communal grazing during the dry season (ZC) and (iii) zero grazing during the rainy season and Communal grazing during the dry season with concurrent irrigation activities (ZCI). The prevalence for paramphistomosis, fasciolosis and schistosomosis for each stratum were, ZZ (36%, 29.7% and 0%), ZC (15%, 6.25%, and 3.8%) and ZCI (56.7%, 57.7%, and 1.03%) respectively. The ZCI stratum had higher prevalences of fasciolosis (58%) and paramphistomosis (57%) compared to ZZ (30% and 36%) and ZC (6.3% and 15%) strata, while the ZC stratum had a higher prevalence of schistosomosis (3.8%) than the ZCI (1.0%) and ZZ (0%) strata. The differences between strata were

significant for fasciolosis ($p<0.001$) and paramphistomosis ($p<0.05$) but not for schistosomosis. The high prevalence of fasciolosis and paramphistomosis in the ZCI stratum as compared to ZZ and ZC strata could be accounted for by the irrigation activities during the dry season when cattle were unconfined. The higher prevalences of fasciolosis and paramphistomosis in ZZ stratum to the ZC stratum were unexpected and attributed to the practice of farmers in ZZ stratum buying fodder for their cattle obtained from pastures in ZCI villages infected with metacercaria of Fasciola and Paramphistomum species. Sourcing fodder from alternative areas might provide an opportunity for control.

10/04/2013 Session 5A - Parasites and food security (BAVP) - Chair Eric Morgan 9:30 AM - 9:45 AM (15 mins)

Assessment and Management of emerging nematode pests of Northern Ireland grassland and cereals

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Plant parasitic nematode (PPN) damage in pastures and cereals is often subtle and difficult to detect, however when combined with abiotic stresses, crop damage can be significant. There is currently little information on the PPN species present in Northern Ireland pasture and cereal fields, but given the reliance of NI agriculture on these crops and the expected future increases in average soil temperature, the impact of these parasites is of increasing concern. This research project will determine which PPNs are currently causing crop damage and identify those species likely to emerge as more serious pests in the future. Initial sampling data across a range of soil types has shown a diverse range of PPNs in agricultural land, including economically important species such as root knot nematodes (Meloidogyne naasi and M. minor) at unexpectedly high occurrence levels. The occurrence of these endoparasites appears to be increasing, highlighting them as the most likely threats to future crop production. Management of PPNs in pasture and cereal crops will be investigated using a range of approaches including plant resistance, biostimulants and fungal endophytes. Initial results on the use of biostimulants in enhancing growth in stressed cereals and grasses will be presented.

10/04/2013 Session 5A - Parasites and food security (BAVP) - Chair Eric Morgan 9:45 AM - 10:00 AM (15 mins)

Risky business: Worm control practices on UK cattle farms

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Anthelmintics are administered frequently to control gastrointestinal nematode infections in grazing cattle. However, little information has been published on the pattern of anthelmintic administration, alternative control measures adopted on UK cattle farms or sources of information on parasite control strategies. A questionnaire survey covering farm demographics, pasture management, anthelmintic usage and parasite control information sources were conducted on UK cattle farms (n= 84). A cohort of respondents (n=20) conducted faecal egg count reduction tests (FECRT) to investigate efficacy of ivermectin in first season grazing calves. General trends were examined within respondents as a whole and univariate analyses of risk factors associated with practices considered likely to select for anthelmintic resistance performed. In total, 62 questionnaires were from beef producers and the remainder from dairy or mixed cattle farms. Eighty-seven percent of all respondents had used a pour-on topical application in the past and 80% of respondents had used a macrocyclic lactone (ML) anthelmintic in the last year. Around one third of respondents never changed anthelmintic class used on their farm and 45% did not administer a quarantine anthelmintic treatment. Forty-four percent determined anthelmintic dose on individual weights or to the weight of the heaviest animal in the group. Through comparison of current best practice guidelines and on farm management practices, the information gathered here can help identify potential areas of “good” and “bad” practice and will direct future information dissemination, to ensure that the message of responsible anthelmintic usage is adopted.

10/04/2013 Session 5A - Parasites and food security (BAVP) - Chair Eric Morgan 10:00 AM - 10:15 AM (15 mins)

Resistant sheep select for increased fitness in their parasitic nematodes (Teladorsagia circumcincta): experimental evidence

Caroline Chylinski, Chylinski Caroline, Schmidt Enrique, Gruner Luca, Cabaret Jacques

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Gastrointestinal nematode species are the greatest parasitic threat to ruminant farming worldwide. By forcing evolution in the sheep host towards increased resistance to infection, we explored whether reciprocal adaptation would take place in the gastrointestinal nematode Teladorsagia circumcincta following five generations of exposure to resistant sheep. We evaluated T. circumcincta adaptation in terms of fitness i.e. their ability to survive and reproduce, by comparing various aspects of their life-history biology against T. circumcincta lines which were maintained in susceptible sheep. The results showed exposure to resistant sheep significantly increased the relative fitness of the T. circumcincta. While those traits pertaining to reproduction (fecundity) remained unchanged, their capacity to survive was significantly augmented both in the parasitic phase (establishment of infective larvae) and external free-living stages (egg to larval development on pasture). The results of this study provide the first known demonstration of gastrointestinal nematodes coevolving in their sheep host. These results carry important implications on the future disease dynamics of the infection should sheep which are selectively bred for gastrointestinal nematode resistance become a mainstay of control.

10/04/2013 Session 5A - Parasites and food security (BAVP) - Chair Eric Morgan 10:15 AM - 10:30 AM (15 mins)

Aquatic Parasitology - Chair Jo Cable

Life cycle complexity and disease ecology

Beth Okamura, Beth Okamura

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Proliferative kidney disease (PKD) causes widespread economic loss on fish farms and is an emerging disease in wild salmonid populations. The disease is thus relevant for both food security and fish conservation. Since all salmonids are susceptible, PKD may imperil some of our most iconic freshwater residents. Outbreaks of PKD are consistently linked with environmental change but understanding the ecology of PKD was greatly hampered until the discovery of the disease source - the myxozoan endoparasite, Tetracapsuloides bryosalmonae, which develops in colonial invertebrates (bryozoans). Freshwater bryozoans act as primary hosts of the parasite and are widely distributed but poorly known invertebrates that form spreading colonies on surfaces in both running and still water habitats. Our discovery of bryozoan hosts has opened up new research avenues to gain a better understanding of the ecology of PKD. We have focused in particular on examining host-parasite interactions through combined field and laboratory studies to identify the multiple drivers that underly the development and proliferation of both the parasite and its primary host. Collectively, our studies provide insights on the strategies that the parasite employs to exploit its highly clonal bryozoan hosts and how these, in turn, help us to understand recurrent disease outbreaks and observed patterns of disease spread. More fundamentally, by revealing the unique opportunities provided by colonial organisms for exploitation by parasites we demonstrate how life cycle complexity in both parasite and host contributes to the ecology of this emerging disease.

10/04/2013 Session 6A - Aquatic Parasitology - Chair Jo Cable 2:00 PM - 2:30 PM (30 mins)

Unravelling the riddle of Radix: DNA bar-coding of important intermediate hosts of digeneans of zoonotic importance in the UK

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Radix spp. (family: Lymnaeidae) are important in the transmission of numerous helminth parasites of medical and veterinary significance. Species identification based on shell morphology and anatomical traits is unreliable, resulting in systematic and taxonomic inaccuracy. A variety of molecular markers have therefore been deployed for vector species discrimination. In this study, COX 1 and ITS 2 markers were used to identify Radix species as part of a survey on digenean intermediate host diversity in the UK and to establish barcoding protocols to identify snail vectors. Populations of Radix spp. sampled from lakes in Hampshire, Norfolk and Surrey, and lochs in the

Scottish Highlands were identified as Radix auricularia (Linnaeus, 1758) or R. balthica (Linnaeus, 1758). Initial identification based on morpho-anatomical characters had described these snails as R. peregra (Müller, 1774) (=R. ovata (Draparnaud, 1805)). The genus Radix has a Palaearctic distribution, but probably an East Asian origin. Maximum likelihood (ML) phylogenetic analysis revealed two distinct lineages of R. auricularia, suggesting separate introductions of this species into the UK from northern and southern Europe. The ML tree for R. balthica, by comparison, showed less diversity and more recent and multiple colonization events from mainland Europe. COX 1 differentiated species to a higher resolution than ITS 2, and was able to differentiate between geographical lineages. Therefore, the standard international COX 1 barcode is proposed as the more reliable marker for snail species discrimination.

10/04/2013 Session 6A - Aquatic Parasitology - Chair Jo Cable 2:30 PM - 2:45 PM (15 mins)

Analysis of excretory/secretory cysteine proteases of Euclinostomum heterostomum (Digenea: Clinostomidae)

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Cysteine proteases of parasite organisms play numerous indispensable roles in tissue penetration, extracorporeal digestion, immunoevasion, virulence, egg hatching and metacercarial excystment. They are critical key enzymes in the biology of parasites and have been exploited as serodiagnostic markers, therapeutic and vaccine targets. In the present study, the cysteine proteases in the in vitro released excretory/secretory (ES) products of the digenetic trematode parasite, Euclinostomum heterostomum have been analysed. The encysted progenetic metacercariae of E. heterostomum collected from the infected liver and kidney of snake headed fish, Channa punctatus were excysted in vitro and incubated in phosphate buffer at 37±1 0C and the ES products released were analysed. The spectrophotometric analysis of the proteases revealed active hydrolysis of chromogenic substrate, Azocoll, in a time, temperature and pH dependant manner. Maximum activity was observed at pH 7.0 at 37±1 0C, and 1 mM each of various protease inhibitors (Mini Protease Inhibitor Cocktail, EDTA, PMSF, Iodoacetamide, 1,10-Phenanthroline) used, significant inhibition was observed by iodoacetamide and almost complete inhibition at a concentration of 2 mM, suggests that the cysteine protease is the major component in the ES of this parasite. Four discrete protease bands of Mr 36, 39, 43 & 47 kDa were identified by gelatine-substrate zymography. Maximum gelatinolytic activity was observed at pH 7.0, and among various inhibitors used, almost complete disappearance of protease bands was observed by 2 mM iodoacetamide.

10/04/2013 Session 6A - Aquatic Parasitology - Chair Jo Cable 2:45 PM - 3:00 PM (15 mins)

Plastic parasites: Extreme dimorphism in the Microsporidia

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Field observations of highly statistically significant co-occurrence with histopathological, ultrastructural and molecular phylogenetic analyses, provide evidence for extreme morphological plasticity in a microsporidium parasite infecting crabs. The parasite alternates between lineages of either bizarre needle-like spores in heart and skeletal muscle fibres (reminiscent of Nadelspora canceri infecting Cancer magister) and Ameson-like spores with pronounced surface projections, in the skeletal muscles (as for Ameson pulvis, previously described infecting Carcinus maenas). Both lineages occur in direct contact with the cytoplasm of host muscle cells and can exist simultaneously within the same cell. Pathological data reveals a remarkable shift in morphology during pathogenic remodelling of host tissues. Sequence analysis of multiple clones derived from amplification of the ssrRNA gene from infected regions of the heart and skeletal muscles confirm the genetic identity of the two lineages. Derived ssrRNA gene sequences are more similar (>99%) to N. canceri than to the coparasite Ameson michaelis infecting Callinectes sapidus (93%). Although molecular phylogenetic data support transfer of A. pulvis into the genus Nadelspora, expansion in the generic description required to include such divergent characteristics is so significant as to be unfeasible within the current taxonomic framework of the phylum. At present, it is preferable to propose that the parasite forms a clade with other morphologically diverse but phylogenetically and ecologically similar muscle-infecting microsporidians from marine crustacean hosts. The strong evidence for plasticity in morphology amongst members of the phylum require novel approaches to phylogeny, based predominantly upon the informed use of molecular sequence data.

10/04/2013 Session 6A - Aquatic Parasitology - Chair Jo Cable 3:00 PM - 3:15 PM (15 mins)

Emerging issues in veterinary parasitology - Chair Jane Hodgkinson

Fasciola hepatica is associated with failure to diagnose bovine tuberculosis in dairy cattle – implications for the current BTB eradication programme.

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The parasite Fasciola hepatica, the common liver fluke, is a significant cause of morbidity and mortality in farmed livestock around the world. In the UK prevalence of infection is increasing, the parasite is spreading into new parts of the country and climate change is likely to exacerbate incidence of disease. It has been known for a number of years that fluke infection impacts on its host's immune system, increasing susceptibility to other infections such as Salmonella Dublin and Clostridium spp. Mice infected with F. hepatica are more susceptible to Bordetella pertussus infection and vaccine responses are suppressed in co-infected animals. Similarly calves infected

with fluke have reduced Th1 responses, characterised by suppressed interferon-gamma secretion and calves infected with avirulent Mycobacterium bovis BCG, had reduced responses to PPD-B when co-infected with fluke. These observations suggested that the single intradermal comparative cervical tuberculin test used to diagnose bovine tuberculosis might be compromised in fluke infected cattle. Over 3000 dairy herds were tested for exposure to fluke and data were collected on the TB status of each herd. There was a significant negative association between fluke and diagnosed BTB in these herds, moreover the magnitude of the SICCT test was significantly reduced in cattle experimentally co-infected with M. bovis and F. hepatica. These data suggest the test used to diagnose BTB is compromised in fluke infected cattle and may in part explain the continuing spread of BTB and the failure of the current eradication programme in the UK.

10/04/2013 Session 7A - Emerging issues in veterinary parasitology - Chair Jane Hodgkinson 4:10 PM - 4:40 PM (30 mins)

Species identification of British paramphistomes and their implications for the diagnosis of fasciolosis.

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The liver fluke, Fasciola hepatica, is endemic in Britain. To detect infection and assess efficacy of fasciolicide treatment, the faecal egg count (FEC) and faecal egg count reduction test (FECRT) are widely used. Rumen fluke are increasingly reported in sheep and cattle in Britain. Their eggs are morphologically similar to those of liver fluke, which may lead to erroneous diagnoses of F. hepatica infection or treatment failure. An alternative method for detection of F. hepatica is the commercial coproantigen ELISA (cELISA). The potential for this test to cross-react with rumen fluke species has not been fully evaluated. Rumen and liver fluke from naturally co-infected British sheep were subjected to immunohistochemistry (IHC) using cELISA antibodies. Intense staining of the gastrodermis was observed in F. hepatica but no cross-reactivity with rumen fluke was seen. Faecal samples from naturally co-infected British sheep flocks were examined by FEC and cELISA. All samples positive for rumen fluke but not liver fluke were negative by cELISA. Rumen fluke specimens from British and Irish cattle and sheep were identified to species level using DNA sequencing of the ITS-2 region. All rumen fluke specimens examined, including those used in IHC, were identified as Calicophoron daubneyi, and not Paramphistomum cervi - the species presumed most common in the British Isles. We conclude that C. daubneyi is the most common rumen fluke of domestic ruminants in the British Isles and that cELISA reduction testing may be a valuable alternative to FECRT where co-infection with liver and rumen fluke.

10/04/2013 Session 7A - Emerging issues in veterinary parasitology - Chair Jane Hodgkinson 4:40 PM - 4:55 PM (15 mins)

Characterisation of IgE antibody responses to Anoplocephala perfoliata in horses.

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Anoplocephala perfoliata is the most common intestinal tapeworm of horses. Infected horses have IgG antibodies specific for Anoplocephala excretory secretory (ES) antigens but the role of IgE antibody in unknown. Serum samples collected from horses with a post mortem diagnosis of A.perfoliata infection had IgG(T), IgA and IgE antibodies to E/S antigens measured by ELISA, although the OD values for IgE were very low. Some horses showed strong IgE antibody binding to the surface layers of the proglottids by immunohistology, while IgG gave only a marginal signal suggesting a novel antigenic target of IgE on the worm urface. Parasite surface carbohydrate exhibited strong binding of the lectin Ulex europaeus agglutinin (fucose) and to a lesser extent peanut agglutinin (galactose). Dual staining showed that IgE and lectin binding co-localized and pre-incubation with IgE antibody completely blocked lectin binding implying the IgE antibodies are directed at a carbohydrate epitope. Immunohistology of colon sections revealed large numbers of IgE+ve cells in the lamina propria along with mast cells and eosinophils. Increased numbers of lymphoid follicles containing IgE+ve cells were also seen at the site of A.perfoliata attachment and QRT-PCR confirmed active IgE transcription at these locations. Furthermore A.perfoliata specific IgE was detected in the supernatant of gut explant cultures indicating that local IgE synthesis and the accumulation of IgE mediated effector cells are characteristic of the immune response to A.perfoliata infection in horses.

10/04/2013 Session 7A - Emerging issues in veterinary parasitology - Chair Jane Hodgkinson 4:55 PM - 5:10 PM (15 mins)

Genetic Analyses of P-Glycoprotein-9 in Two UK Teladorsagia circumcincta Isolates

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Teladorsagia circumcincta is the most important gastrointestinal nematode parasite of small ruminants in temperate regions and the major resistant species in the UK. The worldwide control of parasitic nematodes is reliant on chemotherapy but is compromised by the emergence of anthelmintic resistance (AR). The genetic factors which underpin AR are still poorly understood. Previous work has identified a P-glycoprotein (Pgp) gene, Tci-pgp-9, which is highly expressed in unrelated ivermectin resistant T. circumcincta isolates from the UK and New Zealand. The present study takes this work forward and has identified a number of sequence variants within the internucleotide binding domain-77 of Tci-pgp-9 in two UK isolates of T. circumcincta, one resistant and the other susceptible to ivermectin. Eight out of twelve sequence variants identified shared a high level of identity with sequence variants identified in NZ strains. A 3.7-fold increase in Tci-pgp-9 gene copy number was shown in the UK AR-isolate when compared to the susceptible-isolate, which was consistent with an increase in copy number of Tci-pgp-9 observed in NZ strains. The precise role of this P-glycoprotein gene and its alleles, in the phenotypic expression of AR in T. circumcincta remains to be determined. To this end, we are now attempting to identify which, if any of these Tci-pgp-9 alleles is linked to phenotypic ivermectin resistance using lab-based bioassays.

10/04/2013 Session 7A - Emerging issues in veterinary parasitology - Chair Jane Hodgkinson 5:10 PM - 5:25 PM (15 mins)

Apicomplexan Genomic - Chair Damer Blake

Genomics of apicomplexan parasites and their photosynthetic ancestors

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The genomics era of apicomplexan parasites had started with the publication of two Plasmodium genomes just over a decade ago. Subsequently, with the advent of second and third generation sequencing technologies, at least 15 different species of apicomplexan parasite genomes have already been sequenced to various levels of perfection and many more are in the process of being sequenced. These studies have already provided a wealth of new information on the genome biology of some of these human and animal parasites with diverse life styles and host preferences. In addition, large-scale population-based genome re-sequencing studies in Plasmodium, Toxoplasma and other parasites have just started shedding lights on population structure and natural genome diversity in these parasites. How apicomplexan species have become successful parasites among diverse hosts remains a fundamental question in biology and medicine. In order to answer this question, we have produced a draft nuclear genome sequence of Chromera velia, a free-living algae with ancestral relationship to the apicomplexan parasites. Comparative genomics analysis between C. velia and apicomplexan parasites shows that the core apicomplexan genes, which are conserved among the majority of these parasites, are highly conserved in C. velia. We also found ancient and lineage-specific expansions of gene families, suggesting that the primitive molecular toolkit required for parasites was further evolved to adapt to specific host environments. We will be presenting highlights of our analyses on C. velia nuclear genome.

10/04/2013 Session 5B - Apicomplexan Genomic - Chair Damer Blake 9:00 AM - 9:30 AM (30 mins)

Insights into the role of surface antigens in Eimeria species infecting chickens

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Eimeria spp. cause coccidiosis in a range of livestock, causing the most serious disease in poultry. Apicomplexans such as Eimeria spp., Toxoplasma gondii and Plasmodium falciparum possess large

gene families which are expressed on cell surfaces and act as important regulators of host-parasite interactions. In Toxoplasma gondii the srs gene family is thought to be involved in attachment to host cells and immune invasion, while in Plasmodium falciparum var genes are involved in immune evasion through a process of switching. The principle family of surface antigens in Eimeria (sag) is distinct from that of the relatively closely related Toxoplasma gondii and indeed they have quite different life cycles, which suggest their surface antigens ought to have different roles. We have sequenced the genomes of all seven Eimeria species infecting chickens and through bioinformatic classification and experimental investigation we explore the possible role of the sag gene family in Eimeria biology.

10/04/2013 Session 5B - Apicomplexan Genomic - Chair Damer Blake 9:30 AM - 9:45 AM (15 mins)

A Single Cell Genomics Approach for Malaria Parasites

Ian Cheeseman, Shalini Nair 1, Standwell Nkhoma 1, Peter Zimmerman 2, Karla Gorena 3, Benjamin Daniel 3, François Nosten 4, Timothy J.C. Anderson 1, Ian H. Cheeseman 1.

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Malaria infections frequently contain multiple distinct parasite genotypes, the presence of which have great influence on the spread of drug resistance and the evolution of virulence and greatly complicate genetic analysis. Despite their importance, the tools required to probe the composition of human malaria infections are sorely lacking. We have developed a single-cell genomics approach which combines fluorescence-activated cell sorting (FACS) with single genome amplification (SGA) to generate sufficient high quality material for high-throughput genotyping. By testing multiple combinations of FACS and SGA protocols for over 400 single parasite genomes we optimized and validated a single cell approach to provide >95% accuracy and minimize allelic dropout during targeted genotyping. Through application of this approach to >160 single genomes from 3 multi-clonal, mono-species infections of both Plasmodium falciparum and P. vivax we were able to identify the component genotypes present. Within these infections we see several highly related individuals, perhaps due to repeated inbreeding. Comparison of allele frequencies from single cell genotyping and next generation sequencing of the original infections shows our approach is highly accurate and suggests we have sampled the haplotypes present in single infections in an unbiased fashion. This novel approach has allowed us to characterize the composition of infections with a malaria parasite species (P. vivax) that cannot be maintained in long-term culture. Crucially, these methods provide a framework for dissecting complex infections which is broadly applicable for malaria parasite species, and enable the genomic investigation of complex infections at an unprecedented resolution.

10/04/2013 Session 5B - Apicomplexan Genomic - Chair Damer Blake 9:45 AM - 10:00 AM (15 mins)

Genetic diversity in Eimeria species parasites of poultry.

Emily Clark, Emily Clark1, Kimberley Fornace1, Sarah Macdonald1, Alma Yrjö-Koskinen1, Olaf

Thieme2, Fiona Tomley1, Jonathan Rushton1 and Damer Blake1

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Protozoan parasites of the genus Eimeria cause coccidiosis, a severe enteritis that affects many livestock species, most notably poultry. Recently, cost effective recombinant anticoccidial vaccines have become a realistic prospect due to the identification of several immunoprotective antigens. To predict the likely efficacy and longevity of such vaccines in the field it is important to know the prevalence of naturally occurring genetic (antigenic) diversity. To date the majority of vaccine development has been based on established laboratory strains from Europe and North America and little is known about genetic diversity of Eimeria species in other regions. Using molecular phylogenetics we have analysed genetic variation in sequences encoding the vaccine candidates Apical Membrane Antigen-1 and Immune Mapped Protein-1, alongside the ITS-1/-2 region from field isolates collected from areas of chicken production across the globe. Using Africa, one of world's poorest regions, as an example, five countries were sampled and all seven Eimeria species that are known to infect chickens were detected, in addition to two of the three genetic variants (operational taxonomic units) identified outside of Australia for the first time. Economic analysis revealed that pathogenicity of eimerian infection was correlated with decreased farm profitability, demonstrating a threat to profitable, sustainable small scale poultry enterprises in Africa. With the detection of genetic variants, with unknown pathogenicity in regions where they have not been previously described, our findings indicate that basing novel anticoccidial control strategies solely on species and strains relevant in Europe and North America is unwise.

10/04/2013 Session 5B - Apicomplexan Genomic - Chair Damer Blake 10:00 AM - 10:15 AM (15 mins)

Seroprevalence of Neospora Caninum in several dog populations and study of risk factors in Algeria

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Neospora caninum is an apicomplexa parasite responsible for paresis and neuromuscular problems in dog and for abortion in cattle. Dog is the definitive host and cattle is the major intermediate host. The aim of this work was to evaluate the seroprelavence of N. caninum in several dog populations in Algeria. The serum of 781 dogs were sampled: 337 stray dogs, 209 city dogs, 91 police dogs and 144 farm dogs and the presence of specific antibodies was detected. The overall prevalence was 21.9% but significant differences were present among dog populations. The lower prevalences were present in police dogs with 6.59% and in city dogs with 11.96% and the higher prevalences were present in stray dogs (22.55%) and in farm dogs (44.44%). Risk factors have been studied. The factors race, origin, vaccination and season have a significant effect on seroprevalence. For race, the seroprevalence in mixed breed dogs is higher than in pure breed dogs or than in dogs without pedigree. For origin, the dogs originated from Algeria were significantly more positive than the imported dogs. The dogs vaccinated against classical dog diseases showed a significantly lower prevalence than the non vaccinated dogs. For season, the

seroprevalence was significantly higher in summer than in other seasons. The high prevalence in farm dogs can be explained by the presence of cattle in the farm allowing the complete biological cycle. Most of the seropositive dogs remained asymptomatic. Nevertheless, N. caninum should be considered in the diagnosis

10/04/2013 Session 5B - Apicomplexan Genomic - Chair Damer Blake 10:15 AM - 10:30 AM (15 mins)

Helminth biology III - Chair Eileen Devaney

Small RNA secretion in Heligmosomoides polygyrus: a new mode of parasite-host communication?

Amy Buck, Amy Buck

University of Edinburgh

The secretion and subsequent uptake of vesicular bodies provides a mechanism of cell-to-cell communication and enables RNA transport in mammals. Here we examine whether the gastrointestinal nematode parasite, Heligmosomoides polygyrus, secretes RNAs during its residence in the mouse small intestine. Secretion product was collected from adult worms harvested at 14 days post infection. Small RNA libraries were prepared from the secretion product as well as the eggs, infective larve and duodenal adults. From the 49 million reads analyzed a total of 799 putative pre-miRNAs were identified, 260 of which are represented by reads from both arms. The majority of these miRNAs are conserved in other nematodes and display development-specific expression patterns similar to those reported in C. elegans. In the secretion product a total of 186 miRNAs are present at a frequency of > 10 reads/million. Several of the most abundant miRNAs have homologous seed sites to mouse miRNAs associated with regulation of inflammatory responses. The secreted miRNAs are stabilized against degradation by RNases and associate with structures that pellet upon ultracentrifugation. Transmission electron microscopy reveals vesicle-like structures of 50-100 nM in the ultracentrifugation pellet. Analyses with flow cytometry and confocal microscopy suggest that these vesicles are taken up by mouse small intestinal cells in vitro. This work suggests that RNA secretion by parasitic nematodes could be a mode for cross-species transport of RNA.

10/04/2013 Session 6B - Helminth biology III - Chair Eileen Devaney 2:00 PM - 2:30 PM (30 mins)

Comparison of antibody responses to native and Caenorhabditis elegans-expressed Haemonchus contortus H11 vaccine

Brett Roberts, A Brett Roberts1 Stuart Haslam2 Alison Dicker3 Dave Knox3 Collette Britton1

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A major hurdle in novel parasite control is the production of an effective recombinant vaccine. For the gastrointestinal nematode of sheep Haemonchus contortus, a number of proteases have been identified which induce significant protective immunity when administered in native form isolated from parasite gut extracts. These include cathepsin B cysteine proteases, aspartic and metallo proteases, as well as aminopeptidases. However recombinant forms of these proteases expressed in E. coli, yeast or insect cells have failed to replicate the high level protection of native extracts. This may be due to incorrect folding and/or glycosylation or indicate that combinations of proteases are required. We are using the free-living nematode Caenorhabditis elegans to try to express nematode proteases with similar folding and glycosylation to native enzymes. We have focussed initially on aminopeptidase H11. All H11 isoforms were expressed in C. elegans and co-expression of H11-4 and H11-5 isoforms resulted in highest levels of aminopeptidase activity. Glycan analysis identified similar modifications to native H11. The results of a vaccine trial with C. elegans recombinant H11-4 and H11-5 and comparison of immune recognition of recombinant and native H11 will be presented. This will be important in helping identify what may be required for protective immunity.

10/04/2013 Session 6B - Helminth biology III - Chair Eileen Devaney 2:30 PM - 2:45 PM (15 mins)

Developing a rapid throughput screen for detection of nematicidal activity of plant cysteine proteinases: the role of C. elegans cystatins

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Plant cysteine proteinases (CPs) from papaya are capable of killing parasitic nematode worms in vitro and also possess anthelmintic effects in vivo. The acute damage reported in gastrointestinal parasites has not been found in free-living nematodes such as Caenorhabditis elegans nor among the free-living stages of parasitic nematodes. This apparent difference in susceptibility might be the result of active production of cysteine proteinase inhibitors (such as cystatins) by the free-living stages or species. To test this possibility, a supernatant extract of refined papaya latex (PLS) with known active enzyme content was used. The effect on wild type (Bristol N2) and cystatin null mutant (cpi-1-/- and cpi-2-/-) C. elegans was concentration-, temperature- and time-dependent. Both cystatin null mutant strains were highly susceptible to PLS attack irrespective of the temperature and concentration of exposure, whereas wild-type N2 worms were generally resistant but far more susceptible to attack at low temperatures. PLS was able to induce elevated cpi-1 and cpi-2 cystatin expression. We conclude that C. elegans deploy cystatins CPI-1 and CPI-2 to resist CP attack. The results suggest that either null mutant (or a double mutant combination of the two) could provide a cheap and effective rapid throughput C. elegans-based assay for screening plant CP extracts for anthelmintic activity.

10/04/2013 Session 6B - Helminth biology III - Chair Eileen Devaney 2:45 PM - 3:00 PM (15 mins)

Effects of Cyclosporin A and synthetic PPIase inhibitors in Caenorhabditis elegans and parasitic

nematodes

David Pertab, David Pertab, Tony Page

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Parasitic gastrointestinal nematodes of ruminants are a major economic and welfare burden for the livestock industry. Multidrug resistance in has been reported on a worldwide scale, hence there is a pressing need for the development of novel anthelmintics. To this end, we have been targeting collagen synthesis in nematodes as a potential route for intervention. Collagen synthesis has been well characterised in the model nematode Caenorhabditis elegans, and is believed to be mostly conserved in other Clade V nematodes, such as Haemonchus contortus and Teladorsagia circumcincta. By inhibiting the rate-limiting step of collagen synthesis (peptidyl-prolyl cis-trans isomerisation) using the immunosuppressant Cyclosporin A (CsA), significant morphological phenotypes have been observed in both C. elegans and H. contortus. Furthermore, novel, synthetic, non-immunosuppressive PPIase inhibitors have been shown to produce similar phenotypes and may present a potential new class of anthelmintic agents. C. elegans has been used to study the system-wide effects of CsA and the synthetic PPIase inhibitors by utilising transcriptomics and metabolomics approaches. A mutagenesis screen has also been performed in C. elegans to produce CsA- resistant and sensitive strains. These approaches have been used with the aim of producing further evidence that supports the proposed mechanism of action, as well as shedding light on likely routes of metabolism for the compounds. Yang, Y., Moir, E., Kontopidis, G., Taylor, P., Wear, M. A, Malone, K., Dunsmore, C. J., et al. (2007). Structure-based discovery of a family of synthetic cyclophilin inhibitors showing a cyclosporin-A phenotype in Caenorhabditis elegans. BBRC, 363(4), 1013–9.

