

## STRATEGY & TERMS OF REFERENCE FOR THE INFECTION AND IMMUNITY RESEARCH NETWORK

### Overview

The Infection and Immunity (I&I) Research Network supports studies of the **immune system** in health and illness, and research focussed on the cause, spread, treatment and prevention of **infectious disease**. The Network encompasses studies of emerging infections relevant to the Global Challenges Research Fund (GCRF), and likely to extend their geographic range because of climate change and modern travel; chronic inflammatory conditions that consume significant resources from the public health provisions of first-world economies; and the application of novel methods and technologies to study and impact these conditions. While the reach of the research in the I&I Network is very broad, there are several areas of focus that provide important points of co-ordination for the 250+ members of the Network. Our research seeks to provide solutions with immediate relevance to modern demands.

I&I is a network of staff and students with expertise ranging from fundamental studies of mechanism and structure to population-based research e.g. tackling the management of antibiotic resistance in general practice. Our key research areas are the pathogenesis of infection, population and human health research and immune regulation. Embracing our diversity there remains a real sense of being part of a shared community and I&I enjoys a strong brand identity both internally and externally.

Our expertise is drawn from multiple Schools and Faculties, with strong links incorporating the Bristol Medical School (BMS), the Bristol Dental School (BDS), the School of Cellular and Molecular Medicine (CMM) and the Bristol Veterinary School (BVS), but also extending to Biochemistry, Biological Sciences, Physics, Mathematics and Engineering. The Network works closely with the Elizabeth Blackwell Institute for Health Research (EBI) to foster research across these multi-disciplinary groupings.

### Objectives and Aims

I&I exists to enhance and facilitate infection and immunity research activity and strategic planning. This includes identifying and resourcing key equipment, the improvement of internal communication and collaboration, the identification of key relevant funding priorities and opportunities, and developing better external communication of our research to scientific and healthcare professionals, schools and the general public. The main visible activities of the Network are a series of events and structures which aim to unify and showcase research activity across large number of researchers and include annual symposia and an annual Early Career Researchers' event.

### The Landscape

Research focused on infection and immunity is a key priority of all the major funding organisations [[UK Research and Innovation](#) (UKRI), [Wellcome Trust](#), [Gates Foundation](#), [National Institute for Health Research](#) (NIHR)]. Beyond the traditional silos of microbiology, veterinary medicine and clinical medicine, it interfaces with societal challenges such as

migration, population growth and ‘health across lifetimes’. Immune responses play a critical role in many diseases beyond the arena of infectious diseases, including chronic inflammatory conditions such as type II diabetes, autoimmune disease, ischaemic heart disease, strokes; and neurodegenerative diseases such as Alzheimer’s and conditions associated with aging such as age-related macular degeneration. Some of the most exciting recent advances in treatments for cancer have come from [exploiting the immune response](#) by ablating co-inhibitory molecules or engineering novel targeting receptors into T cells (a sub-type of white blood cell). Chimeric antigen receptor or [CAR-T cells](#) were recently approved for treatment of leukaemia by the US Food and Drug Administration (FDA), and anti-IL1 has been reported to prevent both heart attacks and lung cancer.

High level initiatives have driven funds from multiple organisations towards investigation of anti-microbial resistance (AMR); similar top-down strategies are in for vaccines and most recently for whole genome sequencing directed to cancer, rare inherited diseases and infection.

Within the University, [BristolBridge](#) [an [Engineering and Physical Sciences Research Council](#) (EPSRC)-funded project] has successfully pioneered the co-ordination of interdisciplinary research, focused on AMR, across a broad range of disciplines from microbiologists to biomaterial scientists. As of June 2017, Bristol was the largest recipient of [Research Council UK](#) (RCUK) cross-council AMR initiative funding in the UK.

Because I&I research at Bristol encompasses a broad cross-section of disciplines, one way to leverage this strength is to identify opportunities that coalesce research around key areas of strength that align closely with national and international research priorities.

Three areas where such opportunities are apparent include; antimicrobial resistance, application of vaccines and data science integration.

## 1. Antimicrobial Resistance (AMR)

**Why:** The publication, in March 2013, of the [annual report of Dame Sally Davies](#) focusing on the threat of antimicrobial resistance concentrated the attention of many different funding bodies in this direction. In fact, the UK government made **AMR the first research priority ever to receive cross-council funding** from all UK Research Councils [[Medical Research Council](#) (MRC), [Biotechnology and Biological Sciences Research Council](#) (BBSRC), EPSRC, [Natural Environment Research Council](#) (NERC), [Economic and Social Research Council](#) (ESRC) and [Arts and Humanities Research Council](#) (AHRC)].

