Trends in Parasitology

CellPress

TrendsTalk

Hydra 2022: return of the interactive conference on helminth parasitology after the pandemic

Caitlin M. McManus [1,*,@], Tiffany Bouchery [2,*,@], Mona Suleiman, [3,*,@] Anna O. Kildemoes [4,*,@], Annabel Ferguson [5,*], Tao Wang [6,*], Conor M. Finlay [7,*,@], Ryan Chan [8,*,@], Tess Renahan [9,*], Ananya Mukundan [10,*], Gyaviira Nkurunungi [11,*,@], and Sarah D. Bobardt [12,*]

The Hydra helminth conference series, formally titled 'Parasitic Helminths: New Perspectives in Biology and Infection', has been serving the community of helminth research as a platform for interactive discussions and collaboration opportunities since its original launch in 1997. After a break in 2020 and 2021 due to the pandemic, this long-awaited conference returned at the Bratsera Hotel in Hydra, Greece, from August 28 to 2 September this year, with 100 delegates from 19 countries across the globe. Opening with Richard Davis' keynote lecture, the conference included 12 wide-ranging presentation sessions and two busy poster sessions, covering all major areas of helminth research. In this *TrendsTalk*, we invite 12 young scientists and early-career researchers to highlight the exciting science presented in these sessions. Stay tuned for details of the Hydra 2023 conference scheduled for September 3–8 next year (https://hydra.bio.ed.ac.uk/)!

Caitlin M. McManus

Session 1: helminth infections – big pictures

The first session on the Greek island of Hydra (Ύδρα) focused on the big picture of helminth infections, covering both human and animal helminth infections. The keynote speaker of the session, Meta Roestenberg (Leiden University Medical Center), introduced the controlled human helminth trials currently undertaken in The Netherlands to discover new treatment targets, explore the development of immunity to helminth infection, and test the efficacy of potential vaccines. Meta and her team perform controlled infection with hookworm *Necator americanus* and platyhelminth *Schistosoma mansoni* and have been testing the effect of single-sex infection with *S. mansoni* and the response to repeated infection with *N. americanus*. Next, Francesco Vacca (Malaghan Institute of Medical Research) presented an overview of the peripheral immunological changes that occur during the first year of controlled human hookworm infection; from changes in the immune populations in the blood, to microbiota in the feces and the physiology of the infected gut and the worms who reside there. Tatiana Küster (Boehringer Ingelheim Vetmedica) introduced the major veterinary parasite *Dirofilaria immitis* (heartworm) that can infect both canine and feline hosts and has a high mortality rate. Tatiana investigates new treatment strategies for heartworm to combat increasing resistance to the only effective anthelmintic (macrocyclic lactones) in *D. immitis* populations. Finally, Maria Yazdanbakhsh (Leiden University Medical Center) rounded off the session with a presentation on the role of environment in vaccine responses. Maria compared the immune responses of individuals living in rural versus industrialized areas of helminth endemic regions as well as those from non-endemic areas. Together, these presentations gave a fantastic introduction to human helminth infection, both natural and controlled, as well as covering the emerging anthelmintic resistance in the veterinary field.

Tiffany Bouchery

Session 2: immune phenotypes

With a focus on immune phenotypes, the second session illustrated a recent turn in the immunoparasitology field, where our models and questions are now encompassing more complex life traits. Andrew MacDonald (University of Manchester) and Hermelijn Smits (Leiden University Medical Center) both reported that mixed-sex schistosome infection (in which eggs are released), but not single-sex infection, causes a microbiome change without bacterial translocation, despite tissue damage. Interestingly, Andrew's laboratory shows that transfer of feces from infected mice (with eggs removed) to germ-free mice is sufficient to recapitulate the parasite-induced interleukin (IL)-4, IL-10, and IL-17 upregulation in mesenteric lymph nodes and colon. Hermelijn's laboratory reports, after fecal transfer, induction of regulatory B cells (Bregs) and regulatory T cells (Tregs) in the spleen that are sufficient to decrease allergic asthma in a house dust mite mouse model. Benjamin Dewals (University of Liège) built upon his previous work on helminth-induced expansion of virtual memory CD8 T cells (Tvm). By conducting single-cell RNA sequencing of infected spleen, his laboratory has identified that IL-4-activated Tvm expressed a specific surface receptor, up to this point considered restricted to B cells. Upregulation of this receptor in IL-4-induced Tvm is associated with the expression of effector molecules such as granzyme A. William Horsnell (University of Cape Town) reported maternal protection against helminths through nursing from a dam with prior exposure, increasing CD4 T cells in pups. Surprisingly, protection is not antibody-mediated but rather occurs by mother-to-pup transfer of cells. IL4R deficiency in the nursing dam is sufficient to limit goblet and tuft cell expansion in the pup during infection. Low vaccine effectiveness is common in helminth-endemic tropical countries. Gyaviira Nkurunungi (MRC/UVRI and LSHTM) found higher vaccine-specific immune responses in an urban Ugandan setting than in a schistosomiasis-endemic rural setting. High-dimensional immune characterization highlighted urban–rural differences and a subtle impact of praziquantel treatment on prevaccination cellular phenotype and function. Similarly, treatment and urbanicity were associated with decreased levels of intestinal inflammation markers.

