

# INFECTION AND IMMUNITY NETWORK NEWSLETTER



Elizabeth Blackwell Institut  
for Health Research

**MARCH - APRIL 2017**

## £7.5M boost for Health Research

The [Elizabeth Blackwell Institute](#) (EBI) has been awarded the Wellcome Trust's Institutional Strategic Support Fund (ISSF), designed to support biomedical research and related activities in the UK over the next five years. The ISSF award of £3.75M is being matched by the University. It is the third and largest ISSF award for the EBI and recognises the successful work the Institute has delivered during the previous five years. The Institute will continue to invest in supporting the next generation of health research leaders by offering fellowships

and support for clinical and non-clinical early career researchers. Clinical researchers in particular will benefit from opportunities offered by the EBI and the recently announced [Wellcome Trust-funded clinical PhD programme for the South West](#). I (GW4-CAT).

The Institute will also prioritise work on diversity and inclusion, as well as public engagement with focus on building capacity, creating and developing partnerships to co-design and increase the impact of the University's research.

[GW4-CAT](#) is the clinical PhD programme which will run between the GW4 member universities of Bristol, Exeter and Cardiff. It will offer trainees access to a broad range of training opportunities with world leading researchers in population health; epidemiology; cardiovascular health; neuroscience and mental health; molecular cell biology; cancer; infection; immunity and repair.



**Bristol Events / Other Events**

**Infection and Immunity Research and Staff News**

**Elizabeth Blackwell Institute Funding Schemes**

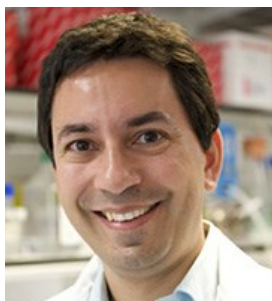
**Funding Opportunities in Infection and Immunity**

**This Issue's Showcased Article**

**Contacts**



# UoBRISTOL EVENTS



[GW4-BristolBridge: "Systems Approaches to Antimicrobial Resistance in Different Environments"](#)

16 March 2017, 9.30 - 16.00. Old Council Chamber, Wills Memorial Bldg

[Dendritic cells in regulation of immunity to infection and cancer](#)

21 March 2017, 13.00 - 14.00. Prof Caetano Reis e Sousa (Francis Crick Institute), Lecture Theatre C42, Biomedical Sciences Building



[Sir Paul Nurse: My life in research](#)

**FOR PGRs ONLY** 22 March 2017, 12.00 - 13.00. UoB Students' Union

[Data Science meets AMR \(antimicrobial resistance\) workshop](#)

29 March 2017, 9.45 - 15.00. Engineers' House, Clifton

[Bridging the Gaps between Academia, Translation and Commercialisation](#)

3 April 2017, 9.30 - 15.00. LT3 and East Foyer, School of Chemistry



[MRC portfolio and funding seminar and 1:1 sessions](#)

5 April 2017, 13.00 - 14.00. Dr Adam Babbs (Programme Manager, Molecular and Cellular Medicine Board, MRC) and Dr Mariana Delfino-Machin (Cancer Lead, Molecular and Cellular Medicine Board, MRC). SM2, Maths Building

[Amelie Baud, Sir Henry Wellcome Fellow, European Bioinformatics Institute](#)

6 April 2017, 16.00 - 17.00. Seminar Room, Oakfield House



[Biotechnology Showcase](#)

3 May 2017, 13.00 - 18.00. Amsterdam

[HerStories: Career seminar series - Getting Your Voice Heard](#)

3 May 2017, 13.00 - 14.00. Prof Havi Carel (Philosophy), Old Council Chamber, Wills Memorial Building

[Research without Borders: A festival of postgraduate research](#)

8 - 12 May 2017

[How Staphylococcus aureus uses decoys to dodge daptomycin](#)

9 May 2017, 13.00 - 14.00. Dr Andrew Edwards (Imperial College), Lecture theatre C42, Biomedical Sciences Building

[BristolBridge Annual Conference and Industry Day](#)

10 - 11 May 2017, Lecture Theatre 3 and East Foyer, School of Chemistry

[Skeletal systems mechanobiology and personalized medicine](#)

*From top: Caetano Reis e Sousa, Amelie Baud, Havi Carel, Andrew Edwards*

## UoBRISTOL EVENTS



23 May 2017, 13.00 - 14.00. Ralph Müller (ETH Zürich), seminar rooms A&B, Level 1 Learning & Research, Southmead Hospital

[How to prepare a good research bid \(Medical Faculties\)](#)

8 June 2017, 10.00 - 16.30. Dr Pamela Johnstone, Brunel Room, Hawthorns

[Bristol Population Health Science Institute launch](#)

9 June 2017, 9.30 - 16.30. Prof Nancy Krieger (Harvard University), Arnolfini Contemporary Arts Centre



### **Infection and Immunity Early Career Researchers' event**

**21 June 2017, 9.30 - 14.00** Seminar rooms G13 and G14, Life Sciences Bldg

**CALL FOR ABSTRACTS NOW OPEN– SEE [WEBSITE](#) FOR DETAILS**

[Symposium and Launch: GW4 Cryo-EM Facility](#)

1 September 2017, 9.30 - 17.00, Life Sciences Building



## OTHER EVENTS

[Science Past and Present: Does Gender Matter?](#)

16 March 2017, 18.00 - 19.00. Dr Patricia Fara (University of Cambridge), University of Bath

[Women in STEM screening](#)

16 March 2017, 19.00 - 21.00. Planetarium, At-Bristol

[Data Challenges in Systems Immunology](#)

6 June 2017, 9.00 - 17.00. Top Floor Seminar Room, Cardiff University Brain Research Imaging Centre

[Big Bang Bristol](#)

6 - 7 July 2017, Trinity Centre

[13th World Congress on Inflammation](#)

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

*From top: Ralph Müller, Nancy Krieger, Patricia Fara*

## NEWS

### NIHR Biomedical Research Centre success

University Hospitals Bristol NHS Foundation Trust, in partnership with the University of Bristol, has been awarded £21.8M over five years by the National Institute for Health Research (NIHR) to fund cutting-edge research. The Biomedical Research Centre (BRC) will come into being in April 2017 and will allow the two ex-

isting Biomedical Research Units (BRUs) to continue the world class research they have been carrying out in the areas of Cardiovascular Disease and Nutrition, Diet and Lifestyle. Alongside this UH Bristol have been funded in three new themes – Surgical Innovation, Mental Health and Perinatal and Reproductive Medicine. The partner-

ship is one of 20 NHS and university partnerships across England to have been awarded funding; each BRC will host the development of new, ground-breaking treatments, diagnostics, prevention and care for patients in a wide range of diseases like cancer and dementia.

