

INFECTION AND IMMUNITY NETWORK NEWSLETTER



MARCH– APRIL 2018

Hub to tackle global vaccination

Established with almost £10 million of funding by the Department for Health, a new research hub to increase global immunisation coverage and improve response to viral outbreaks through the rapid and cost-effective deployment of vaccines has been created. The Future Vaccine Manufacturing Hub is led by Imperial College London and features four other UK universities and three UK institutes, including UoB. Managed by the [Engineering and Physical Sciences Research Council \(EPSRC\)](#), the Hub will address two major challenges:

- How to design a production system that can produce tens of thousands of new doses within weeks of a new threat being identified
- How to improve current manufacturing processes and change the way vaccines are manufactured, stabilised and stored so that existing and new diseases can be prevented effectively, and costs reduced

The hub will collaborate with the [Developing Countries Vaccine Manufacturing Network](#) on manufacturing projects in India, Vi-

etnam, Bangladesh, Uganda and China. Currently, nearly one in five infants across the world - 19.5 million children - do not have access to basic vaccines, and almost one third of deaths among children under five could be prevented through the use of vaccines.

[Read the full story](#)



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UoBRISTOL EVENTS

Dr Alex Thompson (University of Nottingham) - title TBC

1 May 2018, 13.00 - 14.00, Lecture theatre C42, Biomedical Sciences Building

The success of genomics for innovative therapies

2 May 2018, 13.00 - 14.00, Dr Sebastian Nijman (Managing Director, Scenic Biotech), G13/14 Life Sciences Building

Statistics Clinic - 2 May 2018

2 May 2018, 14.00 - 15.30, SM4, Main Mathematics Building

Unlocking molecular secrets of the kidney

2 May 2018, 18.15 - 19.30, Inaugural Lecture by Professor Richard Coward, Lecture Theatre 1, School of Chemistry

Beyond the Pixels: Phenotypic Discovery using Machine Learning and Image Analysis Method

8 May 2018, 13.00 - 14.00, Dr Peter Horvath (Institute for Molecular Medicine Finland), Lecture theatre C42, Biomedical Sciences Building

Inaugural Bristol BioDesign Institute Conference

10 May 2018, 9.00 - 17.00

ERC Workshop

10 May 2018, 14.00 - 16.30, Hepple Lecture Theatre – Geographical Sciences

DNA: Not Merely the Secret of Life

10 May 2018, 18.00 - 19.00, Professor Nadrian C. Seeman (Professor of Chemistry at New York University), School of Chemistry

Open Presentation from Professor Duncan Wingham, Chief Executive NERC

11 May 2018, 11.30 - 12.30, Professor Duncan Wingham (Chief Executive of NERC), G1S Hepple Lecture Theatre, Geographical Sciences

International Clinical Trials Day

14 - 20 May 2018, University Hospitals Bristol NHS Trust

Royal Society open presentation

17 May 2018, 11.00 - 13.00, G1S Hepple Lecture Theatre, Geographical Sciences

Mediation analysis with high-dimensional mediators

17 May 2018, 12.30 - 13.30, Rhian Daniel (Reader in Medical Statistics, Division of Population Health, Cardiff University), Room OS6, Second Floor, Oakfield House

Decoding the Microbiome: Structural and Functional Analysis of an Elusive Genotoxin

23 May 2018, 13.00 - 14.00, Alan R Healy (University of Yale), G13/14 Life Sciences Building

UoB EVENTS

Changing Minds about Changing Behaviour

23 May 2018, 14.30 - 16.00, Professor Dame Theresa Marteau (Director of Behaviour and Health Research Unit, University of Cambridge), Lecture Theatre 1, Chemistry Building

STFC Public Engagement Visit

24 May 2018, 12.00 - 15.30, Room 4.10, School of Education, 35 Berkeley Square

Statistics Clinic - 30 May 2018

30 May 2018, 14.00 - 15.30, SM2, Main Mathematics Building

Professor Michael Dustin - title TBC

5 June 2018, 13.00 - 14.00, Professor Michael Dustin (The Kennedy Institute of Rheumatology, Oxford University), Lecture theatre C42, Biomedical Sciences Building

The public health record of the 2010-2018 UK Government

7 June 2018, 18.00 - 19.00, Professor Danny Dorling (University of Oxford), Bill Brown Design Suite, New Atrium, Queen's Building

Statistics Clinic - 13 June 2018

13 June 2018, 14.00 - 15.30, SM3, Main Mathematics Building

Infection and Immunity Early Career Researchers' Symposium

21 June 2018, 9.30 - 13.15, G13, G14 and foyer, Life Sciences Building

Forming an immune targeted spin-out

29 August 2018, 13.00 - 14.00, Richard Lee (University of Bristol), G13/14, Life Sciences Building

OTHER EVENTS

Integrating molecules with taxonomy and systematics

14 - 18 May Natural History Museum, London

Bath pain forum at Bristol

24 May 2018, 16.00 - 18.00, Dr Andreas Goebel (University of Liverpool), Lecture Theatre 3, UHB Education Centre, Upper Maudlin Street

UoB EVENTS

Infection and Immunity Early Career event 2018

21 June 2018, 9.30 - 13.45

G13-G14, Life Sciences Building

The Infection and Immunity Research Network will be hosting its next Early Career Researchers' (ECRs) symposium in June 2018. This morning event will comprise oral and poster presentations from ECRs as well as a keynote talk.

Abstract Submission

The Network's Steering Group invites all Early Career Researchers conducting research in any Infection and Immunity area to submit an abstract for consideration.

Download the abstract submission form from the event website, or email catherine.brown@bristol.ac.uk.

Abstract submission deadline is 18 May 2018 at 12 noon

£££ PRIZES TO BE WON FOR BEST ORAL AND POSTER PRESENTATIONS £££

Please REGISTER to attend. Registration includes refreshments and a buffet lunch in the atrium. Registration closes 15 June 2018 at 12 noon.

The Infection and Immunity Research Network's Early Career Researchers' event is a fantastic opportunity for Early Career Researchers, junior and senior staff to hear about all the different research taking place across the wider Infection and Immunity community.

PhD students and post-docs are invited to share their methodologies, results, frustrations and skills to a wider audience in the expectation that discussions could lead to greater inter- and multi-disciplinary understanding of the research in question and its potential relevance to other research areas.

Encouraging dialogue between researchers can reveal pools of experience and knowledge that can be applied elsewhere. This fosters not just the creation of new research directions but new ways of working, new ways to support and enable our academic community, and new learning experiences.