10/04/2013 Session 6B - Helminth biology III - Chair Eileen Devaney 3:00 PM - 3:15 PM (15 mins)

microRNAs and drug resistance in Caenorhabdites elegans

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Drug resistance in veterinary nematodes represents a major challenge to the food and livestock industry worldwide. However the molecular mechanisms by which resistance arises in parasite populations are poorly understood. We are investigating the hypothesis that resistance is correlated with alterations in microRNA (miRNA) activity. miRNAs are small non-coding RNAs that bind to target mRNAs and regulate their expression. They are important modulators of drug sensitivity in tumour cells and we propose that they may play similar roles in parasitic nematodes. miRNAs could influence the expression of drug transporters or sub-units of various ion channels and thus affect sensitivity to drug. We compared miRNA expression by microarray in ivermectin-resistant and wild type Caenorhabditis elegans. The drug resistant worms were selected by continuous growth on increasing concentration of ivermectin. This analysis demonstrated that a single miRNA (mir-85) was over-expressed (x40-fold) in ivermectin-resistant worms compared to wild type worms. In contrast, one miRNA (mir-788) was significantly down-regulated (6.5-fold reduction). Both up and down-regulated miRNAs are predicted to be regulated by DAF-3. As over-expression of mir-85 in wild type C. elegans did not confer resistance to ivermectin, the over-

expressing line has been backcrossed to a mir-788 mutant for additional analysis. Our on-going studies are aimed at defining the role of this miRNA in ivermectin resistance.

10/04/2013 Session 6B - Helminth biology III - Chair Eileen Devaney 3:15 PM - 3:30 PM (15 mins)

Helminth immunology III - Chair Karl Hoffman

A Helminth Cathelicidin-like Protein Suppresses Antigen Processing and Presentation in Macrophages via Inhibition of Lysosomal vATPase.

Mark Robinson, Mark W. Robinson, Raquel Alvarado, Joyce To, Andrew T. Hutchinson, Maria Lund, Bronwyn A. O`Brien, John P. Dalton and Sheila Donnelly.

Queens University, Belfast, Northern Ireland; The ithree Institute and The School of Medical & Molecular Biosciences, University of Technology, Sydney, Australia; Institute of Parasitology, McGill University, Canada.

We previously reported the identification of a novel family of immunomodulatory proteins (termed helminth defence molecules; HDMs) that are secreted by medically-important trematode parasites. Since HDMs share biochemical, structural and functional characteristics with mammalian cathelicidin-like host defence peptides (HDPs), we proposed that HDMs modulate the immune response via molecular mimicry of host molecules. In the present study, we report the mechanism by which HDMs influence the function of macrophages. We show that the HDM secreted by Fasciola hepatica (FhHDM-1) binds to macrophage plasma membrane lipid rafts before being internalised by endocytosis. Following internalisation, FhHDM-1 is rapidly processed by lysosomal cathepsin L to release a short C-terminal peptide (containing a conserved amphipathic helix that is key to HDM function) which then prevents the acidification of the endolysosomal compartments by inhibiting vacuolar (v) ATPase activity. The resulting endolysosomal alkalisation impedes macrophage antigen processing and prevents the transport of peptides to the cell surface in conjunction with MHC class II for presentation to CD4+ T cells. Thus, we have elucidated a novel mechanism by which helminth pathogens alter innate immune cell function to assist their survival in the host.

10/04/2013 Session 7B - Helminth immunology III - Chair Karl Hoffman 4:40 PM - 4:55 PM (15 mins)

Improving the success of vaccine candidate superfamilies? Unravelling the Fatty Acid Binding Protein Superfamily of Fasciola hepatica and Fasciola gigantica

Russ Morphew, Morphew, R. M.1, Wilkinson, T.1, Mackintosh, N. M.1, McVeigh, P.2, Abidi, S. M. A.3, Saifullah, M. K.3, Ravikumar, G.4, Raman, M.4, Maule, A. G.2 & Brophy, P. M.1

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The Fatty Acid Binding Protein (FABP) superfamily from the temperate and tropical liver flukes,

Fasciola hepatica and F. gigiantica, have been the subject of many recent scientific studies as potential immune-diagnostic/therapeutic candidates. Despite initial promise, development of a Fascioliasis vaccine based upon FABP has stalled. An incomplete understanding of the FABP superfamily in Fasciola sp. may be responsible for the lack of success. Therefore, we have investigated the FABP superfamily from both F. hepatica and F. gigantica combining high resolution 2DE proteomics and next generation sequencing projects to gain a more complete picture of this vaccine candidate superfamily. To this end, four new FABP isoforms, present in both species, have been identified; deemed FABP IV to FABP VII. The antigenic profile of the complete FABP superfamily has also been investigated. Recombinant forms of novel FABPs have been produced to allow a biochemical and immunological analysis of each.

10/04/2013 Session 7B - Helminth immunology III - Chair Karl Hoffman 4:55 PM - 5:10 PM (15 mins)

Parasite-vector interactions II - Chair Wendy Gibson

Taking leishmaniasis transmission research from the lab to the field

Paul Bates, Paul Bates

Lancaster University

Investigating the transmission mechanism of human parasites is an important area of research as detailed understanding can help in both the design and testing of new ways to prevent disease occurring. Progress in defining the transmission mechanism of leishmaniasis has not only helped to reveal interesting biology but has also informed the process of vector incrimination in the field. This has practical implications in understanding new outbreaks and foci of disease, for example in Ghana, Sri Lanka, Thailand and Australia, as well as the spread of disease in established areas, for example urban visceral leishmaniasis in Brazil. I will discuss these various examples to show how both basic laboratory-based research on transmission mechanisms as well as field–based investigations on vectors and reservoir hosts are both necessary and mutually interdependent means of improving disease control in leishmaniasis, and by implication other vector-borne diseases

10/04/2013 Session 5C - Parasite-vector interactions II - Chair Wendy Gibson 9:00 AM - 9:30 AM (30 mins)

Genomic confirmation of hybridisation and recent inbreeding in a vector-isolated Leishmania population

James Cotton, Matthew B. Rogers1,2, Tim Downing1, Milena Svobodova3 , Barbara A. Smith2, Hideo Imamura1,4, Petr Volf3, Matt Berriman1, James A. Cotton1, Deborah F. Smith2

1 Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Cambridge, CB10 1SA, UK 2 Centre for Immunology and Infection, Department of Biology, University of York YO10 5DD, UK 3 Department of Parasitology, Fac. Sci., Charles University, Vinicna 7, Prague 2, CZ 128 44, Czech Republic 4 Unit of Molecular Parasitology, Department of Parasitology, Institute of Tropical

Medicine, 2000 Antwerp, Belgium

Despite the medical importance of Leishmania parasites, knowledge of their life-history in the wild, and specifically the importance of a sexual cycle, remains limited. While asexual reproduction via clonal propagation has been proposed as the principal reproduction mechanism across the genus, sexual recombination has long been suspected, based on hybrid marker profiles detected in field isolates. Importantly, sex has now also been demonstrated experimentally in both L. major and L. donovani. Here, we use whole genome sequencing to investigate 12 unusual L. infantum isolates isolated from sandflies in a focus of cutaneous leishmaniasis in southeast Turkey as part of a large-scale survey of both vectors and patients in this region. Genomic diversity in these isolates suggests these were all derived from a single hybridisation. A genome-wide pattern of patchy heterozygosity and SNP density was observed both within individual strains and across the set. Comparisons with other genome sequences suggested that these isolates were derived from a single cross of two diverse strains that was altered by subsequent recombination within the population. Phylogenetic analysis indicated that the two parents were phylogenetically distinct. Patterns of linkage disequilibrium indicated that this population reproduced primarily clonally since this original hybridisation event, but that some recombination has occurred, allowing us to estimate the relative rates of sexual and asexual reproduction within this population, to our knowledge the first quantitative estimate of the Leishmania life cycle. This is the first genome-wide examination of a vector-isolated population of Leishmania.

10/04/2013 Session 5C - Parasite-vector interactions II - Chair Wendy Gibson 9:30 AM - 9:45 AM (15 mins)

African Trypanosome in the Tsetse fly: going forward

Brice Rotureau, ROTUREAU Brice, PERROT Sylvie, HUET Diego and BASTIN Philippe

Trypanosome Cell Biology Unit, Institut Pasteur & CNRS URA 2581, 25 rue du Dr Roux, 75015 Paris, France

African trypanosomes are flagellated parasites transmitted by the bite of the tsetse fly and causing sleeping sickness in humans. Trypanosoma brucei development in the fly requires about three weeks during which trypanosomes differentiate successively in at least seven different stages. This complex development is precisely orchestrated in time and in space. Trypanosomes travel through five organs from the midgut to the salivary glands, through the proventriculus. Flagellum beating allows trypanosomes to move in these different environments. By studying the movements and paths of trypanosomes in vivo and ex vivo, we characterized the motility of the different forms of the parasite in relation to their morphology and demonstrated the adaptation of their mobility to specific functions during the parasite life cycle. Group behaviour was also observed during parasite migration in the vector's gut. Functional in vivo studies revealed that parasite forward motility impairment by axonemal dynein knockout causes a loss of infectivity due to the absence of migration from the midgut to the foregut as well as to an absence of differentiation into the epismastigote stage. The essential role of trypanosome motility during the parasite cycle is demonstrated for the first time in vivo.

10/04/2013 Session 5C - Parasite-vector interactions II - Chair Wendy Gibson 9:45 AM - 10:00 AM (15 mins)

Going the distance: a Trypanosoma brucei phosphagen kinase important for infectivity to tsetse

CherPheng Ooi, Ooi, C.P., Subota, I., Julkowska, D., Bastin, P.

Institut Pasteur 25, rue du Docteur Roux 75015 Paris

Trypanosoma brucei has the most complex life cycle within the tsetse vector amongst African trypanosomes, starting from the fly midgut and culminating in the salivary glands after traversing almost the length of the fly alimentary tract and crossing multiple biological compartments. As the primary organelle for locomotion, the T. brucei flagellum has been proposed to feature evolutionary adaptations to facilitate this journey. One such adaptation would be a system to buffer for energy requirements. AK3 is a T. brucei flagellar-targeted phosphagen kinase that we found enriched in the procyclic flagellum, and thus hypothesized it to be important for trypanosome infectivity to tsetse. With AK3-knockout and AK3-overexpressing trypanosome cell lines (both constitutive and tetracycline-inducible), we demonstrated that the lack of AK3 does not impart any growth impairment in vitro, while the overexpression of AK3 does. Conversely this situation is reversed when the knockout and overexpressing cell lines were used to infect tsetse, where the lack of AK3 reduces both the infection rate, as well as competitiveness in co-infection experiments with AK3 knockout and AK3 overexpressing parasites. Interestingly, knockout and overexpression of AK3 appears to increase the profusion of glycosomes within the trypanosome cell body. We are currently investigating this interaction between the glycosome and flagellum, and we postulate that this may be due to the trypanosome attempting to compensate for altered cellular ATP levels when the energy buffering system within the flagellum is affected.

10/04/2013 Session 5C - Parasite-vector interactions II - Chair Wendy Gibson 10:00 AM - 10:15 AM (15 mins)

Vizualization of meiosis and mating in Trypanosoma brucei

Wendy Gibson, Lori Peacock (a,b), Mick Bailey (b), Mark Carrington (c), Wendy Gibson (a)

a. School of Biological Sciences University of Bristol, Bristol BS8 1UG, UK. b. Department of Clinical Veterinary Science, University of Bristol, Langford, Bristol BS40 7DU, UK. c. Department of Biochemistry, University of Cambridge, Tennis Court Road, Cambridge CB2 1QW, UK.

Sexual reproduction in parasites has particular significance in spreading genes for traits such as virulence, disease phenotype or drug resistance. In the protozoan parasite Trypanosoma brucei, mating occurs during the developmental cycle within the tsetse fly vector. We showed previously that three functionally-distinct, meiosis-specific genes were expressed during the early phase of colonisation of the tsetse salivary glands by T. b. brucei. Here we extend this finding to all three subspecies of T. brucei, including the human pathogens T. b. rhodesiense and T. b. gambiense groups 1 and 2. For all strains we were able to demonstrate that YFP-tagged, meiosis-specific fusion proteins were expressed in the nucleus of a single specific cell type, defining a new developmental stage occurring within the tsetse fly salivary gland. Expression occurred in clonal infections indicating that the meiotic programme is an intrinsic but hitherto cryptic part of the developmental cycle of trypanosomes. In experimental crosses, expression of the meiosis-specific

proteins usually occurred before cell fusion. In vitro observation of insect-derived trypanosomes during the window of peak expression of the meiosis-specific genes revealed a further new cell type that engages in fusion and cytoplasmic exchange. The morphology and characteristics of this putative gamete stage will be described.

10/04/2013 Session 5C - Parasite-vector interactions II - Chair Wendy Gibson 10:15 AM - 10:30 AM (15 mins)

Public Engagement: How to do it - Chair Tansy Hammarton

Public Engagement: why bother?

Tansy Hammarton, Tansy Hammarton

University of Glasgow

Engaging with the public is becoming increasingly important. The Concordat to Support the Career Development of Researchers and the Researcher Development Framework both highlight the need for researchers to become skilled at transferring and sharing their research knowledge beyond academia to increase the impact of their work. Grant applications now require an impact statement outlining knowledge exchange activities, and impact will be assessed as part of the 2014 Research Excellence Framework. Public opinion can strongly influence government policy, such as in the ongoing debate about badger culling to curb bovine tuberculosis, while public misinformation can dramatically influence public health, as illustrated by outbreaks of measles and mumps following reduced uptake of the Measles/Mumps/Rubella vaccine after it was falsely linked to children developing autism. Thus, it is highly desirable for researchers to engage with the public to discuss current/contentious issues surrounding their research, to disseminate the aspirations and outcomes of their work, and to inspire an interest in science more generally. Engaging with the public can be highly rewarding but is not without its challenges and pitfalls. This session aims to showcase a wide variety of successful public engagement (PE) activities, to provide insights into how they were conceived and brought to fruition as well as to highlight problems encountered along the way and how these were overcome. It is hoped that this session will inspire more researchers to get involved and will bring together PE novices with researchers experienced in PE. The session will end with a general discussion of how best to share PE experience, expertise and resources amongst BSP members in the future.

10/04/2013 Session 6C - Public Engagement: How to do it - Chair Tansy Hammarton 2:00 PM - 2:15 PM (15 mins)

Public Engagement: Next Gen.

Tansy Hammarton, Tansy Hammarton

University of Glasgow

Science is an important part of the school curriculum, but teachers can sometimes find it hard to deliver inspiring, hands-on and up-to-date biology lessons because of a lack of the necessary

science background (particularly at primary level), because of a lack of funding or availability of resources and equipment, or because of health and safety restrictions. Pupils often view science subjects as difficult options, can struggle with the transition from primary to secondary school science, and concerns over reduced uptake of science subjects by senior pupils leading to fewer university science graduates has resulted in a UK government long-term strategy to promote STEM subjects in schools. Scientists willing to develop activities for schools are generally welcomed with open arms by teachers and pupils alike and usually find it very rewarding to inspire the next generation and promote awareness of their research and science in general amongst pupils, teachers and parents. But how do you get started and what problems might you encounter along the way? We have developed a range of science activities in partnership with local teachers to enhance the curriculum that have now reached >2000 pupils and teachers, including primary school talks and workshops, parasitology labs for senior secondary pupils, and more recently, through a Royal Society Partnership Grant, a year-long microbiology Science Club project for S2 pupils at two local secondary schools. Although it has not been plain sailing throughout, these projects have in the end been very successful and could easily be adapted by others wanting to run their own PE activities.

10/04/2013 Session 6C - Public Engagement: How to do it - Chair Tansy Hammarton 2:15 PM - 2:30 PM (15 mins)

Making an exhibition of yourself

Sonya Taylor, Sonya Taylor

University of Glasgow

Communication has never been more important for everyone involved in science. If there ever was a time when the research community could afford to lock itself away in a laboratory, oblivious to the views of the world outside, that time has surely passed. As members of the research community, we should communicate with the public to ensure they understand the value and relevance of science and technology, and how research affects our lives today but also to highlight what their hard earned tax money is being spent on. Beyond the media and the lecture theatre there are museums, science centres and science festivals, all of which are excellent vehicles to convey our research. However, these events depend on the willingness of active researchers to provide lectures, content for exhibitions, conduct demonstrations and generally make themselves available. So, how can we, as the research community, all make an exhibition of our(research)selves and what are the pros and cons involved?

10/04/2013 Session 6C - Public Engagement: How to do it - Chair Tansy Hammarton 2:30 PM - 2:45 PM (15 mins)

ArtReach: illustrating science

Mhairi Stewart, Mhairi Stewart

University of Glasgow

Just as one well-presented figure in a paper can convey more data than several pages of text, the most reliable and rapid method to engage people and articulate complex ideas is to use striking artwork with good, clear design. While presenting our science using art is a powerful way of raising awareness, there is more scope to 'ArtReach' than designing materials intended to create curiosity. A more engaging method of conveying complex ideas is to encourage artistic creativity using science as inspiration. So how can we run creative workshops as scientists? What are the basics of good design in outreach materials? If we aren't artistic ourselves, how do we go about commissioning the art we want? Where do we find an artist that understands our ideas? And, what will it cost

10/04/2013 Session 6C - Public Engagement: How to do it - Chair Tansy Hammarton 2:45 PM - 3:00 PM (15 mins)

Real science and real engagement: the value of citizen science

Michael Pocock, Michael Pocock

NERC Centre for Ecology & Hydrology

Public engagement is ever so important, but research is too. Citizen science is a superb way of combining the two. Involving members of the public also allows data to be gathered at much larger scales than would be cost-effective with paid researchers, making it a genuinely important form of research. So, how can citizen science be successful? From small beginnings, through to a national project that addressed hypotheses about parasitism of an invasive insect by engaging thousands of 'field assistants', I'll explain my journey in citizen science. Drawing on my review of hundreds of environmental citizen science projects, I'll show that citizen science is more diverse than many people realise, and consider what makes a really successful citizen science project.

10/04/2013 Session 6C - Public Engagement: How to do it - Chair Tansy Hammarton 3:00 PM - 3:15 PM (15 mins)

Malaria : Epidemiology & elimination - Chair David Conway

Multimodel Insights into the Optimal Temperature Regime for Malaria Transmission

Paul Parham, Edwin Michael

Dr Paul E. Parham, Centre for Health Economics and Medicines Evaluation, Institute of Medical and Social Care Research, Dean Street Building, Bangor University, Bangor, Gwynedd LL57 1UT; and Grantham Institute for Climate Change, Department of Infectious Disease Epidemiology, Praed Street, St. Mary's Campus, Imperial College London, W2 1PG. Prof Edwin Michael, Department of Biological Sciences, Eck Institute for Global Health, University of Notre Dame, Notre Dame, IN 46556-0369, USA.

Climatic and environmental variables play a significant role in malaria transmission through influences on Anopheles population dynamics, parasite development, and host behaviour. Understanding the optimum conditions for transmission is important for identifying regions where

climatic factors may be most influential on transmission, assessing the associated impact on designing intervention strategies in different settings, and evaluating how different regions may be affected by climate change over the coming decades. Recent work has suggested that the optimal temperature regime for Plasmodium falciparum malaria, as quantified by the Entomological Inoculation Rate, is around 25oC, while previous estimates, based on the basic reproduction number, are closer to 31oC. However, it is important to realise that identification of optimal temperature depends not only on model parameterisation, but crucially on the transmission metric and underlying model; current estimates are based on one model, despite the considerable suite of available models. Multimodel approaches are an accepted means of improving projection robustness in climate modelling and include the identification and quantification of uncertainties across a multimodel ensemble, but this approach has not been widely adopted in disease modelling. Here, we highlight the value in ensemble modelling in understanding how the optimal temperature depends ultimately on (a) structural uncertainty across host-vector models, (b) the transmission metric of interest, and (c) parameter uncertainty. This approach provides a deeper understanding of the sensitivity of optimal transmission with temperature by accounting for differences in model assumptions and parameterisation, as well as the role of heterogeneities in Anopheles bionomics and parasite strain.

10/04/2013 Session 7C - Malaria : Epidemiology & elimination - Chair David Conway 4:40 PM - 4:55 PM (15 mins)

Genetic diversity and distribution of drug resistance markers among Plasmodium falciparum in sites the Arabian Peninsula

Hamza Babiker, Salama Al-Hamidhi1, Zainab S. Al-Hashami1, Hissa M. Al-Farsi1, Saad M. Bin Dajem2, Adel Ali H. Al-Sheikh3 ,Mohammed Mahdy4, Mohamed Idris1, Albano Beja-Pareira5 and Hamza Babiker1* Hamza A Babiker1* 1 Faculty of Medicine, Sultan Qaboos University, Oman. 2 Biology Department, College of Science, King Khalid University, Abha, Saudi Arabia 3National Centre for Training and Research, MOH, Jazan, Saudi Arabia. 4Department of Parasitology, Faculty of Medicine, Sana'a University, Sana'a, Yemen 5Research Centre in Biodiversity and Genetic Resources (CIBIO), University of Porto, Rua Padre Armando Quintas 7, Vairão 4485-661, Portugal

Faculty of Medicine, Sultan Qaboos University, Oman

Successful malaria control in the Arabian Peninsula, that brought transmission to halt in many sites (e.g Kuwait, United Arab Emirates and Oman), is faced with challenges to contain transmission in active foci and prevent introduction of drug resistant parasites via asymptomatic travellers. Here we examined genetic diversity of Plasmodium falciparum in Yemen and Saudi Arabia, to elucidate parasite structure and distribution of drug resistance genotypes in the region We examined 179 and 108 Plasmodium falciparum isolates for Yemen and Saudi Arabia, respectively. We examined examined 5 polymorphic loci (MSP-2, Pfg377 and 3 microsatellites) not involved in antimalarial drug resistance, and 4 drug resistance genes (Pact, Pfmdr1, duff and dips). There was a high diversity in non-drug resistance genes (He range, 0.88-0.72), and a large effective population size (Ne). The genetic differentiation between the two populations was low (FST < 0.03). Two distinct Pfct genotype, CVIET and SVMNT, existed at high prevalence in Yemen and Saudi Arabia. In addition, Pfmdr1 genotypes YFCDD and YFSND were common in both sites. However, limited mutations in dhfr, associated with SP resistance, and no mutation in dhps were seen in both sites.

The high level of diversity and extensive gene flow between the parasites in Yemen and Saudi Arabia, are indicative of a large parasite reservoir, which represents a challenge to control efforts in the region. Migration is a plausible source of drug resistance genotypes, therefore, monitoring of imported malaria is of high priority for control/eradication programs in the region.

10/04/2013 Session 7C - Malaria : Epidemiology & elimination - Chair David Conway 4:55 PM - 5:10 PM (15 mins)

Development and evaluation of simplified molecular diagnostic platform for malaria: the direct on blood PCR-NALFIA system

Henk Schallig, P.F. Mens, H.M. de Bes, P. Sondo, N. Laochan, L. Keereecharoen, A. van Amerongen, J. Flint, J.R.S. Sak, S. Proux, H. Tinto and H.D.F.H. Schallig

MALACTRES consortium (www.malactres.eu) at Royal Tropical Institute, Parasitology Unit, Meibergdreef 39, 1105 AZ Amsterdam, The Netherlands

Molecular tools allow for specific/sensitive malaria diagnosis, but current formats, like PCR with gel-electrophoresis, are difficult to implement in resource poor settings. Therefore, a simple, fast, sensitive/specific molecular diagnostic platform, direct on blood PCR combined with nucleic acid lateral flow immunoassay (NALFIA) to detect amplified PCR products of Pan-Plasmodium and human GAPDH (internal control) was developed and evaluated under laboratory conditions, a multi country ring trial and in two malaria endemic countries. Analytical sensitivity/specificity of PCR-NALFIA in a single laboratory evaluation was >95% and able to detect 1 parasite/µl blood. All laboratories in the ring trial reported ease of use of the system and could successfully perform the protocol. Overall laboratory inter variability was low and the agreement of reported results was high. Overall k-value was 0.89 (95% CI: 0.83 – 0.94; $p<0.001$). Overall test sensitivity and specificity was >95% with very small confidence intervals. Field evaluations in disease endemic countries, Thailand and Burkina Faso, were performed. In Burkina Faso the relative sensitivity was 94,8% and relative specificity 82,4% compared to microscopy and 93,3% and 91.4% compared to RDT. In Thailand the relative sensitivity and relative specificity was 93,4% and 90,9 respectively compared to microscopy and 95,6% and 87.1 % compared to RDT. These numbers are under estimation of test performance as the results are not PCR corrected. Funding: EU FP7 grant 201889 Multi drug resistance in malaria under combination therapy: assessment of specific markers and development of innovative rapid and simple diagnostics (MALACTRES)

10/04/2013 Session 7C - Malaria : Epidemiology & elimination - Chair David Conway 5:10 PM - 5:25 PM (15 mins)

HIV Screening status and Malaria Prevelance in Pregnant Women in Ikwuano L.G.A, Abia State Nigeria

Onyinye Mkpola Ukpai, +UKPAI, ONYINYE M AND UDO-UDO, EDIKAN, S

DEPARTMENT OF ZOOLOGY AND ENVIRONMENTAL BIOLOGY,MICHAEL OKPARA UNIVERSITY OF AGRICULTURE, UMUDIKE, P.M.B 7267 UMUAHIA, ABIA STATE. NIGERIA

HIV screening status and prevalence of malaria in pregnant women attending ante-natal clinics in Amawom and Ndoro health centres in Ikwuano L.G.A, Abia State were assessed. A total of 150 consenting pregnant women had their blood samples screened for HIV infection and examined for malaria parasites using thin and thick giemsa stained blood smears and Determine HIV 1/2 and Unigold kits for HIV. Ninety two percent(92.0%) were positive for malaria while 5.33% were sero-positive for HIV 1 and 2; and 2.67% fell within the indeterminate HIV group. Malaria-HIV co-infection stood at 10.0%. The highest prevalence of 98.48% was in the age-group 27-31years for malaria and 6.56% for HIV. Malaria infection was highest in blood group AB individuals(100%)but had no HIV case. HIV cases were in blood groups A(4.88%), B(8.82%)and O(4.29%). Women with genotype AA had the highest prevalences of malaria infection(92.78%) and HIV infection(5.77%). Malaria was highest in women in the second trimester(93.99%) and the secundigravidae group(95.45%). The most common possible cause of malaria reported was the bites of mosquitoes(76.67%)while that of HIV was sharing of shaving sticks and clippers(64.0%). Some reported symptoms associated with malaria were headache(26.6%), fever(13.33%), loss of appetite(13.33%), body weakness(12.0%)while those of HIV were continuous fever(42.0%), body weakness(16.0%) and cough(13.33%). Preventive measures employed against HIV were not sharing needles and syringes(36.0%), use of condom(42.67%) and for malaria were the use of mosquito nets(14.0%)and anti-malaria drugs(80.67%). Major sources of information about HIV and malaria were radio(45.33%) and television(30.0%).

10/04/2013 Session 7C - Malaria : Epidemiology & elimination - Chair David Conway 5:25 PM - 5:40 PM (15 mins)

Applying Ecology and Evolution (1) (BES SIG) - Chair Jo Lello

Within-host population ecology and the evolution of drug and vaccine resistance

Andrew Read, Andrew Read

Penn State, USA

Ecological interactions between coinfecting strains of pathogens in the same host can generate powerful evolutionary forces. Medical and public health interventions like drugs and vaccines can alter these interactions. Using experimental data from rodent malaria infections, I will discuss the consequences of medically-imposed ecological disturbances for the evolution of drug and vaccine resistance.

10/04/2013 Session 5D - Applying Ecology and Evolution (1) (BES SIG) - Chair Jo Lello 9:00 AM - 9:30 AM (30 mins)

Seroprevalence of Toxoplasma gondii in the Eurasian otter (Lutra lutra) in England and Wales

Willow Smallbone, Elizabeth A. Chadwick1, Willow Smallbone1, Jo Cable1 Janet Francis2, Edward Guy2, Eleanor F. Kean1, Sarah E. Perkins1 and Ellie Sherrard-Smith1

1School of Biosciences, Sir Martin Evans Building, Cardiff University, Cardiff, CF10 3AX, UK.

2Toxoplasma Reference Unit, Public Health Wales Microbiology, Singleton Hospital, Swansea SA2 8QA, UK.

Toxoplasma gondii, a zoonosis of global importance, has the ability to infect all endothermic vertebrates, with potentially devastating health implications. Transmission occurs through ingestion of cysts in infected meat, oocysts in soil or contaminated water, or congenitally. Epidemiological data collection for T. gondii has been recommended by the World Health Organisation, but the prevalence of T. gondii is seldom monitored in wildlife even though there are links between human, domestic animal and wildlife infection. The current study uses the Sabin-Feldman Dye Test to test for T. gondii in >600 Eurasian otters (Lutra lutra) found dead, mainly as road-kill, in England and Wales. It is the first spatially widespread study of T. gondii in UK wildlife, and the first extensive survey of T. gondii in Eurasian otters. T. gondii infected 24% of UK otters with more infection in the east of the UK than the west. This relatively high prevalence of T. gondii in a semi-aquatic mammal suggests widespread contamination of freshwater, marine and terrestrial ecosystems with oocysts. Continued surveillance of the Eurasian otter for T. gondii is valuable because of conservation concerns and because of the host's role as a sentinel for freshwater health.

10/04/2013 Session 5D - Applying Ecology and Evolution (1) (BES SIG) - Chair Jo Lello 9:30 AM - 9:45 AM (15 mins)

Direct life cycle has implications for chemotherapy of Spironucleus vortens

Jo Cable, Catrin Williams, David Lloyd and Jo Cable

University of Cardiff

Spironucleosis causes devastating losses in the production of both ornamental and food fish. The causative agent, Spironucleus, is an opportunistic protozoan parasite found primarily in the intestinal tract; however some species can cause systemic infections, which in the case of Spironucleus vortens reportedly results in 'hole-in-the-head" disease. For the first time, we demonstrated prolonged survival of S. vortens trophozoites in host faeces, which suggests a direct life cycle without encystment. This novel finding allowed development of a non-invasive method to quantify the degree of intestinal colonization in the host, which was then applied to determine the efficacy of new and existing chemotherapeutics against S. vortens. The current drug of choice, metronidazole and the garlic-derived compound, ajoene, act synergistically against S. vortens both in vitro and in vivo. These treatments cause severe oxidative stress leading to gross cellular morphological damage and ultimately cell death. Further biochemical investigations into the antioxidant defence system and metabolism of S. vortens provided insight into the success of this organism as a parasite, reflected in its ability to withstand fluctuations in O2 and nutrition during its life cycle.

10/04/2013 Session 5D - Applying Ecology and Evolution (1) (BES SIG) - Chair Jo Lello 9:45 AM - 10:00 AM (15 mins)

Differential sources of host species heterogeneity influence the transmission and control of multi-host parasites

Andy Fenton, Andy Fenton, Amy B. Pedersen and Daniel G. Streicker

Institute of Integrative Biology, University of Liverpool, UK. Centre for Infection, Immunity and Evolution, University of Edinburgh, UK. Odum School of Ecology, University of Georgia, USA.

