

Multidisciplinary integrated approaches to understand evasion of host immune responses by pathogens

Wednesday, 20 June 2012
The Penridge Suite, 470 Bowes Road, London N11 1NL

Infectious disease are still a major cause of morbidity and mortality worldwide. Successful treatment and prevention are still hampered by insufficient understanding of the subtle interactions that govern the infectious processes. Evasion of the natural or vaccine-induced immune response is often at the basis of the onset and escalation of disease and can also result in the persistence of the pathogen in chronic infections. This EuroSciCon meeting will be a premier forum for the presentation of cutting-edge research on key mechanisms used by different classes of pathogens to evade host innate and acquired immunity. The meeting will contribute to steer the course of future research into more rational measures to prevent disease in humans and animals.

Meeting Chair: Dr Pietro Mastroeni, Cambridge University, UK

This event has CPD accreditation and will have a discussion panel session.

On registration you will be able to submit your questions to the panel that will be asked by the chair on the day of the event

- 9:00 – 9:45 Registration
- 9:45 – 10:00 **Introduction by the Chair:** Dr Pietro Mastroeni, Cambridge University, UK
- 10:00 – 10:30 **Molecular mechanisms of immune evasion in African trypanosomes**
Dr. Gloria Rudenko, Imperial College, London
The African trypanosome *Trypanosoma brucei* is a parasite causing African Sleeping Sickness. Trypanosomes are unusual, in that they multiply extracellularly in the blood where they are exposed to continuous immune attack. Key to their survival is a highly sophisticated strategy of antigenic variation of a protective Variant Surface Glycoprotein (VSG) coat. We have discovered that VSG synthesis is monitored during the *T. brucei* cell cycle, and blocking its synthesis triggers a very precise cell cycle arrest. In addition, we are trying to understand how VSG expression is controlled at the level of transcription.
- 10:30 – 11:00 **Fungal sensing of mammalian cytokines for adaptation and evasion of host immune defenses.**
Dr Rossana Iannitti, University of Perugia, Italy
Infections by opportunistic fungi have traditionally been viewed as the gross result of a pathogenic automatism which makes a weakened host more vulnerable to microbial insults. However, fungal sensing of a host's immune environment might render this process more elaborate than previously appreciated. As a consequence, microbes must possess specialized systems that sense and promptly respond to immune activation. IL-17A binds fungal cells, likely acting on both host and fungal structures in experimental settings of host colonization and/or chronic infection. The augmented adhesion and filamentous growth eventually translated into enhanced biofilm formation and resistance to local antifungal defenses. This might exemplify a mechanism whereby fungi have evolved a means of sensing host immunity to ensure their own persistence in an immunologically dynamic environment and evasion of host immune defenses.
- 11:00 – 11:30 **Speakers' photo then mid-morning break and trade show**
Please try to visit all the exhibition stands during your day at this event. Not only do our sponsors enable EuroSciCon to keep the registration fees competitive, but they are also here specifically to talk to you
- 11:30 – 12:00 **Host entry by herpesviruses**
Dr Philip Stevenson, University of Cambridge, UK
Herpesvirus infections are common and cause much disease. Viral immune evasion makes them hard to clear. Inhibiting host entry is therefore important for infection control. However, how host entry occurs remains largely unknown. We have identified the olfactory neuroepithelium as an entry point for two unrelated herpesviruses - MuHV-4 and HSV. Both bind to heparan sulfate (HS). While most differentiated epithelia express only basolateral HS, neuroepithelial HS is also apical, allowing incoming virions to bind. Many herpesviruses bind to HS, and there is circumstantial evidence that several infect nasally. Therefore neuroepithelial interventions could be broadly effective at herpesvirus infection control.
- 12:00 – 12:30 **The impact of Salmonella on adaptive immunity**
Professor Adam Cunningham, University of Birmingham

The interaction between the adaptive immune system and Salmonella after systemic infection will be discussed. The innate immune system plays a vital role in preventing the uncontrolled expansion of the infection. Nevertheless, to resolve infection and prevent further re-infection CD4 T cells and antibody are required and mechanisms used by the organism to avoid the engagement or function of adaptive responses may provide an advantage to the pathogen. Our recent findings show that this can happen in unexpected ways, suggesting that Salmonella interferes with adaptive immunity on a systemic level, including sites where bacteria do not colonize.