[More info...](#)

### Clinical Primer leads to Training Fellowship

As a Renal registrar Dr [Emily Bowen](#) (pictured) manages patients with both acute and chronic kidney disease, but she wanted to pursue research interests as well. The [EBI Clinical Primer Scheme](#) allowed her to take a break from her clinical commitments in London to join Bristol Renal, headed by Prof [Moin Saleem](#).

The team made significant breakthroughs in the study of podocytes and glomerular endothelial cells and their interaction in the kidney's filtration barrier, including causation and treatment when the filtration barrier breaks down. Emily's research, su-

pervised by Profs Saleem and [Richard Coward](#) involved exposing cultures of human and mouse podocytes and human glomerular endothelial cells to different concentrations of Shiga toxin for between 30 minutes and 24 hours. This showed that while mouse podocytes were resistant to the Shiga toxin, in humans cellular stress pathways were activated after just one hour.

The preliminary data obtained during the EBI Primer formed the basis of her PhD Clinical Fellowship applications for external funding. She was successful in her first fellowship interview and began her PhD in October 2016:

**A Kidney Research UK** Clinical Training Fellowship went to Dr [Emily Bowen](#) under PI Prof [Richard Coward](#) (£220,890) for *The role of the podocyte in Shiga toxin associated haemolytic uraemic syndrome*. The three-year project will allow Emily to study the molecular biology underpinning Haemolytic Uraemic Syndrome which is the leading cause of Acute kidney injury or failure in children.



## H2020 €28.9M initiative into diabetic kidney disease

Prof [Richard Coward](#) will be leading the BEAt-DKD (Biomarker Enterprise to Attack Diabetic Kidney Disease) project, part of a major pan-European €28.9 million initiative, which will explore the molecular mechanisms underpinning DKD. The project will allow the teams in the School of Clinical Sciences, led by Prof Coward together with Prof [Moin Saleem](#) and Dr [Simon Satchell](#), to work closely together

on this issue. The Bristol element of the project comes to £396,825.

BEAt-DKD is a unique five-year public private partnership funded by the Innovative Medicines Initiative (IMI), member companies from the European Federation of Pharmaceutical Industries and Associations (EFPIA), the Juvenile Diabetes Research Foundation (JDRF) and the state of Switzerland. At the moment,

there are no means to effectively prevent or cure DKD, which has reached epidemic dimensions and is the leading cause of end-stage renal disease. DKD patients are a very sick population with mortalities exceeding most cancers and who are underserved by inefficient and unsuccessful drug development. DKD remains a large unmet medical need.

[More info...](#)

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## Lassoing from the mouth to the heart

Infective endocarditis occurs when bacteria cause unwanted blood clots to form on heart valves. Untreated it is fatal; even treated mortality rates are ~ 30%. There are over 2,000 cases diagnosed in the UK annually, and cases are rising.

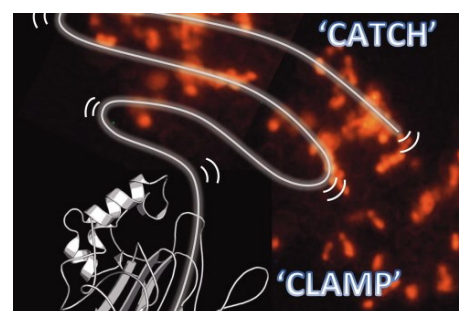
Using the X-ray microscope at [Diamond Light Source](#) a UoB team were able to visualise the structure and dynamics of protein CshA which was believed to play an important role in targeting the oral bacterium *Streptococcus gordonii* to the tissues of the heart. They were intrigued to find that CshA acts as a 'molecular lasso' to enable *S. gordonii* to bind to the surface of human

cells. Such adhesive interactions are critical first steps in the ability of this bacterium to cause disease. The study, which appears as 'Editors' Picks' in the [Journal of Biological Chemistry](#), was conducted in collaboration with Prof Rich Lamont at the University of Louisville, USA.

The work has revealed a completely new mechanism by which *S. gordonii* and related bacteria are able to bind to human tissues, which they have named 'catch-clamp'. The team demonstrated that the terminal portion of CshA is very flexible, allowing it to be cast out like a lasso. When the lasso contacts fibronectin on the surface of human cells

(the 'catch'), it brings CshA and fibronectin into close proximity. This then enables another portion of CshA to tightly 'clamp' the two proteins together, anchoring *S. gordonii* to the host cell surface.

The work opens up new possibilities for designing anti-adhesive agents that target disease-causing bacteria.





## Elizabeth Blackwell Institute funding

**Early Career Fellowships** are designed to support exceptionally talented and motivated researchers who wish to further their career by applying for independent, externally-funded fellowships to be held at Bristol. Dr Vicky Hunt was successful in her application for *The roles of MIRNAS in parasitic nematode infection*.

The **Catalyst Fund** offers up to £30k to pump-prime an ambitious, interdisciplinary project. Dr **Ariel Blocker** received backing for *Rational vaccine design: can one identify protective antigens systemati-*

*cally in silico? A pilot study focusing on epitope design for Shigella and Salmonella vaccines.*

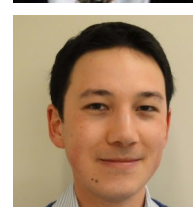
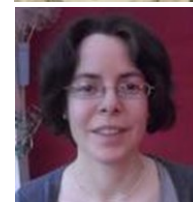
**Translational Acceleration and Knowledge Transfer (TRACK)** awards support health-related translational projects and those at the stage of concept development. Dr **Michele Barbour** can now pursue *A novel, emulsion gel formulation of sustained release chlorhexidine to prevent umbilical cord infection and improve outcomes for neonates in developing countries.*

Dr **Paddy Horner** was also awarded TRACK

funding for *Detection of seminal bacterial sialidase activity in men provides a new therapeutic opportunity for infertile couples.*

The **Confidence in Concept (CiC)** scheme is designed to support projects which are at the proof of concept stage. Dr **Colin Chu** received funding for *Viral Gene Therapy for Glaucoma using CRISPR-Cas9.*

*Pictured right are, from top to bottom: Vicky Hunt, Ariel Blocker, Michele Barbour, Paddy Horner and Colin Chu.*



## Funding successes: Part 1

In the area of veterinary pathology, £225,486 has been awarded to Dr **Doug Wilson** from The Horse Trust for *A pilot study of oral immunotherapy as a treatment to desensitise horses with insect bite hypersensitivity to Culex Spp (Sweet Itch)*. From Oct 2016 for three years.