Mona Suleiman

Keynote lecture and Session 3: genomes and cells

The keynote lecture and the third session consisted of five fascinating talks about the role and function of the genome and cells in influencing parasitism and host genes. A challenge to the notion of genome stability and integrity in organisms was first observed and described in ascarid parasitic nematodes where portions of chromosomes are eliminated. Programmed DNA elimination eliminates sequences from the germline genome to generate a somatic genome. The elimination of germline-expressed genes to form the somatic genome permanently silences these genes in somatic tissues of the parasites. Richard Davis (University of Colorado) first introduced this topic in the opening keynote lecture on Sunday evening. A major focus in his laboratory has been to develop and use molecular methods to investigate atypical mechanisms of gene expression in helminths. In his talk, he emphasized that specific repetitive and unique sequences (including ~1000 genes) are reproducibly lost during the DNA elimination process that generates the somatic genome in *Ascaris*. Both specific DNA breaks (internally in chromosomes as well as at the ends of all chromosomes) and dynamic changes in centromeric histone CENP-A and centromeres/kinetochores in chromosomes define which portions of chromosomes are retained and lost. Following Richard' talk, Jianbin Wang (University of Tennessee) discussed the establishment of the free-living nematode *Oscheius tipulae* as a model to study DNA elimination in the third session. Through genomics and molecular biology, he highlighted that DNA elimination of chromosome ends occurs during early embryogenesis. He compared these

mechanisms with *Ascaris*, but also showed how *O. tipulae* behaves differently and contains a conserved sequence motif that is required for DNA elimination.

David Bird (North Carolina State University) discussed the mechanisms underlying parasitic interactions between the root-knot nematode, *Meloidogyne hapla*, and plant development. His main question 'what nematode genes influence expression of host genes' was answered by exploiting the facultative, meiotic parthenogenetic reproductive mode of *M. hapla* and identifying several pleiotropic loci that modulate the expression of multiple plant genes. Next, Teresa Attenborough (Wellcome Sanger Institute) described an approach to build a single-cell atlas for the first free-living stage of *S. mansoni* – the miracidium larva. She showed that a miracidium is composed of ~365 cells, and there are 19 transcriptionally distinct cell populations that include stem and differentiated somatic cell types, some of which are specific larval features such as the ciliary plates. Investigating these cells may lead to a deeper understanding of the fundamental biology of *S. mansoni* and, therefore, parasitism. The final talk of the session was carried out by Friederike Sonnet (Leiden University Medical Center). She illustrated the potential of immune cell profiling in controlled human hookworm infections to understand hookworm-induced immune-modulations and the development of protection following repeated rounds of challenge and treatment. Overall, this was a well-presented, insightful session that showed an array of different techniques used by genome and cell analysis to examine the biology of parasites.

