

# INFECTION AND IMMUNITY NETWORK NEWSLETTER



Elizabeth Blackwell Institut  
for Health Research

## JUNE - JULY 2017

### New EBI Director from 1 August 2017

Following an open, internal, competitive appointment process, Prof [Rachael Gooberman-Hill](#) has been appointed to the role of Director of the Elizabeth Blackwell Institute, which she will commence on 1 August 2017.

Rachael is Professor of Health and Anthropology in the School of Clinical Sciences and currently leads the STAR Programme of Research to improve treatment for long-term pain after knee replacement as well as numerous other research projects. She also works on the Engaged Univer-

sity Steering Group, the Ethics of Research Committee, the Digital Health Steering Group, and the School of Clinical Sciences Equalities Committee. Thanks have been extended to Prof Jeremy Tavaré has led the Institute since its inception in 2011. During his tenure EBI has established itself as an asset to this institution in building collaborative research activities, providing seed-corn funding for early career and established staff and secured significant external funding particularly through the Wellcome Trust ISSF funds. Jeremy will now take up the position

of Director of Health Research in the University.



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## UoBRISTOL EVENTS

### What makes a good drug target

6 July 2017, 12.00 - 14.00. LifeArc (formerly MRC Technology), Verdon Smith Room, RFH

### AMR Policy workshop

7 July 2017, 9.30 - 13.00. Graduate School of Education, 35 Berkeley Square

### Mendelian randomization in the age of large-scale accessible genomics data

11 - 13 July 2017. Keynotes: George Davey Smith and Marcus Munafó. Colston Hall

### Statistics Clinic - 12 July

12 July 2017, 14.00 - 15.30. SM4 School of Mathematics

### Wrap-up: Infection and Immunity Early Career Researchers' event

Thank you to everyone who participated in the landI ECR event which took place on 21 June 2017 in the Life Sciences Building. We were delighted to welcome as our keynote speaker Dr Daniela Ferreira of the Liverpool School of Tropical Medicine who gave a talk entitled *Controlled human infection model with pneumococcus: what have we learned so far?*

#### Prize winners:

Congratulations are extended to Marcus Eales and Amy Thomas who won best poster and best oral presentation prize, respectively. Each received £50 and a certificate.

#### Programme and presentations:

A copy of the full programme is available to download on the Network's intranet, along with some of the presentations. If you cannot access the intranet files are also available on OneDrive.

### Total knee replacement and non-surgical treatment of knee osteoarthritis

13 July 2017, 10.30 - 11.30. Søren Thorgaard Skou (Syddansk Universitet), Seminar Rooms A&B, Learning and Research Building, Southmead Hospital

### NIHR Public Health Research Information Event

14 July 2017, 9.30 - 16.00

### Wellcome Trust visit

20 July 2017, 12.00 - 14.00. OS6, Oakfield House

### Symposium and Launch: GW4 Cryo-EM Facility

1 September 2017, 9.30 - 17.00, Life Sciences Building

### UHBristol Research & Innovation Showcase

31 October 2017, 10.30 - 16.00. Education Centre, Upper Maudlin Street

## OTHER EVENTS



### **Elizabeth Blackwell Annual Public Lecture**

2 November 2017, 16.00 - 17.30. Prof Helen Stokes-Lampard FRCGP

### **OTHER EVENTS**

### **Big Bang Bristol**

6 - 7 July 2017, Trinity Centre



### **11th Mammalian Genes, Development & disease (MGDD) meeting: Neurotrophins in development and diseases of the nervous system**

7 July 2017, 9.00 - 17.00. 6th Floor Seminar Room, Sir Martin Evans Building, Cardiff

### **13th World Congress on Inflammation**

8 - 12 July 2017. Plenaries: Janet Lord (Birmingham University) & Michal Schwartz (Weizman Institute of Science)



### **6th International Meeting on Conversation Analysis and Clinical Encounters**

12 - 14 July 2017. Plenary speakers: Tanya Stivers (UCLA), Anna Lindström (Uppsala), Ruth Parry (Nottingham), Elizabeth Stokoe (Loughborough). Engineers' House, The Promenade

### **PreScribed (a Life Written for Me)**

15 August 2017, 15.30 - 16.30. The Sanctuary, ZOO Venues, Edinburgh



### **BAS Autumn meeting 2017: The Role of Immunometabolic Pathways in Atherosclerosis**

14 - 15 September 2017. Murray Edwards College, Cambridge

### **Big Data in Biology and Health 2017**

25 - 27 September 2017. Keynote: Sarah Teichmann (Wellcome Trust Sanger Institute), Wellcome Genome Campus, Cambridge

*Images from top: Helen Stokes-Lampard, Janet Lord, Elizabeth Stokoe, Sarah Teichmann*

# NEWS

## Launch of SRIs and Networks

In Dec 2016 the University of Bristol announced the formation of Specialist Research Institutes (SRIs) following a competitive application process. Under the University's new strategy plan, an SRI represents a field in which Bristol is acknowledged to be a world leader and where there is significant alignment with regional, national and international ambitions. SRIs will complement existing disciplinary strengths in Schools and Faculties and will be limited in number to have an effective role in institutional branding. An external launch of the SRIs took place in March 2017.