To Dr **Andrew Davidson**, £95,027 from the British Council for *Rapid PCR test at*

*the point of care to determine dengue virus serotype*, from Aug 2016 for two years.

From the BBSRC, £396,729 to Prof **Christiane Berger-Schaffitzel** for *Membrane protein insertion and quality control by the bacterial holotranslocon and FtsH chaperone/protease complex*, from Oct 2016 for three years.

The University's **International**

**Strategic Fund** awarded Dr **Jo Murrell** £1955 for *Development of objective measures of central sensitization in cats with degenerative joint disease (DJD)-associated pain*, in association with Prof Duncan Lascelles at North Carolina State University.

### High Blood Pressure Study Requires Volunteers in the 35-60 year age range

#### What is this study?

This is a study investigating whether brain blood flow autoregulation is preserved in hypertension. The study involves ~1 hour of screening at CRIC Bristol and ~2 hours on a Thursday afternoon at the Bristol Heart Institute for an MRI scan of the head and chest during lower body negative pressure.

#### Contact?

If you are think you might be eligible, please contact [Sandra Neumann](#) (t: 0117 342 1503) for more information

## David Telling Charitable Trust award

Dr [Catherine Pennington](#) (pictured) was recently awarded a David Telling pilot grant that will serve to bring together a new multi-disciplinary group involving multiple specialities, including Renal (Drs [Fergus Caskey](#), [Albert Power](#)), Ophthalmology (Dr [Denize Atan](#)), Urology (Prof [Marcus Drake](#)),

Stroke (Dr [Phil Clatworthy](#)) and Clinical (Pennington, Hughes) and Preclinical Neurosciences (Prof [Pat Kehoe](#)) to test the feasibility of study to investigate the impact of advancing Kidney disease and outcomes on the development of complex outcomes including cognitive Impairment, bladder func-

tion and pathology of the eye.



## Microscopy facilities opened

A purpose-built microscopy suite to accommodate expansion of the Wolfson Bioimaging Facility was officially opened by Paul Ramsbottom, Chief Executive of the Wolfson Foundation, on 8 July 2016. The facility currently houses imaging systems covering a broad range of advanced fluorescence and electron microscopy techniques. The ar-

rival of new systems including multiphoton, super-resolution and fluorescence lifetime imaging alongside expansion of confocal and widefield microscopy required more space.

A donation of £1M by the Wolfson Foundation was vital in helping to create six purpose-built microscope rooms to accommodate new equipment.

The new imaging suite is situated adjacent to existing microscope rooms and provides the controlled and stable environment required for high-resolution microscopy. The facility has also recently increased the level of support it offers for image processing and analysis to equip its users with the expertise to fully quantify and interpret microscopy data.

Details of the facilities are available on the [website](#).



## Antimicrobial Resistance (AMR) Force

AMR research at the School of Veterinary Sciences is promoted and facilitated by the AMR Force, who work in the South West, nationally and internationally, and are interested in decreasing antibiotic use while improving animal health through a plurality of approaches addressing differing styles and attitudes.

The group currently stewards over £1.7M funding from Research Councils UK (BBSRC, EPSRC, MRC, NERC), industry (AHDB Dairy, MSD Animal Health, Zoetis UK, WD Farmers, Coombe Farm), charity funders (Soil Association, The Langford Trust) and international bodies (EU H2020, Formas - Sweden).

Major questions addressed include:

- Can we use medicine audits to encourage responsible medicine use by veterinarians?
- Can we impact the way veterinarians prescribe medicines?
- Can we assist in developing medicines use policy with policy-makers, veterinarians and farmers (using participatory or other approaches)?
- Does reducing antimicrobial use impact patterns of resistance?
- How do microbes and AMR genes cycle in the environment?

The group are uniquely placed to combine a veterinary focus with close collaborations, including those with social science interests, [animal welfare research](#) and pol-

icy-making concerning animals, animal welfare and veterinary practice. They are presently performing medicines audits and clinical governance on antibiotics in all [Langford Veterinary Services](#) clinics and advise for a number of other practices nationally. They are heavily involved in influencing medicines use UK-wide and in national control programmes on farms. They also work closely and have collaborations with [BristolBridge](#) and a number of basic and social science researchers at the Universities of Bristol and Exeter.

Join the [Antimicrobial Resistance Force](#) by contacting [Kristen Reyher](#).

## Fund UK-China Antimicrobial Initiative

Dr [Helen Lambert](#) (ESRC AMR Champion) and colleagues were awarded £882,688 (UK)/£1,828.878 (combined with National Natural Science Foundation of China contribution) to undertake a project on *Pathways to optimising antibiotic use in Anhui*

*province: Identifying key determinants of antibiotic consumption and prescribing in community and clinical settings.* The successful bid includes co-investigators from Bristol, UCL, the LSHTM, the Health Protection Agency and China. The Bristol co-investigators

are Prof Alasdair MacGowan (Southmead Hospital/North Bristol NHS Trust), Prof [Alastair Hay](#), Prof [Matthew Hickman](#), Dr [Caroline Coope](#), Dr [Christie Cabral](#) (all UoB) and Dr Isabel Oliver of Public Health England.





## Support for Data Science

The University's youngest research institute, the [Jean Golding Institute for Data-intensive Research](#), has started running a data science support service dubbed 'Ask JGI'. The service is available to all staff (and PhD students through their supervisors) and provides advice, support and guidance on all data science queries, in-

cluding for instance statistical, computing, data management, visualisation, and storage questions.

Support is available via email and 1-1 meetings. The Institute works closely with 'data champions' throughout the University and can therefore triage questions to experts and

foster collaborations if they are unable to help directly. Staff can also signpost to other data intensive research facilities in the University such as on Advanced Computing (ACRC) and data storage (RDSF).

Get in touch via [ask-jgi@bristol.ac.uk](mailto:ask-jgi@bristol.ac.uk).

