

I&I NETWORK NEWSLETTER



2022 - ISSUE 2



Valneva COVID-19 vaccine approved in UK

The Medicines and Healthcare products Regulatory Agency (MHRA) has authorised the Valneva COVID-19 vaccine for use in the UK.

This follows rigorous clinical trials supported by the National Institute for Health and Care Research (NIHR) and a thorough analysis of the data by experts at the MHRA. The UK's independent medicines regulator concluded the vaccine met its strict standards of safety, quality and effectiveness, and is the first in the world to ap-

prove the Valneva vaccine. It follows the Pfizer/BioNTech, Oxford/AstraZeneca, Moderna, Janssen and Novavax vac-



cines to be approved for use by the MHRA.

It is the sixth COVID-19 vaccine to be approved by the MHRA, but becomes the first, whole-virus inactivated COVID-19 to

gain regulatory approval in the UK. Prof [Adam Finn](#) (School of Cellular and Molecular Medicine) is Chief Investigator of the Cov-Compare study.

This type of vaccine (similar to the production of flu and polio vaccines) sees the virus grown in a lab and then made completely inactive.

This is done so it cannot infect cells or replicate in the body, but can still trigger an immune response to the COVID-19 virus.

[Read the full press release](#)

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[Read more about Bristol AMR](#)



EVENTS

Spatial control of gene expression during angiogenesis

16 June 2022, 13.00 - 14.00, Dr Guilherme Costa (Queen's University Belfast), E29 Biomedical Sciences Building

Carcinoma cells repel immune attack by forming a CXCL12-chemokine shield

16 June 2022, 14.00 - 15.00, Prof Douglas T. Fearon FRS FRCP FMedSci (Cold Spring Harbor Laboratory, Weill Cornell Medicine, CRUK Cambridge Institute), online

Vaccination as a strategy to combat Antimicrobial Resistance

17 June 2022, 12.00 - 14.00, online

Stemness, Regeneration and Immunity: from development to therapy

20 - 21 June 2022, 16.50, The Francis Crick Institute, 1 Midland Road, London and online

Infection & Immunity Research Network Symposium: Vaccines, Discovery to Uptake

21 June 2022, 10:00 - 15.05, Geographical Sciences Building

Attendance is FREE and includes a buffet lunch

[More information and to register](#)

Balancing research and clinical commitments

21 June 2022, 13.00 - 14.00, Ema Swingwood (NIHR Clinical Doctoral Research Fellow and Respiratory Physiotherapist), online

BNSSG CCG Research Showcase Seminars

22 June 2022, 10.00 - 11.00, online

Bristol Cats Study meeting

22 June 2022, 10.30 - 12.00, online

Managing Imposter Syndrome in Academic-Policy Engagement

22 June 2022, 12.30 - 13.30, Dr Camila Devis-Rozental, online

Festival of Enterprise

27 June 2022, 9.00 - 16.00, Wills Memorial Building, Queens Road, Bristol BS8 1QE

Living systematic reviews: Preventing obesity in children systematic review

28 June 2022, 13.00 - 14.00, Lena Schmidt and Francesca Spiga (University of Bristol), online

Inaugural Lecture - 'Whose Bugs are they Anyway?'

30 June 2022, 17.00 - 19.00, Prof Kristen Reyher (Bristol Veterinary School), Churchill Building Lecture Theatre (and online)

NEWS

Insomnia could increase people's risk of type 2 diabetes

Insomnia, not getting enough sleep, and having a later bedtime, have been linked in previous studies to a greater risk of type 2 diabetes. In this study, the research team assessed whether these associations are explained by causal effects of sleep traits on blood sugar levels.

The study showed that people who reported that they often had difficulty getting to sleep or staying asleep had higher blood sugar levels than people who said they never, rarely, or only some-

times had these difficulties. The research team found no clear evidence for an effect of other sleep traits on blood sugar levels.