There are three Institutes which will sit in the biomedical / health space:

- **Bristol BioDesign Institute** (Dir: Dek Woolfson)
- **Bristol Heart Institute** (Dir: Gianni Angelini)
- **Bristol Population Health Science Institute** (Dir: Caroline Relton)

From 2017 University Research Themes will cease to

be formally endorsed and presented at an institutional level. This means that the Infection and Immunity *Theme* has been transformed into the

**Infection and Immunity Research Network.** Networks, which also include Cancer, Neuroscience and Fundamental Biosciences, have migrated from the University's Research pages and now sit under the [Elizabeth Blackwell Institute](#). (This also applies to the external face of PURE, Explore Bristol).

There are guidance notes further explaining the roles of SRIs and Networks [online](#) (Single Sign-on required).

Despite the shift it is still very much business as usual for landl. The steering group is continuing to meet, Newsletters and digests are still being produced and the website is being regularly updated with news and events.

It might be worth noting that People Profiler is no longer being supported and will

eventually be replaced by PURE, which will act as an interim profiling tool until new software can be brought in. The People listing on the Infection and Immunity website will eventually point to PURE once People Profiler is phased out. Membership to a Research Network on PURE must go through an approved Research Groups Administrator (which is Catherine Brown, Administrator for the Network). If you or people you know within your research groups should/would like to be added to the mailing list and/or the PURE group, please [contact Catherine](#).



## Gene may hold key to bowel disease

A key gene that helps to explain an underlying cause of incurable bowel disorders such as Crohn's disease has been identified by UoB and Edinburgh. Blocking the gene harms vital parts of the cell and leads to bowel disease, while targeting these vital cell parts with drugs can reverse damage.

Inflammatory Bowel Disease (IBD) includes Crohn's Disease and Ulcerative Colitis. The causes of these disorders are unknown and there is currently no cure. The gene, MDR1, governs an extractor system for toxins in the gut. Edinburgh showed that

MDR1 function was lower in colonic biopsies from people with inflamed IBD compared with those without inflammation.

To demonstrate how MDR1 dysfunction leads to bowel damage, they then showed that mice lacking MDR1 had faulty mitochondria; this dysfunction resulted in colitis. They further implicated the role of mitochondria by linking IBD to a large number of genes involved in their regulation through analysis of genetic data from 90,000 people, 40,000 of whom had IBD. The study also showed that a drug called Mitoqui-

none – which protects the mitochondria against toxins – can reduce colitis and promote bowel recovery in the mice lacking MDR1, which scientists say is a significant step forward.

The research, carried out in collaboration with researchers (Prof John Iredale) at UoB, the USA and Japan, was funded by the MRC and Crohn's and Colitis UK.

Ho J-T *et al.* (2017). [MDR1 deficiency impairs mitochondrial homeostasis and promotes intestinal inflammation](#). *Mucosal Immunology*. Published online 12 April 2017.

## Funding successes: Part 1

An award from the **University Strategic Fund** has gone to Dr [Eric Morgan](#) (Veterinary Sciences), Dr [Debbie Watson](#) (Policy Studies) and Dr [Katy Turner](#) (Veterinary Sciences) for *Behaviour change to reduce effects of dog fouling on child health*.

An **NIHR i4i** Award to Prof [Julian Hamilton-Shield](#), Co-applicant Dr [Elsa Marques](#) (both SOCS), of £750,000 for *AmBeR Evaluation and validation of a breath ammonia*

*measurement technology for the improved management of patients with urea cycle defects*. The aim of this research is to establish whether the AmBeR system can be used to improve the management of children with rare but potentially devastating Urea Cycle Defects. Working with colleagues at UWE and an industry partner Breath Dx, we will trial this entirely novel device to assess its utility as a near to patient ammonia measuring device in collaboration

with clinical services in Bristol, Great Ormond St, Guy's Hospital and Birmingham Children's Hospital.

To Prof [Moin Saleem](#) and Dr [Gavin Welsh](#) (Co-Investigator), **Kids Kidney Research** project grant of £100k for *Personalised immunomonitoring in nephrotic syndrome - towards a molecular re-classification of disease*. This project is for T and B cell transcriptomics in patients with relapsing nephrotic syndrome.



## Cystic fibrosis study

Cystic fibrosis is a common life-shortening inherited disease that affects over 70,000 people worldwide. Individuals living with cystic fibrosis carry faults in a single gene that disables or destroys protein CFTR (cystic fibrosis transmembrane conductance regulator). CFTR plays a crucial role in cells by forming a gated pathway for chloride ions to stream across cell membranes. Loss of CFTR leads to ducts and tubes in the body becoming blocked by thick, sticky mucus, causing breathing difficulties in the lungs and problems digesting and absorbing food in the gut.

Since 1989, when CFTR was first identified, more than 2,000 changes have been reported in its gene, 1,700 of which lead to cystic fibrosis. Among the remaining 300 replacements are a group of silent changes which have long been considered without effect on how proteins are made and how they work in cells.