## Student Health Sciences Research Journal

The *INSPIRE Student Health Sciences Research Journal* is produced by a team of student editors from Bristol, Exeter, Plymouth and Cardiff and plays a key part of a collaborative project under the national INSPIRE scheme funded by the Wellcome Trust and administered by the Academy of

Medical Sciences.

The scheme aims to encourage student doctors, dentists and vets to consider a career in research, and encourages publication of their work. Since the scheme began in 2013 the southwest INSPIRE partnership has supported more

than 70 vacation studentships as well as prize awards. Together with local matched funding, this has enabled students to undertake research projects under the supervision of senior scientists and clinicians.

Following a competition in 2015, a team of seven senior editors came together to set up the journal from scratch in order to provide a platform for publication of student project results, as well as to have direct experience of academic peer review.

The first issue of the journal is [available online](#).



## Funding successes: Part 2

An **NIHR Doctoral Research Fellowship** to Dr [Anna Bibby](#) (supervisors Profs Nick Maskell & Rachael Goberman-Hill). £418,414 for *Treating mesothelioma with Intra-pleural bacterial immunotherapy (the TILT Trial): A feasibility study using the 'Trial within a Cohort' methodology*. A feasibility study of intra-pleural immunotherapy using the streptococcal preparation OK-432 in patients with mesothelioma. The trial

will use an innovative and highly pragmatic methodology called the 'Trial Within a Cohort' design and will include embedded qualitative interviews with participants to explore their experiences of participating in the trial.

A **Society of Endocrinology Early Career Grant** to Dr [Felicity Stubbs](#), £10k for *The role of glucocorticoids on P53 dependent cell-cycle control*. Synthetic glucocorticoids are widely used clinically due to

their potent anti-inflammatory properties; they promote cell cycle arrest through the P53 pathway. There are suggestions of another essential key 'player' which could mediate this mechanism by directly interacting with the glucocorticoid receptor (GR) and P53. The study will perform co-immunoprecipitation studies, proteomics and flow cytometry cell cycle analysis to determine whether this key 'player' is ARID1a.

## Algorithm to reduce antibiotic use

A new technique will help GPs identify which children with coughs and respiratory tract infections (RTIs) are most at risk of future hospitalisation. Using this algorithm to its full potential could reduce the amount of antibiotics prescribed to these children by as much as 10%.

Primary care practitioners are responsible for 80% of all antibiotic prescriptions in the UK. Around half of these are for RTIs, despite the fact that their effectiveness in treating RTIs has been shown to be limited. GPs and nurses find making decisions about prescribing

antibiotics in children with RTIs difficult. On the one hand, the over-prescription of antibiotics is recognised as a serious concern but on the other, they want ensure adequate treatment of a significant infection.

The team found seven characteristics that can be used to identify children with cough and RTI at very low, normal and high risk of future hospitalisation: short ( $\leq 3$  days) illness; high temperature; age ( $< 24$  months); recession; wheeze; asthma; and vomiting giving the mnemonic *STARWAVE*.

If children have one or none, there is a very low risk of future hospitalisation; if three or more of these symptoms are present, there is a higher risk they will be hospitalised in the following 30 days.

[Hay AD, Redmond NM, Turnbull S et al. \(2016\). Development and internal validation of a clinical rule to improve antibiotic use in children presenting to primary care with acute respiratory tract infection and cough: a prognostic cohort study. \*Respiratory Medicine\*. 4\(11\), pp902–910.](#)

## Amendment: Student s' Award for Outstanding Teaching

The last issue of the I and I Newsletter had Matthew Avison down as the winner of the 2016 award for Outstanding Teaching (Biomedical Sciences). With many apologies, the editor would like to point out that the winner was actually Dr [Steve Fitzjohn](#), Teaching Fellow in the School of Physiology, Pharmacology and Neuroscience. Matthew was

shortlisted in the same category for 2016. Apologies for the confusion.

The image shows Steve being presented

with his award on 7 June 2016.



## Diabetes and Metabolism Research Group news

Dr [Kathleen Gillespie](#), Alistair Williams and Anna Long have received £95,308 for a **Diabetes UK Scholarship** which will allow Claire Williams to investigate the mechanisms underlying natural regulation of the autoimmune response to Zinc Transporter 8.

In the funding award letter for the scholarship the committee described the group as *an exceptional training environment for postgraduate students*; well-deserved recognition for their excellent research.

Diabetes expert Prof [Colin Dayan](#) began a joint role linking his current post at Cardiff University with a new appointment as **Professor of Diabetes and Endocrinology**

at UoB. From Jan 2017 the role will involve building collaborations between the Universities of Bristol and Cardiff, and later Exeter and Bath, to create a world-leading **GW4** centre for Diabetes and Endocrinology. Dayan has a long-established interest in translational research in the immunopathology of Type 1 diabetes and is currently conducting early phase clinical trials into the development of antigen-specific immunotherapy.

Research Associate Dr [Jody Ye](#) was awarded a **Diabetes Research and Wellness Foundation Non-Clinical Fellowship**. Worth £179,774, her project will focus on how the environment is increasing the risk of childhood type 1

diabetes over multiple generations of the same families participating in the Bart's Oxford family study.

Dr [Kathleen Gillespie](#) has been awarded a supplement of \$34,635.41 towards the **Juvenile Diabetes Research Foundation** award *What protects islet antibody positive T1D relatives who do not progress?*

*Dr Kathleen Gillespie, below, leads the research group*





## Bayer Global Ophthalmology Award

Dr [Sofia Theodoropoulou](#) received a Global Ophthalmology Award 2016 from Bayer. The award recognises ophthalmologists' outstanding commitment and ambition to develop their skills and improve the lives of patients living with ophthalmic diseases.

The award provides research funding of US\$50,000 to support *The role of an immunomodulatory cytokine*

*and its associated pathways in the pathogenesis of age-related macular degenera-*

*tion* which is a collaboration with Prof Andrew Dick.



## Nematodirosis risk in lambs

An online risk forecast has been developed by Sustainable Control of Parasites in Sheep (SCOPS) and UoB to predict when Nematodirosis eggs will hatch and when outbreaks are likely to happen. Nematodirosis, caused by the gut-worm *Nematodirus battus*, affects young lambs. Eggs

deposited on pasture by lambs the previous year hatch together in spring, triggered by a period of chilling over winter followed by warmer weather. Young lambs take in large numbers of larvae as they graze, which damage their gut leading to foetid black diarrhoea (black scour) and death.