Parasites, including many relevant to human and wildlife health, are known to infect multiple host species. Because each host species rarely contributes equally to parasite transmission and persistence, identifying 'key hosts' that dominate transmission is a central goal of applied disease ecology. However, it is rarely acknowledged that heterogeneity in species' contributions to transmission can arise through a variety of processes, potentially requiring different approaches for control. Surprisingly, neither theoretical nor empirical frameworks exist to partition the underlying drivers of host species heterogeneity or to examine how this variation impacts the success of disease control efforts. Using a novel theoretical framework we evaluate the relative importance of three distinct processes that underlie host species heterogeneity in disease transmission: host abundance, infection prevalence and per capita infectiousness. Applying this framework to data on 11 gastrointestinal parasites in varoius small mammal communities reveals variation not only in the magnitude of heterogeneity among host species, but also in the processes driving this heterogeneity; the key hosts of each parasite species arise through distinct, though not necessarily mutually exclusive processes. By simulating different control plans in these host communities we show that these different sources of heterogeneity influence the efficiency by which different control strategies reduce transmission. Tools such as that developed here, which can identify and tailor management efforts to the type of key host in question using quantifiable ecological data, may enable more effective control of multi-host parasites.

10/04/2013 Session 5D - Applying Ecology and Evolution (1) (BES SIG) - Chair Jo Lello 10:00 AM - 10:30 AM (30 mins)

Malaria : Control strategies - Chair Frederic Tipet

Population structure of malaria vectors and implications for malaria control

Kenneth D. Vernick

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Historically, all successful malaria control efforts have included measures targeted at the vector. New approaches to understanding the genetics of vector populations allow rational design of vector control strategies tailored to local vector characteristics. Understanding how vector population subgroups differ for susceptibility to P. falciparum infection, behavior, and ecology is indispensable for the development of effective malaria control measures. Towards this end, we combined experimental infections and capture of naturally infected adult mosquitoes with high-throughput genotyping to determine population subgroup membership in order to measure the natural wide heterogeneities of the malaria vectorial system.

10/04/2013 Session 6D - Malaria : Control strategies - Chair Frederic Tipet 2:00 PM - 2:30 PM (30

mins)

Mosquitos salivary gland, a small treasure island

Hiroyuki Matsuoka, Hiroyuki Matsuoka and Mohamad Reza

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Mosquitos bite the skin to find blood vessels to take blood. They inject their saliva to anesthetize skin and to extend blood vessels for inserting the proboscis. Once starting to take blood, Anopheles stephensi, a malaria transmittable mosquito, drinks her saliva with the blood. In the midgut, blood does not coagulate more than one hour. In the saliva of An. stephensi mosquito, we first found an anti-coagulant protein. We named it as Anopheline anti-platelet protein (AAPP) because it prohibited the attachment of platelets. Without coagulation, An. stephensi mosquitoes can concentrate red blood cells in the midgut and excrete fluid part of blood (plasma) from their anus as prediuresis. Maybe red blood cells contain much nutrition than the plasma. We next found xanthurenic acid (XA), which stimulated male gametoes of malaria parasites to start exflagellation. Compare to the midgut, the salivary gland contains XA very much. We third found that Anopheline mosquitoes drank much saliva when they took blood. After taking blood, the salivary glands of An. stephensi shrink completely, but the salivary glands of Culex and Aedes does not change the shapes. Taken together, we conclude that Anopheline mosquitoes can transmit malaria parasites because male gametoes can start exflagellation and succeed fertilization in the midgut with these substances supplied from the salivary gland. The salivary gland contains many unknown molecules that we can use for our benefits. We should find out some more treasures from the salivary gland.

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Towards release control programs of the malaria mosquito Anopheles gambiae: Can heterozygotic supermales solve the reproductive performance deficiencies of laboratory-produced males?

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The success of vector control strategies aiming to decrease disease transmission via the release of sterile or genetically-modified male mosquitoes critically depends on mating between laboratory-reared males and wild females. Mosquito colonization and laboratory maintenance lead to profound genetic and phenotypic changes that may negatively affect male mating performance. Exploiting heterosis, we produced 'supermales' of the malaria mosquito Anopheles gambiae by crossing the KIL and Mopti strains colonized 25+ and 7 years ago. In large group mating cages, no difference in female insemination rate between supermales and males from their inbred parental strains was found. However, the sperm of supermales transferred to females was found to be significantly larger and more active than that of older strains. The potential fitness advantage of supermales was further demonstrated through detailed fitness experiment of

individual male reproductive success. Whilst males of the old KIL strain achieved significantly higher rates of female insemination than the Mopti strain and heterozygous supermales, they were also frequently infertile as a result of inbreeding. In contrast, females from the two inbred parental strains mated with supermales produced significantly more eggs than when mated with inbred ones, and this ultimately resulted in a 4.2-fold increase in the mean number of larvae fathered by supermales compared to the KIL strain. These results validate the use of heterosis for creating males with improved reproductive success from inbred mosquito lines and have important implications for malaria control strategies relying on

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Utilizing copper at a relatively low concentration in ovitraps: a simple low-cost alternative to Integrated Vector Management

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Ovitraps have been used in vector control, especially in Integrative Vector Management (IVM). However, they are used not only for surveillance or sampling, but also to kill mosquito larvae. Bacillus thuringiensis-based ovitraps show promise, but other larvicides are urgently needed. The ability of copper to kill mosquito larvae led us to test its use in ovitraps. We found that 10 ppm of copper was lethal to larvae of four species of mosquito (Anopheles stephensi, Anopheles sinensis, Aedes albopictus, and Culex pipiens) under laboratory conditions. This result suggests the possibility of utilizing copper at relatively low concentrations in ovitraps as an alternative to IVM and malaria eradication programs.

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Genetic and behavioural mechanisms of speciation in the Anopheles gambiae complex

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The sibling species of the Anopheles gambiae complex are important vectors of human malaria, and Anopheles gambiae sensu stricto is responsible for a large proportion of malaria transmission on the continent. It is believed that An. gambiae s.s. underwent rapid and recent divergence through peripatric and/or parapatric speciation events. Genome-wide studies have shown that

speciation in this species occurs through the divergence of a few loci characterized by reduced recombination and divergent selection. Such 'islands of speciation', located in pericentromeric regions of chromosomes X, 2L and 3L are thought to contain genes responsible for the assortative mating observed in complex An. gambiae populations. we selectively introgressed the largest islands of speciation located on the X chromosome from the S form into an M Mopti form resulting in pairs of recombinant strains differing only in the molecular form of their X-island. We conducted mate choice experiments using recombinants An. gambiae strain differing only at the X-chromosome island of speciation locus. We identified that most of the recombinant BSS individuals mated assortatively thereby broadly mapping assortative mating genes to the X-chromosome island of speciation. Genotyping of the 2L and 3L peri-centromeric islands in recombinant strains revealed no linkage disequilibrium between the X and 2L and 3L islands of speciation, thus confirming the central role played by the X-chromosome island. These results and the availability of a laboratory-model for studying assortative mating constitute fundamental steps towards the identification of behavioral and genetic determinants of pre-mating reproductive isolation in this important vector species complex.

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Applying Ecology and Evolution (2) - Chair Andrea Graham

Evolutionary phage therapy

Angus Buckling, Angus Buckling

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Viruses of bacteria, bacteriophages, have long been used as antimicrobials, but their extreme specificity of action, lack of systemic activity, ease at which bacteria can evolve resistance to them and legislative issues has greatly limited their development in clinical contexts. However, the rapid rise in antibiotic resistance has sparked a resurgent interest in clinical phage therapy. Here, I describe experiments that take advantage of both the evolutionary potential of phages and synergistic interactions between phage and antibiotics to increase the effectiveness of phage therapy (in test-tubes).

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Biliary trematodes of the Eurasian otter

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An understanding of parasite life cycles is essential for the prevention, control and management of diseases, but is particularly challenging for cryptic organisms with complex life cycles. We report novel hosts for Pseudamphistomum truncatum and Metorchis albidus (Trematoda:

Opisthorchiidae), identified recently in otter Lutra lutra populations in the UK. We confirm that intermediate snail and fish hosts for these parasites belong to the Bithyniidae and Cyprinidae taxa. To examine how the distributions of these parasite populations are determined across England and Wales, we tested whether prevalence and mean intensity were associated with abiotic and biotic factors. Most notably, high temperatures were positively associated with the distribution of both parasite species across England and Wales. The empirical data recorded was then used to parameterise a simple, but realistic, model exploring the host population dynamics for this group of parasites.

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Mekong schistosomiasis - snail population trends and the impact of hydropower projects

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Recently concerns have been voiced over the impact of dams planned in the Mekong Basin, with the suggestion that they could lead to an increase in schistosomiasis as observed in similar situations in Africa. The snails transmitting Mekong schistosomiasis, however, exhibit very different habitat requirements from those involved in Africa. In view of these differences, and the lack of suitable baseline data, snail intermediate host population density estimates were made in the Mekong river in 2011 and compared with earlier estimates made between 1992 and 2005. The data set spanned the period before and after the closure of the Nam Theun 2 dam (NT2) project in central Laos. Consequently, analysis of the data, for significant changes in population trends, enabled some assessment of the impact of impoundment on snail populations in the Mekong river and relevant tributaries. In this talk, the results of the population survey are presented and their implications for water resource development and schistosomiasis control are discussed. In addition, the need for specific models which accommodate the particular features of the disease ecology of Mekong schistosmiasis is highlighted.

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Giardiasis in northwest England: a neglected (not so much) tropical disease

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Giardiasis, caused by the protozoan Giardia duodenalis, is a common gastrointestinal infection of humans and domesticated mammals worldwide. G. duodenalis is also a heterogeneous parasite, with seven morphologically identical genetic assemblages that can be characterized by using molecular markers. Giardiasis has received relatively little public health attention in the United Kingdom, but is suspected to be underreported. Between 2007 and 2012 we undertook a giardiasis surveillance programme in northwest England as a collaboration between the Health Protection Agency and the local Environmental Health Departments, with the aim of understanding the actual burden of disease in the area. Socio-demographic and clinico-epidemiological information was collected through questionnaires from confirmed cases of giardiasis. The parasite genotypic assemblage was determined from a subset of these cases by faecal DNA extraction and sequencing of Giardia genes. Results show that giardiasis occurred more frequent than previously reported, particularly in males. Infection was also associated with relatively high morbidity and seemed to be acquired mostly locally, rather than through foreign travel as has been commonly suspected. Some associations between the parasite assemblages and clinico-epidemiological features of the cases were identified. In this talk we also discuss our attempts to genotype further the various assemblages directly from clinical samples by adapting next generation sequencing technologies as novel tools for understanding the molecular epidemiology of Giardia parasites.

10/04/2013 Session 7D - Applying Ecology and Evolution (2) - Chair Andrea Graham 5:10 PM - 5:25 PM (15 mins)

Endoparasites of nestling seabirds affect siblings unequally

Hanna Granroth-Wilding, Hanna Granroth-Wilding (1,2), Sarah Burthe (2), Sue Lewis (1), Francis Daunt (2) & Emma Cunningham (1)

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Parasitic infection during early life has the potential to shape an organism's development. This could have life-long fitness consequences for the individual, with implications for population processes. However, individuals may not be affected equally. Even within a brood, siblings often differ in their susceptibility to poor environmental conditions, and may similarly differ in how they are affected by parasitism. Here, we investigate how parasitism and environmental conditions interact to affect the development of nestling European shags, Phalacrocorax aristotelis, a species with a pronounced brood hierarchy in which last-hatched chicks have higher mortality rates. We treated broods of three chicks with an anti-parasite drug across four years of variable success and measured nestlings' growth rate and behaviour in the nest. The growth of last-hatched siblings was more heavily impacted by parasitism than that of older siblings. Environmental conditions were also important, with a greater difference between siblings in less productive years. Treatment also affected the behaviour of last-hatched chicks more than that of older siblings. This suggests that the impact of parasites for individual development could be modulated by intra-brood conflict dynamics. Parasitism interacts with other external stresses in different ways for different brood members, with potential consequences for their contribution to future

generations.

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Veterinary Parasitology : Stop right there! Mass treatment programmes - lessons from veterinary parasitology - Chair Jacqui Matthews

Anthelmintic resistance in nematode parasites of animals is out of control: can we use the knowledge gained to prevent the same from happening in helminth parasites of humans?

Ray Kaplan, Ray Kaplan

University of Georgia

Anthelmintic resistance in important gastrointestinal nematode (GIN) parasites of ruminants and horses is reaching critical levels worldwide. The situation is most severe in sheep and goats, but the problem is rapidly escalating in horses and cattle as well. And most recently are reports of resistance in the dog heartworm, Dirofilaria immitis. Resistance in the filarial worm D. immitis is especially concerning, considering the pathogenic potential of this worm and the close phylogenetic relationship it has with the important filarial worm pathogens Wuchereria bancrofti and Onchocerca volvulus. To say it quite simply, anthelmintic resistance in parasites of animals is out of control. Multiple-resistance is the status quo, and in many parts of the world it is no longer possible to control GIN parasites of livestock using drugs alone. But this situation did not develop overnight, and years of experience have taught us a great deal about the biological and epidemiological factors that drive the evolution of resistance. We now know that resistance is an inevitable consequence of anthelmintic use, but the rate with which resistance evolves and spreads is directly related to the selection pressures placed on worm populations. Consequently, mass treatment strategies whereby whole herds of animals are treated at regular intervals are no longer recommended; in fact this approach is now broadly condemned as being unnecessary and unsustainable. This new reality is causing the veterinary parasitology community to reevaluate parasite treatment and control recommendations, and a new paradigm is emerging. At the same time, however, we are witnessing a large escalation of mass treatment strategies in humans for the control and elimination of helminth parasites. These helminth control and elimination programs have yielded great benefits in public health, and have the ability to produce long-term improvements in health and educational outcomes in many impoverished areas of the world. But, as we have seen in veterinary medicine, mass treatment strategies carry with them a heavy risk for resistance selection. Because the number of anthelmintic drugs available for helminth control in humans is so limited, widespread resistance to any of the drugs would carry with it severe consequences in the sustainability of helminth control programs. Thus, it seems logical that we should take note of the lessons we have learned in veterinary medicine and use this knowledge to reduce the likelihood that anthelmintic resistance will develop in human parasites. Unfortunately, good in vitro and molecular diagnostic tests to detect the early stages of resistance in human parasites still do not exist for most drugs. Financial resources must therefore also be directed to improve the detection and surveillance of resistance. Such tests are critical for detecting emerging resistance, and would provide a means to test hypotheses about factors that are most important in the selection of resistance in human helminths. Knowledge gained would provide an evidence-based means to modify helminth control programs to meet public health goals while remaining

sustainable. Intensive use of anthelmintics in animals has taught us a great deal about the biology and epidemiology of anthelmintic resistance; let's use this knowledge to prevent the same problems from developing in parasites of humans.

11/04/2013 Session 8A - Veterinary Parasitology : Stop right there! Mass treatment programmes - lessons from veterinary parasitology - Chair Jacqui Matthews 9:00 AM - 9:30 AM (30 mins)

Genetic evidence for hybridization between parasitic nematodes Haemonchus contortus and Haemonchus placei and its implications for the spread of anthelmintic resistance

John Gilleard, John Gilleard, Umer N. Chaudhry, Ramen Muthusamy, Mohammad Abbas, Elizabeth Redman

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There are many aspects of anthelmintic drug resistance that remain poorly understood including how resistance mutations originate and spread in parasitic nematode populations in the field. Resistance is particularly widespread in the highly pathogenic small ruminant parasitic nematode Haemonchus contortus providing us with a valuable model system in which to study such questions. For this parasite, three different mutations (P200, P198 and P167) in the isotype-1 β-tubulin gene have been associated with benzimidazole (BZ) resistance. We will present our current experimental evidence that suggests these mutations arise frequently and recurrently in parasite populations under selection. In addition, our work investigating the possibility of interspecies transfer of anthelmintic resistance genes will be presented. H. contortus and H. placei are phylogenetically closely related species and experimental co-transplantation of adult parasites can result in inter-species hybridization. Although these parasite species have strong host preferences, H. contortus can infect multiple host species and is sympatric with H. placei in many regions of the world . H. contortus is most commonly found in sheep and goats, whereas H. placei is most common in cattle. We present molecular genetic evidence that co-infection of individual hosts with these two parasite species is common in some regions and that interspecies hybridization occurs in natural field populations. This opens up the potential for genetic introgression as a mechanism for the interspecies transfer of resistance genes between different parasitic nematode species.

11/04/2013 Session 8A - Veterinary Parasitology : Stop right there! Mass treatment programmes - lessons from veterinary parasitology - Chair Jacqui Matthews 9:30 AM - 9:45 AM (15 mins)

Using faecal egg counts to reduce anthelmintic usage in horses

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Frequent anthelmintic usage in horses has contributed to the development of drug resistance which, for certain classes of anthelmintic, is widespread. The use of targeted-treatment strategies has been advocated for helminth control. The over-dispersed nature of strongyle nematode infections in equids, means it is possible to identify and target horses that excrete moderate to high numbers of parasite eggs in their faeces. This approach would reduce treatment frequency and protect a proportion of the parasite population from anthelmintic exposure with the aim of reducing selection pressure for resistance. We investigated the prevalence and distribution of nematode eggs in faecal samples from horses on 16 non-Thoroughbred yards using two faecal egg count (FEC) methods (McMaster and centrifugal-flotation, CF) over a nine-month period. A total of 368 horses were screened for the presence of eggs. Of these, 21% and 16% of horses met/exceeded the 200 eggs per gram (EPG) threshold for treatment when using McMaster or CF, respectively, resulting in 79% or 84% reductions in anthelmintic use depending on FEC method employed. A cost/benefit analysis was performed and, by applying a targeted-treatment protocol, an average saving of £244/annum per yard was calculated. These results indicated the real value of applying targeted treatment strategies for equine parasite control.

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First evidence for on-farm multi-drug resistance in sheep parasites in Northern Ireland

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The over-reliance on a small portfolio of anthelmintics, coupled with their misuse means that their utility as long-term parasite control options has been undermined. Supporting evidence includes ever-increasing reports of anthelmintic resistance in sheep flocks (Besier 2007; Jones et al. 2012; Mitchel et al. 2010). However, there has been a significant lack of data on anthelmintic resistance levels in Northern Ireland (NI). A recent faecal egg count reduction test (FECRT) study via postal survey conducted by McMahon et al. (2013) reported resistance levels of 77% to Benzimidazoles (BZ) and 47% to Avermectins (AVM) in flocks from across NI. This study encompasses a FECRT study to determine both BZ and AVM resistance across 23 sheep farms in NI. To ensure experimental consistency and data integrity, all sample collections, drug administrations and FERCTs were performed by the lead author. Egg count reductions post treatment of less than 95% (where pre treatment counts were over 150 eggs per gram of faeces [EPG]) were seen 8-10 days post BZ treatment on 35% of farms and 14-17 days post AVM treatment on 26% of farms. There was a post treatment reduction of less than 95%, indicating resistance to both drugs on 26% of farms, while the remaining 13% of farms showed reductions of more than 95%, indicating no resistance. To our knowledge, this is the first report of multi-drug resistant sheep parasites on farms in NI and demands an alteration to the prevailing parasite control strategies in use in the province.

11/04/2013 Session 8A - Veterinary Parasitology : Stop right there! Mass treatment programmes - lessons from veterinary parasitology - Chair Jacqui Matthews 10:00 AM - 10:15 AM (15 mins)

Genomic exploration of the genetic resistance to Haemonchus contortus in sheep

Guillaume Sallé, Guillaume Sallé1,2,3, Carole Moreno3, Julien Ruesche3, Mathias Aletru4, Jean-Louis Weisbecker4, Frédéric Bouvier5, Françoise Prévot1,2, Jean-Paul Bergeaud1,2, Cathy Trumel2, Christelle Grisez1,2, Dominique François3, Andres Legarra3, Emmanuel Liénard1,2, Philippe Jacquiet1,2 Presenting author: Guillaume Sallé

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Gastro-intestinal nematodes such as Haemonchus contortus are of major concern to sheep health worldwide. Selectively breeding sheep for increased resistance could help sustain production targets in the face of increasing anthelminthic resistance. Identifying and characterizing the causative genes responsible for resistance would augment the efficacy of selective breeding programs by directly targeting the genes involved in this trait, while also shedding light on the complexities of the sheep-nematode interplay. This study reports the first known attempt to functionally characterize a chromosome segment associated with resistance to H. contortus infection using a genetic mapping approach. Following analysis of a dense SNP map and a thousand fecal egg count (FEC) records from H. contortus challenged back-cross (BC) lambs, a segment of chromosome 12 explained a significant proportion of the observed variation in resistance of both immune-naïve and primed lambs. To further characterize this region, the BC sheep were selectively mated to produce BCxBC individuals which carried either two favorable or two unfavorable alleles. Sixty-one BCxBC lambs were then experimentally infected with 10,000 H. contortus larvae and various measures were taken (FEC, haematocrit, worm burden and fertility, gene expression). The results showed the BCxBC sheep with the resistance favourable alleles had lower FEC, better maintain their haematocrit and better limited the fecundity of female worms. Gene expression analysis revealed they also had a higher Th2-biased environment in the abomasal mucosa compared to their more susceptible counterparts. The genotyping of such limited region should contribute to predict the intrinsic resistance level of sheep.

11/04/2013 Session 8A - Veterinary Parasitology : Stop right there! Mass treatment programmes - lessons from veterinary parasitology - Chair Jacqui Matthews 10:15 AM - 10:30 AM (15 mins)

Helminth neurobiology: Target identification / validation & gene silencing I - Chair Angela Mousley

Helminth Neurobiology: Identifying the moving targets of cholinergic anthelmintics

Richard J. Martin, Richard J. Martin1, Jeffrey K. Beetham2, Nathan M. Romine2, Alan P Robertson1, Samuel K. Buxton1, Liang Dong3, Claude L. Charvet4, Cedric Neveu4 and Jacques Cabaret4

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We are seeking new ways to study how anthelmintics act and to study mechanisms of resistance. We will describe the application of recently introduced techniques to study modes of action and mechanisms of resistance. We use levamisole-sensitive and -resistant isolates of the pig nematode, Oesophagostomum dentatum and apply: microfluidics techniques on L3 larvae; transcriptomic techniques on adults; in vivo electrophysiology on muscle preparations of adults and; cloning & expression of nicotinic acetylcholine receptor in Xenopus oocytes to examine effects of different cholinergic anthelmintics. The new microfluidic techniques allow very high-resolution concentration-response phenotyping of anthelmintic-sensitive and -resistant isolates using measurements of velocity and muscle force produced by single larvae. The transcriptomic techniques allow expression levels of signaling pathway genes to be studied. The in vitro expression techniques have allowed separation and molecular characterization of different subtypes of cholinergic receptors. It is now possible to study actions of different cholinergic anthelmintics at whole-worm levels and at single-channel levels in sensitive and resistant worms. The intact worm studies show that resistance is associated with a reduction in the number of active receptors and changes in their pharmacological properties; the microfluidic techniques show that the larvae are less sensitive to levamisole and, actually, can swim faster; the transcriptomic approach suggests that a number of pathway genes are involved, rather than a single gene. Our current understanding suggests that the development of resistance is polygenic, allowing a less anthelmintic sensitive phenotype to appear which retains fitness for survival.
Supported by

11/04/2013 Session 8B - Helminth neurobiology: Target identification / validation & gene silencing I - Chair Angela Mousley 9:00 AM - 9:30 AM (30 mins)

Functional diversification of levamisole receptors in the trichostrongylid nematode Haemonchus contortus

Thomas Duguet, Thomas Duguet * (1) (presenting) Claude Charvet (2) Sean G. Forrester (3) Claudia M. Wever (4) Jospeh A. Dent (4) Cédric Neveu (2) Robin N. Beech (1)

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Pentameric cys-loop ligand-gated ion channels (pLGIC) are key mediators of fast ionotropic neurotransmission and are invaluable as drug targets in parasitic nematodes. The anthelmintic levamisole paralyses nematodes by binding to an acetylcholine-gated pLGIC, L-AChR, in the model free-living worm Caenorhabditis elegans. The C. elegans L-AChR is composed of five different subunits encoded by unc-63, unc-38, lev-8, lev-1 and unc-29. However, the parasitic nematode of small ruminants, Haemonchus contortus shows a major difference compared to the C. elegans model by the presence of four unc-29 paralogs. Receptors were reconstituted by injection of cRNA into Xenopus oocytes and identified by two-electrode voltage clamp electrophysiology. The role of each unc-29 paralog was evaluated by sequential replacement of UNC-29.1 in the H. contortus L-AChR-1. Two new channels produced with Hco-unc-29.3 and Hco-unc-29.4 were identified, revealing high but similar affinity of both receptors to acetylcholine with respective EC50s of 2.94

± 1.03 µM and 2.90 ± 1.01 µM as well as to levamisole with EC50s of 0.83 ± 1.02 µM and 1.63 ± 1.05 µM. Saturating concentration of pyrantel, nicotine or bephenium produced weak responses of both receptors compared to acetylcholine and levamisole. Also, acetylcholine currents were entirely inhibited by d-tubocurarine whereas dihydro-β-erythroidine did not affect signals in all cases. No receptor could be produced using Hco-unc-29.2, despite a similar level of sequence divergence to the other copies. These results confirm functional divergence among the four Hco-unc-29 paralogs and highlight their potential consideration in levamisole resistance and as novel parasite specific anthelmintic targets.

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In vivo and in vitro effects of ivermectin treatment on Brugia malayi microfilariae

Ashley Rogers, Ashley M. Rogers, Andrew R. Moorhead, Mike T. Dzimianski, Balazs Rada and Adrian J. Wolstenholme

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Filarial nematodes that cause lymphatic filariasis, Brugia malayi, Wuchereria bancrofti, and B. timori, affect over 120 million people in 80 countries worldwide. Ivermectin, one of the drugs used in current mass drug administration (MDA) programmes, has a fast acting and long lasting microfilaricidal effect. Its mode of action is still unclear. In vitro, the concentration of ivermectin required to paralyze B. malayi microfilaria (mf) is much higher (>1 µM) than achieved in people receiving MDA. Recently published data show that ivermectin treatment of mf inhibits secretion of Excretory/Secretory products, suggesting that host factors may have a synergistic role with ivermectin in removing B. malayi mf from the circulation. When B. malayi mf were co-incubated with human neutrophils and with ivermectin, there was a drug-dose-dependent increase in the level of neutrophil attachment to the mf. In an attempt to identify possible gene products that might be responsible for this phenomenon, we carried out RNASeq analysis of B. malayi mf isolated from Mongolian jirds (Meriones unguiculatus) that had received two doses of ivermectin at 0.2 mg/kg one month apart. This revealed 74 nematode-specific gene transcripts that were significantly differentially expressed between mf isolated from treated and control animals. Of the 74 nematode-specific genes, 59 of them are annotated with a known or putative function. Further investigation of the up- and down-regulated genes may help elucidate the mode of action of ivermectin against the causative agents of lymphatic filariasis.

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Neuropeptides as Transgenic Nematicides

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Plant parasitic nematodes impose a significant economic burden on plant cultivation efforts

worldwide. Recent estimates predict losses across all sectors of approximately $125 billion annually. Conventionally, an integrated approach to PPN management has relied heavily on various nematicides. As environmental concerns rise over the systemic effects of sustained nematicide use, withdrawal has left a significant shortcoming in our ability to manage this problem and highlights the need for novel and robust control methods. It has been discovered that nematodes can assimilate exogenous peptides through retrograde transport along the chemosensory amphid neurons. These peptides accumulate within cells of the central nerve ring and can elicit physiological effects when released to interact with receptors on adjoining cells. We are harnessing bioactive neuropeptides from the neuropeptide-like protein (NLP) and FMRFamide-like peptide (FLP) families of plant parasitic nematodes as novel nematicides which will be secreted into the apoplastic space of crop plants, and into the rhizosphere. So far we have identified 15 discrete neuropeptides that impact on chemosensation and/or neuromuscular activity in the root knot nematode Meloidogyne incognita, through RNAi-based gene functional studies and exogenous peptide addition.

11/04/2013 Session 8B - Helminth neurobiology: Target identification / validation & gene silencing I - Chair Angela Mousley 10:00 AM - 10:15 AM (15 mins)

FLP-21 as a broad-spectrum transgenic nematicide

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Plant parasitic nematodes (PPNs) are responsible for significant reductions in crop yield globally. Recent estimates predict losses across all sectors of approximately $125 billion annually. PPN management relies heavily on various nematicides, however, recent EU legislation is forcing withdrawal of many environmentally damaging plant protective products in an effort to maintain soil floral and faunal diversity. One forecast predicts that nematicide withdrawal could double the economic implications of Potato cyst nematodes to £56 million annually in the UK alone. The FMRFamide-like peptide (FLP), FLP-21 shares the same sequence identity in many different PPN species, including the potato cyst nematode Globodera pallida, and the root knot nematode Meloidogyne incognita. It has been discovered that nematodes can assimilate exogenous peptides through retrograde transport along the chemosensory amphid neurons. These peptides accumulate within cells of the central nerve ring (CNR) and can elicit physiological effects when released to interact with receptors on adjoining cells. We have studied the function of FLP-21 using RNAi, and have established a function in coordinating host-finding for both nematode species. Immunocytochemistry indicates expression in the amphid neurons and cells of the CNR. Exogenous application of FLP-21 is potent at 1 pM for G. pallida, and 1 µM for M. incognita. FLP-21 will be expressed in crop plant roots, and will be secreted into the apoplasm and rhizosphere by a plant signal peptide sequence, inhibiting PPN host-finding, and reducing infection levels.

11/04/2013 Session 8B - Helminth neurobiology: Target identification / validation & gene silencing I - Chair Angela Mousley 10:15 AM - 10:30 AM (15 mins)

Helminth neurobiology: Target identification / validation & gene silencing II - Chair Collette Britton

Molecular Mechanisms of Infection by Sedentary Plant-Parasitic Nematodes

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Sedentary plant-parasitic nematodes, like cyst (Heterodera, Globodera spp.) and root-knot nematodes (Meloidogyne spp.), induce redifferentiation of plant root cells into specialized feeding cells (syncytia and giant-cells, respectively) to enable their sedentary life styles. Infecting nematodes secrete effector proteins through their stylets into host root cells, and these proteins most likely trigger the formation of feeding cells and mediate susceptibility through the suppression of plant defenses. Consequently, the identification of nematode effector proteins is of high importance. A new method for effector identification relies on transcriptomic analyses of the three nematode cells producing such effectors and is yielding unprecedented views into the effector repertoires of diverse nematode taxa. In addition to effector identification, the functional characterization of their effects on plant cells is of high interest. It has become clear that the massive gene expression changes that occur in redifferentiating root cells are mediated transcriptionally as well as in a post-transcriptional and post-translational manner. In one example, a cyst nematode effector protein is phosphorylated by a cytoplasmic plant kinase, which results in translocation into the plant nucleus. There the effector interacts with a plant transcription factor, presumably resulting in gene expression alterations. Much more dramatic is our discovery that as a result of cyst nematode infection, microRNAs change expression in the developing syncytium. In particular, the Arabidopsis microRNA396 regulatory network has strong impact on cyst nematode parasitic success. This microRNA post-transcriptionally regulates the expression of the Growth Regulating Factor 1 (GRF1) and GRF3 transcription factor genes in the syncytium. The miR396-GRF1/GRF3 regulatory unit is involved in the initiation of the syncytium induction/formation phase and then the transition into the maintenance phase. Expression modulations of miR396 and its GRF target genes resulted in reduced syncytium size and arrested nematode development. Genome-wide gene expression profiling revealed major roles of the microRNA396 regulatory unit in controlling host plant gene expression, altering the expression of approximately 50% of the genes differentially expressed in the syncytium. miR396, and probably other microRNAs that we have shown to change abundance in the syncytium, thus, represent powerful molecular targets for the cyst nematode to modulate plant cell development. Ongoing functional characterizations of additional microRNAs as well as identification and characterization of all nematode effectors promise to provide an understanding of how plant-parasitic nematodes drive normal root cells toward novel developmental pathways required for successful parasitism. Ultimately, such progress will show the way towards solving these pest problems.