The findings could improve researchers' understanding of how sleep disturbance influences type 2 diabetes risk. The study also suggests that lifestyle and/or pharmacological interventions that improve insomnia might help to prevent or treat diabetes. Currently, there are some treatments for insomnia, e.g. cognitive behavioural therapy

(CBT) and short-term treatment of sleeping tablets or treatment with melatonin if CBT does not work. Future studies to assess the impact of these insomnia treatments on glucose levels in people with and without diabetes could establish potential new treatments for the prevention and treatment of diabetes.

Liu J et al. (2022). [Assessing the causal role of sleep traits on glycated haemoglobin: a Mendelian randomization study](#). *Diabetes Care*.

Bristol Clinical Research Facility funding bid successful

Bristol Clinical Research Facility (CRF) is one of five new CRFs across the country to have been awarded funding by the National Institute for Health and Care Research (NIHR) in their latest round of funding. The bid was led by David Wynick, Director of Research of University Hospitals Bristol and Weston NHS Foundation Trust and North Bristol NHS Trust and was for £3.5 million. CRFs support the delivery of early translational and experi-

mental medicine research, from first-in-human trials through to early safety and efficacy trials, and provide purpose-built facilities and expertise for their delivery. Starting from September 2022, the 5-year pump priming will be supported by commercial early phase trials income, thereby offering more cutting-edge research, driving

forward innovation and helping to identify new treatments for patients.

The Bristol CRF will bring together early phase translational and experimental medicine research studies across Bristol under a single management and governance structure, covering research in a variety of areas that include cancer and immunity-based treatments, vaccine development and testing, cardiovascular medicine, neuroscience, and respiratory medicine.



Clinical Research Network West of England awards

The winning nominees for the [Clinical Research Network \(CRN\) West of England Research Awards](#) were announced at the inaugural ceremony on 24 March 2022.

Stephen McGlynn, Deputy Chief Operating Officer said: "A huge congratulations to our winners and short-listers alike. We really enjoyed having the opportunity to share and showcase some of the brilliant work that is happening across the West of England. We hope you all feel very proud of the contributions you have made and continue to make to research."

The full ceremony is available to watch on [YouTube](#).

The winning nominees include:

COVID-19 Collaboration in Research

Regional Covid-19 vaccine trial teams

Collaborative Investigator of the Year

Rajeka Lazarus (right)

Rajeka is a Consultant in Infection at the University Hospitals Bristol & Weston NHS Foundation Trust. She is the Principal Investigator for the COVID-19 vaccine trials for

the West of England Clinical Research Network.

Investigator of the Year category

Catherine Hyams, AvonCAP (below)

Cat is the Principal Investigator for The Avon CAP study. This study seeks to determine the burden of adult acute respiratory disease and assess how the emer-



gence of COVID-19 may lead to changes in adult respiratory disease. By conducting comprehensive surveillance at both acute care NHS Trusts in Bristol, they aim to estimate accurate incidence for acute lower respiratory tract disease and determine the effect the current and novel vaccination would impact patient morbidity and mortality.



Contribution to Clinical Research award

Adam Finn (below)



In his role as Professor of Paediatrics, Adam's research interests are elucidation of the nature of naturally acquired mucosal immunity to pneumococcus, meningococcus and other respiratory bacteria, the determinants of bacterial transmission and vaccine indirect effects and development of tools to assess human immune responses to candidate vaccine antigens. He also leads and supports numerous clinical trials of drugs and medicines in children. He is an honorary consultant in paediatric immunology and infectious diseases at Bristol Royal Hospital for Children, President of the European Society for Paediatric Infectious Diseases and a member of the United Kingdom Department of Health Joint Committee on Vaccines and Immunisation.

Hesitant, rather than opposed to, the COVID-19 vaccine

A study that explored the attitudes of vaccine hesitant adults in the UK towards uptake of the COVID-19 vaccine found that participants were hesitant rather than opposed to the vaccine. Concerns were exacerbated by a lack of trust in government and misunderstanding of science. Researchers interviewed people aged 18-29 who had not had the vaccine, and 30-49 who had not had the second dose of the vaccine after 12 weeks, to under-



stand what the barriers were and what facilitated uptake. Although hesitant about receiving a first or second dose of a COVID-19 vaccine, the majority of participants did not consider themselves to be anti-vaccine, and were usually able to recognise the possible benefits of being vaccinated for themselves and those around them. Younger people did not consider themselves to be at risk of becoming ill from COVID-19, did not think the vaccination was effective in preventing trans-

mission, and did not think sufficient research had been done regarding possible long-term side-effects.