ATTENDANCE IS FREE AND ALL ARE WELCOME

REGISTER NOW

NEWS

New I&I co-lead, Strategy and Terms of Reference

Infection and Immunity is delighted to announce a **new co-Lead for the Research Network**, Dr [Ruth Massey](#). Ruth joined the School of Cellular and Molecular Medicine in 2017 from the University of Bath; her current research focus is the study of several aspects of the pathogenicity of the Gram-positive pathogen *Staphylococcus aureus*.



Ruth takes over from Dr Lindsay Nicholson, also in CMM, who has been the basic

science co-Lead since 2011. Grateful thanks are extended to Lindsay for his dedication to the Network and in pulling together a coherent strategy for I&I which is [available to view online](#). I&I research at Bristol encompasses a broad cross-section of disciplines across Schools and Faculties. The Network has identified three key areas which Bristol has demonstrated strengths in which align with what we believe to be national and international research priorities: **antimicrobial resistance, application of vaccines and data science integration**.

The strategy also incorporates

the [Terms of Reference for the Network's Steering Group](#). We are still keen to **recruit a new clinical lead** for the Network as the current incumbent, Adam Finn, has been in post far beyond the recommended 3 years. If you are a clinician (human or animal) and have a few hours a year to spare to continue to build up the community and bring Infection and Immunity research to the fore, we would be delighted to hear from you. Similarly we are looking to recruit an Early Career Representative, from any research area. Please contact catherine.brown@bristol.ac.uk in the first instance.

New I&I icons

You may have noticed a fantastic new visual representation for the Research Network on the cover of this Newsletter.

[Kate Oliver](#), PhD student in the School of Physics, beat

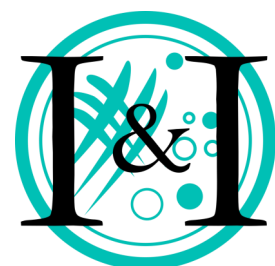
off stiff competition and won the £50 prize for designing the icon. Please do feel free to use the icon for *internal purposes only*; there is a full version and a shorter, round version, as reproduced below. Both available to [download as](#)

[high-res images from the website](#).

Thanks are extended to everyone who submitted to the competition.



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Health Economics @ Bristol updates

The Health Economics at Bristol (HEB) team works closely with local and national policymakers and carries out methodological and applied research. Our three key research themes are the economics of health and care across the life course, efficiency and equity in decision-making, and methods for applied health economics.

Christopher Fawsitt & Nicky Welton



Direct-acting antivirals are successful in curing hepatitis C virus (HCV) in over 95% of patients treated for 12 weeks. However, the cost of a 12-week treatment course is high, with prices ranging from £30,000 to £60,000 per patient in the UK. Shortened treatment durations, which have lower cure rates, have been proposed to reduce costs. With colleagues from Imperial College London and University of Bristol, HEB members Christopher and Nicky evaluated the cost-

effectiveness of different shortened treatment durations for non-cirrhotic patients with HCV genotype 1. Shortening treatment to eight or six weeks is cost-effective, while shorter durations are not. Christopher shared these findings at the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) conference,

[The evolution of value in healthcare](#), held in Glasgow on 4-8 November 2017. The poster, presented on Wednesday 8 November 2018, was entitled *A cost-effectiveness analysis of shortened direct-acting antiviral treatment for mild chronic Hepatitis C virus*.

Christopher and Nicky are now attempting to identify patients for whom shortened treatment is likely to be effective, with treatment duration optimised accordingly.

Myles-Jay Linton, Tim Jones, Will Hollingworth

NHS England is currently analysing public feedback following a national consultation in 2017 on the availability of gluten-free (GF) foods through NHS prescriptions. GF

foods are prescribed to patients with Coeliac Disease (CD), an autoimmune disease characterised by gastrointestinal symptoms following the ingestion of grains containing gluten (wheat, barley and rye). Clinical Commissioning Groups (CCGs) are increasingly opting to restrict these provisions in the face of increasing financial pressures.

HEB members Myles, Tim and Will have been using prescription data linked to GP characteristics to investigate how further policy changes may impact patients and expenditure within CCGs. The availability of GF food on prescription highlights an important question concerning what should constitute 'healthcare', and a much broader moral ambiguity concerning what the NHS has a responsibility to provide.

Go to the [Health Economics at Bristol](#) website for more information on HEB and their work.



Investing in medical research yields healthy returns

Every £1 invested in medical research delivers a return equivalent to 25p every year, a new study shows. Through taxes and donations, the government, charities and the public invest significant sums of money into medical research. The peer-reviewed 'What's it worth?' study shows that this investment delivers outstanding benefits for the economy, as well as for people's health.

What's medical research worth?

Over the past 10 years, Wellcome and other funders have supported a number of 'What's it worth?' studies to better understand the economic impact of medical research.

economic impact of medical research.

This latest study, the third in the series, focuses on musculoskeletal diseases. These conditions, which include inflammatory forms of arthritis, osteoarthritis, back pain and osteoporosis, affect around 10 million people in the UK. The research team was led by Prof Jonathan Grant from King's College London and Prof Martin Buxton from Brunel University. They calculated investments into musculoskeletal disease research over several decades, and worked with disease experts to link research findings to changes in clinical practice.

Their findings show that every £1 of public or charity money invested in musculoskeletal disease research yields patient benefits and economic gains equivalent to a return of 25p a year, forever. On average it takes 16 years for an initial investment to lead to new NHS therapies for musculoskeletal conditions, showing the importance of long-term support for research. The study sits alongside previous research focusing on cancer, cardiovascular disease and mental health.

A [What's it worth? \[PDF 149KB\]](#) briefing is available summarising the findings of this study.

Professor Tavaré to lead new Faculty of Life Sciences

Prof Jeremy Tavaré will take up the role of Dean when UoB's new Faculty of Life Sciences is officially launched on 1 August this year.

Jeremy, a Biochemist and the current Director of Research (Health & Life Sciences) is ideally placed to lead the new faculty which will bring together the schools of Biochemistry, Biological Sciences, Cellular & Molecular Medicine, Experimental Psychology, and Physiology, Pharma-

cology & Neuroscience. His career began at UoB where he obtained a BSc and PhD in Biochemistry, before holding a succession of key roles including Director of Bristol's Wolfson BioImaging Facility, Chair of the Bristol Proteomics Facility, Faculty Research Director for the Faculty of Medical and Veterinary Sciences, Deputy Director of the EPSRC-funded [SPHERE Interdisciplinary Research Centre](#) and Co-Director of the

£5.2M Wellcome Trust-funded [GW4 Clinical Academic PhD Training Programme](#). He was also the inaugural Director of the [Elizabeth Blackwell Institute](#) for Health Research from 2012 -2017.

