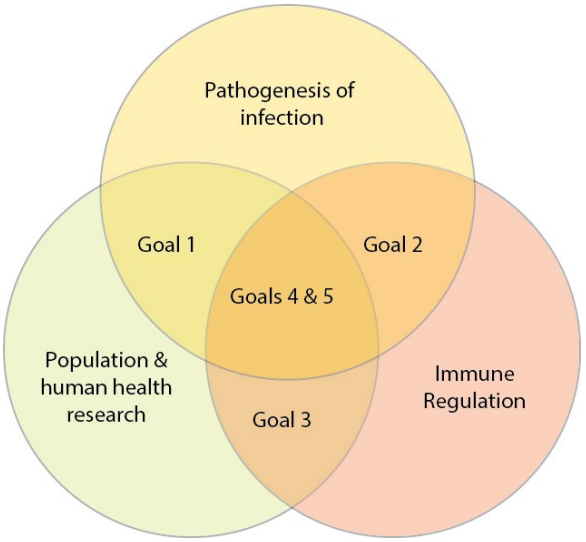
INFECTION AND IMMUNITY THEME NEWSLETTER

University of BRISTOL
Elizabeth Blackwell Institute for Health Research

October / November 2015

What does I and I do?

The Infection and Immunity research theme studies the mechanisms that cause and spread disease. From emerging infections, spread around the world by modern travel or by environmental change, to chronic inflammatory conditions that strain the resources of first-world economies to breaking point, research in this area has immediate relevance to diseases that affect us all.



Inside this issue:

THE MEDICAL RESEARCH COUNCIL GW4 BIOMEDICAL DOCTORAL TRAINING PROGRAMME

Call for Projects: deadline 26 November 2015

The GW4 Alliance universities (Bath, Bristol, Cardiff and Exeter) have recently been awarded 13 MRC PhD studentships per year for the next three years, through the MRC GW4 BioMed Doctoral Training Partnership (DTP). The universities have agreed to provide some additional funding to increase the number of studentships to c. 18 per year.

The three strategic themes for this DTP are: **Infection, Immunity and Repair**; Neuroscience and Mental Health; and Population Health – and PhD projects are expected to align with one of these themes. The DTP will also place a strong emphasis on cross-cutting skills priorities (quantitative skills, interdisciplinary skills and *in vivo* skills), and we have the flexibility to support (occasionally) excellent candidates working on projects that sit outside the themes, so long as the training is focused on one or more of the skills priorities.

The strongest projects will be those that meet the traditional criteria of scientific excellence, training opportunities (noting skills priorities), and supervisory track record, but also where there is added value from collaboration/ cross-partner (GW4) supervision. The DTP is committed to a target of >50% of projects being co-supervised across at least two of the GW4 universities, so we encourage you to start consider developing new as well as existing partnerships.

Project proposals will be evaluated against the following **criteria**:

i) Evidence of high quality doctoral training:

- Significance, originality, feasibility and degree of challenge presented by the proposed research
- Research training, including use of novel, cutting-edge/innovative technologies, approaches and/or special resources
- Added-value features, e.g. exposure to working across disciplinary boundaries, opportunities for collaboration with other academic centres or industries
- Strategy for knowledge transfer and maximising the impact of the doctoral research

Ii) Evidence of an excellent research and training environment:

- Track record of the supervisors in attracting research funding
- Publication of research outputs in high quality journals
- Critical mass of academic and research staff, and doctoral students
- Project supervisors' PhD submission rates in the last 5 years

Iii) Evidence of alignment with:

- Cross-cutting skills priority areas (e.g. quantitative skills; in vivo science; interdisciplinary skills – e.g. imaging, health economics, engineering, chemistry)
- The strategic aim to support collaboration across the partner institutions: as the norm, PhD projects are expected to involve collaboration in supervision and/or specialist training
- The strategic aim to support the development of early career researchers as supervisors.

Supervisors are limited to one proposal as a main supervisor but can be a collaborating supervisor on any number of other projects. Supervisors can apply to be the lead on a project in two of the three intakes.

The GW4 Management Board will assess and score the proposals with reference to the criteria set out above, which will be linked to a numerical scale. The Board will rank the proposals and recommend up to 45 projects (18 x 2.5) to be advertised. (Note that the number of projects advertised exceeds the number of studentships available to ensure that the final selection is on the basis of the quality of the applicant).

The call for projects is now open and closes at 9:00 Thursday November 26th 2015. Supervisors are invited to obtain application forms and further particulars, and submit proposals for PhD projects, to

GW4BioMed@Cardiff.ac.uk

BRISTOL EVENTS

- School of Biochemistry Seminar: macromolecular assemblies
  5 November 2015 13.00-14.00. Neil Ranson (University of Leeds), C42 Biomedical Sciences Bldg
- The Immune Function of Wild Mice, Mus musculus domesticus
  5 November 2015, 16.00 - 17.00. Mark Viney (UoB) Seminar Room, OS6, Oakfield House
- Big Data in Translational Medical Research
  6 November 2015, 12.00 - 13.00. Ewan Birney (EMBL-European Bioinformatics Institute), OS6 Oakfield House
- Phys & Pharm Snapshots: Extracellular calcium-sensing receptors in physiology and disease
  9 November 2015, 13.00-14.00. Daniela Riccardi (Cardiff University), Lecture Theatre 1, Chemistry
- Epstein Barr virus transcription factor Zta acts through distal regulatory elements to control cellular gene expression during its replication
  10 November 2015, 13.00-14.00. Alison Sinclair (University of Sussex), C42 Biomedical Sciences Bldg

2 November 2015
18:00 - 19:00

Prof Dame Anne Johnson
(Professor of Infectious Disease Epidemiology, University College London)

Wills Memorial Building

- launch of BristolBridge
  11 November 2015, 16.00-18.00. Chemistry
- School of Biochemistry Seminar: macromolecular complexes
  12 November 2015, 13.00 - 14.00. Christiane Berger-Schaffitzel (University of Bristol), C42 Biomedical Sciences Bldg
- Introduction to Research Grant Applications (Medical Faculties)
  12 November 2015, 2.00 - 17.00. Hawthornes
- Building a flagellum at the bacterial cell surface
  17 November 2015, 13.00-14.00. Gillian Fraser (University of Cambridge), C42 Biomedical Sciences Bldg
- The MRC-NIHR Methodology Research Programme
  18 November 2015, 11.30 - 12.30. LG.03A, Canynge Hall
- School of Biochemistry Seminar: transfusion medicine
  19 November 2015, 13.00-14.00. Cedric Ghaevert (University of Cambridge), C42 Biomedical Sciences Bldg
- M1/Inhibit and M2/Heal Macrophages: The Chicken and the Egg of Immunity
  20 November 2015, 13.00-15.00. Charles Mills, C44 Medical Sciences Bldg
- From Surgical Robots to Nanomedicine: Cancer Show and Tell
  20 November 2015, 14.00-15.00. NSQI seminar room
- Control of tissue resident macrophage phenotype and function
  24 November 2015, 13.00-14.00. Philip Taylor (Cardiff Institute of Infection and Immunity), C42 Biomedical Sciences Bldg
- Materials and Devices for Wounds
  27 November 2015, 12.30 - 16.00 . Amber Young (Clinical lead, South West Children's Burns Network), NSQI seminar room
- Snapshots: TRPV4 channel in epithelial physiology and pathology
  30 November 2015, 13.00-14.00. Miguel Valverde (Universitat Pompeu Fabra, Barcelona), Lecture

Theatre 1, Chemistry

- School of Biochemistry Seminar: molecular microbiology
  3 December 2015, 13.00-14.00. David Grainger (University of Birmingham), C42 Biomedical Sciences Bldg
- University Hospitals Bristol Research & Innovation Day
  4 December 2015, 9.30-16.00
- Application of biosensors for cell monitoring
  15 December 2015, 13.00-14.00. Richard Luxton (UWE), C42 Bio medical Sciences Building
- Infection and Immunity Annual Symposium 2016
  12 January 2016, 9.30 -14.30. G13/14, Life Sciences Bldg
- Introduction to Research Grant Applications (Medical Faculties)
  1 March 2016, 14.00-17.00. Zoe Holland (RED)
- Surgical Showcase 2016
  18 March 2016, 9.00–17.00. M-Shed

12 January 2016
9:30 - 14:30

Infection and Immunity Annual Symposium

Putting models into action in Infection and Immunity Research

Life Sciences Building

OTHER EVENTS

- UK Veterinary Vaccinology Network Conference 2016
  5 January 2016, 10.30 - 6 January 2016, 17.00. Manchester Conference Centre
- Angiotensin Gordon Research Conference
  21 February 2016, 9.00 - 26 February 2016, 17.00. Il Ciocco Resort & Spa, Barga, Lucca, Italy
- The Oxford Chemical Immunology Conference
  4 April 2016, 9.00 - 5 April 2016, 17.00. Keble College, Oxford

EARLY CAREER EVENT 23 June 2015

I and I hosted a morning ECR event and lunch over the summer. It included a series of oral research presentations by early career researchers and postgraduate students. Presentations were 10-12 minutes with 5 minutes for questions.