Safety concerns were frequently mentioned by participants, with many describing a range of side-effects they or friends and family had experienced, or that they had been exposed to through the media.

Denford S *et al.* (2022). [Exploration of attitudes regarding uptake of COVID-19 vaccines among vaccine hesitant adults in the UK: a qualitative analysis](#). *BMC Infectious Diseases*.

Genetic study gives further details into severe COVID-19

The National Institute for Health and Care Research (NIHR)-supported GenOMICC study, the world's largest study of the genetics of critical COVID-19, has revealed details about some of the biological mechanisms behind the severe form of the disease.

Involving more than 57,000 people, the trial has discovered 16 new genetic variants associated with severe COVID-19, including some related to blood clotting, immune re-

sponse and intensity of inflammation. These findings will act as a roadmap for future efforts, opening new fields of re-



search focused on potential new therapies and diagnostics with pinpoint accuracy, experts say.

Researchers from the [GenOMICC consortium](#) – a global collaboration to

study genetics in critical illness – led by the University of Edinburgh in partnership with Genomics England, made these discoveries by sequenc-

ing the genomes of 7,491 patients from 224 intensive care units in the UK.

So far 94 patients have been recruited at University Hospitals Bristol and Weston NHS Foundation Trust, with the study planned to recruit for the next 10 years.

[Read more](#)

Childhood obesity increases risk of type 1 diabetes

Being overweight in childhood increases the risk of developing type 1 diabetes in later life. The study, co-led by researchers from the Universities of Bristol and Oxford, also provides evidence that being overweight over many years from childhood influences the risk of other diseases including asthma, eczema and hypothyroidism.

The number of individuals being diagnosed with type 1 diabetes has increased drastically in the last 20 years.

One possible explanation is the rising prevalence of childhood obesity in an increasingly obesogenic environment. Poor diets with high fat, salt and carbohydrate may compromise early life health-promoting effects of the bacteria in the gut and pancreatic beta-cell fragility in childhood and subsequently increase type 1 diabetes risk. In contrast to type 1 diabetes, there is irrefutable evidence that children who are overweight are more likely to develop type 2

diabetes and that weight loss can lead to its sustained remission. However, detecting reliable evidence for the factors that contribute to type 1 has been challenging, particularly given that individuals are typically diagnosed early in life before reaching adulthood.

Richardson T *et al.* (2022). [Childhood body size directly increases type 1 diabetes risk based on a lifecourse Mendelian randomization approach.](#) *Nature Communications.*

Patient response to surgical disruption in hormones

Major surgery and critical illness produce a potentially life-threatening systemic inflammatory response, which is counterbalanced by changes in adrenocorticotrophic hormone (ACTH) and cortisol. The body's stress response system, known as the hypothalamic-pituitary-adrenal (HPA) axis, controls the production of these hormones as a vital part of patients' response to surgery, but researchers have found that there is no simple graded HPA response to cardiac surgery.

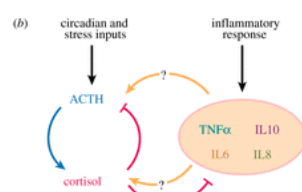
Research by experts at the Uni-

versities of Birmingham and Bristol shows cardiac surgery causes major dynamic changes in concentration of ACTH and cortisol, as well as their pattern of secretion. Using novel mathematical techniques, researchers developed a model of HPA axis activity that predicts the physiological mechanisms responsible for different patterns of cortisol secretion.

They found that the HPA axis response can be classified into one of three dynamic phenotypes: single-pulse, two-pulse and multiple-pulse dynamics.

These patterns may reflect underlying physiological differences in each person's HPA axis, but inflammation caused by surgery also appears to be contributing to changes in at least one of these patterns, the single pulse phenotype, suggesting that patients showing this dynamic could be experiencing the greatest inflammatory response to cardiac surgery.