The creation of the new Faculty of Life Sciences is part of the University's Vision and Strategy to become a life sciences destination for students, academics and research funding.

Funding successes: Part 1

GCRF pump-priming 2017-18 to [Andrew Davidson](#) (CMM) for *Proteomic identification of serum biomarkers for dengue disease severity*, £19,284. Start date 1 Mar 18. UK Co-Is: David Matthews, Andrew Dowey. John McLauchlan, Uni of Glasgow. Partners: Philipines.

GCRF pump-priming 2017-18 to [Katy Turner](#) (Vet School) for *Livestock vaccines for resilient and productive small holder farming*

systems and to reduce reliance on antimicrobials: development of collaborative project, £15,133. Start date 1 Apr 18. UK Co-Is: Mick Bailey, Mark Eisler, Kristen Reyher, Ellen Brooks-Pollock, Katharine Looker, Maria Escobar-Tello, Taro Takahashi. Partner countries: Nigeria, Tanzania, Ethiopia.

BBSRC award to Dr [Paul Race](#) (Biochemistry) for *Structural and Mechanistic Investigations of Antibiotic Production in Bacteria*. £26,929 starting

9 Apr 18 - 9 Apr 21.

BBSRC award to Dr [Ruth Massey](#) (CMM) for *Phenol soluble modulins and their role in the establishment and maintenance of a commensal status for Staphylococcus aureus*. £389,251 from 1 May 18 to 1 May 21.

National Eye Research Centre to Dr [Lindsay Nicholson](#) for *The tissue specific signature of immune cells in persistent uveitis*. £10,000 from 1 Dec 17 to 1 Oct 18.

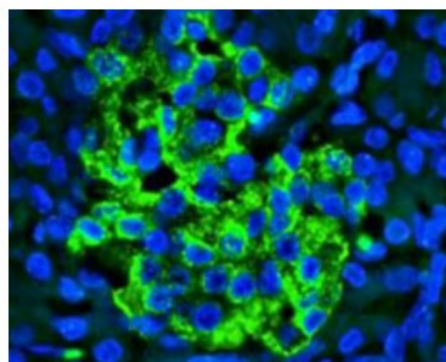
Recognition and public engagement

Ashley Blom and the Musculoskeletal Research Unit team won Best Quality Research Innovation at the Exceptional Healthcare Awards. They were nominated for their five-year research project, RESTORE which looked at improving the experience of joint replacement patients. See the [full list of awards](#).

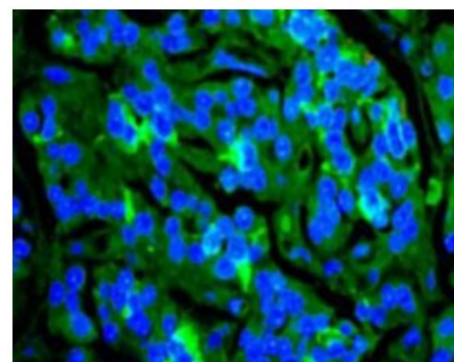
The **Diabetes and Metabolism team** took part in a **Women in Science Outreach Event** on 1

December 2017. PhD students and research technicians based in the Learning and Research building at Southmead hospital ran a stall which aimed to highlight the work of the [Diabetes and Metabolism group](#) and the

variety of career paths in academic science. Secondary school pupils were able to predict and diagnose diabetes by testing for the presence of glucose in Troll "urine".



An islet from a healthy individual: insulin producing beta cells (stained in green).



An islet from an individual with type 1 diabetes: only a few insulin producing cells remain (stained in green).

Tackling antibiotic resistance worldwide

Antimicrobial resistance (AMR) is a serious and growing global health challenge. As such, it is an urgent global threat which requires a coordinated cross-government, academic and industry response. A **GW4 research community** has brought together leading AMR expertise across four universities to help tackle this issue.

To explore how AMR bacteria are transmitted in different environments, a GW4 community identified synergies in research areas in which the four universities hold complementary expertise but are not currently collaborating, such as genomic characterisation of resistant

bacteria, environmental detection and novel sensors. The community built on GW4's research strengths across engineering, physical, life, environmental, veterinary, clinical and social sciences.

The community held a workshop at the University of Bristol to coincide with a 'Bristol Tackles Global Challenges' week, which brought together international AMR researchers from Thailand, Malaysia and Kenya to plan opportunities for funding through the [Global Challenges Research Fund](#).

The one day workshop on 'Systems Approaches to AMR in Different Environments' brought together leading

AMR investigators from all the GW4 universities alongside representatives from some of the most important research centres involved in environmental AMR research, including the NERC [Centre for Ecology and Hydrology](#) and [Cefas](#).

The workshop led to a joint bid to the MRC-led UKRI and Department of Health's 'AMR in a Global Context' call from GW4 universities and key Thai delegates. The resultant development award for '[One Health Drivers of Antibacterial Resistance in Thailand](#)', led by Dr [Matthew Avison](#), has provided £87k to develop a GW4-UK-Thai network to tackle the challenge of antibacterial drug resistance in Thailand. [Read more](#)

Funding successes: Part 2

Daire Shanahan, Sarah George and Angela Nobbs received a David Telling Grant of £16,027 for *Enhanced PPAR-delta expression in patients with periodontitis promotes the inflammatory and pro-atherosclerotic properties of monocytes/macrophages*. The most common cause of heart attacks is atherosclerosis, which involves deposition of cholesterol and inflammation of the arteries that supply the heart, causing them to

thicken and harden. It has been shown that oral bacteria which drive periodontal (gum) disease such as *Aggregatibacter actinomycetemcomitans* (A.a) can trigger such inflammation, and patients suffering from periodontal disease are particularly susceptible to atherosclerosis. However, the precise mechanisms by which these oral bacteria give rise to inflammation are largely unknown. This pilot project seeks to determine whether

A.a. influences and change the behaviour of monocytes in patients with periodontitis via the signalling molecule PPAR-delta. The longer-term benefit of the research will be to develop new treatments that suppress the effects of periodontal bacteria on monocytes and consequently retarding inflammation, stopping the formation of blockages within arteries and preventing heart attacks.

Funding boost for healthcare research centres

Three interdisciplinary research consortia, including the University of Bristol's SPHERE project, have been allocated more than £11 million to continue healthcare sensing systems research that is revolutionising how we identify and respond to outbreaks of infectious diseases, diagnose and manage lung diseases, and recognise and solve emerging health and wellbeing issues in the home environment.

