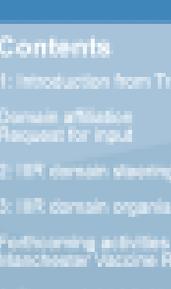


# Infection, Immunity, Inflammation and Repair (IIR)

Research Domain  
newsletter

News, events and translational innovation at the interface of infection, immunity, inflammation and repair

## 01 Introduction from Tracy Hussell



A warm welcome to primary and secondary affiliates to the IIR Domain that spans basic, clinical and translational science at the interface of infection, immunity, inflammation and repair. It unites over 300 researchers from across the University (Figure 1 below), providing the pool of expertise necessary to formulate larger strategic bids. Remember, the Domain does not replace School or Division research strategy, but examines novel opportunities at the interface. The domain links seamlessly with the Manchester Academic Health Science (MAHSC) domain for Inflammation and Repair, and benefits from strong partnerships with the local NHS trusts. We are one of the largest university domains encompassing membership across all 3 schools in the Faculty of Biology, Medicine and Health.

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## Domain affiliation

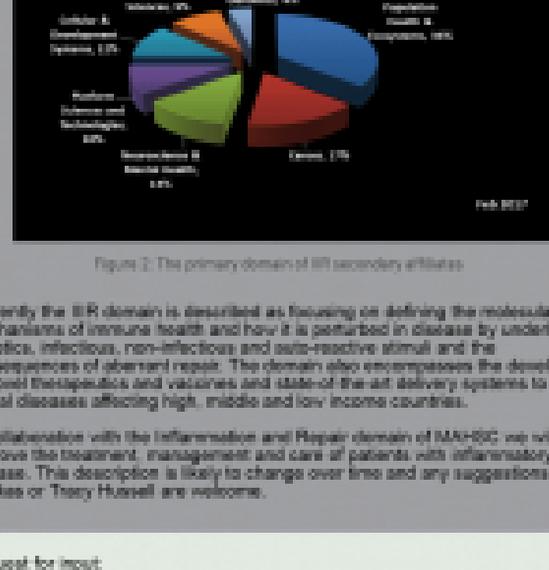


Figure 1. Primary and secondary affiliates to each domain

The cross-fertilisation of disciplines can be seen in the primary domain of secondary affiliates and we are already developing links in those areas.

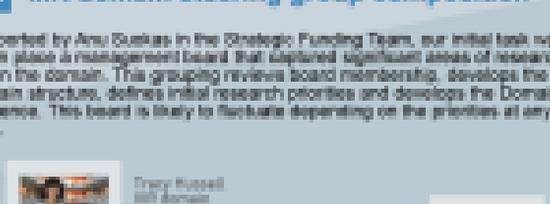


Figure 2. The primary domain of IIR secondary affiliates

Currently the IIR domain is described as focusing on defining the molecular mechanisms of immune health and how it is perturbed in disease by underlying genetics, infectious, non-infectious and auto-reactive stimuli and the consequences of aberrant repair. The domain also encompasses the development of novel therapeutics and vaccines and state-of-the-art delivery systems to combat global diseases affecting high, middle and low income countries.

In collaboration with the Inflammation and Repair domain of MAHSC we will investigate the treatment, management and care of patients with inflammatory disease. This description is likely to change over time and any suggestions to Anu Suckas or Tracy Hussell are welcome.

## Request for input

The Domain steering group would welcome feedback on proposals for:

- 1) Cross-Division/School/Faculty initiatives that require a more strategic approach.
- 2) Areas/Items that would benefit from sharing across the domain.
- 3) Comments on areas lacking in the domain management board.

## 02 IIR domain steering group composition

Deputed by Anu Suckas in the Strategic Funding Team, our initial task was to put in place a management board that captured significant areas of research within the domain. This grouping reviews board membership, develops the sub-domain structure, defines initial research priorities and develops the Domain web presence. This board is likely to fluctuate depending on the priorities at any given time.

- Tracy Hussell, IIR Director
- Jane Barton, Professor of Rheumatology
- Elaine Sigwell, Reader in Applied Myology
- Jeremy Derrick, Professor of Molecular Microbiology
- Richard Dennis, Professor of Immunology
- Olivia Griffiths, Professor of Dermatology
- Judith Hayland, Professor of Molecular Pathology
- Andrew MacCombs, Professor of Immunology
- Daniela Montali, Chair in Memory Neuroscience
- Werner Müller, Ed Ford Chair of Cellular Immunology
- Angela Simpson, Professor of Respiratory Medicine
- Mark Travis, Senior Lecturer Immunology
- Jane Worthington, Professor of Chronic Disease Genetics
- Anu Suckas, Strategic Funding Manager Strategic Funding Team

## 03 IIR domain organisation

The Domain is currently organised across four overlapping and complementary subdomains (Figure 3): Explorative immunology: across the life course; Regenerative medicine: exploring matrix biology; Chronic inflammatory diseases: focusing primarily on musculoskeletal, dermatological and respiratory conditions; Infection including mycology, bacteriology and parasitology. Centres of excellence will be embedded in this structure with separate web-links.