Galvis D *et al.* (2022). [Modeling the dynamic interaction of systemic inflammation and the hypothalamic-pituitary-adrenal \(HPA\) axis during and after cardiac surgery.](#) *Royal Society Interface.*



The right eczema moisturiser is... the one you like

The Best Emollients for Eczema trial has found that no one type of moisturiser is better than another. This study, the first in the world to directly compare different types of moisturisers, highlights the importance of patient education and choice when deciding which moisturisers to use for children with eczema. Moisturisers are recommended for the one in five children who have eczema, which causes dry and itchy skin. Over



100 different moisturisers are prescribed in the NHS, costing over £100 million a year. Lack of research in this area means NHS guidelines vary widely in what is recommended, which leads to confusion and waste.

Used alongside other eczema treatments, there was no difference in effectiveness of the four types of moisturiser used in the study. Skin reactions such as itching or redness were common with all moisturiser

types. Awareness of the different types of moisturiser was low, and users had different preferences based on how the moisturisers look and feel.

Ridd M et al. (2022) [Effectiveness and safety of lotion, cream, gel, and ointment emollients for childhood eczema: a pragmatic, randomised, phase 4, superiority trial](#). The Lancet Child & Adolescent Health.

Sutton E et al. (2022). [How parents and children evaluate emollients for childhood eczema: a qualitative study](#). British Journal of General Practice.

Awards successes

Professor of Primary Health Care [Matthew Ridd](#) (Bristol Medical School: Population Health Sciences) received £1,243,212 from the **National Institute for Health and Care Research (NIHR)** for *Trial of IGe tests for Eczema Relief (TIGER)*, starting Aug '22 for 40 months.

An **NIHR** Health Technology Assessment award of £143,841 was bestowed upon Senior Lecturer Dr [Hayley Jones](#) (Bristol Medical School: Population Health Sciences) for *Surveillance of cirrhosis*, starting July 2022 for 20

months.

Prof in Restorative Dentistry [Nicola West](#) (Bristol Dental School) was successful with her **NIHR** application for a feasibility study *To assess whether reducing periodontal infection (gum disease) slows the progression of cognitive impairment associated with Alzheimer's disease*. The project, supported by a £203,613 award, will start in July 2022 and is expected to complete in June 2025.

Dr [Chrissy Hammond](#), Associate Professor in Developmen-

tal Genetics in the School of Physiology, Pharmacology and Neuroscience, received an £48,815 award from the **Dunhill Medical Trust** for *Response of the ageing immune system in fracture healing*. The project started in June 2022 (length: 10 months).

The role of IL-27 during ocular inflammation has been supported by £20,609 award from **Wellcome**. Principal Investigator Dr [Amy Ward](#) (Cellular and Molecular Medicine) started the project in June 2022 and will complete by October 2022.

Imre Berger: Fellow of the Academy of Medical Sciences

Imre Berger, Professor of Biochemistry and Chemistry and Director of Bristol's Max Planck Centre for Minimal Biology has been elected as a Fellow of the Academy of Medical Sciences for his outstanding contributions to biomedical science and notable discoveries during the COVID-19 pandemic.

His work includes a number of significant breakthroughs in



the fight against COVID-19. His team [discovered a druggable pocket](#) in the SARS-CoV-2

Spike protein that could be used to stop the virus from infecting human cells, blocking transmission and forestalling severe COVID-19 disease.

The findings are being used to develop new cost-effective treatments against all pathogenic coronavirus strains by Bristol-based [Halo Therapeutics Ltd](#). The biotech compa-

ny, co-founded by Imre, is currently preparing for in-human clinical trials.

Other notable breakthroughs include the discovery that SARS-CoV-2-infected individuals could have [several different SARS-CoV-2 variants](#) hidden away from the immune system in different parts of the body. He is also pioneering new vaccine technologies, having developed the ADDomer™, a platform for highly adaptable, rapid-response vaccines.