Anna O. Kildemoes

Session 4: host–parasite interactions

The host–parasite interaction session was kicked off in the realm of plant-parasitic nematodes by Sebastian Eves-van den Akker (University of Cambridge). A truly high-throughput semiautomated phenotyping pipeline involving custom low-cost 3D printed petri dish-imaging machines and artificial intelligence (AI) image analyses of 0.6 million *Arabidopsis thaliana* plants infected with the cyst nematode *Heterodera schachtii* has been developed by his team and collaborators (Ji Zhou, NIAB). In combination with genetic modifications, these tools will revolutionize the identification of plant genes involved in infection and hence progress towards improved pest control and food security. Taking the stage next was Tess Renahan (Max Planck Institute for Biology Tübingen) who shared insights on tripartite relationships of insect–nematode–bacterial interactions and phenotypic plasticity in an ecological context. Based on field experiments, she discussed effects of population density and dispersal events of the necromenic nematode *Pristionchus pacificus*. A nematode stage-specific pheromone is involved in deciding fate as a predatory or bacterivorous form in a density-dependent manner. Changing the setting from ecological context to chronic intestinal helminth infections, Marta Campillo Poveda (University of Glasgow) and Danielle Karo-Atar (McGill University) shared insights on molecular mechanisms behind intestinal barrier function and epithelial programming during helminth infections. Through comparison of mice infected with *Nippostrongylus brasiliensis* and *Heligmosomoides polygyrus,* Marta discussed the importance of induction of chemosensory cells in parasite expulsion. Excretory/secretory (ES) products from *H. polygyrus* or L3 larvae can suppress genes and change morphology of the chemosensory cell compartment in organoids underlining the parasite's capacity to actively change the intestinal environment beyond immunomodulation. In the final talk of the session, Danielle elegantly demonstrated how adult *H. polygyrus* worms reprogram the intestinal stem cell niche into a fetal-like state both *in vivo* and in organoid cultures. She highlighted the involvement of oxidative stress induced by *H. polygyrus* in initiating this fetal reversion and

expansion of clusterin-expressing revival stem cells. Finally, she discussed evidence indicating that fetal reversion of the epithelium favors the chronicity of infection and essentially counters the induction of the host type 2 immune response.

Annabel Ferguson

Session 5: immune modulators

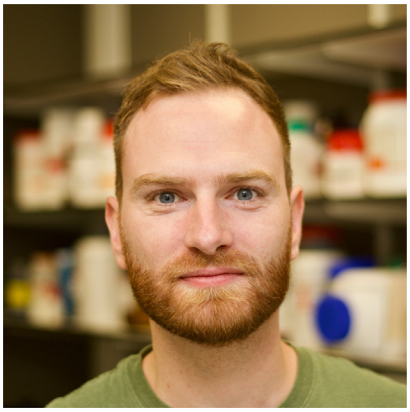
The fifth session on immune modulators showcased the repertoire of ES products from parasitic helminths, highlighting some surprising mechanisms of immune suppression and metabolic regulation that could have therapeutic benefits. Alex Loukas (James Cook University) discussed results of a human-hookworm Phase 1 randomized controlled trial. Skin administration of infective hookworm larvae to human subjects with metabolic syndrome was well tolerated and associated with improved insulin sensitivity. Experiments in mice demonstrated that ES products protect against metabolic disorder, and ongoing work will screen the effects of individual ES molecules. Roland Ruscher (James Cook University) identified three lead compounds that elicit protection from colitis in a mouse model by screening 91 hookworm ES molecules derived from a cell-free expression system. These lead compounds are in distinct families but share lipid/retinol binding characteristics and reduced inflammatory cytokine secretion by stimulated human gut T cells *ex vivo*. William Harnett (University of Strathclyde) discussed protection against rheumatoid arthritis by phosphorylcholine-containing protein ES-62 secreted by *Acanthocheilonema viteae*. ES-62 're-wires' the epigenetic landscape of pathogenic synovial fibroblasts (SFs) to a functional state that resembles nonpathogenic SFs, but with a distinct DNA methylation pattern. Ananya Mukundan (University of Pittsburgh) revealed striking structural details of a transforming growth factor-beta (TGF-β) mimic family of ES products from *H. polygyrus* (Hp-TGM), which potently induce Tregs differentiation via TGF-β receptor binding. Hp-TGM sequences are distinct from mammalian TGF-β yet elicit the same response by binding to the same receptors. Protein structure analysis found that TGM-1, TGM-4, and TGM-6 bind to the same receptor residues as TGF-β via convergent evolution of binding domains. Henry McSorley (University of Dundee) discussed the Hp ES product family, HpARI, and their opposing influences on host immunity. While HpARI2 suppresses the function of 'alarmin' cytokine IL-33, HpARI3 increases IL-33 responses. A key difference between the two is that HpARI2 binds both DNA and IL-33, preventing release, while HpARI3 binds only IL-33, increasing its half-life.

