

I&I NETWORK NEWSLETTER



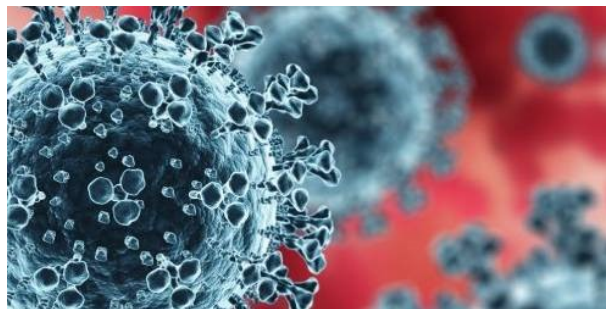
JUNE - AUGUST 2020

COVID-19 research priorities

As the COVID-19 pandemic hit the world, [researchers across the University of Bristol](#) have united to collaborate on finding ways to overcome the disease. Inside will be details of individual projects being undertaken covering everything from the search for a vaccine; online consultations for patients; overcoming isolation and loneliness and maintaining good mental health; determining the impact on financial services and industry; environmental impact; and how technologies can help address challenges.

The University's COVID19
Emergency Research Group

(UNCOVER) are working around the clock looking at how the virus works, survives and transmits. There are teams modelling the coronavirus' spread and infection rates; looking at the relationships between symptoms and the development of immunity in people who get the infection; and how to create and manufacture a safe and effective vaccine.



A number of experts have been making themselves heard in the [press, radio, television and social media](#) helping to dispel fake news, share research and inform the wider public on the challenges coronavirus is presenting and how best to meet them.

University of Bristol academics looking to pursue research into COVID-19 should look at the [list of funding opportunities](#) pulled together by the University's Research Development team.

[Read more about the University's response to the pandemic](#)

Bristol Events / Other Events

2-3

Infection and Immunity Research and Staff News

4-31

Elizabeth Blackwell Institute Funding Schemes

32

Funding Opportunities in Infection and Immunity

33-34

This Issue's Showcased Article

35

Contacts

36



UoBRISTOL EVENTS

After the cancellation and/or postponement of many events due to the COVID-19 situation, there are a number of seminars and meetings which have been transitioned to online platforms. A few teams are also meeting virtually to share research and keep the channels of communication open. A few (that I know of!) examples of active groups include:

- The School of Cellular and Molecular Medicine virtual coffee mornings are on a Friday at 10:30, contact cmm-admin@bristol.ac.uk if you'd like to take part.
- Bristol Veterinary School's [Animal Welfare and Behaviour](#) group have set up a SharePoint site and a Yammer Group, contact Jo.Hockenhull@bristol.ac.uk for access or search on Office365 and request to join. They are also holding regular science meetings 12:00-13:00, contact grp-labmeeting@groups.bristol.ac.uk to join.
- Bristol Veterinary School are holding their research mingles online; contact Chris Whiting (c.v.whiting@bristol.ac.uk) if you'd like an invite.
- The Infectious Disease and Epidemiology research group are holding regular online meetings Tuesday afternoons, contact Aaron Lim (aaron.lim@bristol.ac.uk) to join the mailing list.
- Bristol Veterinary School's Infection, Inflammation and Immunotherapy research group are also meeting regularly online, normally on a Tuesday. Contact Laura Peachey (laura.peachey@bristol.ac.uk) to be added to the mailing list.

Childhood Obesity and Poverty

25 June 2020, 11.00 - 12.30, online

Careers after Research - for PGRs and ECRs

25 June 2020, 13.00 - 14.30, Dr Kevin Parker, online

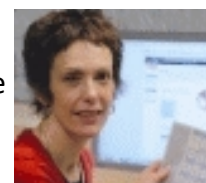


ID&Epi seminar

30 June 2020, 14.00 - 15.00, Tom Hoare (University of Bristol), online

Bristol BioDesign Institute seminar

1 July 2020, 13.00 - 14.00, Prof Christine Orengo (University College London), online



ID&Epi seminar

7 July 2020, 14.00 - 15.00, online

Bristol Veterinary School Research Mingle

8 July 2020, 16.00 - 17.00, Dolberry seminar Room, Langford campus

MESS meeting

14 July 2020, 12.00 - 13.00

UoB EVENTS

ID&Epi seminar

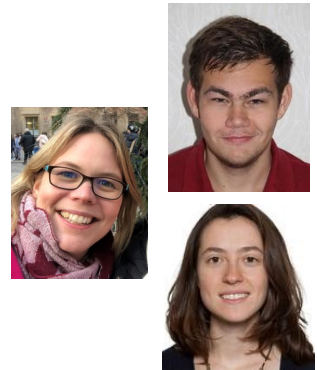
21 July 2020, 14.00 - 15.00, Jack Stone (University of Bristol), online

ID&Epi seminar

4 August 2020, 14.00 - 15.00, Hannah Fraser (University of Bristol), online

ID&Epi seminar

18 August 2020, 14.00 - 15.00, Josephine Walker (University of Bristol), online



OTHER EVENTS

Change in the Animal Industries

25 June 2020, 9.00 - 16.00, online

Covid-19 & Anti-Asian Prejudice: The Virus of Racism

25 June 2020, 17.00 - 17.45, Binna Kandola OBE, online

Cancelled: 2020 Salzburg Conference in interdisciplinary poverty research: Health and Poverty
2 - 5 July 2020, Salzburg

Data X Biomedical Science: Start-up Masterclass Series 2020

7 July 2020, 4.00 PM - 7 July 2020, 6.00 PMonline

RoB 2: Learning Live webinar series: Bias due to deviations from the intended interventions

21 July 2020, 9.00 - 10.00, Julian Higgins (Professor of Evidence Synthesis,) and Jonathan Sterne (Professor of Medical Statistics and Epidemiology), Department of Population Health Sciences, University of Bristol, online

RoB 2: Learning Live webinar series: Bias due to missing outcome data

4 August 2020, 16.00 - 17.00, Julian Higgins (Professor of Evidence Synthesis,) and Jonathan Sterne (Professor of Medical Statistics and Epidemiology), Department of Population Health Sciences, University of Bristol, online

NEWS

Obesity and fatty liver disease in young adults

Fatty liver disease, a condition in which fats build up in the cells of the liver, is broadly split into non-alcoholic fatty liver disease (NAFLD), which is usually seen in people who are overweight or obese, and alcohol-related fatty liver disease. Both can lead to scarring. Participants of the Avon Longitudinal Study of Parents and Children (ALSPAC) were invited for assessment, and researchers found that over 20% displayed evidence of fatty liver and one in forty has already developed fibrosis. As a com-

parison, at 17 years of age, 2.5% of participants had moderate to severe levels of fatty liver, whilst at the age of 24 this number had increased to 13%.

The data has highlighted the potential importance of liver health amongst young adults. This age group remains a blind

spot for clinicians, as they are typically considered a "healthy" age group that are rarely studied. If the obesity epidemic and culture of alcohol abuse aren't tackled nationally, we may see increasing numbers of patients presenting with end-stage liver disease, and at earlier ages.

Abeysekera KWM *et al.* (2020). [Prevalence of steatosis and fibrosis in young adults in the UK: a population-based study.](#) *The Lancet Gastroenterology & Hepatology.*



Funding successes: Part 1

Bristol secured £1m of funding from **UK Research and Innovation** for policy-related research projects. Profs [Mark Eisler](#) and [John Tarlton](#) and Drs [Kristen Reyher](#) and [Siobhan Mullan](#) (Bristol Veterinary School) have been awarded over £55,000 from this for projects and workshops, including:

- ◇ Evidence-gathering for antimicrobial resistance ([AMR Force](#) Research Excellence Framework (REF) case study
- ◇ AMR policy development

- ◇ AMR policy conference to showcase AMR Force work and generate impact
- ◇ Workshop in sustainable control of trematode parasites in African smallholder livestock
- ◇ Sustainable and ethical livestock production - Linking Research to policy and policy to Impact

Prof [Matthew Hickman](#) (Bristol Medical School: Population Health Sciences) received £142,644 from the **Medical Research Council**

(**MRC**) for his project *Co-production of an educational package for the universal HPV vaccination programme tailored for schools with low uptake: A participatory study*, starting January 2020 for one year.

The **Royal Society** awarded Dr [Wuge Briscoe](#) (Chemistry) £12,000 to pursue *Understanding Hepatitis C Protein Adsorption onto Lipid Droplets*, starting December 2019 for two years.

Eliminating Hepatitis C in Pakistan

An internal quality-related (QR) Global Challenges Research Fund (GCRF) pump-priming award to Dr [Aaron Lim](#) (Bristol Medical School: Population Health Sciences) and his overseas partners has paved the way for important Hepatitis C virus (HCV) modelling to be undertaken in Pakistan. Pakistan has one of the highest rates of Hepatitis C infection in the world, accounting for over 10% of the global HCV infections, so reducing new infections to meet the WHO tar-

get is a public health priority. A follow-on study, a collaboration between the University of Bristol, Médecins Sans Frontières, the Pakistan HCV Task Force, US Centers for Disease Control and Prevention, Aga Khan University, and the Pakistan Kidney and Liver Institute, used mathematical modelling to provide the first country-level estimates of the screening and treatment needed for achieving the WHO elimination targets for HCV incidence in Pakistan,

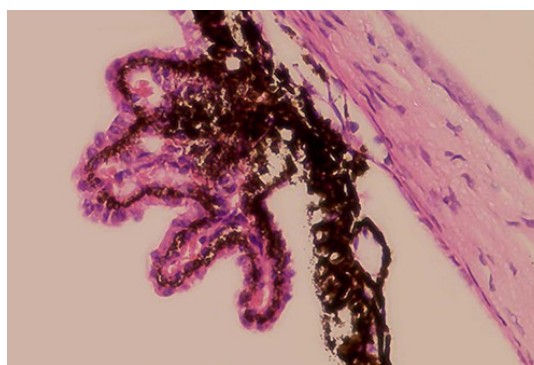
and the possible costs of doing so. An investment of at least US\$39b would be needed to eliminate HCV in the country. Media coverage of the study has generated more than 20 news articles across 8 countries.

Lim A *et al.* (2020). [Effects and cost of different strategies to eliminate hepatitis C virus transmission in Pakistan: a modelling analysis.](#) *The Lancet Global Health.*

[Read the full story](#)

Treating glaucoma with gene therapy

A research team tested a new approach that could provide additional treatment options and benefits for those suffering from glaucoma, a disease affecting over 64 million people worldwide and which is currently treated with eye drops and/or surgery. They designed a gene therapy and demonstrated proof of concept using experimental mouse models of glaucoma and human donor tissue. The treatment targeted eye's ciliary body (pictured), which produces the fluid that maintains pressure within the eye. Using CRISPR gene editing technology, a gene



(Aquaporin 1) in the ciliary body was inactivated leading to reduced eye pressure.