Predicting when outbreaks might happen is becoming increasingly difficult due to variation in spring temperatures

from year to year. As the damage is done by the larvae, faecal egg counts are of little use. The forecast takes advantage of the temperature-driven synchronised hatching of the *Nematodirus* larvae and uses weather data from 140 weather stations provided by the Met Office and Forecast.io. The interactive Google map allows farmers and advisers to select the nearest or most representative weather station and provides advice on how to relate the predicted risk to their particular farm and treatment options.

[More info....](#)



## Early career training and support

The Faculties of Biomedical Sciences and Health Sciences have a dynamic postgraduate community enrolled in taught or research-based programmes. Postgrads receive their training in internationally renowned research groups which span the biomedical science disciplines of Biochemistry, Cellu-

lar and Molecular Medicine and Physiology, Pharmacology and Neuroscience through to the disciplines associated with population health which include life course epidemiology, genomics, primary care and public health with a particular emphasis on methodology. Research takes place in laboratories within the

University and in clinical settings across Bristol, including the University Hospitals Bristol Trust, North Bristol Trust, as well as general practices and other community health services. For further details go to page 19 or the [Elizabeth Blackwell Institute \(EBI\) website](#).

## BristolBridge news

BristolBridge has been awarded a **GW4 Building Communities Initiator** award to hold a workshop in preparedness for the anticipated Phase 2 of the MRC-led cross-council AMR funding initiative which will focus on systems approaches to tackling AMR in different environments in low to middle income countries. The team is led by [Katy Turner](#) (UoB), Will Gaze (Exeter), Barbara Kasprzyk-Horden (Bath) and Tim Walsh (Cardiff).

The workshop, held on 16 March 2017, formed part of [Bristol Tackles Global Challenges](#) week. The aim was to build interdisciplinary global partnerships for AMR research and develop potential collaborative projects. Dr Andrew Singer from the NERC Centre for Ecology and Hy-

drology and Prof Visanu Thamlikitkul, Director of the Thailand WHO Collaborating Centre for AMR Prevention and Control, delivered keynote presentations.

BristolBridge Co-I [Annala Seddon](#) (Physics) was awarded a **Newton Fund RAEng Researcher Exchange Programme** for *Combating Antimicrobial Resistance through Engineering and Education*. Co-I is Dr Huey Ling Tan, Universiti Teknologi MARA in Selangor, Malaysia. The project will look at antimicrobial natural peptides and their interactions with lipids, with part of the grant focused on developing an outreach programme in AMR for Malaysian schools. As part of the programme Dr Tan will spend 3 months in Bristol and Annala will spend

3 months in Malaysia during the summer.

A discussion between [Michele Barbour](#) and [David Barrett](#) at the World Cafe held at Bristol Zoo in January 2016 has led (via a student's summer research project) to a **BBSRC SWBio DTP iCASE Studentship**. The academic supervisors are David Barrett and [Jim Spencer](#); the industry supervisor is Michele Barbour and the CASE partner is [Pertinax Pharma Ltd](#). The candidate, Liam Cundy, will undertake his PhD on *A novel, sustained efficacy, biocide-based treatment for bacterial foot disease in ruminants*.

## Health Research Strategy Committee

Professor John Iredale, Pro Vice-Chancellor for Health, has created a new [Health Research Strategy Committee](#) with broad membership across the Faculties of Health and Biomedical Sciences including Deans, Faculty Research Directors, Heads of Schools and the Elizabeth Blackwell Institute. The com-

mittee will be chaired by the new Director of Research for Health, Professor [Jeremy Tavaré](#) (pictured right). The Committee will debate and develop a unified health research and innovation strategy across the two faculties and take an overview of its delivery by the Faculties and Schools with support from the

Research and Enterprise Development team.

Terms of reference and minutes of meetings are available on the [Committee's intranet](#). If you have any questions regarding the committee, please email [healthresearch-committee@bristol.ac.uk](mailto:healthresearch-committee@bristol.ac.uk)



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## Results of the Big Tick Project

The Big Tick Project, the largest ever study of ticks in dogs in the UK, was active throughout 2015. It demonstrated that almost one third of dogs checked at random during a visit to a vet were found to be carrying a tick. Researchers found a wide geographical spread of ticks right across the UK with the highest risk areas in the South West, Scotland and East Anglia.

A total of 14,711 dogs took part. Five dogs were selected at random for a tick check each week by participating veterinary prac-

tices, with 1,400 taking part in the study. They also found that dogs were at risk of ticks regardless of whether they were urban or rural.

Ticks carry a range of diseases including Lyme disease and potentially fatal canine babesiosis, a disease found in the UK earlier this year for the first time in dogs that had not travelled abroad. Climate change, an increase in hosts carrying ticks and changes to environmental management are all thought to be factors affecting increased tick

numbers and activity. In the study, 56 dogs had travelled outside the UK in the previous two weeks, 43 of which were infested by one of three species of tick. In some dogs that had travelled abroad, the Brown Dog Tick was found which can cause infestations within the home.

For more information on the project go to [www.bigtickproject.co.uk](http://www.bigtickproject.co.uk).





## Funding successes: Part 3

Prof [Margaret May](#) received £15,671 from the **North Bristol NHS Trust** To develop *within Primary Care IT systems a computer program for flagging patients with risk factors for HIV who would benefit from having an HIV test*. Awarded Dec 2016 for six months.

Prof [Julian Hamilton-Shield](#) has lift off for **i4i NIHR** study (£713,000 over 24 months with industrial collaborator Breath Dx) to undertake a study on *Evaluation and validation of a breath ammonia measurement technology for the improved management of pa-*

*tients with urea cycle defects.*

A **GW4 Building Communities Initiator Grant** was awarded to Dr [Katy Turner](#) for *Systems approaches to antimicrobial resistance in different environments.*

*From top: Margaret May, Julian Hamilton Shield, Katy Turner*

## External engagements

An **INSPIRE** summer student, Cherry Phypers, supervised by Linda Wooldridge, Emma Place and Hugo van Oostrom, was awarded an RCVS Knowledge Student Bursary to attend the **Veterinary Evidence Conference** held in Edinburgh in November 2016. INSPIRE is a national initiative co-ordinated by the Academy of Medical Sciences and supported with funding from the Wellcome Trust.

Prof Adrian Mulholland was a consultant on new **comic book series** [Surgeon X](#).