Tao Wang

Session 6: helminth development

The session on helminth development opened with a keynote lecture by Phillip Newmark (University of Wisconsin-Madison) with an exciting study on planarian sexual development. He described his laboratory's ongoing work to identify signals that regulate regeneration of planarian germ cells from the animal's somatic stem cells. James Collins (University of Texas Southwestern Medical Center) described his team's ground-breaking discovery that the dipeptide β-alanyl-tryptamine (BATT) is the male-derived signal that controls virgin female schistosome sexual development. The combined work of the Collins and Newmark laboratories demonstrates how comparative studies of free-living and parasitic flatworms can lead to unexpected and novel biological insights. Anne Lespine (INRAE) demonstrated that the nuclear receptors DAF-12 of *D. immitis* and *Brugia malayi* can be specifically activated by Δ4-dafachronic acid (DA, a natural ligand of DAF-12) containing mammalian sera. RNAseq data showed a switch-off of DA synthesis at the infective stage of filarial nematodes, highlighting the indispensable role of host serum in resumption of filarial development. Adrian Streit (Max Planck Institute for Biology Tübingen) explored how and when male-determining

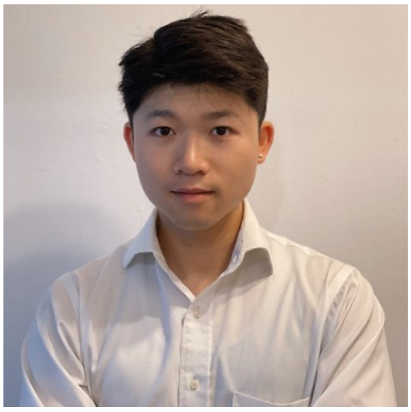
sperm is eliminated during sexual reproduction in free-living *Strongyloides* spp.. Using differential interference contrast (DIC) and electron microscopy, immunohistochemistry, and fluorescent *in situ* hybridization, it was shown that, although nullo-X spermatocytes are originally formed during meiosis, virtually all mature sperm have an X chromosome. In addition, sperm-like structures with no DNA (but with proteins) were observed, suggesting that spermatocytes without an X-chromosome might undergo cell programming and turn into these structures. Taking a different approach, Gabriel Rinaldi (Wellcome Sanger Institute, currently Aberystwyth University) described an ongoing project to characterize the molecular basis underlying the establishment of schistosome sexual dimorphism during the early intramammalian development. Despite his demonstration that sexual dimorphism is morphologically established *in vivo* between day 13 and 17 postinfection, single-cell transcriptomics suggest that a sexual dimorphic transcriptome may be already established in earlier stages. A combination of new genomic and molecular technologies will provide a novel approach to understand schistosome development.



Conor M. Finlay

Session 7: immune cells

The session on immune cells explored divergent dynamics of leukocytes in four different helminth infections. Maaike Scheenstra (Leiden University Medical Center) showed data on two immunomodulators from *S. mansoni*, the well-known Omega-1 and the novel smX protein. Both molecules targeted dendritic cell (DC) function, but in different ways; Omega-1 prevented DC trafficking to draining lymph nodes while smX modulated metabolic pathways. Next, Caitlin McManus (University of Glasgow) presented an important single-cell RNA-sequencing dataset. *H. polygyrus* is a natural nematode parasite of mice that has long been known to induce profound immune regulation. Indeed, it has been the source of multiple novel immunomodulatory molecules that promote Treg development. Caitlin's dataset contained T cells from *H. polygyrus*-infected 'susceptible' C57BL/6 and 'partially resistant' BALB/c mice which captures the full gambit of T cells from Tregs to T helper 2 (Th2) cells. This dataset will be useful to probe T cell biology in response to infection. Matthew Darby (University of Cape Town) provided important information about how platelets regulate immune-mediated tissue damage mediated by the transmigration of *N. brasiliensis* through the lung. Infection increased neutrophil–platelet interactions, inducing altered activation in neutrophils after platelet binding. Platelet depletion increased neutrophil-dependent tissue damage. Mark Siracusa (Rutgers University) shared an early look at an impressive story of neurotoxicity caused by *Trichinella spiralis.* Infection led to the detection of parasite protein transcripts in the brain despite larva being undetectable in the brain. Preventing monocyte recruitment induced lethality that was associated with the production of inflammatory cytokine production by activated microglia and peripheral cachexia, suggesting a surprising and complex interplay of mononuclear phagocytes in the brain during peripheral nematode infection with global effects.