Using funding from the EPSRC, BristolBridge enabled the consolidation of an integrated multidisciplinary community to explore novel and multidisciplinary ways of tackling the escalating threat of AMR.

This initiative developed effective cross-disciplinary integration with active and integrated research in medicine, veterinary and dental sciences, including social science and health economic capabilities. The community of more than 100 researchers is poised to move

forward by achieving a more co-ordinated communication strategy and outward facing identity that can highlight Bristol's key strengths.

Within the community there is appetite for greater direct clinical collaboration and engagement with the [Global Challenges Research Fund](#) (GCRF) to strengthen the existing collaborative partnerships with [Overseas Development Assistance](#) (ODA) countries including Thailand, Kenya, Pakistan, China, Malaysia and India.

**Key stakeholders:** AMR research in Bristol is a thriving community incorporating biomedical scientists, clinicians, veterinary scientists, dental scientists, chemists, physicists, engineers, computer scientists, mathematical modellers, biomaterials scientists, nanoscientists and social scientists. This has raised £11.2m in funds for research and training over the last 3 years. With the wind-up of the EPSRC funded BristolBridge partnership, follow-on funding that build on this Initiative are being sought, including opportunities for further regional alignment (GW4) and collaboration.

## 2. Application of vaccines

**Why:** Manipulation of the immune system for therapeutic benefit, as exemplified by vaccination, remains a crucial health challenge whose exploitation requires a broad range of expertise that goes beyond simply identifying and producing antigens. Veterinary medicine and clinical medicine are both converging on the opportunities for developing next-generation mucosal vaccines which will be informed by novel analyses of the microbiome. The far-reaching impact of most universal vaccine programmes on mucosal colonisation and transmission of infection drives vaccine effectiveness at the population level and also provides powerful tools to combat the spread of antimicrobial resistance. There is opportunity here to bring together experts across human and veterinary medicine and combines expertise in mucosal immunology, molecular microbiology, clinical vaccine trials and epidemiological modelling to make research into population-wide vaccine effects on transmission of infections a strength area. Within synthetic biology (led by [Dek Woolfson](#) in the School of Chemistry and [Imre Berger](#) in the School of Biochemistry) novel vaccine formulations using the technologies that are being developed are an obvious next step.

**Key stakeholders:** [Bristol Children's Vaccine Centre](#) co-ordinates a wide range of studies on the efficacy of vaccine interventions. It focuses on the relationship between vaccination and the normal microbial ecology. It has extensive collaborative programmes involving public health and epidemiology and strong links with industry both for sponsored studies and investigator-led industry-funded research. Related studies, focused around Bristol Veterinary School, are targeting the response of the microbiome of pigs in the context of vaccination and diet and investigating viral-bacterial interactions in the upper respiratory tract in cattle using vaccine probes. [BrisSynBio](#) has framework technologies for delivering 3D antigen targets that may offer significant advantages over linear antigen epitopes.

## 3. Data Science Integration

**Why:** There is a widely appreciated need for more effective integration of large data sets. This need has been recognised at the University of Bristol by the establishment of the [Jean](#)

[Golding Institute](#) for data-intensive research. Within infection and immunity there is relevant expertise in combining transcriptomics and proteomics, and cross-disciplinary collaborations applying bioinformatics approaches to imaging data. The overarching concept is of data fusion between different modalities to increase the sensitivity, specificity and quantification of information obtained from different large data sets.

**Key stakeholders:** The digital health strategy group at the University of Bristol and the new Faculty of Life Sciences have both identified data integration and exploitation as crucial cross-cutting themes. Bristol's state of the art imaging facility, the [Wolfson Bioimaging Facility](#), that supports fundamental cell biology, produces very large data sets whose curation and exploitation remain pressing problems. The integration of imaging data as exemplified by correlative electron light microscopy, leading to improved quantitative and computational analysis, is a shared goal of many different investigators that include virologists, immunologists and engineers from the [Visual Information Laboratory](#). In the area of transcriptomics and proteomics systems virology approaches have been successfully applied to the analysis of the recent Ebola epidemic and informatics platforms to the analysis of lymphocyte repertoire in autoimmune disease and cancer. [Andrew Davidson](#) leads on two MRC grants that aim to solve these integration problems to identify prognostic markers for dengue disease using serum from dengue infected patients in the Philippines and Indonesia. On a broader horizon, there is an ongoing explosion in publicly available data repositories that are critical national and international resources for investigators. Increased capacity and proven ability in these areas are crucial for future proofing biomedical research.