11/04/2013 Session 9B - Helminth neurobiology: Target identification / validation & gene silencing II - Chair Collette Britton 11:10 AM - 11:40 AM (30 mins)

Identifying microRNAs and target genes associated with development in parasitic nematodes

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MicroRNAs are short, endogenous, non-coding RNAs that negatively regulate gene expression. They are found in almost every organism and are known to regulate key developmental decisions in the free-living nematode, Caenorhabditis elegans. Recently, 192 miRNAs were discovered in the parasitic nematode, Haemonchus contortus (Winter et al, 2012) and microarray analysis indicates that 56 show temporal variation. The majority (77%) of these temporally expressed miRNAs are conserved, suggesting that they have an important regulatory role during H. contortus development. Studying this potential role requires us to identify the potential targets of each miRNA and their biological significance. We are currently focusing on the miRNAs that show significant differential expression between the L3 (free-living) and L4 (parasitic) stages which may relate to developmental arrest in the environment and activation in the host. Bioinformatic algorithms, designed for use in C. elegans, have identified many potential target genes. Highly significant target gene predictions are analysed using qRT-PCR in both C. elegans mutant strains and various H. contortus life cycle stages. A recently developed technique, cross-linked immunoprecipitation (CLIP), is being adapted for use in H. contortus and will be used to identify and compare targets in different life cycle stages. We hope to identify miRNAs that regulate important developmental genes and determine whether small RNA mimics or inhibitors have potential as therapeutic agents. Winter AD, Weir W, Hunt M, Berriman M, Gilleard JS, Devaney E and Britton C (2012) BMC genomics. 13(1): 4

11/04/2013 Session 9B - Helminth neurobiology: Target identification / validation & gene silencing II - Chair Collette Britton 11:40 AM - 11:55 AM (15 mins)

RNA interference in adult Ascaris suum: New tricks for an old model

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RNA interference (RNAi) is a reverse genetics technique which can be utilized to probe target gene function and to validate novel antiparasite-drug targets. The efficiency of RNAi in nematodes varies between species, life-stage, and gene target. The large size of Ascaris suum has facilitated its development as a key model species for nematode parasite biochemistry, neurobiology and physiology research, driving discovery biology and comparative studies with the free-living model Caenorhabditis elegans. Whilst RNAi has been reported in L3 larval stage A. suum, it has not been demonstrated in adults, limiting the utility of this gene silencing tool. Here we report the development of an RNAi platform for adult A. suum. Double stranded (ds)RNAs targeting genes expressed in a variety of tissue types (nerve, muscle, all cell types) were injected into the pseudocoelomic cavity of adult female A. suum; successful induction of RNAi was determined by monitoring target-gene transcript levels, encoded protein expression and worm phenotype. The data presented demonstrate: (i) a functional RNAi pathway in adult A. suum that can be triggered by the injection of dsRNA into the pseudocoel; (ii) the RNAi-susceptibility of target genes with disparate expression patterns; and, (iii) the ability to induce RNAi in tissues remote from the site of dsRNA injection. The optimisation of an RNAi platform in adult A. suum has significant appeal

due to its tractability as a model for experimentation, the availability of genomic/transcriptomic resources and its negative impacts on food security and human health.

11/04/2013 Session 9B - Helminth neurobiology: Target identification / validation & gene silencing II - Chair Collette Britton 11:55 AM - 12:10 PM (15 mins)

RNAi transcript and protein dynamics in juvenile Fasciola hepatica

Paul McVeigh, Paul McVeigh1, Russell M Morphew2, Paul McCusker1, Erin M McCammick1, Angela Mousley1, Ravikumar Gopalakrishnan3, Raman Muthasamy3, Abbas Abidi4, Khalid Saifullah4, Nikki J Marks1, Peter M Brophy2, Aaron G Maule1

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While Fasciola spp. liver fluke continue to present a major challenge to global food security and human health, basic research into fundamental fluke biology that might identify the next generation of anti-fluke drug and vaccine targets is under-served within global agricultural and health science research programmes. In order to capitalise on the on-going expansion of liver fluke genome/transcriptome sequence datasets, we have focused on development and optimisation of RNA interference (RNAi)-based gene silencing tools in Fasciola hepatica. Our data illustrate that newly-excysted juvenile (NEJ) fluke of the widely-used US Pacific Northwest strain, are very amenable to RNAi triggered by simply soaking flukes in target-complementary double-stranded (ds)RNA. Focusing on three virulence genes, representing established vaccine antigen candidates (cathepsin B, cathepsin L, and a sigma class glutathione S transferase (sigmaGST)), we have tracked the responses of target transcripts and proteins following dsRNA challenge. We find that while transcript knockdown occurs in these three targets within 24 hours, persists for at least 21 days, and may be triggered by as little as a 60 min burst exposure to 50 ng/ul dsRNA, there is a target-specific lag period before the detection of significant protein suppression. This lag time may vary from 9 days (sigmaGST), to >21 days (cathepsin B). Ongoing work focuses on: (i)Developing in vivo assays to measure the impact of virulence-gene RNAi on worm viability/infectivity, and (ii)Manipulation of in vitro maintenance conditions in order to accelerate post-RNAi protein turnover rates. Funded by BBSRC grant BB/H009477/1.

11/04/2013 Session 9B - Helminth neurobiology: Target identification / validation & gene silencing II - Chair Collette Britton 12:10 PM - 12:25 PM (15 mins)

Searching for potential marker genes that indicate the activation or not of the RNA interference (RNAi) pathway

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RNAi is a reverse genetic mechanism that causes highly specific gene silencing. It was initially described in Caenorhabditis elegans, in which it has been broadly used as a tool for the functional

analysis of its genome. Nevertheless, its application on parasitic nematodes was more difficult than anticipated. The major problem confronting the use of RNAi in parasitic nematodes is the inconsistency of knockdown among different parasitic species and among different genes within the same species. In cases where the RNAi is unsuccessful, it is not known whether the dsRNA is penetrating the parasite and whether the RNAi pathway is activated in response to the exogenous dsRNA. Thus far, there is no information on the status of RNAi pathway gene transcription in C. elegans. Are these genes constantly transcribed or are they "switched on" in response to the dsRNA? The aim of the study was to determine whether there were RNAi pathway genes that potentially could be used as markers which indicate the activation of the RNAi pathway. To achieve this, two targets were selected, namely the Ce-cpr-4 and Ce-sod-4, which had been proven to be consistently susceptible and refractory to RNAi in C. elegans, respectively. After the exposure to the dsRNA the transcript levels of candidate marker genes (Ce-dcr-1, Ce-ego-1 and Ce-rsd-3) were examined. The results showed that those genes cannot be used as markers for the activation of the RNAi pathway since their transcript levels are the same regardless the activation or not of the RNAi pathway.

11/04/2013 Session 9B - Helminth neurobiology: Target identification / validation & gene silencing II - Chair Collette Britton 12:25 PM - 12:40 PM (15 mins)

Schistosomes I: Biology - Chair Mike Doenhoff

Antibody responses to developmentally expressed S. mansoni glycan antigens

Cornelis Hokke, Cornelis H Hokke, Cornelis H Smit, Nicole N Driessen, R Lynh Nguyen and Angela van Diepen

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The parasitic blood fluke Schistosoma mansoni, like all multicellular organisms, expresses a wide range of complex glycans as part of glycoproteins and glycolipids. The expression and biosynthesis of functional and immunogenic glycan elements is developmentally regulated and cell- and species-specific. The glycans and glycoconjugates expressed by schistosomes play a prominent role in the parasite's biology, in particular in the interaction with the human and snail hosts. While previously schistosome glycoconjugates have been identified as diagnostic targets, we currently focus our research on glycans associated with the induction and modulation of immune responses in the host, with the aim of identifying glycans as intervention targets. Among the different mechanisms of interaction, in particular an intense anti-glycan antibody response is mounted in the mammalian host. At present it is unclear if (a subset of) such anti-glycan antibodies can confer protection from (re-)infection or not. To address the latter issue, we have first filled the gaps in our knowledge of the schistosome glycome by unravelling N- and O-glycan profiles of S. mansoni, including the invasive larvae, juvenile as well as adult worms, eggs and miracidia. These profiles indicated that the expression of many potentially antigenic glycan motifs gradually shifts between the different stages, but that also glycan motifs exist that are unique for a particular life cycle stage. A library of defined anti-glycan monoclonal antibodies in combination with immune fluorescence microscopy was applied to study the parasite surface expression of glycan motifs during development. Subsequently, we have printed the hundreds of glycans purified during these structural studies on glass slides to create glycan microarrays. The arrays were then screened with

sera from cohorts of S. mansoni-infected individuals or animals to study responses to the individual glycan antigens printed. The hypothesis that subsets of such responses may be associated with susceptibility or resistance to schistosome infection will be discussed. Supported by NWO-CW ECHO grant 700.58.003 and the EU-FP7 project TheSchistoVac 242170

11/04/2013 Session 8C - Schistosomes I: Biology - Chair Mike Doenhoff 9:00 AM - 9:30 AM (30 mins)

Functional Mapping of Protein Kinase A in Adult Schistosoma mansoni

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Cyclic AMP (cAMP)-dependent protein kinase/protein kinase A (PKA) is the major transducer of cAMP signalling in eukaryotic cells. Here, using laser scanning confocal microscopy and 'smart' anti-phospho PKA antibodies that exclusively detect activated PKA, we provide a detailed in situ analysis of PKA signalling in intact adult Schistosoma mansoni. In both adult male and female worms, activated PKA consistently associated with the tegument, oral and ventral suckers, oesophagus and somatic musculature. In addition, the seminal vesicle and gynaecophoric canal muscles of the male displayed activated PKA whereas in female worms activated PKA localized to the ootype wall, the ovary, and the uterus particularly around eggs during expulsion. Exposure of live worms to the PKA activator forskolin (50 µM) resulted in striking PKA activation in the central and peripheral nervous system including at nerve endings at/near the tegument surface. Such neuronal PKA activation was also observed without forskolin treatment, but only in a single batch of worms. In addition, PKA activation within the central and peripheral nervous systems visibly increased within 15 min of worm-pair separation when compared to closely coupled worm pairs. Finally, exposure of adult worms to forskolin induced hyperkinesias in a time and dose dependent manner with 100 µM forskolin significantly increasing the frequency of gross worm movements to 5.3 times that of control worms ($P \leq 0.001$). Collectively these data are consistent with PKA playing a central part in motor activity and neuronal communication, and possibly interplay between these two systems in S. mansoni.

11/04/2013 Session 8C - Schistosomes I: Biology - Chair Mike Doenhoff 9:30 AM - 9:45 AM (15 mins)

Linking parasite genetics with host disease phenotype, the case for human schistosomiasis.

Tine Huyse, Tine Huyse,1,2 Nele Boon1,2, Frederik Van den Broeck1,2, Lynn Meurs2, Filip A.M. Volckaert1 & Katja Polman2

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Schistosomiasis is a major, poverty-related disease affecting more than 200 million people in

developing countries, 85% of them in sub-Saharan Africa. It has a complex epidemiology with a large variation in infection intensity, immune responses to infection, and schistosome-related pathology. Besides host-related factors, there are numerous parasite and environmental factors involved, which have been largely overlooked in epidemiology and control-oriented research. To untangle the importance of these factors, knowledge about the influence of parasite genetics on host's disease patterns is fundamental. We conducted a large epidemiological study in northern Senegal. We genotyped 1692 S. mansoni larvae collected from 45 human hosts with nine microsatellite loci and linked this with host data such as age, gender, infection intensity, liver and bladder morbidity. We found a positive relationship between schistosome infection intensity (measured as eggs per gram feces (epg)), and the frequency of a certain parasite allele. We corrected for age, sex, and co-infection with S. haematobium. This trend is found with linear regression and redundancy analysis. Two other alleles in this locus were negatively correlated with epg. This microsatellite locus is located in the untranslated region (UTR) of a protein kinase gene. Further characterization of this region will be discussed.

11/04/2013 Session 8C - Schistosomes I: Biology - Chair Mike Doenhoff 9:45 AM - 10:00 AM (15 mins)

Developing microsatellite markers to assess genetic diversity of Schistosoma haematobium: a new tool to measure the impact of control programmes.

Aidan Emery, Aidan M. Emery(1), Travis C. Glenn(2), Stacey L. Lance(3), Anna M. McKee (2), Bonnie L. Webster(1) Adhemar Zerlotini(4), Guilherme Oliveira(4), David Rollinson(1), and Brant C. Faircloth(5)

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The Schistosomiasis Consortium for Operational Research and Evaluation (SCORE) is a multi-centre collaborative project to answer strategic questions about schistosomiasis control and elimination. Control programmes for schistosomiasis rely on the use of mass drug administration (MDA), using Praziquantel. One of the SCORE research aims is to evaluate the effect of different MDA regimes on the prevalence, intensity and population genetics of both Schistosoma haematobium and Schistosoma mansoni. For S. haematobium, the project required the development and optimization of a new suite of microsatellite markers. By sequencing over a million random DNA fragments from a single S. haematobium isolate from Zanzibar, we identified over 13,000 unique loci, of which 15 were chosen and fully optimized using a geographically diverse range of S. haematobium samples archived in SCAN, the Schistosomiasis Collection at the Natural History Museum. As the SCORE project progresses, and samples become available to compare baseline and post-treatment surveys, the microsatellite panels are now being used to study the effect of

MDA on parasite genetics.

11/04/2013 Session 8C - Schistosomes I: Biology - Chair Mike Doenhoff 10:00 AM - 10:15 AM (15 mins)

Genetic diversity within Schistosoma haematobium: DNA barcoding reveals two distinct groups

Bonnie Webster, 1. Bonnie L Webster 2. Joanne P Webster 3. Aiden E Emery 4. David Rollinson

1 and 2 Department of Infectious Disease Epidemiology, Imperial College, London 3 and 4 Parasites and Vectors, Life Sciences, The Natural History Museum, London N.B This study was carried out by Bonnie Webster when she was employed at the Natural History Museum, London.

Schistosomiasis is a disease caused by parasitic blood flukes of the genus Schistosoma. Species that infect humans are prevalent in developing countries, having a major impact on public health and well-being as well as an impediment to socioeconomic development. More people are infected with Schistosoma haematobium than with all the other schistosome species combined, however mainly due to the inability to maintain S. haematobium in the laboratory system empirical studies on this parasite are minimal. The genetic variation of this Schistosoma species on a wide geographical scale has never been investigated. In this study, we have used a DNA 'barcoding' approach to document the genetic variation and population structure of S. haematobium sampled from 18 countries across Africa and the Indian ocean Islands. The study reveals a distinct genetic separation of S. haematobium from the Indian Ocean Islands and the closely neighbouring coastal regions from S. haematobium found throughout the African mainland, the latter of which exhibited extremely low levels of mitochondrial diversity within and between populations of parasites sampled. The data suggests that at some point in the recent evolutionary history of S. haematobium in Africa the population may have passed through a genetic 'bottleneck' followed by a population expansion. This study provides novel and extremely interesting insights into the population genetics of S. haematobium on a large geographic scale, which may have consequence for control and monitoring of urogenital schistosomiasis.

11/04/2013 Session 8C - Schistosomes I: Biology - Chair Mike Doenhoff 10:15 AM - 10:30 AM (15 mins)

Schistosomes II: Elimination of schistosomiasis - fact or fiction? - Chair Russell Stothard

Schistosomiasis elimination: fact or fiction?

Stefanie Knopp, Stefanie Knopp1,2,3, Khalfan A. Mohammed4, Fiona Allan3, Muriel Rabone3, Jürg Utzinger1,2, David Rollinson3

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Schistosomiasis is a chronic and debilitating disease, caused by the blood fluke of the genus Schistosoma. Globally, more than 200 million people are infected. Gaining and sustaining control

of schistosomiasis and, whenever feasible, achieving local elimination are the year 2020 targets put forward by the World Health Organization. Control of schistosomiasis is problematic in some countries because of factors such as high endemicity, rapid re-infection of the population after treatment, environmental modifications (e.g. large dams), agricultural practices (e.g. irrigation systems), and animal reservoirs. However, great progress towards elimination has been achieved in several settings. For example, S. japonicum transmission was remarkably reduced in China by the integration of snail control, health education, improvement of sanitation and access to clean water, with mass treatment of the at-risk population. In countries where schistosomiasis has been eliminated, economic development, strong political commitment, the recognition of schistosomiasis as public health problem, and the use of local resources and health systems plus the application of integrated control measures have been the key to success. Elimination of urogenital schistosomiasis has become a priority on the agenda of the Zanzibar government and the international community in 2011. Over the next 3–5 years, the whole at-risk population will be administered praziquantel (40 mg/kg) biannually. Additionally, snail control and behaviour change interventions will be implemented in selected communities and the impact measured in a randomized intervention trial. The study will provide an evidence-base for decisions about schistosomiasis elimination in Zanzibar and can guide future elimination programmes in Africa.

11/04/2013 Session 9C - Schistosomes II: Elimination of schistosomiasis - fact or fiction? - Chair Russell Stothard 11:10 AM - 11:40 AM (30 mins)

Contrasting colonization history and genetic structure of two parasite species in northern Senegal

Frederik Van den Broeck, Frederik Van den Broeck (1,2) Philippe Lemey (4) Gregory Maes (2) Kim Vereecken (1) Filip Volckaert (2) David Rollinson (3) Katja Polman (1) Tine Huyse (1,2)

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About thirty years ago, two dams were constructed in the Senegal River Basin in order to improve the agricultural conditions in Northern Senegal. The subsequent ecological changes stimulated the spread of Bulinus and Biomphalaria snail species, intermediate hosts of the human parasites Schistosoma haematobium and S. mansoni, respectively. Both parasite species could rapidly colonize northern Senegal following the massive population expansion of their intermediate snail hosts and the increasing human immigration for agriculture. While S. mansoni colonization was characterized by an explosive spread, S. haematobium expansion occurred more slowly. This is a unique system where the origin of an epidemic outbreak is exactly known, providing an opportunity to study the molecular evolution of pathogens in a relative short time frame. We therefore assessed the genetic variability at microsatellite loci within and between natural populations of S. mansoni and S. haematobium in several villages along several waterways in northern Senegal. F- and R-statistics revealed a tenfold higher genetic differentiation between S. haematobium populations than between S. mansoni populations. As the level of human host mobility is the same for both parasite species, these results can either be explained by (or a

combination of) a difference in the level of snail host mobility and/or by a different demographic history of the snail host or the parasite itself. Various demographic and genealogical histories will therefore be explored using MCMC simulation programs.

11/04/2013 Session 9C - Schistosomes II: Elimination of schistosomiasis - fact or fiction? - Chair Russell Stothard 11:40 AM - 11:55 AM (15 mins)

A rapid antibody-detection test for diagnosis of schistosomiasis at the point-of-care (POC)

Emily Dawson, Dawson, E. M. Doenhoff, M. J.

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Diagnosis of schistosomiasis is still widely reliant on traditional parasitological methods, i.e. the Kato-Katz faecal smear for Schistosoma mansoni and urine filtration for S. haematobium. Since these methods are insensitive, relatively laborious and expensive to perform, much effort has been expended into developing alternative ways of diagnosing the disease. Antibody-detection is the best method for diagnosis in areas of low endemicity. It has the merit of high sensitivity and is likely to be useful for schistosomiasis control as programmes are expanded and accelerated towards meeting the WHO's 2020 goals for neglected tropical diseases. A rapid diagnostic test (RDT) for use at the point-of-care (POC) is much more likely to be useful in low-middle income countries than the current assays that are available for antibody-detection. We have therefore been working to develop such a test that incorporates S. mansoni cercarial transformation fluid (SmCTF) for the detection of anti-schistosome antibodies in human blood. Evaluations have been carried out in multiple countries and across different age groups, and results are promising. The SmCTF-RDT is at least as sensitive as two Kato-Katz smears for the diagnosis of S. mansoni infections and one urine filtration for the diagnosis of S. haematobium infections. Specificity of the RDT is low when parasitological methods are the reference standard, but this is likely to be because of the relative insensitivity of the latter. Further evaluations are necessary to determine true specificity, but current results indicate the SmCTF-RDT may be suitable for mapping schistosomiasis prevalence in areas of low endemicity.

11/04/2013 Session 9C - Schistosomes II: Elimination of schistosomiasis - fact or fiction? - Chair Russell Stothard 11:55 AM - 12:10 PM (15 mins)

The dynamics of faecal occult blood and calprotectin in young children with intestinal schistosomiasis in Uganda

Amaya Bustinduy, Amaya Bustinduy*, Jose C. Sousa-Figueiredo, Martha Betson, Moses Adriko, Narcis Kabtereine, Alan Fenwick, J. Russell Stothard

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The search for field-applicable tools of morbidity attributable to schistosomiasis continues, especially for surrogate markers of disease in young children. Moreover, their short-term dynamics following anti-parasitic treatment is yet to be assessed. In this study, we examined a

total of 211 Ugandan children of which 63.5% were egg-patent for Schistosoma mansoni and all were given praziquantel at standard dosing (40 mg/kg). After 24 days, 183 children were re-examined to find 28.3% to remain egg-patent with intestinal schistosomiasis. The prevalence of faecal occult blood and calprotectin, as measured by rapid diagnostic tests, was 13.1% and 53.4% [positive criterion of > 50 µg/g] at baseline and then 8.1% and 47.1% at follow-up, respectively. Between inspection time-points, there was a significant difference in the distribution of cases within calprotectin intensities. Both faecal occult blood and calprotectin were associated with egg-patent schistosomiasis at baseline and at follow-up. At baseline, faecal occult blood and host anaemia were correlated, suggesting a potential causal mechanism of morbidity in intestinal schistosomiasis. Whilst faecal calprotectin assays were informative, but were relatively expensive, we suggest that faecal occult blood tests have a more promising future for measuring short-term dynamics of morbidity.

11/04/2013 Session 9C - Schistosomes II: Elimination of schistosomiasis - fact or fiction? - Chair Russell Stothard 12:10 PM - 12:25 PM (15 mins)

New insights into the epidemiology of intestinal schistosomiasis in Uganda: analysis of Schistosoma mansoni in pre-school children and mothers reveals similar patterns of genetic diversity

Martha Betson, Jose C. Sousa-Figueiredo, Narcis B. Kabatereine, J. Russell Stothard

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In Uganda, intestinal schistosomiasis is the dominant form of the disease and is caused by Schistosoma mansoni. Patent infections can be found in early childhood although such afflicted children are not yet included in control programmes. The longitudinal Schistosomiasis in Mothers and Infants study aimed to investigate the epidemiology and dynamics of S. mansoni in pre-school children and their mothers in six Ugandan lakeshore communities, three on Lake Albert and three on Lake Victoria. During the study, parasites were sampled from children, their mothers and local Biomphalaria snails (intermediate host). A total of 1800 parasites were genotyped by “DNA barcoding”, sequence analysis of the mitochondrial cytochrome c oxidase gene. Genetic diversity within the sample was high with over 230 unique DNA barcodes identified, of which 184 were novel. As expected, there was evidence of schistosome population divergence between lakes. Surprisingly, however, parasite populations sampled from children showed a similar diversity to those sampled from their mothers, pointing towards a non-linear relationship between duration of exposure and the accumulation of parasite diversity. The genetic diversity six months after praziquantel treatment was similar to pre-treatment diversity suggesting that medication had no discernible effect on the diversity of re-infection(s). There was no correlation between infection intensity and genetic diversity, nor any association between treatment history and parasite diversity. Analysis of how the parasite population structure changes over time is underway, but overall these results provide insight into the dynamics of S. mansoni and reveal some counterintuitive patterns of population diversity.

11/04/2013 Session 9C - Schistosomes II: Elimination of schistosomiasis - fact or fiction? - Chair Russell Stothard 12:25 PM - 12:40 PM (15 mins)

Ecological Interactions During Infections - Chair Mike Begon

Ecological interactions during murine malaria infections: using pattern to infer process

Jess Metcalfe, Jess Metcalfe

University of Oxford

Within-host ecology can drive the dynamics of disease. For example, the peaks and troughs of parasitemia may be shaped by both resource limitation (via target cell depletion; a bottom-up effect) and immune clearance (a top-down effect, akin to predation). In murine malaria, simple non-parametric one-time-step look-ahead models offer power to partition these different aspects; yielding insights into fluctuations of the relative importance of top-down and bottom-up effects over the time-course of infection, as well as revealing a protective role of apparent immune pathology, and the impact of inocula size. The approach can be applied to understanding strain diversity in pathology. Interesting questions linked to this work include the fundamental biology underlying why one time-step look-ahead methods are applicable.

11/04/2013 Session 8D - Ecological Interactions During Infections - Chair Mike Begon 9:00 AM - 9:30 AM (30 mins)

Genetic signature of coevolution in an insect virus

Lena Wilfert, Lena Wilfert Frank Jiggins

(1) Centre for Ecology and Conservation, University of Exeter, Cornwall Campus, Penryn, TR10 9EZ, UK (2) Department of Genetics, University of Cambridge, Cambridge, CB2 3EH, UK

The fruitfly Drosophila melanogaster is entangled in an ongoing arms-race with its vertically transmitted parasite, the sigma virus. Previous work has shown that a selective sweep of a resistant allele of the ref2(P) gene in the fruitfly was followed by the rapid spread of a virulent viruses that were able to overcome this resistance mutation in natural populations. By analyzing the phenotype and genome of a large panel of natural isolates of the sigma virus, we have shown that a recent sweep of the virulent virus coincided with a viral population expansion. This genomic data also shows that virulence might be costly for the sigma virus: several independent mutations have led to a reversal to the avirulent phenotype, which cannot transmit in flies carrying the ref2(P) resistance allele. However, these mutations can only be found at the tips of the viral phylogeny, indicating that avirulent viruses cannot persist in nature and that selection for virulence is ongoing in these populations.

11/04/2013 Session 8D - Ecological Interactions During Infections - Chair Mike Begon 9:30 AM - 9:45 AM (15 mins)

Are there energetic and genetic trade-offs between parasite resistance and predator defence? A test using the crustacean Daphnia magna

Job de Roij, Job de Roij Philip J. Wilson Rebecca Muir Andrew P. Beckerman Tom J. Little

Institute of Evolutionary Biology, University of Edinburgh, UK

In the wild, organisms are exposed to parasites and predators simultaneously, and often they will have evolved defences against both of these natural enemies. Parasite defence and predator defence may interact, but this idea has yet to be tested thoroughly. We carried out an experiment to investigate energetic and genetic trade-offs between parasite resistance and a predator-induced life history shift in the freshwater crustacean Daphnia magna. Individuals from 40 D. magna genotypes were exposed sequentially to a fish predator, the three-spined stickleback, Gasterosteus aculeatus, and the sterilising bacterial parasite, Pasteuria ramosa. All D. magna genotypes responded to predator exposure by lowering their age at first reproduction, i.e. a life history shift. Exposure to the fish predator had no overall effect on parasite susceptibility, but genotypes varied in their response, with many showing an increase or decrease in parasite susceptibility. This suggests that there is no general energetic cost of the predator-induced life history shift in terms of parasite susceptibility, or perhaps that it is variable among host genotypes. There was also no genetic correlation between the strength of the predator-induced life history shift (predator defence) and parasite resistance (parasite defence) across host genotypes. The absence of a genetic trade-off suggests that there is no shared genetic control of predator defence and parasite defence in D. magna. Therefore, it seems that, in this system, predator defence and parasite defence are neither physiologically nor evolutionarily constrained by each other.

11/04/2013 Session 8D - Ecological Interactions During Infections - Chair Mike Begon 9:45 AM - 10:00 AM (15 mins)

Cross-phylum shared antigens and apparent competition during nematode-malaria co-infection

Andrea Graham, Karen Fairlie-Clarke1, Christina Hansen2, Adam Rosenthal2, Judith E. Allen3 & Andrea L. Graham2 *

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Helminths and protozoa may interact via various ecological mechanisms within a co-infected host. For example, they may compete for resources (e.g., if both feed upon host red blood cells), and/or one may alleviate immunological pressure for the other (e.g., if helminth-induced immune responses suppress responses against protozoa). However, resource competition and facilitation are not the only mechanisms of interaction observed. Apparent competition may also occur, if an immune response induced by one parasite species can kill the other. Our experimental studies of Nippostrongylus brasiliensis and Plasmodium chabaudi chabaudi AS co-infection in laboratory mice suggest that antibody responses induced by one parasite bind the other. The binding was high affinity, titres of cross-reactive antibody increased with increasing dose, and cross-absorption assays suggested that the cross-reactivity was not due merely to polyclonal B cell stimulation by malaria parasites. Furthermore, Western blot analysis revealed the size and abundance of the shared antigens. Most surprisingly, only rodent parasitic nematodes that have a blood-dwelling

stage shared these antigens with P. c. chabaudi. Finally, co-infected hosts were better able to control malaria density than hosts infected only with malaria. Shared antigens thus potentially generate apparent competition among parasites from different phyla.

11/04/2013 Session 8D - Ecological Interactions During Infections - Chair Mike Begon 10:00 AM - 10:30 AM (30 mins)

Immune responses in an ecological context - Chair Andy Fenton

Tolerance and resistance in helminth infection: the mechanistic immunology perspective

Judith Allen, Judith Allen

University of Edinburgh

Awaiting content

11/04/2013 Session 9D - Immune responses in an ecological context - Chair Andy Fenton 11:10 AM - 11:40 AM (30 mins)

Inhibitory priority effect rules the establishment and transmission of Lyme disease strains in immunocompetent hosts.

Godefroy Devevey, G. Devevey, S. Murray, M.J. Voordouw, T. Nguyen, C. Grave, D. Brisson

University of Pennsylvania & University of Edinburgh

In the seemingly generalist pathogen responsible for Lyme disease (Borrelia burgdorferi s.s.), up to seventeen strains co-exists in the wild even though they do not have the same host niches. Co-infection of hosts in the wild is very common and we hypothesized that the diversity of strains is maintained thanks to interaction between strains (priority effect, cooperation or competition). These relationships have fundamental outcomes for strategies of control. We conducted an experiment of sequential co-infection of mice with several strains. We measured in parallel the transmission of each strain to the natural vector and the host immune response directed against each one. We found that strains differ for their transmission and immunogenicity when single infecting. After the second infection, there is a strong priority effect that excludes the second arriving strains, regardless of the types of the first and the second strain. Contrary to expectation, the inhibitory priority effect is not mediated by the host immunoglobulin. These results suggest that the phenology of the vector and the host community play fundamental roles in the maintenance of the diversity of strains.

11/04/2013 Session 9D - Immune responses in an ecological context - Chair Andy Fenton 11:40 AM - 11:55 AM (15 mins)

Individual variation in the transfer of maternal antibodies to the embryonic environment.

Christina Coakley, Christina M. Coakley1, Vincent Staszewski, Katherine A. Herborn and Emma J.A.

