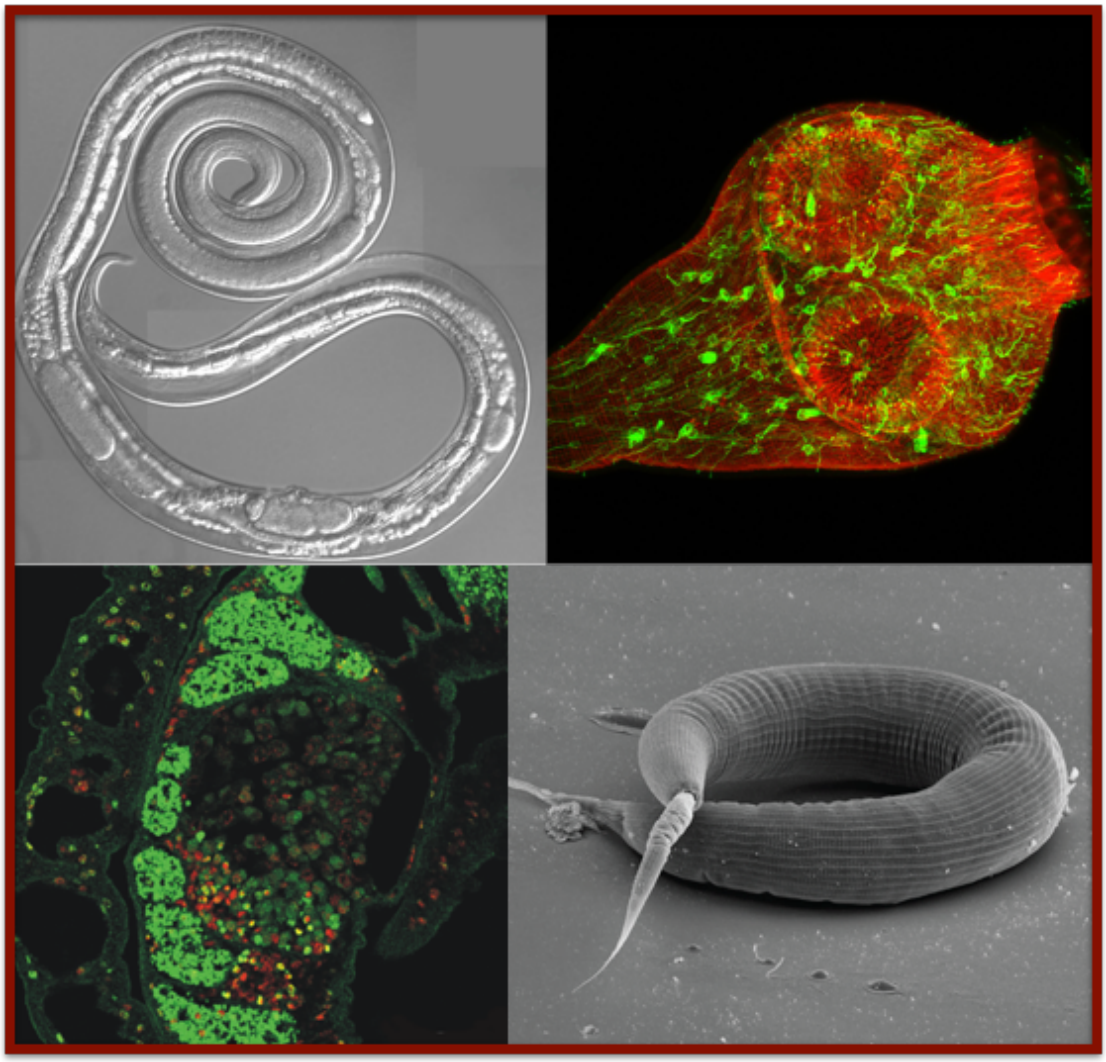
Molecular and Cellular Biology of Helminths X



4 - 9 September 2016

Bratsera Hotel, Hydra, Greece

MOLECULAR AND CELLULAR BIOLOGY OF HELMINTH PARASITES

I. 6-9 September 1997, Edinburgh, UK
'Parasitic Helminths from Genomes to Vaccines'

II. 8-11 July 1999, Edinburgh, UK
'Parasitic Helminths from Genomes to Vaccines II'

III. 14-19 September 2002, Hydra, Greece
'Molecular and Cellular Biology of Helminth Parasites III'
Special Issue of *International Journal of Parasitology* **33 (11):** 1127-1302

IV. 6-11 September 2005, Hydra, Greece
'Molecular and Cellular Biology of Helminth Parasites IV'
Special Issue of *International Journal of Parasitology* **36 (6):** 615-733

V. 12-17 September 2008, Hydra, Greece
'Molecular and Cellular Biology of Helminth Parasites V'

VI. 5-10 September 2010, Hydra, Greece
'Molecular and Cellular Biology of Helminth Parasites VI'
Special Issue of *Experimental Parasitology* **132** (1) : 1-102

VII 2-7 September 2012, Hydra, Greece
'Molecular and Cellular Biology of Helminth Parasites VII'

VIII 1-6 September 2014, Hydra Greece
'Molecular and Cellular Biology of Helminth Parasites VIII'

XI 31 August – 5 September 2015, Hydra Greece
'Molecular and Cellular Biology of Helminth Parasites IX'

Dates of MCBHP-XI Meeting: 3-9 September 2017

ORGANISERS, 2016
Richard E Davis (University of Colorado, School of Medicine, USA)
Kleoniki Gounaris (Imperial College, UK)
Rick Maizels (University of Glasgow, UK)
Edward J Pearce (Max Planck Institute & University of Freiburg, Germany)
Murray Selkirk (Imperial College, UK)

ADMINISTRATION FOR 2016
Jennifer Hurst
Centre for Immunity, Infection and Evolution & Edinburgh Infectious Diseases
Ashworth Laboratories, Charlotte Auerback Road, University of Edinburgh, Edinburgh, EH9 3FL
Tel: (+44) 131 651 3688, E-mail: jennifer.hurst@ed.ac.uk

Cover photos : **Top Left**, *Strongyloides stercoralis* parasitic female - *image from James B Lok, University of Pennsylvania*; **Top Right,** *Echinococcus multilocularis* protoscolex stained for muscle (red) and nephridia (green)- *image from Uriel Koziol in laboratory of Klaus Brehm, University of Würzburg;* **Bottom Left**, *Schistosoma mansoni* ovary stained for apoptotic cells following treatment with ILK kinase inhibitor - *image from Christoph Grevelding, University of Giessen.* **Bottom Right**, Predation by *Pristionchus pacificu*s, feeding on a larva of *C. elegans* - *image from Ralf Sommer. Max-Planck-Institute, Tübingen.*

	Sunday 4 September	Monday 5 September	Tuesday 6 September	Wednesday 7 September	Thursday 8 September	Friday 9 September
	ARRIVE	Session 1 Lives Of Helminth	Session 4 New Strategies For Drugs	Session 7 Parasitism	Session 10 Parasite Regulatory Molecules	DEPART
09:00		Richard Davis	**Erik Andersen**	**Phil LoVerde**	Ed Pearce	
09:20		Warwick Grant			Ron Hokke	
09:40		Adrian Streit	Nicole Liachko	Mark Blaxter	Sasisekhar Bennuru	
10:00		Christoph Grunau	Robin Beech	John Parkinson	Karl Hoffmann	
10:20		Klaus Brehm	Jim Collins	David Bird	Peter Nejsum	
10:40-11:10	Coffee break					
		Session 2 New Tools For Helminths	Session 5 Innate Immunity	Session 8 Host Parasite Interaction	Session 11 Host Parasite Interface	
11:10		Paul Brindley	Bart Everts	Emily White	Alex Loukas	
11:30		James Lok	William Horsnell	Daniel Price	Javier Sotillo	
11:50		Jianbin Wang	Michael Povelones	Hermelijn Smits	Spencer Gang	
12:10		Wormbase Workshop Bruce Bolt	Irma van Die	Susanna Fleurkens	Jaap Van Hellemond	
12:30			Katherine Smith	Wiebke Hartmann	Bruno Guigas	
12:50-4:30	Afternoon break					
		Session 3 Induction & Impact Of Type 2 Responses	Session 6 Development	Session 9 Helminthic Therapy	Session 12 Adaptive Immunity	
4:30	Registration Opens at Bratsera Hotel	**Tom Nutman**	**Sophie Jarriault**	**P'ng Loke**	**David Vöhringer**	
4:50						
5:10		Graham LeGros	Andy Fraser	John Croese	Clarissa da Costa	
5:30		Poster Pitches, 20 x 2 minutes	Celine Cosseau	Poster Pitches 19 x 2 minutes	Cristin Bock	
5:50			Christoph Grevelding		Bill Harnett	
		6:10 Break/End of Sessions				
6:30	Pre-lecture drinks	Poster Session 1		Poster Session 2		
7:30	Keynote Lecture: Ralf Sommer		Vlychos Taverna Dinner (Boat leaves 7:00 PM)		Bratsera Farewell Dinner (8:30 PM)	
8:30	Welcome Reception	End of Session		End of Session		

NOTES

Sunday 4 September

Chair: **Rick Maizels**, University of Glasgow	
19:30	Keynote Lecture: **Ralf Sommer**, *Max Planck Institute for Developmental Biology* **How important are novel and fast evolving genes for your nematode? A case study in *Pristionchus*.**
20:30	**Welcome Reception and Dinner, Bratsera Hotel**

Monday 5 September

09:00 - 10:40 Session 1: Lives Of Helminths

Chair: **Murray Selkirk**, Imperial College London		
09:00	**Richard Davis,** *University of Colorado School of Medicine*	*Ascaris*: Resources, Attributes, and Experimental Tools
09:20	**Warick Grant,** *La Trobe University*	Genetic analysis by GWAS of the facultative switch between free-living and parasitic life in *Parastrongyloides trichosuri*
09:40	**Adrian Streit,** *Max Planck Institute for Developmental Biology*	Making daughters only - the reproductive organ in free-living *Strongyloides* spp. (nematoda)
10:00	**Christoph Grunau,** *University of Perpignan Via Domitia*	Epigenetic bases of infection success in the human blood-fluke *Schistosoma mansoni*
10:20	**Klaus Brehm,** *University of Wuerzburg*	How to turn an embryo into a cancerous monster: the *Echinococcus* case

11:10 – 12:50 Session 2: New Tools For Helminths

Chair : **Anna Protasio,** *Gurdon Institute, University of Cambridge*		
11:10	**Paul Brindley,** *George Washington University*	Genome editing with CRISPR/Cas9 for functional genomics of schistosomes
11:30	**James Lok,** *University of Pennsylvania*	Insertional mutagenesis in *Strongyloides stercoralis* via CRISPR/Cas9
11:50	**Jianbin Wang,** *University of Colorado School of Medicine*	Genome analysis of programmed DNA elimination in nematodes
12:10 – 12:50	**Wormbase Workshop** with Bruce Bolt and Kevin Howe	

16:30 - 18:10 Session 3: Induction & Impact Of Type 2 Responses

Chair : **Clarissa da Costa,** *Technische Universität München*		
16:30	**Tom Nutman,** *National Institutes of Health, Bethesda*	Chronic filarial (and other helminth) infection imposes bystander controls on the responses to the *Mycobacterium tuberculosis* in human co-infections
17:10	**Graham LeGros,** *Malaghan Institute for Medical Research*	Diversity of Th2 subtypes in helminth infection and their involvement in immunity
17:30	**Pitches for Poster Session 1**	

<u>Monday 5 September</u> - 17:30-18:10 (2 min poster presentations, 1 slide each)

Chair: **Niki Gounaris,** Imperial College London			
1	**Jennifer Auret**	University of Cape Town	Helminth-virus co-infection reveals enhanced control of respiratory syncytial virus infection in mice
2	**Allison Bancroft**	University of Manchester	Vaccination using the Major Excreted Secreted Protein of *Trichuris muris*
3	**Rita Berkachy**	Imperial College London	Functional characterisation of *Heligmosomoides polygyrus* secreted apyrases
4	**Alisha Chetty**	University of Cape Town	Influence of *Nippostrongylus brasiliensis* infection on subsequent murid gammaherpesvirus infection
5	**Benjamin Dewals**	University of Liege	Helminth-driven type 2 inflammation enhances CD8+ T cell-mediated control of acute gammaherpesvirus infection
6	**Aifang Du**	Zhejiang University	Structural and functional characterization of a novel gene, Hc-daf-22, from the strongylid nematode *H. contortus*
7	**Maria Duque Correa**	Sanger Institute	Exploring host intestinal epithelia (goblet cell) - whipworm early interactions
8	**Kathy Geyer**	Aberystwyth University	SmMBD2/3 and its interaction partner SmCBX help maintain proliferating somatic cells (PSCs) in schistosomes
9	**Catherine Gordon**	QIMR Berghofer Medical Research Institute	Real-time polymerase chain reaction-based diagnosis of *Schistosoma japonicum* infections in areas of China with low levels of schistosomiasis transmission
10	**Melissa Govender**	University of Cape Town	Specific targeting of IL-4Rα signalling on keratinocytes does not affect experimental murine Schistosomiasis
11	**Alessandra Guidi**	CNR (National Research Council)	Discovery and characterization of novel anti-schistosomal properties of perhexiline and its impact on *Schistosoma mansoni* male and female reproductive systems
12	**Steffen Hahnel**	Justus-Liebig University Giessen	The potential neuropeptide receptor SmNPYR1 is pairing-dependently expressed in the testis of adult *Schistosoma mansoni* males and involved in spermatogenesis
13	**Shannon Hedtke**	La Trobe University	Insights on sub-optimal drug response from whole genome sequencing of populations of the filarial nematode *Onchocerca volvulus*
14	**Kevin Howe**	EMBL European Bioinformatics Inst.	Curation, analysis and display of helminth genomic data by WormBase ParaSite
15	**Min Hu**	Huazhong Agricultural Univ.	Genetic analysis of β-tubulin isotype-1 gene of *Haemonchus contortus* populations from small ruminants in China
16	**Anna Kildemoes**	University of Copenhagan	Host immunopathology outcomes in response to alteration of gut microbial composition and *Schistosoma mansoni* infection in a murine model
17	**Marije Kuipers**	Leiden University Medical Center	Immune modulation by *Schistosoma mansoni* released extracellular vesicles
18	**Dominik Laetsch**	University of Edinburgh	Analysing patterns of gene family evolution within the phylum Nematoda
19	**Eva Loffredo Verde**	Technical University of Münich	The interaction of hepatitis B or C virus infection and *Schistosomiasis* in chronic pathogen-induced liver inflammation
20	**Zhigang Lu**	Justus-Liebig University Giessen	Gonad-specific and pairing-dependent gene expression in *Schistosoma mansoni*

18:30-20:30 Poster Session 1 and Drinks, Bratsera Hotel Courtyard

Tuesday 6 September

09:00 - 10:40 Session 4: New Strategies For Drugs

Chair: **Alex Loukas,** *James Cook University*		
09:00	**Erik Andersen,** *Northwestern University, Illinois*	Discovery of anthelmintic resistance mechanisms using *C. elegans* natural diversity
09:40	**Nicole Liachko**, *Veterans Affairs Puget Sound Health Care System*	Screening in *Caenorhabditis elegans* identifies three novel anthelmintic compounds capable of rapid clinical repurposing
10:00	**Robin Beech,** *McGill University*	Structural organization of the nematode levamisole sensitive acetylcholine receptor
10:20	**Jim Collins,** *UT Southwestern Medical Center*	Functional genomic studies to identify novel therapeutic targets against *Schistosoma mansoni*

11:10 – 12:50 Session 5: Innate Immunity

Chair: **Richard Grencis,** *University of Manchester*		
11:10	**Bart Everts**, *Leiden University Medical Center*	*Schistosoma* egg antigens prime dendritic cells for Th2 polarization via a prostaglandin E2-dependent mechanism
11:30	**William Horsnell,** University of Cape Town	Regulation of immunity to helminths by surfactant protein D
11:50	**Michael Povelones,** University of Pennsylvania	Activation of *Aedes aegypti* mosquito immune signaling reduces infection by heartworm *Dirofilaria immitis*
12:10	**Irma Van Die,** *VU University Medical Center*	*Trichuris suis* dampens pro-inflammatory immune responses by modulation of monocyte-to-macrophage differentiation via an epigenetic mechanism
12:30	**Katherine Smith,** *Cardiff University & University of Cape Town*	Systemic alterations to innate immunity by the gastrointestinal nematode *H. polygyrus*

16:30 – 18:10 Session 6: Development

Chair: **Dick Davis,** *University of Colorado School of Medicine*		
16:30	**Sophie Jarriault,** *IGBMC Strasbourg*	How can cells change their identity? *C. elegans* as a model to understand the nuts and bolts of transdifferentiation
17:10	**Andy Fraser,** University of Toronto	Dissection of the Rhodoquinone synthesis pathway in *C.elegans*
17:30	**Celine Cosseau,** *Université de Perpignan*	Dosage compensation status in *Schistosoma mansoni*: from global to gene specific compensation during the sex differentiating development.
17:50	**Christoph Grevelding,** *Justus Liebig University Giessen*	Integrin/SmVKR 1 signaling pathway cooperation in the ovary of *Schistosoma mansoni* females

Wednesday 7 September

09:00 - 10:40 Session 7: Parasitism

Chair: **Lorna Proudfoot,** *Edinburgh Napier University*		
09:00	**Phil LoVerde** *University of Texas*	*Schistosoma sp.* Genetic basis of drug resistance, drug mode of action and drug discovery
09:40	**Mark Blaxter** *University of Edinburgh*	The hidden history of *Wolbachia* coevolution with nematodes
10:00	**John Parkinson,** *Hospital of Sick Children, Toronto*	Metabolic reconstruction and constraints based modeling reveal the *Wolbachia* endosymbiot of *Onchocerca* volvulus provides significant pathway redundancy
10:20	**David Bird,** *NC State University*	Population engineering: Can a Gene Drive reduce reproduction of *Meloidogyne hapla* to below economic relevance.

11:10- 12:50 Session 8: Host Parasite Interaction

Chair: **Mark Viney,** *University of Bristol*		
11:10	**Emily White,** *University of Manchester*	Infection by the gastrointestinal nematode *Trichuris muris*: Defining the microbiota of the pathogen and the host
11:30	**Daniel Price,** *Moredun Research Center*	Niche-specific expression of immunomodulators by the parasitic nematode *Teladorsagia circumcincta*
11:50	**Hermelijn Smits,** *Leiden University Medical Center*	Molecular characterization of helminth antigens and pathways leading to splenic Breg cell development
12:10	**Susanna Fleurkens,** *ETH Zurich*	Carbohydrate-based vaccines against *Haemonchus contortus*
12:30	**Wiebke Hartmann,** *Bernhard Nocht Institute for Tropical Medicine*	Filariae-retrovirus coinfection in mice is associated with suppressed virus-specific IgG immune response and higher viral loads

16:30 – 18:10 Session 9: Helminthic Therapy

Chair: **Irma van Die,** *VU University Medical Center*		
16:30	**P'ng Loke,** *New York University*	Interactions between helminth colonization and the gut microbiota
17:10	**John Croese,** James Cook University	The background, structure and translational implications of an RCT testing *Necator americanus* and escalating gluten exposure in Coeliac Disease
17:30	**Pitches for Poster Session 2**	

Wednesday 7 September

17:30-18:10 **(2 min poster presentations, 1 slide each)**

Chair: **Niki Gounaris,** Imperial College London			
21	**Mary MacLean**	University of Georgia	In vivo effects of drugs used in lymphatic filariasis MDA programs on *Brugia malayi* in gerbils
22	**Francesca Martini**	Malcisbo AG, ETH Zürich	Glyco-conjugate vaccine against the dog's heartworm *Dirofilaria immitis*
23	**Karen McCulloch**	La Trobe University	Incorporation of population genetic parameters into spatial models for the transmission of Onchocerciasis.
24	**Laura Myhill**	University of Copenhagen	The effect of dietary prebiotics on immune function and helminth infection.
25	**Gyaviira Nkurunungi**	MRC (Uganda Unit) & LSHTM	Assessing glycan-specific IgE profiles associated with *S. mansoni* infection and allergy in Uganda
26	**Christian Owusu**	Wellcome Trust Sanger Institute	Exploring the role of leukotrienes in the immunopathology of schistosomiasis
27	**Anna Protasio**	Gurdon Institute, University of Cambridge	MiRNAs miR-277/novel255 regulate transcriptional landscape during juvenile to adult transition in *Schistosoma mansoni*
28	**Lorna Proudfoot**	Edinburgh Napier University	Development of mitochondria- and protease-specific prodrugs in the potential treatment of parasitic helminth infections
29	**Thomas Quack**	Justus-Liebig University Giessen	Current progresses on isolating and culturing of cells from *Schistosoma mansoni*
30	**Gabriel Rinaldi**	Wellcome Trust Sanger Institute	Schistosome infection modulates the intestinal microbiome
31	**Franca Ronchese**	Malaghan Institute, New Zealand	Transcriptional diversity of dendritic cells during the priming of Th2 immune responses in vivo
32	**Julia Schulz**	University Clinic Bonn	Murine miRNAs that post-transcriptionally regulate the TLR- and NLR-mediated signaling pathways are up-regulated in BALB/c mice but down-regulated in C57BL/6 mice during *Litomosoides sigmodontis* infection
33	**Linda Schönfeld**	EUROIMMUN AG	Usage of recombinant antigens improves sensitivity and allows species differentiation in echinococcosis diagnostics
34	**Christian Schwartz**	Trinity College Dublin	ILC2-T cell crosstalk during helminth infection
35	**Mark Viney**	University of Bristol	*C. elegans* pheromone induces reproductive plasticity
36	**Dongying Wang**	Guangxi University	Excretory secretory products (ESP) from *Fasciola gigantica* induce an M2 macrophage-like phenotype in vivo
37	**Phurpa Wangchuk**	James Cook University	Metabolic profiling and anti-colitic properties of hookworm small molecule extracts
38	**Shona Wilson**	University of Cambridge	Naturally occurring regulation of human IgE-mediated hypersensitivity by hookworm infection
39	**Ya-Yi Michelle Yang**	Leiden University Medical Center	Dynamics of anti-glycan antibody responses in *Schistosoma japonicum*-infected rhesus macaques studied by schistosome glycan microarray

Thursday 8 September

09:00 - 10:40 Session 10: Parasite Regulatory Molecules

Chair: **Hermelijn Smits,** *Leiden University Medical Center*		
09:00	**Ed Pearce,** *Max Planck institute & Univeristy of Freiburg*	Metabolic regulation of alternative macrophage activation
09:20	**Ron Hokke**, Leiden University Medical Center	Developmental expression of schistosome glycan motifs implicated in parasite-host biology
09:40	**Sasisekhar Bennuru,** *NIAID/NIH*	Comprehensive transcriptome and proteome analyses define stage-specific processes and novel biomarkers in the filarial parasite *Onchocerca volvulus*
10:00	**Karl Hoffmann,** *Aberystwyth University*	*Schistosoma mansoni* extracellular vesicles contain a rich collection of host regulatory biomolecules.
10:20	**Peter Nejsum,** *University of Copenhagen*	Identification and characterization of extracellular vesicles in parasitic nematodes of pigs

11:10 – 12:50 Session 11: Host Parasite Interface

Chair: **Wiebke Hartmann,** *Bernhard Nocht Institute for Tropical Medicine*		
11:10	**Alex Loukas,** *James Cook University*	Worm secretions and cancer
11:30	**Javier Sotillo,** *James Cook University*	Extracellular vesicles from trematodes: purification methods and roles in host-parasite interactions
11:50	**Spencer Gang**, *University of California Los Angeles*	Host-seeking and infection strategies of parasitic nematodes
12:10	**Jaap Van Hellemond**, *Erasmus University Medical Center*	Haemostatic changes occur in vivo already in the early non-hepatosplenic, phase of schistosomiasis.
12:30	**Bruno Guigas,** *Leiden University Medical Center*	The schistosome-derived glycoprotein omega-1 inhibits gluconeogenesis by a dual glycan- and RNAse-mediated mechanism in primary mouse hepatocytes

16:30 – 18:10 Session 12: Adaptive Immunity

Chair: **Ed Pearce,** Max Planck Institute & University of Freiburg		
16:30	**David Vöhringer,** *University Clinic Erlangen*	Adaptive immunity license basophils for protection against gastrointestinal helminths
17:10	**Clarissa Prazeres da Costa,** *Technische Universität München*	Chronic helminth infection during pregnancy epigenetically reprograms T cell differentiation
17:30	**Cristin Bock,** *Freie Universität Berlin*	Th2/Th1 hybrid cells: A multifunctional subset with different characteristics in nematode infected humans and mice
17:50	**Bill Harnett,** *University of Strathclyde*	Therapeutic potential of novel sulfone compounds based on the anti-inflammatory phosphorylcholine moiety of the the secreted *Acanthocheilonema viteae* glycoprotein, ES-62

20:30	**Farewell Banquet, Bratsera Hotel**

ABSTRACTS

KEYNOTE LECTURE

How important are novel and fast evolving genes for your nematode? A case study in Pristionchus.

RALF SOMMER

MAX PLANCK INSTITUTE FOR DEVELOPMENTAL BIOLOGY, TÜBINGEN, GERMANY

Genome sequencing projects have revolutionized biology and together with functional tools, such as RNA interference and gene knockout by CRISPR/Cas9, allow novel insight into non-model organisms including parasites of human, livestock and agricultural plants. One unexpected finding from genome sequencing projects over the last decade is that essentially all organisms harbor a large number of genes that are not conserved over larger evolutionary distances. Basically, two distinct evolutionary mechanisms can be responsible for such taxonomically restricted genes, often called “orphan” genes. First, such genes might evolve rapidly, for example under the influence of positive selection, resulting in the (near) absence of sequence homology between distantly related taxa. Second, such genes might also evolve *de novo*. Indeed, recent studies in molecular evolutionary biology provide evidence for *de novo* gene evolution. Considering that orphan genes are present in all parasitic genomes, it is an important question, if such orphan genes are of functional importance for biology and for the functional understanding of the organisms, i.e. its parasitic life style.

I will provide insight from the nematode *Pristionchus pacificus* that we have established as model system in evolutionary biology to integrate developmental biology and other laboratory approaches with fieldwork in ecology and population genetics. *P. pacificus* lives in association with scarab beetles. One key feature of its life style is a mouth-form dimorphism that enables predatory feeding. The development of teeth-like denticles of two different forms represents an example of developmental plasticity and we test the hypothesis that developmental plasticity is a facilitator of phenotypic diversification and the evolution of novelty. Similarly, we study the regulation of dauer development, another example of phenotypic plasticity. By studying the regulation of plastic traits in *P. pacificus* by forward and reverse genetic tools and genome-wide association stuides, we made the surprising finding that taxonomically restricted orphan genes seem to be functionally overrepresented. I will provide several case studies to highlight this finding. Therefore, orphan genes seem to play key roles in the interaction of the organism with the environment. I will argue that similar patterns might be the rule in parasites as well, as parasitism is essentially the interaction of the parasite with the host “environment”. Thus, functional approaches that aim to elucidate the role of orphan genes are most likely inevitable for a thorough analysis of animal parasitism.