Prof [Adam Finn](#) commented on research from Utrecht University which shows that children prescribed antibiotics before the age of two

have a higher chance of developing hay fever or eczema later in life. He was quoted in the [Daily Mirror](#), [Huffington Post Australia](#), [Reuters](#), [Daily Mail](#), [Closer magazine](#), [The Mumbai Mirror](#) and [Medical Daily](#).

Prof [Alastair Hay](#) has been appointed to the National Institute of Health and Care Excellence (**NICE**) management of common infections committee. NICE committees are independent advisory groups that consider evidence and develop national guidance and advice to improve health and social care. Prof Hay will work with the new committee to develop prescribing guidelines for the management of common in-

fections, including respiratory and urinary tract infections. The guidelines will help tackle the problem of antimicrobial resistance (AMR). The committee will be looking at ways to reduce unnecessary antibiotic prescribing in both primary and secondary care. Together with partners and colleagues, Alastair has conducted internationally recognised research to improve the management of acute infections and the use of antibiotics in primary care. This has included research into antibiotic prescribing for children with respiratory infections and flu, and adults with urinary tract infections, sore throats and coughs.

## Farming and the battle against antibiotic resistance

A survey of over 300 farmers, farm managers and farm workers conducted by the Royal Association of British Dairy Farmers in collaboration with UoB assessed attitudes to and use of antibiotics in dairy and beef farming. It was carried out in the wake of the Government-commissioned O'Neill Review on Antimicro-

bial Resistance (AMR) published earlier in 2016. At a media briefing in London held on 3 Oct '16, Dr [Kristen Reyher](#) expressed that, in analysing the results, her team was very encouraged that dairy farmers thought it possible to achieve a median reduction of 30% in antibiotic dry cow therapy use within the next five years. As well as

this, reductions of 15% in antibiotic use to treat calf diseases, most probably pneumonia and calf scour, and 20% to treat clinical mastitis in milking cows are thought possible.

[More info...](#)

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## New insights for treating stomach infections

Researchers have discovered a new approach to preventing or treating a stomach bacterium associated with an increased risk of stomach cancer as well as gastritis and duodenal ulcers. The team included researchers from the Technical University of Munich (TUM), the University of Duisburg-Essen at Essen University Medical Centre and UoB.

*Helicobacter pylori* lives in the lining of the stomach. Infections commonly occur during childhood; once an infection occurs, *H. pylori* will stay in the stomach throughout life and can be fatal, unless treated with particular

antibiotics. At a time when *H. pylori* infection is developing increasing resistance, this new discovery could prove vital in treating diseases caused by it.

The team found that *H. pylori* attach to the epithelial cells in the gastric mucosa and were able to detect a highly specific and exceptionally strong variant of this adhesion, in which the bacterial surface molecule, HopQ, binds to the Carcinoembryonic Antigen-related Cell Adhesion Molecules (CEACAMs) inside the stomach. In contrast to previously known binding partners of the bacterium, this

bond is independent of sugar structures. They found that this ensures that it is stable in the acidic environment of the stomach. CEACAMs are not produced in healthy stomach tissue, but primarily when there is an inflammation of the gastric mucosa caused by the infection. The adhesion of the bacterium to stomach cells could be prevented with a soluble version of HopQ or parts of the protein, and its damaging effects could potentially be suppressed.

[More info...](#) (links to Nature Microbiology article)



## Sheep disease treatment studies

Prior to 1992 farmers across the UK were required by law to treat sheep to prevent scab, an infectious condition caused by the presence of a parasitic mite. At that time there were only around 40 outbreaks per year. After compulsory treatment was removed the number of outbreaks rose dramatically and there are now 5 - 10k outbreaks each year, at a cost to

the UK sheep industry of £10M pa. The failure to reduce scab incidence is often blamed on those farmers who are unwilling to use routine preventative treatments.

A new economic study funded by the BBSRC shows that many of these farmers are being blamed unfairly; analysis suggests that under current conditions, it is actually

only cost-effective for farmers to use preventative treatments in areas where the scab risk is highest - Scotland, Northern England and Wales and where high risk grazing strategies (particularly common grazing) are used. For farmers in other areas, it is more cost-effective in the long run for them to only pay to treat if and when their flock gets scab. [More info...](#)

## Bacteria resists 'last-resort' antibiotic

In 2016 a team, led by Dr [Jim Spencer](#), in collaboration with colleagues from Oxford, Cardiff, Diamond Light Source, Thailand and China, identified mcr-1 as the first colistin-resistance gene that could be passed between bacteria, enabling resistance to spread rapidly within a bacterial population. Colistin is a 'last resort' antibiotic used to treat life-threatening bacterial infections that do not respond to other treatment options.

Since then the mcr-1 gene has been detected in common bacteria such as *E. coli* in China, the United States and across Europe first in farm animals and recently in human patients.

The spread of mcr-1 has been linked to agricultural use of colistin, indicating that transmission between animals and humans may take place. In response to these findings the Chinese government has now banned use of colistin in animal feed.

Colistin acts by binding to, and disrupting, the outer surface of bacteria. Bacteria carrying the mcr-1 gene make a protein that modifies the bacterial surface to reduce colistin binding, making the organism resistant. In their work the team used X-rays produced at Diamond's crystallography beamlines to generate detailed pictures of the portion of this protein responsible for the modification, and with this infor-

mation identified key features that are necessary for it to function. They also constructed computer models of the chemical reaction that leads to resistance.

This provides the first clues as to how mcr-1 acts within the bacterial cell, as well as information essential to efforts to identify ways of blocking MCR-1 function that could restore the activity of colistin against bacteria carrying mcr-1.

*Image caption: X-ray crystal structure of the catalytic domain of the MCR-1 protein. © Dr Phil Hinchliffe*

## Schools conference on AMR

[BristolBridge](#), with support from the [Bristol Chem-LabS](#) outreach team, organised a cross-faculty schools conference for post-16 biology and chemistry students held to examine why AMR is an escalating global threat. Around 160 students and 15 teachers from nine schools across the south west attended the lectures, hands-on displays and discovery-led demonstrations.

Workshops and displays, presented by a team of post-graduates from across the University, looked at a number of different areas including how penicillin works, using maths to fight AMR, modelling bacteria using robot swarms and a game zone where the students could play a 'superbugs' game.

Held on 9 November 2016, the programme is available to [view online](#).

*Below, Matthew Avison opens the proceedings.*



## Stewardship policy reduces antimicrobial use on farms

The new stewardship policy, facilitated by the [AMR Force research group](#), is already informing industry and legislative bodies, allowing them to deliver real, on-farm changes while maintaining or improving herd health and welfare.