[Read the full press release](#)

Siblings and the genetics of disease

Genetic studies aim to find regions of the genome that associate with diseases or other outcomes. A new study has shown that for social traits these genetic effects are due to a mixture of direct effects (e.g. biological effects of DNA), and indirect effects (e.g. family or social environment). Whereas biological traits are mainly driven by direct effects.

An international group of 100 scientists studied 178,076 siblings to estimate the effects of genetics and environment on health and social outcomes. They found that the genetic factors on

more social traits – like educational attainment, age of first child and depression – are strongly influenced by either the family or social en-



vironment. In contrast, the genetic influences on more biological traits – such as cholesterol and BMI – were found to be less socially influ-

enced.

The findings suggest large-scale family datasets provide new opportunities to quantify direct effects of genetic variation on human traits and diseases. Looking at sociological questions and genetics together is a powerful tool for understanding why different health and social outcomes happen, providing better insight for potential interventions and treatments.

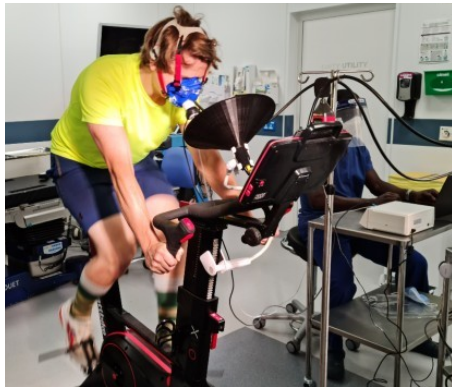
Howe L *et al.* (2022). [Within-sibship GWAS improve estimates of direct genetic effects](#). *Nature Genetics*.

Aerosols from exercise and speaking are similar

Vigorous exercise does not produce significantly more respiratory particles than speaking, but high-intensity exercise does, finds new University of Bristol-led research. The study is the first to measure exhaled aerosols generated during exercise, to help inform the risk of airborne viral transmission of SARS-CoV-2 for indoor exercise facilities and sporting and physical group activities.

Transmission of SARS-CoV-2 is considered to occur predominantly by inhalation of infectious aerosol. In the first published study of its kind, a UK-wide collaborative team

of clinicians and researchers conducted a series of experiments to measure the size and concentration of exhaled particles (up to 20 µm diameter)



ter) which are generated in our respiratory tracts and breathed out, during vigorous and high-intensity exercise.

The team found that the size

of airborne particles emitted during vigorous exercise was consistent with that of a person breathing at rest. However, the rate at which individuals exhale aerosol mass during vigorous exercise was found to be similar to speaking at a conversational volume.

Orton CM *et al.* (2022). [A comparison of respiratory particle emission rates at rest and while speaking or exercising](#). *Communications Medicine*.

Image: Male participant using a cardiopulmonary exercise test (CPET) as part of the PERFORM 2 study

Academic Foundation Programme Conference

The study *Associations between certainty of Covid infection status and reporting of long COVID symptoms: the role of placebo* by Associate Pro Vice-Chancellor (Research Culture) Prof [Marcus Munafò](#) (Psychological Science, pic-



tured below right), Dr [Maddy Dyer](#) (Psychological Science, pictured below left) and Catherine Macleod-Hall (NHS England) has been selected for an oral presentation at the national Academic Foundation Programme Conference.

The [conference](#), held at the University of Bristol on 11 June 2022, will be trainee-centred and will be of interest to foundation doctors, medical students and any faculty/senior colleagues who are involved in academic founda-

tion training. Themes of academic research, education and leadership training will be included.



Antimicrobial resistance study begins on Welsh farms

Bacterial sampling is now underway to assess the abundance and types of antimicrobial resistance (AMR) in bacteria on Welsh dairy, beef and sheep farms. The study, which researchers at the University of Bristol are co-ordinating, is part of Arwain DGC – a project designed to help combat antimicrobial-resistant bacteria in animals and the environment in Wales. Launched last year, Arwain DGC aims to reduce the need to use antimicrobi-

als such as antibiotics by improving productivity, animal health and welfare through



new and innovative technology and 'good practice'. Data obtained by analysing environmental faecal samples from a selected group of

Welsh farms over 12 months will assist researchers in learning more about what factors are associated with AMR on farms. These data will also help inform the design of a robust AMR surveillance system for Wales in the future.