Ascaris: Resources, Attributes, and Experimental Tools

RICHARD DAVIS

UNIVERSITY OF COLORADO SCHOOL OF MEDICINE, USA

Ascaris is an important parasite of humans and pigs. *Ascaris* is estimated to infect ~1 billion people leading to significant morbidity, particularly in young children where infections are associated with retardation in physical and cognitive development. Since the late 19th century, *Ascaris spp.* have been used as an experimental system to address a variety of biological, cellular, and molecular questions. *Ascaris spp.* were used by Boveri to describe the chromosome cycle, centrosomes, and programmed DNA elimination (also known as chromatin diminution), while in the same period, van Beneden described meiosis in *Ascaris spp.*. During the early part of the 20th century, *Ascaris spp.* were used in a variety of biochemical studies on energy metabolism as well as neuroanatomy studies. These studies have continued to this day. In recent years, extracts from the *Ascaris* germline and particularly the early embryo have been used to carry out in vitro studies on RNA transcription, mRNA splicing, mRNA translation, and mRNA decay. While most of these studies used *Ascaris* extracts to address mechanistic aspects of spliced leader trans-splicing, these extracts are likely to be useful for a variety of other biochemical studies. Methods for transfection into early embryos have also been developed and used and several studies have used RNAi approaches in A*scaris*. More recently, comprehensive *Ascaris* genome and transcriptome (mRNA and non-coding RNA) resources have been developed enabling comprehensive molecular and cellular studies in *Ascaris*. For example, a renaissance of studies on programmed DNA elimination have recently been carried out on *Ascaris.* The large size of *Ascaris*, its enormous reproductive output, and other biological attributes also make *Ascaris* a unique model for studies on nematodes. In this presentation, the resources, attributes, and tools, of *Ascaris* as a model for studies on parasitic nematodes will be described and discussed.

Genetic analysis by GWAS of the facultative switch between free-living and parasitic life in _Parastrongyloides trichosuri_

SHILPA KAPOOR[1], STEPHEN DOYLE[1,2], SHANNON HEDTKE[1] & **WARWICK GRANT[1]**

[1]ANIMAL PLANT & SOIL SCIENCES, AGRIBIO, LA TROBE UNIVERSITY, AUSTRALIA; [2]WELLCOME TRUST SANGER INSTITUE, CAMBRIDGE, UK

Parastrongyloides trichosuri is a facultative parasitic nematode in the *Strongyloides* clade, capable of indefinite free-living culture provided low population density and abundant food are maintained. We have shown previously that the switch between the free living and parasitic life cycles is triggered primarily in response to an environmental cue analogous to dauer pheromone in *Caenorhabditis elegans* and that there is considerable heritable variation in the sensitivity to the cue, such that selection of high and low responsive inbred lines is possible. We have now identified candidate genes under selection in high and low response parasites by genome re-sequencing of pools of worms selected at the extreme ends of the life-cycle switch distribution. These candidates encode proteins that are likely to play a role in pheromone reception and neuronal transmission from sensory neurones. “Dauer” genes identified in mutational screens in *C. elegans*, such as insulin signalling pathway genes, are notable by their absence from this candidate list. Selection imposed on naturally-occurring genetic variation in this important life-history trait has therefore revealed novel genes that are genetically variable and “visible” to selection in natural populations of a facultative parasite. We hypothesise that these genes mediate plasticity in the choice between parasitism and free-living life histories and are therefore relevant to the evolution of parasitism in this clade. This work is, to our knowledge, the first detailed genetic analysis of naturally-occurring variation in a complex life history trait in a parasitic nematode and demonstrates the utility of the *Strongyloides* as models for investigation of the genetic basis of parasitic life history evolution.

Making daughters only – the reproductive organ in free-living *Strongyloides spp*. (nematoda)

ARPITA KULKARNI, ANJA HOLZ, CHRISTIAN RÖDELSPERGER, DOROTHEE HARBECKE, JAMES W. LIGHTFOOT, **ADRIAN STREIT**

MAX PLANCK INSTITUTE FOR DEVELOPMENTAL BIOLOGY, TÜBINGEN, GERMANY

Strongyloides spp. are intestinal parasites of vertebrates including man. They alternate between parthenogenetic parasitic and facultative free-living sexual generations. The latter produce only female parasitic progeny. Although the free-living *Strongyloides* spp. superficially resemble the model nematode *C. elegans*, there are dramatic differences between them. Combining light and electron microscopy, immunohistochemistry and quantitative DNA and RNA sequencing we characterized the germ line of free-living *S. ratti* and compared it with the germ lines of other nematodes of various phylogenetic distance. We particularly focused on two features, which have puzzled investigators for several generations. First we characterized a population of non-dividing giant nuclei with a very high DNA content in the distal gonad. In *C. elegans* this regions is populated by mitotically dividing germline stem cells and early meiotic cells. We found that the chromatin of these giant nuclei is rich in histone modifications normally associated with high transcriptional activity and that in these nuclei autosomes are present in higher copy numbers than X chromosomes. Consistently, autosomal genes are expressed at higher levels than X chromosomal ones. This suggests that these worms use differential chromatin amplification for controlling gene expression. Second, we addressed the lack of males in the progeny of the free-living generation. We found that male determining (nullo-X) sperm are present in the sister taxon *P. trichosuri*, which produces male progeny and absent in *S. papillosus*, which does not. Surprisingly, nullo-X sperm and very young embryos with a male karyotype appear to be present in *S. ratti*, even though this species does not produce any surviving male progeny. Interestingly, also the patterns of some histone modifications in spermatogenic cells differ between these three species. These findings suggest that different species of *Strongyloides* employ various strategies to prevent the formation of males in the progeny of the free-living generation.

Epigenetic bases of infection success in the human blood-fluke *Schistosoma mansoni*

SARA FNEICH[1,2,4], ANDRÉ THÉRON[1], CÉLINE COSSEAU[1,2], ANNE ROGNON[1,2], BENOIT ALIAGA[1,2], JÉRÔME BUARD[3], DAVID DUVAL[1,2], NATHALIE ARANCIBIA[1,2], JÉRÔME BOISSIER[1,2], GUILLAUME MITTA[1,2] & **CHRISTOPH GRUNAU[1,2]**

[1]UNIVERSITÉ DE PERPIGNAN, PERPIGNAN, FRANCE; [2]CNRS – IHPE, PERPIGNAN, FRANCE; [3]CNRS- IGH, MONTPELLIER, FRANCE; [4]UMR BDR, INRA, ENVA, UNIVERSITÉ PARIS SACLAY, FRANCE

In all parasites in which the underlying mechanisms were sufficiently well analyzed, there is evidence that development and infection success is based on a complex interplay of genetic determinants and epigenetic regulations. Our laboratory has shown that the platyhelminth *Schistosoma mansoni,* agent of intestinal bilharzia, is no exception to this rule and that genome-wide histone modification profiles change in a developmental stage specific way. The human seeking larvae of *S. mansoni* develop in an intermediate snail host (*Biomphalaria sp.*). Interestingly, even in endemic areas where more than 90% of the human population can be infected, no more than 5% of snails carry the parasite. The interaction between parasite and the mollusk is characterized by a compatibility polymorphism *i.e.* some strains of the parasite can infect a references snail strain (they are compatible) and other cannot (incompatible). The principal molecular marker for compatibility (infection success) of the parasite is the expression pattern of a group of polymorphic mucins (*Sm*PoMuc). Using pedigree studies and chromatin structure profiling, we show here that histone modification changes at the *Sm*PoMuc promoters are the cause for *Sm*PoMuc transcription polymorphism leading to phenotypic novelty and increase in infection success *i.e.* fitness. We establish that epigenetic changes can be the major if not only cause of adaptive phenotypic variants in *S. mansoni*, suggesting that epimutations can provide material for adaptive evolution in the absence of genetic variation in this parasitic flatworm.

How to turn an embryo into a cancerous monster; the *Echinococcus* case

URIEL KOZIOL[1,2], RAPHAEL DUVOISIN[1], FRANCESCA JARERO[3], PETER OLSON[3] & **KLAUS BREHM[1]**

[1]INSTITUTE OF HYGIENE AND MICROBIOLOGY, UNIVERSITY OF WÜRZBURG, GERMANY; [2]UNIVERSIDAD DE LA REPUBLICA, MONTEVIDEO, URUGUAY; [3]NATURAL HISTORY MUSEUM, LONDON, UK

Larval development of *Echinococcus multilocularis* is unusual in so far as its invading oncosphere does not directly develop into a head-like structure (scolex), as in most tapeworms, but into a continuously growing, cancer-like mass of vesicles (the metacestode) which infiltrates host tissue. Contrasting to the oncosphere and the scolex, the cyst-like metacestode does not display clear body axes, so we hypothesized that modifications of the anterior-posterior (AP) axis might be an underlying principle for metacestode evolution. In free-living planarians, the AP axis is specified by the canonical Wnt pathway, where Wnt signaling defines the posterior and expression of Wnt antagonists (e.g. sFRP) the anterior pole. Using the *Hymenolepis* model, we show that this also applies to tapeworm oncospheres where Wnt orthologs are expressed posteriorly (close to the hooks) and sFRP orthologs anteriorly. In the *E. multilocularis* metacestode, we found ubiquitous expression of posterior Wnt factors which, as in planarians, were produced by muscle cells, thus explaining the retention of a muscle layer in the immotile cysts. Only in later stages of the infection, Wnt antagonists were locally expressed in metacestode tissue, which preceded the formation of protoscoleces. This indicates that *E. multilocularis* larvae temporarily give up their anterior pole to exclusively proliferate as posterior tissue, followed by local expression of sFRP to achieve protoscolex production (asexual multiplication). According to our data, canonical Wnt signaling plays a crucial role in metacestode development and, accordingly, RNA-interference against the central Wnt component beta-catenin resulted in metacestode tissue disorganization and prevented the formation of vesicles from parasite stem cells. Interestingly, aberrant regulation of Wnt signaling is also observed in many human cancers, pointing to similarities of malignant transformation of human tissue and metacestode formation. Finally, our data also settle a long-standing dispute concerning the true polarity of the AP axis in cestodes.

Genome editing with CRISPR/Cas9 for functional genomics of schistosomes

CHRISTINA J. COCHRAN[1], VICTORIA H. MANN[1], ARNON D. JURBERG[2], WANNAPORN ITTIPRASERT[1], GABRIEL RINALDI[3] & **PAUL J. BRINDLEY[1]**

[1]GEORGE WASHINGTON UNIVERSITY, USA; [2]FIOCRUZ RIO DE JANEIRO, BRAZIL, [3]WELLCOME TRUST SANGER INSTITUTE, HINXTON, UK

The *Streptococcus pyogenes* Type II CRISPR system is the keystone of the CRSIPR revolution. The system centers on a programmable endonuclease that catalyzes a double stranded break (DSB) in target DNA. The system is active in human, mouse, zebra fish, fruit fly, malarial parasite and yeast and non-model species. It has revolutionized experimental genome editing, and portends hitherto unparalleled advances and positive prospects for gene therapy, biomedicine, and biological systems at large. Adaption and adoption of CRISPR technology for editing the genome of schistosomes and other parasitic platyhelminths would be desirable. Here we targeted the IPSE gene of *Schistosoma mansoni* for 'knockout' - deletion mutation in the coding region of the gene. First, using a double reporter plasmid system, NIH 3T3 fibroblasts were transfected with pX330-IPSE1 and pRGS-tgt-IPSE1. By FACS, ~9% cells were RFP+ve, GFP+ve, indicating cleavage of exon 1 of SmIPSE gene (within pRGS-tgt-IPSE1). Second, *in vitro* incubation of pRGS-tgt-SmIPSE1 with a complex of guide RNA (gRNA) and Cas9 linearized the plasmid, presumably the consequence of a directed DSB catalyzed by Cas9. Third, cultured schistosomula were transfected using square wave electroportation with Cas9 of *S. pyogenes* complexed with gRNA matching residues 22 - 44 of exon 1 of the IPSE gene. Indels were evident by two hours later, detected by quantitative PCR, in ~13% of the cells of the parasites. The Type II Cas9 System is active in schistosomes.

Insertional mutagenesis in *Strongyloides* stercoralis via CRISPR/Cas9

JAMES LOK, HONGGUANG SHAO, HOLMAN MASSEY, JR., XINSHE LI

DEPARTMENT OF PATHOLOGY, SCHOOL OF VETERINARY MEDICINE, UNIVERSITY OF PENNSYLVANIA, USA

The search for new interventions against parasitic nematodes is hampered by the lack of robust methods to study gene function. Their ability to undertake generations of free-living development makes parasites in the genera *Strongyloides* and *Parastrongyloides* more tractable in this regard. Transgenesis has been achieved in both these genera, opening the possibility of using the Cas9 endonuclease guided by short RNAs based on clustered regularly interspaced short palindromic repeats (CRISPR) as a means of gene disruption and editing. We have now achieved specific gene mutation in *S. stercoralis* via CRISPR/Cas9. We selected *Ss-daf-16* as a target in this exploratory study. This gene encodes an insulin-regulated FOXO transcription factor homologous to the dauer regulatory factor DAF-16 in *C. elegans*. We employed CRISPR/Cas9 to insert a 24 bp oligonucleotide, containing stop codons in all reading frames, into exon-5 of *Ss-daf-16*, which is expressed in all message isoforms, presumably creating a null mutation. Our method involved transforming free-living female worms with plasmids encoding the Cas9 endonuclease, the insert with homology arms for 50 bp regions flanking the expected double stranded break (DSB) in the target, and guide RNAs specific for the primary target in *Ss-daf-16* and for flanking targets in the insert donor plasmid, the latter serving to excise the insert with homology arms designed to mediate homology directed repair. To confirm insertion, we used a novel priming site within the insert in nested PCR with three reverse priming sites in the 5' flanking region of the target. Secondary and tertiary reactions yielded products of the expected size (380 and 140 bp) in two independent experiments. Sequencing these products revealed the oligonucleotide inserted precisely at the DSB flanked 5' by predicted stretches of *Ss-daf-16* genomic sequence. This result demonstrates the potential for gene editing and disruption in *S. stercoralis* via CRISPR/Cas9.

Genome analysis of programmed DNA elimination in nematodes

JIANBIN WANG[1], YULIA MOSTOVOY[2], MARTIN K. NEILSON[3], YONGQIAO SUN[4], YUANYUAN KANG[1], LAURA K. WHITE[1], BING ZHANG[4], SONGNIAN HU[4], PUI-YAN KWOK[2], RICHARD E.DAVIS[1]

[1]BIOCHEMISTRY & MOLECULAR GENETICS, UNIVERSITY OF COLORADO SCHOOL OF MEDICINE, USA; [2]CARDIOVASCULAR RESEARCH INSTITUTE, UCSF SCHOOL OF MEDICINE, CA, USA; [3]GLUCK EQUINE RESEARCH CENTER, UNIVERSITY OF KENTUCKY, LEXINGTON, KY, USA; [4]BEIJING INSTITUTE OF GENOMICS, CHINESE ACADEMY OF SCIENCES, BEIJING, CHINA

Maintenance of genome integrity is essential. However, programmed DNA elimination removes specific DNA sequences from the genome during early development. In the human and pig parasitic nematode *Ascaris,* we found that ~13% of the genome is eliminated during DNA elimination. The eliminated DNA consists of specific repetitive and unique sequences, including ~700 genes. The eliminated genes are primarily expressed in the germline, suggesting that DNA elimination in *Ascaris* is an irreversible mechanism for silencing a subset of germline-expressed genes in somatic tissues. We identified ~50 sites where chromosomes break and are healed by telomere addition. A closely related horse parasitic nematode *Parascaris* also undergoes DNA elimination. The majority of the DNA breaks and eliminated genes are conserved between *Ascaris* and *Parascaris*, suggesting a regulated and specific mechanism for DNA elimination in these nematodes. Intriguingly, we found no sequence motifs or other characteristics that might mark the conserved breakpoint regions for chromosomal breakage. We hypothesize that (1) histone modifications, (2) small RNAs, (3) chromosome structure and organization, and/or (4) DNA replication timing may be involved in the identification and generation of chromosomal breaks for DNA elimination. To facilitate a better understanding of DNA elimination, we are building chromosomal level genome assemblies using PacBio long reads and BioNano optical maps. A chromosomal level comparison between these nematodes will not only provide information on DNA elimination and the consequent re-organization of the chromosomes, but will also allow us to determine if DNA elimination serves to generate a specific set of somatic chromosomes (1n = ~36) from drastically different numbers of germline chromosomes (1n = 1 vs. 24) in the two nematodes. We will also describe the updated genome resources for both *Ascaris* and *Parascaris*.

Chronic filarial (and other helminth) infection imposes bystander controls on the reponses to the *Mycobacterium tuberculosis* in human co-infections

THOMAS B. NUTMAN, SUBASH BABU & SOUMYA CHATTERJEE

LABORATORY OF PARASITIC DISEASES, NIAID, NIH, BETHESDA, MD, USA

Examination of the effects of helminth infections on diseases that range from atopy and autoimmunity to other infectious diseases (e.g. HIV, tuberculosis, malaria) have prompted interest not only in the mechanisms involved in the bystander regulation by helminths of ongoing non-helminth antigen-specific immune responses but also in the potential secondary effect (both positive and negative) of these helminth infections on the clinical outcome of non-helminth infectious diseases. While helminth infections (relatively early in infection) induce a predominant Th2-associated immune response, with longstanding infection these (and Th1- and Th17-associated responses) are modulated largely through adaptive Treg production of IL-10. Because the immune response to the intracellular *Mycobacterium tuberculosis* (Mtb) is characterized by a predominant Th1/Th17 response, in areas of helminth/Mtb co-endemicity, the responses induced by the extracellular helminths and those induced by the Mtb are often mutually antagonistic and, as a consequence, can result in impaired (or cross-regulated) host responses to either of the infecting pathogens. Thus, we will discuss the nature of the immune responses induced by infections with helminths and Mtb and provide data from both experimental models and human studies that illustrate how the immune response engendered by helminth parasites modulates Mtb-specific responses in helminth/Mtb co-infection and discuss some of the potential underlying mechanisms involved in this cross-regulation.

Diversity of Th2 subtypes in helminth infection and their involvement in immunity

RYAN KYLE, MELANIE PROUT, FRANCA RONCHESE & **GRAHAM LE GROS**

MALAGHAN INSTITUTE OF MEDICAL RESEARCH, WELLINGTON, NEW ZEALAND

The induction and activation of Type 2 immune responses is a characteristic feature of infection by helminths. We use IL4/IL-13 dual reporter mice to follow the various immune cell subtypes induced by parasites that contribute to a Type 2 response in the lymph node and skin and lung. We identify that there are quite different activation requirements for the development of IL4 and IL-13 Th2 subsets in tissues vs lymph nodes and we discuss the implications of these findings in the context of protective immunity to helminths and reactions associated with allergic diseases.

Discovery of anthelmintic resistance mechanisms using *C.elegans* natural diveristy

ERIK C. ANDERSEN

NORTHWESTERN UNIVERSITY, ILLINOIS, USA

Many neglected tropical diseases (NTD) are caused by parasitic nematodes. Within the last twenty years, a massive campaign to administer anthelmintic drugs was performed. Unfortunately, few anthelmintic classes exist and resistance is growing rapidly, prompting an urgent need to identify resistance genes. In addition, nematode-borne diseases of livestock and plants are major agricultural problems, resulting in severe economic losses. Effective future treatments of parasitic nematode infections require knowledge of which genetic variants cause resistance to a particular drug. In order to identify conserved nematode drug responses, we use two model roundworms, *Caenorhabditis elegans* and *Caenorhabditis briggsae*, and a new massively scaled quantitative phenotyping pipeline to measure population variation and perform statistical mapping procedures. Our platform utilizes automated robotic devices to rapidly and accurately measure fitness traits, such as offspring production, growth rate, and muscle behaviors for hundreds of individuals in parallel. We mapped drug resistance to ten of the most prescribed anthelmintic compounds. I will present our results on resistance to benzimidazole (BZ) and macrocyclic lactone (ML) class compounds. Resistance to ML compounds is more complex than previously appreciated with over five different genomic regions implicated. I will discuss our progress on cloning the resistance genes in one interval. Surprisingly, we found that resistance to the BZ compounds mapped to regions of the genome with few protein-coding genes in both *Caenorhabditis* species. We re-sequenced and re-analyzed the genomes of the two species to facilitate an interspecies comparison that identified an abundant class of small RNAs encoded by genes in the conserved regions. These small RNAs could lead to heritable trans-generational resistance to anthelmintic compounds in parasitic roundworms.

Screening on *Caenorhabditis elegans* identifies three novel anthelmintic compounds capable of rapid clinical repurposing

NICOLE F. LIACHKO[1,2], ALEEN SAXTON[1], KRISTIN J. ROBINSON[3], CAITLYN LEASURE[4], BRIAN M. SUZUKI[5], WILLIAM M. ROBERTS[3], JANIS C. WEEKS[3], JOHN M. HAWDON[4], CONOR R. CAFFREY[5], THOMAS D. BIRD[1,2] & BRIAN C. KRAEMER[1,2]

[1]VETERANS AFFAIRS PUGET SOUND HEALTH CARE SYSTEM, SEATTLE, USA; [2]UNIVERSITY OF WASHINGTON, SEATTLE, USA; [3]UNIVERSITY OF OREGON, EUGENE, USA; [4]GEORGE WASHINGTON UNIVERSITY, WASHINGTON D.C, USA; [5]UNIVERSITY OF CALIFORNIA SAN DIEGO, LA JOLLA, USA

More than 1.5 billion people world-wide are estimated to be infected with parasitic nematodes, resulting in major economic and personal impacts from the years of life lost to poor health and premature mortality. The identification of drugs that can cheaply and effectively treat parasitic nematode infections is a critical global health need. However, the journey from initial drug development to approval for use in humans is long and costly, and screening directly on parasitic nematodes has intrinsic difficulties caused by the requirements for culturing and maintaining populations of parasites. It is likely that compounds that kill *C. elegans* will also kill parasitic nematodes, making *C. elegans* a cost-effective and rapid screening tool to identify new anthelmintics. To expedite the identification of drugs that can be rapidly translated into clinical use for parasite treatment, we have screened the NIH clinical collection (281 drugs approved for use in humans). This collection represent drugs with known safety, bioavailability, and dosage information that can be rapidly repurposed for treatment of parasitic nematode infections. From this screen, we identified three drugs that effectively kill *C. elegans* at multiple life stages. Two of these are used clinically as SSRI anti-depressants while the third drug is a dopamine receptor antagonist anti-psychotic. All three significantly affect hatching and development of *Ancylostoma caninum* hookworms, and are also active against *Schistosoma mansoni* somules. Using a microfluidics based electrophysiology device, we found that all three drugs rapidly inhibit *C. elegans* pharyngeal pumping. *C. elegans* mutants with resistance to known anthelmintic drugs such as ivermectin are equally or more susceptible to these three drugs, indicating these may represent new classes of anthelmintic drugs. Taken together, our results indicate *C. elegans* can provide a powerful powerful surrogate for large scale anti-nematode drug screening.

Structural organization of the *nematode levamisole* sensitive acetylcholine receptor

ROBIN BEECH[1,2], THOMAS DUGUET[1,2], CLAUDE CHARVET[3,4], CÉDRIC NEVEU[3,4]

[1]INSTITUTE OF PARASITOLOGY, MCGILL UNIVERSITY, CANADA; [2]CENTRE FOR HOST-PARASITE INTERACTIONS, QUEBEC, CANADA; [3]INRA, TOURS, FRANCE; [4]UNIVERSITY FRANCOIS RABELAIS DE TOURS, FRANCE

Acetylcholine is a neurotransmitter of major importance for animal life and is a primary target of the pharmaceutical industry. The nematode model, Caenorhabditis elegans, was originally developed to study all aspects of neurobiology, and its levamisole sensitive acetylcholine receptor (L-AChR) was the focus of the first general mutagenesis screen. Genetic analysis subsequently identified several ligand-gated ion-channel subunit genes and accessory proteins as essential components of the (L-AChR), which were verified experimentally in a landmark publication reporting reconstitution of the receptor in Xenopus oocytes. This has since sparked a resurgence of interest in the L-AChRs of parasitic nematodes and reconstitution of L-AChRs from *Ascaris suum*, *Oesophagostamum dentatum* and *Haemonchus* contortus have all been reported. In each case, receptor composition is surprisingly plastic, compared to the fixed composition in *C. elegans*. Understanding the mechanisms behind this phenomenon provides an understanding of receptor assembly in the nematodes and the ways in which evolutionary change can lead to the appearance of novel anthelmintic targets. We identified multiple, independent duplications of the *unc-29* L-AChR subunit throughout clade V nematodes, suggesting this receptor is inherently unstable in evolutionary terms. We were able to define the position of each subunit within the C. elegans L-AChR using expression of subunit concatamers in *Xenopus* oocytes. Using admixtures of C. elegans and H. contortus subunits we were able to show how species specific subunits replace one another and how evolutionary adaptation has led to structural rearrangements in the receptor. We identified specific functional incompatibilities between subunits, providing evidence for the mechanisms responsible for changing subunit composition. Taken together, we propose a model for nematode L-AChR assembly that is distinct from that observed in vertebrates. We highlight the consequences that this has for characterization of ion-channels in other parasitic nematodes.

Functional genomic studies to identify novel therapeutic targets against *Schistosoma mansoni*

JIPENG WANG[1], JULIE N.R. COLLINS[1], ALAN TRACEY[2], KAREN BROOKES[2], HELEN BEASLEY[2], MATT BERRIMAN[2] & **JAMES J. COLLINS III[1]**

DEPARTMENT OF PHAMACOLOGY, UT SOUTHWESTERN MEDICAL CENTER, DALLAS TX, USA; THE WELLCOME TRUST SANGER INSTITUTE, WELLCOME GENOME CAMPUS, HINXTON, CAMBRIDGE, UK

High-quality genome sequences are available for the three major schistosome species that infect humans. Unfortunately, we only know the function of a small handful of genes in these important parasites. To address this issue, we have established a pipeline to systematically characterize gene function in *Schistosoma mansoni* using a combination of high-throughput *in situ* hybridization and RNA interference. We have identified ~3000 genes to initially characterize in adult parasites including genes encoding putative therapeutic targets (enzymes, receptors, and channels) and hypothetical proteins. To date, we have examined several hundred of these genes by RNA interference and have identified novel phenotypes for ~10% of these genes including defects in survival, neuromuscular activity, and stem cell maintenance. We anticipate these approaches will set the framework for large-scale analyses of gene function in these worms and may lead to the identification of novel therapeutic targets to treat schistosome infection.