### ***Aims of the I&I Network***

- 1) *To provide a forum for discussions about I&I research strategy including horizon-scanning, and a mechanism to feed these outcomes to senior management*
- 2) *To contribute to business cases for key academic appointments, capital investments and wider funding bids, to maximise, maintain and create research capacity*
- 3) *To support our Early Career Researcher and Postgraduate student communities*
- 4) *To extend our work facilitating the interfacing of different disciplines and to continue to raise the profile of I&I's work with both internal and external stakeholders, including funders and industrial partners*

### **Management of the Network**

A steering group and website for Infection and Immunity was set up in 2009 with the combined aim of building a cross-faculty community and showcasing research. The current committee is co-led by Prof Adam Finn (clinician) and Dr Ruth Massey (basic science), who are supported by representatives of key research areas at different levels of academic progression and pathways drawn from different faculties.

The Network maintains a mailing list and a website that incorporates news, upcoming seminars and events. We also produce weekly digests and quarterly newsletters with news, events, activities and funding opportunities relevant to the I&I community. We are supported by the Network Facilitator and Administrator, both based in Research and

Enterprise Development (RED).

Any individual involved in infection and immunity-related research at the University of Bristol may consider themselves a member of the I&I Network. Any member of I&I may ask to attend a steering group meeting to discuss an issue or ask for an item to be raised in their absence. Minutes of meetings can be found on the Network's [intranet site](#) (accessible via its [internet site](#)).

### **The *Infection and Immunity steering group (I&Isg)*: composition and rotation**

1. *The I&Isg* will be led by the Network's co-Leads, one clinician and one basic scientist, who are supported by 10-12 academics and representatives from different areas of the community. The *I&Isg* may be led temporarily by a single clinical or basic science focused individual when circumstances demand. Appointments will be made by the steering group.
2. A Facilitator (RED) and an Administrator (funded by EBI) will service the *I&Isg* for as long as funding allows.
3. The *I&Isg* will meet approximately every three months.
4. The co-Leads will be selected from the membership of the I&I Network. Any incoming Lead should possess the requisite skills and experience to act as a Network lead.
5. The term of office of *I&Isg* members, including the co-Leads, will be three years, with the potential for a one-year extension by mutual consent. If a Lead is chosen from within the *I&Isg* itself their three-year term of office will begin from the date they take over as Lead.
6. Former members of the *I&Isg* will be ineligible for re-appointment to the committee for a period of one year from the expiry of their membership.
7. When a steering group member steps down, new members will be recruited through a process of open application from the wider I&I community. If more people wish to join the steering group than there are places available, then admission will be via a vote by the current steering group members. Issues of equality, diversity and diversity of expertise will be taken into consideration.
8. Members of the *I&Isg* who are unable to attend two or more meetings per year, or nominate appropriate substitutes, will be asked to reconsider their commitment.
9. Where it is not possible to meet in person and there are matters of interest or decisions required for specific action, such as expenditure, convening virtually through telephone conference or through specific email correspondence as a group will be permitted.
10. The *I&Isg* reports to the Director of the EBI, who will act as conduit to senior management through the Health and Life Sciences Research Strategy Committee.
11. Changes to these terms require the agreement of at least two thirds of the steering group.

## **APPENDIX 1: Current steering group composition** *(in alphabetical order)*

- Borko Amulic - Lecturer in Immunology (CMM)
- Philip Bright – Clinical Immunologist (Southmead)
- Andrew Davidson - Senior Lecturer in Virology (CMM)
- Adam Finn - Professor of Paediatrics (Bristol Medical School: Translational Health Sciences)
- Hannah Fraser - Senior Research Associate in Infectious Disease Mathematical Modelling (Bristol Medical School: Population Health Sciences) – Early Career Researcher representative
- Wendy Gibson - Professor of Protozoology (Biological Sciences)
- Kathleen Gillespie - Reader in Molecular Medicine, Head of the Diabetes and Metabolism Research Group (Bristol Medical School: Translational Health Sciences)
- Melanie Hezzell – Senior Lecturer in Cardiology (Bristol Veterinary School)
- Ruth Massey – Reader in Microbiology (CMM)
- Peter Muir - Clinical Virology (University Hospitals Bristol NHS Trust)
- Lindsay Nicholson - Reader in Research (Bristol Medical School: Translational Health Sciences)
- Angela Nobbs - Lecturer in Oral Microbiology (Bristol Dental School)
- Annela Seddon - Senior Lecturer and Director of the Bristol Centre for Functional Nanomaterials (Physics)
- Collette Sheahan - Research Development Network Facilitator (RED)
- Katy Turner - Senior Lecturer in Veterinary Infectious Diseases (Bristol Veterinary School)
- Peter Vickerman - Professor of Infectious Disease Modelling (Bristol Medical School: Population Health Sciences)
- Linda Woolridge - Chair in Translational Immunology (Bristol Veterinary School)
- Catherine Brown - Research Development Administrator for the Network (RED/EBI)