Competition was tough, but the two prizes for best talk were awarded to:

- **Martin Challand** (*FISHing for antibiotic resistant bacteria with Methylation Sensitive Bait*), Research Assistant in the School for Cellular and Molecular Medicine, and
- **Ashley Bryce** (*Prevalence of antibiotic resistance in paediatric* E. coli *urinary tract infections and associations with primary care antibiotic prescribing: a systematic review and meta-analysis*), PhD student in the Centre for Academic Primary Care

Each of them received a £25 Amazon voucher. Thanks are extended to the Faculty of Medicine and Dentistry Research Office (as it was still called then) for supplying the prizes, and the Infection and Immunity Theme, with support from the Elizabeth Blackwell Institute, for hosting and catering the

event. Feedback from the day was overwhelmingly positive, with respondents agreeing that their expectations of the day had been met and that the speakers were both interesting and informative. Presentations from the event are now available from the I and I intranet site. Please note that ALL are very welcome to attend these events, staff ***and*** *students, although only ECRs are invited to speak.*

RESEARCH AND STAFF NEWS

- **The winners of the 2015 Bristol Teaching Awards**, a joint venture between the University and Bristol Students' Union, were announced last month. The Bristol Teaching Awards recognise and reward those members of staff who have made an outstanding contribution to teaching, providing support for students, and enhancing the student learning experience. The University Award for Education (Medical and Veterinary Sciences) this year went to Dr Matthew Avison from the School of Cellular and Molecular Medicine.

World Health Organization

25 May 2015

The *WHO* endorses a global action plan to tackle AMR, affordable vaccines and nutrition

- **On 25 May 2015 The World Health Assembly** agreed resolutions to tackle antimicrobial resistance, improve access to affordable vaccines, and address over- and under-nutrition. Delegates endorsed a global action plan to tackle AMR which is occurring everywhere in the world, compromising our ability to treat infectious diseases, as well as undermining many other advances in health and medicine. The plan sets out 5 objectives: improve awareness and understanding of antimicrobial resistance; strengthen surveillance and research; reduce the incidence of infection; optimise the use of antimicrobial medicines; ensure sustainable investment in countering antimicrobial resistance. The resolution urges Member States to put the plan into action, adapting it to their national priorities and specific contexts and mobilising additional resources for its implementation. Through adoption of the global plan, governments commit to have in place, by May 2017, a national action plan on AMR that is aligned with the global action plan. It needs to cover the use of antimicrobial medicines in animal health and agriculture, as well as for human health. WHO will work with countries to support the development and implementation of their national plans.

- **The NIHR Clinical Research Network** has made significant progress and achievement in the growth and delivery of their commercial research portfolio over the last five years. Performance in studies recruiting the required numbers of patients has risen from 21% in 2010 to 73% in 2014. The Network was keen to recognise the contributions of key PIs towards these achievements, and a call for nominations in four commercial categories was launched– these included Adam Finn and Athimailapet Ramanan. In February the successful nominees were invited to London to an event which closed with a speech by Professor Dame Sally Davies (Chief Medical Officer, Department of Health). Professor Ramanan (Consultant Paediatric Rheumatologist, University Hospitals Bristol NHS Foundation Trust) was nominated in three

categories, and said of the day:

> *Professor Dame Sally Davies highlighted the importance of the UK doing well in commercial research and how the lessons learnt in commercial research can be applied to public sector funded research. Global firsts are an important indicator for the pharmaceutical industry and this was highlighted by the speakers representing industry; the UK is doing better with recruitment to commercial studies and the NIHR values recruitment to commercial studies and links with industry as pivotal to its primary goal of funding research in UK.*

- **Research collaborators from Bristol**, Dresden, Munich, Vienna and Denver have successful completed the first step in the development of an insulin vaccine to prevent type 1 diabetes. The Pre-POINT study found a positive immune response in children at risk of type 1 diabetes who were given oral doses of insulin, and adverse reactions such as hypoglycaemia were not observed. The findings support the need for a next phase of testing, which will determine whether an insulin vaccine can prevent the outbreak of the disease over the longer term. In the study, children at high risk of developing type 1 diabetes were treated with oral insulin once daily over periods averaging half a year. The control group was given only a placebo with no effect. The active substance group ingested the insulin in powder form together with food at varying dosage levels that were increased in the course of the study. In the highest dosage (67.5 mg), the insulin powder then induced the desired immune response. Professor Polly Bingley confirmed that "the ultimate prevention of type 1 diabetes is the major research focus of our team in Bristol. The results are encouraging and we hope that they will provide the basis for a larger study in young infants in the future."

Reference:

Bonifacio, E., Ziegler, A-G., Klingensmith, G., Schober, E., Bingley, P. J., Rottenkolber, M., Theil, A., Eugster, A., Puff, R., Peplow, C., Buettner, F., Lange, K., Hasford, J. & Achenbach, P. (2015). Effects of High-Dose Oral Insulin on Immune Responses in Children at High Risk for Type 1 Diabetes: The Pre-POINT Randomized Clinical Trial. *Journal of the American Medical Association. 13(15).*

- **The first human trials** of lab-produced blood to help create better-matched blood for patients with complex blood conditions has been announced by Dr Ashley Toye at UoB and Professor Dave Anstee from NHS Blood and Transplant. The process involved the use of stem cells from adult and umbilical cord blood to create a small volume of manufactured red blood cells; it is hoped that when the production is scaled up, it will offer an alternative to specialist patients with blood disorders such as sickle cell anaemia and thalassemia who require treatment with regular transfusions and for whom it is difficult to find compatible donors.

- **Bovine tuberculosis (BTB)** is most likely to be nearly under control in both species taken in isolation, however together, control is likely to be considerably more challenging. In the UK, a test-and-slaughter surveillance scheme forms the basis of BTB control, as well as badger vaccination and culling being trialled in select areas. Until now, studies have tended to focus on the disease in cattle or badgers, but not together. This work, published in the Proceedings of the Royal Society B, demonstrates that feedback between cattle and badgers is critical for understanding and controlling BTB.

Using mathematical modelling techniques combined with data from a range of sources including badger and cattle population data and BTB infection rates, researchers from UoB and Cambridge were able to model the cycle of infection between cattle and badgers and predict the impact of BTB controls.

The findings showed that while infection in both cattle and badgers is most likely nearly under control on their own, targeting badger-to-badger transmission has only had a modest impact on cattle infection. More effective strategies are reducing badger-to-cattle and cattle-to-cattle transmission.

Our findings show that in areas with badger infection, cattle-to-badger and badger-to-cattle transmission is critical to the whole system

Dr Ellen Brooks-Pollock, Lecturer in Infectious Disease Mathematical Modelling, said: "Bovine TB has had a serious impact on the cattle industry in the UK, as well as across Europe. Our findings show that in areas with badger infection, cattle-to-badger and badger-to-cattle transmission is critical to the whole system. You can't just consider one species in isolation. Reducing badger-to-cattle transmission is likely to be more effective than reducing prevalence in badgers alone. This may have particular implications for badger vaccination programmes, depending on local incidence of badger infection."

Reference:
Brooks-Pollock, E. and Wood, J. L. N (2015). Eliminating bovine tuberculosis in cattle and badgers: insight from a dynamic model. *Proceedings of the Royal Society B*, 282(1808).

- **Global declines and extinctions of amphibian populations**, accelerating over the past 20 years, have attracted much media publicity and concern amongst conservation biologists. A number of factors are involved but one major cause has been the rapid worldwide spread of a lethal fungus infection, *Batrachochytrium dendrobatidis* (Bd).

One prominent theory implicates African clawed toads, *Xenopus laevis*, in dispersal of the disease. These animals have been exported from South Africa worldwide since the 1930s, initially for use in human pregnancy testing, but also as pets and as one of the major species for research on

human disease. It has been thought that escaped or released toads, infected with the fungus, had been involved in spreading the infection to native species. This so-called 'out-of-Africa' theory was originally based on circumstantial evidence and has never been confirmed directly.

Research carried out by Professor Richard Tinsley with Professor Matt Guille and colleagues at the University of Portsmouth, has examined the occurrence of Bd in the two areas of the UK where *Xenopus* has been released and has established breeding colonies. Extensive testing of the two colonies showed heavy infections with Bd in the *Xenopus* in these areas. The researchers commented that "most people, including ourselves, would have expected to find infection in the native amphibians sharing the same habitats." However, samples of these frogs, toads and newts gave no evidence of transfer of infection nor of declines in their populations that might have resulted from past disease.