The team hope to advance towards clinical trials in the near future. If it's successful it could allow a long-term treatment of glaucoma with a single eye injection, which would improve the quality of life for many patients whilst saving

the NHS time and money. The academics are currently in discussion with industry partners to support further laboratory work and rapidly progress this new treatment option towards clinical trials.

Wui J *et al.* (2020). [Gene therapy for glaucoma by ciliary body Aquaporin 1 disruption using CRISPR-Cas9.](#) *Molecular Therapy.*



Funding successes: Part 2

To Dr [Melanie Hezzell](#) (Bristol Veterinary School), £30,200 from the **University of Bristol** for *The Genetics of Myxomatous Mitral Valve Disease in Dogs*, starting Nov 2019 for one year.

The School of Chemistry's Prof [Jonathan Reid](#) was awarded £236,987 from **Biral** for a project entitled *A Prototype Instrument for Assessing Bacterial Viability in the Aerosol Phase*, starting Nov 2019 for 18 months.

Dr [Bryony Sands](#) (Biological Sciences) was successful in

her application to **MSD Animal Health** for £10,000 for her project *Distribution and abundance of Dermacentor reticulatus*, starting Jan 2020 for one year. This tick is a vector of various disease organisms including *Babesia canis* and several *Rickettsia* species.

[Amberly Brigden](#) (Bristol Medical School: Population Health Sciences) received a **National Institute for Health Research** (NIHR) Research Capability Funding award of £15,225 for *Exploring treatment for younger children*

with CFS/ME, starting Nov 2019 for 5 months.

Dr [Katy Turner](#) (Bristol Veterinary School) has been awarded funds to complete an economic evaluation of the **NIHR**-funded trial "*Safetxt*": *A randomised controlled trial of an intervention delivered by mobile phone messaging to reduce sexually transmitted infections (STI) by increasing sexual health precaution behaviours in young people*, led by the London School of Hygiene and Tropical Medicine.

Insect wings for improved medical implants

Some insect wings such as cicada and dragonfly possess nanopillar structures that kill bacteria upon contact. To date, the precise mechanisms that cause bacterial death have been unknown. Using a range of advanced imaging tools, functional assays and proteomic analyses, a recent study has identified new ways in which nanopillars can damage bacteria. The findings will aid the design of better antimicrobial surfaces for potential biomedical applications such as medical implants and devices that are not reliant on antibiotics. The study

shows that the antibacterial effects of nanopillars are actually multifactorial, nanotopography- and species-dependent.

Alongside deformation and subsequent penetration of the bacterial cell envelope by nanopillars, particularly for Gram-negative bacteria, the team found the key to the antibacterial properties of

these nanopillars might also be the cumulative effects of physical impedance and induction of oxidative stress. They hope to translate this expanded understanding of nanopillar-bacteria interactions into the design of improved biomaterials for use in real world applications.

Su B *et al.* (2020). [Antibacterial effects of nanopillar surfaces are mediated by cell impedance, penetration and induction of oxidative stress](#). *Nature Communications*.

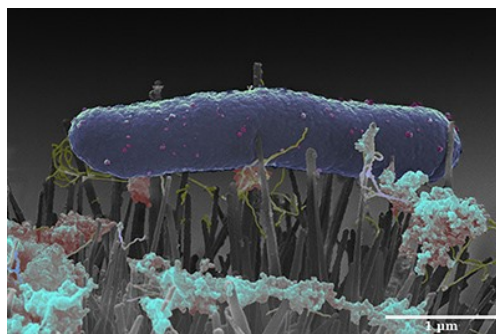


Image: An E-coli bacteria lying on a bed of nanonails. © Prof Bo Su (Bristol Dental School)

Elizabeth Blackwell Institute COVID-19 funding call

The [Elizabeth Blackwell Institute](#) (EBI) opened a [rapid response funding scheme](#) to support research in Coronavirus in March 2020. The initial round received over 50 applications; the scheme is now open on a rolling deadline until funds are depleted. Among the approved projects are:

- Prof [Ian Collinson](#) (Biochemistry), £4,916 for *Characterisation of the dynamic interaction of COVID19 spike protein with the human receptor ACE2*
- Prof [Nicholas Timpson](#) (Bristol Medical School: Population Health Sciences), £5,650 for *Extraordinary COVID_19 questionnaire – Avon Longitudinal Study of Parents and Children*
- Dr [Sarah Sauchelli Toran](#) (Bristol Dental School), £922 for *Digitalising diabetes support groups in response to the coronavirus COVID-19 outbreak*
- Dr [Hannah Christensen](#) (Bristol Medical School: Population Health Sciences), £3,350 for *Social contacts and mixing patterns under COVID19 social distancing measures*
- Dr [Ellen Brooks-Pollock](#)

(Bristol Veterinary School), £1,976 for *Healthcare seeking behaviour and contact patterns during the COVID-19 pandemic: informing predictive modelling*

- Prof [Adam Finn](#) and Drs [Andrew Davidson](#) & [David Matthews](#) (Cellular and Molecular Medicine), £4,980 for *Setting up quantitative realtime PCR testing for CoV2*
- Drs [Darryl Hill](#), [Andrew Davidson](#), [Anu Goenka](#) and Prof

£4,870 for *Hyperinflammation and immunity in COVID-19: establishing a robust and safe immunophenotyping methodology*

- Prof [Imre Berger](#) (Biochemistry), £25,000 for *ADDomer-COVID19 VLP vaccine to combat and defeat COVID19 outbreak*
- Prof [Linda Wooldridge](#) (Bristol Veterinary School), £3,885 for *Identification of T-cell epitopes using a novel MHC-binding prediction tool for the generation of tools to study the T-cell response against SARS-CoV-2*

• Prof [Pete Cullen](#) and [Boris Simonetti](#) (Biochemistry), £4,998 for *Investigation of SARS-CoV-2 S interaction with Neuropilins, a novel*

gateway for infection?

- Prof [Dek Woolfson](#) (Chemistry), £7,587 for *Structure-function studies of the SARS-CoV-2 Envelope (E) Protein*
- Dr [Aisling O’Kane](#) (Computer Science), £3,912 for *Amazon Echo Show for health, care and wellbeing needs for residents and carers during self-isolation*

There are many more funded projects under this call, [view the whole list on the EBI website](#).



[Adam Finn](#) (Cellular and Molecular Medicine), £4,606 for *Understanding the immunomodulatory effects of BCG on subsequent exposure to SARS-CoV2 in human mucosal cells using air liquid interface models*

- Drs [Andrew Davidson](#) & [David Matthews](#) (Cellular and Molecular Medicine), £5,000 for *an Imaging platform for rapid antiviral and neutralising antibody assays against SARS-CoV-2*
- Dr [Laura Rivino](#) (Cellular and Molecular Medicine),

Trial for advanced chronic kidney disease

A new UK-wide clinical trial is looking to recruit around 500 patients aged over 65-years with low kidney function and other health problems to better understand the pros and cons of different options should their kidneys fail. Current evidence around treatment options for patients with the advanced stages of kidney disease, which include dialysis, transplantation and conservative care, a form of treatment that aims to maintain a patient's quality-of-life through symptom management without the intervention of surgery or dialysis, is limited. Some studies have shown that

some older people with other medical problems do just as well with conservative care as they would be expected to do with dialysis, but more evidence is needed.

The [Prepare for Kidney Care trial](#) is the first ever randomised controlled trial to compare the benefits of preparing patients for dialysis versus conservative care. Importantly, the study will provide high-



quality data on quality-of-life and survival rates – something that the patients involved in designing the trial considered essential. The results will be used to inform future patients, relatives and clinical teams on the outcomes that can be expected with each option so that a patient's choice can be matched to their individual preferences and priorities.

The results of this trial will bridge this knowledge gap through more-informed NHS guidance for clinicians and more reliable information on what to expect for patients faced with making the decision.

RECOVERY trial

Fifty recovering COVID-19 patients at University Hospitals Bristol NHS Foundation Trust and Weston NHS Foundation Trust have joined the national clinical trial to test the effectiveness of different drug treatments. Natalie Blencowe from the Surgical Innovation theme is co-ordinating the recruitment in Bristol.

A range of potential treatments have been suggested for COVID-19 but nobody knows if any of them will turn out to be more effective

in helping people recover than the usual standard of hospital care which all patients will receive. The [RECOVERY Trial](#) will begin by testing some of the suggested treatments to identify the most effective quickly to make them available to all patients, among them:

- Lopinavir-Ritonavir (commonly used to treat HIV)
- Low-dose Dexamethasone (a type of steroid, which is

used in a range of conditions typically to reduce inflammation)

- Hydroxychloroquine (related to an anti-malarial drug)
- Azithromycin (a commonly used antibiotic)
- Tocilizumab (an anti-inflammatory treatment given by injection)
- Convalescent plasma (collected from donors who have recovered from COVID-19 and contains antibodies against the SARS-CoV-2 virus).

RECOVERY
Randomised Evaluation of COVID-19 Therapy

Peace and mind and attitudes towards vaccines

Many people experience peace of mind from getting their children vaccinated; however, this benefit is currently being ignored when health bodies weigh up vaccine benefits to make decisions about whether or not to introduce vaccines or expand their coverage. A study found that peace of mind should be considered in the health economic framework used by decision makers, but that more research is required to further define and quantify it. Many different factors are consid-

ered by the [Joint Committee on Vaccination and Immunisation](#) who advise UK government, but peace of mind is not currently one of them. Researchers found that whether a person experienced peace of mind from vaccination depended on their knowledge of its benefits; the reassurance



they experienced came from the knowledge that some level of protection against a disease would be gained. Though peace of mind benefits are only experienced by some parents, the added value to their health could still influence decisions on whether or not a government should fund a vaccine.

Lasseter G *et al.* (2020). [Understanding the role of peace of mind in childhood vaccination: A qualitative study with members of the general public](#). *Vaccine*.

Funding successes: Part 3

Dr [Laura Peachey](#) (Bristol Medical School) received a **Royal Society** International Exchanges award worth £5,900 for overseas travel between collaborators in the UK and New Zealand for *The role of the microbiome in providing protection against gastrointestinal nematodes*.

Prof [Carmen Galan](#) (Chemistry) was awarded £746,198 from the **Engineering and Physical Sciences Research Council** (EPSRC) for *Bio-inspired nanoparticles for point of care tuberculosis detection*, starting Apr 2020 for two years.

Diabetes UK awarded Prof

[Kathleen Gillespie](#) (Bristol Medical School: Translational Health Sciences) a £95,700 studentship to look into *Genetic regulation of immune response genes in Slow Progressors to type 1 diabetes*, starting Oct 2020 for 3 years.