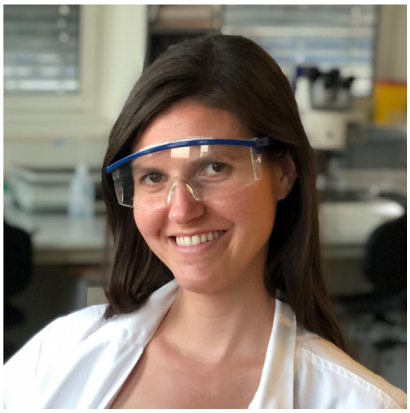


Ryan Chan

Session 8: drugs and drug targets

In the first talk of the session on drugs and drug targets, Andrew Fraser (University of Toronto) presented his research on rhodoquinone-dependent metabolism as targets for new anthelmintics. He explained the importance of rhodoquinone in the unique anaerobic metabolism of soil-transmitted helminths and their ongoing search for potential inhibitors using a combination of *in vivo* and *in silico* approaches. His team have currently identified four enzymes with unique active sites that could be targeted without affecting the host. Plant-parasitic nematodes destroy billions of dollars' worth of food

and crops yearly. Jessica Knox (University of Toronto) addressed this global issue in her work on bioactivated nematicides for the selective control of plant-parasitic nematodes. She introduced Cyproside-3, a novel nematicide that is broadly active across many nematode species. Her work postulated that the nematode-selective activity of Cyproside-3 is achieved via nematode-specific metabolic conversion into a lethal product. Robin Beech (McGill University) uncovered potential novel drug targets through a new class of neurotransmitter receptors in nematodes. He explained the interesting subunit composition of pentameric ligand-gated ion channels and the selective pressure leading to their evolution. Robin explores a new receptor related to ACR-16 with characteristics of a sensor. Sina Bohnacker (Helmholtz Center Munich) presented her research on *H. polygyrus* glutamate dehydrogenase and the regulation of type-2 immunity. She specifically showcased the ability of *H. polygyrus* glutamate dehydrogenase to modulate macrophage metabolism, especially the arachidonic acid metabolic pathway, and proposed that it may be used to develop novel immunomodulatory strategies for the treatment of inflammatory diseases. Klaus Brehm (University of Würzburg) scrutinized the current treatment against alveolar echinococcosis and stressed the parasitostatic limitations of albendazole. He suggested and reviewed a combination therapy of albendazole complemented with triclabendazole to target both the differentiated cells as well as the stem cells of the *Echinococcus* parasite.



Tess Renahan

Session 9: helminths, microbes, vectors

From leaping nematodes summersaulting in the air to sweet injection-based revenge on universally loathed mosquitoes, the enchanting 'Helminths, microbes, vectors' session was filled with intriguing insights and images that captivated the audience. The flying worm teased as an entertaining glimpse into Adler Dillman's (University of California Riverside) exploration of entomopathogenic nematode host-seeking and attachment behaviors, though his illuminating talk centered on how deep studies of *Steinernema carpocapsae* have enabled the utilization of this worm and insects as a model system to understand human parasitic nematodes, focusing on the multifaceted ES products that both damage hosts and trigger host immune responses. Typically, these ES products are extracted from infective juveniles *in vitro*, but the laboratory questioned whether these collections are reflective of what happens *in vivo*, and determined this with single-worm transcriptomics. Now armed with congruous crude products, the biologists tested the immunomodulatory influence of ES proteins conserved across parasitic nematodes. In establishing a model host, Adler turned to a classic: *Drosophila melanogaster*. The flies were injected with one of three protein families of interest: FAR, sPLA2, and ShK domain-containing. Overall, infected flies displayed decreased survival and diminished resistance to bacterial pathogens; lipid signaling is a suspected immunity player. Michael Povelones' (University of Pennsylvania) depiction of blood-sucking *Aedes aegypti* and its unfavorable spreading of heartworm disease-causing *D. immitis* to our beloved canine friends kept the spectators engrossed. Endeavoring to curb dirofilariasis, Michael investigates potential disturbances to nematode growth in the malevolent mosquito vector. In a rare instance of satisfying vengeance, his team injected mosquitoes, but with double stranded (ds)*Cactus* RNA to observe whether Toll pathway activation affected the infesting worms. Excitingly, young larvae in the Malpighian tubules became developmentally stunted. By contrast, more advanced L3 in the proboscis were not affected. The worms' ability to persist was hypothesized to be linked to ES products; worm proteins found in mosquito hemolymph are being inspected as imperative immunomodulators. We eagerly await updates from both worm scientists.