Our aims are to understand: i) The fundamental processes driving and regulating immune health; ii) How immune health is perturbed by infection, underlying genetics, auto-reactive stimuli, biological timing and cancer; iii) The process of healthy repair and regeneration and the consequences of its dysregulation; iv) The optimal therapeutic, vaccination or delivery processes that alleviate inflammatory diseases.

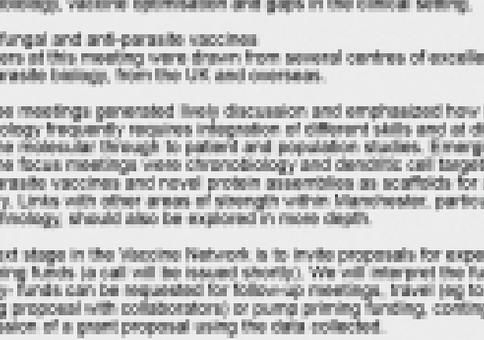


Figure 3. IIR domain structure

## Forthcoming activities:

Invitation to a Single Cell Biology in Health & Disease Workshop Wednesday 5th and Thursday 6th July 2017

This workshop, funded by the MRC Discovery Award for "Capacity Building in Single Cell Inflammation", is a joint initiative between the Infection, Immunity, Inflammation and Repair, and the Platform Sciences and Technologies Domains. This will provide a unique opportunity to interact with internal and external leaders in this rapidly expanding technology and will highlight the breadth of single cell research at The University of Manchester.

Deputed speakers include Professor Mughith Haniffa (Newcastle University, UK), Professor Wolf Kisk (Kaiserlin Institute, Cambridge, UK) and Dr Hervé Lucike (INSERM, Paris, France) at the event. Further speaker/chairs will be announced shortly.

There will also be ample opportunity for people to interact and hear about the latest advancements in single cell research at the genomic, epigenomic and proteomic level including CyTOF.

If you would like to attend please register using the event/for address below. Places are limited so please register soon to avoid disappointment.

[tinyurl.com/singlecellbiology](http://tinyurl.com/singlecellbiology)

Prof Ilkka White  
Prof Tracy Hussell

Infectious disease: bridging the gap between lab and clinic Wednesday 6th September, 12- 5pm

A meeting will be held on Wednesday 6th September, 12-5pm to bring together academics and clinicians with an interest in infectious disease across the Manchester Academic Health Science Centre (MAHSC). The aim is to showcase the wide range in infectious disease research across the MAHSC domains, from bacteriology and genomics, through to clinical studies of antibiotic treatment in hospitalised patients and the emergence of antimicrobial drug resistance.

Through exploring the interface between basic biological research and its clinical applications, we hope to identify areas of potential, particularly in Translational Medicine, which Manchester can develop in the future.

The meeting will consist of a series of short talks, followed by a discussion session. Invitation and registration details to follow.

Prof Jeremy Derrick  
Prof Paul Dalk  
Prof Tracy Hussell

## Manchester Vaccine Research Network - an update:

Vaccines are one of the oldest and most effective health interventions, and are currently undergoing renewed interest and investment from research councils and charities. This is driven by several factors, including the need for cost-effective medical interventions in developing and developed countries, the implementation of new technologies or delivery systems, greater understanding of underlying mechanisms, the rise in antibiotic resistance and the potential global spread of infectious diseases. Using funding from The University of Manchester Research Initiative (UMRI), we developed a network which is designed to link individuals from across the three Faculties and promote innovation in vaccine studies in the broadest sense, from technical innovations and understanding of the underlying immunology, to clinical, public health and social applications. In particular, we wanted to include researchers who would not necessarily regard themselves as vaccine specialists, but who have valuable skills to contribute in technical development or other areas.

We started the network with three meetings which highlighted areas of strength within Manchester, and have potential for interdisciplinary research:

1. Vaccines and Synthetic Biology. This meeting explored the interface between vaccinology and the exciting potential of Synthetic Biology.
2. Innate Immunity and Rheumatology. This discussion included a series of short talks by academics and clinicians, followed by a meeting and future planning. Topics covered included dendritic cell biology, rheumatology, vaccine optimisation and gaps in the clinical setting.
3. Antifungal and anti-parasite vaccines. Speakers of this meeting were from several centres of excellence in fungal and parasite biology, from the UK and overseas.