Dr [David Matthews](#) (Cellular and Molecular Medicine) received £100,000 from **Public Health England** for his project *Constructing a recombinant 2019-NCOV*, starting Apr 2020 for 8 months.

The **National Institute for Health Research** School for Primary Care Research (NIHR-SPCR) awarded Dr [Rupert Payne](#) (Bristol Medical

School: Population Health Sciences) £76,500 for *COVID19 risk stratification*, starting Apr 2020 for three months.

Dr [Tristan Cogan](#) (Bristol Veterinary School) was awarded £25,000 from the **Department for Environment, Food and Rural Affairs** (DEFRA) for *Investigation of bacteria in canine uterine and renal glomerular vasculopathy (CRGV) cases*, starting Nov 2019 for five months.

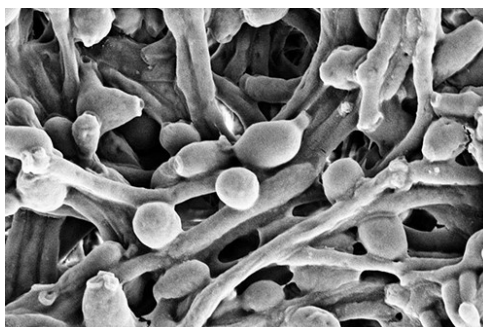
To Dr [Melanie Hezzell](#) from the **National Institute for Health** (USA), £2,739 for *Prognostic value of circulating cortisol in canine congestive heart failure*, from Jan 2020.

New drug formulation could treat *Candida* infections

Candida albicans, usually seen in the mouth, skin, gut and vagina, is reported to form biofilms and cause mild to life threatening infections. Fluconazole, an antifungal drug widely used to treat *Candida* infections is completely ineffective in treating *Candida* biofilms and new drugs are needed to treat them. However, developing antifungal drugs is very challenging because yeast cells are structurally similar to human cells; as a result, there is a greater chance of unwanted side effects. A better alternative would be to improve the efficiency of currently approved antifun-

gal drugs but with minimal side effects. Studies have shown that microorganisms can communicate using chemical signals, with some using these signals to control competing microorganisms; these signals could therefore potentially be used as antimicrobial drugs. The team found that a specific chemical signal released from a major bacterial pathogen can be

successfully used to significantly improve the activity of fluconazole against *Candida* biofilms by packaging them to small lipid molecules and delivering them together. It is hoped pharmaceutical industries will explore the antimicrobial properties of microbial chemical signals so they can be developed into cost effective treatments.



Bandara HMHN *et al.* (2020). A novel, quorum sensor-infused liposomal drug delivery system suppresses *Candida albicans* biofilms. *International Journal of Pharmaceutics*.

Bringing vaccine technology to Vietnam

Prof Imre Berger, Director of the [Max Planck-Bristol Centre for Minimal Biology](#), visited [Vabiotech](#) in Hanoi in Nov 2019 as part of an ongoing initiative to share state-of-the-art vaccine technology with developing countries. Vabiotech and the University of Bristol are partners in the [Future Vaccine Manufacturing Research Hub](#) (FVMR Hub), a collaborative initiative led by Imperial College London and supported by the

Engineering and Physical Sciences Research Council. Scientists from Vabiotech are being trained by Prof Berger and his team in MultiBac, a powerful recombinant production technology the Berger team pioneered. MultiBac is uniquely suited for producing

novel vaccines in large quantities in insect cells that can be easily cultured at low cost. The objective is to master the MultiBac technique and implement the technology in large-scale biofermenters in Vietnam. Together with Vabiotech and supported by the FVMR Hub, Prof Berger is targeting the use of MultiBac towards the production of vaccines for pandemic (avian) influenza, as well as rabies and other pathogens.



Coronavirus behaviour change website

An evidence-based, behaviour change website, already proven successful in reducing infection transmissions for seasonal and swine flu, has been rapidly redeveloped and adapted in response to coronavirus. The researchers behind 'Germ Defence' from the Universities of Bristol, Bath and Southampton hope that the quick redevelopment of the site for COVID-19 will help the public



to shift behaviours.

The researchers suggest it can help all of us move from current lockdown measures towards a so-called 'new normal', where social distancing measures look likely to apply for the foreseeable future.

'Germ Defence' draws on behaviour change techniques to

help users think through and adopt better home hygiene and stronger infection control. Developed by

health experts and psychologists, previous research into its effectiveness involving a study of over 20,000 people, found that users of the site were less likely to catch flu or other viruses; and if they did become ill, on average, their illnesses were shorter and milder.

Little P *et al.* (2020). [Reducing risks from coronavirus transmission in the home—the role of viral load](#). *BMJ*. Published 6 May 2020.

Research to track frontline NHS staff in Bristol

Healthy frontline NHS staff in Bristol will be studied as part of a research project led by infectious disease and immunology specialists from Bristol Royal Hospital for Children and the University of Bristol. The LOGIC project will monitor 125 healthy frontline NHS staff from the Emergency Department of the Bristol Royal Hospital for Children to inform potential vaccines and treatment. The team will track their symptoms (or lack of), the presence (or absence) of the virus in their mouths and noses and the development (or not) of the protective antibodies in their blood over a three-

month period.

While it is widely known that Covid-19 is caused by the virus SARS-CoV-2, there is little understanding about the SARS-CoV-2 infection and the relationship between the symptoms, viral and immune dynamics which is needed in order to inform public health control measures and the development of a vaccine. The study will be carried out by researchers from the Univer-

sity's COVID-19 Emergency Research Group (UNCOVER) in partnership with clinical staff. UNCOVER pools resources, capacities and research efforts to combat this infection and includes clinicians, immunologists, virologists, synthetic biologists, aerosol scientists, epidemiologists and mathematical modellers and has links to behavioural and social scientists, ethicists and lawyers.



The research is being funded initially by [Wallace and Gromit's Grand Appeal](#), the dedicated charity for the children's hospital as part of the charity's [emergency Coronavirus Appeal](#).

External engagements: Part 1

Drs [Andrew Davidson](#) and [David Matthews](#) (Cellular and Molecular Medicine) were interviewed by correspondent Deborah Cohen on [BBC Newsnight 5 March 2020](#), during which they discussed their Coronavirus work and the work they are doing with Public Health England and colleagues at the University of Liverpool.



Andrew was also interviewed by Adam Walton on BBC Radio Wales' *The Arts Show* and

Science Café on 25 February 2020 to discuss Coronavirus and other epidemics, to understand how viruses spread across the globe, and what ways we can all prevent infection. You can listen [here](#) on BBC Sounds.

Dr [Aiden Foster](#) and Sam Pearce (Bristol Veterinary School) were interviewed about Sam's project on *Enteric Pathogens in Deer* by [BBC Farming Today](#).

Prof [Adam Finn](#) (Bristol Medical School:), in addition to appearing in [BBC Points West](#) to discuss the UK's response to control the spread of COVID-

19, discusses the virus from a paediatric standpoint on the [BBC Radio 4's 'PM' current affairs](#) programme.

Prof [Gabriel Scally](#) (Bristol Medical School: Population Health Sciences and Associate Fellow at the Institute for Public Policy) was interviewed by Adam Vaughan at *New Scientist* to find out [Why have there been so many coronavirus deaths in the UK?](#) He has also been interviewed by The Guardian and New Statesman.

See the list of many more interviews and opinion pieces by University of Bristol staff relating to COVID-19

Big Beat Challenge shortlist

The British Heart Foundation's [Big Beat Challenge](#) is a global competition that will see teams of world-class scientists competing for a research award of up to £30 million. International, multi-disciplinary groups of researchers were asked to identify and propose a transformational solution to a significant problem in any heart or circulatory disease. The most compelling proposal will win the funding, and the opportunity to accelerate breakthroughs that could transform

lives across the globe.

The University of Bristol is part of the consortium whose idea for next generation cardiovascular health technology is one of just four that have been shortlisted. ECHOES - Enhancing Cardiac care through Extensive Sensing (ECHOES) - is based on the principle that the single greatest obstacle to prevention, diagnosis and treatment of major chronic cardiovascular diseases (CVD) is the lack of medically relevant patient data obtained in daily life. The

team will develop wearable technology that can be used in daily life to capture more data than ever before. From symptoms and physical activity to heart function and air quality, this information could be used alongside genetic and healthcare data to transform diagnosis, monitoring and treatment of heart and circulatory diseases by creating a digital twin. ECHOES is led by Prof Frank Rademakers at KU Leuven, Belgium. The winner is expected to be announced at the end of 2020.

Funding for Bristol's Health Protection Research Unit

A £4m funding boost from the National Institute for Health Research (NIHR) will fund a new [Health Protection Research Unit \(HPRU\) in Behavioural Science and Evaluation](#). The funding is part of the [NIHR's £58.7 million investment](#) into research to protect the public's health from threats such as antimicrobial resistance, air pollution and infectious diseases. The funds will be used to create 14 Health Protection Research Units that will con-

duct high-quality research enhancing the ability of Public Health England (PHE) to use innovative techniques to protect the public's health and minimise the health impact of emergencies. These are multidisciplinary centres of excellence which launched in April and will run for five years.

The partnership between the University of Bristol and PHE, in collaboration with University College London, Cam-

bridge Medical Research Council (MRC) Biostatistics Unit and University of the West of England, the Bristol HPRU will co-design a programme of research to support PHE tackle some of the biggest health threats nationally and globally and will build on their previous successful partnership and expand research capacity in behavioural science.

Funding successes: Part 4

Dr [Kristen Reyher](#) (Bristol Veterinary School) is part of an international team which has been awarded £200,000 for the Joint AMR in the Environment 'Pan-Program' Integration Project, to build upon the consortium's award for AMR research in Argentina.

Dr [Emily Blackwell](#) (Bristol Veterinary School) has secured £47,000 from **Cats Protection** towards the annual running costs of the [Bristol Cat Study](#).

Dr [Katy Turner](#) and Prof [Andrew Dowsey](#) (Bristol Veterinary School) lead a new award of £14,797 from the **Elizabeth Blackwell Institute's Health Data Strand** with colleagues in

Bristol Medical School, Cellular and Molecular Medicine, Computer Science, Electrical and Electronic Engineering and Engineering Maths, and North Bristol NHS Trust for the study *Severn Pathology: Opening up a goldmine for Antimicrobial Resistance (AMR) health research and beyond 2*.

Dowsey and Turner are also leading the AMR theme of a successful **David Telling** Infrastructure award of £225,000 for *A nationally leading resource for linked BNSSG health and social care data, with exemplar research on antimicrobial resistance and pathways between health and social care*, led by Prof Jonathan

Sterne (Bristol Medical School: Population Health Sciences).