Schistosoma egg antigens prime dendritic cells for Th2 polarization via a prostaglandin E2-dependent mechanism

MARIA KAISAR[1], HULDA JÓNASDÓTTIR[2], MARTIN GIERA[2], MARIA YAZDANBAKHSH[1*], **BART EVERTS[1*]**

*LEIDEN UNIVERSITY MEDICAL CENTER, THE NETHERLANDS: [1]DEPT.PARASITOLOGY; [2]CENTER OF PROTEOMICS AND METABOLOMICS (*CONTRIBUTED EQUALLY)*

Helminth-derived molecules (HDMs) are well known for their ability to induce T helper 2 (Th2) polarization via functional modulation of Dendritic Cells (DCs). Yet the molecular mechanisms through which HDMs condition DCs for Th2 polarization are still incompletely understood. To this end, we used human monocyte-derived DCs that were stimulated with *Schistosoma* soluble egg antigen (SEA), a potent Th2-polarizing antigen mixture. We found that DCs stimulated with SEA rapidly produced Prostaglandin E2 (PGE2). This effect was not driven by omega-1, a major glycoprotein present in SEA known to prime Th2 responses, as omega-1 did not promote PGE2 synthesis and SEA from which omega-1 had been depleted (SEADw1) retained its ability to prime DCs for PGE2 synthesis. Importantly, neutralization of PGE2 during stimulation of DCs with SEADw1 abrogated their capacity to prime a Th2 response, while stimulation of DCs with exogenously added PGE2 was sufficient to recapitulate the Th2-priming effect of SEADw1. Mechanistically, we found PGE2 synthesis to be dependent on signalling via syk, suggesting a role for Dectin in this process. Moreover, SEA and PGE2 induced OX40L expression in these DCs, a costimulatory molecule that has been linked to priming of Th2 responses. In summary, we identified a novel pathway in DCs involving syk-PGE2-OX40L through which *Schistosoma* egg derived antigens induce Th2 responses. As this pathway appears to be distinct from the earlier described mode of action through which omega-1 primes Th2 responses, it highlights the complexity of mechanisms involved in Th2 polarization by helminths such as schistosomes. Currently, studies are underway to identify the molecules and/or molecular structures present in the schistosome eggs that drive the PGE2-dependent Th2 polarization.

Regulation of immunity to helminths by surfactant protein D

SUMAIYYA THAWER[1], JENNIFER AURET[1], CORINNA SCHNOELLER[3], KATHERINE SMITH[4], MURRAY SELKIRK[3], HOWARD CLARK[2], **WILLIAM HORSNELL[1]**

[1]INSTITUTE OF INFECTIOUS DISEASE AND MOLECULAR MEDICINE AND DIVISION OF IMMUNOLOGY, UNIVERSITY OF CAPE TOWN, SOUTH AFRICA; [2]CLINICAL & EXPERIMENTAL SCIENCES ACADEMIC UNIT, SOUTHAMPTON GENERAL HOSPITAL, SOUTHAMPTON, UK; [3]DEPT OF LIFE SCIENCES, IMPERIAL COLLEGE LONDON, LONDON, UK; [4]INSTITUTE OF INFECTION AND IMMUNITY, UNIVERSITY OF CARDIFF, CARDIFF, UK

Epithelial cell responses can drive the induction of type 2 immunity against nematode infections. An important epithelial product, especially in the lung, is the collectin Surfactant Protein D (SP-D). We have found that SP-D concentrations increase in the lung following *Nippostrongylus brasiliensis* infection and this increase was IL-4/13 and IL-4Ra dependent. Loss and gain of function studies established that SP-D was required for optimal immunity to the parasite. *N. brasiliensis* infection of SP-D-/- mice resulted in profound impairment of host innate immunity and ability to resolve infection. Raising pulmonary SP-D levels prior to infection enhanced parasite expulsion and type 2 immune responses, including increased numbers of IL-13 producing type 2 innate lymphoid cells (ILC2), elevated expression of markers of alternative activation by alveolar macrophages (alvM) and increased production of the type 2 cytokines IL-4 and IL-13. Adoptive transfer of alvM from SP-D-treated parasite infected mice into naïve recipients' enhanced immunity to *N. brasiliensis.* Protection associated with selective binding by the SP-D carbohydrate recognition domain (CRD) to L4 parasites to enhance their killing by alvM. These findings are the first demonstration that the collectin SP-D is an essential component of host innate immunity to helminthes. We suggest helminth induced SP-D may also contribute to parasite regulation of immune-pathologies caused by other diseases.

Activation of *Aedes aegypti* mosquito immune signalling reduces infection by heartworm *Dirofilaria immitis*

YUKWAH KWOK[1], BRITTANY WATSON[2], ELIZABETH M. FULLER[3], LETITIA K. THOMPSON[1], THOMAS J. NOLAN[1], JAMES B. LOK[1] & **MICHAEL POVELONES[1]**

DEPARTMENTS OF [1]PATHOBIOLOGY AND [2]CLINICAL STUDIES, UNIVERSITY OF PENNSYLVANIA SCHOOL OF VETERINARY MEDICINE, PHILADELPHIA, PA; [3]CHARLESTON ANIMAL SOCIETY, NORTH CHARLESTON, SC

Dirofilaria immitis is a canid-infecting nematode. The mosquito is essential for the *D. immitis* life cycle serving as both an intermediate host and vector. Transmission requires that ingested *D. immitis* microfilariae develop into infective L3 larvae over an approximately 2-week period. As it develops in the mosquito, *D. immitis* interacts with different tissues and immunological barriers. In this study, we address the role of immune signaling pathways in controlling infection using a *D. immitis* susceptible laboratory strain of *Aedes aegypti*. Previous studies have shown that the Toll and Imd pathways are important regulators of immune signaling in mosquitoes. Activation of these pathways protects *A. aegypti* from infection by various pathogens such as dengue virus and malaria parasites. Therefore, we hypothesized that activation of the Toll or Imd pathway may decrease *D. immitis* infection. To test this, we assayed *D. immitis* infection in mosquitoes following RNAi-mediated silencing of pathway-specific negative regulators. We found that Toll pathway activation led to a significant decrease in the prevalence of infection and in the median number of larvae as assayed at six days post infection. In contrast, Imd pathway activation led to a modest but significant increase in the number of larvae. Preliminary data from genome-wide transcriptomic analyses, as well as ongoing studies to address the role these pathways have in a *D. immitis* refractory strain of *A. aegypti* will be discussed. These data suggest that the mosquito immune system may influence susceptibility to heartworm infection and implicate targets of the Toll pathway in general immune defense against a variety of pathogens. These findings also raise the possibility of novel transmission blocking strategies targeting *D. immitis* in the mosquito vector.

Trichuris suis dampens pro-inflammatory immune responses by modulation of monocyte-to-macrophage differentiation via an epigenetic mechanism

IRMA VAN DIE[1], MARTEN HOEKSEMA[2], LISA LAAN[1], JULIETTE POSTMA[1], RICHARD D. CUMMINGS[3], CHRISTINE D. DIJKSTRA[1], MENNO P.J. DE WINTHER[2] & GIJS KOOIJ[1]

[1]DEPARTMENT OF MOLECULAR CELL BIOLOGY AND IMMUNOLOGY, VU UNIVERSITY MEDICAL CENTER, AMSTERDAM, THE NETHERLANDS; [2]DEPARTMENT OF MEDICAL BIOCHEMISTRY, ACADEMIC MEDICAL CENTER, AMSTERDAM, THE NETHERLANDS; [3]DEPARTMENT OF SURGERY, HARVARD MEDICAL SCHOOL, BOSTON, USA

Probiotic helminth administration of the porcine nematode *Trichuris suis* has immunomodulatory capacities that may be applied in the treatment of chronic inflammatory disorders, such as inflammatory bowel disease and multiple sclerosis (MS). We previously established that soluble compounds of *T. suis* (TsSP) have the potential to strongly ameliorate clinical parameters in a murine model for MS. In addition, we showed that these compounds have a direct effect on the human innate immune system by inducing a dendritic cell population with reduced pro-inflammatory properties and a Th2 skewing potential. In addition to dendritic cells, macrophages are essential players of the innate immune response. Macrophages display remarkable plasticity, which enables them to dynamically respond to their environment and acquire specialized functional phenotypes. These phenotypes can be viewed as a spectrum, with a cytotoxic, pro-inflammatory subset (M1) on one side and a regenerating, anti-inflammatory subset (M2) on the other side. In MS, M1 macrophages are essentially involved in myelin breakdown leading to nerve damage in patients, whereas M2 macrophages help to suppress inflammation and may have more neuroprotective properties. Our major hypothesis is that during chronic inflammation, and a concomitant administration of *T. suis*, monocytes encounter worm products in the circulation before they are recruited to tissue and differentiate into a monocyte-derived macrophage subset. Recently, we studied the effect of TsSP treatment on human monocytes, and on monocyte-to-macrophage differentiation and showed that TsSP treatment increases a subset of patrolling monocytes, and in addition generates naïve macrophages with enhanced anti-inflammatory (M2) properties. Furthermore, TsSP treatment profoundly dampens the induction of pro-inflammatory (M1) macrophages. Our data indicate that TsSP induce a long lasting effect in monocytes that drives macrophage skewing via epigenetic reprogramming of monocyte-to-macrophage differentiation. We here propose a distinct form of trained innate immunity in which no secondary microbial encounter is required.

Systemic alterations to innate immunity by the gastrointestinal *nematode H. polygyrus*

MARTYNA SCRIBIOREK[1], WILLIAM HORSNELL[2], **KATHERINE SMITH[2,3]**

[1]ERASMUS UNIVERSITY ROTTERDAM, HOLLAND; [2]INSTITUTE OF INFECTIOUS DISEASES AND MOLECULAR MEDICINE, UNIVERSITY OF CAPE TOWN, SOUTH AFRICA; [3]CARDIFF UNIVERSITY, UK

Gastrointestinal helminth infections can have a profound impact on the systemic immune system, modulating inflammatory disorders of the skin, respiratory tract and nervous system. Although some immune cell populations have been implicated in mediating this mucosal cross-talk, a current consensus on those mechanisms modulating disease is absent. In this work, we investigated the impact of gastrointestinal helminth infection with the mouse nematode *H. polygyrus* on lung inflammation following intranasal administration of the protease allergen papain. Our experiments indicated that *H. polygyrus* infection can protect against immune-mediated pathology in papain-treated mice. There were no differences in the signature inflammatory responses associated with papain treatment (IL-33 alarmin production and innate lymphoid cell induction) in the lung digest and bronchoalveolar lavage (BAL) of naïve or *H. polygyrus* infected mice, however, we found a predominance of granulocytes in cytospins of *H .polygyrus* infected tissues. Closer inspection of these cytospins revealed a population of ring-shaped granulocyes within the lung of *H. polygyrus* infected mice resembling granulocytic myeloid derived supressor cells (MDSCs). An increased proportion and number of MDSCs was confirmed in the lung of *H. polygyrus* infected mice by multi-parameter flow cytometry. This increase was apparent at earlier time points of infection, co-inciding with the presence of the helminth in the intestinal tissue. MDSCs are potent inhibitors of T cell proliferation and play an important role in regulating tissue inflammation, as well as in dampening anti-tumor responses. Systemic induction of this cell population folowing gastrointestinal helminth infection has important implications for the evolution of lung inflammatory disorders in endemic populations.

How can cells change their identity?

***C. elegans* as a model to understand the nuts and bolts of transdifferentiation**

SOPHIE JARRIAULT

IGBMC, STRASBOURG, FRANCE

Whereas postmitotic somatic cellular identity is generally a stable feature of multicellular organisms, natural interconversions between functionally distinct somatic cell types (aka transdifferentiation or Td) have been reported in species as diverse as jellyfish and mice. Direct reprogramming can also be induced experimentally, however at a very low frequency, and remains rare *in vivo*. Why do some cells but not their neighbours, change their identity and how in some cases, Td events occur with remarkable precision and efficiency. For example, our laboratory has shown that a rectal cell suddenly looses its differentiated identity and is reprogrammed into a motoneuron with invariant precision, in 100% of the wild type *Caenorhabditis elegans* animals. I will present how we have used this conversion, a defined, single cell, natural transdifferentiation event to investigate the cellular steps involved, the molecular mechanisms promoting this event and those ensuring its invariance, or how extrinsic cues and the intrinsic context impact on the ability of a cell to change its identity.

Dissection of the Rhodoquinone synthesis pathway in *C.elegans*

MARK SPENSLEY, DJINA PAJKIC, SAM DEL BORELLO, MARGOT LAUTENS, AMY CAUDY & **ANDREW FRASER**

THE DONNELLY CENTRE, UNIVERSITY OF TORONTO, CANADA

Most parasitic helminths (PHs) undergo major shifts in their metabolism following host infection. While PHs use standard aerobic metabolism during their free-living stages, many PHs live in hypoxic conditions in their host — to survive they use unusual metabolic pathways to make ATP. In particular they rely on malate dismutation and the reduction of fumarate — this needs a Ubiquinone derivative, Rhodoquinone (RQ). Humans do not make RQ and do not use fumarate reduction. The RQ pathway is thus a perfect drug target but (a) no commercial drugs exist that target RQ synthesis or malate dismutation and (b) the key enzymes required for RQ synthesis are unknown. One key difficulty in studying RQ synthesis is the lack of a tractable genetic system — one cannot study this in yeast/mammals since they lack this pathway. *C.elegans* however does make RQ and can use malate dismutation. I will present the work we have done to establish *C.elegans* as a powerful model for studying RQ synthesis and for identifying new drugs that target this pathway. So far we have identified a novel gene family that is likely to be required for RQ synthesis and we are characterizing these now. We showed *C.elegans* can survive inhibition of both aerobic respiration and glycolysis by using a fumarate-stimulated pathway. Finally, we established assays to screen for drugs that inhibit FR/RQ. These use a very high throughput drug screening methodology that we have developed that would be applicable to study of a wide range of helminths. Together, we think this has been significant progress in dissecting a pathway that is central to the ability of a wide variety of parasites to infect their human hosts. We'd love to talk to researchers working directly with parasites to understand how to take our results forward into parasites directly.

Dosage compensation status in *Schistosoma mansoni*: from global to gene specific compensation during the sex differentiating development

MARION PICARD, CHRISTOPH GRUNAU, DAVID ROQUIS, ANNE ROGNON, JÉRÔME BOISSIER, **CÉLINE COSSEAU**

UNIV. PERPIGNAN VIA DOMITIA, IHPE UMR 5244, CNRS, IFREMER, UNIV. MONTPELLIER, PERPIGNAN, FRANCE

Dosage compensation is a regulatory mechanism that adjusts the expressed dose of genes encoded on heteromorphic sex chromosomes. This mechanism aims at reducing the disparity of the dose of sex linked genes and autosomal genes that result from the sex difference in copy number of sex chromosome genes. Complete dosage compensation has been described in model species and is generally present in male-heterogametic systems whereas partial dosage compensation is met in female heterogametic species. Among more than 20,000 parasitic flatworms that are hermaphrodites, Schistosomatidae are intriguing because they are gonochoric. Sex of schistosomes is genetically determined by the presence of ZZ or ZW sex-chromosomes, respectively in males or in females. There is, however, (i) no phenotypic dimorphism between males and females in the larval stages: sexual dimorphism appears only in the vertebrate host, during the schistosomulum stage. (ii) There are apparently no female specific genes and the major part of the sex chromosomes is pseudoautosomal. This makes all evolutionary process linked to sex determination/differentiation pathway enigmatic. Using sex-specific RNA-Seq and ChIP-Seq data on different histone marks on larval stages, sex-differentiating stages (schistosomula) and adults, we show here that a change of the dosage compensation mechanism occurs during the development of the parasite: global compensation is observed in larvae, whereas gene specific compensation occurs during sex differentiating stages. ChIP-seq data further reveals that this change in the regulation of dosage compensation status is linked to different chromatin structures which happen between male and female but also, from larvae to adults. Altogether, these elements argue in favor of the epigenetic commitment to modulate gene dosage compensation during the parasite development and we hypothesize that this change in dosage compensation is necessary to trigger the sexual dimorphism in Schistosomes.

Integrin/SmVKR 1 signaling pathway cooperation in the ovary of *Schistosoma mansoni* females

CHRISTOPH G. GREVELDING[1], COLETTE DISSOUS[2], MARION MOREL[2], MATHIEU VANDERSTRAETE[2], KATIA CAILLIAU[3], VERENA GELMEDIN[1]

[1]BFS, INSTITUTE FOR PARASITOLOGY, JUSTUS-LIEBIG-UNIVERSITY GIESSEN, GERMANY; [2]UNIV. LILLE, CNRS, INSERM, CHU LILLE, INSTITUTE PASTEUR DE LILLE, LILLE, FRANCE; [3]UNIV. LILLE, CNRS, UMR 8576-UGSF, LILLE, FRANCE

Molecular studies in *S. mansoni* have provided evidence that signaling pathways control proliferation and differentiation of the female gonad following pairing. Next to cellular tyrosine kinases (CTKs) directly cooperating in one complex, upstream-interacting transmembrane receptor were identified such as the venus kinase receptor SmVKR1 and the beta-integrin receptor Smβ-Int1[5]. Results of yeast-two-hybrid and co-immunoprecipitation experiments have indicated the interaction of these molecules, which co-localize in the ovary. Knock-down approaches by specific inhibitors and/or RNAi demonstrated not only interaction of these molecules but also comparable phenotypes exhibiting their importance for gonad differentiation, especially in the ovary. Based on these findings and evidence from other biological systems we hypothesized that schistosome integrin receptors may cooperate with SmVKR1 as part of communication processes integrating environmental signals via different receptors to regulate complex operations inside the cell. To this end we cloned and characterized SmILK, SmPINCH, and SmNck2, three bridging molecules that were speculated to mediate Smβ-Int1/SmVKR1 cooperation. Besides colocalization of their transcripts in the schistosome ovary, all molecules were expressed in *Xenopus* oocytes. Here germinal vesicle breakdown (GVBD) was induced only if all members were expressed. Co-immunoprecipitation confirmed formation of a Smβ-Int1-SmILK-SmPINCH-SmNck2-SmVKR1 complex leading to SmVKR1 activation by phosphorylation in the absence of a ligand. RNAi and inhibitor studies to knock-down SmILK as a representative complex member concurrently revealed effects on the extracellular matrix surrounding the ovary and oocyte localization within the ovary, oocyte survival, and egg production. By TUNEL assays, confocal microscopy, and caspase-3 transcript profiling we finally obtained evidence for processes mediating cell death that occurred in immature and primary oocytes. These results suggest that SmVKR1 can be activated in a ligand-independent manner by integrin-receptor interaction, which could be important for the maintenance of the differentiation status of oocytes and their survival.

Schistosoma sp. Genetic basis of drug resistance, drug mode of action and drug discovery

STACEY R. STAHL[1], ALEXANDER B. TAYLOR[2], XIAOHANG CAO[2], P. JOHN HART[2], STANTON F. MCHARDY[3], AMBROSIO LOPEZ[3], FRÉDÉRIC D. CHEVALIER[4], TIMOTHY J. C. ANDERSON[4], **PHILIP T. LOVERDE[2]**

[1]DEPT. MICROBIOLOGY AND IMMUNOLOGY, UTHSCSA, SAN ANTONIO, TX 78226; [2]DEPT. BIOCHEMISTRY AND PATHOLOGY, UTHSCSA, SAN ANTONIO, TX 78226; [3]SOUTHWEST RESEARCH INSTITUTE, SAN ANTONIO TX 78266; [4]TEXAS BIOMEDICAL RESEARCH INSTITUTE, SAN ANTONIO, TX 78245

Human schistosomiasis is a disease caused by species of the genus *Schistosoma,* which globally affects over 260 million people. The major species affecting humans are *S. mansoni, S. haematobium,* and *S. japonicum.* There is currently only one method of treatment (monotherapy), the drug Praziquantel. Constant selection pressure through mass chemotherapy - this year alone will see the administration of over 250 million doses - has yielded evidence of resistance to PZQ. This has been observed in both the laboratory and field. The goal of this research is to develop a second drug for use in conjunction with PZQ**.** Previous treatment of *S. mansoni* included, among others, the use of oxamniquine (OXA), a prodrug that is enzymatically activated in *S. mansoni* but is ineffective against *S. haematobium* and *S. japonicum.* The OXA activating enzyme was identified, described, and crystallized by our laboratories as being a sulfotransferase (SmSULT). The focus of this research is to reengineer OXA to be effective against *S. haematobium* and *S. japonicum*. In this regard we isolated the *S. haematobium* (ShSULT) and *S. japonicum* (SjSULT) sulfotransferases. Over 130 OXA derivatives were synthesized, of which twelve showed schistosomicidal activity as good as or better than OXA that may potentially be used to treat schistosomiasis mansoni. *In vitro* tests demonstrated that some of these derivatives had activity against *S. haematobium* and *S. japonicum*. This iterative process of using structural data to inform chemical synthesis of derivatives, which are then tested *in vitro*, continues to provide us with novel compounds with improved anti-schistosomal activity. The information gleaned from these early studies will be used to optimize OXA derivative design. The most active derivatives will be used in an *in vivo* model of schistosomiasis to evaluate efficacy before moving to safety and toxicity studies.

The hidden history of _Wolbachia_ coevolution with _nematodes_

MARK BLAXTER & GEORGIOS KOUTSOVOULOS

IEB, UNIVERSITY OF EDINBURGH, EDINBURGH, EH9 3TF

Symbiotic interactions shape the diversity of the natural world. *Wolbachia* are common alphaproteobacterial endosymbionts of terrestrial arthropods and nematodes. In most arthropods, *Wolbachia* behave as reproductive parasites, while in nematodes they may be essential, mutualist symbionts that provide services to their hosts. The main group of nematode hosts, the vertebrate-parasitic Onchocercidae ("filarial nematodes") are important human and veterinary parasites, and antibiotic treatment (killing the nematodes *via* killing of their symbionts) is already used in clinical practice. The filarial nematodes harbour a range of different strains of *Wolbachia* that are classified into different supergroups. How these different supergroups invaded filarial nematode species, whether there was one primary infection or many independent ones, and whether there has been symbiont replacement in some nematode lineages remain open questions. Different symbionts are likely to have different relationships with their hosts, and understanding whether they are primary or replacement/secondary symbionts may impact treatment and control strategies. Using genomic data we have tracked the evolution of the association between *Wolbachia* and their nematode hosts. *Wolbachia* DNA is frequently laterally transferred into the host genome, and persists after the *Wolbachia* infection has been cleared. We have used these insertions to extend our study into the phylogenetic past to reveal the palaeobiology of extinct symbionts and the dynamics of symbiont acquisition and loss.

Metabolic reconstruction and constraints based modelling reveal the *Wolbachia* endosymbiot of *Onchocerca volvulus* provides significant pathway redundancy

NIRVANA NURSIMULU[1], ALEXANDRA GROTE[2], SARA LUSTIGMAN[3], ELODIE GHEDIN[2] & **JOHN PARKINSON[1]**

[1]HOSPITAL FOR SICK CHILDREN, UNIVERSITY OF TORONTO, TORONTO, CANADA; [2]NEW YORK UNIVERSITY, NEW YORK, USA; [3]NEW YORK BLOOD CENTRE, NEW YORK, USA

Constraints based modeling has emerged as a powerful route to interrogate the metabolic potential of pathogens and identify essential enzymes that may be targeted for therapeutic intervention. With the recent availability of genome sequences for the filarial nematodes *Onchocerca volvulus* and *Loa loa,* we performed metabolic reconstructions and constraints based modeling to examine their respective metabolic capabilities, as well as the contribution of the Wolbachia endosymbiont of *O. volvulus*. The resultant networks comprise 771 reactions, provided by 378 distinct enzymes for *O. volvulus* and 652 reactions provided by 301 distinct enzymes for *L. loa*. Most of the additional reactions present in the *O. volvulus* reconstruction (100 reactions) are contributed by Wolbachia, none of which are encoded in the genome of *L. loa* (which lacks Wolbachia). To identify essential reactions that might serve as candidates for therapeutic intervention, we performed Flux Balance Analysis (FBA) to investigate the impact of single reaction knockouts on parasite growth, the first for any nematode. For *O. volvulus*, only 71 reactions were predicted to be essential, with 70 of these also predicted to be essential for *L. loa*. For *L. loa*, 112 reactions were predicted to be essential. Many essential reactions are associated with nucleotide and lipid metabolism, energy production, biosynthesis of co-factors and transport. Unlike *Loa loa* which relies on a greater number of salvage pathways, *O. volvulus* benefits from Wolbachia contributions to fatty acid metabolism, heme synthesis, and purine and pyrimidine metabolism. For example, our model predicts that Wolbachia provides *O. volvulus* with IMP, a crucial precursor in purine metabolism, whereas *L. loa* depends exclusively on adenine import. This raises the exciting possibility of developing inhibitors of purine-nucleoside phosphorylase as a route to selectively target *O. volvulus* over *L. loa*.

Population engineering: Can a Gene Drive reduce reproduction of *Meloidogyne hapla* to below economic relevance?

DAVID BIRD

BIOINFORMATICS RESEARCH CENTER, AND DEPT. ENTOMOLOGY AND PLANT PATHOLOGY, NC STATE UNIVERSITY, RALEIGH NC 27695

Driven by the growing affluence of a growing human population, the demand for food will soon outstrip supply. Absent new farmlands, controlling pests is one of the few avenues open to increasing yield. Plant-parasitic nematodes (PPN) are the major source of biotic damage to staple and cash crops alike. They contribute to malnutrition in subsistence farming, and broadly diminish agricultural profitability; losses are estimated to approach $170 billion per year. Eliminating the major species of PPN would ameliorate this impact. To this end, we established *Meloidogyne hapla* as a robust platform for genetic, genomic and biochemical analysis. Based on natural field variation we have identified loci in the nematode able to regulate specific genes in the host. We have solved the structure of numerous signaling molecules, and have performed extensive molecular dynamic simulations to predict biological interactions. Using this information, we have begun to design a suite of CRISPR/Cas9-based, Gene Drive constructions to sweep genes into PPN populations. Our initial targets include genes in the sex determination pathway, with the objective of a masculinizing the wild population of *M. hapla*. We suspect this will present some challenges.

Infection by the gastrointestinal nematode *Trichuris muris*: Defining the microbiota of the pathogen and the host

EMILY WHITE, ASHLEY HOULDEN, ALLISON BANCROFT, KELLY HAYES, RICHARD GRENCIS, IAN ROBERTS

FACULTY OF LIFE SCIENCES, UNIVERSITY OF MANCHESTER, UK

Intestinal dwelling parasites live in close association with the complex microbiota that inhabit our intestinal tracts. The intestinal helminth, *Trichuris muris*, depends on these bacteria for egg hatching and successful establishment of infection within the epithelium of the caecum and colon. Infection induces significant dysbiosis in the host intestinal microbiota impacting on host health. However, the importance of the host microbiota for this pathogen and the role of its own intestinal microbiota is unknown. We found that *T. muris* requires its own diverse intestinal microbiota that is derived from, but distinct to, that of its host using 454 pyrosequencing of 16S rRNA gene amplicons. A core microbiota is selected and maintained by the parasite regardless of the surrounding host microbiota. The parasite microbiota is important for its fitness and is able to produce the short-chain fatty acid butyrate, which the parasite is unable to make itself yet secretes at high levels. Butyrate is important for maintaining intestinal homeostasis and has potent immunomodulatory effects, both of which would be beneficial to the parasite for reducing local inflammation in the host intestine. Furthermore, *T. muris* induced dysbiosis reduces egg hatching, therefore inhibiting further rounds of infection to control parasite numbers within the host intestine. Together these strategies promote the long term survival of *T. muris* within the intestinal niche, adding a new level of complexity to the interaction between the pathogen, the host and their respective microbiotas that underpins successful chronic nematode infection.