All three meetings generated lively discussion and emphasized how innovation in vaccinology frequently requires integration of different sites and at different levels, from the molecular through to patient and population studies. Emerging themes from the focus meetings were chronobiology and dendritic cell targeting, fungal and parasitic vaccines and novel protein assemblies as scaffolds for antigen delivery. Links with other areas of strength within Manchester, particularly Industrial Biotechnology, should also be explored in more depth.

The next stage in the Vaccine Network, is to invite proposals for expenditure of the remaining funds in call will be issued shortly. We will interpret the funding remit broadly - funds can be requested for follow-up meetings, travel (eg to discuss a funding proposal with collaborators) or pump priming funding, contingent on submission of a grant proposal using the data collected.

Nationally, there have also been research funding developments in vaccinology. Of particular note are the results from the GCRF Call in partnership for Vaccine R&D, which was open in Autumn 2016 (<https://tinyurl.com/vxyvngp>). Official announcements of the funded networks are expected imminently. These networks will function in a similar manner to the GBSRC Networks in Industrial Biotechnology and Bioscience (IIBIOs), including organisation of meetings to promote new collaborations and the distribution of pump priming funds. They are an excellent opportunity for anyone who wishes to become more involved in vaccine research and a possible outlet for development of projects which have been initiated by the Manchester network.

Prof Jeremy Derrick

## 04 Research highlights

Biological timing  
Understanding the rhythms of life  
[tinyurl.com/comeclock](http://tinyurl.com/comeclock)

The University of Manchester is home to the largest biological timing research community in Europe. Led by Professor David Ray, the group brings together world-leading researchers with a multidisciplinary approach to cellular timers and circadian clocks. The biological timing group works closely together with the Public Programmes Team at Central Manchester University Hospitals NHS Foundation Trust and volunteers from across the grouping to improve the reach and understanding of timing research in both patient and public communities.

Here David tells about the group's achievements and how research into immunity and inflammation is a fundamental part of their work.



Prof David Ray

"A review of research strengths in the new Faculty of Biology, Medicine and Health revealed that our strengths in biological timing research is a major and unique research pillar. Consequently, the Faculty wanted us to formally link together our respective multidisciplinary groupings to enhance progress, and to provide a focus of research excellence across the University." The new timing group - officially launched in May 2017 - has more than £50million in active research funding and brings together 33 principal investigators and 168 research staff.

Disturbance of circadian rhythms impacts negatively on our health and wellbeing including the immune system. The circadian clock exerts regulatory control over immune processes through finely tuned molecular mechanisms. We believe that the immune system is reprogrammed, whereas the circadian clock is subject to inflammation-mediated reprogramming, with eventual disruption in the clock mechanisms.

We recently won a major programme grant from MRC to work on finding mechanisms in chronic inflammatory disease, capitalising on our recent discovery that inflammation regulates the coupling of the core clock oscillator to output pathways. We propose that an initially adaptive response to inflammation requires regulation of the circadian clock, mediated by cross-talk between core clock components, regulators of energy metabolism, and inflammatory signals, to meet the bioenergetic demands of the inflammatory process. In chronic inflammation this change is maladaptive and imposes a bioenergetic cost, with consequences for inflammatory resolution, organismal energy metabolism, and also in the response to therapeutic intervention.

Inflammation plays a critical role in most human diseases, and safe effective treatments remain an urgent and unmet clinical need. Our research into biological control mechanisms spans from cell biology to clinical translation, and significant progress has been made in a number of areas associated with the IIR Domain. Links between timing researchers and Prof Tracy Hussell, Prof Andrew MacCombs and Dr John Gearing at the Manchester Collaborative Centre for Inflammation Research have proved highly productive with recent major MRC funding (led by Dr David Bechtold), and addressing timing mechanisms controlling the immune-epitope interface. Biological timing provided elements for the successful, recently completed musculoskeletal biomedical research unit, and now to the newly funded, and far larger Manchester Biomedical Research Centre (Director: Prof Ian Bruce).

The recent visit from the Wellcome Trust to the newly-funded Wellcome Trust Centre for Cell Matrix Research also provided an opportunity to show how timing mechanisms affect matrix formation and function. Prof Ilkka White and colleagues led a highly successful GBSRC-funded programme of research looking at timing as an encoder of information within the inflammatory signalling NF-kB circuit, with a major computational aspect; a feature of much timing-focused research. The timing group runs an on-going clinical trial programme in asthma and rheumatoid arthritis, and our work has revealed the profound impact of the clock in pulmonary and joint inflammation. In addition, wider links to the clinical research community have opened up new fields of research into electronic health records, and into the impact of the circadian system on the UK public through the UK BioBank."

## Contact:

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