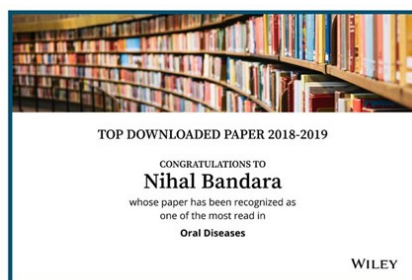
Prof [Helen Lambert](#) (Bristol Medical School: Population Health Sciences) was awarded £21,600 from the **British Council** for *The Challenge of AMR*.

An award of £557,000 was made to Prof [Andrew Dick](#) (Bristol Medical School: Translational Health Sciences) from **MeiraGTx** for *Gene therapy for Glaucoma with MeiraGTx*, starting Oct 2019 for 2 years.

The Grand Appeal awarded £58,513 to Prof [Adam Finn](#) (Cellular and Molecular Medicine) for LOnGitudinal Study of COVID-19: Symptoms, Virology & Immunity (LOGIC Study).

Achievements

Dr Nihal Bandara (Bristol Dental School) was informed by the journal *Oral Diseases* that his paper, [Biodiversity of the human oral mycobiome in health and disease](#), is among the top 10% most downloaded papers of last year.



[Peter Cullen](#), Professor of Biochemistry and Wellcome Trust Senior Investigator, has been elected to a Fellowship

by the Academy of Medical Sciences. Fellows have been chosen for their exceptional contributions to advancing biomedical science via world-leading research discoveries, running national science communication and engagement programmes and translating scientific advances into benefits for patients and the public. Prof Cullen is internationally recognised for his identification and characterisation of the molecular mechanisms that orchestrate protein and lipid transport through the endosomal network, a complex intracellular maze found in all human cells. His world-leading research has laid the

foundations for understanding how altered function of the network contributes to an array of human diseases, ranging from cardiovascular disease and neurological disorders, most notably Alzheimer's disease and Parkinson's disease, through to metabolic disorders such as type 2 diabetes, hypercholesterolemia and non-alcoholic fatty liver disease, and subversion of the network by a wide range of viruses and bacteria.



COVID-19 Disease-Target Atlas

Dr [Jie Zheng](#) (Vice Chancellor's Fellow, Bristol Medical School: Population Health Sciences) and colleagues from the [MRC Integrative Epidemiology Unit](#) have evaluated the tissue-specific effects of COVID-19 drug targets on a range of infectious and non-infectious disease outcomes to support rapid target prioritisation. Using Mendelian randomization the team have analysed 353 candidate COVID-19 drug targets and es-

timated their effect (in 11 tissues relevant to SARS-CoV-2 infection) on 619 disease traits, identifying 726 targets, which show evidence of effects on other diseases (including targets of Leflunomide, Cilengitide and Bari-

tinib).

The results are openly available as a COVID-19 target-disease atlas in EpiGraphDB, <http://epigraphdb.org/covid-19/ctda/>.

Zheng J *et al.* (preprint). [Multi-omics study revealing tissue-dependent putative mechanisms of SARS-CoV-2 drug targets on viral infections and complex diseases.](#) *medRxiv*.

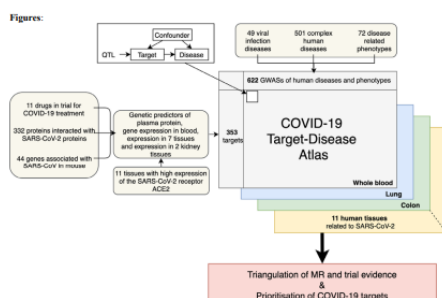


Figure 1. Study design of this multi-omics MR study of COVID-19 targets on human phenome and drug target prioritization. The diagram on the top left corner is the Mendelian randomization model been used in this study. The QTL refers to the genetic variant(s) robustly associated with the protein/gene expression levels of the COVID-19 target genes.

Hepatitis C intervention found to be effective by GPs

The first UK clinical trial to increase the identification and treatment of hepatitis C (HCV) patients in primary care has been found to be effective, acceptable to staff and highly cost-effective for the NHS. The Bristol-led Hepatitis C Assessment to Treatment Trial (HepCATT) provides robust evidence of effective action GPs should take to increase HCV testing and treatment. An electronic algorithm was devised to flag patients with HCV risk mark-

ers and invite them for an HCV test by letter, or opportunistically through pop-up messages during consultations. Practice staff received HCV educational training, and HCV posters and leaflets were placed in waiting rooms to increase patient awareness. Around 5% of all patients were flagged with HCV risk markers; 16% of the flagged patients were tested for HCV in HepCATT intervention practices compared to 10% in control practices, a

59% increase after adjusting for the characteristics of different practices. Five times as many patients were assessed for treatment in the HepCATT intervention practices, compared to control.

Macleod J *et al.* (2020). [Cost effectiveness of an intervention to increase uptake of hepatitis C virus testing and treatment \(HepCATT\): cluster randomised controlled trial in primary care](#). *BMJ*. Published 26 February 2020.

Funding successes: Part 5

Dr [David Morgan](#) (Cellular and Molecular Medicine, CMM) and Prof [Linda Wooldridge](#) (Bristol Veterinary School, BVS) were awarded a **Wellcome Trust** Translational Partnership Award of £100,000 for one year to look at *Targeting CD8 using blocking anti-CD8 antibodies as a strategy to disable autoreactive CD8+ T-cells in Type 1 diabetes*.

Prof [Andrew Dowsey](#) and Dr [Katy Turner](#) (Bristol Veterinary School) are Associate Directors and part of a South West team of NHS and academic partners (directed by Prof Jonathan Sterne, Bristol Medical School) which has received a large award from [Health Data](#)

[Research UK](#). The award (£1.2m total of which £250k to the Vet School) is for three years; within this award, Katy and Andy are leads for the sub-project [Precision antimicrobial prescribing: safeguarding patient outcomes and preserving future efficacy – HDR UK](#).

Dr [Georgina Russell](#) (Bristol Medical School: Translational Health Sciences) was awarded £98,205 from **Above & Beyond** for *Neuro-endo-immunomodulation in glucocorticoid based therapeutics*, starting Feb 2020 for 18 months.

Dr [Laszlo Talas](#) (Biological Sciences) received £14,769 from the **Engineering and Physical**

Sciences Research Council Impact Acceleration Account for *Exploratory: Automatic thermal and behavioural monitoring for disease detection in foals*, starting Apr 2020 for one year.

The **Elizabeth Blackwell Institute** has awarded £21,000 to Prof [Linda Wooldridge](#) (BVS) and Dr [Laura Rivino](#) (CMM) for the purchase of *Peptide Libraries* for the study of Immunity in COVID-19.

Dr [Parthive Patel](#) (CMM) was awarded a Sir Henry Dale Fellowship by the **Wellcome Trust/Royal Society**. Parthive's research looks into how tissues maintain epithelial integrity under stress/damage.

Drug used widely to treat eye condition has 'no benefit'

A team from the University of Bristol and University Hospital Southampton have found that a drug used to treat a common eye condition has “no benefit” and should no longer be used. Eplerenone, which is primarily used to treat heart failure, is widely offered by ophthalmologists as a treatment for central serous chorioretinopathy (CSCR) based on limited clinical data. It is the fourth most common retinal disease. Eplerenone, which is one of a group of drugs that decrease the activity of hormones that regulate salt and water in the body, was found to improve vision in a

small number of patients in early-stage research. However, it is also associated with side effects including raised potassium levels and a decrease in blood pressure. Prof Andrew Lotery, a consultant ophthalmologist at University Hospital Southampton, launched the first study into the long-term efficacy and safety of the drug for CSCR. The £1 million trial, funded by the Medical Research Council and the National Institute for Health Research Efficacy and Mechanism Evaluation Programme, saw 111 patients at 22 sites across the UK receive either the medication or an identi-

cal placebo tablet for up to 12 months. The results showed there was no benefit of treating patients with eplerenone compared to those who took a placebo. The study was managed by researchers from the Bristol Trials Centre at [Bristol Medical School](#) which co-designed the study and analysed the data.

Lotery A *et al.* (2020). [Eplerenone for chronic central serous chorioretinopathy in patients with active, previously untreated disease for more than 4 months \(VICI\): a randomised, double-blind, placebo-controlled trial](#). *The Lancet*.

AMR project launch in Thailand

The OH-DART ([One Health Drivers of Antibacterial Resistance in Thailand](#)) Bristol-led project launched officially in Bangkok, Thailand in late December 2019. OH-DART is an MRC-funded project whose aim is to define and prioritise the drivers of AMR in Thailand using a multi-disciplinary approach by a consortium comprising AMR investigators from the universities of Bristol, Exeter, Bath, the UK Centre for Ecology and Hydrology, Mahidol University and the

Chulabhorn Research Institute. The project consortium is led by Prof [Matthew Avison](#) (Cellular and Molecular Medicine) and includes members Dr [Kristen Reyher](#), Dr [Katy Turner](#) and Dr [Ross Booton](#) (all Bristol Veterinary School). The study was presented to the Thai Government and the

national press. The study was presented to the Thai Government and the national press. The launch was announced on Thailand's TV news and an [excellent educational video](#) was also broadcast.



Funding successes: Part 6

Prof [Sorrell Langley-Hobbs](#) (Bristol Veterinary School) and Prof [Eithne Comerford](#) (University of Liverpool) have been awarded funds for a **Petsavers** Student project entitled *Characterising Implant-associated Infection and Aseptic Loosening of Total Hip Replacements in a Large Cohort of Dogs from the British Veterinary Orthopaedic Association (BVOA) - University of Liverpool (UoL) Canine Hip Registry*.

The **Worldwide Universities Network (WUN) Research Development Fund** has granted awards to two Bristol researchers who are co-investigators on projects:

- Prof [John Bower](#) (Chemistry) for *On the Search for Potential Trypanocidal Compounds: Synthesis and Evaluation of new Drug Candidates*; lead WUN Partner Universidade Federal de Minas Gerais.
- Dr [Yiming Wang](#) (Policy Studies) for *Low-Carbon Transport*,

Individual Wellbeing & Planetary Health in the Era of Smart Cities and New Mobilities; lead WUN Partner The Chinese University of Hong Kong.

Dr [Jim Spencer](#) (Cellular and Molecular Medicine) and Dr [Charlie Colenso](#) (Biochemistry) were awarded a **Biotechnology and Biological Sciences Research Council** FTMA Innovation Fellowship for *In silico Ligand Discovery for Glycan-based Bacterial Pathogen Detection in Urinary Tract Infections*

Bristol pioneers use of VR for designing new drugs

Many drugs are small molecules, and discovering new drugs involves finding molecules that bind to biological targets like proteins. In the study, users were able to use VR to 'step inside' proteins and manipulate them, and the drugs binding to them, in atomic detail, using interactive molecular dynamics simulations in VR (iMD-VR).

Using iMD-VR, researchers 'docked' drug molecules into proteins and were able to predict accurately how the drugs bind.