Professor Tinsley emphasised that the results certainly don't support the 'out-of-Africa' theory in the conditions found in the UK. He said: "Our field studies provide a particularly robust test of the possibility of disease transfer: the population in Wales was established in the wild over half a century ago, so we would have expected any ill-effects to have become evident here. But, there is still a need for similar comprehensive testing in countries elsewhere in the world where *Xenopus* has been introduced."

The extent of this deadly pandemic has been a result of human activities, especially the international trade in amphibians

Despite the lack of transfer of infection from *Xenopus*, nevertheless Bd has been introduced from other sources into some areas of the UK. "We still need to understand what prevented the spread of infection from *Xenopus* in our study areas – potentially including variations between strains of the fungus and natural resistance to these strains by native amphibians. Knowledge of these factors controlling infection may help in regions where spread of the fungus is occurring rapidly."

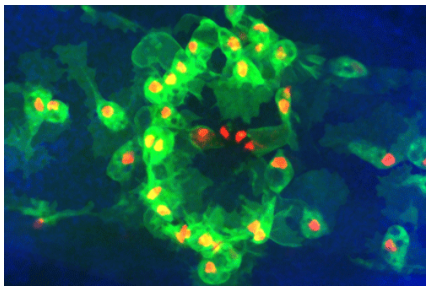
Reference:

Tinsley, R. C., Coxhead, P. G., Stott, L. C., Tinsley, M. C., Piccinni, M. Z. and Guille, M. J. (2015). Chytrid fungus infections in laboratory and introduced Xenopus laevis populations: assessing the risks for U.K. native amphibians. *Biological Conservation*. 184, pp.380-388.

- **Immune cells play an important role in the upkeep** and repair of our bodies. New research has identified the triggers which lead these cells to react and respond in cell repair.

Previous studies had found that the earliest signal produced at a wound site responsible for attracting immune cells to the damaged site is H_2O_2. However, it was still unclear how these cells detect it, and what signalling occurs in these cells downstream of H_2O_2 detection to power their rapid

migration. Using *Drosophila melanogaster* and time-lapse microscopy, the team led by Professor Will Wood, were able to study the process *in situ* and identify what causes the cells to migrate to sites of damage where they then detect, ingest and degrade debris, dying cells and invading pathogens.



After dissecting the signalling occurring in immune cells responding to wound induced (H_2O_2), the team found that it involved a well-established immune signalling pathway used in vertebrate adaptive immune responses. The results suggest that adaptive immune signalling pathways important in distinguishing self from non-self in vertebrates appear to have evolved from a more ancient response designed to distinguished 'damaged self' from 'healthy self'.

Will Wood said, "While inflammation is critical to prevent infection, too much of a response by immune cells can cause or worsen a wide range of human diseases and conditions including autoimmunity, atherosclerosis, cancer and chronic inflammation. This research is therefore critical... and (will) allow us to design therapies to direct immune cells away from sites where they are doing damage and send them into places where they are needed."

This research is... critical for improving human health as it enables us to discover novel points of intervention to manipulate immune cell behaviour

Reference:

Evans, I. R., Rodrigues, F. S. L. L., Armitage, E. L. and Wood, W. (2015). Draper/CED-1 mediates an ancient damage response to control inflammatory blood cell migration *in vivo*. *Current Biology*. 25(12), pp. 1606-12.

- **PIs Professor Elek Molnar together with** Professor Aniko Varadi (UWE) and Reader in Molecular Medicine Dr Kathleen Gillespie (SOCS) have been awarded a three-year PhD Studentship from the University of the West of England for C.H. Caygill.

University Policy on Open Access to research publications

Senate has approved a mandate for the institutional policy on Open Access to research publications, and this will take effect from 1 October 2015. Academics and research students are required to deposit, at the point of acceptance from the publisher, eligible research outputs in the institutional repository (Pure). The mandate is to ensure that all research outputs that will be submitted to the post-2014 REF are eligible, under new requirements from HEFCE. Further information about the mandate and help available. For the full policy please see the Institutional Policy web page.

- **Bristol social scientist appointed ESRC Champion to tackle antibiotic overuse.** Dr Helen Lambert, Reader in Medical Anthropology, has accepted the new position of AMR Research Champion. 'The rise of microbial resistance to antibiotics is largely a consequence of human action, and is as much a societal problem as a technological one,' says Dr Lambert.

The solution to AMR is widely thought to lie in the development of new antibiotics and diagnostic tests. However, on beginning the role of Champion, Dr Lambert stressed that social science research 'is as important as laboratory research in tackling this global health problem'.

Social organisation is just as important as what happens in the laboratory. We need to find answers to questions such as why antibiotics are often overused, how pharmaceutical supply chains and the organisation of healthcare affect access to antibiotics, or what part farming practices might play in AMR transmission. In this role, I aim to engage with a broad range of social scientists - from economists and psychologists to anthropologists and geographers - in undertaking research relevant to AMR, as well as highlighting the need for social science evidence that will help improve our understanding and lead to new ways of dealing with the threat of infections caused by antibiotic resistant bacteria.

E·S·R·C ECONOMIC & SOCIAL RESEARCH COUNCIL

Over the coming year the team will be organising a range of activities to engage researchers and highlight relevant research.

- **A new technology which could increase protection against antibacterial** and antifungal infection is likely to have significant impact across a number of areas including dentistry, where one in seven composite fillings fail within seven years and 86 per cent of these failures are caused by bacterial infection.

Michelle Barbour, Senior Lecturer in Biomaterials. Image credit: Bhagesh Sachania, UoB

Bristol Biobank

The Bristol Biobank (funded by the David Telling Charitable Trust with stakeholders from the University of Bristol and University Hospitals NHS Foundation Trust) stores samples collected from patients and healthy volunteers for use in biomedical research. The samples form a biorepository to which researchers can apply for use in their research. The collection of a wide range of samples will provide a platform for research into complex conditions.

Researchers may request to deposit samples into the Biobank following the end of a NHS Research Ethics Committee approved study. Consent must have been taken using study specific documentation for the storage and use of these samples in research beyond the study.

The team will also be happy to receive applications to deposit samples for specific projects you wish to set-up using Biobank permissions and documentation.

The Bristol Biobank is licensed by the Human Tissue Authority (licence 12512) to store human tissue for research and has ethics approval from Wales Research Ethics Committee 3 as a research tissue bank to collect and issue biomaterials for biomedical research across a range of therapeutic areas. If you are interested in finding out more about the opportunities of working with the Biobank please contact Manager Claire Matthews, claire.matthews@bristol.ac.uk.

Developed by Dr Michele Barbour and her research group in Oral and Dental Sciences, Pertinax is a new formulation of the antimicrobial agent chlorhexidine, widely used to prevent and treat a range of infections, but which is effective for only a very short length of time. Pertinax increases chlorhexidine's uses by improving its persistence where it is applied. This innovation has won Dr Barbour and Pertinax the £25,000 Materials Science Venture Prize awarded by The Worshipful Company of Armourers and Brasiers.

"Our initial focus will be in the dental market," explains Dr Barbour. "Research shows there is a clear need for long-acting antimicrobial products used in fillings and cements for crowns, bridges and orthodontic braces which will treat and prevent persistent bacterial infections over a much longer time frame than is currently possible." Other potential areas for use include catheters and wound-care products, which are especially prone to infection by antibiotic-resistant bacteria such as MRSA. The money will be used in developing a robust and scalable manufacturing process for commercial application.

- **The Ebola virus outbreak in West Africa** has been going on for over a year and there have been fears about the speed of virus evolution and the corresponding effect on vaccines, diagnostics and treatment. Dr David Matthews, whose team led the Bristol component of the study, used blood samples taken from patients and compared changes in the genetic material of the virus from throughout the outbreak. They were able to show that the outbreak had a single point of origin and predicted that diagnostics and treatment would be effective on the current form of the virus.

They used Bristol's Supercomputer, Blue Crystal, to analyse raw data on the Ebola virus in 179 patient blood samples to determine the precise genetic make-up of the virus in each case. This allowed the team to examine how the virus evolved over the last year, informing public health

policy in key areas such as diagnostic testing, vaccine deployment and experimental treatment options. The process took 560 days of processing time, generating 9,000bn letters of genetic data before reaching the virus' 18,000 letters long genetic sequence for all blood samples.

The €1.8M study was funded by the European Union's Horizon 2020 programme and also involved researchers at the University of Edinburgh as well as from throughout the EU and Guinea.

Reference:

Carroll, M. et al. (2015). Temporal and spatial analysis of the 2014-2015 Ebola virus outbreak in West Africa. *Nature*. 524, pp.97-101.