12:30 – 13:30

Lunch and trade show

This is also a good time to fill out your feedback forms

13:30 – 14:30

Question and Answer Session

Delegates will be asked to submit questions to a panel of experts. Questions can be submitted before the event or on the day

14:30 - 14:45

Suppressors of cytokine signaling (socs) induced by fish pathogens: an immune evasion strategy?

Bartolomeo Gorgoglione, Scottish Fish Immunology Research Centre, Institute of Biological and Environmental Sciences, University of Aberdeen, Scotland

The intracellular suppressors of cytokine signaling (SOCS) family members, including CISH and SOCS1 to 7 in mammals, are important regulators of cytokine signaling pathways. Most SOCS proteins are induced by cytokines and therefore act in a classical negative-feedback loop to inhibit cytokine signal transduction. However, they are also induced by various other stimuli, such as pathogen associated molecular patterns (PAMPs), and bacterial, viral, and parasitic infection. Pathogens can escape from host defence by induction of SOCS expression. So far, the orthologues of all the eight mammalian SOCS members have been identified in fish, with several of them having multiple copies. The expression of different SOCS members in rainbow (*Oncorhynchus mykiss*) and brown trout (*Salmo trutta*) was studied in kidney, which in fish plays an important role as an haematopoietic and lymphopoietic organ. RT-qPCR screening was carried out to detect SOCS expression during infection with several relevant diseases for salmonids in aquaculture: a viral (Viral hemorrhagic septicemia caused by a *Novirhabdovirus*), a bacterial (Enteric RedMouth Disease caused by the Gram negative bacterium *Yersinia ruckeri*), and a parasitic infection (Proliferative Kidney Disease caused by the Myxozoan *Tetracapsuloides bryosalmonae*). In all the cases, the expression of SOCS1 and 3 was found to be up-regulated, while other SOCSs showed specific patterns. Interestingly, the expression of these two SOCS members was much higher in the kidney of rainbow trout compared to that of brown trout, and could relate to the differences in disease susceptibility seen between these two closely related species. Thus, we suggest that SOCS genes expression may have value as a biomarker of disease resistance in fish. In addition, inhibition of SOCS genes expression may be a potential target in future studies aimed at modulating T-helper cell development and function, with a view to improving vaccine efficacy, and enhancing disease resistance in fish.

14 45 – 15:15

Afternoon Tea/Coffee and trade show

15:15 – 15:45

Spatiotemporal dynamics of Salmonella enterica infections

Dr Andrew Grant, University of Cambridge, Cambridgeshire

Salmonella enterica are a major threat to public health. Current treatments are not sufficiently effective, and there is a need to develop new therapeutic strategies. Our multidisciplinary approach provides an unprecedented insight into the dynamics of bacterial infection biology at different scales; from the direct interaction of an individual bacterium with a host cell, to the analysis of global traits of innate host resistance and in vivo spread and distribution of bacteria in the body. This work in the long term will provide knowledge and a technological basis for targeting individual bacterial components in vivo with novel drugs and vaccines.

15:45– 16:15

Immunomodulation by Helminth Parasites - a Molecular and Cellular Dialogue

Professor Rick Maizels, University of Edinburgh, Scotland

Helminths are multicellular worm parasites which are highly prevalent in humans and animals in many parts of the world. Helminths effectively down-regulate host immunity, and in so doing significantly reduce allergies and autoimmunity. Our laboratory is decoding the molecular and cellular interactions between helminths and the host immune system which underpin these observations. For example, we have identified a parasite mimic of TGF-beta which induces immunosuppressive Foxp3+ regulatory T cells. Understanding the pathways of helminth immunomodulation may identify new strategies to both boost immunity to infections in endemic countries and ameliorate the immunopathological disorders of developed countries.

16:15– 16:30

Chairman's summing up



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This meeting was organised by Euroscicon (www.euroscicon.com), a team of dedicated professionals working for the continuous improvement of technical knowledge transfer to all scientists. Euroscicon believe that they can make a positive difference to the quality of science by providing cutting edge information on new technological advancements to the scientific community. This is provided via our exceptional services to individual scientists, research institutions and industry.

About the Chair

Pietro Mastroenis' research is multidisciplinary and focuses on pathogenesis and immunity to bacterial infections and on vaccine development. His group has developed new biological and mathematical approaches to study the interaction of bacteria with individual cell in vivo and to analyse the interplay between bacterial virulence genes and host resistance genes/mechanisms.