Niche-specific expression of immunomodulators by the parasitic nematode *Teladorsagia circumcincta*

DANIEL PRICE, ALASDAIR J. NISBET, DAVID FREW, STEWART T.G. BURGESS, HARRY WRIGHT, DAVE BARTLEY, YVONNE BARTLEY, TOM N. MCNEILLY

MOREDUN RESEARCH INSTITUTE, PENTLANDS SCIENCE PARK, BUSH LOAN, PENICUIK, MIDLOTHIAN, UK

The primary cause of parasitic gastroenteritis in small ruminants in temperate regions is the brown stomach worm, *Teladorsagia circumcincta*. This parasitic nematode has a direct life cycle, with sheep becoming infected by ingestion of third-stage larvae from pasture. These larvae invade gastric glands of the abomasum (which is analogous to the monogastric stomach) where they develop to fourth-stage larvae (L4); emerge from gastric pits as fifth-stage larvae; and finally complete their development to adult worms in the lumen. Host immunity to this parasite is slow to develop, consistent with the ability of *T.circumcincta* to suppress the host immune response. To better understand immune modulation, we focused on L4 worms, as they are most closely associated with host tissue and are targeted by the local host immune response. We demonstrate that within the abomasum there are two subpopulations of L4, those associated with the gastric glands ("mucosal larvae") and those either loosely associated with the mucosa or free-living in the lumen ("luminal larvae"). Comparative genomic and proteomic analyses of each sub-population identified a suite of genes and secreted proteins that are specific to each population. We hypothesized, based on the ability of *T.circumcincta* to modulate the host immune response, that excretory-secretory (ES) products of mucosal larvae contain immunomodulatory molecules. Here, using *in vitro* assays we demonstrate that mucosal larvae ES proteins, including a ShK-domain containing protein (TcK6) and a peroxiredoxin (TciPRX) have potential immunomodulatory properties. Specifically, we demonstrate that TcK6 inhibits cytokine production by T cells, and TciPRX is an antioxidant, with potential to modulate macrophage function. In conclusion, by comparing L4 niche-specific gene expression and protein secretion, coupled with *in vitro* assays we have identified *T.circumcincta* immunomodulatory proteins. Current work is underway to assess these proteins as vaccine candidates, with the aim of generating host antibodies that neutralize parasite immunomodulation.

Molecular characterization of helminth antigens and pathways leading to splenic Breg cell development

SIMONE HAEBERLEIN[1*], KATJA OBIEGLO[1*], ARIFA OZIR-FAZALALIKHAN[1], MATHILDE CHAYÉ[1], NICOLE N. DRIESSEN[1], ECATHERINA SAULOVA[2], GABRIELE SCHRAMM[3], MAX ARTIMOV[2], CORNELIS H. HOKKE[1], MARIA YAZDANBAKHSH[1] & **HERMELIJN H. SMITS[1]**

[1]DEPARTMENT OF PARASITOLOGY, LEIDEN UNIVERSITY MEDICAL CENTER. LEIDEN, THE NETHERLANDS; [2]DEPARTMENT OF PATHOLOGY & IMMUNOLOGY, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, ST LOUIS, USA; [3]RESEARCH CENTER BORSTEL, BORSTEL, GERMANY

Infection with the helminth *Schistosoma mansoni* drives the development of IL-10-producing regulatory B cells (Breg cells). Knowledge about the mechanisms of Breg induction allows the development of novel therapies against allergic disorders by enhancing Breg cell activity. Therefore, we investigated whether schistosomal egg antigens (SEA) directly interact with B cells and which pathways are involved in helminth-induced Breg development. Both intraperitoneal injections of (fluorescent) SEA in vivo and stimulation of B cells in vitro resulted in a significantly upregulated IL-10 and CD86 expression by marginal zone (MZ) B cells which was further enhanced by CD40-ligation. Importantly, SEA-induced Breg cells triggered Treg cell development in co-culture experiments in vitro. Among the major antigens in SEA, natural IPSE was capable of inducing IL-10 in naïve B cells, whereas omega-1 and kappa-5 had no effect. Interestingly, SEA depleted from IPSE still efficiently induced Breg cells, which indicates that other molecules are involved as well. To further elucidate which receptors and pathways are important for (the induction of) regulatory B cells in the context of helminth infections, we investigated the transcriptome profile of splenic MZ B cells during chronic S. mansoni infection (15wk) by RNAseq analysis. Differentially expressed genes were identified using the R/Bioconductor package DEseq2, and subjected to downstream analysis using Inguinity Pathway Analysis (IPA). MZ B cells show a highly distinct transcription profile, including the expression of several Breg cell-associated markers (e.g. Il10, Cd1d, Cd5). In response to infection, changes in genes encoding for e.g. proliferation, cytokines/cytokine-receptors, toll-like receptors (TLRs) and downstream signalling cascades, immunoglobulins, Fc-receptors and complement factors were found. We furthermore observed transcriptional differences in the cellular metabolism compartment. Currently, we are following up on the most interesting leads for subsequent validation and functional studies.

Carbohydrate-based vaccines against *Haemonchus contortus*

SUSANNA FLEURKENS[1,2], CHIA-WEI LIN[1], CHRISTINE NEUPERT[2], BRUNO OESCH[2], MARKUS AEBI[1]

[1]*INSTITUTE OF MICROBIOLOGY, ETH ZÜRICH, SWITZERLAND;* [2]*MALCISBO AG, SCHLIEREN, SWITZERLAND*

The development of a safe and effective vaccine offers a sustainable solution to the problem of increasing parasitic nematode drug resistance. For *Haemonchus contortus*, native extracts enriched for specific glycoproteins have shown to be highly protective, but recombinant forms do not induce protective immunity. This might be due to differences in glycosylation and/or conformation between native and recombinant proteins. Therefore, we have examined glycoengineered insect cells to test its suitability as an alternative system to produce known glycoprotein antigens carrying nematode-specific glycan structures. We focused on the *H. contortus* aminopeptidase H11 family, which is enriched in the protective native extract. All five isoforms share 65-76% amino acid identity and possess between 2 and 8 N-glycosylation sites. Sequencing analyses of the H11 isoforms amplified from cDNA of a Swiss field isolate revealed a polymorphism in the isoforms H11-1, H11-2 and H11-5, resulting in many different unique sequences with up to 7% amino acid replacements. In contrast, isoform H11-4 showed no polymorphism. Specific nucleotide mutations lead to the loss or gain of N-glycosylation sites. Most interestingly, the mutations were affecting exclusively amino acid residues on the surface of the protein when modeled on the crystal structure of the human aminopeptidase N (hCD13). Surfaces most exposed to the *H. contortus* gut lumen showed the most mutations, whereas few mutations were found on the surface directed towards the microvilli membrane. H11 isoforms were co-expressed in insect cells with the nematode-specific galactosyltransferase GALT-1. Analysis of site-specific N-glycosylation revealed differences in the site-specific N-glycosylation but confirmed nematode-specific glycan structures of the recombinant proteins. The high surface variability of the different H11 proteins observed in *Haemonchus* populations might explain the low levels of protection using recombinant variants of these proteins as vaccines.

Filariae-retrovirus coinfection in mice is associated with suppressed virus-specific IgG immune response and higher viral loads

KIRSTEN KATRIN DIETZE[1], ULF DITTMER[1], DANIEL KARIM KOUDAIMI[1], SIMONE SCHIMMER[1], MINKA BRELOER[1], **WIEBKE HARTMANN**[2]

[1]*INSTITUTE OF VIROLOGY, UNIVERSITY HOSPITAL ESSEN, UNIVERSITY OF DUISBURG-ESSEN, ESSEN, GERMANY;* [2]*BERNHARD NOCHT INSTITUTE FOR TROPICAL MEDICINE, HAMBURG, GERMANY*

Worldwide more than 2 billion people are infected with helminths. Coinfections with viruses are common due to the geographical overlap of these pathogens in developing countries. Helminths modulate the immune response of their hosts and induce a Th2-biased immune response while virus infections skew the immune response towards a proinflammatory type 1 immune response. To test whether helminths affect the outcome of a virus infection we set up a filarial/retrovirus coinfection model. C57BL/6 mice were first infected for 14 days with the filarial nematode *Litomosoides sigmodontis* and subsequently with the murine Friend retrovirus (FV). We monitored the course of FV infection at day 20 and day 35 post virus infection and analysed the virus-specific immune response. Control of FV was impaired in C57BL/6 mice that were infected with *Litomosoides sigmodontis* and superinfected with FV. Interestingly, neither numbers of FV-specific $CD8^+$ effector T cells nor their cytokine response or the induction of regulatory T cells were changed by concurrent *L. sigmodontis* infection. Increased viral loads in coinfected mice were rather associated with a reduced FV-specific neutralizing IgG2b/c response, suggesting that helminth infection interfered with the control of retrovirus infection by inhibiting the virus-specific antibody response.

Interactions between helminth colonization and the gut microbiota

P'NG LOKE

NEW YORK UNIVERSITY, NEW YORK, USA

Both helminths and the gut microbiota can exert powerful systemic immunoregulatory effects. Changes to the prevalence of helminth infections and the microbiota may be environmental factors contributing towards the "hygiene hypothesis" and the rising incidence of autoimmune diseases in developed nations. Dysbiosis (dysregulation of microbial communities) is a common feature of many human diseases, especially those with an inflammatory component. We have studied the effects of helminth colonization on the microbiota of indigenous Malaysians, called the "Orang Asli". Our preliminary results have identified an antagonistic relationship between microbial communities dominated by either Bacteroidales or Clostridiales communities. The expansion of Clostridiales over Bacteroidales communities can be driven by type 2 cytokines (IL-4 and IL-13), which promote increased mucus production by goblet cells. Mucus can directly promote the growth of human Clostridial strains. Using mouse models, we could demonstrate that a cocktail of Clostridial strains could directly inhibit a Bacteroides dominated community, even in the absence of helminth infections. We hypothesize that the expansion of Clostridiales communities by helminth colonization promotes anti-inflammatory responses within the host.

The background, structure and translational implications of an RCT testing *Necator americanus* and escalating gluten exposure in Coeliac Disease

JOHN CROESE, PAUL GIACOMIN AND ALEX LOUKAS

CENTRE FOR BIODISCOVERY AND MOLECULAR DEVELOPMENT OF THERAPEUTICS, AUSTRALIAN INSTITUTE OF TROPICAL HEALTH AND MEDICINE, JAMES COOK UNIVERSITY, QLD, AUSTRALIA

Coeliac disease (CeD) is a gluten-sensitive autoimmune enteropathy. A gluten-free diet is effective treatment, but compliance is demanding. Because human immunity is in part defined by co-evolution with helminths that must induce tolerance in the host to survive, we have investigated the therapeutic potential of both live infection with the human hookworm *Necator americanus* (Na) to improve gluten tolerance in people with CeD, and hookworm derived products to suppress autoimmune inflammation. This presentation focuses on the clinical application of live hookworm infection. In people with CeD once infected with Na, gluten stimulation promoted mucosal IFN-γ responsiveness, but IL-23 and IL-17A responses were suppressed, and IL-5 and TGF-β responsiveness developed. On the basis that this platform might promote gluten tolerance, we trialled an escalating gluten challenge in healthy participants with CeD. Two of twelve participants were withdrawn immediately after micro-challenge because of adverse responses to gluten. Thereafter, 10 completed a modest and sustained 12 week challenge designed to mimic twice weekly inadvertent exposures to gluten, after which mean quality of life and coeliac symptom index (CSI) scores remained unchanged. Histological indices did not deteriorate. Frequencies of intestinal intraepithelial T cells expressing IFN-γ were reduced and mucosal $Foxp3^+$ regulatory T cells increased. After a 12 week washout, 8 of 8 subjects completed a 2 week moderate gluten challenge equivalent to a small bowl of pasta daily during which CSI values and tissue transglutaminase titres progressively declined. Based on these remarkable outcomes, we have initiated a randomised multi-stage clinical trial designed to restore gluten tolerance through micro-challenge in the context of Na infection, then progressively increase gluten consumption to a level consistent with a liberal diet. The trial protocol will be described.

Metabolic regulation of alternative macrophage activation

EDWARD J. PEARCE

DEPARTMENT OF IMMUNOMETABOLISM, MAX PLANCK INSTITUTE OF IMMUNOBIOLOGY AND EPIGENETICS, AND FACULTY OF BIOLOGY, UNIVERSITY OF FREIBURG, FREIBURG, GERMANY

Changes in metabolism can be initiated in response to signals received from other cells. An example of this is provided by macrophages that have been stimulated by IL-4 to become alternatively/M2 activated. In these cells, lysosomal lipolysis of triacylglycerols to release fatty acids, and the oxidation of these fatty acids, are increased, and these processes are critical for M2 activation. Compared to resting macrophages, M2 macrophages also exhibit changes in glucose metabolism that we have found are essential for activation. In other cell types, mTORC2 has been linked to enhanced glycolysis. We have found that mTORC2 operates in parallel with the IL-4Ra/Stat6 pathway to facilitate increased glycolysis during M2 activation. Our data implicate signaling initiated by M-CSF, and involving PI3K, in the activation of mTORC2, and indicate that downstream of mTORC2 induction of IRF4 expression is critical for metabolic reprograming to support M2 activation. We show that loss of mTORC2 in macrophages decreases immunity to a parasitic nematode.

Developmental expression of schistome glycan motifs implicated in parasite-host biology

CORNELIS H. SMIT, D. LINH NGUYEN, MICHELLE Y. YANG, A. VAN DIEPEN, **CORNELIS H. HOKKE**

DEPARTMENT OF PARASITOLOGY, LEIDEN UNIVERSITY MEDICAL CENTER, LEIDEN, THE NETHERLANDS

During their entire life cycle, schistosomes express an abundance of proteins and lipids with complex specific glycosylation patterns. In the mammalian host antigenic glycans of larvae, worms and eggs induce specific antibodies to numerous glycan motifs, and glycans initiate or modulate innate immune responses and cellular uptake of glycoconjugates *via* host lectins. In the snail host specific miracidium and sporocyst glycans interact with glycan-binding proteins in the hemolymph determining aspects of snail-schistosome compatibility. To provide a clear map of schistosome glycosylation in support of functional studies of host-parasite glycobiology we applied a mass spectrometric glycomics approach to determine the expression profiles and structural identity of hundreds of glycans expressed in the schistosome life stages. Striking shifts and switches in the expression of glycan motifs during the maturation of the worm and the egg were identified. Subsequently, we have generated a microarray of hundreds of N-, O-, and lipid-glycans covering the entire glycome of *S. mansoni*. We have used this array to determine IgG and IgM to each glycan specifically in a number of human and animal infection cohorts, as well as to characterize anti-glycan monoclonal antibodies that were used to study the localization of various glycan antigens in and on the parasite during development. To cercarial glycans carrying unique Fucα1-2Fucα1-3GlcNAc motifs exposed at the surface of schistosomula, sustained antibodies are present in baboons that have successfully been vaccinated with irradiated cercariae of *S. mansoni*. In humans anti-glycan Abs are quite variable and dependent on multiple factors including age and infection intensity. The schistosome glycome will be discussed in view of the immunological and biological properties that have been attributed to schistosome glycans and glycans of other parasitic helminths.

Comprehensive transcriptive and preteome analyses define stage-specific processes and novel biomarkers in the filarial parasite *Onchocerca volvulus*

SASISEKHAR BENNURU[1], JAMES A. COTTON[2], ALEXANDRA GROTE[3], JOSE M.C. RIBEIRO[4], ELODIE GHEDIN[3,5], MATTHEW BERRIMAN[2], SARA LUSTIGMAN[6], THOMAS B. NUTMAN[1]

[1]LABORATORY OF PARASITIC DISEASES, NIAID, NIH, BETHESDA, MD, USA; [2]WELLCOME TRUST SANGER INSTITUTE, WELLCOME GENOME CAMPUS, CAMBRIDGE, UK; [3]CENTER FOR GENOMICS & SYSTEMS BIOLOGY, NEW YORK UNIVERSITY, NEW YORK, USA; [4]LABORATORY OF MALARIA & VECTOR CONTROL, NIAID, NIH, ROCKVILLE, MD, USA; [5]COLLEGE OF GLOBAL PUBLIC HEALTH, NEW YORK UNIVERSITY, NY, USA; [6]NEW YORK BLOOD CENTER, NEW YORK, NY, USA

Onchocerciasis ('river blindness') is a neglected tropical disease that has been targeted for control and elimination through mass drug administration (MDA) of ivermectin that ultimately interrupts transmission. Control of onchocerciasis has had considerable success in Africa. However, as efforts shifted from control to disease elimination better tools are needed to identify the presence of viable parasites that can be used in surveillance and for the certification to determine when the end game of post MDA is reached. To identify biomarkers of viable adult females and/or microfilariae (mf), we first compared the transcriptomes and proteomes of all of the major mammalian and vector stages of the *O. volvulus* (Ov) parasites (L1, L2, L3, molting L3, L4, adult males (AM), adult females (AF), nodular and skin mf. We have been able to identify 45 potential candidates based on their stage specific enrichment in OvAF (or mf). Using recombinant proteins or fusion constructs, and antibodies raised against them, we have developed several assay formats that have enable the detection of Ov-specific circulating antigens. Furthermore, using an "immunomics" approach, in which a subset of selected proteins (398) were gridded on protein arrays and screened for isotype-specific (IgG1, IgG3, IgG4, IgE) responses with infected and appropriate control sera, we identified heretofore-unrecognized novel diagnostic biomarkers (based on high IgG4 reactivity). To validate these biomarkers, we tested the corresponding fusion proteins of candidate biomarkers in a luciferase immunoprecipitation system (LIPS) that allowed for rapid identification of *O. volvulus*- (but not related filarial parasite-) specific targets of antibody reactivity. Thus, using the Ov genome and its putative proteome as a framework, we have identified multiple novel stage-specific proteins that will constitute the basis for the next generation of immunoassays that can be performed at the point of contact.

Schistosoma mansoni extracellular vesicles contain a rich collection of host regulatory biomolecules

FANNY C. NOWACKI[1], MARTIN T. SWAIN[1], FRANKLIN CHOW[2], JUAN F. QUINTANA[2], OLEG I. KLYCHNIKOV[3], PAUL J. HENSBERGEN[3], AMY H. BUCK[2], CORNELIS H. HOKKE[4] & **KARL F. HOFFMANN[1]**

[1]IBERS, ABERYSTWYTH UNIVERSITY; [2]CIIE, UNIVERSITY OF EDINBURGH; [3]CENTER FOR PROTEOMICS AND METABOLOMICS, LEIDEN UNIVERSITY MEDICAL CENTER (LUMC); [4]DEPARTMENT OF PARASITOLOGY, LUMC

The ability of schistosome parasites to successfully modulate host physiological and immunological responses is a prerequisite for establishing and maintaining long-lived molluscan and mammalian relationships. Identifying the parasite components responsible for these host-regulatory activities will contribute to the development of innovative schistosomiasis control strategies. Here, we continue our characterisation of schistosome extracellular vesicles (EVs) and illustrate that these excretory/secretory (E/S) components contain a rich diversity of putative host-modulatory biomolecules including small non-coding RNAs (sncRNAs), proteins, glycoproteins and glycolipids. Schistosome EVs, isolated from *in vitro* cultivated schistosomula, are remarkably uniform in size (mode = 86 nm; mean = 101 nm as assessed by tunable resistance pulse sensing) and morphology (measured by transmission electron microscopy). These characteristics are consistent with EVs derived from the fusion of multivesicular bodies with the plasma membrane and suggest that the predominant vesicle type released and detected during *in vitro* schistosomula culture are exosome-like. sncRNA characterisation of these schistosomula exosome-like EVs revealed hundreds of gene-regulatory micro (mi)RNAs (205) and tRNA-derived small RNAs (tsRNAs; 33). Putative parasite and host mRNA targets of the schistosomula miRNAs have been identified. Schistosomula exosome-like EV proteomes are also enriched for previously-described vaccine candidates (e.g. SmTSP2, SmGST, Sm29/Ly6D, Sm14, Sm20.8, Sm21.7), hypothetical antigens and conserved EV-like markers (e.g. rab11 proteins, annexins, 14-3-3 isoforms). Glycosylation analysis of the protein and lipid EV constituents identified immunologically-relevant glycans including LeX and fucosylated LacdiNAc motifs. Total EV glycopeptide analyses and EV surface glycosylation characterisations are ongoing. Together, our results indicate that schistosome exosome-like EVs contain a diverse collection of putative host-modulatory biomolecules. Characterising the function of these players in host/parasite interactions represents an exciting new aspect of schistosome biology useful in identifying novel anti-schistosomal targets.

Identification and characterization of extracellular vesicles in parasitic nematodes of pigs

ELINE P. HANSEN[1], KASPER L. ANDERSON[1], MERETE FREDHOLM[1], AAROM R. JEX[2], ROBIN B. GASSER[2], ANTONIO MARCILLA[3], STIG M. THAMSBORG[1], **PETER NEJSUM[1]**

[1]DEPARTMENT OF VETERINARY DISEASE BIOLOGY, UNIVERSITY OF COPENHAGEN, DENMARK; [2]FACULTY OF VETERINARY SCIENCE, THE UNIVERSITY OF MELBOURNE, AUSTRALIA; [3]DEPARTMENTO DE BIOLOG'A CELULAR'Y PARASITOLOG'A, UNIVERSITAT DE VALE', NCIA, VALENCIA, SPAIN

Endoparasites from all major parasitic groups (protozoa, nematodes, flukes and cestodes) have been shown to release extracellular vesicles (EVs) containing protein and RNA species and seem to be important in the host-parasite interplay e.g., host invasion or acquisition of immunity. The aim of this study was to examine EVs in secretions from three nematodes of pigs *Ascaris suum*, *Trichuris suis* and *Oesophagostomum dentatum* and then to determine their possible role(s) in host-parasite interactions. These parasites have different patterns of host adaptation, i.e. migration in the host, location within the gastrointestinal tract and the immunological response that they evoke. Therefore, they could represent suitable candidates to explore unique as well as common modes of parasite-host interactions and immune modulation in host animals. Adult worms of *A. suum*, *T. suis* and *O. dentatum* were incubated in RPMI 1640 under sterile conditions for 24-72 hours. EVs were purified from parasite-depleted RPMI by an initial filtering step (200 nm), followed by differential centrifugations with two ultracentrifugations at 110,000 x g. EVs in the size of ~100 nm were identified using transmission electron microscope, and RNA was purified. miRNAs were sequenced using the Illumina® platform and reads were aligned to the genomes of *A. suum, T. suis* and *O. dentatum*, respectively. A range of miRNAs unique and common for the three helminth species were identified using the miRDeep2 algorithm. One common miRNA was let-7a which has been suggested to inhibit the production of the anti-parasitic cytokine IL-13 and suppress the function the porcine miRNA ssc-let-7d-3p. Predicting targets and potential functions of these miRNAs in greater detail is part of an on-going analysis, in addition to a proteomic analysis of the EVs. With this, we may unravel the complex interplay between parasites and their hosts, and potentially discover novel targets for diagnostic test and parasite control.

Worm secretions and cancer

ALEX LOUKAS

AUSTRALIAN INSTITUTE OF TROPICAL HEALTH AND MEDICINE, JAMES COOK UNIVERSITY, CAIRNS QLD, AUSTRALIA

The oriental liver fluke *Opisthorchis viverrini* is considered a group 1 carcinogen by the International Agency for Research on Cancer. The only other helminth parasite to have earned this status is Schistosoma haematobium due to its association with squamous cell carcinoma of the bladder. The mechanisms by which *O. viverrini* induces cancer are multi-factorial, but we have shown an important role for excretory/secretory (ES) products in this pathogenic process. Both soluble fluke proteins (growth factors) and secreted extracellular vesicles (exosomes) can promote growth of human cholangiocytes, drive angiogenic processes and induce inflammatory cytokine production. Using high-resolution 3D-SIM microscopy and proteomic analyses we showed that liver fluke exosomes are internalised by human cell lines and that exosome proteins can be detected in bile fluid from infected humans and hamsters. Importantly, antibodies against tetraspanin proteins on the exosome surface can block vesicle uptake by host cells, providing a unique target for development of vaccines against parasitic helminths.

Extracellular vesicles from trematodes: purification methods and roles in host-parasite interactions

JAVIER SOTILLO[1], SUJITTRA CHAIYADET[2], MARK PEARSON[1], THEWARACH LAHA[2], ALEX LOUKAS[1]

[1]CENTRE FOR BIODISCOVERY AND MOLECULAR DEVELOPMENT OF THERAPEUTICS, AUSTRALIAN INSTITUTE OF TROPICAL HEALTH AND MEDICINE, JAMES COOK UNIVERSITY, CAIRNS QLD, AUSTRALIA; [2]DEPARTMENT OF PARASITOLOGY, FACULTY OF MEDICINE, KHON KAEN UNIVERSITY, KHON KAEN, THAILAND

Studies on host-trematode interactions have traditionally focused on the proteins and other molecules secreted by the parasites; recently, however, various groups have shown that trematodes and other helminths secrete small extracellular vesicles (EVs) that are internalised by host cells and impact upon cellular function. While EVs have been characterised for a number of trematodes including the liver flukes *Fasciola hepatica*, *Opisthorchis viverrini* and the blood flukes *Schistosoma mansoni* and *Schistosoma japonicum*, there is an increasing need to develop standardised methods to purify the different subpopulations of EVs (such as exosomes) so that comparable functional studies can be performed across different trematodes. In the case of *S. mansoni*, different parasite stages (adults and schistosomula) secrete exosome-like EVs that contain many vaccine candidates, potential virulence factors and molecules implicated in feeding such as different tetraspanins, saposin B, Sm29 and several annexins. In the case of *O. viverrini*, the carcinogenic adult flukes secrete EVs that contain conserved and unique proteins, including tetraspanin transmembrane proteins. Internalization of EVs by cholangiocytes resulted in cell proliferation and secretion of IL-6, and induced major changes in expression of proteins associated with processes such as phagocytosis, wound healing and cancer. We showed that antibodies to a recombinant *O. viverrini* surface tetraspanin blocked the uptake of *O. viverrini* EVs by cholangiocytes, highlighting a novel potential approach to vaccine development for this chronic infectious cancer. The discovery of EVs from trematodes has revealed an entirely new phenomenon by which parasites communicate with their hosts, and their study can reveal new innovative means by which to target parasitic helminths.