The findings are important as they show whether the treatment and vaccination programmes in place have and will be effective in controlling… the largest known outbreak of Ebola

- **In countries with a high prevalence of HIV**, provision of antiretroviral therapy (ART) programmes in the workplace can be cost saving for companies due to reductions in healthcare costs, absence from work and staff turnover. Recent analysis conducted by Peter Vickerman (UoB) and Gesine Meyer-Rath (Boston University) was the result of a long-standing collaboration with the London School of Hygiene and Tropical Medicine and the Aurum Institute in South Africa.

ART suppresses the HIV virus and stops the progression of HIV disease. It has led to huge reductions in rates of death and suffering, particularly in early stages of the disease. The research developed a mathematical model to evaluate the past and future impact and costs to the employer of an antiretroviral treatment program provided since 2002 by a coal mining company operating at a number of South African mines. The company was one of the first to provide services for HIV-infected employees in a poor country, and provided HIV therapy years before it was available in the government sector. By the end of 2010, 1,149 out of 9,252 employees had tested HIV positive in confirmatory tests and had been enrolled in the company's wellness programme.

The model estimated that, as ART coverage increased from 10 per cent to 97 per cent of eligible employees, increases in the survival and retention of HIV-positive employees and reductions in absen-

New translational research centre

The £5.3 million Translational Biomedical Research Centre (TBRC), currently under construction at Langford, aims to get research out of the laboratory and ensure patients worldwide can access ground-breaking treatments as quickly as possible. Funded by UoB, MRC and BHF, the centre's 'topping-out' was celebrated in September, led by the Centre's Director, Professor Raimondo Ascione.

TBRC will use experimental models relevant to human disease and anatomy and procedures will be tracked in living animals using non-invasive scanning techniques. This will help test new treatments to NHS standards while reducing the number of animals needed. It will operate under the One-Health concept for the benefit of people, animals and environment. This is a key development in the University's vision for a research culture that feeds directly and rapidly into tangible and lasting benefits for the health and welfare of humans and animals alike.

teeism and benefit payments would lead to overall cost savings compared to a scenario of no antiretroviral treatment provision. Specifically, the annual cost of HIV to the company would decrease by five per cent and the average cost per HIV positive employee would decrease by 14 per cent by 2022.

It is rare that a health care intervention saves money...supplying comprehensive HIV care to company employees being one of those rare examples. Our analysis suggests that all businesses should supply for the HIV health needs of their employees to minimise costs

Although the study did limit its scope (e.g. it did not examine the impact of HIV prevention policies on the miners or their families), the changes in costs were robust and translated into average savings of nearly $1 million US dollars per year for the company. Importantly, they found that even in a country with very low HIV prevalence, ART would still save companies money compared to no ART provision. These savings mainly accrue from reductions in benefit payments for death and retirement due to ill-health and in employee healthcare costs.

Reference:

Meyer-Rath G, Pienaar J, Brink B, van Zyl A, Muirhead D, Grant A and Vickerman, P. (2015). The Impact of Company-Level ART Provision to a Mining Workforce in South Africa: A Cost–Benefit Analysis. PLOS Medicine. Available online 1 September 2015.

- Dr Emily Porter from the School of Veterinary Sciences has been awarded the European Advisory Board on Cat Diseases (ABCD) & Merial Young Scientist Award 2015 for her contribution to feline infectious disease research. Her work involves the genetics of feline coronaviruses (FCoV) and the complex interactions between the virus and the feline host during the development of feline infectious peritonitis (FIP), a systemic disease that is a frequent cause of death in young cats. Emily was presented with her award at the congress of the International Society of Feline Medicine (ISFM), held 1-5 July 2015 in Porto.

The European ABCD & Merial Young Scientist Award recognises innovative and outstanding work by promising young professionals in the field of feline infectious diseases or immunology. Emily's research focused on a comparison of the genomic sequences of FCoVs in cats with and without FIP. Her analysis showed that viruses shed in

Dr Emily Porter receiving her award from Jean-Christophe Thibault of Merial Animal Health and Karin Moestl, Chairman of the ABCD group

the faeces of healthy cats and those in the tissues of cats with FIP were genetically closely related but a small number of mutations distinguished the virulent from the avirulent forms.

Additionally, Emily found that viral sequence mutations reported to be associated with FIP virulence were actually associated with systemic infection of the virus rather than FIP per se. These studies have laid the foundation for the development of a robust reverse genetics system that can be applied to field strains of FCoV and, in the longer term, genetically modified recombinant FCoVs as candidate vaccine strains.

- **Grace Edmunds (CMM) has been awarded an EBI Clinical Veterinary Primer** to pursue research into *Proteomic analyses to assess the effects of adenosine on CD8+ tumour-infiltrating lymphocytes: A step towards the restoration of effective anti-tumour immunity*. Her placement will begin their placements later this year.

- **An investment of £150,000 on behalf of the Elizabeth Blackwell Institute** for Health Research, through its Wellcome Trust ISSF Award (match funded by the University of Bristol), will fund three new posts that will be openly available to help support all health and biomedical researchers across the University in their informatics needs. These posts will come into full effect in the early part of 2016, and will comprise:

EBI has funded three new posts that will help support all health and biomedical researchers across the University in their informatics needs

i) A *Biomedical Research Computing Analyst* based in the Advanced Computing Research Centre who will enable researchers working with high throughput, multi-omic data and complex modelling to have enhanced access to the University's HPC and Research Data Facilities in order to generate, refine and optimise the research software they specifically need.

ii) A *Genome Informatician* located in the Life Science Building 'Omics Hub' with expertise in Galaxy software and who will support researchers analyse deep sequencing, RNA-seq and CHiP-seq

iii) A *Microscopy Image Analyst* based in the Wolfson BioImaging Facility in the Biomedical Sciences Building to help researchers with their image processing and analysis needs. Dr Stephen Cross has been appointed into this role and is expected to be in post on 1 February 2016.

- **Professor Neil Williams has been appointed the new Director of Strategic Alliances** for EBI, with the responsibility for implementing the University's new Strategic Alliance Framework in which they will develop productive strategic partnerships with pharmaceutical and biotechnology industries. Together with Director of Regional Health Partnerships Professor Lars Sundström, they will ensure that Bristol's environment and capability for health and biomedical research translation is fully optimised.

- **This year's Vice-Chancellor's Impact Award**, which recognises innovative research that benefits society by enhancing quality of life, health and creative output, increasing the effectiveness of policy-making or public services or fostering economic success, was presented to Dr Hannah Christensen and Professor Matt Hickman. The winning project is entitled *Infectious*

disease and health economic modelling of vaccination against capsular group B meningococcal disease to support vaccine decision making and introduction. This research was critical to the Department of Health deciding to introduce a new vaccine into the UK immunisation schedule.

From September 2015 the UK will be the first country to offer all babies the Bexsero vaccine against group B meningococcal disease, a leading infectious cause of death in infants. Starting in 2007 when the vaccine was in clinical trials, Dr Christensen, working with a team of modellers and epidemiologists, developed new mathematical models to predict the cases which could be averted by introducing the vaccine and estimated the maximum price the Government should pay for the vaccine to provide value for money to the NHS.

From 2011 to 2014, these models were substantially developed as more data became available and the vaccine licensed. In March 2014, the Joint Committee on Vaccination and Immunisation recommended the introduction of Bexsero into the routine infant immunisation schedule in the UK subject to a cost-effective vaccine price, based principally on this modelling work. The strategy chosen was the one from the model developed by Dr Christensen's team that offered the greatest direct protection at reduced cost. After negotiation between the Department of Health and the manufacturer the vaccine will now be offered to all babies in the UK and will form part of the ongoing national immunisation schedule.

ELIZABETH BLACKWELL FUNDING SCHEMES

Clinical Primer Scheme
Closing date: 11-Dec-15

The awards are aimed at Medical & Veterinary clinical graduates considering a career as a clinical academic but wishing to experience life as a researcher before deciding. They are designed to give outstanding early career clinicians the chance to experience a world-class research environment for the first time. Applications from suitably qualified clinical graduates are invited for six month biomedical research primer projects to be undertaken at the University of Bristol.

EBI Workshops Funding
Support for interdisciplinary workshops in health research at a new or emerging interface between two or more disciplines. Applications are reviewed on a rolling basis.

EBI Catalyst Fund

Pump priming awards can support the most promising and ambitious ideas across the widest inter-disciplinary boundaries. These projects will be identified largely through the running of workshops to explore new possibilities and identify the big questions. Applications are reviewed on a rolling basis.

Returning Carers Scheme

UoB has introduced a Returning Carers' Scheme (RCS) to support academic staff across all faculties in re-establishing their independent research careers on return from extended leave (16 weeks or more) for reasons connected to caring - such as maternity leave, adoption leave, additional paternity leave, or leave to care for a dependant. The deadline for applications is 30 April and 31 October each year.