Many drugs work by binding to proteins and stopping them working. To bind well, a

small molecule drug needs to fit snugly in the protein. An important part of drug discovery is finding small molecules that bind tightly to specific proteins, and understanding what makes them bind tightly, which helps to design better drugs. To design new therapies, researchers need to understand how drug molecules fit into their

biological targets. To do this, we use VR to represent them as fully three-dimensional objects. Users can then fit a drug within the 'keyhole' of a protein binding site to discover how they fit together. Tests showed that users were able to predict how a drug binds to the targets; pulling the drug into the protein, they could build structures similar to the structures of the drug complexes found from experiments.



Deeds H *et al.* (2020). [Interactive molecular dynamics in virtual reality for accurate flexible protein-ligand docking](#). *PLOS One*.

ASTUTE trial for uveitis

Two in 10,000 people are at risk of serious sight loss from a form of eye inflammation known as uveitis. A new clinical research study, led by the University of Bristol and University Hospitals Bristol and Weston NHS Foundation Trust (UHBW), will evaluate a drug combination treatment for the eye disease thanks to funding of £2.5 million by the National Institute for Health Research (NIHR). The study will be co-ordinated by the University's Bristol Trials Centre (CTEU). Three recent studies suggest fortnightly adalimumab is an effective way to treat uveitis in some

patients. However, drugs like adalimumab can have serious side effects and more evidence is required to identify which patients with uveitis benefit the most from adalimumab, both with respect to their vision and quality of life, including treatment side effects.

The ASTUTE trial aims, first, to identify patients who are most likely to benefit from adalimumab. All eligible patients who consent will be given adalimumab for a 16-week test period, if necessary, in combination with low dose of steroids. Patients who are successfully

treated with adalimumab and low-dose steroids (inactive disease at the end of 16-weeks) will enter the main study and will be randomly assigned to receive adalimumab or a placebo treatment, in combination with their other medications (including low-dose steroids). Patients will be treated and followed up for 12 to 30 months to find out whether adalimumab is better at preventing recurrence of uveitis than the placebo treatment and whether adalimumab is cost-effective compared to the placebo treatment.

[Read the full article](#)

Engagement

On 1 June 2020 [Dr Ellen Brooks-Pollock](#) (Lecturer in Infectious Disease Mathematical Modelling, Bristol Veterinary School) gave evidence to the Lords Science and Technology Committee for their inquiry into the science of COVID-19 and the role of modelling in the response. You can watch the session [here](#).

[GW4](#), in collaboration with the [Jean Golding Institute](#) and [The Alan Turing Institute](#), has launched a Data Science Network. The Network will

act as a hub for news, events and funding opportunities in data science research that are available to staff and students throughout GW4.

The [Bristol City Fellows Programme](#), funded by a £118,000 Impact Acceleration Account grant from the [Economic and Social Research Council](#), is led by the University of Bristol with Bristol City Council's [City](#)

[Office](#) and the Social Justice Project. They will work with charities and community groups to ensure marginalised voices have a say in decision-making and in turn tackle systemic inequalities across Bristol. One of the fellows, Lucie Martin-Jones, Head of Community Services at The West of England Centre for Inclusive Living, will look at improving healthcare and support for disabled people, ultimately creating new systems which are person-centred and allow disabled people more independence and control.



COVID-19 vaccine trials

Researchers at University Hospitals Bristol and Weston NHS Foundation Trust (UHBW) and the University of Bristol are set to begin trials of a vaccine pioneered in the UK which could protect against COVID-19. The study will involve healthy volunteers between 18 and 55 with up to 150 participants to be recruited in Bristol.



Work on the vaccine, developed by clinical research teams at the University of Oxford's Jenner Institute and Oxford Vaccine Group, began in January. It is called ChAdOx1 nCoV-19 and is made from a weakened version of a common cold virus (adenovirus) from chimpanzees that has been genetically changed so that it is impossible for it to grow in humans. This has been com-

bined with a gene that makes a protein from the COVID-19 virus (SARS-CoV-2) called spike glycoprotein which plays an essential role in the infection pathway of the SARS-CoV-2 virus. The vaccine aims to turn the virus' most potent weapon, its spikes, against it – raising antibodies that stick to them allowing the immune system to lock onto and destroy the virus.

[Read the full story](#)

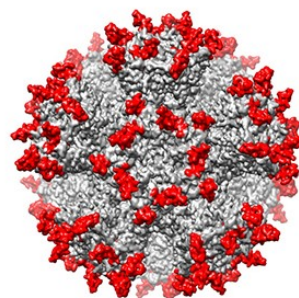
New vaccine platform used to develop COVID-19 candidates

University of Bristol and spin-out company [Imophoron](#) have been heavily involved in testing COVID-19 vaccine candidates, having produced multiple COVID-19 vaccine candidates, based on its novel vaccine platform (ADDomer®) within weeks of the virus sequence being made available. The start-up has developed a new, highly adaptable, easy-to-manufacture, rapid-response platform for vaccines to combat present and future infectious diseases. The vaccines produced are extremely stable and require no refrigeration, potentially enabling un-

restricted distribution worldwide. Importantly the high specificity of the vaccine particle promises a reduced risk of potentially dangerous side effects, seen with some novel vaccines. COVID-19 (SARS-CoV-2) infects cells using its so-called 'Spike' protein. Most COVID-19 vaccines now being fast-tracked present the complete Spike to the immune system, which reacts

by making antibodies. This approach risks inducing antibodies that bind to the wrong parts of the Spike and could make the disease even worse. In vaccines for SARS-CoV-1, this sometimes resulted in severe lung tissue damage; Imophoron's vaccines, in contrast, present only very specific parts of the Spike essential for cell entry and are potentially much less prone to this risk.

COVID-19 Spike



ADDomer-COVID19 Candidate Vaccine

COVID-19 Spike protein is shown. Parts mediating cell entry are coloured red. Imophoron's ADDomer®-based candidate vaccines present exactly these parts to the immune system, giving rise to antibodies to neutralise the virus and protect against infection

What does a blood test mean for CFS patients?

Chronic fatigue syndrome (CFS) affects 17 million people worldwide and 250,000 in the UK alone. It usually presents with flu-like symptoms and chronic pain, along with difficulty walking, exercising and sleeping. Extreme tiredness is often seen as the defining characteristic of CFS. Living with it is a difficult and unpredictable journey, with symptoms and severity unique to each patient and changeable day-to-day. This makes accessing disability facilities a daily struggle. Despite not knowing exactly what causes the disease to manifest, there has been a recent break-

through in the field – [a blood test to detect the disorder has recently been explored](#), with promising results. A research group led by Dr Ron Davis at Stanford University used a test that detected the ATP used in immune cells to withstand the stress caused by a high salt environment. Cells that are healthy should be able to use ATP to adapt to a high salt environment very efficiently. Cells from a group of healthy people and a group



of CFS patients were tested for this ability, and cells from these CFS patients adapted to the high salt environment less efficiently than the healthy controls. This suggests that there is a biomarker for CFS, meaning we are closer than ever to diagnosing CFS with a single blood test. If these results are confirmed to be accurate, the test could provide a definite and reliable diagnosis for people struggling with the disorder, and thus help with quick access to treatment and support.

[Read the full blog](#) written by Amy Preston, undergraduate student

Genomic analysis of SARS-CoV-2

Clinical vaccine trials to help fight the pandemic against COVID-19 have been helped by a team based at the School of Molecular and Cellular Medicine. They have been growing the live human SARS-CoV-2 virus in a controlled lab to investigate what the virus is doing inside cells. The team isolated parts of the virus to find out how it instructs the cell to make virus proteins, which can either be used to form virus particles or slow our immune response, and also investigated whether the

genome of the virus changes during growth in cells. They found that when the virus is grown in the laboratory in monkey cells it can make significant changes to the protein found on the surface of the virus - the "spike glycoprotein" - which promotes entry into the host cell and is an important target for the human immune system in its fight against the virus. They describe that many of the proteins the virus makes are also decorated with important modifications

(phosphorylations) which can alter how the virus protein functions and may provide clues about the kinds of drugs that would help treat it.

Davidson AD *et al.* (preprint). [Characterisation of the transcriptome and proteome of SARS-CoV-2 using direct RNA sequencing and tandem mass spectrometry reveals evidence for a cell passage induced in-frame deletion in the spike glycoprotein that removes the furin-like cleavage site.](#) *bioRxiv*.

Daily moisturiser cannot prevent childhood eczema

The [Barrier Enhancement for Eczema Prevention study \(BEEP\)](#) was led by experts from at the School of Medicine at the University of Nottingham in collaboration with the [Centre for Academic Primary Care](#) at the University of Bristol. Eczema is a very common skin problem affecting around one in five children in the UK. It usually starts in infancy, and a generally dry skin is often one of the first symptoms in babies who go on to develop the condition. It is thought that a

faulty skin barrier could be the first step in the development of eczema. Moisturisers improve skin barrier function by providing a covering to the outermost layer of skin and trapping in water. BEEP aimed to determine whether the regular use of moisturisers had any impact on preventing the development of eczema.



The team looked at 1394 newborn babies who were born to families with eczema, asthma or hayfever who were split into two groups. The study found no evidence that the daily use of moisturiser during the first year of life could prevent eczema in the study children. There was however, a small increase in the risk of skin infections. The results also showed early indications that daily use of these creams may increase the risk of food allergy.

[Read the full story](#)

Excess weight increases risk of diabetes and heart disease

Obesity in childhood is known to have a detrimental impact on various health conditions and disease risk in later life including coronary heart disease, type 2 diabetes and cancer. However, it is unclear whether being overweight as a child directly influences risk of these diseases or whether they can be reversed through lifestyle changes, particularly as those who are obese in early life tend to remain obese as adults. Researchers from Bristol Medical School sought to investigate this by using [Mendelian randomisation](#), which allows scientists to separate the genetic influence of risk factors, such as

being overweight as either a child or as an adult, on risk of disease. The technique was applied using human genetic data from 453,169 individuals from the UK Biobank study and four large scale genome-wide association studies using measures of BMI in adulthood (average age 57) and self-reported perceived body size at age 10. They found evidence that childhood obesity is associated with increased risk of coronary heart disease and type 2 diabetes due to a persistent, long-term effect of obesity over many years. This indicates that within a population, individuals who are overweight as

children are more likely to be at risk of these diseases as they tend to remain overweight as adults. However, encouragingly this suggests that lowering weight in adulthood could reduce the long-term adverse effects of childhood obesity. The authors point to some of the study limitations, such as relying on self-reported early life body size.

Richardson TG *et al.* (2020). [Use of genetic variation to separate the effects of early and later life adiposity on disease risk: mendelian randomisation study.](#) *The BMJ*.