The University of Edinburgh IEB Ashworth Laboratories Kings Buildings Edinburgh

Maternal antibodies transferred from mother to offspring are key to protecting young animals from disease and can impact on responses to infection and offspring fitness. While there has been much work on factors that affect an individual's immune response, far less is known about factors affecting the level of antibody transferred to offspring. Here we show in Chinese painted quail, (Coturnix chinensis), that significant variation exists between females in the relative amount of specific blood antibodies they transfer to the embryonic environment. Furthermore, within-individual variation in transfer levels is low, both across different phases of their immune response and when challenged with different vaccine types . Females that produced a high antibody response therefore did not necessarily transfer the greatest number of antibodies to offspring. The amount of antibody transferred was related negatively to the female's body condition but their own antibody responses were not. We found no evidence for any trade-offs between the total amount or relative amount of antibody transferred with other measures of reproductive investment. These results suggest that the amount of antibodies raised by an individual in response to challenge and the proportion of antibodies transferred to offspring may be separate traits on which selection acts.

11/04/2013 Session 9D - Immune responses in an ecological context - Chair Andy Fenton 11:55 AM - 12:10 PM (15 mins)

Complex associations between circulating antibody levels, body mass, parasite burden and survival in a wild mammal population

Daniel Nussey, Daniel Nussey(1, 2), Kathryn Watt(1), Josephine Pemberton(1), Jill Pilkington(1), Rose Zamoyska (2), Andrea Graham (3), Tom McNeilly(4)

(1) Institute of Evolutionary Biology & (2) Institute of Infection and Immunity Research, University of Edinburgh, The Kings Buildings, Edinburgh, UK; (3) Princeton University, Princeton NJ, USA; (3) Moredun Research Institute, Pentlands Science Park, Midlothian , UK.

The relationship between immunity and host demography remain poorly characterised in wild mammals. Antibody-mediated immunity is known to play an important role the development and maintenance of resistance to micro- and macro-parasites, but very few studies have been able to examine the links between circulating antibody levels and health, reproduction and survival in natural conditions. We addressed this using a uniquely detailed long-term study of feral Soay sheep on the St Kilda archipelago. We had previously established that, in adult females, high circulating levels of anti-nuclear antibodies (ANA) predicted improved survival of harsh winters. We have now followed this up to examine a range of circulating antibodies of different isotypes and specificities in sheep sampled in three years preceding high mortality winters. Although the antibody measures were generally positively correlated, most correlations were low suggesting limited redundancy in our 11 different antibody measures. Associations with weight at the time of sampling were complex, with different antibodies showing independent effects on weight in different directions. Only anti-strongyle IgE levels predicted from faecal egg counts at the time of sampling – but surprisingly, it was individuals with intermediate IgE levels that had the highest egg counts. Importantly, independent of age, year, weight or faecal egg counts, ANA and anti-stronglyle IgG levels were found to positively and independently predict subsequent over-winter

survival. The anti-strongyle IgG effect was of comparable magnitude to that of body mass, suggesting circulating antibody levels can predict important aspects of fitness in the wild.

11/04/2013 Session 9D - Immune responses in an ecological context - Chair Andy Fenton 12:10 PM - 12:40 PM (30 mins)

POSTER ABSTRACTS

Schistosomiasis in African infants and preschool children: let them now be treated! (P1)

Russell Stothard, J. Russell Stothard*, José C. Sousa-Figueiredo, Martha Betson, Amaya Bustinduy and Jutta Reinhard-Rupp

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The occurrence of schistosomiasis within African infants and preschool children has been much better documented in recent years, revealing an important burden of disease previously overlooked. Despite mounting evidence showing that treatment with praziquantel is safe, beneficial and could be delivered within ongoing public health interventions, young children still do not have satisfactory access to this drug. Indeed, a significant treatment gap exists which is inflicting unnecessary suffering on those least able to make a demand for treatment. Progress towards resolution of this unfortunate health inequity is now highlighted, including an update on the development of an appropriate paediatric praziquantel formulation, and present blocks are identified on securing this issue within the international health agenda for control of neglected tropical diseases.

Schistosomiasis in African infants and preschool children: let them now be treated! (P2)

Russell Stothard, J. Russell Stothard*, José C. Sousa-Figueiredo, Martha Betson, Amaya Bustinduy and Jutta Reinhard-Rupp

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The occurrence of schistosomiasis within African infants and preschool children has been much better documented in recent years, revealing an important burden of disease previously overlooked. Despite mounting evidence showing that treatment with praziquantel is safe, beneficial and could be delivered within ongoing public health interventions, young children still do not have satisfactory access to this drug. Indeed, a significant treatment gap exists which is inflicting unnecessary suffering on those least able to make a demand for treatment. Progress towards resolution of this unfortunate health inequity is now highlighted, including an update on

the development of an appropriate paediatric praziquantel formulation, and present blocks are identified on securing

Urogenital schistosomiasis morbidity in pre-and primary school-aged children in rural Zimbabwe. (P3)

Welcome Mkululi Wami, W.M. Wami (1), N. Nausch (1), N. Midzi, (2), T. Mduluza (3), M.E.J. Woolhouse (1), F. Mutapi (1).

(1)Institute for Immunology and Infection Research, Ashworth Laboratories, University of Edinburgh, Edinburgh EH9 3JT, UK (2)National Institute of Health Research, PO Box CY 573, Harare, Zimbabwe and Research Council of Zimbabwe, Mount Pleasant Business Park, Harare, Zimbabwe (3)Department of Biochemistry, University of Zimbabwe, PO Box 167, Harare, Zimbabwe

Purpose: Pre-school children (less than 5 years) so far are being excluded from most schistosomiasis treatment control programs for reasons that are now widely refuted. The aim of this study is to assess urogenital schistosomiasis morbidity prevalence in young children and the effect praziquantel (PZQ) treatment on infection levels in this age group. Methods: Children aged 1-10 years meeting the study protocol were recruited into the study and received PZQ treatment at the recommended dose of 40mg/kg body mass, with a six weeks post-treatment efficacy check. Infection levels for S. haematobium were measured using egg counts/10ml urine. Urinary dipsticks were used to measure several morbidity markers, chiefly haematuria and proteinuria. An additional proxy for urinary tract damage, the Urine-Albumin/Creatine Ratio (UACR) was also determined. Anthropometry measures were captured prior to treatment to assess the growth and nutrition status. Results: The pre-treatment prevalence for haematuria was over 60% and a prevalence of 75 % abnormal UACR, which decreased after treatment was observed. Other additional morbidity markers measured in the study support the results that indicate morbidity is apparent even in the very young children. No severe malnutrition or stunting was observed, prevalence less than estimated national levels. Evidence of treatment efficacy was demonstrated by a 95% egg reduction rate 6 weeks post-treatment with a cure rate of 93%. Conclusions: Morbidity is significant in young children. Treatment is equally effective in these young children, further reiterating the need for them to be included in the control.

Molecular Characterization of Acanthoparyphium sp. (Digenea: Echinostomatidae) from Kuwait Bay Using ITS1 and mtCO1 Sequences (P4)

Wafa Al-Kandari, Suzanne A. Al-Bustan, Majed Alnaqeeb and Asha Merine Isaac

Department of Biological Sciences, Kuwait University, Kuwait

The Prosobranch snail Cerithidea cingulata from Kuwait Bay was infected with the larval stages of Acanthoparyphium sp. (Digenea: Echinostomatidae). The cercariae and metacercariae are characterized by having 23-collar spines. Previous identification of the Acanthoparyphium sp. from Kuwait Bay was based on morphological characteristics. In the present study, sequences of the first internal transcribed spacer region of ribosomal DNA (ITS1) and mitochondrial cytochrome

oxidase subunit 1 (mtCO1) were used for genetic characterization and examination of the phylogenetic relationship between the isolate from Kuwait Bay and other isolates available from GenBank database. Sequences of ITS1 and mtCO1 for rediae and metacercariae were identical in length and composition with no intraspecific variations. Phylogenetic analysis revealed that Acanthoparyphium sp. from Kuwait Bay formed a clade with Acanthoparyphium sp. from New Zealand. Their ITS1 and mtCO1 sequences showed 97% and 84% similarity. The taxonomic status of Acanthoparyphium sp. from Kuwait Bay needs to be confirmed and revised using more sequences of the genus from different regions in the world.

SchisTEM: an agent-based model of schistosomiasis and water temperature (P5)

Nicky McCreesh, Nicky McCreesh and Dr Mark Booth

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More than 200 million people are estimated to be infected with schistosomiasis. Both the intermediate host aquatic snail species and the Schistosoma parasite are sensitive to a wide range of different environmental factors, including temperature and rainfall. Schistosomiasis will therefore be affected by climate change, and the effectiveness of different control strategies will vary according to season. Little work has been done on modelling schistosomiasis and temperature however, or on developing agent-based models of schistosomiasis transmission. The Schistosomiasis Transmission and Ecology Model (SchisTEM) is an agent-based model of schistosomiasis and water temperature. Snails, schistosome worms, cercariae and miracidia, and humans are represented as agents. Birth, development, mortality and transmission rates for the snails and parasites are temperature dependent. The model has a time step of one hour meaning that diurnal fluctuations in water temperature can be modelled. The model has been parameterised using available experimental and field data. This includes extensive field data collected over a number of years at a site on Lake Albert, Uganda. Further data will be collected over the coming year to improve the parameterisation and fitting of the model. The model will be used to predict the effects of rising temperatures on schistosomiasis transmission at the field site, and a generalised version of the model will be applied throughout East Africa. In both cases, climate predictions which include diurnal and seasonal variation will be used.

Mitochondrial marker development for European schistosomiasis: insights into the molecular diversity of mitochondrial genomes of Schistosoma turkestanicum in Hungary (P6)

Scott Lawton, S. P. Lawton1, J. P. Dukes1 and G. Majaros2

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Schistosoma turkestanicum (syn. Orientobilharzia turkestanicum (Dutt and Srivastava, 1955)) is a major agent of animal schistosomisis throughout Asia, especially in China, India, Pakistan and Iran.

The disease primarily affects domestic cattle causing intestinal and hepatic schistosomiasis but has also been attributed to causing significant losses to herds by increasing morbidity in adult animals and mortality in lambs and calves. The parasite is also an agent of cercarial dermatitis in humans, a neglected disease which is now considered to be of increasing concern due to its association with neurological disease. Recently, S. turkestanicum was identified in Hungary utilising red deer as a definitive host and molecular clock data suggested that the parasite had been occupying Eastern Europe since the last ice age. In order to identify suitable molecular markers for the differentiation of schistosome populations in Hungary, large fragments of mitochondrial genomes were sequenced that incorporated the majority of protein-coding genes in the genome. Analysis of these genes showed the diversity to vary considerably across the genome indicating that different rates of evolution occur in closely linked genes. Also, further analysis showed the bar coding gene cox 1 not to be the most diverse gene and may not provide the true resolution required to differentiate populations of parasites for epidemiological studies.

Are there antigens in Taenia crassiceps that can be used in the diagnosis of cystic hydatid disease? (P7)

Amy Marsden, Marsden, A.N., Bodell, A.E., Craig, P.S. & Rogan, M.T.

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Cystic hydatid disease is a zoonosis caused by the cestode Echinococcus granulosus, the dog tapeworm, which results in hydatid cysts, usually in the liver or lungs of the intermediate host, commonly sheep. Accidental infection in humans can lead to debilitating, and sometimes fatal disease. The cysts caused by E. granulosus are often asymptomatic for a number of years and may only be diagnosed once the cyst is grossly enlarged, pressing on the internal organs causing pain. Diagnosis is reliant on ultrasound or CT scans and immunoassays with techniques being refined over the past 30 years. Hydatid cyst fluid is the most frequent source of diagnostic antigens but batches of cyst fluid can show significant variability and may in some cases produce false negative results. The present study investigates whether Taenia crassiceps , another cestode parasite of the same family, has cross reacting antigens with E. granulosus which may be useful in diagnosis and disease follow up. This parasite has the advantage of being maintained in experimental murine hosts. Crude Taenia crassiceps cysticerci extract was immune- affinity purified on a Sepharose CL4B column coupled with human post infection IgG and the eluate tested in ELISA against individual hydatid sera with different WHO cystic types. Results indicated that cross reacting antigens were present.

Small Molecule Analogues of an Immunomodulatory Helminth Product Provide a Novel Approach to Dissecting Dendritic Cell Signal Transduction Pathways (P8)

Felicity Lumb, F.Lumb*, C.J.Suckling+ and W.Harnett*

*University of Strathclyde Strathclyde Institute of Pharmacy and Biomedical Sciences G4 0RE + University of Strathclyde Pure and Applied Chemistry

ES-62 is a phosphorylcholine (PC) containing glycoprotein actively secreted by the rodent filarial nematode Acanthocheilonema viteae during parasitism of its host. ES-62 is a key immunomodulator during filarial infection and is known to target multiple cell types including T and B lymphocytes, antigen presenting cells – macrophages and dendritic cells- and mast cells to generate an overall anti-inflammatory immunological phenotype. The unusual post-translational modification of addition of PC appears to be responsible for many of the immunomodulatory properties of this molecule as PC conjugated to ovalbumin can mimic ES-62 action. In mouse models of autoimmune diseases such as collagen-induced arthritis (CIA) and asthma ES-62 has been shown to have a therapeutic and preventative effect and as a result has raised the possibility of ES-62 being a potential drug candidate. However, such a large and hence immunogenic molecule is not an ideal drug. Therefore the focus has now moved to small molecule analogues (SMAs) of ES-62 that are based around its active PC moiety. To identify SMAs that mimic the action of ES-62 an initial screening system was set up. SMAs were selected based on their ability to down-regulate the LPS-induced cytokine response of dendritic cells in in vitro inflammation assays. Interestingly, certain SMAs show a selective inhibitory effect on production of inflammatory cytokines and so could be used to dissect the key signalling pathways responsible for the inflammatory phenotypes of DCs.

Observations of the over winter survival of ovine endoparasites. (P9)

Hazel Wilkie, H.E. Wilkie P. Sirl E.R. Morgan

Biological Sciences University of Bristol Woodland Road Brisol BS8 1UG

Two of the most important nematode species in British sheep are Teladorsagia circumcincta and Haemonchus contortus. The free-living stages (egg to L3) are heavily climate dependent. These parasites are able to suspend their development at the early fourth larval (EL4) stage inside the host, in a process known as hypobiosis, which bury into the abomasal glands only emerging when outside environmental conditions are optimal for continuation of the lifecycle. Climate change is affecting the epidemiology of the parasites and their over winter survival affects the infection levels for the following year, thus influencing the best times to treat the flock. The over wintering strategies used by these nematodes were monitored in a sheep flock in south west England by counting the number of infective larvae on pasture and the number of adult nematodes and hypobiotic larvae present in the host abomasum over the winter of 2011/12. Our results suggest that overwintering strategies might be changing with climate warming, with less reliance on hypobiosis and greater importance of free-living stages on pasture.

The effectivenss of exogenously administered probiotic feed additives at reducing endoparasitic burden in domestic sheep. (P10)

Owen Gethings, Gethings, OJ

Hartpury College

The frequent systematic treatment of parasite-infected sheep with chemotherapeutic agents has led to the development of drug resistance in gastrointestinal nematodes to all three classes of anthelmintics, calling for new and improved alternative control practices. The effectiveness of exogenously administered probiotics at reducing endoparasitic burden in sheep was evaluated over a 5-week period. N=20 sheep were selected from n=220 using simple random sampling, split into a control and treatment group and segregated for the duration of the trial. A probiotic feed additive containing Saccharomyces cerevisiae (1010 cfu/g of DM, BIOSAF) was administered orally to the treatment group daily and faecal egg counts were conducted on fresh faecal samples taken from both the treatment and control group weekly using a modified McMaster Technique. Overall mean worm burden was measured overtime in both the treatment and control group to evaluate egg gain/loss using a One-Way Analysis of Variance (ANOVA). Individual parasite species identified per week were also tested for significant gain/loss overtime in both treatment and control groups. Overall worm burden and individual parasite species were also compared between the control and treatment group for significant difference using an Independent Samples T-Test. No significant difference was identified between the mean overall worm burdens overtime in either the treatment (p=0.697) or control (p=0.081) group. A significant difference was identified in the numbers of Haemonchus contortus eggs isolated over the 5-week period for the treatment group (p=0.038), whereas no similar reduction was seen in the control group (p=0.561).

Immune and cellular impacts in the autogenous aedes caspius larvae after experimentally-induced stress: effects of bacillus thuringiensis infection (P11)

Ashraf Ahmed, Ashraf M. Ahmed

Ashraf M. Ahmed

Insects possess effective defense mechanisms against pathogens via induction of antimicrobial immune and oxidative stress responses. In this study, immune impact and histological damages in the gastric caeca have been investigated in the 3rd instar larvae of the autogenous Aedes caspius upon infection with Bacillus thuringiensis (Bt). Data showed a significant increase in phenoloxidase (PO) activity by 1.23 folds at 4h post-infection then reduced to the normal level at 8h post-infection and until larval death. Besides, nitric oxide (NO) titer was significantly increased by 1.4 folds at 4h post-infection, then, reduced down to its normal level at 8h post-infection, after which, it was significantly decreasing by time until being hardly detected at 44h post-infection compared to that of control mosquitoes. Moreover, percentages of cellular apoptosis were significantly elevating from 6 to 48h post-infection. Consequently, cytological damages in the epithelium and microvillii of the gastric caeca were observed at 48h post-infection. Finally, larval body sizes were significantly smaller prior to death (at 48h post-infection). Taken together, these data suggest further modes of action of Bt as inhibiting the antibacterial immune responses, inducing cellular apoptosis prior to damaging the epithelium of gastric caeca. This may explain - partially at least - the irresistibility and high pathogenicity of Bt against mosquito vector, which may help understanding, and hence, overcoming developing resistance by some mosquito vectors to some mosquitocidal bacteria. This may help improving the biocontrol measures against mosquito vectors.

Effect of infestation of Pyxinia firma on the Total Haemocyte Counts (THC) and Larval Growth of the Dermestes vulpinus (Dermestidae : Coleoptera) (P12)

Mohammed Siddiqui, Mohammed Iqbal Siddiqui* and Mohammed Saleh Al-khalifa**

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Pyxinia firma has not previously been recorded in the mid gut of the larvae of scavenger beetle Dermestes vulpinus. Infected larvae of the scavenger beetles were investigated in order to determine the effects of their infection by the eugregarine, Pyxinia firma. Infected larvae were found to have higher total haemocyte counts and greater weight gain than uninfected ones. Infected larvae that were starved , however, lost weight much faster than uninfected larvae. The impact of infection on the physiology of the insect is also discussed and it is observed that the variation in the pattern of the total haemocyte counts between infected and uninfected larvae is indicative of the effect of the infection on the immune system of D. vulpinus.

Genetic characterization of Leishmania in wild carnivores, dogs and humans from Spain (P13)

Ana Isabel Cubas Atienzar, Cubas Atienzar, Ana Isabel

University of Murcia (Spain)

Leishmaniasis is a worldwide distributed re-emerging zoonotic parasitic disease. Genetic characterization of Leishmania spp. began in the 1980s to improve our understanding of its epidemiology, control, treatment and prognosis. The present study uses recent advances in DNA sequencing to confirm the presence and characterize genetically Leishmania spp. in wild carnivores from the Basque Country and dogs and people from Murcia, previously diagnosed using with a real-time PCR kinetoplast DNA. To do this we proceeded to amplify by classic PCR Internal Transcribed Spacer 2 and to sequence and analyze phylogenetically the results obtained. Sequencing analysis revealed 6 different haplotypes based on 1 or 2 nucleotides mutations of L.infantum, haplotype 1 (hap1) (76.7% of the samples) was present in all species, hap2 present in two foxes, hap3 in a polecat and a badger, hap4 in a human and a wild cat and hap5-6 belonging to a fox and a human, respectively. A review in the Genebank confirmed the worldwide predominance of hap1 and the phylogenetic study corroborated the monophyletic nature of L.infantum. In summary, this the first time that L. infantum has been sequenced in wild carnivores from Spain and results show that it is the same species that infects dogs and people. Moreover, the presence of parasite in wild carnivores of the Basque Country, a region traditionally considered to be non endemic, could be related to the pioneering use of PCR diagnosis and/or to changes in geographical distribution of infection.

The metabolomic and lipidomic profiles of miltefosine-resistant Leishmania donovani and

quantification of drug uptake using liquid chromatography â€“ mass spectrometry (P14)

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Currently the only safe and effective oral treatment for visceral leishmaniasis is the phospholipid drug miltefosine. Resistance to the drug can easily be induced in the laboratory and unrestricted use in endemic regions makes the threat of resistance in the field a possibility. In this study, Leishmania donovani isolates from Nepal with different inherent resistance to antimonial drugs were made resistant to miltefosine by step-wise exposure of promastigotes to miltefosine and cloned. Previous genetic studies have shown a reduction in the expression of two transporter genes LdROS (encoding L. donovani Ros protein) and LdMt (encoding L. donovani Miltefosine transporter) in miltefosine-resistant (MIL-R) parasites compared to wild type (WT) parasites indicating that resistance may be due to a reduced uptake of drug. The metabolome and lipidome of WT parental lines and their MIL-R counterparts were analysed using liquid chromatography – mass spectrometry (LC-MS) and compared to determine key changes. The analyses identified 685 putative metabolites, 81 of these were lipids that were either up- or down- regulated in MIL-R strains compared to their WT counterparts. In addition, the rate of uptake of MIL by WT and MIL-R promastigotes was quantified at different times post-MIL treatment using LC-MS. MIL-resistant promastigotes imported significantly less MIL from the medium compared to their WT counterparts. These data suggest that induced MIL resistance in Leishmania is associated with significant changes in metabolism, particularly lipid composition, and a decreased MIL uptake

Development of a model to study the energetics of African Trypanosome infection (P15)

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African trypanosomiasis is a disease caused by the protozoan parasite Trypanosoma brucei. Cachexia and parasite induced anorexia are symptoms of infection with considerable veterinary and economic importance in livestock although their significance in human disease is unclear. The mechanisms underlying these physiological effects are thought to be associated with a dysregulated inflammatory immune response.In an experimental model to study African trypanosomiasis; we observed a hitherto undescribed period of anorexia and body weight loss at 7-8 days post infection. We want to understand the immunological and physiological mechanisms underlying this phenomenon as well as evaluating the energetic consequences of T. brucei infections. A standardised infection-host model was developed using male C57/BL6 mice infected intraperitioneally with 1 x 10^3 Trypanosoma brucei brucei (AnTat1.1p clone). Inflammatory

responses, changes in food intake, body weight and energy excretion in relation to parasitaemia were measured over a period of 4 weeks. A period of anorexia occurred consistently after the first parasitaemic peak at day 6p.i. with typically a 10% weight loss and 79% reduction in food intake compared to uninfected controls at day 8p.i. Infected mice recovered from this profound period of anorexia and recovered body weight by day 12p.i. without any hyperphagic response. Daily energy expenditure (DEE) and digestive efficiency data of T.b. brucei infected mice have been measured and we are presently analysing the inflammatory cytokine responses to test the hypotheses that pro-inflammatory cytokines IL-6 and/or TNF-α are driving this phenomenon.

Human Immune Response to Sand Fly Salivary Proteins in Leishmania Endemic and Non Endemic Areas in Jordan. (P16)

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The role of sand fly saliva in the Leishmania transmission is well established. Recent studies on mice have shown that immunity to sand fly saliva would enhance the immune response against the transmission of Leishmania infection when co-injected with salivary gland homogenate. New approaches are investigated to study the possibility of integrating sand fly salivary protein to Leishmania vaccine that would post the immune response and protect against the transmission of the infection. In this study, we are investigating the role of sand fly salivary content on immune response of human in Leishmania endemic area and being exposed to sand fly bite compared to unexposed naïve. In this study,blood samples were collected from donors living in endemic area with leishmania and sandfly as exposed infected (Swaymeh), donors living in areas with sandflies as exposed (Mafraq) and donors living in sandfly free areas as unexposed (Amman). The serum was probed for antibodies specific to sand fly salivary proteins (Isolated from field collected Phlebotomus papatasi) using western blot. Also, peripheral blood monocytes (PBMC) were separated and used to determine the effect of sand fly salivary lysate to induce lymphocyte proliferation.

Assessing the Risk of an Emerging Salmonid Disease (P17)

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Proliferative kidney disease (PKD) is an emerging disease that is linked with environmental change and causes mortality of both wild and farmed salmonids across Europe and North America. The causative agent of PKD is the myxozoan parasite Tetracapsuloides bryosalmonae (Tb) which exploits the freshwater bryozoan Fredericella sultana (Fs) as primary host. Fs is a colonial

invertebrate that reproduces asexually through budding and by the production of “statoblasts” (over-wintering dormant stages). In bryozoans the parasite cycles between overt and covert infection stages, the former being constituted by sacs filled with spores infective to fish and the latter by single cells infecting the bryozoan body wall. This project focuses on Tb development in bryozoans to assess the risk of PKD. The objectives of the research are to: 1) characterise bryozoan population dynamics and the dynamics of Tb development within this host; 2) establish risk factors associated with Tb prevalence/burden in bryozoans and subsequent transmission to fish; 3) create a protocol to sample bryozoans instead of wild fish in order to monitor parasite levels and to produce a PKD risk map. Results presented here include: levels of vertical transmission in bryozoan hosts (through fragmentation of bryozoan colonies and via statoblasts); presence of infectious spores in water samples; and prevalences of overt/covert/uninfected bryozoans in populations sampled every 45 days from two rivers in southern England. A major aim of the research is to reduce direct sampling of valuable fish stocks for disease detection helping to conserve the health and diversity of wild fish populations.

Toxoplamsa gondii Tyrosine Hydroxylase 2 Expression and Intermediate Host Altered Neuromodulation Mechanisms (P18)

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Toxoplasma gondii (T. gondii) is a microorganism that causes infection worldwide; its seroprevalence ranges from 20 to 95%.Studies demonstrated that T. gondii alters the intermediate host’s behaviour to increase the organism’s transmission to the definitive host (cat) and complete its life cycle. Studies found that some of this altered behaviour is found in infected humans. Some explanations have been proposed but not yet proven; including that T. gondii changes the intermediate host brain’s neuromodulation process. Studies established that T. gondii produces tyrosine hydroxylase (TH) (rate-limiting step of catecholamine biosynthesis). TH is responsible for the transmission of tyrosine to L-dopa. Recent study showed that 6–8 weeks infected mice neurons have an increase in TH and dopamine levels. Aims of the study are to further elucidate functioning of T. gondii TH, its structure and phosphorylation. In this study, TgAaaH2 is produced using the isopropyl-beta-D-thiogalactoside induction and purified using cobalt affinity chromatography. Phosphorylation assays and structural studies will be conducted on the purified protein in the future. The activity of TH produced by T. gondii growing in human foreskin fibroblast (HFF) cells is going to be determined by monitoring the conversion of tyrosine to L-dopa in the presence of tyrosine, and tetrahydrobiopterin. Then, high-performance liquid chromatography with electrochemical detection (HPLC-ED) used to detect L-dopa levels. Further, this research expolre whether T. gondii plays a role in completing dopamine synthesis through converting L-dopa to dopamine by producing L-dopa decarboxylase using TH activity assay. T. gondii TgAaaH2 was produced and purified but with

Antiparasitic activity of Lactoferrin bound to Chitosan nanoparticles in Plasmodium berghei infected mice (P19)

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Lactoferrin protein is known as antimicrobial, antiparasitic, antitumor and immunomodulating in nature. But till now no study has shown its inhibitory effect on malarial parasites. The present study has shown the effect of alginate enclosed chitosan-calcium phosphate-Lactoferrin nanoparticles on mice infected with Plasmodium berghei when given orally mixed with mice diet. The malaria disease was developed in only 40% of the infected mice. While mice with normal diet started dying on day 9 post infection. The mice given these nanoparticles orally resulted in survival upto 25 days. The weight of spleen and liver of mice was also measured. The mice having normal diet showed enlargement of spleen and liver due to parasite sequestration as compared to mice which were on nanoparticles diet. The mice given nanoparticles has shown no parasitemia at day three post infection and only one mice out of three showed parasite at day 6. At day 9 the parasitemia in case of normal diet mice was found to be >50% as compared to nanoparticles diet mice which showed only 10-15% parasitemia. Two mice died at day 9 in case of normal diet group, Nanoparticle diet mice survived till day 25. The present study indicates that the nanoparticles are preventing the invading of malarial parasites to the RBC's. As also the malaria burden was more in reticulocytes till day 12 p.o.i as compared in old RBC's. Present study has thus shown a good inhibitory effect on rodent malarial parasite P .berghei in a mouse model.

Hepatic oxidative stress in gerbils experimentally infected with Babesia divergens (P20)

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The present study aimed to investigate oxidative stress, DNA damage, and histopathological alterations in hepatic tissues of Mongolian gerbils experimentally infected with Babesia divergens. It was found that parasitemia reached approximately 77% at day 5 post infection. The liver became dark-brown and extremely friable and hepatic sinusoids were dilated and contained macrophages and parasite-containing erythrocytes. Infection also induced inflammation and injury of the liver. This was illustrated by (1) an increase in inflammatory cellular infiltrations, (2) a decrease in total antioxidant capacity, as indicated by lowered glutathione and catalase levels, (3) increased production of nitric oxide-derived products (nitrite/nitrate) and malondialdehyde, and (4) increased lactic acid dehydrogenase activity and protein carbonyl content in the liver. Infection also interfered with the normal cell cycle of the hepatic tissue, as indicated by a significant

increase in the percentage of liver cells at G0/G1 from approximately 86.2 % to 97.5 % and in S phases from 0.28 % to 2.2 %. Collectively, the present data suggests that B. divergens infection could induce cell-cycle alteration following oxidative stress and DNA damage in hepatic tissue. Further work is required to investigate the mechanism by which this hepatic tissue damage takes place.

Introducing the COSMIC consortium: Community-based scheduled screening and treatment of malaria in pregnancy for improved maternal and infant health: a cluster-randomized trial (P21)

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A EU funded interdisciplinary research consortium, COSMIC, comprising partners from Medical Research Council (The Gambia), Centre de Recherches Entomologiques de Cotonou (Benin), Centre Muraz (Burkina Faso), Institute of Tropical Medicine (Belgium), Imperial College (UK), WHO - Special Programme for Research and Training in Tropical Diseases and Royal Tropical Institute (Netherlands) has recently started their activities. The consortium aims at implementing scheduled intermittent screening of pregnant women with RDT by Community Health workers (CHW) at community level and treat positive women with anti-malarials (SST). CHWs will also encourage pregnant women to attend antenatal clinics (ANC) for other pregnancy-targeted interventions such as IPTp/SP, thereby improving its coverage. This approach combines existing IPTp/SP with SST at village level as an extension of home based management of malaria (HMM). This simple (diagnosis by RDTs) and low cost intervention capitalizes on an already existing interventions (HMM) to improve maternal and newborn health. The project aims at determining the added value of community SST of pregnant women implemented through the CHW involved in HMM (as compared to IPTp/SP alone implemented in health facilities). Objectives are: 1) to identify bottlenecks for implementation of SST by CHW involved in HMM; 2) to determine the impact of introducing SST in pregnancy on the quality of HMM; 3) to determine the impact of SST on ANC attendance and IPTp/SP coverage; 4) to determine the impact of SST on LBW, anaemia and placenta malaria; 5) to estimate cost-effectiveness of the intervention, and 6) to formulate recommendations for implementation.

The curative and prophylactic effects of xylopic acid on Plasmodium berghei in mice (P22)

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Efforts have been intensified to search for more effective antimalarial agents because of the

observed failure of some Artemisinin - Based Combination Therapy (ACT) treatment of malaria in Ghana. Xylopic acid, a pure compound isolated from the fruits of the Xylopia aethiopica was investigated to establish its attributable prophylactic and curative antimalarial properties. These antimalarial properties were determined by employing xylopic acid (10 - 100 /kg) in ICR mice infected with Plasmodium berghei. Xylopic acid exerted significant ($P<0.05$) effects on P. berghei infection similar to artemeter - lumefantrine, the standard drug. Furthermore, it significantly, ($P<0.05$) reduced the lipopolysaccharide (LPS) induced fever in Sprague-Dawley rats similar to prednisolone. Xylopic acid therefore possesses prophylactic and curative antimaalarial as well as antipyretic properties which makes it ideal antimalarial agent.