The additional investment will enable vital collaborations to continue addressing many of the most pressing health and wellbeing issues, boosting the UK's status as an innovation nation.

EPSRC's IRCs are centres of internationally acknowledged scientific and technological excellence, bringing together researchers, clinicians, industry and other professionals to make a real impact in areas of key future industrial rele-

vance to the UK.

[**SPHERE**](#) (Sensor Platform for HHealthcare in a Residential Environment), led by the University of Bristol, is developing sensors for use in the home in order to spot health and wellbeing problems ranging from depression and obesity to cardiovascular and musculoskeletal diseases .

Elizabeth Blackwell Institute staffing updates

Dr **Richard Seabrook** MBA joined EBI in January 2018 as **Director of Business Development**. Richard will provide leadership to support the growth of partnerships and alliances with industry in the space across the health arena (ranging from pharmaceuticals, to devices, analytics and novel genomic and informatics methodologies) and assist with maximising opportunities to benefit from external funding streams to support these activities such as the government's new Industry Strategy Challenge Fund. He will also play a central role in identifying new opportunities to translate fundamental research across

UoB's entire health research portfolio into commercial impact.

Lauren Curtis started as the EBI **Diversity & Inclusion Champion** (Mon-Wed) in late 2017. Lauren's focus is on championing and challenging equality, diversity and inclusion within health and biomedical research communities at UoB.

Karen Wallace is now job-sharing the EBI **Executive Assistant** (Wed-Fri) role with **Jocelyn Egginton** (Mon-Wed). Contact ebih-admin@bristol.ac.uk if you need to contact the team.

Jo Barrell began her role as

EBI **Senior Communications Officer** (Tues and Thurs) role in February 2018. Jo has a lot of experience in communications in a range of contexts; her most recent role was Communications Manager at 'Together for Short Lives', the UK charity for children's palliative care.

Didier Laval is the EBI **Public Engagement Associate**, covering for Georgia Bladon who is currently on secondment to the Wellcome Trust. **Ellie Shipman** acts as the EBI **Public Engagement Officer/Fun Palaces Ambassador**.

All EBI staff are based in Royal Fort House.

Funding successes: Part 3

Dr [Richard Lee](#) (BMS/THS) from the **National Eye Research Centre** for *Minimising steroid side-effects in patients with sight-threatening intraocular inflammation*, £58,500 for one year.

Dr [Fernando Sanchez-Vizcaino Buendia](#) (BVS) from the **Jean Golding Institute** for *Fostering collaborations with UK livestock diagnostic laboratories to integrate data sources on antimicrobial resistance into a multi-use data resource*, £2,600 from Dec '17 for 3 months.

Dr [Anna Long](#) (BMS/THS) from the **Juvenile Diabetes**

Research Foundation for *Adult onset Type 1 Diabetes: Slow Progressors or Late Starters?*, £283,873 from Jan '18 for 3 years.

Prof [Matthew Hickman](#) (BMS/PHS) from **NIHR - PGfAR** for *Evaluating the Population Impact of Hepatitis C Direct Acting Antiviral Treatment as Prevention for People Who Inject Drugs* (EPIToPe), from Feb '18 for 5 years.

Prof [Helen Lambert](#) (BMS/PHS) from the **Wellcome Trust** for *Regulating resistance, resisting regulation: New regimens to tackle drug-resistant infections in*

European and Asian healthcare systems, £91,984 from Mar '18 for 1 year.

Dr [Kathryn Garner](#) (BMS/THS) from the **BBSRC** for *Engineering a synthetic light-controlled system to investigate fast insulin oscillation sensing by kidney podocytes*, £50,804 from Aug '18 for 1 year.

Dr [Josephine Walker](#) (BMS/PHS) from the **Liver Institute and Foundation** for *Economic evaluation of the Hepatitis C virus elimination program in Georgia*, £13,920 from Feb '18 for 8 months.

How bone size, shape & structure affects arthritis

How the size, shape and structure of bones and joints contribute towards the development of common age-related diseases such as osteoarthritis and osteoporosis will be investigated thanks to a £1.6 million Wellcome Trust award. Musculoskeletal disorders are a leading cause of disability in the UK's rising ageing population, primarily due to low back pain, fractures and diseases such as osteoarthritis. The total cost of joint replacement and hip fracture surgery is approach-

ing £9.5 billion annually and represents a major burden on society and the NHS. The study is intended to reduce the impact of these common musculoskeletal disorders by providing a basis for improved means of disease prediction, prevention and treatment.

The study, led by Prof [Jon Tobias](#), will involve a collaboration between Bristol, Manchester, Southampton, Aberdeen, Cardiff and Queensland universities.

Using a combination of scans and genetic data from around 100,000 40-to-69-year-old men and women, the team will explore how the size, shape and structure of hips, knees and spines contribute to the development of fractures, osteoarthritis and back pain. The findings will then be used to develop novel strategies for identifying those at risk, slowing disease progression and treating those with established disease.

[Read more](#)

Complementary medicine may decrease antibiotics use

GP surgeries with doctors who also have training in complementary and alternative medicines appear to be less likely to prescribe antibiotics to patients and may hold the key to reducing over-prescribing of these drugs, suggests a study led by researchers at the Centre for Academic Primary Care.

The UK, German and Dutch research team set out to examine what differences there may be in antibiotic prescription rates between

conventional GP surgeries and those with GPs who had also been trained in integrative medicine using NHS Digital monthly prescribing data for 2016.

Data from 7,274 GP surgeries was studied and compared with nine practices that had GPs who had training in integrative medicine, looking at overall prescribing of antibiotics, as well as prescribing of these drugs for respiratory tract infections and for urinary tract infections.

Analysis showed that practices that employed GPs with additional training in IM had significantly lower antibiotic prescribing rates than those with conventional GPs. Prescribing of antibiotics for patients with respiratory tract infections was also noticeably less in practices with IM-knowledgeable GPs. However, there was no difference between the two types of practice when it came to levels of antibiotic prescribing to patients with urinary tract infections. [Read the full story](#)

How cells rebuild after division

When cells divide, they need to rebuild their nucleus and organise their genome. New research demonstrates how cells achieve this through the unexpected deployment of filamentous actin (F-actin) to the nucleus. The study provides the first evidence that actin polymerisation in the nucleus helps in reshaping the nucleus and reorganising the genome after cell division (mitosis).