The team, led by Prof Zoya Ignatova (Hamburg) and Prof [David Sheppard](#) (UoB) with colleagues in the Netherlands and the USA investigated the impact on the CFTR protein of a silent change in gene T2562G. T2562G changes how the CFTR protein is

made; it causes the CFTR pathway for chloride ions to become narrowed. This change is the result of how the cell reads genetic information; T2562G causes ribosomes to slow down the speed with which CFTR is made, resulting in an altered protein with impaired chloride transport. This reveals a new unexpected way by which silent changes in genes alter how proteins are made and how they work in cells.

Kirchner S et al. (2017). [Alteration of protein function by a silent polymorphism linked to tRNA abundance](#). *PLOS Biology*. Published online 16 May 2017.

## Cost-effectiveness of Hep C treatments

Josephine Walker, Linda Campbell and Joanna Coast of the [Health Economics at Bristol](#) team are working in collaboration with Médecins Sans Frontières (MSF) to evaluate the impact and cost-effectiveness of new direct acting anti-viral (DAA) treatments for Hepatitis C virus (HCV) in Cambodia and Pakistan. Chronic HCV infection is a major global health problem, with 80m infections worldwide. The World Health Organization targets elimina-

tion of viral hepatitis as a public health concern by 2030 through prevention and access to highly effective DAAs. DAAs are prohibitively expensive in high-income countries (~\$80,000 per treatment), and although generic versions and negotiated rates bring the cost of the drug down in low and middle income countries, access to this cure requires introducing a diagnostic and treatment pathway for HCV where very little infrastructure was previ-

ously available to identify or treat liver disease. The team is measuring costs and modelling HCV disease progression and transmission to project the impact and cost-effectiveness of screening and treatment programmes run by MSF. The results will be used to support advocacy for governments to implement public treatment programmes and to identify strategies for elimination.

## New drug combination could help children with arthritis



Over 5,000 children and adolescents with juvenile idiopathic arthritis (JIA) in the UK are likely to develop uveitis. A clinical trial found that adalimumab, in combination with methotrexate, was an effective therapy in children and adolescents with JIA-associated uveitis. The majority (75%) of those treated with ada-

limumab experienced a significant reduction in eye inflammation. An early analysis of the data was so convincing that the trial was stopped early. There are 15,000 children and adolescents in the UK with the auto-immune disease JIA. With one third of those likely to develop uveitis, leading to more serious visual im-

pairments such as blindness, the results could prove an effective treatment in future.

Ramanan AV *et al.* (2017). [Adalimumab plus Methotrexate for Uveitis in Juvenile Idiopathic Arthritis](#). *The New England Journal of Medicine*. 376(17).

## Elizabeth Blackwell Institute funding successes

### Postgraduate Discipline Hopping Fellows 2017

The scheme supports a small number of postgraduate researchers currently enrolled on one of the University of Bristol Wellcome Trust-funded 4 year PhD programmes who receive funding that enables them to 'discipline hop' and experience a new field.

Recently in receipt of an award is [Dylan Bergen](#) (SOCS) for *In silico prioritisation and validation of causal genes that underpin osteoporosis pathogenesis*.

### Confidence in Concept

CiC awards fund larger proof of concept studies which provide robust evi-

dence to funders of the feasibility of a proposed solution to a health, clinical or product development need.

They are intended to accelerate the translation of discovery research into new therapies, diagnostics and medical devices by supporting preliminary work or feasibility studies to establish the viability of an approach – before seeking more substantive translational funding. Recently in receipt of such an award are:

### [Massimo Antognozzi](#)

(Physics, pictured above right) for *Developing a mobile device for rapid antimicrobial resistance detection in primary care*, and



### [Richard Lee](#)

(SOCS, below) for *Selective calcineurin inhibition for the treatment of corticosteroid resistant diseases*.



## Improved life expectancy for HIV sufferers

Life expectancy of 20-year-olds starting treatment for HIV has increased by around a decade in the EU and North America since the introduction of antiretroviral therapy in the mid-1990s.

The findings could help to reduce stigmatisation and help people with HIV gain employment and obtain medical insurance, as well as encouraging those diagnosed to start treatment as soon as possible and continue it fully. Their projections suggest that life expectancy of a 20-year-old who began treatment from 2008 onwards and had a low viral load after a year of treatment may approach that of the general population (around 78 years old). However, life expectancy for people with HIV most-

ly remains lower than that of the general population.

The research illustrates a success story of how improved HIV treatments coupled with screening, prevention and treatment of health problems associated with HIV infection can extend the lifespan of people diagnosed with HIV. Combination antiretroviral therapy has been used to treat HIV for 20 years, but newer drugs have fewer side effects, involve taking fewer pills, better prevent replication of the virus and are more difficult for the virus to become resistant to. The improvements are likely to be a result of the transition to less toxic antiretroviral therapy with more drug options for people infected with a drug-resistant HIV strain, better

adherence to treatment, improved treatment of co-occurring conditions and opportunistic infections, and increased use of screening and prevention programmes for conditions such as cardiovascular disease and cancer.

The study used data for 88,504 people with HIV who started antiretroviral treatment between 1996 and 2010 from 18 European and North American studies. In order to estimate life expectancy, it tracked how many people died during the first three years of their treatment, their cause of death, HIV viral load, immune cell (CD4 cell) count and whether they were infected through injecting drugs.