The Wellcome Trust new Strategic Framework

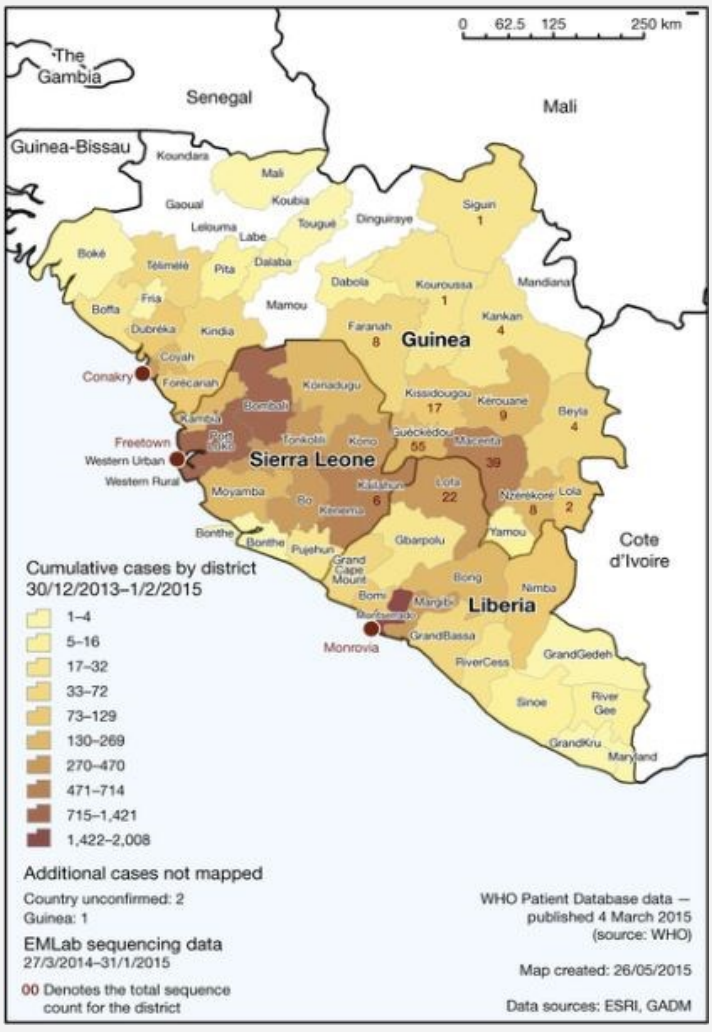
Wellcome's new framework consists of three complementary approaches across science, research and engagement with society:

1. Advancing Ideas. Wellcome will continue to respond to great ideas and inspired thinking that address the fundamental health challenges of our time.
2. Seizing opportunities. Wellcome brings ideas together to make a big difference, providing intensive support that creates real change. They identify times when concerted intervention can accelerate progress towards better health. Priorities will evolve as new challenges arise, drawing on insights from a rich history of achievement and a network of experts from different disciplines around the world. Initial priorities include:
   - Drug-resistant infection. Growing resistance to antibiotics and other drugs threatens many of the benefits of modern medicine. Wellcome will explore how best to use and protect the treatments we have, and to encourage the development of new ones.
   - Vaccination. Too many lives are still lost to diseases that could be prevented by vaccines, mostly in low and middle-income countries. Wellcome will investigate how best to stimulate research, technology development and policy to address this critical unmet need.
   - Our Planet, Our Health. Human health is intimately linked to the environment in which we live. Wellcome will build understanding of how global food systems and urbanisation connect to health, improving the evidence base for public policy.
   - Science education. An appreciation of science, for the future scientist or the informed citizen, begins with learning in school and beyond. Wellcome will help give young people an engaging, relevant and inspiring science education.
3. Driving reform. Wellcome changes ways of working so more ideas can flourish, leading by example and campaigning for wider reform. Their record in areas like open access to research results, public engagement, and research careers has earned us the credibility to challenge ways of working, and to propose better alternatives.

More information on the Wellcome Trust Strategy page.

THIS ISSUE'S SHOWCASED ARTICLE

West Africa is currently witnessing the most extensive Ebola virus (EBOV) outbreak so far recorded. Until now, there have been 27,013 reported cases and 11,134 deaths. The origin of the virus is thought to have been a zoonotic transmission from a bat to a two-year-old boy in December 2013. From this index case the virus was spread by human-to-human contact throughout Guinea, Sierra Leone and Liberia. However, the origin of the particular virus in each country and time of transmission is not known and currently relies on epidemiological analysis, which may be unreliable owing to the difficulties of obtaining patient information. Here we trace the genetic evolution of EBOV in the current outbreak that has resulted in multiple lineages. Deep sequencing of 179 patient samples processed by the European Mobile Laboratory, the first diagnostics unit to be deployed to the epi-centre of the outbreak in Guinea, reveals an epidemiological and evolutionary history of the epidemic from March 2014 to January 2015. Analysis of EBOV genome evolution has also benefited from a similar sequencing effort of patient samples from Sierra Leone. Our results confirm that the EBOV from Guinea moved into Sierra Leone, most likely in April or early May. The viruses of the Guinea/Sierra Leone lineage mixed around June/July 2014. Viral sequences covering August, September and October 2014 indicate that this lineage evolved independently within Guinea. These data can be used in conjunction with epidemiological information to test retrospectively the effectiveness of control measures, and provides an unprecedented window into the evolution of an ongoing viral haemorrhagic fever outbreak.



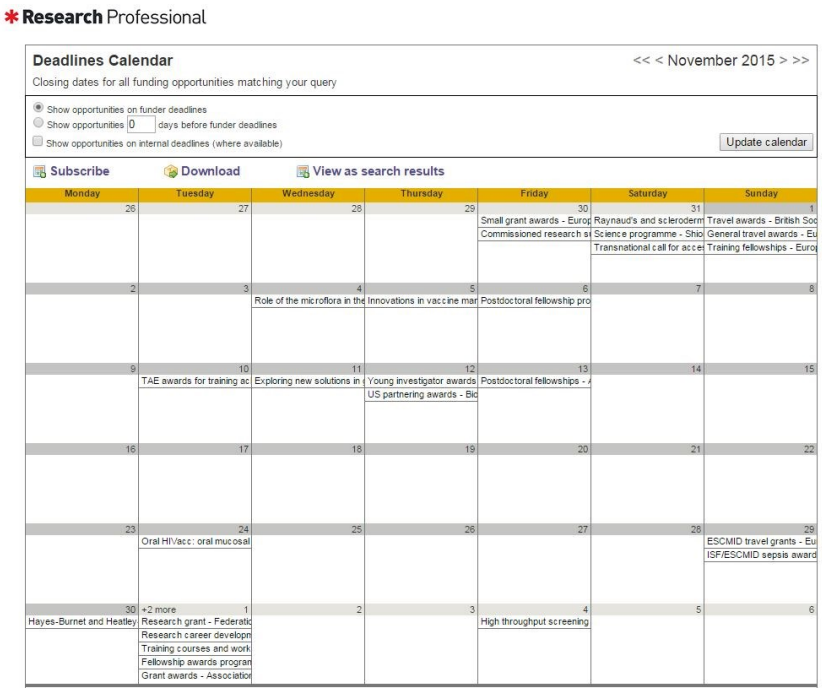
Reference:

Carroll, M. et al. (2015). Temporal and spatial analysis of the 2014-2015 Ebola virus outbreak in West Africa. *Nature*. 524, pp.97-101.

FUNDING OPPORTUNITIES IN INFECTION AND IMMUNITY

Calendar of potential funding opportunities for I and I

Set up via Research Professional (RP), a full calendar of funding opportunities for Infection and



Immunity Research is available online. Subscribing to a calendar will place the entries in your own calendar, which will automatically update according to pre-specified search criteria. Staff and students have FREE access to Research Professional online from all computers on the University network. You can create your own personalised funding opportunity e-mail alerts by registering with RP. Find out all about it on the RED website.

Henry Smith Charity

Medical research grants

Closing Date: none Award amount: not specified

Support research on child health, bowels and gastroenterology, lung diseases, pancreatic disease, urinary and faecal incontinence. Grants do not support projects on liver disease, tuberculosis or diabetes. Applications are not accepted from individuals or NHS trusts. Grants are tenable for up to three years and may be used towards refurbishment, capital projects or equipment as well as project and salary costs.