In mammals the cell nucleus packages and protects the genome. When human cells divide, the nucleus is dissembled to allow segregation of the chromosomes. Once

chromosome segregation is complete, new cells need to re-build their nucleus and organise their genome. This process, although essential for life, was poorly understood. [Alice Sherrard](#) (pictured) developed and implemented complementary and interdisciplinary methods to visualise nuclear structure and genome organisation after cells division. In so doing, she revealed that disruption of the formation of F-actin results in cells failing to expand their nuclear volume as well as their inability to de-compact their genome. Because of these defects, cells become inefficient in

retrieving genetic information encoded in their DNA; thus, they divide slower.



This discovery advances our fundamental knowledge of genome regulation in space and time, and could have major implications in understanding cancer and degeneration.

Baarlink C *et al.* (2017). [A transient pool of nuclear F-actin at mitotic exit controls chromatin organization](#). *Nature Cell Biology*. 19(12):1389-1399.

Funding successes: Part 4

Prof [Jonathan Tobias](#) (BMS/THS) from the **Wellcome Trust** for *Causal inference in the aetiology of osteoporosis, osteoarthritis and scoliosis: Musculoskeletal Imaging-Derived Phenotypes in UK Biobank*, £711,189.

Dr [Massimo Antognozzi](#) (Physics) from the **Jean Golding Institute** for *Development of machine learning algorithms for antimicrobial resistance testing*, £3,142 from Feb '18 for 4 months.

Prof [John Bower](#) (Chemistry) from the **Royal Society** for *Strategies To-*

wards Potent Trypanocidal Drugs: Synthesis of Substituted Naphthoquinoidal Systems and their Evaluation Against Trypanosoma cruzi, £99,949 from Dec '17 for 1 year.

Prof [Chris Willis](#) (Chemistry) from the **BBSRC** for *Structural and Mechanistic Investigations of Antibiotic Production in Bacteria*, £697,421 from Apr '18 for 3 years.

Dr [Tom Williams](#) (Biological Sciences) from the **Royal Society** for *Modelling lateral gene transfer on a new bacterial tree*, £9,740 from Mar

'18 for 2 years.

Dr [Jennifer Bailey](#) (BVS) from the **EBI Confidence in Concept** scheme for *Preclinical evaluation of an iron-responsive bacterial therapeutic to prolog periods of remission in inflammatory bowel disease*.

Prof [David Wynick](#) (BMS/THS) from the **EBI Confidence in Concept** scheme for *Use of a novel long-acting GalR2-specific agonist to pre-clinically validate GalR2 for the treatment of multiple sclerosis*.

Antibiotic resistance in children's *E. coli*

Antibiotic resistance in children's *E. coli*, a bacteria that is the most common cause of urinary tract infection, is high against many antibiotics commonly prescribed in primary care and could make them ineffective as first-line treatments.

The research team investigated the prevalence of antibiotic resistance in urinary *E. coli* from pre-school children. They also measured risk factors associated with resistant urinary *E. coli*, including previous antibiotic expo-

sure. They found a high prevalence of antibiotic resistance in urinary *E. coli* against several commonly prescribed antibiotics including amoxicillin, trimethoprim and co-amoxiclav. Almost one third of all *E. coli* were multidrug resistant. There was also an association between exposure to antibiotics within the previous three months and increased likelihood of a resistant urinary *E. coli*.

The study, funded by the National Institute for Health Research School for

Primary Care Research, involved secondary analysis of data from 824 children under 5 years consulting in primary care for an acute illness.

Bryce A et al. (2018). [Comparison of risk factors for, and prevalence of, antibiotic resistance in contaminating and pathogenic urinary *Escherichia coli* in children in primary care: prospective cohort study](#). *Journal of Antimicrobial Chemotherapy*.

[Read more](#)

Annual *Nematodirus* spring threat to young lambs

Responding to the speed with which this parasite can hit, the [Sustainable Control of Parasites in Sheep](#) (SCOPS) group is again providing an invaluable forecasting tool, developed by the [Bristol Veterinary School](#), on its website. An [interactive map](#) with a traffic light system of warnings is provided alongside practice advice for assessing on-farm risk.

Dr [Hannah Vineer](#), who developed the online tool, said:

"We could be in for a high-risk season, if this late cold snap is followed by a rapid increase in temperature. Such conditions will cause the *Nematodirus battus* parasite to hatch in large numbers, posing a massive threat to lambs aged around four to six weeks. Predicting when outbreaks might happen at a local level is becoming increasingly difficult, due to variation in spring temperatures from year to year."

The forecast map is updated daily using data from over 140 weather stations around the UK, tracking changes in risk throughout the spring and early summer. It allows farmers and advisers to select the nearest or most representative weather station, providing advice on how to relate the predicted risk to their particular farm, treatment options and possible management actions.

[Read more](#)

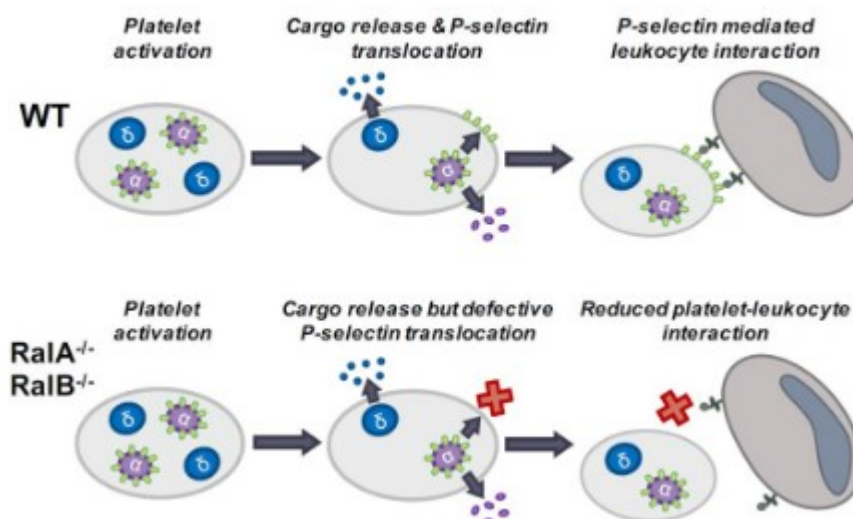
New targets for treatment of inflammatory conditions

Research has shed light on the way our clotting cells and immune cells control their interactions with each other. The findings could lead to the development of new treatments for inflammatory diseases such as inflammatory

bowel disease, rheumatoid arthritis and asthma.

The team studied how two molecular switches, RalA and RalB, control the release of bioactive molecules from platelets. The findings reveal a novel role for RalA and RalB

in controlling how platelets interact with white blood cells and contribute to inflammation. It is hoped that the study will lead to the development of new medicines to target RalA and RalB for the treatment of a range of inflammatory conditions.