[More info](#)

## Funding successes: Part 2

**Arthritis Research UK** Clinical Studies Group grant to Dr [Emma Clark](#) (£587,000). To produce and evaluate a clinical tool to screen older women in primary care with back pain for vertebral fractures.

**MRC Stratified Medicine** - Consortium Building award to Prof [Moin Saleem](#) (£15,000) for *NURTURE - changing the*

*landscape of renal medicine to foster a unified approach to stratified medicine*. Awarded after shortlisting in initial round. To help build the consortium and support the full application.

**Kidney Research UK** Post-Doctoral Fellowship to Dr [Kathryn Garner](#) (£220,472) for *Modelling Angiotensin*

*receptor-associated protein (ATRAP) interaction dynamics to define novel targets for treatment of Chronic kidney disease*. This is to investigate angiotensin II and TNF-alpha signalling in kidney podocytes using high content imaging and mathematical modelling with the aim of identifying novel drug targets for the treatment of CKD.



## Treatment of infected eczema

Eczema is a common condition which affects around one in five children in the UK. Eczema sometimes 'flares', and having particular bacteria on the skin may contribute to its cause. These flares are often treated with antibiotics.

The [CREAM](#) study, led by Cardiff, wanted to find out if oral or topical antibiotics help improve infected eczema severity. Results from the analysis of data from 113 children with non-severely infected eczema showed no significant difference between the groups in the resolution of eczema symptoms at two weeks, four weeks or three months. Researchers found rapid resolution in response to mild-to-moderate strength topical corticosteroids and emollient treatment, and ruled out a clinically meaningful benefit from the addition of either oral or topical antibiotics.

Francis NA *et al.* (2017). [Oral and topical antibiotics for clinically infected eczema in children: a pragmatic randomized controlled trial in ambulatory care](#). *Annals of Family Medicine*. 15(2), pp124-130

## Funding successes: Part 3

Dr [Sebastian Oltean](#) from the [Richard Bright VEGF Research Trust](#), for *Diavit as a new treatment for diabetic nephropathy*. £46,848 awarded; project dates 01/05/2017 to 01/05/2019.

Prof [Adam Finn](#) from **CHC Hospital Pediatrico** (EU) for *Cross-sectional survey of meningococcal carriage in university students in Coimbra 2016 - evaluation of saliva sampling in comparison to oropharyngeal swabs*. £117,255 awarded; project dates 01/09/2016 to 01/01/2018.

Dr [Jim Spencer](#) from the **MRC** for *Determining the clinical and environmental impact, burden and cost of extensively drug resistant Enterobacte-*

*riaceae in China*. £237,274 awarded; project dates 01/12/2016 to 01/07/2019.

Dr [Matthew Avison](#) from the **Medical Research Foundation** for a *National PhD Training Programme in Antimicrobial Resistance Research*. £2,451,007 awarded; project dates 01/09/2017 to 01/01/2023.

Dr [Eric Morgan](#) from the **Worldwide Universities Network** for *New insights into the transmission of Angiostromylus lungworms by gastropods under climate change; a comparative approach was successful*. £8,200 awarded; project dates 01/01/2017 to 01/01/2018.

Dr [Angela Nobbs](#) from the **British Heart Foundation** for *Molecular mechanisms in Streptococcus-triggered endocarditis*. £189,630 awarded; project dates 01/05/2017 to 01/05/2020.

Prof [Peter Vickerman](#) from the **Bill and Melinda Gates Foundation** for *Expanded use of ART for treatment and prevention for female sex workers in South Africa*. £78,313 awarded; project dates 01/11/2016 to 01/04/2018.

Dr [Jennifer Haworth](#) from the **Royal College of Surgeons** for *Mechanisms of oral Streptococcus-induced platelet activation*. £8,700 awarded; project dates 01/03/2017 to 01/03/2019.

## Health Integration Teams: Annual Reviews

The **Bones and Joints HIT** lead the INFORM programme, a randomised control trial of one versus two-stage revision of infected hip replacements; have agreed best-practice standards across the Bristol hospitals for DEXA bone density scans; reviewing the pathways for diagnosing patients with fibromyalgia; and developing unified best practice for patients with vasculitis and the connective tissue diseases, on top of conducting self-management research.

The **Bristol Immunisation Group HIT** aims to improve the local performance and resilience of the national immunisation programmes. The team has evaluated the first year of the childhood flu programme for school age children; findings strongly support the delivery of the programme in school settings and has added to the evidence for future commissioning of these services. They designed and conducted the SPIT study, which looked at giving meningitis B (MenB) vaccine to 16-18 year olds in two local secondary schools. This builds on earlier local carriage and vaccine studies in schools and the University of Bristol, where a

large proportion of undergraduates were given MenB vaccine in 2014. They also facilitated a service change to tackle local issues of long waiting lists and low uptake of the BCG vaccine so that it could be delivered by neonatal community staff.

The **Sexual Health Improvement for Population and Patients Health Integration Team (SHIPP) HIT** works to promote evidence based sexual health improvement. Their focus of the last 12 months has been to support the commissioning of a new integrated sexual health service across Bristol, North Somerset and South Gloucestershire (BNSSG). They provided commissioners with cost effective evidence based advice that has underpinned the procurement process. In November 2016 the contract to provide the new service was awarded to Unity Sexual Health, a coalition involving Bristol Sexual Health Centre, the specialist service provided by University Hospitals Bristol NHS Foundation Trust, and all major third sector providers. SHIPP's leadership in research and service innovation has also helped champion a number of research projects in the past year.