Blocking kidney brain signals could help with treatments

A team have discovered an important cell signalling pathway in the kidney which, if stopped, could hold the key to treating chronic kidney disease as well as other deadly conditions, including heart attack and stroke. The pathway was already known to exist in the brain, where it helps to maintain the body's energy balance, but this is the first time it has been found in the kidney. The researchers identified a substance called Neuropeptide Y (Npy), present in high levels in the brain, in the filtering unit of the kidney. They

found Npy in podocytes, which were sending harmful signals and damaging the filtering unit (glomerulus). This caused large amounts of protein to leak into urine, a condition called proteinuria. Often undiagnosed early on, if left untreated the disorder can lead to kidney failure requiring dialysis or a kidney transplant and it is

related to an increased risk of suffering a heart attack or stroke. The study revealed Npy was produced by the podocyte in the kidney as well as the brain. Furthermore, Npy production was massively reduced in diabetic podocyte cells studied in laboratory dishes and Npy levels were also significantly lower in the glomeruli of patients with diabetes.



Lay AC *et al.* (2020). [A role for NPY-NPY2R signaling in albuminuric kidney disease. PNAS.](#)

Healthcare costs and quality of life

Much available research cannot meaningfully identify the long-term consequences of health conditions for healthcare cost and quality of life. This is because observational studies are prone to bias due particularly to reverse causality and omitted variable. In a Medical Research Council - funded fellowship, Dr Padraig Dixon (Bristol Medical School: Population Health Sciences) has been using quasi-random variation in genetic liability to disease and other phenotypes to

avoid this kind of bias. Using information of genetic variation as instrumental variables, we have demonstrated that conventional methods may substantially underestimate the cost of obesity on the health system. Ongoing work demonstrates a similar relationship with rates of hospital admission. Other work in-progress demonstrates that this kind of evidence can be

used to inform robust causal inference for long-term policy decisions and interventions in relation to both costs and quality of life, particularly in cases where randomized controlled trials may not be feasible.



Dixon P *et al.* (2020). [Mendelian Randomization analysis of the causal effect of adiposity on hospital costs. Journal of Health Economics. 70, 102300.](#)

Reductions in antibiotic resistant infections

A study has found reductions in overall and individual antibiotic dispensing between 2013 and 2016 after evaluating, for the first time, national primary care prescribing policy on community antibiotic resistant infection. They investigated the relationship between primary care antibiotic dispensing and resistance in community-acquired urinary *Escherichia coli* infections from Bristol and the surrounding areas between 2013-16. This period was chosen because the NHS introduced an

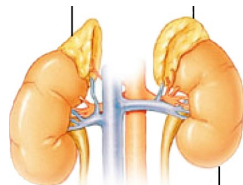
incentive scheme to reduce antibiotic dispensing from 2014 onwards. The work involved multilevel modelling analysis of data from 163 primary care practices (serving 1.5 million patients) and 152,704 urinary *E. coli*. In keeping with national trends, the team found reductions in overall and individual antibiotic dispensing between 2013 and 2016. Antibiotic dispensing reductions were associated with reduced resistance to ciprofloxacin, trimethoprim and amoxicillin. These reduc-

tions happened within three months and persisted for a further three months for trimethoprim and amoxicillin. However, the study found despite reductions in the dispensing of two other antibiotics, cefalexin and co-amoxiclav, resistance to these antibiotics increased over time.

Hammond A *et al.* (2020). [Antimicrobial resistance associations with national primary care antibiotic stewardship policy: primary care-based, multi-level analytic study](#). *PLOS ONE*.

Corticosteroids and adrenal gland inflammation

New research has found evidence that prolonged treatment of synthetic corticosteroid drugs increases adrenal gland inflammation in response to bacterial infection, an effect that in the long-term can damage adrenal function. Synthetic corticosteroid drugs are widely prescribed to treat many inflammatory and autoimmune diseases but taking a high dose over a long period of time can cause adverse side effects. Patients undergoing prolonged corticosteroid treatment can also develop adrenal insufficiency, which in rare occasions can lead to adrenal gland failure.



The team tested the hypothesis that synthetic corticosteroids cause long-term changes in the adrenal gland steroidogenic pathways that are responsible for adrenal suppression.

The research found that the rhythms of glucocorticoid secretions are disrupted following prolonged treatment with synthetic corticosteroid drugs, and that the adrenal steroidogenic pathway is directly affected. Importantly, these changes persist long after discontinuation of the treatment. The study also showed a pro-inflammatory effect of synthetic glucocorti-

coids treatment in the adrenal gland. This is an important finding with high clinical relevance as intra-adrenal activation of the immune system can affect adrenal functionality by interfering with the steroidogenic pathway, damaging adrenal endothelial microvascular cells, and by inducing apoptosis and reducing cell viability.

Spiga F *et al.* (2020). [Prolonged treatment with the synthetic glucocorticoid methylprednisolone affects adrenal steroidogenic function and response to inflammatory stress in the rat](#). *Brain, Behavior, and Immunity*.

Better Care South West Partnership

A new partnership led by the University of Bristol that will join up data and improve patient care in the South West has been announced by Health Data Research UK (HDR UK). The HDR UK Better Care South West Partnership is being awarded £1.2 million over three years to drive forward data-led research projects and join up the region's considerable health data expertise. The partnership is a collaboration of health and social care providers with the Universities of Bristol, Exeter and Bath. Key health-care partners in-



clude Bristol, North Somerset and South Gloucestershire Clinical Commissioning Group, South Central and West Commissioning Support Unit, North Bristol NHS Trust and University Hospitals Bristol and Weston NHS Foundation Trust. It aims to address real-world health problems using the Bristol, North Somerset and South Gloucestershire (BNSSG) system-wide health and social care dataset, which

is one of the largest linked health data sets in the UK. Enabling this joined-up approach is especially vital

during the COVID-19 pandemic. This new initiative represents a step forward in using advanced analytics to benefit patients and partner organisations. The partnership will lead on five data-driven projects, including personalised scores to reduce rates of unplanned admissions to intensive care, and optimised choice of antibiotics based on patients' individual history. The newly-established HDR UK Better Care Northern and South-West Partnerships aim to boost the depth and breadth of expertise in health data research and innovation and complement existing network of HDR UK sites and hubs.

Academic Health Science Centre status

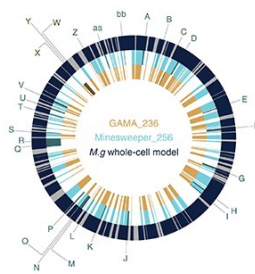
Following a highly competitive process, Bristol Health Partners (BHP) is now one of only eight designated Academic Health Science Centres (AHSCs) in England. The AHSC will drive service change, leading to world-class health, clinical and economic outcomes for the regional population across Bristol, North Somerset and South Gloucestershire (BNSSG). The AHSC designation by the National Institute for Health Research (NIHR), NHS England and NHS Improvement builds upon

BHP's current successes in research, innovation, education and training and recognises the outstanding local collaborations between academia, public health, the NHS, social care and the voluntary and community sector that the Partnership has created across BNSSG. The importance of collaboration across research, health and social care has never been greater than we have seen with COVID-19. From the rapid creation of the NHS Nightingale Hospital Bristol to

supporting national testing and vaccine trials, the strength of these partnerships is reflected in how local expertise and resources are coming together in response to COVID-19. Over the next five years, Bristol Health Partners AHSC will be focusing on six key areas including public health and prevention; mental health and neuroscience; cardiovascular science; surgical innovation; perinatal, reproductive and children's health and delivering integrated, optimal and equitable care across BNSSG.

Technology takes a step forwards in genetic research

New research brings combined computational and laboratory genome engineering a step closer following the design of smaller and smaller genomes, to advance genetic manipulation, using supercomputers. The size of genomes can be vast and vary across organisms. Genetic variety is still being explored and gene functions understood within biology. By minimising genomes, researchers can un-



derstand better what each gene does within a cell. Researchers at Bristol have found a way to design a smaller genome using computational methods. Algorithms run on Bristol's supercomputers allowed the team to design a genome which is smaller, simpler, and can be easily manipulated. The research team tested designs within a computerised cell model to see if the cells are able to grow and divide. The researchers

plan to apply designs like these within real cells in the future. This will allow them to discover how advanced this technology really is. Making smaller genomes can contribute to understanding their properties.

Rees-Garbutt J *et al.* (2020). [Designing minimal genomes using whole-cell models](#). *Nature Communications*.

Comparing the initial genome (outer ring) to two smaller versions produced using supercomputers

New Global Health Challenge Leader

An academic from the University of Bristol has been appointed a Global Health Challenge Leader by UK Research and Innovation (UKRI) and will join the flagship international development research scheme, the Global Challenges Research Fund (GCRF).

Helen Lambert, Professor of Medical Anthropology (Bristol Medical School: Population Health Sciences) has taken up the role GCRF Challenge Leader for Global Health. Prof Lambert has a background of research into antimicrobial resistance, HIV prevention with vulnerable communities,

and the social and cultural dimensions of health systems.

Over the last few years I have become increasingly convinced that to deal with global health challenges, we really need to work across international boundaries and disciplines. The current Coronavirus outbreak highlights the need and urgency to boost



international, multidisciplinary partnerships as combining on-the-ground expertise with specialist skills and knowledge are essential for understanding and tackling contemporary health challenges.

Leaders will forge diverse and exciting equitable partnerships between UK researchers and academics, policy makers and community groups across developing countries to ensure that GCRF funded research responds to the needs of poorer countries and moves the world closer towards achieving the UN Sustainable Development Goals.

Calculating early warning scores for patients

Recording National Early Warning Scores (NEWS) when a patient is urgently referred to hospital can improve the process of care for the sickest patients and reduce the time taken to get to hospital. NEWS help clinicians recognise when patients are at risk of deterioration, for example as a result of infection such as sepsis. The research team, based at the [NIHR Applied Research Collaboration \(ARC\) West](#) in collaboration with the [West of England Academic Health Science Network](#) (AHSN), studied the impact of NEWS scores collected for more than

13,000 urgent GP referrals to hospital. They found that higher scores are associated with patients being taken to hospital by ambulance more quickly. Average transfer time was 94 minutes for patients with the highest scores, compared with 132 minutes for those with the lowest. Patients with high scores were also reviewed more quickly after arriving at hospital. Patients with higher scores were sicker, with longer hospital stays and more of them being admitted to intensive care. Patients with the highest scores were nearly five times more likely to have

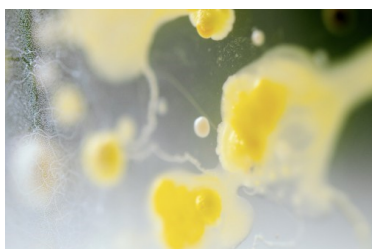
sepsis than those with the lowest scores and eight times more likely to die within two days of hospital admission. Early warning scores (EWS) are designed to help healthcare staff identify patients whose condition is deteriorating, to allow them to get the treatment they need quickly. Higher scores indicate poorer health.