Host-seeking and infection strategies of parasitic nematodes

SPENCER GANG[1], MICHELLE CASTELLETTO[2], TAYLOR BROWN[1], JOON HA LEE[2], ELISSA HALLEM[1,2]

[1]MOLECULAR BIOLOGY INSTITUTE, UNIVERSITY OF CALIFORNIA, LOS ANGELES, USA; [2]DEPARTMENT OF MICROBIOLOGY, IMMUNOLOGY AND MOLECULAR GENETICS, UNIVERSITY OF CALIFORNIA, LOS ANGELES, USA

How the infective juveniles (IJs) of skin-penetrating parasitic nematodes find, infect, and navigate through their host to successfully parasitize the intestinal tract is poorly understood. We hypothesized that skin-penetrating IJs might use chemosensory mechanisms to detect and infect hosts. We asked how the human-parasitic threadworm *Strongyloides stercoralis* and closely related skin-penetrating nematodes respond to three mammalian cues: heat, odorants, and CO_2. We found that elevated temperature increases IJ crawling speed and induces local search behavior. We compared host odorant responses of *S. stercoralis* to six other nematode species and found that olfactory preferences reflect host specificity rather than phylogeny, suggesting that olfaction plays a role in host selection. CO_2 exhaled during respiration is a critical host-seeking cue for many mammalian parasites. Surprisingly, we found that CO_2 was not a host-seeking cue for skin-penetrating IJs. We asked if CO_2 was instead important for establishing an infection inside the host, where CO_2 concentrations are elevated relative to the environment. We found that 5% CO_2 and 37^{o}C are required for IJ activation, an early stage of development inside the host. We are now examining the neural basis of heat-and-CO_2-mediated IJ activation. In *Caenorhabditis elegans*, a family of receptor guanylate cyclase genes *gcy-8, gcy-18,* and *gcy-23* are required for thermosensation in AFD chemosensory neurons. Similarly, the receptor guanylate cyclase gene *gcy-9* is required for CO_2 detection in BAG chemosensory neurons. We identified *gcy-23* and *gcy-9* homologs in *S. stercoralis* and generated *gcy-23::GFP* and *gcy-9::GFP* reporter constructs, which specifically labeled putative AFD and BAG neurons, respectively, based on conserved anatomical position. We are now employing similar reporter-based strategies to quantitatively image heat-and-CO_2-evoked neural activity in *S. stercoralis* AFD and BAG neurons. We are also developing methods to genetically silence AFD and BAG neurons to determine if they are required for IJ activation.

Haemostatic changes occur *in vivo* already in the early non-hepatosplenic, phase of schistosomiasis

MIRJAM M. MEBIUS[1,2], AKIM A. ADEGNIKA[3,4,5], JEANNOT F. ZINZOU[3,4], JEAN-CLAUDE DEJON AGOBE[3,4], CLAUDIA J. DE DOOD[5], MARIA YAZDANBAKHSH[5], GOVERT J. VAN DAM[5], PAUL L.A.M. CORSTJENS[5], ALOYSIUS G.M. TEILENS[1,6], PHILIP G. DE GROOT[2], ROLF T. URBANUS[2], **JAAP J. VAN HELLEMOND[1]**

[1]DEPT. MEDICAL MICROBIOLOGY & INFECTIOUS DISEASES, ERASMUS UNIV. MEDICAL CENTER, ROTTERDAM, THE NETHERLANDS; [2]DEPT. CLINICAL CHEMISTRY & HAEMATOLOGY, UNIV. MEDICAL CENTER, UTRECHT, THE NETHERLANDS; [3]CENTRE DE RECHERCHES MÉDICALES DE LAMBARÉNÉ (CERMEL), BP118 LAMBARÉNÉ, GABON; [4]INSTITUT FÜR TROPENMEDIZIN, UNIV. TÜBINGEN, GERMANY; [5]DEPT. PARASITOLOGY, LEIDEN UNIV. MEDICAL CENTER, THE NETHERLANDS; [6]DEPT. BIOCHEMISTRY & CELL BIOLOGY, FAC. VETERINARY MEDICINE, UTRECHT UNIV., THE NETHERLANDS

Haemostatic abnormalities, such as thrombocytopenia, increased von Willebrand Factor antigen (VWF:ag) levels, decreased levels of coagulation factors, and increased fibrinolysis, are observed in hepatosplenic schistosomiasis. However, in the non-hepatosplenic, early phase of schistosomiasis platelet counts are normal, but it is unknown yet whether other haemostatic parameters are changed in early schistosomiasis. This study investigated haemostasis in early schistosomiasis in citrate plasma obtained from ten individuals with non-hepatosplenic schistosomiasis haematobium and four healthy controls recruited from the Lambaréné area in Gabon. Urine egg count and Circulating Anodic Antigen (CAA) levels were used to confirm an ongoing infection. Levels of VWF:ag, active VWF, ADAMTS13 antigen (ADAMTS13:ag), osteoprotegerin (OPG), thrombin-antithrombin III (TAT) and D-dimers were measured in plasma with ELISA. ADAMTS13 activity was determined with FRETS-VWF73 substrate and ristocetin co-factor activity (VWF:RCo) was assessed with the BC-VWF-reagent. VWF:ag and active VWF levels were elevated in individuals with non-hepatosplenic schistosomiasis haematobium compared to healthy controls ($p=0.002$ and $p=0.004$, respectively). The percentage of active VWF was slightly decreased in patients compared to controls ($p=0.024$). No abnormalities in the VWF degrading protease ADAMTS13 were observed in both patients and healthy controls. VWF:RCo was similar between patients and healthy controls and platelet counts were normal in all individuals. Increased VWF:ag levels could be caused by inflammation-mediated endothelial activation as OPG levels, a marker of inflammation-mediated endothelial activation, were elevated in patients versus healthy controls ($p=0.036$). TAT and D-dimer levels were similar between schistosomiasis patients and healthy individuals. These results demonstrate that in plasma of patients in the early non-hepatosplenic phase of schistosomiasis haematobium VWF:ag, active VWF, and OPG levels are elevated, whereas all other analysed haemostatic factors are not affected. This indicates that in vivo inflammation-mediated endothelial activation occurs already early in infection, while other haemostatic changes are still absent in this phase of the disease.

The schistosome-derived glycoprotein omega-1 inhibits gluconeogenesis by a dual glycan- and RNAse-mediated mechanism in primary mouse hepatocytes

NOEMI GARCIA-TARDÓN[1], LEONIE HUSSAARTS[1], LOTTE B. WESTERHOF[2], RUUD H. P. WILBERS[2], NICOLE N. DRIESSEN[1], GERARD C. VAN DER ZON[3], HELMUT HAAS[4], GABRIELE SCHRAMM[4], ARJEN SCHOTS[2], CORNELIS H. HOKKE[1], MARIA YAZDANBAKHSH[1] & **BRUNO GUIGAS[1,3]**

[1]DEPT. OF PARASITOLOGY, LEIDEN UNIVERSITY MEDICAL CENTER, LEIDEN, THE NETHERLANDS; [2]PLANT SCIENCES DEPT., LABORATORY OF NEMATOLOGY, WAGENINGEN UNIVERSITY & RESEARCH CENTRE, WAGENINGEN, THE NETHERLANDS; [3]DEPARTMENT OF MOLECULAR CELL BIOLOGY, LEIDEN UNIVERSITY MEDICAL CENTER, LEIDEN, THE NETHERLANDS; [4]RESEARCH CENTER BORSTEL, 23845 BORSTEL, GERMANY

Helminths are endemic parasites that infect millions of people worldwide, eliciting strong Th2 immune responses in their hosts. Recently, several studies have shown that both helminth infection and treatment with helminth-derived molecules (HDMs) improve whole-body insulin sensitivity and glucose homeostasis in obese mice. Although part of these beneficial effects are secondary to their immunomodulatory properties, HDMs might also directly target metabolic cells to regulate key metabolic processes. Interestingly, we found that chronic infection with *Schistosoma mansoni* and treatment with soluble egg antigens (SEA) decreased the expression of the gluconeogenic gene *Pck1* in the livers of obese mice. In the present study, we therefore aim to investigate whether HDMs could directly regulate hepatic gluconeogenesis. We first showed that both SEA and one of its major components, the schistosome-derived glycoprotein omega-1, bind to and are rapidly internalized in primary mouse hepatocytes. Remarkably, SEA and omega-1, but neither other mixture of parasite molecules nor other single HDMs, dose-dependently decreased gene and protein expression of key gluconeogenic genes, leading to a significant reduction in glucose production rates. Using various recombinant variants of omega-1 we showed that both its Lewis-X-bearing glycan and RNAse activity play a role in the inhibition of gluconeogenesis. Finally, among the pathways controlling gluconeogenesis, omega-1 was found to increase AMPK and reduce PKA/CREB signaling. In conclusion, our data show that the schistosome-derived omega-1 directly inhibit gluconeogenesis in primary mouse hepatocytes by a glycan- and RNAse-mediated dual mechanism. These findings might provide opportunity for development of a new class of anti-diabetic drug.

Adaptive immunity license basophils for protection against gastrointestinal helminths

DAVID VOEHRINGER

UNIVERSITY HOSPITAL ERLANGEN AND FRIEDRICH ALEXANDER UNIVERSITY ERLANGEN-NUREMBERG, 91054 ERLANGEN, GERMANY

About one third of the human population is infected with gastrointestinal helminths. The infections are often associated with type 2 immune responses characterized by eosinophilia, increased serum levels of IgE and activation of IL-4/IL-13 producing effector cells such as mast cells, basophils, Th2 cells and type 2 innate lymphoid cells (ILC2s). It is well known that expulsion of *Nippostrongylus brasiliensis* during primary infection requires antigen-specific T cells and IL-4- or IL-13-induced activation of STAT6-regulated genes in non-hematopoietic cells. Using conditional IL-4/IL-13-deficient mice we could show that T cell-derived IL-4/IL-13 is critical for IgE production and polarization of alternatively activated macrophages. However, IL-4/IL-13 from cells of the innate immune system was required for goblet cell hyperplasia and worm expulsion consistent with the concept that ILC2s play a crucial role for protective immunity during primary *N. brasiliensis* infection. We further used mixed bone marrow chimeras to demonstrate that basophil-derived IL-4/IL-13 plays an important protective role during secondary infection with *N. brasiliensis* and *Heligmosomoides polygyrus.* Basophil activation was largely dependent on IgE rather than IgG1 antibodies. Next generation sequencing analysis revealed a striking overlap between the IgE and IgG1 repertoire indicating that a large part of the IgE response is generated by sequential class switch recombination. Therefore, Th2 cell-mediated induction of the IgE response is the critical part of the adaptive arm of the immune system to sensitize basophils as innate effector cells for protective immunity during secondary infection with gastrointestinal helminths.

Chronic helminth infection during pregnancy epigenetically reprograms T cell differentiation

KATHRIN STRAUBINGER[1], SOPHIE PERCHERMEIER[1], SONAKSHI BHATTACHARJEE[1], HANI HARB[1], ROUZANNA ISTVANFFY[3], EVA LOFFREDO-VERDE[1], HARALD RENZ[2] & **CLARISSA U. PRAZERES DA COSTA[1]**

[1]INSTITUTE OF MEDICAL MICROBIOLOGY, IMMUNOLOGY AND HYGIENE, TECHNISCHE UNIVERSITÄT MÜNCHEN, MUNICH, GERMANY; [2]INSTITUTE OF LABORATORY MEDICINE AND PATHOBIOCHEMISTRY, MOLECULAR DIAGNOSTICS, PHILIPPS UNIVERSITY MARBURG, GERMANY; [3]III. MEDIZINISCHE KLINIK UND POLIKLINIK, KLINIKUM RECHTS DER ISAR, TECHNISCHE UNIVERSITÄT MÜNCHEN, MUNICH, GERMANY

Schistosomiasis is a non-transplacental helminth infection and chronic infection during pregnancy suppresses the adult offspring´s allergic responses to a heterologous antigen. We sought to determine whether suppression of allergic airway inflammation (AAI) was dependent on *in utero* exposure to chronic schistosome infection (Reg phase) and was transferrable to F2 generation and whether the suppressed AAI phenotype could be recapitulated within the T cell compartment. Therefore, we OVA-induced AAI analyzed in offspring born from *Schistosoma mansoni* infected Reg-phase mothers and breastfed by cage-mated naïve mothers. Furthermore, AAI was induced in F2 offspring from *Schistosoma mansoni* infected Reg-phase mothers. For detailed T cell analyses naïve $CD4^+CD62L^+$ T cells from offspring Reg-phase mothers and naïve cage-mated mothers were subjected to epigenetic and *in vitro* Th1 and Th2 T cell differentiation studies. In addition, the Th1 and Th2 memory T cell compartment of these mice was investigated. The cross foster studies revealed that *in utero* exposure rather than the early postnatal environment mainly shapes the offspring's AAI phenotype and that this phenotype is not transferred to the F2 generation. $CD4^+CD62L^+CD44^+$ memory T cells from Reg-phase offspring produced IL-4 *in vitro* in contrast to naïve offspring. Furthermore, naïve $CD4^+CD62L^+$ T cells from Reg-phase offspring had a strong capacity to differentiate into Th1 cells *in vitro*, whereas their ability to differentiate into Th2 cells was strongly impaired. In accordance, differences in histone acetylation patterns within cytokine promoter regions (IL-4, FoxP3, RORc) of naïve T cells were observed. Taken together our data show that maternal *S. mansoni* infection changes the offspring´s allergen susceptibility already *in utero* and that these effects are lost in the F2 generation. Furthermore distinct epigenetic changes of the naïve T cell compartment affect Th2 and Th1 differentiation with possible effects on T cell driven immune responses such as bacterial infections, allergies or vaccinations.

Th2/Th1 hybrid cells: A multifunctional subset with different characteristics in nematode infected humans & mice

CRISTIN N. BOCK[1], SEBASTIAN RAUSCH[1], MINKA BRELOER[2], SUBASH BABU[3], SUSANNE HARTMANN[1]

[1]INSTITUTE OF IMMUNOLOGY, FREIE UNIVERSITÄT BERLIN, GERMANY; [2]HELMINTH IMMUNOLOGY, BERNHARD NOCHT INSTITUTE FOR TROPICAL MEDICINE, HAMBURG, GERMANY; [3]NATIONAL INSTITUTE OF HEALTH CHENNAL, INDIA

Infection with the intestinal nematode *Strongyloides stercoralis* is an underestimated health risk as the disease is usually asymptomatic in immunocompetent individuals, but often exhibits devastating effects in immunocompromised patients. The potentially dangerous outcome of this infection is based on its capacity to multiply in humans via autoinfection. *Strongyloides* can parasitize undetected for decades and may produce heavy infections in later moments in life due to changes of the immune status of the host. The role of $CD4^+$ T cells, their cytokine response patterns or other immunological marker to assess the state of infection are poorly defined. Therefore we aimed to functionally characterize the T cell response, in particular whether Th2/Th1 hybrids also occur in nematode infected humans. This subset of $CD4^+$ T cells was recently characterized in helminth-infected mice as cells co-expressing the Th2 and Th1 lineage-defining transcription factors and cytokines. Blood samples from patients mono-infected with *S. stercoralis* and healthy control individuals in an endemic region in South India were analyzed by flow cytometry for the expression of GATA-3, T-bet and the associated cytokines IL-4, IL-13, IL-5 and IFN-γ. In parallel, murine $CD4^+$ T cells in infections with the close relative *S. ratti* were analyzed for their transcription factor and cytokine profile. Infected patients and mice mounted a Th2 response and Th2/1 hybrids producing Th2 and Th1 cytokines were detectable. Interestingly, human Th2/Th1 hybrids differed from their murine counterparts by expressing T-bet, high levels of IFN-γ, but very low levels of GATA-3. Furthermore, human Th2/Th1 hybrids were restricted to the IL-4/13 producing population, while $IL\text{-}5^+$ Th2 cells uniformly expressed high levels of GATA-3 and no IFN-γ. Th2/Th1 hybrids occur in both mammalian hosts but appear to be differentially programmed. Studies assessing functional differences of hybrids and their contribution to the outcome of Th2-driven diseases are under way.

Therapeutic potential of novel sulfone compounds based on the anti-inflammatory phosphorylcholine moiety of the secreted *Acanthocheilonema viteae* glycoprotein, ES-62

WILLIAM HARNETT[1], MIGUEL A. PINEDA[2], FELICITY E. LUMB[1], MARLENE CORBET[2], JAMES DOONAN[1], COLIN J. SUCKLING[3] AND MARGARET M. HARNETT[2]

[1]STRATHCYLDE INSTITUTE OF PHARMACY AND BIOMEDICAL SCIENCES, UNIVERSITY OF STRATHCLYDE, GLASGOW, G4 0RE, UK; [2]INSTITUTE OF INFECTION, IMMUNITY AND IMMFLAMATION, UNIVERSITY OF GLASGOW, GLASGOW, G12 8TA, UK; [3]DEPARTMENT OF PURE & APPLIED CHEMISTRY, UNIVERSITY OF STRATHCLYDE, GLASGOW G1 1XL, UK

The ability of a range of parasitic worm species to protect against disease development in mouse models of allergy and autoimmunity has contributed to the belief that anti-inflammatory drugs can be developed from these organisms. Towards this, we have generated novel sulfone compounds that are based around the anti-inflammatory phosphorylcholine (PC) moiety of ES-62, a secreted glycoprotein of *Acanthocheilonema viteae*. Investigation of the effects of these small molecule analogues (SMAs) in mice has revealed that they broadly mirror ES-62 both in protecting against disease in models of rheumatoid arthritis, systemic lupus erythematosus, skin inflammation and asthma and in failing to defend against development of type 1 diabetes, inflammatory bowel disease and multiple sclerosis. Microarray analysis of the effects of SMA 12b on macrophages and mast cells suggests a range of targets and the SMAs can both reduce expression of pro-inflammatory mediators and increase expression of molecules that inhibit inflammatory responses. Active SMAs generally target the same immune system mechanisms as ES-62, e.g., reduction in IL-17 responses, polarisation of dendritic cell maturation, inhibition of mast cell degranulation, induction of regulatory B cells (but not regulatory T cells), but selective results have also been observed in some cases, e.g., NRF2-mediated inhibition of IL-1b production by SMA 12b in arthritis. Contributing to these protective effects is that active SMAs have also been shown to mirror ES-62 in causing autophagolysosmal degradation of MyD88 in a number of immune system cells. Finally, the SMAs have registered favourable ADMET analysis, can inhibit inflammatory responses of human immune system cells *in vitro*, and have recently been found to be protective in a mouse model (collagen-induced arthritis) when administered as dendritic cell therapy. Overall therefore, subject to satisfactory necessary further pre-clinical analysis, the SMAs may be suitable for phase I clinical trials.

NOTES

POSTER SESSION 1

ABSTRACTS

1. Helminth-virus co-infection reveals enhanced control of respiratory syncytial virus infection in mice

JENNIFER AURET[1], CORINNA SCHNOELLER[2], ALISHA CHETTY[1], MURRAY E. SELKIRK[2], FRANK BROMBACHER[1], WILLIAM G.C. HORSNELL[1]

[1]*INSTITUTE OF INFECTIOUS DISEASE AND MOLECULAR MEDICINE, UNIVERSITY OF CAPE TOWN, SOUTH AFRICA;* [2]*DEPARTMENT OF LIFE SCIENCES, IMPERIAL COLLEGE LONDON, UNITED KINGDOM*

Co-infection with multiple pathogens is normal but how different pathogens influence the immune system to control them is not completely understood. Helminths, a common source of underlying infection throughout the world, can change our ability to control other infections. In this study we demonstrate how infection with the model helminth *N. brasiliensis* alters control of a subsequent respiratory syncytial virus (RSV) infection in mice. Here, helminth exposure prior to RSV infection resulted in both reduced weight-loss and reduced RSV titers in the lung. Analysis of host innate immune responses, associated with protective immunity to RSV, revealed that *N. brasiliensis* infected mice demonstrated significantly raised alveolar macrophage populations compared to RSV only infected mice. Additionally, responses associated with enhanced pathology such as IFNg and granzyme B were significantly reduced in co-infected mice. These data indicate that prior exposure to a helminth infection can confer enhanced innate control of RSV infection and pathology.

2. Vaccination using the Major Excreted Secreted protein of *Trichuris muris*

ALLISON BANCROFT, SHEILA BROWN, SEONA THOMPSON, ANDREW MACDONALD & RICHARD GRENCIS

FACULTY OF LIFE SCIENCES, UNIVERSITY OF MANCHESTER, UK

The major excreted/secreted (ES) protein (43 kDa; P43) protein of the intestinal helminth *Trichuris muris* has previously been shown to have a low level of host immunogenicity following a natural infection. P43 is a highly cysteine rich and stable molecule produced in all stages of the parasite. Vaccination with highly purified P43, however, generated resistance reflected by lower worm burdens in lower worm burdens with reduced fecundity. Reduced levels of pathology were also observed in mice vaccinated with both purified P43 and recombinant, R43. Protected mice exhibited reduced intestinal pathology. In vitro studies focussed on the initial interaction between P43 and the dendritic cell demonstrated that Cy3 labelled P43 entered the conventional antigen processing pathway and induced a dose dependent BMDDC up regulation of both MHC Class II and co stimulation markers. Mechanisms underlying both the reduced worm numbers and pathology are currently being investigated.

3. Functional characterization of *Heligmosomoides polygyrus* secreted apyrases

RITA BERKACHY, RACHEL VAUX, MURRAY E. SELKIRK AND KLEONIKI GOUNARIS

DEPARTMENT OF LIFE SCIENCES, IMPERIAL COLLEGE LONDON, SOUTH KENSINGTON CAMPIS, LONDON, SW7 2AZ, UK

Tissue damage results in the release of molecules which activate elements of the immune system. One such class of these molecules is extracellular nucleotides, which can also be released in a regulated manner, exerting a variety of effects via signalling through purinergic receptors. In general, ATP and ADP are pro-inflammatory, whereas adenosine is anti-inflammatory. Nematode parasites are known to secrete nucleotide-metabolising enzymes, which would be predicted to affect the availability and local concentrations of extracellular nucleotides and ensuing cellular responses. We have expressed four apyrases (APY-1-4) from *Heligmosomoides polygyrus* in *Pichia pastoris* and characterised their enzymatic activity. Purified recombinant apyrases and adult *H. polygyrus* total secreted proteins hydrolysed both nucleoside triphosphates and nucleoside diphosphates, but not monophosphates. The activity, optimal over a broad pH range between 7.5 and 10.0, was not dependent on the presence of cations, and showed no distinct preference for any nucleotide except lower activity towards CTP, GTP, CDP and GDP. We have developed a natural parasite of mice, *Trypanosoma musculi*, as a vehicle for heterologous expression and in vivo delivery of helminth secreted proteins in order to assay potential immunomodulatory properties. APY-1 from *H. polygyrus* has been expressed in *T. musculi*, and determination of enzymatic activities of transgenic *T. musculi* confirmed the secretion of an active apyrase. The function of the transgene will be studied *in vivo*.

4. Influence of *Nippostrongylus brasiliensis* infection on subsequent murid gammaherpesvirus infection

ALISHA CHETTY[1], ANNETTE DOUGALL[2], MARION ROLOT[2], MURRAY SELKIRK[3], WILLIAM HORSNELL[1], BENJAMIN DEWALS[2]

[1]INSTITUTE OF INFECTIOUS DISEASE AND MOLECULAR MEDICINE, INTERNALTIONAL CENTRE FOR GENETIC ENGINEERING AND BIOTECHNOLOGY AND DIVISION OF IMMUNOLOGY, UNIVERSITY OF CAPE TOWN, SOUTH AFRICA; [2]IMMUNOLOGY-VACCINOLOGY, DEPARTMENT OF INFECTIOUS AND PARASITIC DISEASES, FUNDAMENTAL AND APPLIED RESEARCH FOR ANIMALS & HEALTH (FARAH), FACULTY OF VETERINARY MEDICINE, UNIVERSITY OF LIÈGE, LIÈGE, BELGIUM; [3]DEPARTMENT OF LIFE SCIENCES, IMPERIAL COLLEGE LONDON, LONDON, UK

Parasitic helminth infections are highly immunogenic, have systemic effects on host immunity and influence host control of unrelated infections. In this study we investigated the influence of exposure to *Nippostrongylus brasiliensis* (Nb) on host control of murid gammaherpesvirus4 (MuHV-4) infection in female BALB/c mice. Mice were infected with Nb 6 days before intranasal infection with 10-4 PfU MuHV-4. Viral infection was monitored by *in vivo* imaging and confirmed by viral titration of the lung to establish viral PfU. We observed that mice exposed to Nb failed to display any virus-induced weight loss when compared to mice infected with MuHV-4 alone. *In vivo* imaging revealed that the lack of weight loss related to a significant reduction in lung viral replication in co-infected mice. Viral titration of the lung also showed a significant reduction in PfU in co-infected mice. Analysis of lung cell populations showed increased populations of alveolar macrophages, neutrophils, eosinophils, monocytes, dendritic cells, natural killer cells, and B and T cells in the lungs of co-infected mice when compared to mice infected with MuHV-4 only, but were equivalent to the populations seen in Nb only infected mice. Additionally, we observed an increase in virus-specific CD8 T cells in the lungs of co-infected mice. This data suggests that prior exposure to Nb enhances host ability to control a subsequent MuHV-4 acute primary infection. However, extended *in vivo* analysis revealed heightened viral reactivation in the genitals of co-infected mice at later time points. This may suggest that while Nb infection may contribute to enhanced early control of MuHV-4 in the lung it also allows the virus located to other tissue and reactivate to a greater extent than that seen in mice infected with MuHV-4 alone.

5. Helminth-driven type 2 inflammation enhances CD8+ T cell-mediated control of acute gammaherpesvirus infection

ANNETTE DOUGALL[1], MARION ROLOT[1], ALISHA CHETTY[2], MURRAY SELKIRK[3], FRANK BROMBACHER[2], FABRICE BUREAU[4], LAURENT GILLET[1], ALAIN VANDERPLASSCHEN, WILLIAM G. HORSNELL[2], **BENJAMIN G. DEWALS[1]**

[1]IMMUNOLOGY-VACCINOLOGY, FARAH, FACULTY OF VETERINARY MEDICINE, UNIVERSITY OF LIÈGE, B-4000 LIÈGE, BELGIUM; [2]INSTITUE FOR INFECTIOUS DISEASE AND MOLECULAR MEDICINE, UNIVERSITY OF CAPE TOWN, SOUTH AFRICA; [3]IMPERIAL COLLEGE LONDON, DEPARTMENT OF LIFE SCIENCES, LONDON, UK; [4]GIGA, MOLECULAR AND CELLULAR IMMUNOLOGY, UNIVERISTY OF LIÈGE, BELGIUM

The first stages of host colonisation with pathogens often determine the efficacy of their control through priming and maintenance of effective adaptive immune responses, which are essential for such control. Infection with different pathogens often occurs concurrently and a better understanding of how our immune system faces multiple aggressions with different sorts of pathogens is therefore important. In this study, we have investigated how helminth-driven Th2-type inflammation affects the control of host colonization by a gammaherpesvirus. We used *in vivo* imaging of murid herpesvirus 4 (MuHV-4) live infection to investigate viral replication in mice and observed that pre-exposed mice to helminth (*Schistosoma mansoni* or *Nippostrongylus brasiliensis*) better controlled lung acute infection and weight loss. The improved control of acute infection was associated with increased virus-specific effector $CD8^+$ T cell responses in the bronchoalveolar lavage, lung, draining LN (dLN) and spleen; whereas depletion of $CD8^+$ cells caused a loss of viral infection control irrespective of the exposure to helminth. Exposure to *S. mansoni* eggs caused increased numbers of dendritic cells (DCs), predominantly $CD11b^+$ conventional DCs in the lung, and in the dLN, which was associated with higher numbers of antigen-loaded lung DCs migrating to the dLN after MuHV-4 infection, suggesting that *S. mansoni* egg-induced inflammation might result in an improved priming of virus-specific $CD8^+$ T cells. To address the role of type 2 inflammation, we next used interleukin 4 receptor α-chain (IL-4Rα) deficient mice exposed to *S. mansoni* eggs and observed the absence of both the enhanced control of viral acute infection and the increased $CD8^+$ T cell response, suggesting that IL-4Rα signalling is involved. Collectively, we present data indicating that IL-4Rα-dependent type 2 inflammation induced in the lung by helminth exposure improves host control of acute viral infection through the induction of an increased virus-specific $CD8^+$ T cell effector response.