The **Respiratory Infections Health Integration Team (RuBICoN) HIT** has been working to improve advice and support for parents and patients, and to reduce antibiotic use in the treatment of respiratory infections, since December 2012. They began the year by looking at work streams again, and agreeing on focus projects. They ran a feasibility pilot for introducing parent advice sessions on common childhood illnesses and one to evaluate an intervention that gives personalised antimicrobial prescribing feedback to GPs. With the aim of improving antimicrobial stewardship.

The **Chronic Kidney Disease Health Integration Team (CKD) HIT** successfully developed a telephone clinic service for kidney transplant patients. On average patients were saved 37 miles of travel to and from the hospital; 100% of patients fed back that that they would recommend the clinics to others. They have developed a dashboard, adopted at UHBT and NBT, which records incidences of acute kidney injury by stage, location and consultant, which is an excellent basis for identifying and addressing issues.

## Funding successes: Part 4



Prof [Julian Higgins](#) (top left) from the **World Health Organisation** for his contribution to protocols for trials on non-specific effects of vaccines. £6,095 awarded; project dates 28/02/2017 to 31/07/2017.

Dr [Esther Van Der Werf-Kok](#) (middle left) from the **Louis Bolk Institute** for *Antibiotic prescription rate study*. £12,000 awarded; project dates 01/01/2017 to 01/01/2018.

Dr [Darryl Hill](#) (bottom left) from the **Wellcome**

**Trust** for *Understanding the contribution of antibodies against meningococcal serogroup B pili, to the bactericidal activity of sera from individuals vaccinated with Bexsero*. £2,000 awarded; project dates 12/06/2017 to 12/08/2017.

## Image Data Resource

The Image Data Resource (IDR) is a collaboration between scientists in the [Open Microscopy Environment](#) (OME), based at Dundee, and groups at Universities of Cambridge and Bristol, and the European Bioinformatics Institute (EMBL-EBI). The collaboration brings together biologists, imaging specialists, big data scientists and computer scientists.

A team headed by Prof Jason Swedlow (Dundee) has built this public database that collects and integrates imaging data related to experiments published in leading scientific journals. This

means that 'Big Data' from imaging experiments conducted by scientists all over the world that were previously too large and difficult to share are now publicly available.

Access to primary research data is vital for the advancement of science but comparing and analysing image datasets produced by individual researchers is notoriously difficult for scientists. The images are large, unwieldy, complex and heterogeneous. They are rarely publicly available and, even if they are, different means of collating and storing image data mean they cannot

be easily reproduced, compared or re-analysed. IDR automates these processes and pulls individual pieces of related research together to create a vast bank of knowledge that can save researchers time, effort and money while serendipitously highlighting previously unexplored areas with the potential to solve scientific mysteries. This free resource is the first general biological image repository that stores and integrates data from multiple modalities and laboratories.

[More info](#)

## Lab mice and immunology research

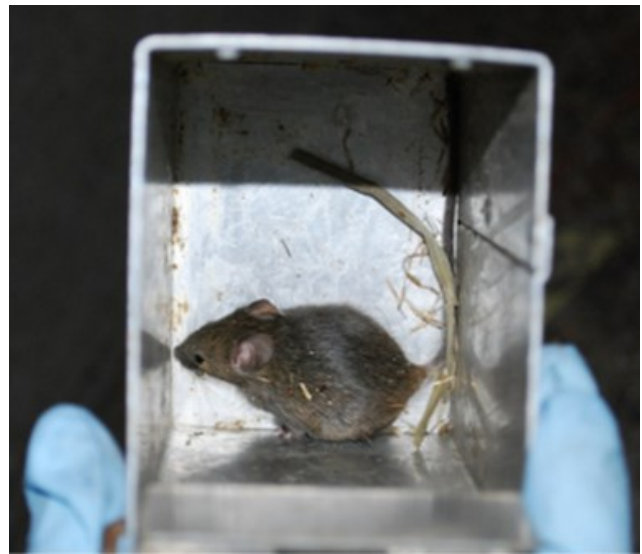
Laboratory mice may not be effective models for studying immune responses to disease, a finding which has implications for all aspects of medical and scientific research. Prof [Mark Viney](#) and colleagues from UoB and London School of Hygiene & Tropical Medicine studied the immune systems of 460 wild mice taken from 12 sites in the UK and compared them with mice bred in captivity.

The study found that these two groups of mice have major differences in their immune make-up. The wild mice had highly-activated

immune systems, most likely because they are more exposed to infections. The wild mice also tightly control their responses to new infections, probably to prevent immune-mediated disease. In 62 immunological measures, 57 differed between wild and laboratory mice. Importantly, the researchers showed that wild mice have more highly-activated myeloid cells. Abolins S *et al.* (2017). [The Com-](#)

[parative Immunology of Wild and Laboratory Mice, \*Mus musculus domesticus\*](#). *Nature Communications*. 8 (14811).