While high use of AMs in food-producing animals may be associated with intensive pig and poultry production, pressures to use medicines more responsibly are increasing in all sectors, and the use of AMs - including those used to treat serious infections in humans - is a growing focus. The new stewardship policy will in-

form industry and legislative bodies to deliver real, on-farm changes while maintaining or improving dairy herd health and welfare.

The process to create a policy, led by Dr [Kristen Reyher](#) and PhD student [Lisa van Dijk](#), enabled groups of dairy farmers to develop an AM livestock health policy to address the challenge of more responsible use of medicines on farms. Dairy farmers, their veterinarians and researchers worked together with the aim of developing a functional and implementable AM policy which was producer-led and benefitted the relevant supply chain. The

policy development process began with two dairy producer groups consisting of 25 organic producers and 48 conventional producers supplying one of the UK's major retailers. It was a focused initiative driven by the producers, but also addressed retailer and consumer needs. The research is an initial step towards a better understanding of how participatory methods with producers can be applied in the UK and more widely. The study serves as a pilot for promoting more responsible use of AMs in other livestock species using such methods.

[More info...](#)

## Research projects funded by BristolBridge

BristolBridge supported six new interdisciplinary projects in the second funding round in February 2016 with Summer 2016 starting dates. For a [full listing see the BristolBridge website](#).

Three new interdisciplinary pump-priming projects were awarded funds in the third funding round in late May 2016. The University awarded BristolBridge funds from its EPSRC Institutional Sponsorship award for Global Challenges. With matched funding from BristolBridge,

this funding has been assigned to tackling the global challenge of antimicrobial resistance with relevance to Official Development Assistance (ODA).

1) *Evaluation of nano-mechanical cantilever-based biosensors as a novel, rapid approach to detect antifungal resistance in pathogenic Candida species*. [Mervyn Miles](#), [Elizabeth Johnson](#), [Mark Fraser](#), [Andy Borman](#) and [Monica Berry](#).

2) *Towards devices for detecting antimicrobial resistance in resource-poor settings; on-chip magnetic separation, concentration and detection of bacteria* (under Global Challenges). [Annela Seddon](#), [Jim Spencer](#) and [Rob Hughes](#).

3) *Mathematical modelling of the impact of novel AMR diagnostics for Neisseria gonorrhoeae* (under Global Challenges). [Katy Turner](#), [Martin Homer](#), [Hannah Christensen](#), [Harriet Mills](#) and [Darryl Hill](#).

## Immunotherapy Clinical Primer

When the body detects cancer it sends CD8+ Tumour Infiltrating Lymphocytes (TILs) into the tumour to de-



stroy it. However, once inside the tumour, TILs are suppressed- often by molecules in the tumour that engage inhibitory receptors on the TILs – so that they fail to kill cancer cells. Targeting these inhibitory pathways so that the TILs can function again may lead to the design

of new anti-cancer drugs.

Drugs that block two known co-inhibitory receptors, PD-1 and CTLA-4, show great promise in clinical trials. However, they only produce anti-tumour responses in a subgroup of patients and can be associated with severe side effects. Nonetheless, these trials suggest that immunotherapies can give better responses than some chemotherapy and radiotherapy

treatments.

Thanks to an [EBI Clinical Primer](#), Bristol graduate [Grace Edmunds](#) won a Wellcome Trust Fellowship to take such research forward. Grace is now 6 months into her PhD and has already contributed data for a paper produced by the [Morgan lab](#), and produced a documentary on tumour immunology in her spare time which won a joint first prize at the [Bristol Science Film Festival](#).

## Funding successes: Part 4

**Meningitis Research Foundation** grant to Prof [Adam Finn](#) and Dr [Jenny Oliver](#), £29,737 for *Feasibility of, and methodological approaches to, a teenage evaluation of MenB vaccination and meningococcal carriage*. This is a study to evaluate prevalence of meningococcal carriage in teenagers (SPIT). This project will run from September 2016 to March 2017.

**Kidney Research UK** grant to Profs [Richard Coward](#) and [Craig McArdle](#), £65,638 for *OAFI: John Feehally - Stoneygate Research Project: Developing new molecular therapies for cystinuria kidney disease*.

Award date: 17 Jan 2017. This is a 1 year project grant starting in April this year.

## Stemming waterborne infections

Every year in low- and middle-income countries, 13 live-stock-related diseases, commonly transmitted from animals to humans through water, cause 2.4 billion cases of human illness and 2.2 million deaths. Since climatic and hydrological conditions create the host environment for these disease-causing organisms, reducing the risk of infection and identifying opportunities for interventions requires a greater understanding of the connection between changing environmental and human factors and health.

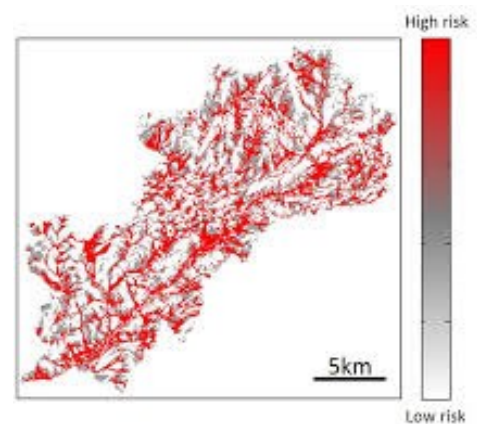
Profs [Thorsten Wagener](#), [Petter Vickerman](#) and Dr [Eric Morgan](#) drew up a proposal

for a cross-disciplinary project with an objective to develop advanced infectious disease modelling that simulates current and future scenarios for waterborne diseases, allowing better planning and interventions. The project was made possible by a grant from the EBI [Catalyst Fund](#). First, the team developed a conceptual model of the interactions between climate, human and animal mobility, hydrology, and infectious disease transmission, using a common language across the different disciplines. Next, they modelled these different components and developed and validated a method for assessing current and future

patterns of liver fluke (*Fasciola hepatica*) in two UK locations. Liver fluke is a common parasite in livestock, which in the UK alone costs farmers £300 million a year due to lost production. Despite efforts to control it, UK fluke outbreaks are on the rise, and this is often attributed to climate change. Their research led to the first integrated model for liver fluke that simulates the suitability of habitat for disease development in space and time, and the life cycle of the organism in connection with key environmental conditions.