6. Structural and functional characterization of a novel gene, Hc-daf-22, from the strongylid nematode *Haemonchus contortus*

XIAOLU GUO[1], HONGLI ZHANG[2], QIANJIN ZHOU[3], YI YANG[1], XUEQIU CHEN[1], **AIFANG DU[1]**

[1]COLLEGE OF ANIMAL SCIENCES, ZHEJIANG UNIVERSITY, CHINA; [2]ZHEJIANG CENTER OF ANIMAL DISEASE CONTROL, CHINA; [3]FACULTY OF LIFE SCIENCE AND BIOTECHNOLOGY, NINGBO UNIVERSITY, CHINA

Haemonchus contortus can form diapause to adapt to hostile environmental conditions in the early fourth stage of this stronglylid nematode. In the present study, a new gene *Hc-daf-22* was identified which is the homologue of *Ce-daf-22* and human SCPx. Genome walking and RACE confirmed the full length gene of *Hc-daf-22* (6939 bp) contained 16 exons separated by 15 introns, and encoded a cDNA of 1117 bp (533 amino acids, estimated at about 59.3 kDa) with a peak in L3 and L4 in trascriptional level analyzed by qRT-PCR using all developmental stages as templates. The Hc-DAF-22 protein was consisted of a 3-oxoacyl-CoA thiolase domain and a SCP2 domain and evolutionarily conserved. The 1548 bp fragment upstream of the 5' flanking region was confirmed to have promoter activity compared with 5'-flanking region of *Ce-daf-22* by micro-injection. The rescue experiment by micro-injection of *daf-22 (ok693)* mutant strain showed significant increase in body size and brood size in the rescued worms with significantly reduced or completely absent of fat granules confirmed by Oil red O staining, indicating that *Hc-daf-22* could partially rescue the function of *Ce-daf-22*. Furthermore, RNAi with *Hc-daf-22* could completely silence the endogenous *Ce-daf-22* in N2 worms and mimic the phenotype of *daf-22 (ok693)* mutants. In general, *Hc-daf-22* shared similar characteristic and function with *Ce-daf-22* and may play an important role in peroxisomal β-oxidation and development in *Haemonchus contortus*.

7. Exploring host intestinal epithelia (goblet cell) – whipworm early interactions

MARÍA A. DUQUE-CORREA[1,2], HAYLEY BENNETT[1], ADAM J. REID[1], MAGDA LOKOWSKA[1], NANCY HOLROYD[1], ALLISON BANCROFT[2], CORDELIA BRANDT[1], SIMON CLARE[1], DAVID J. THORNTON[2], GORDON DOUGAN[1], RICHARD K. GRENCIS[2], MATTHEW BERRIMAN[1]

[1]WELLCOME TRUST SANGER INSTITUTE, WELLCOME TRUST GENOME CAMPUS, HINXTON, CB10 1SA, UK; [2]FACULTY OF LIFE SCIENCES, UNIVERSITY OF MANCHESTER, MANCHESTER, M13 9PT, UK

Whipworms (*Trichuris trichiura*) are soil-transmitted helminths and the etiologic agent of the human disease, trichuriasis. Whipworms live preferentially in the cecum of their hosts where they tunnel through epithelial cells and cause inflammation potentially resulting in colitis. Despite extensive research, the role of whipworm early interactions with host intestinal epithelial cells in triggering parasite establishment remains unclear. Here, we investigated novel interactions of whipworms with the host intestinal epithelia during the first events of infection. Imaging experiments upon three hours, one and three days post infection of mice with *T. muris* (a mouse model of *T. trichiura* infection in humans) have revealed the very first images of whipworm early larvae (L1) infecting the base of the crypts of the intestine of mice. These images suggest a close interaction between the L1 larvae and the host goblet cells. Based on these data, we hypothesize that targeted infection of goblet cells by L1 larvae can support the parasite growth and establishment in the host, potentially by the degradation of mucus. To further understand this whipworm – host intestinal epithelial early interaction, on-going experiments focus in studying the transcriptome of the L1 larvae of *T. muris* and single cell intestinal epithelial cells of infected animals. We aim to elucidate: 1) signals in the whipworm L1 larvae that are triggered uniquely by the host environment and 2) interactions of the whipworm with the host that are required for the establishment of the L1 larvae inside the epithelia. Additionally, whipworm gene expression switched on during the hatching process will give further insights into the biology of the worm and the gene expression of the host epithelia will shed light into the initiation of the immune responses.

8. SmMBD2/3 and its interaction partner SmCBX help maintain proliferating somatic cells (PSCs) in schistosomes

KATHRIN GEYER[1], SABRINA MUNSCHI[1], JIPENG WANG[2], JAMES COLLINS[2], KARL HOFFMANN[1]

[1]IBERS, ABERYSTWYTH UNIVERSITY, ABERYSTWYTH, UK; [2]UT SOUTHWESTERN MEDICAL CENTRE, USA

DNA methylation is an epigenetic modification that commonly involves the recruitment of heterochromatin-associated proteins (e.g. histone deacetylases, histone methyltransferases) via Methyl-CpG Binding domain proteins (MBD). These MBDs represent the readers of metazoan DNA methylation systems and, by specifically binding to methylated loci, attract chromatin-remodelling complexes, leading to transcriptional repression. In addition to their highly conserved N-terminal 5mC-binding domain, several MBDs also have a coiled-coil region at their C-terminus known to mediate protein-protein interactions (PPIs). We have previously identified a MBD homolog in the genome of the medically important blood fluke *Schistosoma mansoni*, and bioinformatic characterisation suggested SmMBD2/3 to be a functional member of this protein family. Here, we demonstrate that the recombinantly expressed protein is indeed capable of binding methylated DNA and predominantly localises within nuclear compartments. Furthermore, PPI studies based on a Yeast Two-Hybrid screen revealed the heterochromatin protein SmCBX (including the chromo shadow domain (CSD) known for PPIs) as a binding partner of SmMBD2/3. The CSD of this transcriptional repressor is likely to interact with the C-terminal coiled-coil region of SmMBD2/3, whereas the chromo domain (CD) at the C-terminus has known affinity to trimethylated histones (H3K9). Subsequent Whole-mount in situ hybridisation (WISH) confirmed the co-localisation of the proposed binding partners in schistosomal mesenchymal-, germ- and proliferating somatic stem cells (PSCs or neoblasts). Moreover, by employing RNAi and EdU Click-iT assays, we provide preliminary evidence suggesting an involvement of SmMBD2/3 and SmCBX in maintaining *S. mansoni* neoblasts. Unlike the *Schmidtea mediterranea* homolog, SmMBD2/3 represents a functional protein capable of binding 5mC. The physical interaction of SmMBD2/3 with the repressor SmCBX further suggests a role for these partners in heterochromatin formation and epigenetic regulation of gene expression. Additionally, a decrease in PSCs following SmMBD2/3 and SmCBX knockdown hints at an involvement of the partners in neoblast biology.

9. Real-time polymerase chain reaction-based diagnosis of *Schistosoma japonicum* infections in areas of China with low levels of schistosomiasis transmission

PEI HE[1], **CATHERINE A. GORDON[2]**, LI YUESHENG[1,2], YUANYUAN WANG[1], JUNJIAN HU[1], GAIL M. WILLIAMS[3], DARREN J. GRAY[4], DONALD P. MCMANUS[2]

[1]HUNAN INSTITUTE OF PARASITIC DISEASES, YUEYANG, PEOPLE'S REPUBLIC OF CHINA; [2]MOLECULAR PARASITOLOGY LABORATORY, INFECTIOUS DISEASES DIVISION, QIMR BERGHOFER MEDICAL RESEARCH INSTITUTE, BRISBANE, AUSTRALIA; [3]DISCIPLINE OF EPIDEMIOLOGY AND BIOSTATISTICS, SCHOOL OF POPULATION HEALTH, UNIVERSITY OF QUEENSLAND, BRISBANE, AUSTRALIA; [4]RESEARCH SCHOOL OF POPULATION HEALTH, THE AUSTRALIAN NATIONAL UNIVERSITY, CANBERRA, AUSTRALIA

Schistosomiasis in the People's Republic of China (PRC) goes back to antiquity. In the past 60 years, the Chinese government has made great strides in its control with elimination in the next ten years as the final declared goal to be reached through the implementation of a comprehensive control strategy. This aims to reduce the role of bovines and humans as sources of infection as a pre-requisite for elimination through transmission interruption. This goal will be achievable only by the formulation of a sustainable surveillance and control system, and sensitive diagnosis will be crucial. Currently used diagnostics lack the necessary sensitivity to accurately determine the prevalence of *Schistosoma japonicum* in areas with low intensity infections. It is of epidemiological importance to find and treat people with low-level infection if control programs are to be effective and sustained. Here, we evaluated a real-time polymerase chain reaction (qPCR)-based assay on 724 human stool samples from 7 villages, and 190 bovine (cattle and water buffalo) stool samples from 4 villages, in Hunan, Hubei, Anhui, and Jiangxi provinces, PRC. The qPCR was shown to be highly sensitive when compared with the Miracidial Hatching Test (MHT), Kato-Katz (KK) method and the Formalin-Ethyl Acetate Sedimentation-Digestion technique (FEA-SD), performed on MHT-positive samples only for quantification purposes. For both the human and bovine samples, a significantly higher prevalence was determined using qPCR (10.91% humans, 23.68% bovines) compared with the MHT (0.55% humans, 7.89% bovines). As the prevalence and intensity of infection of schistosomiasis gradually decreases in China more sensitive diagnostic tests will be required to monitor the reduction in schistosomiasis transmission, and to evaluate the control program leading to elimination. The qPCR assay will be a particularly useful tool for field diagnostics and schistosomiasis surveillance in low-transmission areas.

10. Specific targeting of IL-4Rα signalling on keratinocytes does not affect experimental murine Schistosomiasis

MELISSA GOVENDER, HLUMANI NDLOVU, JUSTIN NONO KOMGUEP, RAMONA HURDAYAL, ABDELAZIZ NADA, RETO GULER, FRANK BROMBACHER

INTERNATIONAL CENTER FOR GENETIC ENGINEERING AND BIOTECHNOLOGY (ICGEB), CAPE TOWN COMPONENT AND INSTITUTE OF INFECTIOUS DISEASES AND MOLECULAR MEDICINE (IDM), DIVISION OF IMMUNOLOGY, UNIVERSITY OF CAPE TOWN, CAPE TOWN, SOUTH AFRICA

Schistosomiasis is a neglected tropical disease that infects approximately 200 million people worldwide, causing approximately 200 000 deaths annually. Murine models of schistosomiasis, which plays an important role in providing a better understanding of the elicited host immune responses, have defined a host-protective role for signalling through the IL-4 receptor α chain (IL-4Rα). Migration of infectious cercariae through the skin of the host may be a key point of study in understanding the parasite-host interaction, but is still poorly understood. The skin is composed of a variety of cells, 90% of these cells being keratinocytes. In the current study, the role of IL-4Rα-responsive keratinocytes in *Schistosoma mansoni* was investigated. We generated a novel mouse model that lacks the expression of IL-4Rα specifically on all keratinocytes ($KRT14^{cre}IL\text{-}4R\alpha^{-/lox}$), in BALB/c mice, by gene targeting and site-specific recombination using the cre/*lox*P system, under the control of the KRT14 promoter. Compared to the littermate control mice, *S. mansoni* infected $KRT14^{cre}IL\text{-}4R\alpha^{-/lox}$ BALB/c mice had similar weights of liver and spleen, no difference in the production of Th1 (IFN-γ) and Th2 cytokines (IL-4, IL-13, and IL-5), similar levels of Type 1 (IgG2a and IgG2b) and Type 2 (IgG1 and IgE) antibody responses, and no difference in infiltrating populations of T and B cells, macrophages, and dendritic cells in the draining lymph nodes. Furthermore, no differences were observed in the egg burden, and associated pathology of the livers of mutant versus wild-type mice, as this also translated into a similar mortality rate between both groups of mice. Taken together, these data demonstrate that IL-4Rα signalling on keratinocytes does not affect immunopathology murine schistosomiasis.

11. Discovery and characterization of novel anti-schistosomal properties of the antianginal drug, perhexiline and its impact on *Schistosoma mansoni* male and female reproductive systems

ALESSANDRA GUIDI[1], CRISTIANA LALLI[1], EMERALD PERLAS[2], GIULIA BOLASCO[2], MARTINA NIBBIO[3], EDITH MONTEAGUDO[3], ALBERTO BRESCIANI[4] AND GIOVINA RUBERTI[1]

[1]NATIONAL RESEARCH COUNCIL, INSTITUTE OF CELL BIOLOGY AND NEUROBIOLOGY, CAMPUS A. BUZZATI-TRAVERSO MONTEROTONDO (ROMA), ITALY; [2]EUROPEAN MOLECULAR BIOLOGY LABORATORY (EMBL), MOUSE BIOLOGY UNIT, MONTEROTONDO, ITALY; [3]IRBM SCIENCE PARK, DEPARTMENT OF PRECLINICAL RESEARCH, POMEZIA, ITALY; [4]IRBM SCIENCE PARK, DEPARTMENT OF BIOLOGY, POMEZIA, ITALY

Schistosomiasis, one of the world's greatest human neglected tropical diseases, is caused by parasitic trematodes of the genus *Schistosoma*. A unique feature of schistosome biology is that sexual maturation of the female and egg production, necessary for both disease transmission and pathogenesis, are strictly dependent on the male. The treatment and most control initiatives of schistosomiasis rely today on the long-term application of a single drug, praziquantel (PZQ), mostly by campaigns of mass drug administration. PZQ, while very active on adult parasites, has much lower activity against juvenile worms. Monotherapy also favors the selection of drug resistance and therefore new drugs are urgently needed.
Following the screening of a small compound library with an ATP-based luminescent assay on *Schistosoma mansoni* schistosomula, we here report the identification and characterization of novel antischistosomal properties of the anti-anginal drug perhexiline maleate (PHX). By phenotypic worm survival assays and confocal microscopy studies we show that PHX, *in vitro,* has a marked lethal effect on all *S. mansoni* parasite life stages (newly transformed schistosomula, juvenile and adult worms). We further demonstrate that sub-lethal doses of PHX significantly impair egg production and increase lipid accumulation within the *vitellarium* of adult female worms. Moreover, we highlighted tegumental damage in adult male worms and remarkable reproductive system alterations in both female and male adult parasites. The *in vivo* study in *S. mansoni*-patent mice showed a notable variability of worm burdens in the individual experiments, with an overall minimal schistosomicidal effect upon PHX treatment. The short PHX half-life in mice, together with its very high rodent plasma proteins binding could be the cause of the modest efficacy of PHX in the schistosomiasis murine model.

12. The potential neuropeptide receptor SmNPYR1 is pairing-dependantly expressed in the testis of adult *Schistosoma mansoni* males and involved in spermatogenesis

STEFFEN HAHNEL, PAULA RIBEIRO, CHRISTOPH G. GREVELDING

[1]INSTITUTE OF PARASITOLOGY, BFS, JUSTUS LIEBIG UNIVERSITY, GIESSEN, GERMANY; [2]INSTITUTE OF PARASITOLOGY, MCGILL UNIVERSITY, MONTREAL, CANADA

Schistosomes exhibit an unusual reproductive biology. Firstly, they belong to the few trematode species which have developed a distinct sexual dimorphism. Secondly, the maturation of the female reproductive organs depends on a permanent pairing contact with the male. This close interaction between both genders is a prerequisite for egg production by the parasite. Therefore, pairing has fatal consequences for the final host as the eggs are the pathogenic agents of schistosomiasis. On the way to find alternative strategies for controlling schistosomiasis, many efforts have been made to identify genes which are involved in schistosome reproduction. Regardless of its importance for flatworm biology in general, a potential role of the nervous system and neuronal processes for gametogenesis in *S. mansoni* has not been considered so far. Here, we report for the first time on the involvement of a G protein-coupled receptor (GPCR), named SmNPYR1, in the spermatogenesis of adult *S. mansoni*. SmNPYR1 was identified by database analyses of receptor genes in the *S. mansoni* genome, and phylogenetic analyses revealed homology to neuropeptide Y receptors of other invertebrate clades. By *in situ* hybridization, transcripts of the receptor gene were localized exclusively in the testis of adult males, which was additionally confirmed by gonad-specific RT-PCRs. Furthermore, qRT-PCR analyses of total RNA obtained from gonads showed a pairing-dependent up-regulation of SmNPYR1 expression in the testis of pairing-experienced males. To elucidate receptor function, RNAi experiments were performed to knock down SmNPYR1 expression in adult schistosomes. Using confocal laser scanning microscopy, a distinct phenotype was observed in the male gonads going along with a drastic reduction of mature sperms in the testicular lobes and the seminal vesical. These results clearly show a pairing-influenced role of SmNPYR1 for spermatogenesis and thus indicate a substantial contribution of neuronal processes for reproduction.

13. Insights on sub-optimal drug response from whole genome sequencing of populations of the filarial nematode *Onchocerca volvulus*

SHANNON M. HEDTKE[1], STEPHEN R. DOYLE[2], SAMUEL K. ARMOO[1,3], MIKE OSEI-ATWENEBOANA[3], WARWICK GRANT[1]

[1]DEPARTMENT OF ANIMAL, PLANT AND SOIL SCIENCES, LA TROBE UNIVERSITY, AUSTRALIA; [2]PARASITE GENOMICS GROUP, WELLCOME TRUST SANGER INSTITUTE, UK; [3]ENVIRONMENTAL BIOLOGY AND HEALTH DIVISION, COUNCIL FOR SCIENTIFIC AND INDUSTRIAL RESEARCH-WATER RESEARCH INSTITUTE, GHANA

Onchocerciasis is a disease caused by the filarial nematode *Onchocerca volvulus*, affecting over 37 million people worldwide. The drug deployed for treatment and elimination is ivermectin, which kills microfilariae and suppresses adult female fertility. In several African communities, evidence suggests that a sub-optimal response to ivermectin in nematode populations has a heritable, genetic basis. We performed a genome-wide association study using whole genome sequences of 59 individual worms collected and phenotyped from 18 communities across a transect in Ghana, with an additional 7 from Mali and Côte d'Ivoire. We used spline analysis of F_{ST} values calculated from SNPs across the genome to identify windows that are highly genetically differentiated between good and poor responders to ivermectin; these windows contain candidate loci for the response phenotype. We compare the resulting candidate list from individual worms to previously-reported candidates based on pooled population sequencing, and discuss differences observed in the context of sampling methodology and geographic variation. We further explore how these differentiated loci are distributed across autosomes compared to the sex chromosome, and whether they derive from recent or retained ancestral mutations. Finally, we summarize challenges and possible solutions towards developing markers that could be deployed to screen African communities for *O. volvulus* with sub-optimal response to ivermectin.

14. Curation, analysis and display of helminth genomic data by WormBase ParaSite

KEVIN HOWE[1], BRUCE BOLT[1], JANE LOMAX[2], MICHAEL PAULINI[1], MYRIAM SHAFIE[2], PAUL KERSEY[1], PAUL W. STERNBERG[3], MATTHEW BERRIMAN[2] AND THE WORMBASE CONSORTIUM

[1]EMBL EUROPEAN BIOINFORMATICS INSTITUTE, WELLCOME TRUST GENOME CAMPUS, HINXTON, CAMBRIDGE, CB10 1SD, UK; [2]WELLCOME TRUST SANGER INSTITUTE, WELLCOME TRUST GENOME CAMPUS, HINXTON, CAMBRIDGE, CB10 1SA, UK; [3]HOWARD HUGHES

The number of publicly available helminth genome sequences has increased dramatically in the past three years, and research interest in helminth functional genomics is now quickly gathering pace in response to the foundation that has been laid by these collective efforts. A systematic approach to the organisation, curation, analysis and presentation of is clearly vital for maximising the utility of these data to researchers. WormBase have approached this problem from two directions. Firstly, our remit of detailed and deliberate curation of the *C. elegans* reference genome annotation has been extended to selected parasitic worms with high-quality (chromosome-level) genome assemblies. WormBase now act as the custodians of the reference annotation for these genomes, and actively engages with the communities in order to identify high-value data sets for integration and targets for curation. Secondly, we have developed a portal for interrogating helminth genomes on a large scale. WormBase ParaSite (http://parasite.wormbase.org) has been built using the Ensembl infrastructure, and integrates data on over 100 nematode and platyhelminth genomes, adding value by way of systematic and consistent functional annotation (e.g. protein domains and Gene Ontology terms), gene expression analysis (e.g. alignment of life-stage specific RNASeq sets), and comparative analysis (e.g. orthologs and paralogs). We provide several ways of exploring the data, including genome browsers, genome and gene summary pages, text search, sequence search, a query wizard, bulk downloads, and a programmatic interface.

15. Genetic analysis of β-tubulin isotype-1 gene of *Haemonchus contortus* populations from small ruminants in China

ZHONGZE ZHANG[1], ROBIN B. GASSER[1,2], XIN YANG[1], FANGYUAN YIN[1], GUANGHUI ZHAO[3], MIN BAO[4], BAOLIANG PAN[5], WEIYI HUANG[6], CUNREN WANG[7], FENGCAI ZOU[8], JUNLONG ZHAO[1], YANQIN ZHOU[1], RUI FANG[1], **MIN HU**[1]

[1]HUAZHONG AGRICULTURAL UNIVERSITY, WUHAN, CHINA; [2]THE UNIVERSITY OF MELBOURNE, VICTORIA, AUSTRALIA; [3]NORTHWEST A&F UNIVERISTY, YANGLING, CHINA; [4]LIAONING MEDICAL COLLEGE, JINGZHOU, CHINA; [5]CHINA AGRICULTURAL UNIVERSITY, BEIJING, CHINA; [6]GUANGXI UNIVERISTY, NANNING, CHINA; [7]HEILONGJIANG BAYI AGRICULTURAL UNIVERSITY, DAQING, CHINA.;[8]YUNNAN AGRICUTURAL UNIVERSITY, KUNMING, CHINA

Haemonchus contortus is one of the most important parasitic nematodes infecting small ruminants worldwide. The control of haemonchosis relies mainly on anthelmintics; however, prolonged and excessive use of anthelmintics has caused serious drug resistance issues. As benzimidazoles (BZs) have been widely used in China, we hypothesized that resistance is widespread. Given the link between known point mutations (designated F167Y, E198A and F200Y) in the β-tubulin isotype-1 gene and BZ resistance, our goal here was to explore these mutations in *H. contortus* representing eight populations from goats and sheep from eight provinces in China. Six distinct genotypes at 198 and 200 SNP positions were identified in the eight populations. Sequence analysis revealed allele frequencies of 0-0.70 at 198A and 0-0.31 at 200Y, respectively. F167Y was not detected in any population. High degrees of diversity in the β-tubulin isotype-1 gene sequence was recorded within individual populations (0.735 to 0.967). Phylogenetic analysis revealed E198A and F200Y to be present in two and seven groups, suggesting multiple origins of these mutations in China. This first analysis of mutations in the β-tubulin isotype-1 signals a clear need for resistance surveillance in China.

16. Host immunopathology outcomes in response to alteration of gut microbial composition and Schistosoma mansoni infection in a murine model

ANNA O. KILDEMOES[1], DENNIS S. NIELSEN[2], SØREN SKOV[3], AXEL K. HANSEN[3], BIRGITTE J. VENNERVALD[1]

[1]*SECTION FOR PARASITOLOGY AND AQUATIC DISEASES, FACULTY OF HEALTH AND MEDICAL SCIENCES, UNIVERSITY OF COPENHAGEN, DENMARK;* [2]*SECTION FOR FOOD MICROBIOLOGY, FACULTY OF SCIENCE, UNIVERSITY OF COPENHAGEN, DENMARK.;* [3]*SECTION FOR EXPERIMENTAL ANIMAL MODELS, FACULTY OF HEALTH AND MEDICAL SCIENCES, UNIVERSITY OF COPENHAGEN, DENMARK.*

The gut associated bloodfluke, *Schistosoma mansoni,* is a potent immunomodulator favouring regulatory responses and a general Th2 milieu related to egg production and migration. Host immune responses forming egg induced granulomas are necessary for egg passage through intestinal tissue to the lumen for host exit via faecal matter and life-cycle propagation. The most severe *S. mansoni* induced pathology in chronic infections is related to eggs carried via the bloodstream to the dead end liver and subsequently induced immune responses. Interestingly, a recent mouse study demonstrated that depletion of gut microbiota resulted in a reduction of intestinal inflammation and less granuloma formation in response to *S. mansoni* eggs lodged in intestinal tissue. However, the effect was local and no differences were observed in liver tissue. Both humans and mice show changes in energy metabolism and gut microbial activity in response to *S. mansoni* infection observed by metabonomic approaches. These indications implicate a role for gut microbiota in *S. mansoni* pathology and egg secretion. In this study we explore the consequences of alteration of gut microbial composition on *S. mansoni* induced granulomatous and regulatory responses in a C57BL/6NTAC model. Gut microbial composition changes are observed by tag-encoded 16S rRNA gene MiSeq-based high-throughput sequencing of faecal samples at multiple time-points. Egg induced inflammation and granulomatous responses are quantified in liver and intestinal tissue by stereological principles. Furthermore, the regulatory capacity is investigated by quantification of $CD4^+CD25^+FOXP3^+$ T-cells from mesenteric lymph nodes and spleen. This data is related to parasitological parameters viewing the gut as a small ecosystem consisting of commensal gut microbiota, helminth parasite infection and host immune responses. The aim of the study is obtaining a better understanding of factors affecting the immune homeostasis, which determines health as an outcome rather than disease in terms of development of autoimmune and inflammatory conditions.

17. Immune modulation by *Schistosoma mansoni* released extracellular vesicles

MARIJE E. KUIPERS[1], ARIFA OZIR-FAZALALIKHAN[1], ALWIN J. VAN DER HAM[1], GER J.A. ARKESTEIJN[2], YAVUZ ARIYUREK[3], NICOLE N. DRIESSEN[1], SIMONE HAEBERLEIN[1], STEFAN J. WHITE[3], CORNELIS H. HOKKE[1], ESTHER N.M. NOLTE-'T HOEN[2], HERMELIJN H. SMITS[1]

[1]*DEPT. OF PARASITOLOGY, LEIDEN UNIVERSITY MEDICAL CENTER (LUMC), LEIDEN, THE NETHERLANDS* [2]*DEPT. OF BIOCHEMISTRY & CELL BIOLOGY, UTRECHT UNIVERSITY, UTRECHT, THE NETHERLANDS* [3]*DEPT. OF HUMAN GENETICS, LUMC, LEIDEN, THE NETHERLANDS*

Secreted components by various life stages of *Schistosoma mansoni* were shown to influence the host immune system and promote their survival in the host. Examples are the conditioning of dendritic cells (DCs) to prime T helper(Th) 2 and regulatory T cell (Treg) responses, and the induction of IL-10 producing $CD1d^{hi}$ Breg cells in infected mice and men. Recently, parasites were shown to release extracellular vesicles (EVs). EVs are nano-sized membrane vesicles containing lipids, proteins and microRNA, which contribute to intercellular communication. The question remains whether EVs from schistosomes have specific biological functions and can influence immune cells of the host regulatory network. We demonstrate that *S. mansoni* adult worms and eggs release EVs, which can be purified from culture medium by density gradient ultracentrifugation and quantified by high-resolution flow cytometry. Using Western blotting, we observed that these EVs contained parasite-specific glycosylated proteins. Additionally, microRNA libraries were constructed from egg and adult worm EVs, and are currently processed for deep sequencing. When splenic mouse B cells were stimulated by adult worm ES, we observed a 2 to 3-fold elevated IL-10 production (but not for the pro-inflammatory IL-6). Interestingly, we found that at least part of this IL-10 producing activity was recaptured by adult worm EVs. In addition, human DCs exposed to adult worm EVs had a ~2-fold increased capacity to induce IL-10 production in naïve T cells. Current experiments are set up to further investigate the regulatory potential of EVs and to dissect the mechanism by which EVs can drive IL-10 producing B and T cells.