Image © Steve Abolins



## Discontinuing medication to prevent acute kidney injury

Kidney function can decrease suddenly when someone becomes unwell, particularly when the person is elderly, has other medical problems or is taking certain medicine. This acute kidney injury (AKI) can mean a higher chance of being admitted to hospital and spending longer there. One in four patients admitted with AKI do not survive; those that do are often left with long term kidney damage.

Experts suggest that stopping

taking certain medicines during illnesses may reduce the chance of AKI. A systemic review looked at six studies: five in people having coronary angiography and one in people having heart surgery. They didn't find any studies on stopping taking medicines when people weren't already in hospital and became unwell. The studies found that people who continued to take their medicines prior to the angiography or surgery had a small increased risk of kidney injury, compared to

those that stopped taking them.

The review shows a need for more research to look at the effect of stopping taking medicines on kidney function in people when they are unwell.

Whiting P *et al.* (2017). [What are the risks and benefits of temporarily discontinuing medications to prevent acute kidney injury? A systematic review and meta-analysis](#). *BMJ Open*. 7(4).



## Informatics service support for research



The Elizabeth Blackwell Institute for Health Research (EBI), through its Wellcome Trust ISSF Award, and match funded by UoB, invested in two posts that are openly available to help support all health and biomedical researchers across the University in their informatics needs.

Dr Stephen Cross (top left), Research Associate in Microscopy Image Processing and Analysis, Wolfson Bi-



imaging Facility: The primary purpose of my role is to assist users with processing and analysis of microscopy images; typical examples of which include 3D segmentation of cells, characterisation of protein colocalisation using the overlap of fluorescent signals and tracking cells and measuring their mobility. Email [Stephen](#) to discuss your project.

Dr David Lee (bottom left), Research Associ-

ate in Bioinformatics, Life Sciences: My speciality is analysing, predicting and comparing the structures and functions of proteins. More recently, I have expanded my expertise at Bristol into transcriptomics, proteomics and statistics and can now assist with truly comprehensive analyses. Email [David](#) to discuss how he could collaborate with you on your project.

## New trial for prosthetic hip joint infection

The first ever randomised trial to investigate why some patients develop infections after their hip or knee replacement surgery, and which type of surgical revision treatment is best, is being run by UoB. Periprosthetic joint infection (PJI) affects approximately one per cent of patients following total hip replacement (THR) and often results in severe physical and emotional suffering. Current treatment options include the removal of damaged or dead tissue, antibiotics and implant reten-

tion; revising the joint replacement; removal of the joint; and amputation. Revision surgery can be done as either a one-stage or two-stage operation. Both types of surgery are well established in the NHS and appear to result in similar rates of re-infection, but little is known about the impact of these treatments from the patient's perspective.

The [NIHR-funded IN-FORM \(Infection Orthopaedic Management\)](#) trial compares one-stage with two-

stage revision for hip PJI. The trial's primary focus is on patient reported outcomes: pain, stiffness, function and wellbeing in the long-term. The trial also compares the cost-effectiveness, complications and re-infection rates between these surgical interventions. Finally, an interview study explores patients' and surgeons' experiences, including their views about trial participation and randomisation.

[More info](#), including a video of the project.

## Preventing progression in diabetic kidney disease

### **EBI Clinical Primer Case**

**Study.** Glitazones are drugs used to treat type 2 diabetes because they improve insulin resistance and reduce progression of associated kidney disease. But how do they work?

The six-month scheme offered Dr [Caroline Platt](#) a chance to further her understanding of the molecular and cellular basis of kidney disease in children, before training in paediatric nephrology.

The ability of the podocyte to respond to insulin is im-

portant for its health and survival, and therefore health and survival of the kidney itself. This is controlled by PPAR- $\gamma$  (peroxisome proliferator activating receptor), which switches on the genes for the insulin signalling pathways within the podocyte. Damage to the podocyte in people with type 2 diabetes is the first step towards the development of diabetic kidney disease. The glitazones protect the podocyte, and therefore kidney function, by activating PPAR- $\gamma$ . Caroline wanted to investigate the role of PPAR- $\gamma$ , its influence

on how insulin works in the podocyte, and how its activation can prevent progression in diabetic kidney disease. Working alongside Prof [Richard Coward](#)'s team, her research showed that the glitazones activate well-established PPAR- $\gamma$  responsive genes in podocytes grown in culture, and also protect podocytes from damage (induced by a toxin called PAN). Further investigation of the influence of the glitazones on the protein make-up of the cell revealed some interesting avenues to explore.

[More info](#)

## Targeting of disease causing cells

### **EBI Translational Acceleration and Knowledge Transfer (TRACK) Award Case Study.**

There is a problem with the traditional treatment of autoimmune and inflammatory conditions. Steroid therapy doesn't always work, and immunosuppressant drugs can have toxic side effects. Dr [Richard Lee](#) and his team are working to overcome this by exploring technology used in cancer therapy to target steroid-resistant immune cells and avoid damaging healthy non-immune tissues. This involves combining the active

therapeutic agent (in this case an immunosuppressant) with a monoclonal antibody that targets a protein (antigen) specifically found on disease causing cells. These therapeutic pairings are known as antibody drug conjugates (ADCs).