[Read more about the announcement](#)

Image: As part of the project bacterial sampling is being undertaken in order to assess the abundance and types of antimicrobial resistance in bacteria on Welsh dairy, beef and sheep farms.

Reducing HIV stigma in African and Caribbean communities

[Common Ambition Bristol](#) brings together people of African and Caribbean heritage, working in equal partnership with healthcare professionals to develop new ways of increasing HIV awareness, encourage more people to get tested and tackle the stigma associated with HIV.

Common Ambition Bristol has launched an exciting programme of initiatives that include:

- A new, myth busting website developed by people of African and Caribbean heritage that talks about HIV, how to test for it and more
- Bristol's only dedicated sex-

ual health drop-in clinic for African and Caribbean heritage communities, based at Charlotte Keel health centre



- Wellbeing sessions to learn about sexual health, relationships, and new ways of preventing HIV
- Working with local barbers to share knowledge about HIV

- Partnership with local community events to increase HIV awareness and knowledge

The results will help Bristol achieve the goals set out by the global Fast Track Cities partnership, which Bristol Mayor Marvin Rees signed up to in November 2019. The partnership aims to reduce new HIV transmissions in the city to zero by 2030 while also working to eradicate the stigma associated with HIV.

Image: Aisha-monic Namurach, project coordinator for Common Ambition Bristol

ELIZABETH BLACKWELL FUNDING

Nurturing
Research.
Improving
Health.



Research for Equality, Diversity & Inclusion in Health and Biomedicine

This includes projects that focus on the way in which research is conducted (careers and research community) as well in projects that focus on the equality, diversity and inclusion in the delivery of research or the analysis of data. Research projects should demonstrate clear pathways to deliverables and next steps, such as impact on practice or submission of applications for external research funding.

Closing date: 25 July 2022

Elizabeth Blackwell Institute support scheme for academic training 2022

This scheme is designed to provide support for attending or accessing externally-provided training courses, including training in research methods and techniques, in all areas of health research.

Closing date: 31 August 2022

Elizabeth Blackwell Institute academic bridging funding scheme 2022

We have funding available to provide bridging funding for salaries of academic staff in health-related research in all Faculties at the University of Bristol.

Closing date: 31 August 2022

Workshop support

We offer support for workshops in health and biomedical research to facilitate new interdisciplinary connections. Applications reviewed all year.

Returning Carers Scheme

The University of Bristol is running a Returning Carers Scheme (RCS) to support academic staff across all faculties in re-establishing their independent research careers. Applications reviewed all year.

FUNDING OPPORTUNITIES

Research Professional provides access to an extensive database of funding opportunities. UoB staff and students have **FREE** online access to the database from any device – once you've registered then you can view upcoming funding opportunities from any device. You can search for funding information by discipline, sponsor, database searches, by recent calls or by upcoming deadlines. If you register for the site and log in, you'll be able to:

- Set up automated funding opportunity email alerts - **tailored according to your discipline and research interests**
- Save searches and bookmarks - store items of interest for future reference, download and email to colleagues
- Sign up for higher education news bulletins

For further information on Research Professional, go to the **RED website**.

*Research Professional

British Society for Immunology

[Communicating immunology grants](#)

Closing date: 1 July 2022

Award amount: £1,000

These enable individuals to stimulate interest, discussion and understanding of immunology amongst a wider audience with a particular interest in reaching new or traditionally hard to reach audiences, as well as support education on immunology.

National Institute of Allergy and Infectious Diseases, US

[Immune drivers of autoimmune disease \(U01 clinical trial not allowed\)](#)

Closing date: 1 July 2022

Award amount: USD \$3,750,000

This invites applications to participate in a co-operative research programme, which will focus on defining the immunologic states and dynamics that drive autoimmune disease. The aim is to enhance our understanding of the immunologic processes, events, and changes that underlie the clinical manifestations of autoimmune diseases, including disease flare, remission, and progression of established disease, as well as the progression from a state of elevated risk to clinical diagnosis of autoimmune disease.