Scott LJ *et al.* (2020). [Association between National Early Warning Scores in primary care and clinical outcomes: an observational study in UK primary and secondary care.](#) *British Journal for General Practice.*

Certain human genes relate to gut bacteria

The role genetics and gut bacteria play in human health has long been a fruitful source of scientific enquiry, but new research marks a significant step forward in unravelling this complex relationship. Its findings could transform our understanding and treatment of all manner of common diseases, including obesity, irritable bowel syndrome, and Alzheimer's disease.

The international [study](#), led by the University of



Bristol, found specific changes in DNA affected both the existence and amount of particular bacteria in the gut, leading them to question whether the microbiome may directly influence human health and disease. The study identified 13 DNA changes related to changes in the presence or quantity of gut bacteria.

... we identified new and robust signals across the three study populations,

which makes the correlation of genetic variation and gut bacteria much more striking and compelling. Now comes the challenge of confirming observations with other studies and dissecting how these DNA changes might impact bacterial composition.

David Hughes, lead author

Hughes DA *et al.* (2020). [Genome-wide associations of human gut microbiome variation and implications for causal inference analyses.](#) *Nature Microbiology.*

Link between Covid-19 and cardiovascular diseases

Improved care for people with heart and circulatory disease suffering from COVID-19 could soon be available after the British Heart Foundation (BHF) and National Institute for Health Research (NIHR) announced support for six flagship research programmes. Researchers from across the UK including the University of Bristol will combine data from hospitals, information about our health and lifestyle, genetic studies, and cutting-edge imaging and artificial intelligence

techniques to better understand how the virus affects the heart and circulatory system.

A team led by researchers from the University of Bristol and University College London (UCL) is linking data from



large cohort studies to uncover which cardiovascular diseases, as well as genetic, demographic or lifestyle factors are associated with increased risk of COVID-19 infection and its severity. It will also look at mechanisms linking COVID-19 to adverse cardiovascular health. This could pave the way for improved treatments or better ways of identifying those at risk.

[Read the full press release](#)

COVID-19: which patients are greatest risk of harm?

A new study by researchers at the [Centre for Academic Primary Care](#) will link hospital and GP practice data to identify patients who are most at risk of harm from coronavirus. The study will link routine health data recorded in GP surgeries to the records of the most severely ill patients admitted to hospital intensive care units.

The linked data will then be analysed to find out which existing health problems, drug treatments, or other factors, such as smoking or pregnancy, are most strongly associated with people

being admitted to intensive care or dying due to the virus. Knowing more about who is most at risk of harm will enable health care professionals to advise patients on how to minimise their exposure to the virus, make decisions about when to treat people – earlier for those most at risk – and prioritise treatments for

those who are most likely to benefit. Data will be drawn from the [Clinical Practice Research Datalink \(CPRD\)](#) and the [Intensive Care National Audit and Research Centre \(ICNARC\)](#).

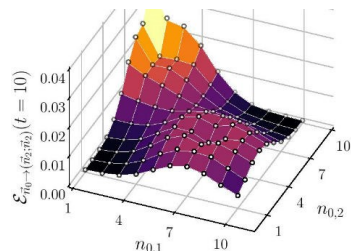
Older people and those with pre-existing health problems who develop COVID-19 are at higher risk of serious disease or death. Better information on who is at risk will help the NHS and public health authorities guide patient care and save lives.

Rupert Payne, Consultant Senior Lecturer in Primary Care and lead researcher



Diffusion equation could predict infection transmission

Dr [Luca Giuggioli](#) (Engineering Mathematics) has solved a 100-year-old problem: the discrete diffusion equation in finite space. The solution could be used to accurately predict encounter and transmission probability between individuals in a closed environment, without the need for time-consuming computer simulations. It describes how to analytically calculate the probability of occupation (in discrete time and discrete space) of a diffusing particle or entity in a confined space - something that until now was only possible



computationally. The diffusion equation models random movement and is one of the fundamental equations of Physics. The analytic solution of the diffusion equation in finite domains, when time and space is continuous, has been known for a long time. However, to compare model predictions with empirical observations, one needs to study the diffusion equation in finite space. It allows us to tackle problems that were

almost impossible in the past because of the prohibitive computational costs.

The finding has far-reaching implications across a range of disciplines and possible applications include predicting molecules diffusing inside cells, bacteria roaming in a petri dish, animals foraging within their home ranges, or robots searching in a disaster area. It could even be used to predict how a pathogen is transmitted in a crowd between individuals.

Giuggioli L (2020). [Exact spatio-temporal dynamics of confined lattice random walks in arbitrary dimensions: A century after Smoluchowski and Polya](#). *Physical Review X*.

Signs of diabetes visible at age 8

Early signs of being more susceptible to type 2 diabetes as an adult can be seen in children as young as 8 years old. The research looked at the effects of a genetic risk score for developing type 2 diabetes as an adult on metabolism measured from blood samples taken from the participants in the study when they were aged 8, 16, 18, and 25 years. The study tracked over 4,000 participants in the [Children of the 90s](#) health study. The team combined genetic information using metabolomics,

which involves measuring many small molecules in a blood sample, to try and identify patterns that are specific to early stages of type 2 diabetes development. The study was conducted among young people who were generally free of type 2 diabetes and other chronic diseases to see how early in life the effects of being more susceptible to adult diabetes become visible. In particular, certain types of HDL cholesterol were reduced at age 8 before other types of cholesterol including LDL were

raised; inflammation and amino acids were also elevated by 16 and 18 years old. These differences widened over time. Knowing what these early signs look like widens our window of opportunity to intervene much earlier and stop diabetes before it becomes harmful.

Bell JA *et al.* (2020). [Early metabolic features of genetic liability to type 2 diabetes: cohort study with repeated metabolomics across early life](#). *Diabetes Care*.

The pandemic: not the great equaliser

A blog written by PhD student [Angelique Retief](#) (Policy Studies) for PolicyBristol explains that the large number of deaths of BAME people due to the coronavirus has quickly disproved the claim that the pandemic is a 'great equaliser' and has instead brought to the fore the many social ills in society. As most determinants of health are socially created, it logically follows that socioeconomic deprivation disproportionately affects BAME people, and will act as a precursor to the impact of the virus on those communities. With living space, gardens, and

local areas (or the lack thereof) dictating our well-being, the gap between the rich and the poor has never been more obvious. The coronavirus will therefore not be felt equally and – compounded by the already profound challenges to well-being in non-OECD countries – will only serve to further entrench existing racial and economic disparities.

The product of centuries of colonialism, apartheid and racial exclusion, South Africa's welfare system has struggled to provide the freedoms promised in 1994. It has been 26 years since

South Africa's first democratic election, and it is still one of the world's most unequal societies. The country has reported the most coronavirus cases in Sub-Saharan Africa and many people are too poor to weather the associated economic fallout and lack the funds to stock up on adequate food. While significant policy achievements and large gains have been made in many socioeconomic areas such as education, welfare services are notoriously underfunded.

[Read the full blog here](#)

COVID-19 rapid evidence reviews

Researchers from across the University of Bristol are contributing to COVID-19 rapid evidence reviews, co-ordinated by the National Institute for Health Research Applied Research Collaboration West (NIHR ARC West). The rapid research aims to answer key questions from the local health and care system, such as how to manage patients with dementia who 'walk with purpose and

intent', how to monitor COVID-19 symptoms remotely and the potential impact of COVID-19 on mental health. Researchers are reviewing the available evidence and offering topic and methodological expertise to help NHS clinical

commissioning groups (CCGs) and local authority public health departments plan how to respond to the COVID-19 pandemic. A pool of over 70 researchers from across the University of Bristol was quickly assembled to respond to requests for help. The researchers are from more than 12 research centres and [the local NIHR infrastructure](#).

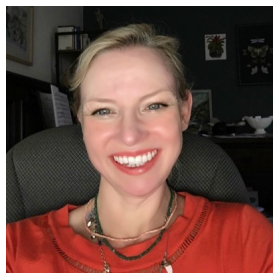
[Read the full press release](#)



Microbiomes in health and disease

Dr [Clare Woodall](#) was recently awarded a Daphne Jackson Fellowship hosted by the Elizabeth Blackwell Institute. The Fellowships support individuals who want to return to their career in research following a break of two years or more taken for family, caring or health reasons.

She will be joining co-supervisors, Principle Inves-



tigator, Professor Alastair Hay and Dr Ashley Hammond (Bristol Medical School: Population Health Sciences) on the METRIC study (Influence of the human Microbiome in the acquisition of acute Respiratory tract Infections in the Community: a prospective cohort feasibility study) to pursue the (informally titled) project, *A sore throat and an upset tummy. Do our own bugs hold all the answers?* She will inves-

tigate how both the gut and respiratory microbiomes differ in healthy adults compared to those that contract seasonal respiratory infection-like symptoms, like a cold. Respiratory disease costs the NHS about £165 billion per year and may result in a course of antibiotics, which will be ineffectual if the infection is caused by a virus, and will contribute to the increasing problem of antimicrobial resistance.

[Read more](#)

Video consultations for chronic kidney disease

Children with chronic kidney disease require specialist renal paediatric dietetic care, regardless of disease severity or geographical location; however, under-resourcing makes this challenging. Video-consultation may offer a solution, but research exploring its acceptability is limited. The present study explored parent/carer and child perspectives of videoconsultation as an alternative or supplement to existing regional dietetic care.

Children and families using a regional paediatric nephrology service were recruited through purposeful sampling techniques. Renal paediatric

dietitians used existing hospital software to host videoconsultations with families. Perspectives were subsequently explored in telephone interviews with the children, their parents and separately with the renal dietitians. Data were transcribed verbatim and an inductive framework analysis conducted. Twelve families took part in the study, and six themes emerged: Logistics, Understanding Information, Family Engagement, Establishing Trust, Willingness to Change, and Preferences. Satisfaction with the videoconsultations was high, with no data security fears and only minor privacy concerns. Parents reported

that screen-sharing software enhanced their understanding, generating greater discussion and engagement compared to clinic and telephone contacts. Parents praised efficiencies and improved access to specialist advice, requesting that videoconsultations supplement care. Children preferred videoconsultations outright.

Trace SL *et al.* (2020). [Using videoconsultations to deliver dietary advice to children with chronic kidney disease: a qualitative study of parent and child perspectives](#). *Journal of Human Nutrition and Dietetics*.