The team had already identified a group of steroid-resistant immune cells as candidates for therapeutic targeting in a range of inflammatory conditions. They now proposed to deliver a calcineurin inhibitor in an ADC directed at a cell surface pro-

tein (CCR6) which they had identified as particular to steroid resistant cells. Pilot data needed to develop this resulted in a partnership with a UCL spinout, Polytherics (now Abzena), to produce the ADC. Their project is also being developed in partnership with US National Institutes of Health.

The work resulted in a US patent application by UoB for ADCs for steroid refractory inflammatory disease.

[More info](#)

# ELIZABETH BLACKWELL FUNDING

## [EBI MRC Confidence in Concept Scheme \(CiC\)](#)

Support health related translational projects. Funding is available to support projects which are at the stage of proof of concept (Confidence in Concept Awards). Applicants successful at the outline stage will be invited to submit a full application for concept development funding.

**Deadline for outline applications: 28 July 2017**

## [EBI Research for Health challenge](#)

Aims to encourage healthcare practitioners and University of Bristol researchers to work together to develop innovative thinking around clinical problems.

**Call opens 13 July 2017**

## [EBI Workshops Funding](#)

Support interdisciplinary workshops in health research at new or emerging interface between two or more disciplines. Applications reviewed all year.

## [EBI Catalyst Fund](#)

Pump priming awards support the most promising and ambitious ideas across the widest interdisciplinary boundaries. They will be identified largely through the running of [workshops](#) to explore new possibilities and identify the big questions. Applications reviewed all year.

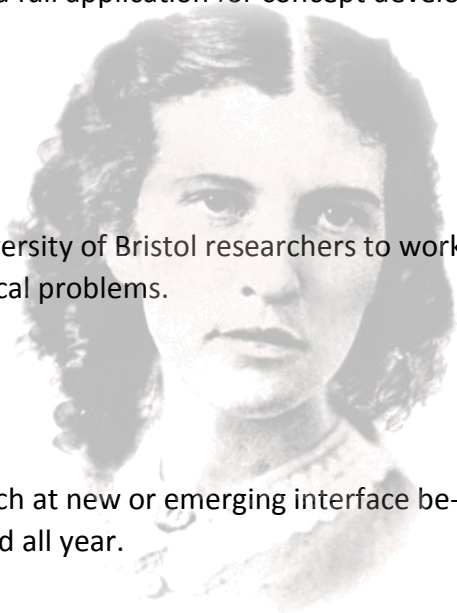
## [Returning Carers Scheme](#)

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 (e.g. maternity leave, adoption leave, additional paternity leave, leave to care for a dependant.).

The deadline for applications is 30 April and 31 October each year.

## [EBI Bridging Funds for Senior Fellows](#)

This scheme is designed to support a small number of academic staff at the University of Bristol who currently hold an externally funded research fellowship. Applications accepted on a **rolling** basis.



# FUNDING OPPORTUNITIES

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 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](#).

The listing below represents a *brief selection* of available funding for the infection and immunity community. Full listings of opportunities are sent out via Schools and are available on the [Research Development website](#).

Note that some calls may be subject to a major bids process, and all details are on the website.

## Healthcare Infection Society

### [Travel grant](#)

Closing date: None

Award amount: £750

Enable trainees and junior members of staff to attend meetings of educational benefit, particularly if work is to be presented.

## European Society of Clinical Microbiology and Infectious Diseases

### [Attendance grants for educational and scientific events](#)

Closing date: None

Award amount: unspecified

Support young European researchers wishing to attend educational and scientific events organised or endorsed by the European Society of Clinical Microbiology and Infectious Diseases. Funding may cover tuition and travel expenses.

## European Society for Paediatric Infectious Diseases

### [General travel awards](#)

Closing date: None

Award amount: €1,000

Enable members to attend scientific meetings by contributing to travel, accommodation and registration costs. Awards are worth up to €1,000 for travel to the US and the Americas, €600 for travel within Europe and €200 for travel within the applicant's own country.

## National Institute of General Medical Sciences

### [Modelling of infectious disease agent study research projects \(R01\)](#)



Closing date: 05-Jul-17

Award amount: unspecified

Supports innovative research that will develop and apply computational tools and methods for modelling interactions between infectious agents and their hosts, disease spread, prediction systems and response strategies. Application budgets are not limited but need to reflect the actual needs of the proposed project.

**US Department of Defense**

[Tick-borne disease research programme – idea award](#)

Closing date: 05-Jul-17

Award amount: USD 250,000

Supports conceptually innovative, high-risk or potentially high-reward research in the early stages of development that could lead to critical discoveries or major advancements that will accelerate progress in improving outcomes for individuals affected by Lyme disease and other tick-borne illnesses.

**US Department of Defense**

[Tick-borne disease research programme – investigator-initiated research award](#)

Closing date: 05-Jul-17

Award amount: USD 700,000

Supports highly rigorous, high-impact studies with the potential to make important contributions to Lyme disease and other tick-borne disease research, patient care and quality of life. Approximately three awards worth USD 700,000 each are available .

**World Health Organization**

[UNITAID grant call for proposals – new tools for vector control in malaria](#)

Closing date: 08-Jul-17

Award amount: unspecified

Supports late-stage product development for new vector control tools in malaria. Projects should last between three and five years.