Wersäll A *et al.* (2018). [Mouse platelet Ral GTPases control P-selection surface expression, regulating platelet-leukocyte interaction. Arteriosclerosis, Thrombosis, and Vascular Biology.](#)

[Read more](#)

Gum disease's devastating impact

A new report has revealed that the number of people affected by tooth decay and gum disease is having a widespread and devastating impact not only on patients' mouths but also on their general health and wellbeing, particularly in the older population.

The study, led by an international team of periodontists including researchers at the Bristol Dental School, reviewed all available data, publishing 15 systematic reviews on the evidence and published consensus findings, and found that

10% of the global population are affected by severe gum disease. Left untreated, gum disease causes tooth loss and in its more severe forms, periodontitis which is independently associated with increased mortality rates due to a higher risk of atherogenic cardiovascular diseases, diabetes and related complications.

The study's recommendations include:

- Dental professionals should be consulted regularly to prevent and treat caries and periodontal diseases effectively

- Bleeding gums are not normal
- Periodontal disease is an indicator of general health issues
- Reducing sugar and starch intake levels and frequency can help prevent periodontal disease and caries
- Brushing twice daily with fluoride toothpaste is essential

[Proceedings of the 12th European Workshop on Periodontology, "The Boundaries between Caries and Periodontal Diseases"](#).

Watch fat cells help heal a wound in a fly

Fat body cells in *Drosophila* play a surprising role in sealing wounds and preventing infection a recent study has found. The cells, which were previously thought to be immobile, propel themselves forward toward wounds with a wormlike wave motion, rather than adhering to and pushing off from other structures like most motile cells do. The fat cells crowd into the wound and waft debris to the edges of it, where the debris can be consumed by the immune cells. The fat cells are large enough that anywhere

from one to four cells can plug the wound, playing a role similar to a clot or scab in vertebrates. The cells physically keep bacteria out of the wound while it heals, while helping increase the production of antimicrobial peptides to quell any infections. The fat cells stay at the wound site until it is healed, then they detach and just swim off.

Whereas most cells use little spikes of actin (filopodia and lamellipodia) to push and pull themselves off from other objects, the fat body cells ap-

pear to use peristaltic constriction to "swim" through the hemolymph. How the cells know to travel to the wound is still unclear. Even in the absence of immune cells, the fat body cells still go to the wound; but once they get there, they do clearly collaborate with immune cells.

Franz A *et al.* (2018). [Fat Body Cells Are Motile and Actively Migrate to Wounds to Drive Repair and Prevent Infection](#). *Developmental Cell*. 44(4), pp 460-470.

[Read more](#)

€10M in European Research Council grants

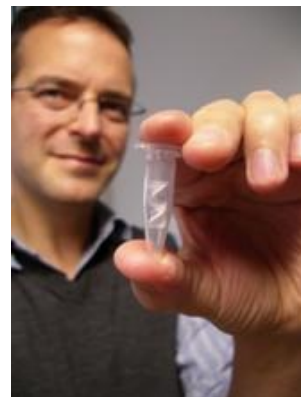
Five senior researchers from the University of Bristol have been awarded over €10M in European Research Council (ERC) Advanced Grants in recognition of their 'excellent science' and potentially ground-breaking research.

The ERC's Advanced Grants support exceptional researchers, who are leaders in their field, in undertaking

ambitious research projects. The grants are awarded under the 'excellent science' pillar of Horizon 2020, the EU's research and innovation programme.

The grantees at Bristol will pioneer research on a wide range of topics across disciplines as diverse as modern slavery, archaeology, evolutionary biology, biochemistry and chemistry. One recipient

is Prof [Mark Szczelkun](#) in the School of Biochemistry for his project 'Molecular mechanisms, evolutionary impacts and applications of prokaryotic epigenetic-targeted immune systems'.



Lung cancer drug resistance explained

Molecular simulations have been used to understand resistance to osimertinib, an anticancer drug used to treat types of lung cancer. Osimertinib binds tightly to epidermal growth factor receptor (EGFR), which is overexpressed in many tumours. EGFR is involved in a pathway that signals for cell proliferation, and so is a target for drugs. Blocking the action of EGFR can switch it off, and so

is a good way to treat the disease. Osimertinib is used to treat non-small-cell lung cancer (NSCLC) in cases where the cancer cells have a particular (T790M) mutant form of EGFR. It is a covalent inhibitor, binding irreversibly to EGFR. Although patients generally respond well to the drug, most acquire drug resistance within one year of treatment. Drug resistance arises because the EGFR protein mutates,

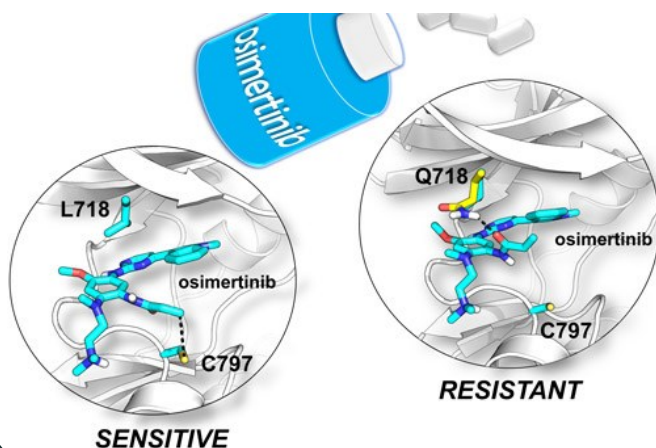
so that the drug binds less tightly.

One such mutation, L718Q, was recently discovered in patients in

the Medical Oncology Unit of the University Hospital of Parma. In this drug resistant mutant, a single amino acid is changed. Unlike other drug resistant mutants, it was not at all clear how this change stops the drug from binding effectively. A collaboration between medicinal and computational chemists and clinical oncologists has revealed exactly how subtle changes in the protein target cause drug resistance.

Callegari D *et al.* (2018). [L718Q mutant EGFR escapes covalent inhibition by stabilizing a non-reactive conformation of the lung cancer drug osimertinib](#). *Chemical Science*. 9: 2740.

[Read more](#)



Best way to treat infected hip replacements?

New research has found treating an infected hip replacement in a single stage procedure may be as effective or better than the widely used two-stage procedure. Hip replacement is a very common operation that is effective at providing pain relief and improving mobility, however, infection can sometimes occur following joint replacement. The findings have wide implications for orthopaedic surgery, the NHS, and health systems worldwide.