Plasmodium malariae in Marigot, South-Eastern Department of Haiti (P23)

Alexandre Existe, Alexandre EXISTE, Micheline CICERON, Jean Semé ALEXANDRE

Haiti, West Indies

Alexandre EXISTE and Micheline CICERON: Laboratoire National de Sante Publique, Angle delmas 33 and rue Charbonnières, Delmas, Haiti Jean Semé ALEXANDRE CDC-Haiti, building of US Embassy in Haiti, Boulevard du 15 octobre, Tabarre, Haiti

Antiparasitic activity of Lactoferrin bound to Chitosan nanoparticles in Plasmodium berghei infected mice (P24)

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The development of a novel workflow for the screening of natural product compounds for malaria (P25)

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The pharmaceutical company drug discovery process has successfully isolated and characterized several active antimalarial compounds from natural products. These products such as artemisinin and chloroquine have been the mainstay of drug treatment for malaria. Evidence has however shown a trend between the purification of natural products to a single active compound and the development of resistance. Furthermore, plant components are believed to have positive and synergistic interactions between their components which act via different mechanisms. This could be a possible reason as to why crude extracts of chloroquine and artemisinin have been used for centuries successfully without resistance. In view of the above, two medicinal plants were chosen based on their ethno pharmacological usage for screening. The in vitro antiplasmodial activity of Bridelia ferruginea and Byrsocarpus cockiness were evaluated a range of fluorescent based assay optimised in our laboratory. Both extracts showed inhibitory activity against the Plasmodium falciparum 3D7 chloroquine sensitive strains. The methanolic extracts showed a higher inhibitory activity and further tests revealed the extract had an early onset of action and was active against parasites at different stages of the erythrocytic cycle. The extract will be purified using HPLC technique and the endpoint guided by proteomics.

A link between epigenetics and severe malaria in humans (P26)

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The majority of infections with the human malaria parasite Plasmodium falciparum result in mild disease or asymptomatic carriage that can last for several months. Some infections, however, lead to acute and potentially fatal malaria. The development of severe disease probably depends on complex interactions between host and parasite. Chronic infections depend on antigenic variation. P. falciparum Erythrocyte Membrane Protein 1, the major parasite antigen expressed on the erythrocyte surface, is encoded by a highly diverse family of 'var' genes which undergo antigenic switching. This is mediated by clonal variation in expression and in vitro studies have demonstrated a central role for epigenetics. PfEMP1 also mediates sequestration of infected cells in the microvasculature, and the expression of particular variants may cause tissue-specific enrichment of parasites - a factor in the development of severe malaria. The genetics of both host and parasite undoubtedly influence disease severity, but the role of epigenetics has not yet been investigated in in vivo human infections. We therefore examined the expression of var genes and epigenetic regulators in parasites taken from Gambian children with severe or mild malaria. We present evidence that infection-induced stress responses in the host may modify var expression via epigenetic mechanisms, creating a feedback loop between the host's immune response and the within-host behavior of the parasite. Our work raises the question: does severe disease represent an adaptive strategy by the parasite to maximize survival; or a loss of control over the process of antigenic switching?

Analysis of simple sequence repeats (SSRs) in full-length cDNA sequences of Eimeria species. (P27)

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Eimeria species are protozoan parasites that cause coccidiosis in domestic fowl. The disease is mainly controlled using chemotherapeutic agents but due to the emergence of drug-resistance strains, alternative control methods are desired. The development of such strategies may be facilitated by a further understanding of the biology of the parasites. Hence, an analysis of simple sequence repeats (SSRs) in full-length cDNA sequences was carried out to gain better insights into the transcriptomes of Eimeria maxima and E. tenella. Results showed that SSRs were present more abundantly in E. maxima (3.67%) than E. tenella (1.5%) with the trinucleotide repeat being the most prominent type of repeat found in both E. maxima (3.08%) and E. tenella (1.29%). The top codon repeat types shared by them were AGC, GCA and CAG, reflecting their close relationship at the sequence level. Similar distribution of SSRs was detected in 5'UTR, ORF and 3'UTR, where trinucleotide repeats were over-represented. In ORFs of E. maxima and E. tenella, dominant trinucleotide repeats were found to be CAG (glutamine) at 29% and 21%, GCA (alanine) at 26% and 36%, and AGC (serine) at 19% and 23%, respectively. Further analysis of SSRs in the coding region of predicted membrane and secreted proteins showed that the SSR content in these molecules was higher compared to that in ribosomal and other housekeeping gene sequences. This study revealed the abundance of SSRs in Eimeria transcriptomes and proposed the possibility of SSRs being associated with the function of membrane and secreted proteins.

Detection of Avian Coccidiosis in local domestic chickens using the loop-mediated isothermal amplification (LAMP) assay (P28)

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Avian coccidiosis is an economically important enteric disease that is caused by seven Eimeria species. Identification of Eimeria species that are present in chicken flocks will aid farmers and relevant authorities in the management of this disease, and contribute towards the development of more efficient control methods. The main objective of this study was to establish a system to detect Eimeria species that infect local domestic chickens based on the Loop-Mediated Isothermal Amplification (LAMP) assay. LAMP assays containing previously described species-specific primer sets were initially shown to be capable of specifically detecting the Houghton strain of all the

seven Eimeria species. Subsequently, the LAMP assays were tested against 18 Eimeria samples collected from local poultry farms. A PCR-based method using previously described real-time quantitative PCR primers was used as a comparison and showed that Eimeria parasites were identified in 16 out of the 18 samples, with the majority of them showing the presence of multiple species. LAMP assays against the 18 samples showed comparable results. However, a few species that were detected by the PCR assays were not detected by the LAMP assays. This may be due to sequence divergence between strains and imply that further optimisation is required to improve the sensitivity of the LAMP assays in detecting local Eimeria populations.

Genetic diversity of African isolates of Toxoplasma gondii (P29)

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Toxoplasma gondii is intracellular protozoa parasite and has the ability to infect all warm-blooded animals including humans. While the three clonal lineages predominate in North America and Europe, strains from other regions in the world appear to have more diverse genotypes. By analysis of isolates from South America, Asia and Africa by using PCR-RFLP or microsatellite markers, it is revealed that the majority of these isolates have type I, II or III alleles which are identical to those in the main three lineages, but also some novel alleles are shown. In this study, multiplex multilocus nested PCR analysis of Toxoplasma gondii samples will be applied using 12 different genetic markers (SAG1, 5'-SAG2, 3'-SAG2, alt. SAG2, SAG3, BTUB, GRA6, C22-8, C29-2, L358, PK1 and Apico) to increase the resolution and discriminative power in detecting the genetic diversity between isolates. Focusing on African isolates, we wish to investigate their genetic relationship to global strains and the level of variation across multiple loci relative to reference type II and III strains. Based on sequencing, we already know some African isolates are type II, some type III and one a recombinant II/III. However, their level of diversity has yet to be fully analysed.

Chemotherapeutic Control of Fasciolosis: Effect of Triclabendazole on the Glutathione Transferases (P30)

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Fasciolosis is a major issue for Food Security and without vaccines can only be controlled by chemotherapeutics. Increasing global reports of emerging Triclabendazole (TCBZ) resistant fluke is concerning since it's the only drug showing activity against pathogenic immature fluke. There is an urgent need to resolve the mechanisms of TCBZ resistance. The Glutathione Transferase (GST)

superfamily contains drug detoxification enzyme members present in high levels within fluke. IBERS have previously shown that the 'Mu' class GST expression alters between TCBZ resistant and susceptible Fasciola isolates on exposure to the active metabolite TCBZ-Sulphoxide (TCBZ-SO) stress in culture. We have incorporated sub-proteomic approaches to measure the GST profile (GST-ome) of TCBZ susceptible Fasciola on TCBZ-exposure in culture. For the first time, sub-proteomic profiles of GST in a single fluke were shown to be measurable. A statistical difference was found for total GST activity within TCBZ-SO treatment groups and no differences in relative expression of individual GST proteins, suggesting TCBZ-SO exposure induces all GSTs. Following sub-proteomic assays optimisation in individual liver fluke we will now investigated the role of GST in the mechanism of drug resistance in populations, using defined isolates of established TCBZ susceptibility/resistance.

Drug repositioning as a viable option for antimalarial drug discovery (P31)

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Artemisinin based combination therapy (ACT) is currently recommended by the World Health Organisation for the treatment of malaria in most endemic regions. However, early evidence of resistance development towards the artemisinins, and many of the selected partner drugs, has already been reported. This no doubt calls into question the longevity of ACT, and with no new drugs in the pipeline alternative strategies for drug discovery are urgently needed. One option is drug-repositioning; screening existing compound libraries, that are already FDA approved, for their activity against the malaria parasite. There are numerous advantages to this approach: firstly, the drugs have known toxicity profiles and bioactivities, secondly, finding more suitable partner compounds for ACT will help prolong resistance development towards the artemisinins, and thirdly, there is a considerably shorter drug development time which may provide a much needed interim solution for malaria treatment while novel candidates are sought. Towards this goal, a panel of compounds have been identified from an existing drug library that are capable of inhibiting parasites development within a nanomolar dose range. Furthermore, these drugs have shown additional suppression when used in combination with dihydroartemisinin and therefore offer promise as potential partner drugs for artemisinin based combination therapy.

The role of microRNAs in the host-parasite relationship in H. contortus (P32)

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Haemonchus contortus is a gastrointestinal nematode that is a significant cause of welfare and economic problems in small ruminants, particularly sheep. There are currently no vaccines available against GI nematodes which, in part, relates to the ability of these parasites to modulate the host immune response. In this project, we are investigating the interaction of microRNAs and the host immune response. miRNAs are short 22 nucleotide long RNA molecules that negatively regulate gene expression. A previous study identified 192 miRNAs in H. contortus, one of which, mir-5352, is the focus of this study. mir-5352 is one of a cluster of four miRNAs, which are conserved only GI tract nematodes. Microarray and qRT-PCR showed that mir-5352 is highly expressed only in parasitic stages within the host. While the function of mir-5352 is unknown, its expression profile indicates that it may have a role in the host-parasite interaction, perhaps by regulating a host mRNA. In order for a parasite miRNA to regulate a host mRNA, it must be released, possibly in the excretory-secretory products (ES). RT-PCR experiments have confirmed the presence of mir-5352 in the ES and bioinformatic prediction programmes have identified a number of possible targets. Two potential targets are the focus of study: CD69 and BCL2L11. Both targets are important in TGF-β signalling, a pathway which is known to be affected by ES products of other G.I. nematodes. Studies are underway to determine whether mir-5352 expression correlates with the immuno-modulatory effects that are observed in nematode-infected hosts.

Molecular Characterisation of Glycogen Synthase Kinase-3 from Eimeria tenella (P33)

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Eimeria tenella is an apicomplexan parasite that causes coccidiosis in poultry animals. Heavy financial losses are reported due to the disease in broilers worldwide and increasing drug-resistance reports emphasise the need to identify new anti-coccidial drug targets. Glycogen synthase kinase-3 (GSK-3) is a multifunctional serine/threonine kinase that regulates many eukaryotic cellular pathways and has been validated as a potential drug target for protozoan parasites such as Plasmodium falciparum and Trypanosoma brucei. In this study, the GSK-3 homologue in E. tenella Houghton strain was isolated and sequenced. Comparison of the deduced 3138bp genomic locus with its cDNA coding sequence revealed 5 exons and 4 introns with all splice sites obeying the canonical GT-AG and non-canonical GC-AG rule. BLAST analysis of the putative 481 amino acids showed high similarities to T. gondii protein kinase 3 and P. falciparum GSK-3. Domain search analysis using Pfam-A databases showed E. tenella GSK-3 (EtGSK-3) belonging to the CL0016 Pkinase clan, which includes the GSK-3 family. Comparison with the Weybridge and Wisconsin strains disclosed the presence of 13 insertion/deletion sites and 18 single nucleotide polymorphisms (SNPs). Only three SNPs at base positions 39, 286 and 632 of exon 1 were detected as coding SNPs of which two were predicted to be non-synonymous (nsSNPs). Although secondary conformational changes were predicted due to the nsSNPs, the mutations occurred outside GSK-3 catalytic domains, which are vital for its function. Hence, GSK-3 remains a suitable candidate in the quest for new anti-coccidial drug targets.

Immunostimulatory and protective effects of sugar cane (Saccharum officinarum L.) bagasse derived fatty acids against coccidiosis in broiler chickens (P34)

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Fatty acids including oleic acid, linoleic acid, α-linolenic acid and γ-linolenic acid were recovered from sugar cane (Saccharum officinarum L.) bagasse by the sponification of its ethanoilc extract. All the fatty acids were characterized for their identification by using gas chromatography equipped with flame ionization detector. Mixture of these fatty acids was evaluated for its immunological and protective efficacy against coccidiosis in chickens. The sugar cane bagasse fatty acids (SCBF) significantly enhanced ($P<0.05$) the in vivo and in vitro lymphoproliferative responses to T-cell mitogens, phytohaemagglutinin-P and Concanavalin-A, respectively in chickens. Significantly elevated B- cell mediated immune response in terms of antibody titres to sheep red blood cells, Newcastle disease (ND) and Infectious bursal disease (IBD) vaccines ($P<0.05$) in SCBF administered chickens were also detected. Results of the challenge experiment revealed that the per cent protection and daily weight gains were significantly higher ($P<0.05$); whereas, mean oocysts per gram of droppings and lesion scores were significantly lower ($P<0.05$) in the SCBF administered chickens as compared to those in the control group. ELISA showed that SCBF significantly elevated ($P<0.05$) antibody titres against the Eimeria species (local isolates) used in the challenge experiment. The differences in organ-body weight ratio of all the lymphoid organs were statistically non-significant ($P>0.05$) in experimental and control groups except thymus and cecal tonsils. On the whole, results suggested that sugar cane derived fatty acids have immunostimulatory potential that persisted against the induced coccidial infection in chickens. Further studies on its commercial feasibility are underway.

Potential mechanisms underlying the increase in permeability of the blood-brain barrier in cerebral malaria: an in vitro study (P35)

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Cerebral malaria (CM) is a major cause of death in children infected with Plasmodium falciparum. A consistent feature of CM is the sequestration of mature parasitized red blood cells (PRBC) in cerebral microvessels. Although increased permeability of blood-brain barrier (BBB) accompanied by the loss of endothelial cell junction protein ZO-1, occludin and vinculin has been shown, the mechanism is still unclear. Here, we examined the indirect effect of PRBC on BBB permeability using an in-vitro model of BBB. Human brain endothelial cells (HBEC) were co-cultured with PRBC (or uninfected red blood cells (uRBC) as control) for 20 hours. The co-culture supernatant was harvested, in order to determine whether any soluble factors produced in response to the interaction between HBEC and PRBC had the ability to alter BBB permeability. Change in the integrity of the BBB in response to the co-culture supernatant was tested in two different assays:

(1) continuous real time trans-endothelial electrical resistance (TEER) using electrical cell-substrate impedance sensing (ECIS) and (2) FITC-dextran permeability assay. Both assays demonstrated that the integrity of HBEC monolayer was reduced up to 2-fold when treated with PRBC/HBEC co-culture supernatant compared to uRBC control. Interestingly, analysis of the co-culture supernatant showed the induction of the ADAMTS family protease, ADAMTS-4. In addition, differential regulation of ADAMTS-1 and the matrix metalloproteases (MMP) family proteases, MMP-2 and MMP-9, was demonstrated. We propose that proteases are released as a result of interactions between PRBC and endothelial cells of the BBB contribute to BBB breakdown in CM.

An Investigation of Transmission Routes and Zoonotic Reservoirs for Giardiasis and Cryptosporidiosis in Malawi (P36)

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The parasites, Giardia sp. and Cryptosporidium sp. infect both humans and animals and are considered to have the potential for zoonotic transmission, although the actual role of animals as reservoirs for human infection remains unclear. G. duodenalis has been categorised into at least seven genotypic assemblages, and multilocus sequence typing (MLST) is a useful approach for detecting the presence of potentially zoonotic genotypes of this parasite. Cryptosporidium species are frequently associated with diarrhoea among HIV patients and cattle. The purpose of this study was to determine the range of Giardia duodenalis genotypes (assemblage prevalence and zoonotic genotypes) and Cryptosporidium species infecting human cases of disease from Malawi by using appropriate markers. Faecal samples were screened for both parasites microscopically using the Immunofluorescence Assay Technique (IFAT) and parasite isolates were typed by using nested PCR and/or sequencing of SSU-rRNA, β-giardin, tpi and gdh genes. Initial results of Giardia sp. confirmed the occurrence of already described and also new assemblage A and B genotypes in humans. The detection rate of Giardia was 11.36% by IFAT and 28.14% by nested PCR. For the detection rate of Cryptosporidium was 23.48% by IFAT and 10.05% by nested PCR. The results demonstrate that nested PCR is more sensitive than IFAT for Giardia whereas IFAT is more sensitive than nested PCR for Cryptosporidium. Therefore, IFAT technique can be helpful in determining the Cryptosporidium spp. infection and it provides a valuable tool for the rapid, specific and sensitive detection of Cryptosporidium in faecal samples.

A new species of Choleoeimeria (Apicomplexa: Eimeriidae) from the lizard (P37)

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Four out of twenty (20%) specimens of the lizard Scincus hemprichii, collected in Saudi Arabia, were found to be infected with a previously undescribed species of Choleoeimeria. Oocysts of Choleoeimeria jazani sp. n. were cylindroidal, 26 × 154m, with a smooth bilayered wall and a shape index of 1.7. Oocyst residuum and micropyle was absent. Sporocysts were subspherical, 10 × 7 4m, with a shape index of 1.3. The Stieda body was absent. Sporozoites were banana-shaped, 10× 3 4m, with one refractile body and enclosed dispersed finely granulated sporocyst residuum. The endogenous development was confined to the gallbladder. Meronts and gamonts were evident.

Detection and differentiation of African trypanosome species in blood through internal transcribed spacer nested PCR (P38)

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Human African trypanosmoiais (HAT) or sleeping sickness is considered a major health problem in Africa, HAT is caused by Trypanosoma brucei spp. According to the World Health Organisation the number of cases has dropped by 10000 cases for the first time in 50 years, as in the last decade the number of reported HAT cases dropped from 37,385 (1998) to 9,589 (2009). Molecular techniques play a major role in controlling the HAT, as they offer a sensitivity and specificity in the detection of the parasite. However, there are some obstacles with the molecular tools especially in the field environment. Therefore, FTA cards are now considered for rapid collection for large scale epidemiological studies using DNA based techniques. In this research 36 samples (20 females and 16 males) of blood from infected patients with Trypanosoma brucei (T.brucei), were collected on FTA cards from a hospital in Angola. The detection of the parasite was optimised by extracting the DNA using a chelex extraction protocol. Followed by detection of trypanosomes using an internal transcribed spacer (ITS) nested PCR that targets inter-specific length variation of the ITS regions of ribosomal genes. Out of the 36 samples, 47% (17) were detected, despite being isolated from patients with sleeping sickness. However, this was an improvement the results (0%) from a previously used method that relied on taking a single punch from the FTA card. By comparing the effort and difficulty of other DNA extraction protocols with the Chelex DNA protocol, it can be concluded that transferring

Molecular and phylogenetic studies on culicine mosquito vectors of infectious diseases in the Arabian Peninsula (P39)

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Saudi Arabia is the largest country in the Arabian Peninsula and has a peculiar position in the

world zoo-geographic regions. About 35 mosquito species were reported theirbased on classical taxonomic keys. These include disease dominant vector species: Aedes aegypti vector of dengue fever and other arboviruses and Anopheles vectors of malaria. However, there is a lack of data on their population genetics in relation to disease transmission. We have amplified and sequenced a 545-547 bp of ITS2 region of the ribosomal DNA gene cluster (rDNA) from many of these mosquito species collected from various parts of Saudi Arabia. The ITS2 DNA sequences from the Saudi mosquitoes were 100% identical i.e. belonging to the same ITS2 haplotype. When this ITS2 haplotype was searched against the GenBank database, it was identical to the most frequent ITS2 haplotype in the GenBank, collected from Iran, Iraq, and UAE. Multiple sequence alignment of ITS2 sequences of Saudi samples with other closely related sequences from GenBank, revealed the presence of 11 single nucleotide polymorphisms (SNPs). The SNPs detected are one or two nucleotide indels. Most of the ITS2 haplotypes were singleton i.e. represented only with one individual sequence. This is a first step towards the development of molecular tools to be used together with pectorial keys for more accurate identification and studying their population structure and dynamics. The significance of these studies for disease epidemiology and control under regional conditions are highlighted.

Choleoeimeria bunpusi sp. n. (Apicomplexa: Eimeriidae) developing in the gall bladder of the tuberculated gecko Bunopus tuberculatus (Reptilia: Gekkonidae) from Saudi Arabia (P40)

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Choleoeimeria bunpusi sp. n. is described from the gall bladder of the Blanford's rock gecko Bunopus tuberculatus in Saudi Arabia. The prevalence of infection was 13.3% (2/15). Oocysts were ellipsoidal and measured 31 (30-33) 5m × 21 (20-22) 5m. Sporocysts were dizoic, elliptical in shape and measured 12 (11-13) 5m × 7 (6 -8) 5m. The endogenous development was confined to the gall bladder epithelium. The hypertrophic parasitized biliary epithelium either remained in one layer or became stratified. Meronts, gamonts, and young oocysts were detected.

Grey squirrel control in Scotland: effectiveness and impacts on parasite dynamics (P41)

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The impacts of invasive species on native species and ecosystems may be mediated by a variety of mechanisms. The grey squirrel (Sciurus carolinensis) has successfully established and spread in the UK, with a subsequent decline of the native red squirrel. As decline is more rapid in the presence of squirrel pox (which is generally harmless to greys and fatal to reds), this is a commonly cited example of disease mediated competition between an invasive and native species. Squirrel

pox is widespread in England but has only recently spread to Scotland. Consequently, intensive control work has been carried out to (a) prevent spread of squirrel pox northwards from the borders, (b) prevent further spread of the grey squirrel population north from the central belt and (c) attempt to eradicate an isolated population of grey squirrels from Aberdeenshire. Using records of trapping effort and captures, and samples obtained using control programmes, this project is investigating both the efficacy of control and the impact of control on disease dynamics. To date, data has been collated and summarised from the different control programmes and samples have been collected to enable the investigation of broad scale patterns in prevalence of a range of parasites across Scotland. Further work will elucidate how control may influence the dynamics of parasites with different life histories and transmission routes. Results will provide information for future grey squirrel management in the UK and for other control programmes aimed at mitigating disease threats.

Parasitre ecology information gained from survey data (P42)

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The European rabbit has become established in many countries across the world and therefore subjected to large range in climates. The free living stages of rabbit parasites are therefore exposed to extremes in temperature and rainfall which could affect both their rate of development and survival. Data were compared from surveys of rabbit parasites from throughout the British Isles, Europe, Australia and New Zealand over a number of years. A comparison of the results of these surveys has been used to gain an insight into the differing ecological requirements of some of these parasites e.g Trichostrongylus retortaeformis tolerates a wider range of climastic exteremes than does Graphidium strigosum. A knowledge of these ecological parameters can be used to extapolate the possible potential impact of climatic change on the distribution of these parasites.

Bioinformatic identification and analysis of the excretory/secretory gene products of the nematode of Strongyloides ratti (P43)

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Strongyloides ratti (S. ratti) is a laboratory analogue of the parasite of humans, S. stercoralis which infects some 100 million people worldwide. The S. ratti - host interaction is likely mediated by proteins excreted and secreted by the parasitic stages inside of the host. To begin to investigate this, we undertook a computational characterization of potentially secreted products of S. ratti. Expressed sequence Tag (EST) cluster sequences were analysed for the presence of putative signal peptides. Among 5152 EST clusters, 81 contained predicted signal peptides. These 81 EST cluster

sequences were then used to find the complete coding region of these genes in the genome of S. ratti. Out of 81 EST clusters, 51 showed clear alignments to the genome; 19 showed partial alignments; 1 showed no alignment, and 10 showed multiple alignments to genes. Gene Ontology (GO) annotation of 70 genes allowed us to assign GO terms; biological process terms were assigned to 68, molecular function terms to 28 and cellular component terms to 29. Together, these findings may provide important information that will help to illuminate molecular, biochemical and immune-modulatory basis of S. ratti - host biology.

The Schistosoma mansoni protein SmShb interacts with and regulates SmVKR1 signaling in oocytes. (P44)

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Venus Kinase Receptors (VKRs) are an atypical family of Receptor Tyrosine Kinase (RTK) formed by an extracellular Venus Fly Trap (VFT) ligand binding domain and an intracellular tyrosine kinase domain. These receptors are found in many invertebrates (Vanderstraete et al., accepted) and quantitative RT-PCR in Schistosoma mansoni have shown that the parasite SmVKRs are expressed in all developmental stages. RNA interference experiments indicated -together with results of localization studies- functions in reproductive activity (Vanderstraete et al., in prep). To further characterize SmVKR1, we focused on the determination of its intracellular interacting partners hoping to find evidence for signaling pathways this receptor is involved in. Screening of a yeast two-hybrid adult cDNA library allowed us to identify an SH2 domain-containing protein, SmShb, which is homologous to members of the Shb adaptor family known to transduce signals induced by activated RTKs. In situ hybridization experiments showed the colocalization of SmShb and SmVKR1 transcripts in mature oocytes. Molecular cloning and characterization of SmShb revealed it specific interaction with the activated/phosphorylated form of SmVKR1. This interaction occurs between the SH2 domain of SmShb and a specific phosphotyrosine residue (pY979) located in the juxtamembrane region of SmVKR1. Expression of these proteins in Xenopus oocytes allowed us to show that the interaction between SmVKR1 and SmShb specifically activates the JNK signaling pathway in oocytes. Finally, preliminary data about potential downstream partners of SmShb identified from yeast two-hybrid experiments using SmShb as bait, suggest a role of the SmVKR1-SmShb pathway in maturation and cell fate oocytes.

Use of highly synchronized parasites to discriminate stage dependent killing rate profiles by antimalarials (P45)

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Killing profile in response to antimalarial treatments is a key property for the drug and is characteristic of the intracellular mode of action. Determination of the rate of killing for a compound allows the selection of fast-acting antimalarials to be used as first-line treatments for malaria control. Parasite killing rate can be estimated in vitro monitoring and quantifying the growth of viable cells after drug treatment (1). This methodology can also be used to determine the most sensitive intraerythrocytic stages of the parasite to an antimalarial compound. In this work, by using highly synchronized cultures, we have determined the specific killing rate profiles of several antimalarial drugs on the different parasite stages. Our results show that the different antimalarial modes of action produce specific patterns in terms of viability. Whereas chloroquine and artesunate are compounds very active against both young and mature intraerythrocytic stages, atovaquone and pyrimethamine display a faster killing rate against the mature forms of the parasite, probably due to the increased metabolic rate of the parasite. (1)Sanz et al. Antimicobial Agents and Chemotherapy. 2011. 55(12):5740-5

Transcriptome overview of the sheep helminth Haemonchus contortus (P46)

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We applied RNA-seq to sequence the transcriptome of the key model parasitic nematode Haemonchus contortus. In total, triplicate samples of six main life-stages, as well as samples taken from the gut of an adult female, were sequenced. This represents one of the most comprehensive transcriptome analyses of a parasitic nematode of veterinary importance. We present here a functional term enrichment analysis for various pair-wise comparisons of the samples, which indicate patterns consistent with parasite development and tissue specificity. The data presented here has already been included in the ongoing effort to annotate the H. contortus reference genome. Additionally, it will provide an important tool for future studies, such as a better understanding of the changes required for an adaptation to parasitism and the study of potential vaccine and drug target candidates.

Evolutionary Processes Affecting Molecular Diversity and Antigenic Variation in Tetraspanin 23 in the human parasite Schistosoma mansoni (P47)

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Schistosomiasis is caused by parasitic blood flukes of the genus Schistosoma with an estimated 220 million people infected in Sub-Saharan Africa, Asia and South America. Tolerance to praziquantel, which is used in mass drug administration programmes, has been documented, making the elucidation of a viable vaccine target important. Tetraspanin 23 (TSP23) is expressed on the schistosome tegument and directly interacts with the host immune system, making it a prime vaccine candidate. The majority of antibodies generated by the host recognize TSP23; however, there appears to be little immune memory towards this protein upon re-infection. Our previous work highlighted the hyper-variability of TSP23 and a large number of allelic isoforms of the protein have been found in several different geographical isolates of Schistosoma. These isoforms possessed altered antigenicity, potentially indicating the establishment of distinct antigenic lineages. Molecular genetic analysis of TSP23 was carried out in populations of Schistosoma mansoni from both field isolates and cultures passaged through a single strain of laboratory mice over time. Different allelic variants of TSP23 were seen at each successive generation resulting from high levels of recombination. Recombination appeared to be highest in parts of the gene responsible for coding the regions of the TSP23 protein that are considered antibody-binding sites. This is indicative of the adaptive response of TSP23 in schistosome populations as an effect of the continuous selective pressures of immunoglobulin interaction.

Neuropeptides as Transgenic Nematicides (P48)

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Plant pathogenic nematodes (PPNs) impose a significant economic burden on plant cultivation efforts worldwide. Recent estimates predict losses across all sectors of approximately $125 billion annually. Conventionally, an integrated approach to PPN management has relied heavily on various nematicides. As environmental concerns rise over the systemic effects of sustained nematicide use, withdrawal has left a significant shortcoming in our ability to manage this problem and highlights the need for novel and robust control methods. It has been discovered that nematodes can assimilate exogenous peptides through retrograde transport along the chemosensory amphid neurons. These peptides accumulate within cells of the central nerve ring and can elicit physiological effects when released to interact with receptors on adjoining cells. We are harnessing bioactive neuropeptides from the neuropeptide-like protein (NLP) and FMRFamide-like peptide (FLP) families of plant parasitic nematodes as novel nematicides. Active neuropeptides will be secreted into the apoplastic space of crop plants, and into the rhizosphere. So far we have identified 15 discrete neuropeptides that negatively impact chemosensation and/or neuromuscular activity in the root knot nematode Meloidogyne incognita, through RNAi-based gene functional studies and exogenous peptide addition.

Prevalence of chicken coccidia in commercial poultry farms of north India (P49)

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Coccidiosis, caused by multiple species of the protozoan Eimeria genus, is among the most economically important diseases of chickens. In the present study, the occurrence of Eimeria in chickens reared under intensive broiler and layer systems was recorded in four north Indian states (Uttar Pradesh, Uttarakhand, Haryana and Punjab). Pooled poultry droppings collected from 66 farms (48 broiler; 18 layer) were screened microscopically for Eimeria, revealing oocysts in 89.4% farms (97.9% broiler; 66.7% layer). No significant difference was observed in occurrence across the four states, although quantitative occurrence (mean oocysts per gram faeces; OPG) was significantly higher in Haryana and Uttar Pradesh (broilers: 72.7x103 and 35.9x103; layers: 5.3x103 and 12.5x103 respectively) compared to Uttarakhand (17.5x103 and 1.3x103; $p<0.05$). Molecular identification was accomplished using Eimeria-genus specific polymerase chain reaction (PCR) targeting internal transcribed spacer-1 (ITS1) with species-specific nested primers. Genomic DNA was isolated from faecal samples collected from 41 broiler and 11 layer commercial poultry farms found to have >500 OPG using a Qiagen stool DNA extraction kit. Results revealed the presence of all seven Eimeria spp. (Eimeria tenella 100%, E. mitis 84.6%, E. acervulina 80.8%, E. necatrix 57.7%, E. praecox 57.7%, E. maxima, 53.8% and E. brunetti 11.5%). Nested PCR using strain specific primers for E. maxima revealed existence of both US-and Australian-type strains in north India. Results for broilers and layers were largely similar, although E. maxima was not recorded in any Punjab broiler farm and E. brunetti was not recorded in any Uttar Pradesh or Haryana layer farm.