**US Department of Defense**

[Peer reviewed medical programme – technology and therapeutic development award](#)

Closing date: 13-Jul-17

Award amount: USD 3,000,000

Supports the translation of promising preclinical findings into clinical applications for prevention, detection, diagnosis, treatment, or quality of life research.

**National Institute of Allergy and Infectious Diseases**

[HIV vaccine research and design programme \(P01\)](#)

Closing date: 14-Jul-17

Award amount: unspecified

Supports multi-component, multidisciplinary projects that address scientific questions relevant to Aids prophylactic vaccine discovery research. Application budgets are not limited, but must reflect the needs of the project. The maximum project period is five years.

**Healthcare Infection Society**

[Major research grants](#)

Closing date: 31-Jul-17

Award amount: £99,000

Support research on the subject of healthcare associated infection.

**Centers for Disease Control and Prevention (CDC)**

[Technical assistance services to improve tuberculosis and other infectious diseases control and prevention efforts under other health initiatives and the president's emergency plan for AIDS relief](#)

Closing date: 29-Sep-17

Award amount: US\$500,000

Supports efforts to provide targeted and on-the-ground technical assistance and interventions for the prevention and treatment of tuberculosis and other infectious diseases.

**National Institute of Allergy and Infectious Diseases**

[Partnerships for development of clinically useful diagnostics for antimicrobial-resistant bacteria \(R01\)](#)

Closing date: 04-Oct-17

Award amount: USD 1,050,000

Supports projects focused on the development of clinically informative diagnostic platforms that identify select antimicrobial-resistant bacterial pathogens and determine associated antimicrobial sensitivity or resistance.

**National Institute of Allergy and Infectious Diseases**

[Partnerships for the development of vaccines and immunoprophylactics targeting multiple antimicrobial-resistant bacteria \(R01\)](#)

Closing date: 04-Oct-17

Award amount: USD 4,050,000

Supports projects focused on discovery, establishment of proof-of-concept for, or preclinical development of, lead candidate vaccines or immunoprophylactics that target multiple antimicrobial-resistant Gram-negative bacterial pathogens prevalent in nosocomial infections.

**Cancer and Polio Research Fund**

[Research grants](#)

Closing date: 15 Oct 17

Award amount: unspecified

## THIS ISSUE'S FEATURED ARTICLE

### Insights into the Classical Genetics of *Clitopilus passeckerianus* – the Pleuromutilin Producing Mushroom

de Mattos-Shipley K, Foster G and Bailey AM (2017). *Frontiers in Microbiology*. 8(1056).

*Clitopilus passeckerianus* is the fungal species responsible for the production of pleuromutilin, a diterpene antibiotic that is gaining in commercial interest. Production of the antibiotic is constrained by the low titers typically obtained from isolates. We therefore set out to investigate the possibility of using classical breeding techniques coupled with genetic manipulation as a means to develop such fungi. We show that the original production strain of *C. passeckerianus* is able to fruit under laboratory conditions, giving viable haploid meiotic basidiospores. The derived progeny displayed the typical physiological and genetic characteristics of a tetrapolar mating system. The monokaryon haploids produced pleuromutilin and haploid lines were amenable to genetic manipulation. Together this shows that the basic requirements for a classical breeding approach are present and the tools required to undertake directed genetic engineering on haploid strains are available, demonstrating that strain improvement may be feasible in this fungus.



*Image caption: A mature Clitopilus passeckerianus fruiting body, 4 weeks after plate inoculation. The brown coloration below the basidiocarp is from the released basidiospores.*

# CONTACTS

## The Infection and Immunity Theme is run by a Steering Group:

Co-Chair: [Lindsay Nicholson](#)

Reader in Research



Co-Chair: [Adam Finn](#)

Prof of Paediatrics



- [Anders Johanson](#) - Senior Lecturer in Systems Engineering
- [Alastair Hay](#) - Professor of Primary Care
- [Andrew Davidson](#) - Senior Lecturer in Virology
- [Angela Nobbs](#) - Lecturer in Oral Microbiology
- [Catherine Brown](#) - Research Development Administrator for the Network
- [Claire Heffernan](#) - Chair in Infectious Disease, Head of Infection and Immunity at the School of Veterinary Sciences
- [Collette Sheahan](#) - Research Development Network Facilitator
- [David Morgan](#) - Reader in Immunology
- [Kathleen Gillespie](#) - Reader in Molecular Medicine, Head of the Diabetes and Metabolism Research Group
- [Katy Turner](#) - Senior Lecturer in Veterinary Infectious Diseases
- [Linda Woolridge](#) - Chair in Translational Immunology
- [Mark Jepson](#) - Reader in Cell Biology
- [Peter Muir](#) - Clinical Virology
- [Peter Vickerman](#) - Professor of Infectious Disease Modelling
- [Victoria Davenport](#) - Senior Lecturer in Immunology (UWE)
- [Wendy Gibson](#) - Professor of Protozoology

e: [infection-immunity@bristol.ac.uk](mailto:infection-immunity@bristol.ac.uk)

w: <http://www.bristol.ac.uk/infection-immunity/>