The research team conducted a study that reviewed

patient data from 44 studies to compare the effectiveness of the two types of surgery currently used to treat infections – one-stage and two-stage revisions. In the two-stage procedure, the existing artificial joint is removed in one operation and the patient is treated for several months with antibiotics. A new joint is then inserted in a second operation. In the one-stage procedure, the artificial joint is removed along with all infected tissue and a new one inserted in the same operation. The study found that the one-stage revision strat-

egy is as good, if not better, as the two-stage strategy. The one-stage strategy may also be better suited for patients with certain types of infection or problems that were previously thought not to be appropriate for this type of surgery.

Kunutsor SK *et al.* (2018). [One- and two-stage surgical revision of peri-prosthetic joint infection of the hip: A pooled individual participant data analysis of 44 cohort studies](#). *Journal of Epidemiology*. Published online 5 Apr 2018.

Academics urge rethink on 28-day prescriptions

The widely adopted practice of issuing 28-day prescriptions for people with long-term conditions lacks a robust evidence base and should be reconsidered; research shows that considerable savings could be made by the NHS switching to longer prescriptions. Over a billion NHS prescription items are issued each year at a cost of over £9 billion. Many of these medications are used for the management of long-term health conditions, such as diabetes or heart disease. Prescriptions for these medications are is-

sued through the 'repeat prescribing' system. Local guidance by clinical commissioning groups in many parts of the country encourages GPs to issue shorter supplies of these repeat medications, partly to reduce wastage.

The study, led by RAND Europe in Cambridge and funded by the NIHR, examined previously published studies that looked at this issue, dating back as far as 1993. The researchers found nine studies that suggested that longer duration prescriptions are as-

sociated with patients being more likely to take their medications. They also found six studies that suggested that shorter prescriptions might be associated with less wastage, although these studies were considered to be very low quality. An analysis of 11 years of UK GP prescribing data found that any savings due to reduced waste resulting from issuing shorter prescriptions were more than offset by greater costs due to the additional work required by GPs and pharmacists.

[Read more](#)

Observing the battle of the stem cells

Stem cells must compete with one another to remain among a smaller number of pluripotent, self-renewing cells rather than transform into a specialised cell. But how does this process play out, and with what effects? Dr [Marc Amoyel](#), a developmental biologist, received an [EBI Early Career Fellowship](#) award to examine stem cell competition in *Drosophila*. The preliminary data from

his work at Bristol yielded a surprising result. It showed that when stem cell proliferation in fruit flies is impaired, the niche itself loses its quiescence and begins to proliferate and give rise to new stem cells. This shows that stem cells signal back to their niche to maintain the right balance of proliferating cells. Dr Amoyel is submitting a paper on these findings, in collaboration with Dr Erika

Bach's laboratory at the New York School of Medicine, which is doing complementary research. He has also secured a five-year Career Development Award from the Medical Research Council.



Understanding the immunobiology of wild mammals

The state of the immune system of wild animals is, remarkably, almost unknown. However, knowing this and knowing what affects the immune state of wild animals is important in understanding how infection and disease affects wild animals. Knowing the immune state of wild animals is also important in understanding the biology of the germs or pathogens that

infect them. This is also directly relevant when trying to understand how germs are passed from one species to another, including to humans.

In a new study, a joint project with the London School of Hygiene and Tropical Medicine and the University of Edinburgh's Roslin Institute, the team investigated the immune ecology of wild house mice – the same species as the laboratory mouse – as an example of a wild mammal, characterising their adaptive humoral, adaptive cellular and innate immune state. They first found that neighbouring populations of wild mice – on different farms, for example – were often in a very different immune state,

the first time that this has been seen.

Secondly, they identified the main factors that underlie the immunological differences among individual mice, showing that mice with good body condition had enhanced immune responses. In general, older mice had a poorer immune state but older animals also had better body condition, allowing them to partially resist the effects of their older age on their immune systems.

Abolins S *et al.* (2018). [The Ecology of Immune State in a Wild Mammal, *Mus musculus domesticus*](#). *PLoS Biology*. Published online 13 April 2018.



ELIZABETH BLACKWELL FUNDING

EBI Postgraduate Discipline Hopping Fellowships

This scheme is designed to support a small number of postgraduate researchers currently enrolled on one of the University of Bristol Wellcome Trust-funded 4 year PhD programmes.

Closing date: 23 April 2018

EBI MRC Confidence in Concept Scheme (CIC)

With support from the MRC, the University has funding available to support health related translational projects.

Closing date: 30 April 2018

EBI Translational Acceleration and Knowledge Transfer (TRACK)

This scheme provides funding to support health related translational projects.

Closing date: 25 June 2018

EBI Identifying Candidates for Wellcome Trust Investigator Awards

This scheme is designed to support a small number of permanent academic staff at UoB within the first five years of their appointment, who are planning to apply for an Investigator Award from the Wellcome Trust. Applications will be accepted on a rolling basis.

Heads of School are asked to nominate members of staff who can be eligible for this scheme by emailing ebi-health@bristol.ac.uk

EBI Workshop Support

Support interdisciplinary workshops in health research at new or emerging interface between two or more disciplines. 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 Research 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.

Medical Research Council

[New investigator research grant – infections and immunity](#)

Closing Date: 16 May 18

Award amount: not specified

This supports researchers who are capable of becoming independent PIs and who are ready to take the next step towards that goal within the areas of infections and immunity. Applicants are expected to combine their time with a portfolio of other activities, such as other research grants or clinical duties, teaching, administration duties, or other time spent in faculty.

Medical Research Council

[Research grants – infections and immunity](#)

Closing Date: 16 May 18

Award amount: £1m

These fund focused research projects that may be short- or long-term in nature related to infections and immunity, as well as method development and continuation of research facilities. Projects may involve more than one research group or institution.

Medical Research Council

[Programme grants – infections and immunity](#)

Closing Date: 16 May 18

Award amount: not specified

The purpose is to help the medical science community to think bigger. A programme is defined as a coordinated and coherent group of related projects that may address an interrelated set of questions across a broad scientific area. The expectation is that not all questions will necessarily be an-

swered within the tenure of the award. Parts of the programme may be continuations of current activity, but other elements must be innovative and ambitious.

National Institute of General Medical Sciences, USA

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

Closing Date: 5 Jun 18 Award amount: not specified

This 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.

National Institute of Allergy and Infectious Diseases, USA

[Research to advance vaccine safety \(R01\)](#)

Closing Date: 5 Jun 18 Award amount: not specified

This announcement supports research that will contribute to the overall understanding of vaccine safety. Studies should address scientific areas potentially relevant to vaccine safety, such as physiological and immunological responses to vaccines and vaccine components; how genetic variations affect immune or physiological responses that may impact vaccine safety; etc.