Wellcome Trust

Four-year PhD studentship programmes

Closing Date: No deadline Award amount: not specified

H2020: 2016-2017 Societal Challenges and LEIT Work Programmes published

The 2016-2017 Work Programmes for Horizon 2020's Societal Challenges and Leadership in Enabling and Industrial Technologies (LEIT) have now been published, with many of the 2016 calls now open. The Societal Challenge Work Packages reflect the policy priorities of the EC and addresses major concerns shared across Europe. The challenge-based approach is expected to bring together resources and knowledge across different fields, technologies and disciplines. Topic areas include Health, Food Security, Energy, Transport, Climate, Security and Inclusive, Innovative and reflective societies.

A minimum of three partners from three different EU countries are required for both Societal Challenges and LEIT proposals, and there are various deadlines over the next two years, starting as early as February 2016.

If you are interested in discussing involvement in one of these calls, either as a lead or partner, or would like more details about what is available in your area of interest please contact Tiernan Williams.

Enable students to undertake in-depth postgraduate training at centres of excellence throughout the UK in the several biomedical research areas including immunology and infectious disease. The first year combines taught courses with laboratory rotations to broaden the student's knowledge of the subject area. Studentships include a stipend, PhD registration fees at UK or EU student rate, laboratory rotation expenses in the first year, research expenses for years two to four, travel and transferable-skills training.

Arthritis Research UK
Programme Grants

Closing date: to be confirmed Award amount: £1.2M

Provide longer-term support where the aim is to answer an interrelated set of questions on a broader front than would be feasible with projects and, at the same time, should provide an opportunity for innovation and creativity. Open to established groups and that have a substantial research track record already supported by project grants.

European Society for Paediatric Infectious Diseases
Fellowship awards programme

Closing date: 1-Dec-15 Award amount: €100,000

Support basic or clinical research that utilises advanced techniques and methods to improve the health of children through the prevention or management of infectious diseases. Applications with emphasis on prevention will receive high priority. Fellowships can take place outside or within the applicant's institution and country. Candidates must be under the age of 40 on the day of the application deadline.

GW4

Initiator Funds (Round 5) and Accelerator Funds (Round 4)

Closing date: expected mid-Dec-15 Award amount: £20,000

Aim to: support enabling activities that bring together communities of academic staff with excellent and complementary expertise and capability; address research questions with potential for high impact that could not be carried out by any single institution; facilitate exploration of novel research concepts to a point at which significant external funding can be sought; promote and facilitate ground breaking interdisciplinary research; demonstrate clearly the added value of the GW4 collaboration.

European Academy of Allergy and Clinical Immunology

Research fellowships

Closing Date: 31 Dec 15 Award amount: €20,000

Support the research and training of EACCI junior members in a European country outside their own. There are three types of fellowships, short, medium and long-term. Fellowships are worth €5,000 for short-term visits over three months, €10,000 for medium-term visits over six months and €20,000 for long-term visits over 12 months. Preference is given to the specific acquisition of new skills, or the establishment of collaborations.

National Institute of Allergy and Infectious Diseases

Characterisation of mycobacterial induced immunity in HIV–infected and uninfected individuals

The MRC, ESRC, BBSRC and the National Natural Science Foundation of China (NSFC) will shortly be launching a call for research proposals focusing on antibacterial resistance

The objective of this call will be to deliver significant 2-3 year research funding for internationally competitive and **innovative collaborative projects between researchers from China and the UK** that will allow the pursuit of shared research interests.

Before the call the funding agencies will hold a **joint workshop on 24-26 November 2015 in Shanghai;** researchers who do not participate in the workshop will not be precluded from applying to the call. The participating funding agencies have identified four areas for this upcoming workshop, which will then be the focus for the call.

It is currently anticipated that the **call will launch in early December 2015** (following the workshop) with a deadline for applications in mid-February 2016. Funds will be channelled via **The Newton Fund**. Further information on the workshop opportunity and the call pre-announcement can be found on the MRC website.

Win £100k to realise your healthcare business idea with One Start

OneStart is the world's largest life sciences and healthcare accelerator programme offering young entrepreneurs the chance to win **£100k**, **free lab space** and on-going advice from an extensive mentor network drawn from McKinsey & Co., Johnson & Johnson Innovation, GlaxoSmithKline, AstraZeneca, SR One, Takeda Ventures etc.

Applications are open until 1 December 2015. Anyone under 36 years old interested in healthcare entrepreneurship is welcome to apply, from ***all disciplines*** and ideas at ***all stages*** of development - from a simple idea to a startup with ample data. Applicants are encouraged to recruit other scientists, engineers, business students, lawyers, and anyone else with talent and motivation to join your team. Have a fantastic idea but no co-founders; why not assemble your team through the co-founder hub, connecting innovators across the globe.

Closing Date: 11-Jan-16 Award amount: US$275,000

Aims to support hypothesis-generating research on innate and adaptive immune responses induced by mycobacterial infection, Bacillus Calmette–Guerin vaccine or other mycobacterium tuberculosis vaccinations. Studies that include evaluation of immune responses by anatomical location in HIV-infected or uninfected individuals are of particular interest. Applications that address the following areas are encouraged:

•characterisation of the timing, anatomical location and contribution to disease outcome of systemic and mucosal immune responses to mycobacterial infection and vaccination;

•development of new technologies and assays to compare key mycobacterial-specific mucosal and systemic immunological parameters and facilitate more sophisticated and comprehensive monitoring of human immune responses during vaccine clinical trials;

•monitoring of immune responses in appropriate animal models during preclinical studies and vaccine candidate selection.

The main objective is to provide novel data advancing new hypotheses that can contribute to the advancement of new tuberculosis vaccines.

Marie Sklodowska-Curie
Innovative Training Network

Closing Date: 12-Jan-16 Award amount:

Aim to train a new generation of creative, entrepreneurial and innovative early-stage researchers, able to face current and future challenges and to convert knowledge and ideas into products and services for economic and social benefit. ITN will raise excellence and structure research and doctoral training, extending the traditional academic research training setting, incorporating the elements of Open Science and equipping researchers with the right combination of research-related and transferable competences. It will provide enhanced career perspectives in both the academic and non-academic sectors through international, interdisciplinary and intersectoral mobility combined with an innovation-oriented mind-set.

A minimum of three partners from three different EU countries are required.

Medical Research Council
Research Grants-Infections and Immunity

Closing date: 13-Jan-16 Award amount: £1M

Suitable for focused research projects that may be short- or long-term in nature. In addition, they can be used to support method development and continuation of research facilities and may involve more than one research group or institution. Any UK-based researcher who can demonstrate that they will direct the proposed research and be actively engaged in carrying it through is eligible to apply.

Medical Research Council
New investigator research grants – infections and immunity

Closing date: 13-Jan-16 Award amount: unspecified

Provide support for clinical and non-clinical researchers while they are establishing themselves as independent principal investigators. For those who already have an institutional post, it provides funding and protected time with which to establish an independent research career. The grant is also a potential source of research funding for fellows whose awards only cover a personal salary or limited research funds.

Agency for International Development
Partnerships for enhanced engagement in research (PEER) call: Middle East – infectious disease in the Middle East

Closing Date: 15-Jan-16 Award amount: US$80,000

Supports projects related to improving infectious disease prevention, detection, and response in the Middle East region. Proposals that address displaced populations such as refugees from the ongoing conflicts in Syria and Iraq are of particular interest.

Each proposal must be submitted by a national of Egypt, Jordan, Lebanon, Morocco or Tunisia, based at an academic institution, non-profit organisation or government-managed research laboratory, centre or institute in one of these countries. Proposals linking research from multiple institutions across the region are strongly encouraged. Women are strongly encouraged to apply. Researchers from non-eligible countries may participate using their own resources, but may not serve as principal investigators. Each applicants must partner with a US government-supported researcher .

Healthcare Infection Society
Small research grants

Closing date: 1-Feb-16 Award amount: £10,000

Support work on the subject of healthcare infection control, to be carried out in the UK or Eire. Funding is to support small-scale research projects or possibly the costs associated with the visit of an overseas research fellow.

National Institute on Drug Abuse
Prevention and treatment of substance using populations with or at risk for hepatitis C virus (R01)

Closing date: 5-Feb-16 Award amount: unspecified

encourages research focused on the prevention and treatment of hepatitis C virus to reduce new infections and identify and treat existing infections more effectively. This FOA supports the initial development of a clinical trial or research project focused on HCV for at-risk substance using populations, including those with or at risk for HIV.

European Federation of Immunological Societies
World Fellowship

Closing date: 19-Feb-16 Award amount: €1,750 per month plus travel

Supports scientific collaboration, advanced training, learning techniques or methods not available in the applicant's current place of work. The main goal is to build a strong international network of immunological research, and fellowships may therefore be held anywhere in the world. Each applicant must be under 35 years of age and a member of a society affiliated with EFIS.