Ananya Mukundan

Session 10: molecular biology

The last full day of the conference started off with the session on molecular biology, which was centered around understanding the role of soluble (s)RNA on parasite pathology. The first speaker of the session, Coleen Murphy (Princeton University), astounded with a narrative into mechanisms of transgenerational epigenetic inheritance (TEI) in *Caenorhabditis elegans*. She showed that *C. elegans* avoidance of the pathogenic strain of *Pseudomonas aeruginosa* (PA14) is vertically transmitted until the F4 generation and can be transferred horizontally by exposing untrained worms to the lysate of the grandprogeny (F2) of trained mothers. This avoidance is mediated by a PA14 sRNA, P11, and further regulated by the Cer1 transposon, a 'gut to germline to neuron' model for *C. elegans* TEI. Mona Suleiman (University of Bath) highlighted the importance of characterizing parasitic sRNAs by identifying a group of piwi-interacting (pi)RNA-like sRNAs targeting transposons in *Strongyloides ratti* that were upregulated in parasitic females but not in free-living female stages. As *S. ratti* does not express piRNAs, Mona's work clearly demonstrates a remarkable adaptation by the parasite to its own lack of piRNA, thus allowing for alternative regulation of transposable elements in the parasitic stage. Denis Voronin (National Institutes of Health, USA) presented mostly unpublished work on the role of parasite miRNA in the mutualistic interactions between the intracellular bacterium, *Wolbachia*, and its host, *Brugia malayi*. Healthy mutualistic association is partly dependent on miRNA-regulated autophagy, an intracellular self-degradative process that controls the bacterial population size in parasite cells. Methods to control these *Wolbachia* populations will potentially lead to new breakthroughs in antifilarial treatments. The final speaker, Thomas Spangenberg (Merck KGaA) tackled miRNA from a different perspective by developing methods to target miRNA-10 stemming from *Schistosoma* extracellular vesicles. Utilizing the secondary structure of pre-miRNA-10 to determine a suitable binding region, the team discovered a compound that can restore NF-kB activity previously downregulated by miRNA-10. These talks highlighted how sRNAs are vital to understanding host–parasite interactions, parasite behavior, and how targeting them can be key for antiparasitic therapeutics.

Gyaviira Nkurunungi

Session 11: helminth interactions

Thewarach Laha (Khon Kaen University) kicked off the session by describing how CRISPR/Cas9-mediated gene knockout of the *Opisthorchis viverrini* granulin-like growth factor (*Ov-grn-1*) results in malignancy suppression in hamsters. Infection with *O. viverrini* ES products carrying mutated *Ov-grn-1* resulted in reduced cholangiocyte hyperproliferation and reduced periductal and liver fibrosis, compared with infection with wild-type *O. viverrini* ES products. Foe turned friend, as the potentially beneficial role of *Ov-grn-1* was demonstrated by Michael Smout (James Cook University). His team developed a granulin-based peptide, GP4a, and explored its wound-healing properties. Experiments utilizing surgically inflicted wounds in mice, a human 3D *ex vivo* skin-wound-healing model, scratch healing assays, and trials in swine, all demonstrated that GP4a accelerates wound healing. Switching gears to trans-kingdom control of helminth development, Amicha Robertson (New York University) reported that *Staphylococcus aureus* induces hatching of *Trichuris muris* eggs *in vitro*. Physical contact between these nonfimbriated bacteria and egg poles was important; however, egg polar contact was not a hatching prerequisite. Hatching was inducible only with live bacteria and accelerated at higher bacterial concentrations. Katie Hildersley (Moredun Research Institute) presented results from immunohistochemical (IHC) labeling of ovine abomasa, and single cell (sc)RNA-seq of abomasal cells following *Teladorsagia*

circumcincta infection. She identified abomasal POU2F3+ cells that expanded similarly to murine tuft cells, and found cross-species conservation between some ovine and murine functional and structural tuft cell genes. Differences were shown too, for example, in some tuft cell surface receptors. To conclude this session, we heard from Ruby White (University of Edinburgh) about her work on helminth extracellular vesicles (EVs) and their role in immunomodulation. She used a 2D gastrointestinal organoid model to show that *H. polygyrus bakeri* EVs are taken up by intestinal epithelial cells and downregulate host genes involved in the response to intestinal nematodes, such as antimicrobial peptide genes.