Innovate UK

[UK-China antimicrobial resistance funding competition](#)

Closing Date: 6 Jun 18 Award amount: £750,000

This aims to support projects that build UK and Chinese academia and industry partnerships to combat antimicrobial resistance by delivering cutting-edge research and having global benefits. Eligible projects must be such that neither country would be able to conduct within the same timeframe without the others expertise, and should develop new products or services against AMR where there is a significant threat to human health. Where appropriate, they should include clinical evaluation.

Innovative Medicines Initiative Joint Undertaking, EU

[H2020-JTI-IMI2-2018-14 IMI fourteenth call for proposals](#)

Closing Date: 14 Jun 18 Award amount: not specified

This supports the development and implementation of research and innovation activities of strategic importance to the EU's competitiveness and industrial leadership, and address specific H2020 societal challenges, in particular European citizens' health and well-being. The initiative should seek to involve a broad range of partners. Proposals may address the following topics:

- IMI2-2018-14-01 targeted immune intervention for the management of non-response and relapse
- IMI2-2018-14-02 non-invasive clinical molecular imaging of immune cells
- IMI2-2018-14-03 development of a platform for federated and privacy-preserving machine learning in support of drug discovery
- IMI2-2018-14-04 centre of excellence – remote decentralised clinical trials

National Institute of Allergy and Infectious Diseases, USA

[Impact of initial influenza exposure on immunity in infants \(U01 clinical trial not allowed\)](#)

Closing Date: 2 Jul 18

Award amount: US\$21,700,000

This supports projects that aim to establish, follow and characterise longitudinal cohorts of infants to determine how initial and repeated natural influenza infections or influenza vaccinations shape infant and childhood immunity to future influenza exposures. The ultimate goal is to provide key information to facilitate design of durable, broadly protective influenza vaccines.

Healthcare Infection Society

[Major research grants](#)

Closing Date: 2 Jul 18

Award amount: £99,000

These support PhD students, MDs or other research workers in the subject of healthcare infection control. Preference is given to translational research rather than pure science topics.

THIS ISSUE'S FEATURED ARTICLE

Co-association between Group B *Streptococcus* and *Candida albicans* promotes interactions with vaginal epithelium

Grace R. Pidwill, Sara Rego, Howard F. Jenkinson, Richard J. Lamont and Angela H. Nobbs (2018). *Infection and Immunity*. 86(4), e00669-17.

Group B *Streptococcus* (GBS) is a leading cause of neonatal sepsis, pneumonia, and meningitis worldwide. In the majority of cases, GBS is transmitted vertically from mother to neonate, making maternal vaginal colonization a key risk factor for neonatal disease. The fungus *Candida albicans* is an opportunistic pathogen of the female genitourinary tract and the causative agent of vaginal thrush. Carriage of *C. albicans* has been shown to be an independent risk factor for vaginal colonization by GBS. However, the nature of interactions between these two microbes is poorly understood. This study provides evidence of a reciprocal, synergistic interplay between GBS and *C. albicans* that may serve to promote their cocolonization of the vaginal mucosa. GBS strains NEM316 (serotype III) and 515 (serotype Ia) are shown to physically interact with *C. albicans*, with the bacteria exhibiting tropism for candidal hyphal filaments. This interaction enhances association levels of both microbes with the vaginal epithelial cell line VK2/E6E7. The ability of GBS to coassociate with *C. albicans* is dependent upon expression of the hypha-specific adhesin Als3. In turn, expression of GBS antigen I/II family adhesins (Bsp polypeptides) facilitates this coassociation and confers upon surrogate *Lactococcus lactis* the capacity to exhibit enhanced interactions with *C. albicans* on vaginal epithelium. As genitourinary tract colonization is an essential first step in the pathogenesis of GBS and *C. albicans*, the coassociation mechanism reported here may have important implications for the risk of disease involving both of these pathogens.

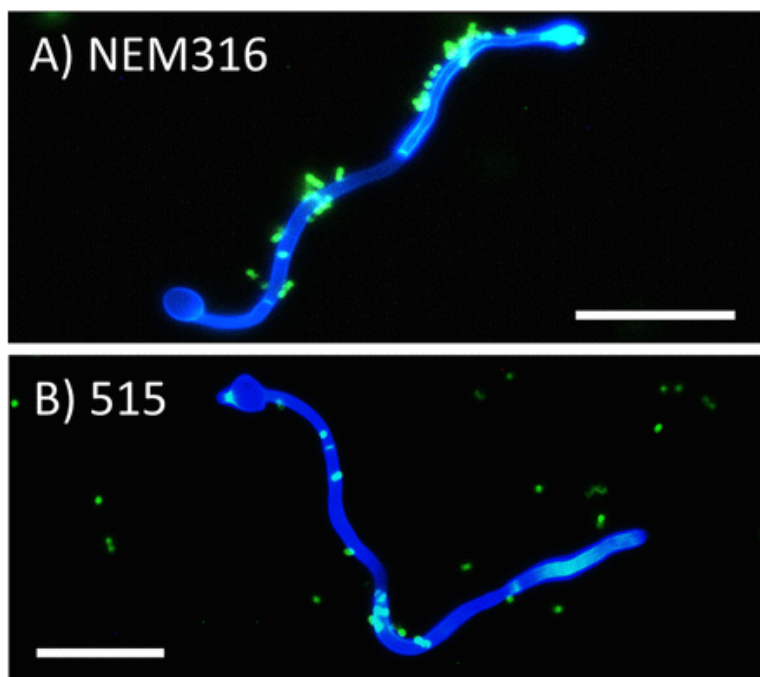


Image caption: Fluorescence micrographs of planktonic interactions between *C. albicans* and GBS. *C. albicans* SC5314 was grown in YNBPTG for 2 h at 37°C and 220 rpm before addition of GBS strain NEM316 (A) or GBS strain 515 (B) and incubation for a further 1 h. GBS was labeled with FITC (green), and *C. albicans* was labeled with calcofluor white (blue). Bars, 20 μm.

CONTACTS

The Infection and Immunity Network is run by a Steering Group:

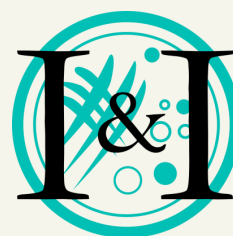
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Reader



Co-Chair: [Adam Finn](#)
Prof of Paediatrics



- [Andrew Davidson](#) - Senior Lecturer in Virology
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- [Collette Sheahan](#) - Research Development Network Facilitator
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