18. Analysing patterns of gene family evolution within the phylum Nematoda

DOMINIK R LAETSCH[1,2,3], PETER J COCK[2], VIVIAN C BLOK[3], MARK L BLAXTER[1]

[1]*INSTITUTE OF EVOLUTIONARY BIOLOGY, UNIVERSITY OF EDINBURGH, UNITED KINGDOM;* [2]*INFORMATION AND COMPUTATIONAL SCIENCE GROUP, THE JAMES HUTTON INSTITUTE, UNITED KINGDOM;* [3]*CELL AND MOLECULAR SCIENCE GROUP, THE JAMES HUTTON INSTITUTE, UNITED KINGDOM*

The field of nematode genomics has thrived in recent years due coordinated sequencing efforts, such as the 50 Helminth Project (coordinated by the Wellcome Trust Sanger Institute) and the Caenorhabditis Genome Project, as well as contributions of individual laboratories. Here, we present the results of a clustering analysis of >2.6 million proteins derived from 112 nematode next generation sequencing datasets, and 9 outgroup species. The putative gene families obtained through this analysis can now serve as a resource for the study of the phylum Nematoda, such as the identification of protein clusters unique to a species or group of species which can then be associated with features of the species' biology. We will present an estimate of the protein sequence diversity of Nematoda and demonstrate the value of this resource based on the analyses of single gene families, such as the nematode-specific "Worm ARGonautes" (WAGOs). In addition, we will show results regarding patterns of gene family evolution within genomes of plant parasitic nematodes of the suborder Tylenchina (Aphelenchoidae and Heteroderidae).

19. The interaction of hepatitis B or C virus infection and schistosomiasis in chronic pathogen-induced liver inflammation

E. LOFFREDO-VERDE[1], S. BHATTACHARJEE[1], A. MALO[2], F. REISINGER[3], M. RINGELHAHN[3], M. HEIKENWÄLDER[3], U. PROTZER[2], C. PRAZERES DA COSTA[1]

[1]INSTITUTE FOR MEDICAL MICROBIOLOGY, IMMUNOLOGY AND HYGIENE, TECHNISCHE UNIVERSITÄT MÜNCHEN, MUNICH, GERMANY; [2]INSTITUTE OF VIROLOGY, TECHNISCHE UNIVERSITÄT AND HELMHOLTZ ZENTRUM MÜNCHEN, MUNICH, GERMANY; [3]INSTITUTE OF VIROLOGY, TECHNISCHE UNIVERSITÄT MÜNCHEN, HELMHOLTZ ZENTRUM MÜNCHEN, MUNICH, GERMANY

One of the main complications of hepatitis B and C virus (HBV, HCV) infection is the development of chronic hepatitis after the acute infection, because affected individuals are at high risk to develop liver cirrhosis and hepatocellular carcinoma. Interestingly, chronicity develops at a higher frequency in developing countries in which co-infections with several helminth species, such as *Schistosoma mansoni* are common. During co-infection, immuneregulatory capacities of helminths may contribute to HBV/HCV persistence by compromising anti-viral effector T cell responses, and may lead to liver disease progression. We experimentally investigated the impact of distinct immune phases induced during *S. mansoni* infection on the outcome of HBV infection and vice versa, focusing on immune responses within the liver. In addition, we analysed the interrelationship between *S. mansoni* and HCV in an epidemiological study. While in combination with HCV, concomitant helminth infection led to an aggravation of the liver disease with enhanced viral replication and induction of regulatory T cells (Treg) with an unique phenotype, co-infection with HBV led to differential outcomes of the viral infection. Here, animals which acquired the viral infection during IFN-Y-prone immune phases of schistosomiasis presented lower viral loads, higher systemic IFN-Y and elevated frequencies of liver-resident HBV-specific $CD8^+$ IFN-Y^+ T cells in comparison to their HBV mono-infected counterparts. The prominent role of schistosome-induced IFN-Y secretion in this context was shown by the fact that co-infected IFN-Y-deficient mice failed to control viral replication. Additionally, we observed that the anti-viral effect of parasite-induced IFN-g dominates over possible Treg effects even during the chronic phase of infection. Taken together, our data indicate a causal relationship between schistosome-induced IFN-Y production within the liver, the induction of anti-viral T cells and clearance of HB/HC Virus.

20. Gonad-specific and pairing-dependent gene expression in *Schistosoma mansoni*

ZHIGANG LU[1], FLORIAN SESSLER[2], NANCY HOLROYD[2], STEFFEN HAHNEL[1], THOMAS QUACK[1], MATTHEW BERRIMAN[2], CHRISTOPH G. GREVELDING[1]

[1] *BFS, INSTITUTE OF PARASITOLOGY, JUSTUS LIEBIG UNIVERSITY, GIESSEN, GERMANY*; [2]*WELLCOME TRUST SANGER INSTITUTE, WELLCOME GENOME CAMPUS, HINXTON, UNITED KINGDOM*

Schistosoma is the only member among the trematodes that lives dioeciously. To achieve sexual maturation and reproduction, female worms need to be constantly paired with males. Pairing-induced gene expression in both genders has been investigated in a few studies, however, little is known about the complexity of transcriptional processes in schistosome gonads. Based on a recently established organ-isolation approach, we performed comparative transcriptomic analyses for ovaries and testes from both paired and unpaired adult worms. Using RNAseq we identified 3,600 and 243 significantly (*padj* < 0.05 or 0.005) differentially (fold change > 1.5) expressed genes (DEGs) in ovaries (unpaired vs. paired origin) and testes (unpaired vs. paired origin), respectively. KEGG pathway mapping confirmed their roles in transcriptional and translational regulation, cellular processes, energy metabolism, and signal transduction. Among these DEGs, 309 showed ovary-specific transcription, including *cpeb1*, *cpeb2*, *zfhx1*, and *syt14,* and 42 appeared to be testis-specifically transcribed, including *cdc25* and *syt1*. In addition, 436 transcripts occurred testis-specific but pairing-independent, including *elav2* and *tll/nhr*. Beyond that, the majority of gonad-transcribed genes demonstrated to be pairing-unaffected in both ovaries and testes (4,100 genes; e.g. *mcm2-8*, *vlg1-3*, *ago*, *pcna* and *vkr2*), or affected by pairing only in ovaries but not in testes (3,152 genes; e.g. *vkr1*, *melk*, *fgfr-a*, *plk1*, and *nanos2*). Furthermore, we identified sets of genes with preferential expression in the gonads and associated to stem-cells/neoblasts (e.g. *plk1* and *ago*) or neural processes (e.g. *melk* and *nk2*). Finally, for many genes whose products still annotated as hypothetical proteins evidence was found for reproduction-associated functions. Overall, our datasets elucidate key aspects of schistosome reproductive biology and will be relevant for basic as well as applied, exploitable research aspects.

POSTER SESSION 2

ABSTRACTS

21. In vivo effects of drugs used in lymphatic filariasis MDA programs on *Brugia malayi* in gerbils

MARY J. MACLEAN[1,2], ASHLEY M. ROGERS[1,2], SALLY M. WILLIAMSON[1,2], MICHAEL T. DZIMIANSKI[1], BOB E. STOREY[1], ADRIAN J. WOLSTENHOLME[1,2]

[1]DEPARTMENT OF INFECTIOUS DISEASES, UNIVERSITY OF GEORGIA, ATHENS, GA, UNITED STATES; [2]CENTER FOR TROPICAL AND EMERGING GLOBAL DISEASES, UNIVERSITY OF GEORGIA, ATHENS, GA, UNITED STATES

Lymphatic filariasis (LF) threatens nearly 20% of the world's population and has handicapped one-third of the 120 million people currently infected. Current control and eventual elimination of LF rely on mass drug administration (MDA) programs with three drugs: ivermectin (IVM), albendazole (ALB), and diethylcarbamazine (DEC). Only the mechanism of action of albendazole is well-understood. For *Brugia malayi*, the *in vitro* IC_{50} for ivermectin against microfilariae (Mf) was 6.1 ± 1.1 µM, 120 times the drug concentration that clears Mf from human patients. IC_{50} values could not be calculated for DEC as no effect of the drug on motility could be observed in vitro. These findings suggest that the rapid clearance of Mf observed after treatment with IVM or DEC is aided by the host immune system and does not simply result from the paralysis of the parasites. To gain a better insight into antifilarial drug action, we treated gerbils with patent *B. malayi* infections with 6 mg/kg DEC, 1 mg/kg ALB, or 0.15 mg/kg IVM to mirror the doses used in human MDA programs. These treatments had no effect on the numbers of worms present in the peritoneal cavity of infected animals. Adults and Mf were collected 1 and 7 days post-treatment and RNA was isolated for transcriptomic analysis. The experiment was repeated three times. Preliminary analysis of the effects of IVM, ALB, and DEC on adult males and females revealed treatment-specific changes in transcripts related to collagen expression, reproduction, embryogenesis, larval development, and lifespan determination. Similar data are currently being collected for the microfilariae. Our analysis of the effects of these drugs *in vivo* should provide a better understanding of how they clear Mf from the circulation of infected individuals.

22. Glyco-conjugate vaccine against the dog's heartworm *Dirofilaria immitis*

FRANCESCA MARTINI[1,2], CHIA-WEI LIN[2], CHRISTINE NEUPERT[1], BRUNO OESCH[1], MARKUS AEBI[2]

[1]MALCISBO AG, SCHLIEREN, SWITZERLAND [2]INSTITUTE OF MICROBIOLOGY OF ETH ZÜRICH, SWITZERLAND

Dirofilaria immitis is a filarial parasite of *canidae* that, upon infection from mosquito bite, causes cardiopulmonary dirofilariasis in dogs, cats, and ferrets, presenting also zoonotic potential. Currently, this parasite is controlled by early chemical treatments, which prevent the infection. The prophylactic treatment presents several disadvantages, the used drugs are highly toxic for the dogs, expensive and their extensive use could result in the raise of resistant strains, therefore new strategies to control this infection are desirable. The goal of this project is to develop the basis for a novel glyco-conjugate vaccine against *D. immitis*. To date, no potential vaccine targets have been found in *D. immitis*, however, several promising vaccine candidates of other blood sucking nematodes have been published, for example of *Ancylostoma caninum*, the dog's hookworm. Searching the *D. immitis* genome for homologous *A. caninum* antigens might therefore be a valuable strategy for vaccine target identification. Moreover, in recent years it has become evident that the protein backbone of an antigen is not the only factor eliciting a protective immune response, its secondary structure and post-translational modifications, like glycosylation, are to be taken into account. Using mass spectrometry and lectin blotting analysis on *D. immitis*' *N*-glycans we identified potentially immunogenic glycan epitopes, such as LacdiNAc and α1,3 core fucosylation. A glyco-conjugate, expressing these modifications on a carrier protein, will be tested for its effectivity as potential vaccine against *D. immitis*.

23. Incorporation of population genetic parameters into spatial models for the transmission of *Onchocerciasis*.

KAREN MCCULLOCH[1, 2], SHANNON M HEDTKE[1], KATIE CRAWFORD[1], JAMES MCCAW[2], JODIE MCVERNON[2,] WARWICK GRANT[1]

[1]ANIMAL, PLANT AND SOIL SCIENCES, AGRIBIO, LA TROBE UNIVERSITY, AUSTRALIA; [2]MELBOURNE SCHOOL OF POPULATION & GLOBAL HEALTH, UNIVERSITY OF MELBOURNE, AUSTRALIA.

Current models for the transmission of Onchocerciasis assume one homogenously mixing population and do not take into account factors such as gene flow (through host migration) and population structure. These models have been relied on heavily as policy and decision making tools upon which many control programs, such as mass drug administration (MDA) of ivermectin, have been based. Gene flow can cause recrudescence if new gene migrants become established, which could happen through human host or vector migration. Recent research has found that parasite populations of *Onchocerca volvulus* (the causative organism of Onchocerciasis) are strongly structured, that is there are readily detectable genetic differences between populations according to geography. By taking a new approach to understanding the transmission of Onchocerciasis, we investigate answers to questions such as: For regions where the elimination of Onchocerciasis has been successful, is recrudescence possible due to infected neighbouring regions and the mobility of human and vector hosts? Here, we derive a mathematical model for the transmission of human Onchocerciasis which incorporates population structure to investigate the dynamics of how multiple populations of *O. volvulus* interact. We use parasite population genetics to define the separate geographical regions which we refer to as `transmission zones'. For each transmission zone i, we derive equations to describe the rate of change of the adult worms (W_i), microfilaria (M_i) and infective larvae (L_i) over time in order to investigate the population dynamics. Using this spatial model framework for the transmission of Onchocerciasis we estimate the rate of host migration and gene flow between transmission zones. This research provides further insight into the underlying driving factors that may have contributed to the sustained transmission of *O. volvulus* in areas where MDA of ivermectin was unsuccessful.

24. The effect of dietary prebiotics on immune function and helminth infection.

LAURA J. MYHILL, ANDREW R. WILLIAMS, HELENA MEJER, STIG THAMSBORG

DEPARTMENT FOR VETERINARY DISEASE BIOLOGY, THE UNIVERSITY OF COPENHAGEN, DENMARK

Helminth infections can result in serious health implications for both humans and animals, due to their strong immunomodulatory effects. In addition to poor health and welfare, huge economic losses in the pig industry can arise from reduced productivity caused by gastrointestinal helminths, such as *Ascaris suum* and *Trichuris suis*, which drives the need for the development of novel anti-parasite control treatments. Previous research from our group has suggested that dietary prebiotics, such as chicory inulin, have the capability of modulating the host immune system and drastically reducing helminth infection in pigs; however the mechanisms of this are still unknown. To further understand the interaction between dietary prebiotics and local gut immunity, we will utilise *in vitro* and *ex vivo* cell cultures to determine the specific role of dendritic cells (DC). Our preliminary studies with DCs cultured with a combination of inulin, helminth antigen and/or lipopolysaccharide (LPS), suggest that inulin alone is not capable of inducing an anti-inflammatory phenotype in DCs. Thus, we will focus on the interaction of DCs and short chain fatty acids (SCFA), the by-products of inulin fermentation in the large intestine. SCFAs are well known for interacting with host gut microbiota, which provides an alternative pathway in which modulation of host immunity may occur, yet we hypothesise that DCs may be directly influenced by SCFAs themselves. Ultimately, our *in vitro* data will fully complement our continuing *in vivo* studies using *Trichuris suis*-infected pigs to provide a powerful insight into the complex interactions between host immunity, diet and helminth infection.

25. Assessing glycan-specific IgE profiles associated with *S. mansoni* infection and allergy in Uganda

GYAVIIRA NKURUNUNGI,[1,2] ANGELA VAN DIEPEN,[3] JOYCE KABAGENYI,[1] RICHARD SANYA,[1] NIELS-CHRISTIAN REICHARDT[4], CORNELIS HOKKE[3], ALISON ELLIOTT[1,2], MARIA YAZDANBAKHSH[3]

[1]MRC/UVRI UGANDA RESEARCH UNIT ON AIDS; [2]LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE, UK; [3]LEIDEN UNIVERSITY MEDICAL CENTER, THE NETHERLANDS; [4]CENTRO DE INVESTIGACIÓN COOPERATIVA EN BIOMATERIALES, SPAIN

Several studies point to the benign nature of carbohydrate antigens as allergenic determinants. Protein glycosylation processes in several nematodes, trematodes (such as *Schistosoma mansoni*) and allergens, but not in mammalian species, involve addition of immunogenic β-1,2-xylose and α-1,3-fucose moieties to the conserved glycan core. We hypothesised that chronic *S. mansoni* infection is associated with enhanced IgE responses to specific glycan structures, which might dominate over allergen protein-specific IgE, resulting in reduced allergic effector responses. In participants from the rural *S.mansoni*-endemic islands of Lake Victoria, we assessed associations between IgE reactivity to synthetic glycan structures containing β-1,2-xylose, α-1,3-fucose and α-1,6-fucose linkages to the common pentasaccharide ($Man_3GlcNac_2$) core and 1) current *S. mansoni* infection 2) SPT reactivity. We also compared anti-glycan IgE profiles between island study participants and participants from a relatively low-helminth-prevalence, urban birth cohort. Microarray technology was used to measure IgE reactivity to the glycan structures. Among island participants, we observed a positive association between current *S. mansoni* infection and IgE reactivity to the core β2-xylosylated N-glycan structure. This association was lost in presence of fucose in the α-1,3 position, although there was no effect of α-1,6-fucose. Mean IgE reactivity to β-1,2-xylose was lower among SPT-reactive individuals. Furthermore, rural island participants had higher IgE responses to most core β2-xylosylated N-glycans than their urban counterparts. Presence of further mannose, galactose, GlcNAc and GalNAc groups in various positions on the core glycan structure had varying effects on the association between *S. mansoni* infection (and/or SPT reactivity) and IgE reactivity. Taken together, our results point out the potential role of IgE to specific helminth-associated N-glycan structures in the modulation of allergic effector responses. Moreover in the Lake Victoria islands, we have the unique opportunity to evaluate the effect of intensive anthelminthic treatment on glycan-specific antibody profiles related to helminths and allergy.

26. Exploring the role of leukotrienes in the immunopathology of schistosomiasis

CHRISTIAN OWUSU[1], ALEX PHYTHIAN-ADAMS[2], ANDREW MACDONALD[2], MATT BERRIMAN[1]

[1]PARASITE GENOMICS, WELLCOME TRUST SANGER INSTITUTE, WELLCOME TRUST GENOME CAMPUS, HINXTON, UNITED KINGDOM; [2]MANCHESTER COLLABORATIVE CENTRE FOR INFLAMMATION RESEARCH, THE UNIVERSITY OF MANCHESTER, MANCHESTER, UNITED KINGDOM

Schistosoma mansoni causes hepatosplenic schistosomiasis, a serious chronic disease that constitutes a major public health burden in endemic countries. Pathology from schistosomiasis arises from the action of the immune system against parasite eggs trapped in host tissue. Like many other helminth infections, schistosomiasis induces a strongly polarised type 2 inflammatory response, resulting in the formation of periovular granulomas, which restrict tissue damage from potentially toxic compounds released by trapped schistosome eggs. Over time, this granulomatous response can lead to fibrosis, ultimately resulting in impaired organ function. While much is known about the major effector cells involved in immunopathological changes in the liver, we are still largely ignorant of the exact molecular triggers leading to the observed pathology. To address this, we conducted transcriptome profiling of infected mouse livers across six time points. The time points were chosen to reflect the progression of the immune response, beginning prior to the onset of egg deposition, and extending all the way through to the chronic stage of the disease. Differential expression analyses revealed overexpression of several genes active in the leukotriene arm of the arachidonic acid (ARA) metabolism pathway, with the 5-lipoxygenase activating protein (FLAP) gene repeatedly identified as the most significantly upregulated gene at 56, 84 and 105 days post infection. As this gene is only active early in the ARA metabolism cascade, we conducted preliminary experiments to determine which of the two main classes of immunologically active downstream ARA metabolites (i.e. LTB_4 and the cysteinyl leukotrienes) were produced in response to *S. mansoni*, and to characterise their role in schistosomiasis.

27. MiRNAs miR-277/novel255 regulate transcriptional landscape during juvenile to adult transition in Schistosoma mansoni

ANNA V. PROTASIO[1], LEONOR QUINTAIS[2], STIJN VAN DONGEN[2], DIOGO RIBEIRO[1], FLORIAN SESSLER[1], MARTIN HUNT[1], ANTON J. ENRIGHT[2], MATTHEW BERRIMAN[1].

[1]WELLCOME TRUST SANGER INSTITUTE, WELLCOME GENOME CAMPUS, CB10 1SA, UK.
[2]EUROPEAN BIOINFORMATICS INSTITUTE, WELLCOME TRUST GENOME CAMPUS, CB10 1SD, UK.

Schistosomes are parasitic helminths that cause schistosomiasis, also called bilharzia, a disease affecting 200 million people primarily in underprivileged regions of the world. *Schistosoma mansoni* is the most experimentally tractable schistosome species due to its ease of propagation and high quality status of its genome assembly and annotation. Although non-coding RNAs, in particular microRNAs are starting to be studied in this system, little is know about the role of these molecules in the context of physiological processes in this trematode. In this report, we used small RNA libraries from several intra-mammalian stages of the parasite to identify novel and conserved miRNAs. We found that one particular miRNA, here called novel255, increases expression as the parasites develop from juvenile to adult. What is more, using a unique combination of high-resolution transcriptome data and bioinformatics techniques we found that changes in the transcriptome of worms undergoing this transition are mainly shaped by the presence of this miRNA and/or members of its family. Finally, we show that the pattern of expression of the targets of these miRNA is significantly different in mature and immature “virgin” females, suggesting that this miRNA could be involved in sexual development of female schistosomes.

28. Development of mitochondria- and protease-specific prodrugs in the potential treatment of parasitic helminth infections

EYITAYO OLUWADARE, AIMAN REHAN, YAO DING, AGNES TURNBULL, EVA MALONE, DAVID MINCHER, **LORNA PROUDFOOT**

SCHOOL OF LIFE, SPORT AND SOCIAL SCIENCES, EDINBURGH NAPIER UNIVERSITY, EDINBURGH, UK

Anthelmintic resistance and the shortage of new drugs represent an urgent need for the development of novel anti-parasite drugs with effective delivery to the target site. Reduced bioavailability and sub-optimal doses can be responsible for generation of anthelmintic resistance, so there is potential to convert proprietary products to new 'smarter' targetable prodrugs, which may circumvent developing resistance and lower general toxicity. *Caenorhabditis elegans* has been used as a parasite model to demonstrate mitochondria- and protease-specific targeting. We have also been able to demonstrate the potential for protease-specific targeting *in vitro* in the case of *Haemonchus contortus* and *Teladorsagia circumcincta*. A series of novel targeted anthelmintic candidate drugs have been synthesized, based on a tubulin disrupting agent; tubulin is a known target of the benzimidazole anthelmintics. New prodrugs are ester-linked to a lipophilic cationic carrier designed to not only pass through cell membranes and localise in mitochondria but also facilitate drug cellular uptake by avoiding p-glycoprotein-type mediated efflux mechanisms. *C. elegans* L4 larvae were treated with mitochondria-specific prodrugs in a 24-well plate assay and the percentage survival was monitored after specific incubation times compared with controls. Preliminary biological evaluation of these prodrugs demonstrated significant toxicity against *C. elegans.* In the case of protease-specific prodrugs, we used a novel fluorogenic rhodamine-based asparagine-containing oligopeptide substrate (SM9) attached to a 'black hole' quencher where selective cleavage by the target protease separates the quencher from the probe, triggering fluorescence. With the SM9 probe, accumulation was detected as fluorescence in specific areas, particularly around neurons associated with the pharynx, vulva (HSN), neurosecretory-motor neuron and pre-anal ganglion regions. Protease-specific probe localization could potentially be exploited to achieve region-specific, protease-mediated prodrug activation and therefore site-specific drug delivery. Work will continue to refine and define structure-activity relationships and to determine the effect of the novel agents on worm viability.

29. Current progresses on isolating and culturing of cells from *Schistosoma mansoni*

THOMAS QUACK, ZHIGANG LU, CHRISTOPH G. GREVELDING

BFS, INSTITUTE OF PARASITOLOGY, JUSTUS LIEBIG UNIVERSITY, GIESSEN, GERMANY

Due to their impact on human and animal health schistosomes have been in the focus of many research initiatives over the last decade(s). Several "-omic" approaches have generated a vast amount of genetic "blue-prints" about schistosomes. In this context, numerous genes were detected, which are of interest to be characterised in more detail. In this era of post-genomic research, however, methods and tools are desperately needed for reverse genetic analyses. Among the desired tools are schistosomal cell lines, which are generally accepted to be required to overcome present research limitations. Recently, we developed a novel organ isolation protocol that provided access to whole intact reproductive tissue from *Schistomoma mansoni* as a source for RNA and proteins but particularly also gonadal cells (Hahnel et al. 2013; PLoS NTD). The latter appear to be promising starting material for cell culture experiments. Here we present novel strategies for the isolation and enrichment of gonadal cells and show first results regarding their characterisation as well as *in vitro* cultivation. To this end molecular and morphological analyses were performed, and we tested varying growth conditions including different types of cell culture media, growth factors, and further supplements, respectively. The results indicate that the establishment of primary cell cultures is possible. This in turn represents an important prerequisite for subsequent experiments such as transfection and in particular immortalisation approaches for establishing permanently dividing cells/cell lines.

30. Schistosome infection modulates the intestinal microbiome

GABRIEL RINALDI[1]*, HONG-BIN YAN[1,2], RAFAEL NACIF-PIMENTA[1,3], JOSEPH F. PETROSINO[4], MICHAEL H. HSIEH[5,6,7], NADIM J. AJAMI[4], PAUL J. BRINDLEY[1]

*[1]DEPARTMENT OF MICROBIOLOGY, IMMUNOLOGY & TROPICAL MEDICINE AND RESEARCH CENTER FOR NEGLECTED DISEASES OF POVERTY, SCHOOL OF MEDICINE & HEALTH SCIENCES, THE GEORGE WASHINGTON UNIVERSITY, WASHINGTON, DC, USA.[2]STATE KEY LABORATORY OF VETERINARY ETIOLOGICAL BIOLOGY, LANZHOU VETERINARY RESEARCH INSTITUTE, CHINESE ACADEMY OF AGRICULTURAL SCIENCES, LANZHOU, GANSU PROVINCE, CHINA. [3]LABORATORIO DE ESQUISTOSSOMOSE, CENTRO DE PESQUISAS RENE´ RACHOU, FUNDACAO OSWALDO CRUZ - FIOCRUZ, BELO HORIZONTE, MINAS GERAIS, BRAZIL. [4]THE ALKEK CENTER FOR METAGENOMICS AND MICROBIOME RESEARCH, DEPARTMENT OF MOLECULAR VIROLOGY AND MICROBIOLOGY, ONE BAYLOR PLAZA, BAYLOR COLLEGE OF MEDICINE, HOUSTON, USA. [5]BIOMEDICAL RESEARCH INSTITUTE, ROCKVILLE, MD, USA. [6]CHILDREN'S NATIONAL HEALTH SYSTEM, WASHINGTON, DC USA. [7]DEPARTMENTS OF UROLOGY AND PEDIATRICS, SCHOOL OF MEDICINE & HEALTH SCIENCES, THE GEORGE WASHINGTON UNIVERSITY, WASHINGTON, DC, USA. *CURRENT ADDRESS: WELLCOME TRUST SANGER INSTITUTE, WELLCOME TRUST GENOME CAMPUS, CAMBRIDGE, UK*

The influence of schistosomiasis on the host microbiome remains largely unexplored. In order to identify the gastrointestinal microbiome profile of *Schistosoma mansoni*-infected mice, we collected large and small intestinal contents 28 and 50 days post infection (dpi), isolated DNA and performed 16S rRNA gene sequencing. In addition, we analyzed the presence of bacteria in parasites obtained under sterile conditions by portal perfusion of infected mice. Changes were detected in the small intestine microbiome of infected vs. non-infected mice; Allobaculum and Turicibacter present in controls were drastically reduced in infected mice at 28 and 50 dpi, respectively. Conversely, Akkermansia and Oscillibacter increased in the small intestine of mice infected for 28 and 50 days, respectively. Bacteroides were more abundant in the large intestine at 50 dpi. Principal components analysis revealed that the highest dissimilarity between the infected and non-infected mice was evident at day 50 post-infection. At 50 dpi the female worms had been already laying eggs for several days, and many of these eggs presumably had traversed the intestinal wall towards the intestinal lumen. Therefore, changes in the gut microbiome at this stage in comparison to an earlier in the infection might be predicted. In addition, we investigated microbiota associated with schistosomes perfused from infected mice. Strikingly, a worm-associated microbiome comprised of > 60 genera of bacteria, including Acinetobacter was observed. No clear differences were evident between worm-associated microbiomes at days 28 vs. 50 dpi. The worm-associated microbiome was dissimilar to the microbiome of the gastrointestinal tract of the infected mice. Understanding the interaction between the parasite, the host and the microbiome may help elucidate host-parasite interactions and immunopathogenesis.