Healthcare Infection Society

[Graham Ayliffe training fellowship](#)

Closing date: 1 September 2022

Award amount: £73,000

This enables clinicians working in the field of infection prevention and control to take a one year paid leave of absence to pursue their specialist area by broadening their knowledge base and imparting that knowledge to the wider scientific and medical community.

European Society of Clinical Microbiology and Infectious Diseases

[Research grants](#)

Closing date: 13 September 2022

Award amount: €50,000

These enable young investigators to conduct research in the fields of infectious diseases and clinical microbiology. Applicants must be principal investigators of the proposed research and must have a medical degree, a PhD or be enrolled in a PhD programme. They must be ESCMID members and must have been born on or after 1 January 1983.

Medical Research Council

[Research grants: Infection and Immunity](#)

Closing date: 13 September 2022

Award amount: unspecified

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.

National Institute of Allergy and Infectious Diseases, US

[Partnerships for development of vaccines against select enteric pathogens \(R01 clinical trial not allowed\)](#)

Closing date: 14 September 2022

Award amount: USD \$3,750,000

This supports research applications focused on advancing development of vaccine candidates against Enterotoxigenic *Escherichia coli*, *Salmonella enterica* serotype Paratyphi A, *Shigella flexneri* and *Shigella sonnei*.

European Society for Paediatric Infectious Diseases

[Small grant awards](#)

Closing date: 31 October 2022

Award amount: €20,000

These provide pump priming funds for research related to paediatric infectious diseases that is designed to produce pilot data for further external funding.

Applicants must be paid-up members of the society at the time of application and be within their medical qualification or PhD for at least 16 years.

THIS ISSUE'S FEATURED ARTICLE

Endothelial glycocalyx is damaged in diabetic cardiomyopathy: angiotensin 1 restores glycocalyx and improves diastolic function in mice

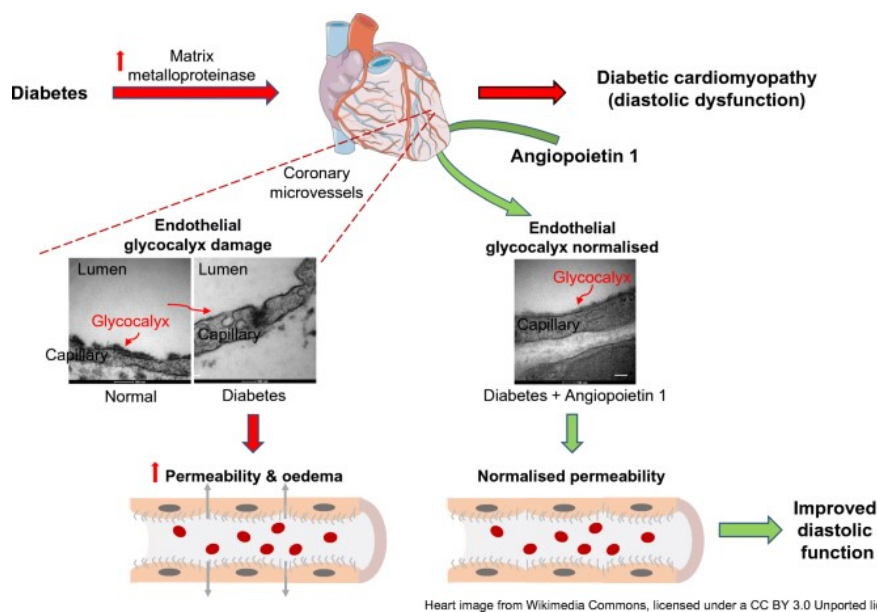
Qiu Y, Buffonge S, Ramnath R *et al.* (2022). *Diabetologia*.