COVID-19 detection system

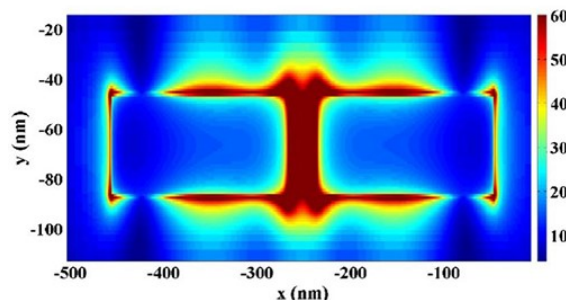
The World Health Organisation has regularly said that rapid testing of patients with COVID-19 is critical to controlling the pandemic, especially with lockdown measures easing across the globe. A new research project will explore the development of a low-cost, rapid, COVID-19 diagnosis system using nanophotonic fluorescence enhancement.

The pilot study will use simulant fluorescently labelled RNA to develop an assay for the detection of coronavirus.

Martin Cryan (Professor of Applied Electromag-

netics and Photonics in the Department of Electrical and Electronic Engineering), principal investigator for the project, has been working in this field for many years and has shown how very small antennas, known as nanoantennas, can enhance the amount of light given out by fluorophores, which can dramatically improve the sensitivity of biosensors. The pro-

ject involves collaboration from the University of Cardiff who are developing DNA and RNA extraction techniques for pathogen detection. Future projects will team up with Cardiff and commercial partners to develop a complete microfluidics-based approach that could lead to a handheld device for use in GP surgeries and hospital wards.



*The **Elizabeth Blackwell Institute**-funded project 'Feasibility study for microfluidic fluorescence-based diagnosis system for COVID-19' will run until 31 January 2021.*

Markers that could predict COVID-19 outcome

There is an urgent need to identify why some patients with COVID-19 do very well whereas others need to be admitted to intensive care. An new observational study aimed at identifying markers that predict how COVID-19 affects patients is being led by clinicians and academics at North Bristol NHS Trust and the University of Bristol. The DISCOVER (**D**iagnostic and **S**everity markers of **C**COVID-19 to **E**nable **R**apid triage) study is focused on blood-based

biomarkers and their ability to predict a patient's disease course alongside demographic factors such as age, sex, frailty and other medical conditions. When patients with suspected or confirmed COVID-19 are admitted to hospital, they will be asked for consent for blood sampling and access to their med-

ical history. They will be followed up for 28 days, remotely, and clinical progress recorded. One biomarker tested will be suPAR (soluble urokinase plasminogen activating receptor) alongside other more conventional tests, such as troponin, NT-proBNP and ferritin. They will also test cytokines to help predict which patients will require hospital admission; this early triage of patients is crucial to manage the pressure on hospital beds safely.



[Watch the video](#)

ELIZABETH BLACKWELL FUNDING

Nurturing
Research.
Improving
Health.



EBI Rapid Response call COVID-19

A funding call for research looking into COVID-19/Novel Coronavirus.

Final closing date: 30 June 2020

Rosetrees Trust Mental Health Research funding call 2020

Funding available for challenge-led research projects addressing mental health.

Closing date: 1 July 2020

EBI Identifying Candidates for Wellcome Trust Investigator Awards

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

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

Closing date: none

EBI Seed Fund: Public Engagement with Health Research

Seed funding is available for health researchers who would like to deliver public engagement events and activities. Applications accepted on a **rolling** basis.

Closing date: none

EBI Workshop Support

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

Closing date: none

Returning Carers Scheme

To support academic staff across all faculties in re-establishing their independent research careers on return from extended leave (16 weeks or more) for reasons connected to caring (e.g. maternity leave, adoption leave, additional paternity leave, leave to care for a dependant).

Closing date: 30 April and 31 October each year

FUNDING OPPORTUNITIES

Would you like to receive timely, tailored funding opps information?

Do you want to know what funding opportunities come up in your research area?

Get tailored funding alerts?

Research Professional provides access to an extensive database of funding opportunities, and can send out tailored alerts based on keywords that you input, ensuring that the funding alerts you receive are the ones you want to hear about. 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 home or away, not just while on the University network.

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**, an easy process that will take just a few minutes to set up through the use of keywords
- **Save searches and bookmarks** - store items of interest for future reference, download and email to colleagues
- **Sign up for higher education news bulletins** – want to hear about what is going on in the broader HE environment? Latest news on the REF, setting up of UKRI etc? Sign up for the 8am play-book or the Research Fortnight news publications and stay up to date with the latest news.

For further information on Research Professional, go to the [RED website](#).

National Institute of Allergy and Infectious Diseases, US

[Partnerships for the development of universal influenza vaccines](#)

Closing date: 2 July 2020

Award amount: US\$1,175,000

This supports the development of promising universal influenza vaccine candidates that protect against both influenza A (IVA) and B (IVB) viruses. The aim is to optimise preventive measures against seasonal influenza by providing broad, durable protection against both IVA and IVB strains.

National Institute of Allergy and Infectious Diseases, US

[Engineering immunity to HIV-1 through next-generation vaccines](#)

Closing date: 28 July 2020

Award amount: unspecified

This supports multi-disciplinary teams in the application of novel and practical bioengineering solutions to solve challenging and persistent problems in the production of a safe and effective preven-

tive HIV-1 vaccine. The aim is to pair bioengineers and immunologists to leverage emerging innovative knowledge in physical and computational sciences.

National Institute for Health Research

[Commissioned call 19/136: Evaluating interventions for the diagnosis and treatment of autoimmune diseases](#)

Closing date: 11 August 2020

Award amount: unspecified

These support studies evaluating interventions that have the potential to make a step-change in the promotion of health, treatment of disease and improvement of rehabilitation or long-term care.

Healthcare Infection Society

[Major Research Grant](#)

Closing date: 1 September 2020

Award amount: £99,999

This supports work on the subject of healthcare-associated infections and infection prevention and control. The grant is suitable for a PhD studentship, MD or other research worker and related consumables and equipment, with a preference towards translational research rather than pure science topics.

European Innovation Council

[Horizon prize for early warning for epidemics](#)

Closing date: 1 September 2020

Award amount: unspecified

This supports projects that develop a scalable, reliable, cost-effective prototype early warning system to forecast and monitor vector borne diseases in order to contribute to the prevention of outbreaks, mitigating their impact at local, regional and global scales and providing support to existing elimination efforts. The prototype early warning system should encompass innovative technological solutions integrating big data derived from the Earth observation domain. The solution must be demonstrated at local level, taking into account any relevant societal factors in the chosen geographical area.

Medical Research Council

[Research grants—infections and immunity](#)

Closing date: 16 September 2020

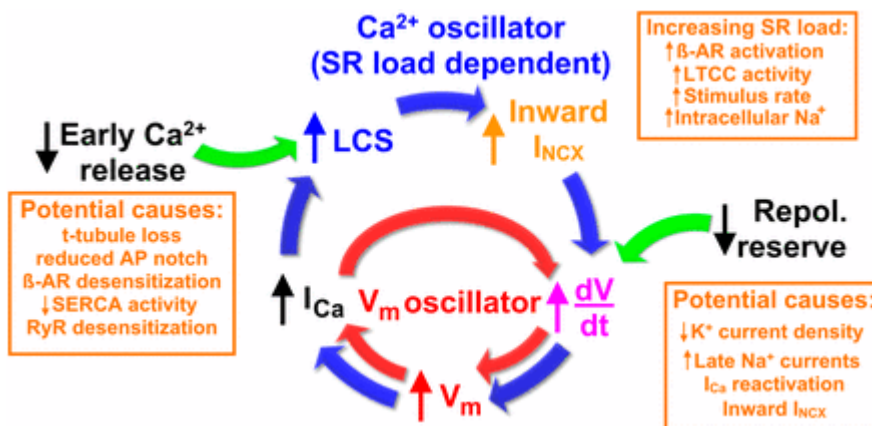
Award amount: £1m

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

THIS ISSUE'S FEATURED ARTICLE

Arrhythmogenic late Ca^{2+} sparks in failing heart cells and their control by action potential configuration

ED Fowler, N Wang, M Hezzell, G Chanoit, JC Hancox & MB Cannell. *Proceedings of the National Academy of Sciences of the United States of America* (PNAS). 117(5), pp2687-2692.



Flow diagram for two interacting positive-feedback mechanisms that can drive V_m and Ca^{2+} oscillations during EADs. The red inner cycle represents the well-established V_m oscillator, wherein an increase in dV_m/dt (caused by a relative increase in depolarizing currents compared to repolarizing currents, e.g., text in orange box at Lower Right) leads to voltage-dependent reactivation of I_{Ca} , which in turn causes

further depolarization. The blue outer cycle represents the stochastic LCS-mediated Ca^{2+} oscillator mechanism for EAD initiation. Reduced early Ca^{2+} release and/or increased SR load increases LCS production, and the resulting increase in inward I_{NCX} tends to depolarize the membrane which then feeds onto I_{Ca} to trigger additional LCS. Green arrows indicate possible factors contributing to EAD initiation. β -AR, beta-adrenoreceptor.

Sudden death in heart failure patients is a major clinical problem worldwide, but it is unclear how arrhythmogenic early afterdepolarizations (EADs) are triggered in failing heart cells. To examine EAD initiation, high-sensitivity intracellular Ca^{2+} measurements were combined with action potential voltage clamp techniques in a physiologically relevant heart failure model. In failing cells, the loss of Ca^{2+} release synchrony at the start of the action potential leads to an increase in number of microscopic intracellular Ca^{2+} release events ("late" Ca^{2+} sparks) during phase 2–3 of the action potential. These late Ca^{2+} sparks prolong the Ca^{2+} transient that activates contraction and can trigger propagating microscopic Ca^{2+} ripples, larger macroscopic Ca^{2+} waves, and EADs. Modification of the action potential to include steps to different potentials revealed the amount of current generated by these late Ca^{2+} sparks and their (subsequent) spatiotemporal summation into Ca^{2+} ripples/waves. Comparison of this current to the net current that causes action potential repolarization shows that late Ca^{2+} sparks provide a mechanism for EAD initiation. Computer simulations confirmed that this forms the basis of a strong oscillatory positive feedback system that can act in parallel with other purely voltage-dependent ionic mechanisms for EAD initiation. In failing heart cells, restoration of the action potential to a nonfailing phase 1 configuration improved the synchrony of excitation–contraction coupling, increased Ca^{2+} transient amplitude, and suppressed late Ca^{2+} sparks. Therapeutic control of late Ca^{2+} spark activity may provide an additional approach for treating heart failure and reduce the risk for sudden cardiac death.

CONTACTS

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

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



Co-Chair (interim): [Katy Turner](#)
Senior Lecturer in Veterinary
Infectious Diseases



- [Borko Amulic](#) - Lecturer in Immunology
- [Matthew Avison](#) - Co-Director, Bristol AMR
- [Andrew Davidson](#) - Senior Lecturer in Virology
- [Stephanie Diezmann](#) - Senior Lecturer in Fungal Pathogens
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- [Hannah Fraser](#) - Research Fellow in Infectious Disease Mathematical Modelling
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