Healthcare Infection Society
Graham Ayliffe training fellowship

Closing date: 1-Mar-16 Award amount: £70,000

Enables a healthcare professional in training to take one year leave of absence from their training programme to develop a special interest in aspects of the prevention and control of infection. Preference will be given to the following topics: work in a specialist service relevant to infection prevention and control; development of specialist skills and expertise with the potential to become a regional or national resource of expertise; undertaking a significant audit project with greater than local scope, completing a full audit cycle; development of a guideline in an area of significant importance or need, including pilot implementation; production of a structured review literature or meta analysis.

National Institute of Allergy and Infectious Diseases
B cell immunology programme for HIV-1 vaccine development (R01)

Closing Date: 17 Mar 16 Award amount: not specified

This supports basic and preclinical research and the analysis of clinical samples to identify and evaluate parameters critical for programming desired B cell functions. The objective is to encourage multidisciplinary teams to explore and exploit emerging knowledge about the complexities and developmental plasticity of B cells, at vaccine priming and at response recall, that are associated with the induction of potent and durable adaptive immune responses against HIV-1. Applications must propose hypothesis-driven research with the goal of defining biological mechanisms of immune response. Novel approaches based on recently identified molecular markers or pathways of immunological relevance are especially encouraged.

British Infection Association
Research fellowship

Closing Date: 31-Mar-16 Award amount: £70,000

Support trainees undertaking infection-related research in an academic centre in the UK, or appropriate UK-linked centre overseas. Applications are open to clinically qualified trainees in infection or infection-related specialities who are not in a consultant level post, or UK-based non-clinical postdoctoral scientists within four years of the award of their PhD who are not in a tenured academic or top-grade scientist post. All applicants must be supported by a named supervisor in the UK or place of study. The fellowship is tenable for one year and is worth up to £70,000, which may consist of up to £55,000 of salary costs, and up to £15,000 of non-salary costs.

RECENT PUBLICATIONS IN INFECTION AND IMMUNITY

Wuelfing, C. & Roybal, K. (2015). *Encyclopedia of Cell Biology*. Cellular structures controlling T cell signaling in time and space. Bradshaw, R. & Stahl, P. (eds.). Waltham, MA: Academic Press, Vol. 3, pp. 677-686.

Cain, L. E., Saag, M. S., Petersen, M., May, M., Ingle, S. & Sterne, J. (2015). Using observational data to emulate a randomized trial of dynamic treatment switching strategies: an application to antiretroviral therapy. International Journal of Epidemiology. In press.

Verasdonck, J., Shen, D., Treadgold, A., Arthur, C., Böckmann, A., Meier, B. H. & Blocker, A. J. (2015). Reassessment of MxiH subunit orientation and fold within native Shigella T3SS needles using surface labelling and solid-state NMR. Journal of Structural Biology. Available online 6 October 2015.

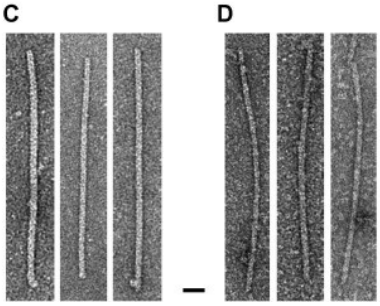


Image: Electron micrographs of purified superlong MxiHL32C and MxiHV68C needles, negatively stained. Bar equals 20 nm.

Foster, A., Mitchell, S. & Wall, R. (2015). Cattle ectoparasites in Great Britain. *Cattle Practice*. 23(2), pp. 280-287.

Boldison, J., Khera, T. K., Copland, D. A., Stimpson, M. L., Crawford, G. L., Dick, A. D. & Nicholson, L. B. (2015). A novel pathogenic RBP-3 peptide reveals epitope spreading in persistent experimental autoimmune uveoretinitis. *Immunology*. 146(2), pp. 301-11.

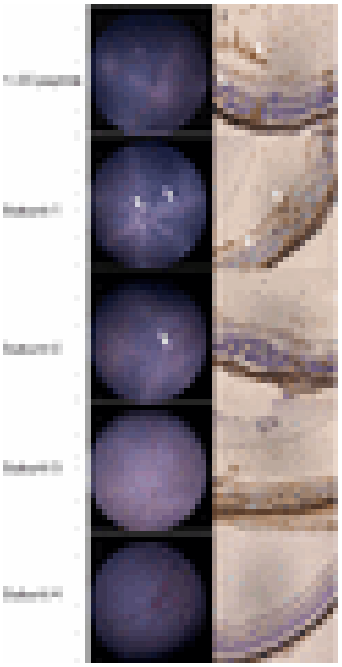


Image: Retinol binding protein-3 (RBP-3) recombinant subunits induce experimental autoimmune uveoretinitis (EAU). C57BL/6J mice were immunized with either 50 µg/ml RBP-3 recombinant subunits 1, 2, 3, 4 or 500 µg/ml 1–20 RBP-3 peptide to induce EAU. Representative topical endoscopic fundal imaging (TEFI) and histology images are shown demonstrating clinical appearance, cellular infiltrate and structural morphology of the retina (vasculitis in the clinical pictures and CD45$^+$ cell infiltrate in the tissue sections are indicated by white arrows). TEFI images taken between days 23 and 25, mice were then killed before the eyes were enucleated, sectioned and stained for CD45$^+$ infiltrate.

Mable, B. K., Kilbride, E., Viney, M. E. & Tinsley, R. C. (2015). Copy number variation and genetic diversity of MHC Class IIb alleles in an alien population of *Xenopus laevis*. *Immunogenetics.* 67(10), pp. 591-603.

Larney, S., Grebely, J., Hickman, M., De Angelis, D., Dore, G. J. & Degenhardt, L. (2015). Defining populations and injecting parameters among people who inject drugs: Implications for the assessment of hepatitis C treatment programs. *International Journal of Drug Policy*. 26(10), pp. 950-7.

Grebely, J., Robaeys, G., Bruggmann, P. *et. al* (2015). Recommendations for the management of hepatitis C virus infection among people who inject drugs. *International Journal of Drug Policy*. 26 (10), pp. 1028-38.

Sen, E. S., Clarke, S. L. N. & Ramanan, A. V. (2015). Macrophage Activation Syndrome. *Indian Journal of Pediatrics.* Available online 24 September 2015.

Marlow, R., Finn, A. & Trotter, C. (2015). Quality of life impacts from rotavirus gastroenteritis on children and their families in the UK. *Vaccine*. 33(39), pp. 5212-6.

Turnbull, S., Redmond, N., Lucas, P., *et. al* (2015). The CHICO (Children's Cough) Trial protocol: A feasibility randomised controlled trial investigating the clinical and cost effectiveness of a complex intervention to improve the management of children presenting to primary care with acute respiratory tract infection. *BMJ Open*. 5(9), e008615.

Thors, V., Morales-Aza, B., Pidwill, G., Vipond, I., Muir, P. & Finn, A. (2015). Population density profiles of nasopharyngeal carriage of five bacterial species in pre-school children measured using quantitative PCR offer potential insights into the dynamics of transmission. *Human vaccines & Immunotherapeutics*. Available online 14 September 2015.

Foster, A., Mitchell, S. & Wall, R. (2015). Cattle mange in Great Britain. *Livestock*, 20, p. 256-261.

Martin, N. K., Vickerman, P., Dore, G. J. & Hickman, M. (2015). The hepatitis C virus epidemics in key populations (including people who inject drugs, prisoners and MSM): the use of direct-acting antivirals as treatment for prevention. *Current Opinion in HIV and AIDS*. 10(5), p. 374-80.

Roybal, K. T., Mace, E. M., Mantell, J. M., Verkade, P., Orange, J. S. & Wuelfing, C. (2015). Early Signaling in Primary T Cells Activated by Antigen Presenting Cells Is Associated with a Deep and Transient Lamellal Actin Network. *PloS one*. 10(8), e0133299.

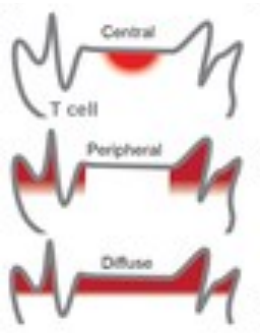


Image: The panel represents six categories to classify spatiotemporal signalling features that reflect underlying cell biological structures. The APC above the T cell is not shown. Central reflects a large central signalling complex, peripheral the part of the actin network stabilizing the interface edge. Diffuse reflects cortical accumulation, invagination enrichment in a transient large T cell invagination suggested to contribute to early signal resetting. Asymmetric reflects individual small lamella and the lamellal pattern is characterised here.

Roybal, K. T., Mace, E. M., Clark, D. J., Leard, A. D., Herman, A., Verkade, P., Orange, J. S. & Wuelfing, C. (2015). Modest Interference with Actin Dynamics in Primary T Cell Activation by Antigen Presenting Cells Preferentially Affects Lamellal Signaling. *PloS one*. 10(8), p. e0133231.