He is actively involved in the study of the cross-talk between different cell populations in the initiation and expression of host immunity to bacteria. His research also investigates the role of innate cell receptors (e.g. TLRs) and acquired immune receptors (e.g. FcR) in infection control and vaccine function.

Other collaborative lines of research are exploring new areas within infection such as the interplay between microbes and autoimmune diseases and the possibility to use recombinant bacteria as anti-cancer agents. He is also involved in the forefront research on emerging diseases such as *Clostridium difficile* infections.

About the Speakers

Gloria Rudenko is a Wellcome Senior Research Fellow and Reader in Molecular Microbiology in the section of Infection and Immunity, Division of Cell and Molecular Biology, Imperial College London-South Kensington. Dr. Rudenko has an MSc. from the University of Leiden, the Netherlands and a PhD from the University of Amsterdam, the Netherlands and Columbia University, NY, USA. The Rudenko lab focuses on investigating the molecular and cellular biology of African trypanosomes, particularly with regards to the molecular mechanisms of immune evasion.

Philip Stevenson, Clinical medicine up to 1993, PhD Oxford 1997 - immune responses to influenza virus infection in the central nervous system, post-doc, Peter Doherty's lab, Memphis, TN - CD8+ T cell response to persistent infection, 1999 - clinical lecturer in virology, Cambridge - T cell evasion by gamma-herpesviruses, 2001 - MRC clinician scientist, Division of Virology, Cambridge - herpesvirus pathogenesis and immune evasion, 2006 - Wellcome Trust senior clinical fellow, Division of Virology, Cambridge - herpesvirus pathogenesis and immune evasion, 2006 - Wellcome Trust senior clinical fellow, Division of Virology, Cambridge - antibody evasion by Murid Herpesvirus-4

Rossana Iannitti is a Research Fellow in the Department of Experimental Medicine and Biochemical Sciences in the section of Microbiology, at the University of Perugia under the guidance of Prof. Luigina Romani. Dr Iannitti has a MSc. in Biology and PhD in Biology and Experimental Medicine at the University of Perugia. The Romani lab focuses on investigating pathogenesis and immunity to fungal infections particularly with regards to approaches to study the interaction of fungi with mammalian host in vivo and to analyze the interplay between fungal virulence and host resistance mechanisms.

Andrew Grant is a Senior Research Associate in the Department of Veterinary Medicine, University of Cambridge. Dr Grant has a PhD (in Molecular Microbiology) and a BSc (in Biochemistry with Pharmacology) from The School of Biological Sciences, University of Southampton. The Grant lab combines state-of-the-art microbiological, molecular, imaging and mathematical modeling techniques to investigate bacterial pathogens of veterinary and clinical significance. Current projects are broad-ranging and multidisciplinary, from understanding the roles of individual bacterial proteins in virulence to studying within-host population dynamics.

Rick Maizels is in the University of Edinburgh's Institute of Immunology and Infection Research. He is an immunologist interested in fundamental questions of how and why parasites manipulate the sophisticated mammalian immune system, and how that system has evolved in the face of parasite immunomodulatory strategies. Before moving to Edinburgh in 1995, Rick was Professor at Imperial College London. Prior to this, he held positions at the National Institute for Medical Research in London, UCLA and California Institute

of Technology. He was elected Fellow of the Royal Society of Edinburgh in 2002, and made a Senior Fellow of the American Asthma Foundation in 2010.

Adam Cunningham was awarded his PhD from Southampton University for studies on the immune response to chlamydial infection. He then did post-doctoral work on mycobacterial infections and on the development of antibody responses in Birmingham. As a RCUK Roberts Fellow he developed a programme of work examining how immune responses develop to vaccines and pathogens such as Salmonella. In 2011 he was appointed Chair in Functional Immunity in Birmingham.

Keywords: Antigenic variation, Trypanosoma brucei, Variant Surface Glycoprotein, Immune evasion, trypanosomes, IL-17A, TOR pathway, autophagy, fungi, herpesvirus, host entry, antibody, pathogenesis, Infection, Dynamics, Bacteria, Pathogenesis, Salmonella, Allergy, Immunity, Nematode, Regulation, Vaccine, Salmonella, T cells, B cells, antibody

Registration Web Site: www.regonline.co.uk/host2012

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- ▯ There may be an independent meeting report published within a few months of this event. If this is published we will send you an email to let you know the reference details
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