The comparison of FECPAK, McMaster and FLOTAC techniques for gastrointestinal strongyle faecal egg counts in cattle (P50)

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The study compared the sensitivity and accuracy of three faecal egg counting techniques, FECPAK, McMaster and FLOTAC, for diagnosis of gastrointestinal (GI) strongyles in cattle, naturally infected with high and low egg burdens. Two composite samples were prepared, one having a low and one having a high GI strongyle eggs per gram (EPG). From each pooled sample, 12 replicates for each of the three methods were analysed using a saturated NaCl as the flotation solution. FLOTAC was the only technique that gave positive results for all replicates of the composite sample with low levels of GI strongyles, thus making it more sensitive than FECPAK (66.7%) and McMaster (41.7%). FLOTAC also produced mean EPG values higher and CV values lower than the other two techniques, both for high and low GI strongyles levels. The results also show that reliability of FECPAK and McMaster techniques for the estimation of the GI strongyles EPG is influenced by the choice of the reading area (volume) both for low and high egg counts. The most striking result was the finding of the highest EPG values (151% for McMaster) where the smallest area of the slide was counted. The higher egg counts in the McMaster slide and lower in the FECPAK indicates that both slides are mis-estimating egg counts and counting eggs under the grid will give incorrect values.

The decline in equine Echinoccus granulosus. (P51)

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In the 1970s E.granulosus in horse livers was very common (60%) due to feeding of raw horse meat to fox hounds. To determine how levels of infection are changing percentages of infected livers were counted in 2002 and ten years later at a licenced horse abattoir in Somerset. Of 921 horses inspected in 2002 17.4% had E.granulosus cysts in their livers. Most livers had 1-2 cysts 1-10 cm in diameter. By 2012 this figure had declined to 5.2% (1205 horses). In 2002 of 18 kennels 18% said they fed horse meat regularly and 59% occasionally. In 2012 of 21 kennels 48% said they fed raw horse meat regularly and 33% occasionally. Praziquantel was used on average 1.76 X per year in all kennels in 2012. Where horse meat was fed regularly the average number of doses per year was 1.4 with 3 kennels using no praziquantel. The decline in infection rates is encouraging and could be much lower in younger horses than the data suggests as most horses taken to the abattoir are about 20 years old. However to ensure eradication of equine E.granulosus more treatment of dogs with praziquantel is required.

Using microsatellite markers to determine Schistosoma mansoni and S. haematobium genetic diversity under contrasting chemotherapy control strategies. (P52)

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The aim of this study is to determine the impact of two contrasting chemotherapy control strategies on schistosome population genetic diversity and structure in Schistosoma mansoni and S. haematobium endemic foci in Tanzania and Niger respectively. For both countries a total of 16 villages are split into two chemotherapy control strategies; community wide (CWT) and school based (SBT). In each village larval miracidia samples are collected prior to treatment from school-aged children (n=30). Samples are retained within the Schistosomiasis Collection At the Natural History Museum (SCAN). Baseline surveys were conducted to determine the population structure and composition pre-treatment. In Tanzania 18649 S. mansoni miracidia were collected from a total of 263 children in 16 villages. In Niger 5130 S. haematobium miracidia were collected from 5 villages. Year 2; 1965 S. haematobium miracidia were collected from 10 schools. Future follow-up collections are planned for 2013 and 2014. A new set of multiplex panels were developed from previously published microsatellites for S. mansoni (up to microsatellite 26 loci) and S. haematobium (18 microsatellite loci). Processing of baseline samples from Niger and Tanzania are now underway. This project aims to determine schistosome population structure and how parasite populations adapt and evolve under different human chemotherapy programmes within

SBT and CBT strategies. Collection methods and data will be presented and microsatellite analysis methods discussed.

Functional studies of the Protein Phosphatase 2A (PP2A) regulation by PhosphoTyrosyl Phosphatase Activator (PTPA) in Plasmodium falciparum (P53)

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Phosphatases are known to be essential for different biological functions like cell growth, differentiation or division. Protein phosphatase 2A (PP2A) is, with protein phosphatase 1 (PP1), considered as a major ser-thr phosphatase involved in dephosphorylation. In eukaryote cells, PP2A is complexed with many regulators which control its activity, its localization and/or its specificity. In Plasmodium falciparum, although PP2A has been described as an essential protein for erythrocytic stages survival, very little is known about its regulators. In our laboratory, in silico studies allowed the identification of several genes homolog to known eukaryotic PP2A regulators. The present work is focused on the molecular and functional characterization of phosphotyrosyl phosphatase activator (PfPTPA) potentially encoded by the gene PF3D7_1430100. This protein has been described to interact and regulate the PP2A activity by potentiating its tyrosine phosphatase activity. The amino acid sequence of PfPTPA deduced from the cDNA sequence obtained by RT-PCR exhibits 30% identity with human PTPA and five residues out of six, known to be involved in the interaction with PP2A are conserved. Using different biochemical and functional approaches, we show that PfPTPA interacts and regulates PP2A activity. Structure-function analysis performed with mutated versions of PfPTPA led to the identification of critical residues required for the function of PfPTPA. We further show that PfPP2A and PfPTPA are co-localized in P. falciparum. Finally, we present evidence that PfPTPA and PfPP2A loci are genetically accessible, allowing future attempts to generate KO parasites.

Prevalence of nematode infection and faecal egg counts in free range laying hens. (P54)

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To investigate the importance of nematodes in free range laying hens faecal samples were collected from 65 week old birds in 19 flocks and counted using FLOTAC accurate to 1 epg. All flocks had at least one nematode species with 17/19 infected with Heterakis, 16 with Ascaridia , 9 with Trichostronglyus and 6 with Syngamus. There was no significant difference between organic (9) and non-organic (10) flocks and between static (n=8) and mobile flocks (n=11). None of the faecal egg counts for any of the species were correlated with egg production or cumulative mortality suggesting the infections were not severe. Faecal egg counts were correlated with a

range of housing, husbandry and management practices which varied between nematode species and included depth of litter, percentage of hens using the range and the number of dead hens. The relationship between faecal egg counts and housing and husbandry variables suggests that these could be used to assist in future control of parasitic nematodes.

Counting of Anoplocephala perfoliate eggs in equine faecal samples (P55)

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A simple reliable method to count cestode eggs in equine faecal samples would be of value. Since FLOTAC is a relatively new egg counting method accurate to 1 epg it was tested with horse faeces containing Anoplocephala perfoliata eggs. Adult A.perfoliata and faeces from horses with negative worm burdens or known numbers of worms were collected from a licensed horse abattoir. Eggs were collected from mature A.perfoliata segments, washed, resuspended and added to 10gr of uninfected horse faeces. When eggs were added directly to the FLOTAC cell the recovery was 100%. Recovery rates using 5% Tween 20 and saturated solutions were sucrose 81%, sodium chloride 79% and zinc sulphate 74%. Best results (72%) with 10 gr faeces were with 10% Tween 20 and 50% sucrose. When eggs were added to different egg free faeces, eggs were always found in the sample, but the results were variable. Egg loss occurred when the faeces were filtered. The repeatability of counts from naturally infected faecal samples from horses with heavy worm burdens was low, varying from horse to horse, suggesting eggs were not evenly distributed in the faeces. By contrast 88% recovery of eggs was obtained when added to cattle faeces. It is suggested that the coarse nature of the fibres in horse faeces traps A.perfoliata eggs making faecal egg counts unreliable. Novel methods of estimating A.perfoliata burdens in horses are therefore required.

Ticks (Acari:Ixodidae) infesting camels(camelus dromedaries) in eastern region of Saudi Arabia (P56)

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Ticks transmit numerous infectious agents to humans and animals. The tick-borne diseases include encephalitis, Tularaemia, tick paralysis, Brucellosis, Crimean-Congo haemorrhagic fever and many other diseases.These diseases cause illnesses, mass mortality, and severe economic losses in livestocks. In Saudi Arabia Alkhurma disease, a dengue-like hemorrhagic fever is suspected to be transmitted by ticks. In Saudi Arabia many genera of hard ticks were found and identified by morphological characters only. In this study we report on the results of studies on the distribution and species composition of ticks collected from camels. These camels under study are from various origins and reared in different farms in the Eastern Province of Saudi Arabia. These ticks were sorted according the site of infestation of the camel for each farm. We will also attempt to develop a molecular PCR assay based on variations of the internal transcribed sequence (ITS) of

the ribosomal DNA genes that might exist between different ticks collected if present. These polymorphisms will be an important tool for further phylogenetic studies on pests and vectors of diseases of these important animals of both economic and cultural importance in the Arabian Peninsula.

Identification of a novel pyrethroid metabolising Cytochrome P450 from the tick: Rhipicephalus (Boophilus) microplus (P57)

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The identification of enzymes involved in the metabolism of pesticides is becoming increasingly important in numerous arthropod species to provide an insight into the molecular mechanisms of pesticide resistance. Cytochrome P450s (CYPs) are the major phase 1 metabolising enzymes and have been shown in mosquito species to be key in metabolising pesticides such as pyrethroids, with members of the CYP6 and CYP9 families being of particular importance. The acari (ticks and mites) are second to mosquitoes as vectors of medically and veterinary important diseases. Like most pest species, ticks are showing increased resistance to commonly used pesticides but the mechanism behind this is poorly understood. Rhipicephalus (Boophilus) microplus - the cattle tick – is an important vector of Babesiosis to cattle and control infestations costs the industry billions of dollars globally each year. In an attempt to gain a better understanding of acaricide metabolism in this tick, our group has employed a combination of transcriptomic data and RACE PCR to identify a novel CYP from R. microplus. Subsequent bioinformatic analysis on the sequence strongly suggests this is CYP may be associated with pyrethroid metabolism and should be included in the key detoxification CYP6/9 clade. This CYP is currently being cloned into a prokaryotic expression system in order to carryout detailed enzymatic characterisation. In addition qRT-PCR data is being collated to determine if there is an association between the expression of this novel CYP and acaricide resistance in 11 R. microplus strains.

The effect of buthionine sulphoximine on the survival of different Leishmania species (P58)

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Glutathione (GSH) is widely distributed in animal cells and is the major intracellular thiol antioxidant in cells. Buthionine sulphoximine (BSO) is irreversible inhibitor of gamma glutamyl cysteine synthetase (γGCS).In this study experiments were carried out to determine whether BSO had a similar effect on L. mexicana and L. major, which are known to have different effects on their host cell. Therefore the effect of BSO treatment on the survival of promastigotes and intracellular amastigotes of L. donovani, L. mexicana, L. major and the expression and inhibitory effect on the activity of recombinant γGCS from each species was determined. As there is

considerable homology (87.6%) in the sequence of the protein for all three species. 97% similarity between L. donovani and L. major, 95% similarity between L. donovani and L. mexicana and 94% similarity between L. major and L. mexicana. Treatment with BSO significant affected the survival of all thre Leishm- ania parasites (n=4), with L. donovani having the highest susceptibility to BSO at both the promastigote (meanIC50±SE, for L. donovani, 1.3±0.29mM; L. major, 1.8±0.017mM; L. mexicana, 2.4±0.68 mM) and intracellular amastigote stage. This differential activity was not mirrored by the effect of BSO on the recombinant protein for all three species as L. mexicana was the most resistant to inhibition (mean % inhibition of specific activity with 1mM BSO (n=4); L. donovani, 86%±0.02; L. mexicana, 45%±0.19; L. major, 63%±0.17). The results of this study indicate that inhibition of GSH production requires development species-specific

Cysteine biosynthesis and thiol balance in Leishmania donovani (P59)

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Cysteine is a key building block of trypanothione, an antioxidant unique to trypanosomatids that plays a pivotal role for the survival of the parasites. Leishmania can obtain cysteine in two ways, using the sulphydrylation and trans-sulphuration pathways. Humans lack the sulphydrylation pathway, thus this, and especially cysteine synthase (CS), of Leishmania could be a potential drug target. In order to determine the relative importance of these pathways, the levels of thiols at different stages of promastigote growth of wild-type, mutants lacking CS (deltacs), and CS episomal re-expressor parasite lines were determined. It was found that during logarithmic phase the mutant parasites have significantly reduced levels of thiols, which is reversed in the CS re-expressing parasite line. The mRNA and protein levels of cystathionine β-synthase (CBS) were found to be increased in deltacs L. donovani, while this increase was reversed in the CS re-expessing line. These data suggest that the reverse trans-sulfuration pathway compensates for the loss of CS to some extent but that this is not sufficient to maintain thiol levels during logarithmic growth. It was further found that ornithine decarboxylase mRNA is upregulated while the protein levels appear to be reduced in the deltacs parasite line; this change is reversed in the CS re-expessing line. The latter was supported by the finding that the deltacs mutant parasites have low sensitivity to difluoromethylornithine, an inhibitor of ornithine decarboxylase. Overall the data suggest that the levels of thiols are dependent on an adequate supply of cysteine through the sulphydrylation pathway.

Gastrointestinal parasites of birds in five zoological gardens in South West Nigeria (P60)

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Infections with gastrointestinal parasites are a major health issue in captive birds. However, prevalence data of gastrointestinal parasites of birds in zoological gardens in Nigeria are scarce. This study was carried out to establish the gastrointestinal parasite profile of birds kept in Zoological gardens in the University of Ibadan, Obafemi Awolowo University, University of Ilorin, University of Lagos and Federal University of Agriculture Abeokuta, all in south-west Nigeria. Fecal samples were examined using three techniques, Sedimentation technique for identification of parasites, McMaster technique for fecal egg/oocyst counts and Harada Mori technique for larvae recovery. A total of 178 fecal samples were examined in 83 birds (27 Species, eight Orders) and 32(18.0%) samples were found positive for infection. Eggs of Ascaris and Capillaria species were observed in 14(7.9%) and 25(14.1%) samples respectively, while the oocyst of Coccidia and cyst of Balantidium were observed in 14(7.9%) and 2(1.11%) samples respectively. Mixed infection was found in 18(10.1%) samples. Strongyloides larvae were observed in 6(3.4%) samples. The Anseriformes and Struthioniformes harbored all the types of parasites detected. The geometric mean intensity of eggs ranged from 101.98 ± 10.36 to 63.00 ± 16.67 epg and oocyst counts ranged from 332.47 ± 16.67 to 297.89 ± 20.41 opg. Cyst count of Balantidium was 324.04 ± 25.00. Count of oocyst of Coccidia species was significantly higher in all the zoos. The fecal culture yielded Strongyloides species. There is a need for regular deworming of birds, improved hygiene, funding and management of Nigerian zoological gardens to ensure sustainability.

Age, gender and climate associations with the seroprevalence of Neospora species infection in horses in Jordan (P61)

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A cross-sectional study was carried out on a systematic sample of 379 horses to determine the seroprevalence of Neospora spp. in Jordan, using the indirect fluorescent antibody test. Five variables, namely; locality (n = 10), climatic zone (n = 5), age group (n = 3), gender and breed were tested as risk factors for Neospora-IgG-seropositivity at 4 cutoff titers (1:50, 1:200, 1:400 and 1:800), using univariable and multivariable logistic regression analyses. A total of 122 (32%; 95% CI: 28, 37) sera had anti-Neospora-IgG at a cutoff titer of 1:50. Increasing Neospora-IgG-seropositivity was associated with horses in three localities (Madaba, Zarka and Petra), cool temperate climate, age group >14 years and female gender. Serpositivity was associated with Madaba at all the cutoff titers, Zarka at titers of > 1: 200, and Petra associated with titer < 1: 200. Cool temperate climate was associated with titers < 1:400. The age group > 14 years associated with titers > 1:200. The female gender was associated with high seropositivity of > 1:800.

Bayesian Geostatistical model-based estimates of schistosomiasis prevalence and Praziquantel treatment requirements in Nigeria (P62)

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The paucity of detailed information on schistosomiasis distribution in Nigeria hampers the implementation of the national control programme. We produced risk maps to facilitate targeting of control activities, planning of future surveys and surveillance. Relevant schistosomiasis prevalence data were extracted from peer-reviewed journals and reports, geo-referenced and collated in a nationwide, geographical information system (GIS) database for the generation of schistosomiasis point prevalence maps. This exercise revealed that schistosomiasis is endemic in 35 of the country's 36 states including the federal capital territory of Abuja. Infections were found in 462 unique locations out of 833 different survey locations. Schistosoma haematobium, the predominant species in Nigeria, was found in 368 (79.6%) locations covering 31 states, S. mansoni in 78 (16.7%) locations in 22 states, and S. intercalatum in 17 (3.7%) locations in two states. The estimated prevalence of S. haematobium, based on Bayesian geospatial predictive modelling with a set of bioclimatic variables, ranged from 0.2% to 74.7% with a mean prevalence of 22.9% (95% confidence interval (CI): 22.8-23.1%) for the country as a whole. The model suggests that mean temperature, annual precipitation and soil acidity significantly influence the spatial distribution of schistosomiasis in Nigeria. Prevalence estimates, adjusted for school-aged children in 2010, showed that the prevalence is <10% in most states with only some reaching 50%. It was estimated that 11.3 million (95% CI: 10.3-12.2 million) school-aged children require Praziquantel annually.

Pyrimidine biosynthesis is not an essential function for Trypanosoma brucei bloodstream forms (P63)

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Background: African trypanosomes are capable of both pyrimidine biosynthesis and salvage of preformed pyrimidines from the host, but it is unknown whether either process is essential to the parasite. Methodology/Principal Findings: Pyrimidine requirements for growth were investigated using strictly pyrimidine-free media, with or without single added pyrimidine sources. Growth rates of wild-type bloodstream form Trypanosoma brucei brucei were unchanged in pyrimidine-free medium. The essentiality of the de novo pyrimidine biosynthesis pathway was studied by knocking out the PYR6-5 locus that produces a fusion product of orotate phosphoribosyltransferase (OPRT) and Orotidine Monophosphate Decarboxylase (OMPDCase). The pyrimidine auxotroph was dependent on a suitable extracellular pyrimidine source. Pyrimidine starvation was rapidly lethal and non-reversible, causing incomplete DNA content in new cells. The phenotype could be rescued by addition of uracil; supplementation with uridine, 2'deoxyuridine, and cytidine allowed a diminished growth rate and density. PYR6-5-/- trypanosomes were more sensitive to pyrimidine antimetabolites and displayed increased uracil transport rates and uridine phosphorylase activity. Pyrimidine auxotrophs were able to infect mice although the infection developed much more slowly than infection with the parental, prototrophic trypanosome line. Conclusions/Significance: Pyrimidine salvage was not an essential function for bloodstream T. b. brucei. However, trypanosomes lacking de novo pyrimidine biosynthesis are completely dependent on an extracellular pyrimidine source, strongly preferring uracil, and display reduced infectivity. As T. brucei are able to salvage sufficient pyrimidines from the host environment, the pyrimidine biosynthesis pathway is not a viable drug target, although any interruption of pyrimidine supply was lethal.

The Fasciola hepatica cathepsin B4 conundrum: Does the Cys/Ser active site substitution create an inactive protease? (P64)

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Fasciola spp. liver flukes cause fasciolosis, a global disease of domestic animals and a neglected tropical disease which infects up to 17 million people. Infection with liver fluke occurs following ingestion of dormant metacercarial larvae which occur encysted on vegetation. Metacercariae are activated and larval parasites excyst in the host duodenum, penetrate the duodenal wall, and migrate to the bile ducts via the hepatic parenchyma. During this invasion phase, juvenile fluke secrete a battery of proteolytic enzymes dominated by multiple cathepsin B and cathepsin L cysteine proteases. Fasciola hepatica expresses at least ten distinct cathepsin B (FhCB) transcripts; we have profiled the expression of these cathepsins in metacercariae, newly-excysted juvenile (NEJ) and adult F. hepatica and Fasciola gigantica using qPCR. We identified expression of FhCB1, 2, 3, 4, 6, 7, 9 and 10 and FgCB1, 2, 3, 4, 6, 7 and 9, with some variation across the life stages; as expected, expression of FhCB1, 2 and 3 predominates in NEJs and then diminishes comparatively in adult stage worms. FhCB4, which is expressed in metacercariae, NEJs and adult parasites,

represents an unusual cysteine protease, in that its active site cysteine residue appears to be replaced by serine. To determine the impact of this Cys-Ser exchange on proteolytic activity, we have expressed recombinant FhCB4, alongside S29C and A27G/A28S/S29C variants, in the pPink alpha Pichia pastoris system. Analyses of proteolytic activity in these variants are underway, with the aim of understanding the unusual cathepsin's biological function.

Down-regulation of TLR3 expression in lymph nodes in a susceptible experimental model of canine Leishmania infantum infection (P65)

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A wide spectrum of clinical manifestations occurs in canine Leishmania infantum infection as a result of complex interactions between the parasite and host innate and adaptive immune responses. Toll-like receptors (TLRs) are essential components of the innate immune system and facilitate the early detection of infection. The TLR signalling pathway is thought to be one of the first systems to defend against Leishmania, although information about TLR expression during canine L. infantum infection is scarce. The objective of this study was to characterize TLR3 transcription in a susceptible model of canine L. infantum infection. Popliteal lymph node samples were taken post-mortem from experimentally infected beagles at different stages of infection [Group 1 (n=6), non-infected clinically healthy control dogs; Group 2 (n=24), dogs euthanized six months post-infection and Group 3 (n=7), sick dogs euthanized 15 months post-infection]. RNA was extracted and cDNA generated from lymph node samples. Transcription of TLR3 and a panel of tissue-specific housekeeping genes were assessed by quantitative real-time PCR. Absolute quantification of lymph node TLR3 transcription revealed statistically significant differences between all groups. TLR3 mRNA levels were down-regulated in both infected groups compared to the control ($p=0.007$). Further down-regulation was noted as the infection progressed (comparing Groups 2 and 3; $p=0.002$). These results demonstrate progressive TLR3 down-regulation in the lymph node with parasite dissemination and disease development. Reports describing the importance of TLR3 in phagocytosis of Leishmania donovani by macrophages suggest a role in immune evasion for the parasite-induced TLR3 down-regulation described here.

Interaction basis and regulation of Protein Phosphatase type 1 by inhibitor 2 of Plasmodium falciparum (P66)

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It is now clear that phosphorylation is one of the most 'if not the most' fundamental process in the biology of Plasmodium. This has been clearly demonstrated by accumulating and converging evidences from studies on Kinases. However the role of the opposed enzymes, the phosphatases which are key keepers of the balance between phosphorylated /dephosphorylated proteins and their regulators remain very poorly understood. Among these phosphatases, Protein Phosphatase type 1 (PP1) was identified in Plasmodium falciparum (Pf) and it was found to be as the major enzyme in this apicomplexan parasite. Our previous work showed that the PfPP1is tightly controlled by regulatory proteins including PfLRR1 (homolog to sds22 of the yeast) and the Pf Inhibitor-3 (PfI3). Genetic studies revealed that these regulators are as essential as PfPP1 itself for parasite survival. Here we report the identification and characterization of Pf Inhibitor-2 falciparum (PfI2) which shared conserved motifs with human inhibitor 2. We present evidence that PfI2 binds to PfPP1 and is able to inhibit its activity. Moreover, PfI2 motifs 12KTISW16 and 102HYNE105 are involved in the PfI2 regulatory activity. PfI2 seems to be involved in the cell cycle regulation as functional studies using the Xenopus oocytes model revealed its ability to trigger the G2/M transition. Finally, reverse genetic manipulations suggest an essential role of PfI2 in the parasite survival. All together, these results strongly suggest that PfI2 could play a crucial role in the regulation of Pf development via its PfPP1 phosphatase inhibitory activity.

Schistosoma mansoni Sirtuins: SmSirt2 is a promising target for drug development against schistosomiasis (P67)

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Sirtuins are protein deacetylases that are involved in a wide variety of cellular processes including the regulation of transcription and apoptosis. They are actively investigated as drug targets, particularly in cancer. In this work, we are investigating the use of sirtuin inhibitors as candidate drugs against schistosomiasis. Five sirtuins, orthologues of mammalian sirtuins (Sirt) 1, 2, 5, 6 and 7, are encoded in the S. mansoni genome and we have cloned and characterized their coding sequences. Quantitative RT-PCR shows that all five are expressed at all parasite life-cycle stages tested. Production of recombinant Schistosoma mansoni Sirt2 (SmSirt2) allowed us to obtain an antibody and show that SmSirt2 is expressed at all parasite stages. Comparison of a 3D model of SmSirt2 with the human Sirt2 crystal structure shows notable differences at the peptide substrate binding site indicating that it should be possible to identify specific inhibitors for the parasite enzyme. Inhibitors of human Sirt1 and 2 induce death of schistosomula via apoptosis. Moreover, treatment with sirtuin inhibitors affects the pairing stability of adult worms, decreases the number of eggs laid in vitro and affects the morphology of the ovary and testis. Recombinant SmSirt2 was subjected to high-throughput inhibitor screening. Several inhibitors show high affinity (IC50 in the

nM range) and were active in in vitro assays on schistosomula and adult worms maintained in culture.

Short interfering RNA-mediated gene silencing in the potato cyst nematode, Globodera pallida (P68)

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The potato cyst nematode Globodera pallida is a burden on potato crop production throughout the UK; losses in Europe are estimated at ~£300 million per annum. Recently, in planta based RNA interference (RNAi), utilising transgenic plants expressing double-stranded RNA (dsRNA) to trigger specific transcript degradation of target genes within plant parasitic nematodes, has been proposed as a novel control strategy. Here we investigate the sensitivity of transcripts expressed in different tissues of infective J2 stage worms for susceptibility to RNAi. Our previous work demonstrated efficient knockdown following soaking in siRNAs of one neuronal (Gp-ace-2) and two gland cell (Gp-cell-1, Gp-cm-1) genes. Here we report expansion of this work to examine the susceptibility of genes expressed selectively within the intestine (cathepsin L; Gp-cp-l), hypodermis (fatty-acid and retinol binding protein; Gp-far-1)), muscle (Gp-unc-54), subventral glands (pectate lyase; Gp-pel-2 and expansin; Gp-exp) and one gene expressed across multiple tissue types (actin; Gp-act) to RNAi. Our experimental design included multiple replicates and post-analysis of transcript using quantitative PCR. So far, knockdown has been demonstrated in Gp-cp-l (~70%), Gp-far-1 (~80%), Gp-unc-54 (between 45% and 70%), Gp-pel-2 (~75%), Gp-exp (~95%); unexpectedly, Gp-act transcript has been upregulated consistently following exposure to selective siRNAs. These data show that gene transcripts in most tissue types are susceptible to RNAi.

Allele frequency changes in a malaria parasite population over a 25 year period related to genomic signatures of selection (P69)

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Analysis of genome-wide polymorphism is widely employed to uncover evidence of selection on particular loci in humans and other eukaryotic genomes. However, data on associated historical changes in allele frequencies are generally unavailable, preventing validation of the proposed selective events. We present a unique study of long term temporal changes and their relationship with signatures of selection in the malaria parasite Plasmodium falciparum, the most important

eukaryotic pathogen of humans. We studied frequencies of alleles at four drug resistance loci using 668 archived blood samples collected in The Gambia between 1984 and 2008, from a time before any resistance was detected locally, through the subsequent periods of failure of chloroquine and sulphadoxine-pyrimethamine until their withdrawal. Frequencies of resistance alleles were very low or undetectable in 1984 but changed significantly over time, peaking in 2000 for chloroquine resistance-associated crt and mdr1 alleles, and at the end of the survey period for the dhfr and dhps alleles associated with pyrimethamine and sulphadoxine resistance. By genome sequence analysis of a population sample of clinical isolates from 2008, we identify multiple loci with evidence of directional selection, and show that three of the drug resistance loci were in the top four signatures genome-wide. The fourth drug resistance locus did not emerge from this genome wide scan, consistent with the declining frequency of the mdr1 resistance allele over the last eight years of the survey, providing a direct demonstration of the transient nature of selective sweeps following a period of intense selection.

Knockdown of Asparagine synthetase A renders Trypanosoma brucei auxotrophic to asparagine (P70)

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Asparagine synthetase (AS) catalyzes the ATP-dependent conversion of aspartate into asparagine using ammonia or glutamine as nitrogen source. There are two distinct types of AS, asparagine synthetase A (AS-A), known as strictly ammonia-dependent, and asparagine synthetase B (AS-B), which can use either ammonia or glutamine. The absence of AS-A in humans and its presence in trypanosomes, point out AS-A as a potential drug target that deserves further investigation. We have for the first time reported the presence of asparagine synthetase A in Trypanosoma cruzi (TcAS-A) and Trypanosoma brucei (TbAS-A). In both parasites, this enzyme converts L-aspartate into L-asparagine in the presence of ATP, ammonia and Mg2+. TcAS-A and TbAS-A use preferentially ammonia as nitrogen donor, but surprisingly can still use glutamine, a characteristic, so far, never described for any AS-A. TbAS-A knockdown by RNAi did not affect in vitro growth of bloodstream forms of the parasite. However, growth was significantly impaired when TbAS-A knockdown parasites were cultured in medium lacking asparagine. Indeed, parasite cell cycle was arrested in G0/G1 phase, and consequently they did not multiply correctly. As expected, mice infections with induced/non-induced T. brucei RNAi clones were similar to the wt strain resulting therefore in the same percentage of mice survival. However, when T. brucei RNAi clones were injected in mice undergoing asparaginase treatment, and thus having reduced levels of asparagine in the blood, mice exhibited lower parasitemia and a prolonged survival in comparison to control mice. Our findings give new insights into functional characterization of AS-A in trypanosomes.

The effects of sex and food resources on vertically acquired covert granulovirus on the Indian meal moth, Plodia interpunctella (P71)

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The vertical transmission of viruses in covert states presents viruses with a means of persisting in host populations where there are low or dramatically alternating host densities. Covert vertical transmission also provides a means of persistence where horizontal transmission only occurs in larval stages and adult stages are highly mobile. The Indian meal moth Plodia interpunctella is a crop pest of stored grain. Plodia interpunctella GV (PiGV) is a Baculovirus, which through horizontal transmission obligately kills its Plodia interpunctella larval host. Using PCR to detect the PiGV granulin gene, levels of covert vertical infection rates for PiGV were detected in progeny of all the different combinations of either PiGV infected or non-infected, Plodia interpunctella females and males. The mechanisms under which covert Baculoviruses are activated to an overt state are poorly understood. As such, this study also sought out to find whether low food quality could activate PiGV from a covert to an overt state. This was done by raising the progeny of the differentially infected first generation Plodia interpunctella on two different qualities of food. Across all treatments no overt, activated PiGV infection was found in the second generation. PCR methods detected the presence PiGV in the progeny of all treatments. Including that of males mated with females, both of which had been dosed with a control solution. This result could suggest that a version of PiGV has been transmitting covertly between generations within the stock population of Plodia interpunctella.