Nicoli, E. J., Ayabina, D., Trotter, C. L., Turner, K. M. E. & Colijn, C. (2015). Competition, coinfection and strain replacement in models of Bordetella pertussis. *Theoretical Population Biology*. 103, p. 84-92.

Dick, A. D. (2015). Enhancing Inflammation as an Adjuvant to Neovascular AMD Therapy. *Investigative ophthalmology & visual science*. 56(9), p. 5431.

Crichton, J., Hickman, M., Campbell, R., Batista Ferrer, H. & Macleod, J. (2015). Socioeconomic factors and other sources of variation in the prevalence of genital chlamydia infections: A systematic review and meta-analysis. *BMC Public Health*. 15, 729.

Nzalawahe, J., Kassuku, A. A., Stothard, J. R., Coles, G. C. & Eisler, M. C. (2015). Associations between trematode infections in cattle and freshwater snails in highland and lowland areas of Iringa Rural District, Tanzania. *Parasitology*. 142(11), pp. 1-10.

May, M. T., Justice, A. C., Birnie, K., *et. al* (2015). Injection Drug Use and Hepatitis C as Risk Factors for Mortality in HIV-Infected Individuals: The Antiretroviral Therapy Cohort Collaboration. Journal of Acquired Immune Deficiency Syndromes. 69(3), pp. 348-3547.

Ramani, P., Sowa-Avugrah, E. & May, M. T. (2015). High proliferation index, as determined by immunohistochemical expression of Aurora kinase B and geminin, indicates poor prognosis in neuro-

blastomas. *Virchows Archiv*. 467(3), pp. 319-327.

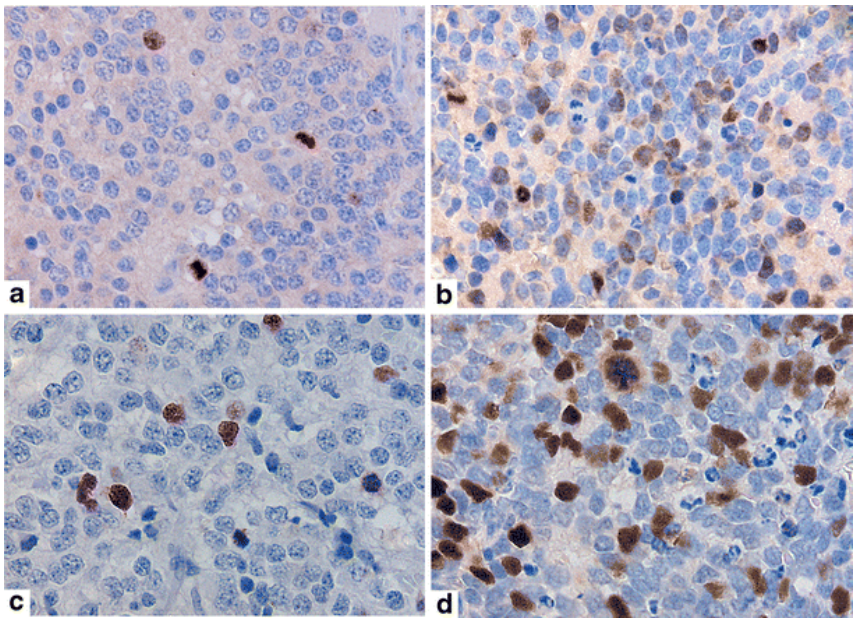


Image: Immunohistochemical expression of Aurora kinase B (AURKB) and geminin (GMNN) in neuroblastoma (NB). ***a*** *AURKB stained <8.5 % neuroblasts in non-high-risk NB,* ***b*** *AURKB stained ≥8.5 % neuroblasts in high-risk NB,* ***c*** *GMNN stained <16.8 % neuroblasts in non-high-risk NB, and* ***d*** *GMNN stained neuroblasts ≥16.8 % in high-risk NB*

Cron, R. Q., Behrens, E. M., Shakoory, B., Ramanan, A. V. & Chatham, W. W. (2015). Does Viral Hemorrhagic Fever Represent Reactive Hemophagocytic Syndrome? *Journal of Rheumatology*. 42 (7), pp. 1078-80.

Cochrane, A., Evlampidou, I., Irish, C., Ingle, S. M., Hickman, M. & Hickman, M. (2015). Hepatitis B infection prevalence by country of birth in migrant populations in a large UK city. *Journal of clinical virology* . 68, p. 79-82.

Jeppesen, C. A., Snape, M. D., Robinson, H., *et. al* (2015). Meningococcal carriage in adolescents in the United Kingdom to inform timing of an adolescent vaccination strategy. *The Journal of Infection.* 71(1), pp. 43-52.

Cabral, C., Lucas, P. J., Ingram, J. C., Hay, A. D. & Horwood, J. P. (2015). "It's safer to ..." Parent consulting and clinician antibiotic prescribing decisions for children with respiratory tract infections: an analysis across four qualitative studies. *Social Science and Medicine*. 136-137, p. 156-164.

Black, V., Adamantos, S., Barfield, D. & Tasker, S. (2015). Feline non-regenerative immune-mediated anaemia: features and outcome in 15 cases. *Journal of Feline Medicine and Surgery*. Available online 26 June 2015.

Wu, W-K., Georgiadis, A., Copland, D. A., *et. al* (2015). IL-4 Regulates Specific Arg-1(+) Macrophage sFlt-1-Mediated Inhibition of Angiogenesis. *American Journal of Pathology*. 185(8), pp. 2324-2335.

Collin, S. M., Granell, R., Westgarth, C., *et. al* (2015). Associations of pet ownership with wheezing and lung function in childhood: Findings from a UK birth cohort. *PloS one*. 10(6), e0127756.

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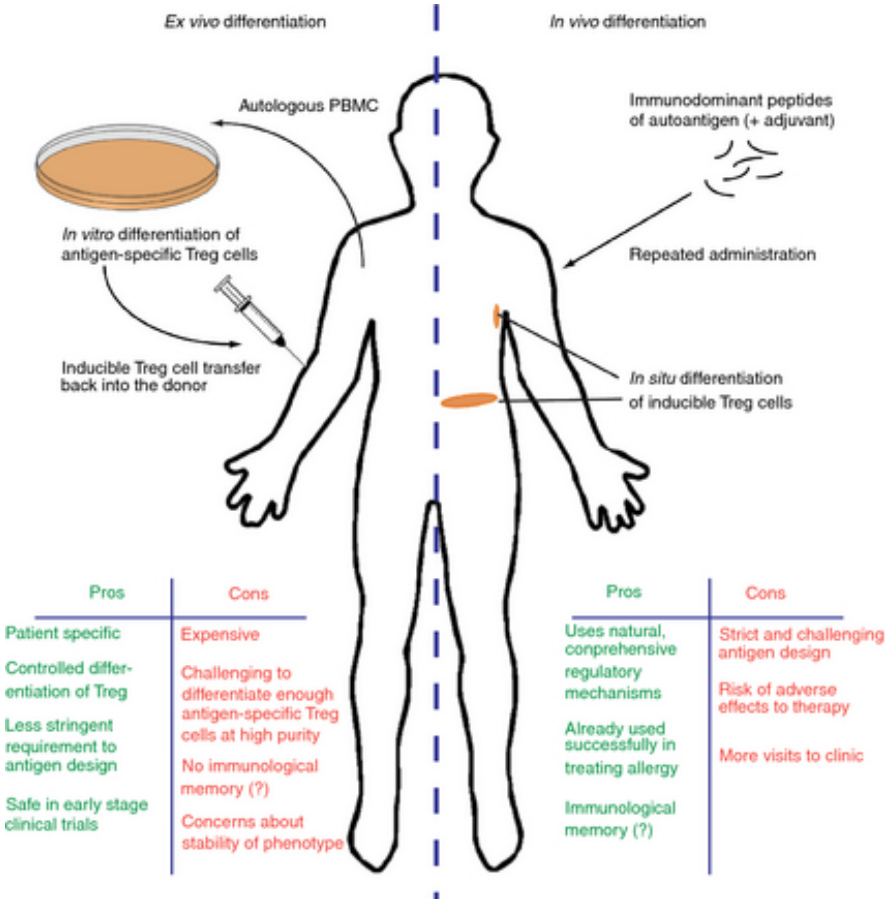

Image: Transfer versus in situ differentiation of inducible regulatory T (Treg) cells in antigen-specific immunotherapy of autoimmune disease. Two different antigen-mediated treatment strategies aimed at using the therapeutic potential of inducible Treg cells are considered for immunotherapy; ex vivo differentiation of autologous $CD4^+$ T cells followed by transfer back into the donor or in situ differentiation by administration of tolerogenic peptide, either alone or in combination with a tolerogenic adjuvant.

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