Sarah D. Bobardt

Session 12: immunology and pathology

In the final session of the conference, the speakers each discussed novel approaches to understanding the immune response to helminth infection and associated tissue pathology. Meera Nair (University of California Riverside) began the session discussing immunomodulation by lipid-derived endocannabinoids, produced by both the mouse host and the parasitic nematode *N. brasiliensis.* Cocultures revealed that macrophages and eosinophils isolated from *N. brasiliensis*-infected lungs lacking the endocannabinoid receptor CBR1 had increased binding to larval parasites. Endocannabinoid treatment also reduced expression of the M2 macrophage gene Relmα in a CBR1-dependent manner, indicating that endocannabinoids regulate macrophage activation and behavior. Single-worm RNA-seq of *N. brasiliensis* life-cycle stages revealed that endocannabinoid genes were expressed highest in infectious larval stage 3. High-resolution sequencing with Hi-C of the *N. brasiliensis* genome has been completed, which will improve *N. brasiliensis* functional analyses. The next two speakers focused on key players in the host immune response to nematode infection. Tiffany Bouchery (Swiss Tropical and Public Health Institute) demonstrated that hookworm infection activates epithelial cells in the lung. Conor Finlay (University of Manchester, currently Trinity College Dublin) evaluated the influence of mouse genotype on macrophage programming in the pleural space. Shifting from mice to human pathogenic nematodes, Paul Chapman (QIMR Berghofer Medical Research Institute) discussed a Phase 1 clinical trial that treated patients with attenuated (infertile) hookworm larvae in the first-ever live-worm vaccine trial. These larvae did cause significant dermal reactions and helped to protect against future challenge infections, demonstrating their effectiveness in engaging the immune system. Finally, Simon Babayan (University of Glasgow) continued the discussion on the helminth vaccines by exploring potential causes of poor response to vaccination in lambs and in wild rodents. Through machine learning and causal inference, complex determinants of vaccine response, such as the age, diet, and prior helminth infection were evaluated, which could be used to improve the overall vaccine response of a population. Altogether these talks explored how our understanding of the interaction between worms and the immune system can be harnessed to identify novel therapeutics and develop effective vaccines against helminth infection.

[1]School of Infection and Immunity, the University of Glasgow, Glasgow, UK
[2]Hookworm Immunobiology Group, Swiss Tropical and Public Health Institute, University of Basel, Basel, Switzerland
[3]University of Bath, Bath, UK
[4]Leiden Parasite Glycobiology Group, Department of Parasitology, Leiden University Medical Center (LUMC), Leiden, The Netherlands
[5]Department of Pathobiology, University of Pennsylvania, Philadelphia, PA, USA
[6]Department of Veterinary Biosciences, Melbourne Veterinary School, The University of Melbourne, Melbourne, Australia
[7]Trinity Translational Medicine Institute, Trinity College Dublin, The University of Dublin, Dublin, Ireland
[8]McGill University, Montreal, Quebec, Canada
[9]Max Planck Institute for Biology, Tübingen, Germany
[10]Department of Molecular Biophysics and Structural Biology, School of Medicine, University of Pittsburgh, Pittsburgh, PA, USA

[11]Immunomodulation and Vaccines Programme, MRC/UVRI and LSHTM Uganda Research Unit; Department of Infection Biology, London School of Hygiene and Tropical Medicine, London, UK
[12]Division of Biomedical Science, School of Medicine, University of California Riverside, Riverside, CA, USA

*Correspondence:
Caitlin.McManus@glasgow.ac.uk (C.M. McManus), tiffany.bouchery@swisstph.ch (T. Bouchery), ms3056@bath.ac.uk (M. Suleiman), akildemoes@lumc.nl (A.O. Kildemoes), aaf6@pennmedicine.upenn.edu (A. Ferguson), tao.wang1@unimelb.edu.au (T. Wang), cofinlay@tcd.ie (C.M. Finlay), Ryan.chan3@mail.mcgill.ca (R. Chan), tess.renahan@tuebingen.mpg.de (T. Renahan), anm276@pitt.edu (A. Mukundan), Gyaviira.Nkurunungi@mrcuganda.org (G. Nkurunungi), and sboba003@ucr.edu (S.D. Bobardt).
@Twitter: @CaitlinMMcManus (C.M. McManus), @tiffanyBouchery (T. Bouchery), @monaaaa_10 (M. Suleiman), @akildemoes (A.O. Kildemoes), @Conorisco (C.M. Finlay), @RyanHChan (R. Chan), and @GyavN (G. Nkurunungi).

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