Diabetic cardiomyopathy (DCM) is a serious and under-recognised complication of diabetes. The first sign is diastolic dysfunction, which progresses to heart failure. The pathophysiology of DCM is incompletely understood but microcirculatory changes are important. Endothelial glycocalyx (eGlx) plays multiple vital roles in the microcirculation, including in the regulation of vascular permeability, and is compromised in diabetes but has not previously been studied in the coronary microcirculation in diabetes. We hypothesised that eGlx damage in the coronary microcirculation contributes to increased microvascular permeability and hence to cardiac dysfunction.

We investigated eGlx damage and cardiomyopathy in mouse models of type 1 (streptozotocin-induced) and type 2 (db/db) diabetes.

In a mouse model of type 1 diabetes, diastolic dysfunction was associated with loss of eGlx from coronary microvascular endothelial cells (CMVECs) and the development of perivascular oedema, suggesting increased microvascular permeability.

We confirmed *in vitro* that eGlx removal increases CMVEC monolayer permeability. We identified increased matrix metalloproteinase (MMP) activity as a potential mechanism of eGlx damage and we observed loss of syndecan 4 consistent with MMP activity. In a mouse model of type 2 diabetes



we found a similar loss of eGlx preceding the development of diastolic dysfunction. We used isolated rat hearts to demonstrate that eGlx damage (induced by enzymes) is sufficient to disturb cardiac function. Ang1 restored eGlx and this was associated with reduced perivascular oedema and amelioration of the diastolic dysfunction seen in mice with type 1 diabetes.

The association of CMVEC glycocalyx damage with diastolic dysfunction in two diabetes models suggests that it may play a pathophysiological role and the enzyme studies confirm that eGlx damage is sufficient to impair cardiac function. Ang1 rapidly restores the CMVEC glycocalyx and improves diastolic function. Our work identifies CMVEC glycocalyx damage as a potential contributor to the development of DCM and therefore as a therapeutic target.

CONTACTS

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

Co-Chair: [Philip Bright](#)
Clinical Immunologist



Co-Chair (interim): [Angela Nobbs](#)
Senior Lecturer in Oral
Microbiology



- [Borko Amulic](#) - Senior Research Fellow in Immunology
- [Matthew Avison](#) - Professor of Molecular Bacteriology
- [Charles Beck](#) - Consultant Epidemiologist & Head of Team, Field Service South West, National Infection Service, UK Health Security Agency
- [Stephanie Diezmann](#) - Senior Lecturer in Fungal Pathogens
- [Hannah Fraser](#) - Research Fellow in Infectious Disease Mathematical Modelling
- [Clare French](#) - Research Fellow in Research Synthesis
- [Anu Goenka](#) - Clinical Lecturer in Paediatric Infectious Diseases and Immunology
- [Melanie Hezzell](#) - Senior Lecturer in Cardiology
- [Jamie Mann](#) - Senior Lecturer in Vaccinology & Immunotherapy
- [Paula MacGregor](#) - Senior Research Fellow and Proleptic Senior Lecturer
- [Adrian Mulholland](#) - Professor of Chemistry
- [Laura Peachey](#) - Lecturer in Veterinary Parasitology
- [Annala Seddon](#) - Director of the Bristol Centre for Functional Nanomaterials
- [Sarah Stuart](#) - Research Development Associate for the Faculties of Health and Life Sciences
- [Peter Vickerman](#) - Professor of Infectious Disease Modelling
- [Linda Woolridge](#) - Chair in Translational Immunology
- [Catherine Brown](#) - Network Administrator



The content of this newsletter is not the intellectual property of the Network, but rather an amalgamation of information obtained through a variety of sources including our [community members](#); research groups such as [Bristol AMR](#) and [Infection, Inflammation and Immunotherapy](#); and University of Bristol [school bulletins](#) and [press releases](#).

Affiliations are stated wherever possible, however please note that omissions do happen and we apologise in advance for any you may come across. All information is merely for educational and informational purposes. We cannot offer medical advice and any queries regarding treatment for a specific medical condition or participation in a clinical trial should be addressed to your healthcare provider. While the information herein has been verified to the best of our abilities, we cannot guarantee that there are no mistakes or errors.

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w: <http://www.bristol.ac.uk/infection-immunity/>
[@BristolandI](#)

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