31. Transcriptional diversity of dendritic cells during the priming of Th2 immune responses in vivo

FRANCA RONCHESE[1]

[1]MALAGHAN INSTITUTE OF MEDICAL RESEARCH, WELLINGTON, NEW ZEALAND

The dendritic cell (DC) signals required for the in vivo priming of IL4-producing T cells are unknown. We used RNA sequencing to characterize DC from skin lymph nodes of mice exposed to two different Th2 stimuli: the helminth parasite Nippostrongylus brasiliensis (Nb), and the contact sensitizer DBP-FITC. Both Nb and DBP-FITC induced extensive but distinct transcriptional changes in DC subsets. Pathway analysis revealed an IFN-I signature unique to DC from Nb-primed mice, and blocking the IFN-I receptor abrogated Th2 development in mice treated with Nb, but not DBP-FITC. Thus the priming of Th2 responses is associated with heterogeneous signatures in DC in vivo, reflecting the diverse strategies through which Th2 immune responses are initiated.

32. Murine miRNAs that post-transcriptionally regulate the TLR- and NLR-mediated signaling pathways are up-regulated in BALB/c mice but down-regulated in C57BL/6 mice during *Litomosoides sigmodontis* infection

JULIA SCHULZ, ACHIM HOERAUF, KENNETH PFARR

INSTITUTE OF MEDICAL MICROBIOLOGY, IMMUNOLOGY AND PARASITOLOGY, UNIVERSITY CLINIC BONN, SIGMUND-FREUD-STR. 25, D-53127 BONN, GERMANY

The genetic background of the host is important in the Th1/Th2 balance in immune response to *Litomosoides sigmodontis* infections. These filarial nematodes successfully establish the full life cycle in susceptible mouse strains such as BALB/c. In contrast, the C57BL/6 strain is less susceptible and eliminates most of the worms before patency. As regulators of post-transcriptional processes, microRNAs (miRNAs) are important in host-pathogen interactions and modulation of immune function. To investigate the role of miRNAs in the regulation of host immunity, differences in the miRNA expression profiles of BALB/c and C57BL/6 strains were analyzed in pleural cavity cells using a PCR-array (SA Bioscience) approach. Several miRNAs: miR-21, miR-155, miR-126 and miR-146 were up-regulated in BALB/c but down-regulated in C57BL/6. These miRNAs are involved in several immune and pathological responses and negatively regulate the TLR- and NLR-mediated signaling pathways NF-kB and AP-1, which also interact with MAPK and TGF-ß/Smad. This work focuses on the characterization of the candidate miRNAs according their impact on the modulation of the host immune response and regarding their regulatory role in signaling pathways by targeting receptor associated signaling molecules as well as functional cytokines and chemokines. Supported by knock-out mice studies we hypothesize that the repressed activity of NF-kB leads to the modulation of IL-6, IL-12, IL-10 and IL-13 levels and reduces the transcription of the IFN-α and -ß genes, which results in a lower proinflammatory immune response. Thus, the up-regulation of specific miRNAs may support the development of the parasite in BALB/c mice. In contrast, the down-regulation of these miRNAs in C57BL/6 mice leads to a higher proinflammatory immune response and control of the worm burden. Consequently, differentially regulated mouse miRNAs in these two backgrounds correlate with different *L. sigmodontis* phenotypes as a result of differential regulation of the immune response.

33. Usage of recombinant antigens improves sensitivity and allows species differentiation in echinococcosis diagnostics

LINDA SCHÖNFELD, THOMAS SCHEPER, WOLFGANG MEYER, JENS MIGUEL WARNECKE

INSTITUTE FOR EXPERIMENTAL IMMUNOLOGY, AFFILIATED TO EIROIMMUN AG, SEEKAMP 31, LUEBECK, GERMANY

Cystic (CE) and alveolar echinococcosis (AE) are infectious diseases caused by the tapeworms *Echinococcus granulosus* and *Echinococcus multilocularis*, respectively. Imaging techniques such as MRI provide initial indications for diagnosis. For species differentiation, blot techniques using recombinant antigens to detect specific antibodies are of increasing significance. We determined the potential of the recombinant specific antigens Em18, Em95 and EgAgB for serological diagnostics of echinococcosis and for differentiation between *E. granulosus* und *E. multilocularis* as causative agent. We tested 329 sera (55 CE, 52 AE, 100 healthy controls, 122 infected with other parasites) for the presence of anti-Echinococcus ssp. specific IgG using a Western blot with electrophoretically separated *Echinococcus multilocularis* metacestode vesicle fluid (EmVF) and 3 membrane chips coated with recombinant *E. granulosus* antigen AgB8 and the *E. multilocularis* antigens Em18 and Em95. Presence and intensity of the bands were automatically evaluated using commercial software (EUROLineScan, Euroimmun). Testing the pre-characterized patient sera revealed a sensitivity of 89% for echinococcosis at a specificity of 100% of the Western Blot and an increased sensitivity of 93% (at 100% specificity) considering the recombinant proteins additionally. A specific algorithm of the EUROLineScan software was developed for species differentiation on the basis of the antibody findings. Considering patients with specific anti-Echinococcus ssp. antibodies in 33/45 of AE patients and 45/52 of CE patients, the causative species was correctly assigned as E. multilocularis and E. granulosus, respectively, by the software. Investigation of a parasite panel showed no cross reactivity of the recombinant antigens while in the Western Blot positive results were obtained in 6 out of 122 samples. The combination of EmVF Western Blot and immobilized recombinant antigens in a single assay (Anti-Echinococcus EUROLINE-WB) improves sensitivity of the diagnostic tool for echinococcosis at constantly high specificity and enables differentiation between the *Echinococcus* subspecies.

34. ILC2-T cell crosstalk during helminth infection

CHRISTIAN SCHWARTZ, ACHILLEAS FLOUDAS, SEAN P. SAUNDERS, EMILY HAMS, PADRAIC G. FALLON

SCHOOL OF MEDICINE, TRINITY BIOMEDICAL SCIENCES INSTITUTE, TRINITY COLLEGE DUBLIN, DUBLIN 2

Innate lymphoid cells are important contributors to type 2 immune responses associated with parasitic infections, allergies and asthma. Previous studies have shown that ILC2s license dendritic cells, express MHC class II molecules and promote Th2 polarization during infections with *Nippostrongylus brasiliensis* or protease allergen challenge. However, it remains unclear, which other factors contribute to the dialogue between ILC2 and CD4 T cells, and whether the crosstalk between T cells and ILC2s contributes to the generation of memory T cells. In particular, the alarmins IL-25, IL-33, and to a lesser extent, TSLP are required for the activation of different ILC2-subsets. IL-25- or IL-33-elicited subsets have been shown to differentially express activation markers including KLRG1, ST2, IL-17RB and IL-7Ra. We identified further differentially expressed activation markers and using alarmin-knockout mice we delineate the cellular and microenvironmental requirements needed for an optimal immune response against *N. brasiliensis* and the generation of memory T cells.

35. *C. elegans* pheromone induces reproductive plasticity

MARK VINEY & BARNEY WHARAM

SCHOOL OF BIOLOGICAL SCIENCES, UNIVERSITY OF BRISTOL, UK

C. elegans produces a pheromone that consists of a complex mixture of ascaroside molecules. This pheromone is used in mate finding and in the induction of dauer larvae. Previously we have shown that there is significant inter-genotype variation in the production of, and sensitivity to, this pheromone. This suggests that a genotype's pheromone can evolve to send precise, genotype-specific information. We have now found a new role for *C. elegans* pheromone – the control of reproductive plasticity, where the pheromone speeds sexual maturity, pre-adult growth rate and gonad proliferation. By comparing the reproductive plasticity-inducing effects of pheromones from a diversity of recently wild genotypes we again find evidence of inter-individual differences in both pheromone production and pheromone sensitivity with respect to reproductive plasticity. (There is also evidence that N2's pheromone is less potent than that of other genotypes.) Our work, paired with recent findings relating to olfaction of food that causes reproductive changes, provide evidence that sensory cues play a pivotal role in regulating nematode reproduction. While these phenomena are described from a free-living species, it would be surprising if the same phenomena did not occur among parasitic nematodes.

36. Excretory secretory products (ESP) from *Fasciola gigantica* induce an M2 macrophage-like phenotype in vivo

YAOYAO ZHANG[1], XUEFANG MEI[1], WEI SHI[1],DONGYING WANG[1] ,WEIYI HUANG[1]

[1]*COLLEGE OF ANIMAL SCIENCE AND TECHNOLOGY, GUANGXI UNIVERSITY*

Macrophages are the body's defensive cells and play important roles in immunity and homeostasis. Macrophages according to its phenotype and the secretion of cytokines can be divided into two types of polarization, the classically activated M1 and alternatively activated M2. M1 macrophages induce the inflammatory response to microbes, mainly display the host's immune function,the body can lead to inflammation of the normal tissue damage.M2 macrophages aim to reduce inflammation and repair tissue.*Fasciola gigantica* is a helminth trematode that migrates through the host tissues until reaching bile ducts where it becomes an adult. In this study, we focused on the effect excretory-secretory products (FgES) on the peritoneal macrophages.So we want to know the interaction between ESP and macrophage.As a begining, BALB/c mice were injected three times per week for 3 weeks with PBS and FgES(200 ug per mouse).Isolated peritoneal macrophages were cultured. After 72 h, supernatants were taken and analysed by NO assay kit. In comparison with the PBS-treated mice,isolated peritoneal macrophages were identified arginine activity by biochemical test.Arg-1, RELMa,Ym-1/2 and iNOS gene expression were measured by RT-PCR in isolated peritoneal macrophages.We found *Fasciola gigantica* infection induces the expression of genetic markers with in peritoneal macrophages that are characteristic of an M2 phenotype: Arg-1, RELMa andYm-1/2. Furthermore, biochemical experiments have proved the result. M2 macrophages are central to the immune response during helminth infection, and the findings in this study provide us with insight into the interaction between *F. gigantica* ES antigens and macrophages.

37. Metabolic profiling and anti-colitic properties of hookworm small molecule extracts

PHURPA WANGCHUK, CATHERINE SHEPHERD, ALEX LOUKAS

AUSTRALIAN INSTITUTE OF TROPICAL HEALTH AND MEDICINE, JAMES COOK UNIVERSITY, CAIRNS, QUEENSLAND, AUSTRALIA

Experimental challenge of human subject with hookworms has been shown to be efficacious in treating numerous inflammatory diseases of the g.i. tract. However, it presents many challenges including apprehension by the patient to readily accept such a radical treatment, safety concerns and regulatory hurdles. Our laboratory has been exploring a more palatable and conventional treatment approach based on the excretory/secretory (ES) molecules released by adult stage hookworms. The proteinaceous component of hookworm ES products has been characterized at the molecular level, and individual proteins with anti-inflammatory properties have been isolated, however the composition and therapeutic potential of small molecules remain unexplored for any helminth parasite. We show here that small molecule extracts derived from both ES products and somatic tissues extracted using both methanol and the mixed solvent hexane:methylene chloride: acetronitrile (1:1:1 v/v)) (HDA) confer protection in a murine model of TNBS colitis. Using gas chromatography mass spectrometry (GCMS) we profiled the metabolomes of these extracts. We identified 24 compounds from the somatic HDA extract, 20 compounds from the somatic methanol extract and 20 compounds from the ES material. The major compounds were free saturated fatty acids and their ester derivatives. Palmitic acid, stearic acid, oleic acid, methyl palmitate and methyl stearate were the major fatty acids present in the active somatic and ES extracts. Since some of these fatty acids have known anti-inflammatory properties, we believe that they are, either alone or in combination through synergistic mechanisms, important contributors in the hookworm'santi-inflammatory armoury.

38. Naturally occurring regulation of human IgE-mediated hypersensitivity by hookworm infection

JAKUB WAWRYZNIAK[1], MOSES ADRIKO[2], EDRIDAH TUKAHEBWA[2], DAVID W DUNNE[1], **SHONA WILSON**[1]

[1]DEPARTMENT OF PATHOLOGY, UNIVERISTY OF CAMBRIDGE, UK [2]VECTOR CONTROL DIVISION, MINISTRY OF HEALTH, UGANDA.

IgE-mediated hypersensitivity is an aggressive reaction believed to have evolved to counter infection by multi-celllular helminths and arthropods, but in the western world it has become synonymous with allergy as opposed to immunity. The long relationship between host and parasite has led to the evolution of powerful immunomodulation absent in the allergic response. Of the helminths, hookworms are some of the best adapted to the human host, capable of potent specific and non-specific immune regulation. In areas where hookworm is endemic, this immune regulation is proposed to provide protection from sensitisation to environmental allergens. For this reason attempts have been made to study regulation of allergen specific responses in rural communities endemic for helminth infection. Mostly concentrating on descriptive analysis of skin-test reactivity and clinical symptoms, these studies are often hindered by the very low prevalence of allergic disease observed in these communities. To counter this, we conducted a case-control study examining regulation at an immunological rather than a clinical level. We selected a cohort of adults resident within 12 villages in Mayuge District, Uganda where transmission of hookworm is persistent despite annual community based mass drug administration. Cases with >1000 hookworm eggs per gramme of faeces were age, sex, village of residence and Schistosoma mansoni infection intensity matched with individuals who had no detectable hookworm eggs. Blood cultures stimulated with schistosome soluble worm antigen (SWA) and dust-mite antigen were set-up to investigate histamine release by basophils. There was no evidence for regulation of SWA-specific histamine release, which was significantly associated with circulating levels of SWA-IgE. However, there was evidence for regulation of dust-mite antigen specific basophil histamine release amongst individuals who had hookworm. The regulation of dust-mite antigen appears to be due to a non-IgG4 mediated de-coupling of IgE from its effector cell response.

39. Dynamics of anti-glycan antibody responses in Schistosoma japonicum-infected rhesus macaques studied by schistosome glycan microarray

YA-YI MICHELLE YANG[1], XIAO HONG LI[2], NIELS-CHRISTIAN REICHARDT[3], R. ALAN WILSON[4], ANGELA VAN DIEPEN[1], CORNELIS H. HOKKE[4]

[1]*LUMC, PARASITOLOGY, LEIDEN*; [2]*MOH NATIONAL INSTITUTE OF PARASITIC DISEASES, SHANGHAI*; [3]*CIC BIOMAGUNE, SAN SEBASTIAN*; [4]*UNIVERSITY OF YORK, CENTRE FOR IMMUNOLOGY & INFECTION, YORK*

Human immunity to the parasitic disease schistosomiasis requires many years of exposure to develop. Unlike humans, rhesus macaques clear an established infection naturally and become immune towards reinfection. In macaques, egg production decreases at 8 weeks post-infection and by week 22, physiological impairment of the worm caused by undefined antibody-mediated processes is observed. Since strong responses are observed against schistosome glycan antigens in human and animal infections, anti-glycan antibodies were studied. Serum IgG and IgM of S. japonicum-infected macaques from in a longitudinal study of 22 weeks were analyzed on a glycan microarray containing a large repertoire of glycans from various life-stages of schistosomes. Additionally, an in vitro schistosomula killing assay was used to investigate the killing potential of infected macaque sera and glycan-directed monoclonal antibodies. Profound increase in IgG was observed 8 weeks post-infection mainly towards glycans that expressed (multi-)fucosylated terminal LDN and LeX motifs. The extent of glycan fucosylation was proportional to its antigenicity. Interestingly, even though many IgG and IgM responses have declined 22 weeks post-infection, IgG towards cercarial O-glycans with highly fucosylated LDN motifs remained. Moreover, macaque serum taken at later infection time points caused more rapid schistosomulae death in vitro than serum from earlier time points. To consolidate this schistosomula killing observed is contributed by the anti-glycan antibodies in macaque serum. We showed that monoclonal antibodies against highly fucosylated LDN motifs were able to kill schistosomula in vitro in a concentration dependent manner, while mAbs against LeX motifs could not. These observations indicate the presence of sustained protective antibodies, possibly against schistosomula surface glycans. Our data also suggests that IgG against highly fucosylated LDN motifs that sustain when worms deteriorate, may be associated with infection clearance and resistance to re-infection in macaques.

NOTES

DELEGATE LIST

LIST OF PARTICIPANTS

Erik	**Andersen**	Northwestern University, Illinois, USA	erik.andersen@northwestern.edu
Jennifer	**Auret**	University of Cape Town	jenniferauret@gmail.com
Allison	**Bancroft**	University of Manchester	allison.j.bancroft@manchester.ac.uk
Robin	**Beech**	McGill University	robin.beech@mcgill.ca
Sasisekhar	**Bennuru**	NIAID/NIH	bennurus@niaid.nih.gov
Rita	**Berkachy**	Imperial College London	r.berkachy14@imperial.ac.uk
Matthew	**Berriman**	Sanger Institute	mb4@sanger.ac.uk
David	**Bird**	NC State University	bird@ncsu.edu
Mark	**Blaxter**	University of Edinburgh	mark.blaxter@ed.ac.uk
Cristin	**Bock**	Freie Universität Berlin	cristin.bock@fu-berlin.de
Bruce	**Bolt**	EMBL European Bioinformatics Institute	bruce.bolt@ebi.ac.uk
Klaus	**Brehm**	University of Wuerzburg	kbrehm@hygiene.uni-wuerzburg.de
Paul	**Brindley**	George Washington University	pbrindley@gwu.edu
Alisha	**Chetty**	University of Cape Town	allychetty@gmail.com
Jim	**Collins**	University of Texas Southwestern Medical Center	JamesJ.Collins@utsouthwestern.edu
Céline	**Cosseau**	Université de Perpignan	celine.cosseau@univ-perp.fr
John	**Croese**	John Cook University	jcroese@bigpond.com
Richard E.	**Davis**	University of Colorado School of Medicine	richard.davis@ucdenver.edu
Benjamin	**Dewals**	University of Liege	bgdewals@ulg.ac.be
Aifang	**Du**	Zhejiang University	afdu@zju.edu.cn
Maria Adelaida	**Duque Correa**	The Wellcome Trust Sanger Institute	md19@sanger.ac.uk
Bart	**Everts**	Leiden University Medical Center	b.everts@lumc.nl
Susanna	**Fleurkens**	ETH Zurich	fleurkens@micro.biol.ethz.ch
Andy	**Fraser**	University of Toronto	andyfraser.utoronto@gmail.com
Spencer	**Gang**	University of California Los Angeles	sgang@ucla.edu
Kathy	**Geyer**	Aberystwyth University	kkg6@aber.ac.uk
Kleoniki	**Gounaris**	Imperial College London	k.gounaris@imperial.ac.uk
Catherine	**Gordon**	QIMR Berghofer Medical Research Institute	Catherine.Gordon@qimrberghofer.edu.au
Melissa	**Govender**	University of Cape Town	millyla579@gmail.com
Warwick	**Grant**	La Trobe University	w.grant@latrobe.edu.au
Richard	**Grencis**	University of Manchester	richard.k.grencis@manchester.ac.uk
Christoph G.	**Grevelding**	Justus-Liebig-University Giessen	christoph.grevelding@vetmed.uni-giessen.de
Christoph	**Grunau**	University of Perpignan Via Domitia	christoph.grunau@univ-perp.fr
Alessandra	**Guidi**	CNR (National Research Council)	alessandra.guidi@ibc.cnr.it

Bruno	**Guigas**	Leiden University Medical Center	b.g.a.guigas@lumc.nl
Steffen	**Hahnel**	Justus Liebig University Giessen	steffen.hahnel@vetmed.uni-giessen.de
William	**Harnett**	University of Strathclyde	w.harnett@strath.ac.uk
Wiebke	**Hartmann**	Bernhard Nocht Institute for Tropical Medicine	hartmann@bni-hamburg.de
Shannon	**Hedtke**	La Trobe University	S.Hedtke@latrobe.edu.au
William	**Horsnell**	University of Cape Town	wghorsnell@gmail.com
Karl	**Hoffmann**	Aberystwyth University	krh@aber.ac.uk
Cornelis	**Hokke**	Leiden University Medical Center	c.h.hokke@lumc.nl
Kevin	**Howe**	EMBL European Bioinformatics Institute	kevin.howe@wormbase.org
Min	**Hu**	Huazhong Agricultural University	mhu@mail.hzau.edu.cn
Weiyi	**Huang**	Guangxi University	wyhuang@gxu.edu.cn
Vicky	**Hunt**	University of Bristol	V.L.Hunt@bristol.ac.uk
Sophie	**Jarriault**	IGBMC, Strasbourg	sophie.jarriault@igbmc.fr
Malcolm	**Kennedy**	University of Glasgow	malcolm.kennedy@glasgow.ac.uk
Anna	**Kildemoes**	University of Copenhagen	amok@sund.ku.dk
Marije	**Kuipers**	Leiden University Medical Center	m.e.kuipers@lumc.nl
Dominik R	**Laetsch**	University of Edinburgh	dominik.laetsch@gmail.com
Graham	**Le Gros**	Malaghan Institute of Medical Research	glegros@malaghan.org.nz
Nicole	**Liachko**	Veterans Affairs Puget Sound Health Care System	nliachko@uw.edu
Eva	**Loffredo Verde**	Technische Universität München	eva.loffredo-verde@tum.de
James	**Lok**	University of Pennsylvania	jlok@vet.upenn.edu
P'ng	**Loke**	New York University	Png.Loke@nyumc.org
Alex	**Loukas**	James Cook University	alex.loukas@jcu.edu.au
Philip	**LoVerde**	University of Texas, San Antonio	loverde@uthscsa.edu
Zhigang	**Lu**	Justus Liebig University Giessen	Zhigang.Lu@bio.uni-giessen.de
Karen	**McCulloch**	La Trobe University	K.McCulloch@latrobe.edu.au
Mary	**MacLean**	University of Georgia	mjmac28@uga.edu
Rick	**Maizels**	University of Glasgow	rick.maizels@glasgow.ac.uk
Francesca	**Martini**	Malcisbo AG, ETH Zürich	fmartini@ethz.ch
Laura	**Myhill**	University of Copenhagen	lauramyhill@sund.ku.dk
Peter	**Nejsum**	University of Copenhagen	pn@sund.ku.dk
Gyaviira	**Nkurununngi**	MRC (UGANDA UNIT) & LSHTM	gyaviira.nkurununngi@mrcuganda.org
Thomas	**Nutman**	National Institutes of Health, Bethesda, USA	tnutman@niaid.nih.gov
Christian	**Owusu**	Wellcome Trust Sanger Institute	co7@sanger.ac.uk

John	**Parkinson**	Hospital for Sick Children	jparkin@sickkids.ca
Edward J.	**Pearce**	Max Planck Inst. & University of Freiburg	Pearceed@ie-freiburg.mpg.de
Michael	**Povelones**	University of Pennsylvania School of Veterinary Medicine	mpove@vet.upenn.edu
Clarissa	**Prazeres da Costa**	Technische Universität München	clarissa.dacosta@tum.de
Daniel	**Price**	Moredun Research Institute	dan.price@moredun.ac.uk
Anna	**Protasio**	Gurdon Institute, University of Cambridge	ap6@sanger.ac.uk
Lorna	**Proudfoot**	Edinburgh Napier University	l.proudfoot@napier.ac.uk
Thomas	**Quack**	Justus-Liebig-University, Gießen	thomas.quack@vetmed.uni-giessen.de
Gabriel	**Rinaldi**	Wellcome Trust Sanger Institute	gr10@sanger.ac.uk
Franca	**Ronchese**	Malaghan Institute of Medical Research	fronchese@malaghan.org.nz
Giovina	**Ruberti**	CNR (National Research Council)	giovina.ruberti@cnr.it
Irma	**Schabussova**	Medical University of Vienna	ischabuss@gmail.com
Linda	**Schönfeld**	EUROIMMUN AG	l.schoenfeld@euroimmun.de
Julia	**Schulz**	University Clinic Bonn	julias3@gmx.de
Christian	**Schwartz**	Trinity College Dublin	christian.schwartz@tcd.ie
Murray	**Selkirk**	Imperial College London	m.selkirk@imperial.ac.uk
Katie	**Smith**	Cardiff University and University of Cape Town	smithk28@cardiff.ac.uk
Hermelijn	**Smits**	Leiden University Medical Center	h.h.smits@lumc.nl
Ralf	**Sommer**	Max Planck Institute for Developmental Biology, Germany	ralf.sommer@tuebingen.mpg.de
Javier	**Sotillo**	James Cook University	javier.sotillo@jcu.edu.au
Adrian	**Streit**	Max Planck Institute for Developmental Biology	adrian.streit@tuebingen.mpg.de
Irma	**Van Die**	VU University Medical Center	im.vandie@vumc.nl
Jaap J	**van Hellemond**	Erasmus University Medical Center	j.vanhellemond@erasmusmc.nl
Mark	**Viney**	University of Bristol	Mark.Viney@bristol.ac.uk
David	**Vöhringer**	University Clinic Erlangen	David.Voehringer@uk-erlangen.de
Dongying	**Wang**	Guangxi University	215500278@qq.com
Jianbin	**Wang**	University of Colorado School of Medicine	Jianbin.Wang@ucdenver.edu
Phurpa	**Wangchuk**	James Cook University	phurpa.wangchuk@jcu.edu.au
Emily	**White**	University of Manchester	emily.white@manchester.ac.uk
Madeleine	**White**	University of Glasgow	Madeleine.White.2@glasgow.ac.uk
Shona	**Wilson**	University of Cambridge	sw320@cam.ac.uk
Ya-Yi Michelle	**Yang**	Leiden University Medical Center	y.m.yang@lumc.nl
Yi	**Yang**	Zhejiang University	yangyi0607@zju.edu.cn

NOTES

NOTES