[More info...](#)

*Image: A map of liver fluke infection risk for a catchment in the UK*





# ELIZABETH BLACKWELL FUNDING

## EBI Workshops Funding

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

## EBI Catalyst Fund

Pump priming awards can support the most promising and ambitious ideas across the widest interdisciplinary boundaries. These projects will be identified largely through the running of [workshops](#) to explore new possibilities and identify the big questions. Applications are reviewed on a **rolling** basis.

## EBI MRC Confidence in Concept Scheme (CiC)

To support health related translational projects which are at the stage of proof of concept (Confidence in Concept Awards). Open to all UoB academic staff. **Deadline: 20 March 2017**

## EBI Translational Acceleration and Knowledge Transfer (TRACK)

Funding to support health related translational projects which are at the stage of concept development. Successful outline applications will be invited to submit a full application for concept development funding. Open to all UoB academic staff. **Deadline: 26 April 2017**

## Returning Carers Scheme

UoB has introduced a Returning Carers' Scheme (RCS) to support academic staff across all faculties in re-establishing their independent research careers on return from extended leave (16 weeks or more) for reasons connected to caring - such as maternity leave, adoption leave, additional paternity leave or leave to care for a dependent. Deadlines: 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.

## EBI Postgraduate Discipline Hopping Fellowships

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 (Dynamic Cell Biology, Neural Dynamics & Molecular, Genetic and Lifecourse Epidemiology). **Deadline: 27 April 2017.**



Elizabeth Blackwell Institute  
for Health Research

# 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 Faculty Research Directors and/or School Research Directors, 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.

## Wellcome Trust

### [Four-year PhD studentships in science](#)

Closing date: none

Award amount: unspecified

Enable students to undertake in-depth postgraduate training at centres of excellence throughout the UK, including in immunology and infectious disease.

## 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.

**British Society for Antimicrobial Chemotherapy**

[Terry Hennessey microbiology fellowship](#)

Closing date: 31-Mar-17

Award amount: £1,500

This enables a young investigator working in the field of infectious diseases to present a paper or poster at the ASM Microbe conference meeting, to be held from 1 to 5 June 2017 in New Orleans, US.

**Department of Health including NIHR**

[Vaccines for global epidemics – clinical](#)

Closing date: 12 Apr 17

Award amount: £3M

Supports projects seeking to develop candidate vaccines and vaccine platform technologies at the clinical stage with the aim to enable an effective and rapid response during future outbreaks of disease. The total budget is £35 million.

**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.

**Cancer and Polio Research Fund**

[Research grants](#)

Closing date: 15 Oct 17

Award amount: unspecified

Support research into cancers, with particular reference to the causes, development and treatment of these diseases, or research into polio and other crippling diseases. Grants may be used for direct costs of research and to support research symposia or lectures for the dissemination of findings.

# THIS ISSUE'S FEATURED ARTICLE

## *Streptococcus thermophilus* NCIMB 41856 ameliorates signs of colitis in an animal model of inflammatory bowel disease

Bailey J, Vince V, Williams N & Cogan T (2017). *Beneficial Microbes*. In press.

**Background:** Treatment of inflammatory bowel disease (IBD) is mainly based on suppression of symptoms, often with numerous side effects. Trials of probiotics in IBD have frequently produced disappointing results. The majority of probiotics are unusual, since they do not require iron for growth, unlike many bacteria resident in the intestine. The IBD intestine is iron-rich due to bleeding and use of oral iron supplements; conventional probiotics would be rapidly outcompeted. We have evaluated an iron-responsive *Streptococcus thermophilus* strain for its potential to reduce signs of colitis.

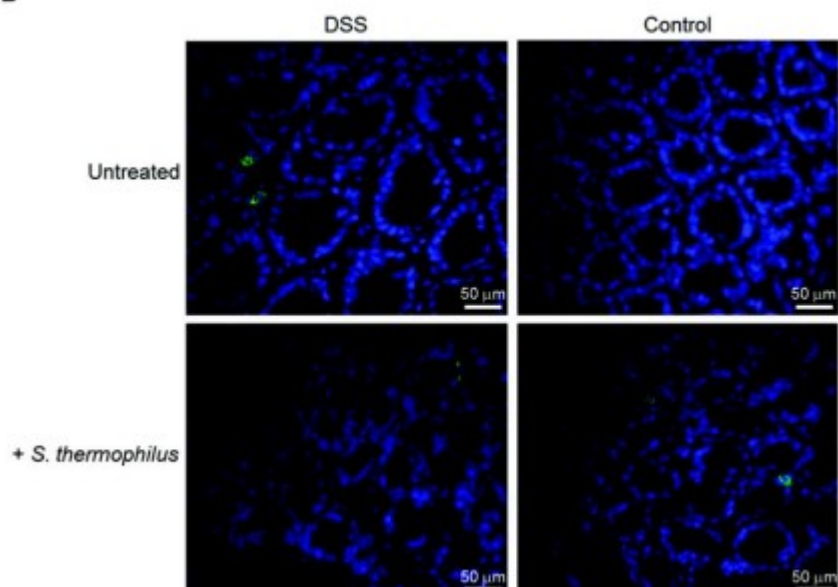
**Methods:** Efficacy of *S. thermophilus* was evaluated in the dextran sodium sulphate (DSS) mouse model of colitis. Treated animals were given  $1 \times 10^8$  cfu *S. thermophilus* per day and clinical observations were taken daily. At termination, gross and histopathological signs of disease, cellular infiltration, location of bacteria, and cytokine expression in the intestine were determined.

**Results:** *S. thermophilus* delayed onset of colitis and reduced clinical signs of disease, including bodyweight loss and gastrointestinal bleeding. It reduced bacterial translocation into the colonic tissue. Increased numbers of CD8+ intraepithelial lymphocytes were seen in control animals treated with *S. thermophilus*. *S. thermophilus* had no effect on gross pathology, histopathology or cytokine production in either colitic or control animals.

**Conclusions:** We propose that *S. thermophilus* promotes maintenance of mucosal barrier function which reduces bacterial translocation, thereby reducing immune stimulation and associated inflammation. This allows mucosal healing, reducing gastrointestinal bleeding and weight loss. This could be studied as a locally-acting adjunct or alternative to current IBD treatments.

B

*S. thermophilus* treatment increased expression of CD8 in control animals, predominantly in the epithelium (CD8+ cells are shown in green and nuclei are stained with DAPI)





# CONTACTS

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

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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
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