Detection of Trypanosoma brucei gambiense infections in humans living in Plateau and Nasarawa states of north central Nigeria. (P72)

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Introduction Human African trypanosomiasis (HAT) is one of the most important vector-borne diseases of sub-Saharan Africa. Approximately 60 million people are at risk of disease, with an estimated 30,000 new cases annually (WHO, 2009). The vast majority of untreated cases are fatal. The causative agent in western and central parts of Africa is a sub-species of the tsetse fly-transmitted parasite Trypanosoma brucei – T. b. gambiense. The present study aimed to calculate the prevalence of T. b. gambiense infections in people from 9 villages located in several local government areas (LGAs) of Plateau State, and 3 villages from bordering Wamba LGA in Nasarawa State, in north central Nigeria. Methods Across the 12 villages, a total of 309 blood samples were collected from randomly selected individuals by thumb pricks. The blood was stored on Whatman® FTA cards. DNA was extracted from samples by washing them with FTA purification reagent and 1x tris-EDTA buffer, before treating them with Chelex® 100 sodium. T. brucei s.l. DNA was amplified by PCR using TBR1/2 primers which target a satellite repeat in the nuclear DNA of all T. brucei sub-species (Moser et al, 1989). Samples which tested positive were subjected to a nested PCR, using primers which target the T. b. gambiense-specific glycoprotein (TgsGP) gene (Picozzi et al, 2005 & Radwanska et al, 2002). PCR products were then analysed by electrophoresis using 1.5% agarose gels. Results of the electrophoretic analysis will be conveyed during the poster session.

Predictive mapping of Schistosoma haematobium infection in Zanzibar and Niger (P73)

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Natural History Museum

Predictive risk mapping in spatial epidemiology can provide valuable insights into the distribution of disease, and therefore assist with accurate estimations of disease burden. Such predictive mapping is of crucial importance in the study of neglected tropical diseases like schistosomiasis, which displays a highly focal distribution. Predictive mapping has been undertaken for Schistosoma haematobium, causal agent of urogenital schistosomiasis at both a fine-level scale in Zanzibar, and at a much broader spatial range in Niger, to examine potential influences on spatial distribution of the disease. Parasitological data for Niger were obtained from SCORE, the Schistosomiasis Consortium for Operational Research and Evaluation, and consisted of a pre-baseline prevalence survey, carried out in late 2010 of 391 villages across 10 districts. Zanzibar data were provided from the 2011- 2012 baseline survey of ZEST- Zanzibar Elimination of Schistosomiasis Transmission, from 90 schools. Probabilities of infection were estimated using univariate and multivariate logistic regression models. For Niger and Zanzibar, site level covariables were analysed, including climate and environmental data, for the 12 months prior to the relevant survey. For Zanzibar, individual level covariates such as age and sex were also examined, and a mixed model was run to allow for school location as a random effect to account for clustering. Mapping was undertaken in Arc GIS version 10, and predictive surfaces were created using joint kriging. Further analysis of the Zanzibar baseline survey will be undertaken in modelling and mapping intensity of infection.

GLOWORM: GLObal changes in parasitic WORMs (P74)

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Gastrointestinal nematodes are a major economic and welfare cost to the European livestock industry. Climate and other environmental change may result in altered seasonal and geographical distribution and risks of gastrointestinal nematode infections, rendering current management practices unsustainable in the long-term. The EU FP7 project GLOWORM (GLObal changes in parasitic WORMs) aims to develop innovative and sustainable strategies to mitigate the impact of

climate change on helminth infections in ruminants by: 1) developing improved diagnostic tests for infection and anthelmintic resistance, 2) predicting the impact of global change on the epidemiology of infection and evaluating potential management strategies to mitigate the altered challenge, 3) mapping and modelling the spatial distribution of key species and anthelmintic resistance, 4) evaluating and optimising treatment strategies which maintain anthelmintic efficacy, and 5) disseminating results to stakeholders.

Schistosoma mansoni methyl-CpG binding domain protein (SmMBD2/3): A component of the epigenetic machinery that may be actively in transcriptional regulation. (P75)

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Methyl-CpG binding domain proteins (MBDs) are fundamental components of the eukaryotic epigenetic machinery. MBDs target and bind 5-methylcytosine(5mC) and can recruit various corepressor complexes to these methylated genomic loci, leading to localised chromatin remodelling and gene expression control. Previous studies in our laboratory have identified an MBD homologue (SmMBD2/3) that is transcriptionally co-regulated with a functional DNA methyltransferase (SmDNMT2) in the pathogenic trematode S.mansoni. Here, using yeast 2 hybrid screens, cell transfections and cell fractionation, we present evidence for the functional role of SmMBD2/3 in chromatin remodelling and therefore transcriptional regulation.

Role of Interleukin-12 family of cytokines during experimental infection with visceral Leishmania infantum (P76)

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The initial encounter of Leishmania sp. with the host immune cells is crucial for the outcome of infection. In this context, the IL-12 family of cytokines plays a central role linking the early immune responses after parasite recognition to the later adaptive events required for parasite clearance. This family of cytokines shapes the immune responses by influencing the development and altering the function of T cell subsets dictating the disease outcome. Therefore, we intended to analyze the precise role of each member of the IL-12 family during visceral leishmaniasis in susceptible (BALB/c) and resistant (C57BL/6) mice. When cultured-BMDCs were infected with L.

infantum protozoan parasites, no significant changes were observed at the transcriptional level of the majority of IL-12 family members, excepted with the IL-12p40 subunit. Since not all BMDCs in the culture became infected, a separate analysis of bystander and infected cells, demonstrated that the upregulation of IL-12p40 transcription was restricted to the bystander population and was Myd88-dependent. Nevertheless, L. infantum induces the secretion of IL-27p28 and bioactive IL-27, irrespective of the mouse strain. Importantly, the transcription of IL-27p28, in opposition to IL-12p35 and IL-12p40, was found to be independent of IL-10. Finally, we only detected in vivo, an increase on IL-27p28 transcription, among all IL-12 family, in splenic macrophages and DCs recovered from L. infantum-infected BALB/c mice. Our data provides new information on the role of IL-12 family of cytokines in immune function against L. infantum, although our current knowledge, particularly for the IL-27, needs to be enhanced.

Optimising composite faecal egg count methods in goats (P77)

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Helminth infection compromises health, welfare and productivity of livestock. Growing awareness of the need for sustainable livestock practices and increasing prevalence of anthelmintic resistance are promoting use of strategic anthelmintic treatment decisions rather than routine prophylactic treatments. A popular method for monitoring nematode burdens is the faecal egg count (FEC), particularly composite FECs. However, there is a tendency for composite FECs to underestimate mean egg density of the total population with error increasing at higher levels of parasite aggregation. The majority of work undertaken in this area has been in sheep with negligible consideration for goats and their distinct behavioural, immunological and physiological characteristics. This study uses a simulation-based approach built on data collected from available literature to consider the relative impacts of sample size, faecal sample weight and detection limit of laboratory tests on error in observed composite FEC at different levels of parasite aggregation and mean egg density in goat herds. The results, validated with field data, show that the number of animals included in composite FECs has a far stronger effect on error than amount of faecal material examined, or accuracy with which individual samples are included; this effect is greater with increasing levels of aggregation. Furthermore, resampling of animals did not significantly compromise composite FEC results, suggesting that sample size can be increased and elements of accuracy in sample collection compromised, reducing the labour and error associated with composite FEC monitoring and therefore promoting its regular use by farmers.

Mapping the highly complex genetic architecture of variation in Caenorhabditis elegans dauer larvae development within growing populations (P78)

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Dauer larvae of the free-living nematode Caenorhabditis elegans are commonly used to model various aspects of the biology of the infective juveniles of parasitic species. One such aspect is the developmental choice, made by C. elegans larvae, between developing as a reproductive adult or as a dauer larva. This choice has clear parallels within the lifecycle of the entomopathogenic insect-parasitic nematodes and in the development of the infective stages of many vertebrate parasites. Commitment (or not) to dauer larvae development in C. elegans also tells us about how worms perceive their environment, a critical issue for understanding the responses of parasitic species to chemical cues from potential hosts. However, little is known about the genetics of natural variation in C. elegans dauer larvae formation, particularly in growing populations. Here, we have analysed dauer larvae development in growing populations of C. elegans wild isolates and introgression lines (ILs) derived from the isolates N2 and CB4856. These analyses reveal extensive variation between wild isolates and identify 24 quantitative trait loci (QTLs) affecting dauer formation, 10 by bin mapping, an additional 8 by analysis of individual ILs and 6 more by sequential IL analysis. These data demonstrate the power of ILs for identifying QTLs underlying complex traits and indicate that the mapping approach can dramatically affect the apparent control of trait variation. This work also indicates that a behavioural polymorphism controlled by the neuropeptide Y receptor homolog npr-1 affects dauer larvae development in growing populations. As npr-1 is known to act in O2

Schistosomiasis: the role of parasite genetics in human infection and disease (P79)

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Schistosomiasis is a major, poverty-related disease affecting more than 200 million people in developing countries. It has a complex epidemiology with a large variation in infection intensity and schistosome-related pathology. It is still not fully understood why certain people living in the same endemic area are heavily infected and develop disease while others do not. It has been shown that factors such as host genetic background and water contact play an important role, but a large part of the variation in infection intensity and pathology in humans remains unexplained. Recent research based on a limited set of microsatellite markers revealed a positive relationship between a specific parasite genotype and schistosome infection intensity (presentation Huyse T. et al.). In this PhD project we will, among others, try to confirm this observation in other populations in Senegal as well as in DRCongo and study in depth the underlying molecular mechanisms. The overall goal of the project is to investigate how parasite genetics influence host infection and disease patterns. Extensive fieldwork to collect parasite samples and epidemiological information about the host forms an essential component of this project. The second step, the genotyping of the parasite, will be technical challenging as the amount of DNA

template is low and contamination with genetic material from other organisms may be high. This is especially the case for field samples, i.e. (hatched) eggs collected from urines or stools. Two different approaches, a candidate gene based method and a Genome-Wide Association Study (GWAS) are considered.

Further Developmental Characterisation of the DOZI Translational Repression Complex in P. berghei. (P80)

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The protein CITH (CAR-I Trailer Hitch homologue) in P. berghei is closely associated with DOZI (Development Of Zygote Inhibited), a DEAD box helicase, in a ribonucleoprotein complex (RNP) which in gametocytes RNP has a central role in conditional translational repression of transcripts vital to zygote development. Reciprocal pull downs of CITH and DOZI from gametocyte extracts have shown similar associated proteins and overlapping, but not identical, RNA species associated with each. In this study an RNA motif previously identified from translationally repressed transcripts and transcripts downregulated on DOZI knock out was used to capture proteins that bind and may influence the repression and release of RNA species. We are also characterising the translational repression complex in ookinetes with respect to protein and RNA species using immunoprecipitation (IP) of GFP-tagged DOZI and CITH. The protein components are very similar to those in the gametocytes but, as expected, microarray analysis of the RNA species recovered from a CITH::GFP IP reveals a very different collection of transcripts. Those that have been previously characterised have roles in the continuing development of the parasite in the mosquito, however many have not been characterised. The generation of knock out lines using pJazz vectors of multiple genes of interest is on-going.

Anthelmintic activities of a plant-derived natural product. (P81)

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Schistosomiasis control is heavily reliant on a single drug, praziquantel (PZQ). With no vaccine on the immediate horizon, and the ever-present spectre of PZQ-resistant schistosomes developing in communities undergoing mass drug administration (MDA) programmes, identifying next generation anthelmintics is urgently needed for sustaining deworming initiatives into the future. Towards this end, and due to the well-characterised therapeutic success of artemisinin, we have begun investigating the anthelmintic activities of natural products derived from temperate plants. Here, we demonstrate that, amongst a library derived from 1000 novel chemical entities (NCEs), a single compound displayed both anti-schistosomal and anti-fasciolicidal activity during in vitro, whole organism assays. Specifically, this NCE displayed an LD50 = 20µM against schistosomula, an

EC50 = 2.5µM against newly excysted juvenile (NEJ) Fasciola hepatica and caused severe phenotypic alterations in adult schistosomes (between 10µM-100µM). These adult schistosome alterations included tegumental disruptions, tubercule abnormalities and irregular oocyte architecture as assessed by scanning electron and confocal microscopy. Reassuringly, this compound displayed no general cytotoxicity (at 50µM) against a human liver cell line (HepG2) . In light of the selective (no toxicity against mammalian cells) and pan-trematode activity (against both blood and liver flukes) of this natural product, further experiments are ongoing to detail additional anthelmintic properties in both in vitro and in vivo models.

Simultaneous Detection of Tick-Borne Pathogens in Nigeria (P82)

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Introduction Ticks and tick-borne pathogens impair cattle fitness and productivity in the whole of sub-Saharan Africa, including Nigeria. This study aimed to assess the occurrence of pathogens of veterinary and zoonotic importance in ticks collected from cattle in an area of central Nigeria where no acaricides are employed on livestock, in spite of the relatively high tick burdens on cattle. Methods Ticks were collected in October 2010 from indigenous (Bos indicus) cattle in Plateau State. Collected ticks were preserved in 70% ethanol and morphologically identified. For each tick, sex and feeding state were also recorded. After DNA extraction, all samples were subjected to a molecular protocol consisting of three simultaneous polymerase chain reactions (PCRs) followed by reverse line blot (RLB) hybridisation of PCR products. In addition, a spotted fever group (SFG)-specific PCR was carried on RLB Rickettsia positive samples. Results 119 adult Ixodid ticks were identified, including 37 Rhipicephalus (Boophilus) decoloratus (23 males, 14 females), 46 Rhipicephalus (Boophilus) annulatus (20 males, 26 females), 12 Rhipicephalus (Boophilus) geigyi (3 males, 9 females), 12 Hyalomma truncatum (6 males, 6 females) and 12 Amblyomma variegatum (6 males, 6 females). Pathogens detected included Anaplasma marginale, Anaplasma bovis, Anaplasma centrale, Ehrlichia ruminantium, Ehrlichia sp. Omatjenne, Theileria mutans and Babesia bigemina, with the most prevalent of these being Anaplasma marginale. A high frequency of co-infection with both Anaplasma marginale and Rickettsia spp. was also seen upon RLB hybridisation. Amongst the 33 Rickettsia spp. positive samples, 14 also tested positive for spotted-fever group rickettsiae.

Do interactions between co-infecting schistosome species affect the outcome of praziquantel treatment? (P83)

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Two human schistosome species are common in Africa, Schistosoma haematobium and S. mansoni. In many areas, both are endemic and co-infection is common. During co-infection, the species may interact, through competition for space, nutrients or mates, or via the immune system. While schistosome co-infection has been shown to alter species-specific infection intensity and morbidity profiles, whether co-infection influences the success of drug treatment with praziquantel (PZQ, the current drug of choice in preventative chemotherapy programmes), has rarely been considered. Using data from two mixed species settings in West Africa, (Senegal and Mali), we examined whether schistosome co-infection affected PZQ-related parasite clearance, re-infection post-treatment, and the ability to reduce infection prevalence over successive treatment rounds. We found asymmetries in the effect of one schistosome species on the other in the context of PZQ chemotherapy, with S. haematobium more affected by S. mansoni co-infection than vice versa. S. haematobium was less likely to be cleared when co-infecting with S. mansoni, an effect that appeared to be driven by higher infection intensity. Furthermore, the intensity of S. haematobium re-infection in the 6 months post-treatment declined with increasing intensity of S. mansoni co-infection at baseline. No effects of S. haematobium co-infection on S. mansoni drug-induced clearance or re-infection were found. Further studies are needed to test the consistency of these preliminary results across different settings. However, if repeatable they suggest the impact of treatment may be influenced by within-host schistosome species interactions, and that optimal treatment strategy may vary with the level of

In silico elucidation of the Notch and Hedgehog developmental pathways in the model tapeworm Hymenolepis microstoma (P84)

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The developmental pathways “Notch” and “Hedgehog” are both highly conserved signalling systems, involved in regulation, cell fate specification and pattern formation. We are interested in how modification of shared developmental systems are able to produce such a wide range of novelty in form, specifically the range of segment body plans seen amongst cestodes. Here we present bioinformatic work that has identified the presence of core components and the absence of some co-receptors and regulators involved in each pathway in the model tapeworm Hymenolepis microstoma. This work will be used to visualise expression patterns within the tapeworm and allow for a broader comparison of developmental gene expression within other major groups of Platyhelminthes (including monogeneans and digeneans).

A bioinformatic approach toÂ the discovery of novel antigens for visceral leishmaniasis diagnosis (P85)

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Leishmaniasis is a vector-bone disease transmitted by Leishmania-infected female sandflies of genera Phlebotomus (in the Old World) and Lutzomyia (in the New World). Visceral Leishmaniasis (VL) may be zoonotic, caused by Leishmania infantum or anthroponotic, caused by Leishmania donovani. VL remains a problem especially in Asia, East Africa and Brazil as current diagnostic tools are far from ideal. Although the antigens rK39 and rK28 are currently widely used, the sensitivity levels are not equally satisfactory in the endemic areas (particularly in East Africa). Therefore, an improved serological diagnostic antigen is urgently needed. The analysis of rK39 and rK28 sequences revealed several region-specific polymorphisms among Indian and East African strains. Using bioinformatics to search and compare the available Leishmania reference genomes, we are currently working to identify novel antigenic epitopes; and investigate further the antigenic epitope of rK39 and rK28.

Characterization of Plasmepsin V substrate specificity. (P86)

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Malaria is caused by the unicellular eukaryote Plasmodium and is responsible for approximately 655,000 deaths every year. During the blood stage of the disease parasites reside inside red cells and export proteins to the cytosol of their host cell where they have a variety of effects. Most exported proteins contain a Host Targeting (HT) motif that is responsible for directing them for export. The HT motif corresponds to the consensus sequence RxLxE/D/Q (where x is any amino acid). Plasmepsin V is an essential aspartic protease localized to the parasite endoplasmic reticulum. It cleaves the HT motif of exported proteins after the leucine residue, which generates a ‘new’ N-terminus starting with the sequence xE/D/Q. Cleavage by Plasmepsin V is essential as it generates a new N-terminal sequence in nascent exported proteins that is both necessary and sufficient to target proteins for export. Previously it has been shown that the R and L positions in the HT motif are important for cleavage by Plasmepsin V. We now show, in vivo, and in vitro using purified Plasmepsin V, that the identity of the residue in the fifth position (E) of the HT motif is also important for efficient cleavage by Plasmepsin V.

Applied evolution: an experimental approach to investigating how the interaction between parasite life history strategies and control measures affects rates of resistance evolution. (P87)

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The problem of overcoming resistance involves finding methods of drug use such that parasite/pest populations are kept at low numbers and the evolution of resistance is minimised. Several factors are known to affect the rate at which populations can evolve resistance, including the type of drug, dosage, timing of application, migration rates between susceptible and resistant populations, the standing frequency of resistance alleles in the population and the specific mechanisms of resistance. In addition, life history characteristics of the parasites and their reproductive strategies could influence the rate at which resistance develops. Current research to date on parasitic organisms has considered many of these factors in isolation but there has been little attempt to explore interactions between life-history traits, mating systems and other factors affecting the rate of resistance. This study will take an experimental evolutionary approach to understanding the influence of such interactions, using free-living Caenorhabditis remanei as a model. The rate of resistance evolution will be evaluated by treating nematodes with anthelmintics, applied at different dosages and rates, under experimentally varied reproductive modes and population demographics.

Broad fish tapeworm Diphyllobothrium dendriticum: Neglected human parasite of growing significance (P88)

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Diphyllobothriosis is a human disease caused by broad fish tapeworms of the genus Diphyllobothrium Cobbold, 1858 (Cestoda: Diphyllobothriidea). Among the total number of 14 Diphyllobothrium species described to be capable of infecting humans, D. latum causes the majority of human infections. However, the real number of D. latum diphyllobothrioses might be overestimated on account of other human-infecting Diphyllobothrium species, namely D. nihonkaiense, D. pacificum and D. dendriticum. Even if the endemic areas of D. nihonkaiense and D. pacificum are northern and southern Pacific region, respectively, the recent globalization of food trade, climate change, increased mobility and changed eating habits of people spread these parasites to originally pathogen-free regions. D. dendriticum has then never been considered an important parasite of man—the human infections were generally thought accidental. Routine diagnostics of diphyllobothriosis is currently based on the morphological observation of relatively small eggs with an operculum or proglottides with median genital pores in stool. Such cases are, however, mostly identified as D. latum or as unidentified Diphyllobothrium infections because Diphyllobothrium egg morphometric values vary considerably within and overlap between individual species thus preventing a correct species diagnosis to be done without the use of molecular tools. Here, we describe recent cases of Europeans infected with D. dendriticum,

revealed and confirmed by the use of sequence data. Our findings call into question the current knowledge of the distribution and epidemiological status of this tapeworm species and demonstrate that causal agents of zoonoses can be readily imported throughout the world.

Endoparasites of nestling seabirds affect siblings unequally (P89)

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Parasitic infection during early life has the potential to shape an organism's development. This could have life-long fitness consequences for the individual, with implications for population processes. However, individuals may not be affected equally. Even within a brood, siblings often differ in their susceptibility to poor environmental conditions, and may similarly differ in how they are affected by parasitism. Here, we investigate how parasitism and environmental conditions interact to affect the development of nestling European shags, Phalacrocorax aristotelis, a species with a pronounced brood hierarchy in which last-hatched chicks have higher mortality rates. We treated broods of three chicks with an anti-parasite drug across four years of variable success and measured nestlings' growth rate and behaviour in the nest. The growth of last-hatched siblings was more heavily impacted by parasitism than that of older siblings. Environmental conditions were also important, with a greater difference between siblings in less productive years. Treatment also affected the behaviour of last-hatched chicks more than that of older siblings. This suggests that the impact of parasites for individual development could be modulated by intra-brood conflict dynamics. Parasitism interacts with other external stresses in different ways for different brood members, with potential consequences for their contribution to future generations.

In vitro comparison of the effect of flavonoids in anthelmintic resistant and susceptible isolates of Haemonchus contortus: preliminary results (P90)

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Gastro-intestinal nematodes (GIN) are responsible for production losses in grazing sheep and goats. Until recent years, control of GIN relied on mass treatment with anthelmintics. Such practice has selected for GIN populations resistant to (multiple) anthelmintic classes, leading in some cases to the impossibility of drenching animals and thus jeopardizing breeding. Further, the reduction of drenching applied to small ruminants will meet social expectations of an environment friendly farming, producing both healthy and safe animal products. Some plants are known to

exert an anthelmintic effect. Even if precise ways of action remain unknown, bioactive principles responsible for anthelmintic activity seem to be plant secondary metabolites like condensed tannins. These compounds belong to the flavonoid group and are responsible of major effect on GIN both in vitro and in vivo. It has been demonstrated that some flavonoids could act on several species of small ruminants GIN, namely Trichostrongylus colubriformis and Haemonchus contortus. However, no tests have been performed on isolates showing different sensitivity toward anthelmintic classes. We measured the effect of five flavonoids against two H.contortus isolates, being either susceptible or resistant to every anthelmintic class, by an in vitro larval exsheathment test. Rutine and quercetin inhibited the exsheathment process in an unequivocal fashion in both isolates ($p<0.01$). Kaempferol was active against the resistant isolates ($p<0.05$) whereas the same trend was observed for the susceptible isolates ($p=0.18$). Our results suggest some condensed tannins may control H. contortus isolates in a fashion independent from the GIN resistance status.

Whole genome assembly from a clinical sample in an unusual case of human cerebral sparganosis (P91)

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Sparganosis is a rare parasitic infection found predominantly in Asia. It is caused by the plerocercoid larval form of cestodes from the order Pseudophyllidea. A patient presented in East Anglia with a range of neurological symptoms and a radiologically migrating lesion was observed. A formalin-fixed paraffin-embedded biopsy sample from the patient was morphologically identified as sparganum. Genomic DNA was extracted and PCR/Sanger sequencing of the cox1 gene refined the species identification to Spirometra erinaceieuropaei, an important distinction from the proliferative Sparganum proliferum, which has a poorer prognosis. Mitochondrial cytochrome oxidase and NADH dehydrogenase genes matched sequences previously reported from China, consistent with the suspected geographical origin of infection. Paired-end 450 bp fragment Illumina libraries were generated for sequencing from 12.5 ng gDNA. The genome was assembled using Velvet, and scaffolded using SSPACE. The fragmented genome will undergo further iterations and improvements with a 3-kb library generated via whole genome amplification. Previously molecular information regarding Spirometra erinaceieuropaei has been limited to the mitochondrial genome. We have built a de novo genome assembly from a clinical specimen, which will allow comparative analysis to other cestode species and hence will be useful in determining the most appropriate treatment strategies in such cases.

Parasites and Pathologies of the European Eel Anguilla anguilla. (P92)

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The European eel, Anguilla anguilla, hosts a diverse range of parasites throughout its geographical range. It is increasingly recognised that some parasites can adversely affect the fitness, survival and reproductive capacity of eels. Much attention has been given to the swim bladder nematode Anguillicoloides crassus, but relatively little is known about the impact, distribution and importance of other infections in the wild. There has also been limited study on parasites in early life stages of eels. The results of parasitological examinations and health investigations in wild UK eels, conducted between 2008 and 2013, are presented. Descriptions of gross and histopathological changes associated with the parasites Anguillicoloides crassus, Pseudodactylogyrus spp., Pomphorynchus laevis, Acanthocephalus anguillae, Daniconema anguillae, Myxidium giardi, Myxobolus portucalensis, Ergasilus gibbus, and Dermocystidium anguillae are described and evaluated. Additional attention is given to disease outbreaks caused by the bacterial pathogens Aeromonas hydrophila, Vibrio anguillarum and the virus Herpesvirus anguillae. The importance of these infections is discussed in relation to the health of individual eels and the wider management of this threatened species.

The Ascetosporea in crustacean hosts (P93)

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The class Ascetosporea, phylum Cercozoa (Cavalier-Smith 2002) is comprised of two important, but understudied invertebrate pathogen orders, the Haplosporida (including the genera Haplosporidium, Minchinia, Urosporidium and Bonamia), and the Paramyxida (containing Marteilia, Paramarteilia and Paramyxa). Haplosporida infect invertebrate hosts from marine and freshwater habitats. Certain species within the representative genera are considered important pathogens of commercially harvested molluscs. Previously, my laboratory described an asporous haplosporidian-like parasite infecting the common shore crab (Carcinus maenas) from the European shoreline. Later, extraction of genomic DNA from the haemolymph, gill or hepatopancreas of infected C. maenas was carried out and the small subunit ribosomal DNA (SSU rDNA) of the pathogen was amplified by PCR before cloning and sequencing. Infected crabs yielded an identical 1736bp parasite sequence. BLAST analysis against the NCBI GenBank database identified the sequence as most similar to the protistan pathogen group comprising the order Haplosporida. Parsimony analysis placed the crab pathogen within the genus Haplosporidium, sister to the molluscan parasites H. montforti, H. pickfordi and H. lusitanicum. The parasite

infecting C. maenas was therefore named Haplosporidium littoralis n. sp. In this presentation, I will place the confirmation of a haplosporidian parasite infecting decapod crustaceans from the European shoreline in to context with knowledge of other haplosporidians infecting molluscan hosts, and with members of the order Paramyxida infecting molluscs, crustaceans and polychaetes. In addition, recent evidence of diversity from eDNA surveys revealing the under-representation of the Ascetosporea within public genetic databases is discussed.

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STUDENT PRIZES VOTING FORM

BEST ORAL PRESENTATION

Student name

Presentation title

Session number

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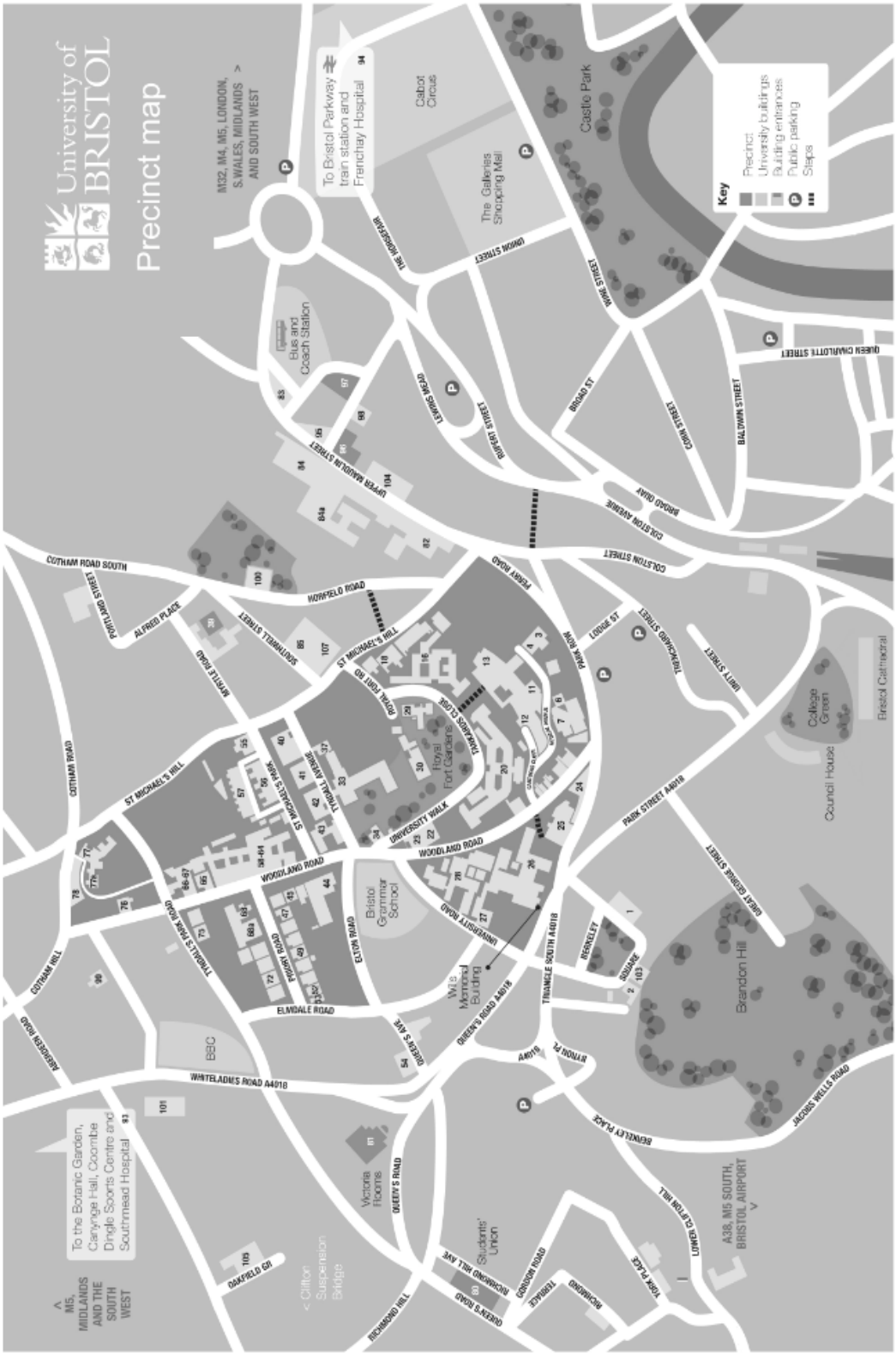
Poster number

Map

The main meeting venue is the Wills Memorial Building – building 26.
The Plenary session and AGM are in the School of Chemistry – building 13.
The Conference dinner is just off the map, below Bristol Cathedral.



Meeting programme - bsp.uk.net

Your guide to Bristol - bsp2013.info