I&I NETWORK NEWSLETTER



for Health Research

An international research team will lead elimination efforts of Hepatitis C in Ethiopia - one of the worst affected African countries of the disease - thanks to funding of £2.2 million by the National Institute for Health Research (NIHR).

The DESTINE project will bring together the Universities of Bristol and Dundee and NHS Tayside with several medical schools and other key institutions in Ethiopia. The team will investigate the extent of Hepatitis C (HCV) in-

2022 - ISSUE 1

Eliminating Hepatitis C in Ethiopia

fection in the country using epidemiological and modelling techniques. They will then design care based around treat-



ment pathways created in the UK but moulded to suit the Ethiopian context.

The World Health Organisation has set a target for the world

to eliminate HCV by 2030 and while many of the more developed countries have put plans in place to reach this target, this has been more difficult in low and middle income countries. For example, in Ethiopia the number of people living with HCV infection is not known, although estimates suggest it may be around 3 million. HCV is a blood borne virus which affects the liver and can lead to cirrhosis, liver failure or liver cancer.

Read the full article

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EVENTS

mRNA vaccines - from treating cancer to preventing COVID

7 April 2022, 13.00 - 14.00, Prof Özlem Türeci (Co-founder and Chief Medical Officer, BioNTech), online

Importance of intellectual property in the pathway to patient benefit

12 April 2022, 13.00 - 14.00, Cameron Fenwick (BRC Translational Manager, University of Bristol), online

Doing it! Participatory Visual Methodologies and Youth Sexuality Research 13 April 2022, 13.30 - 14.30, Prof Sarah Flicker (York University, Canada), online

A therapeutic vaccine to cure HIV infection

20 April 2022, 13.00 - 14.00, Dr Jamie Mann (Bristol Veterinary School), online

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

21 June 2022, 10:00 - 15.05, Chemistry Building

Attendance is FREE and includes a buffet lunch More information and to register

Exploring cellular heterogeneity in human skin

21 April 2022, 13.00 - 14.00, Prof Fiona Watt, FRS (Director of the European Molecular Biology Organization, EMBL Heidelberg), online

The MRC's vision for the Adolescent Health Study (AHS)

21 April 2022, 14.00 - 15.00, Prof Nick Wareham (MRC Epidemiology Unit and Chair of the MRC Population Health Sciences Group), online

Building Equitable Global Partnerships panel discussion 26 April 2022, 10.00 - 11.30, online

Cellular and Molecular Medicine seminar series: Professor Arne Akbar, UCL 26 April 2022, 13.00 - 14.00, Prof Arne Akbar (University College London), C42 Biomedical Sciences Building

Sexual Health Improvement Programme (SHIP) network meeting 26 April 2022, 14.00 - 15.30, online

Post EBMT Update Day

27 April 2022, 8.30 - 16.30, online

VIEW THE FULL LIST OF I&I EVENTS ON OUR WEBSITE

NEWS

Shield for safer dental surgery

Dental patients and practitioners could be better protected from COVID-19 and other airborne viruses and bacteria thanks to the development of a new environment-friendly shield by a multidisciplinary team from the University of Bristol and University Hospitals Bristol and Weston NHS Foundation Trust (UHBW). The shield could also increase the number of patients seen by dentists and help reduce procedure wait times.

(Novel Patient Shield), is designed to protect patients and practitioners from diseases spread through aerosol gener-



ating procedures (AGPs) during dental procedures.

In England 19 million NHS dental appointments and eight million courses of dental treatments were missed between March 2020 and April 2021. Suspension of routine dentistry led to the increased use of antibiotics - by 25% in England - and dental extraction for otherwise treatable dental diseases.

The recommended 15 to 60 minutes fallow period after any AGP has led to most UK dental practices operating at less than half their prepandemic capacity and almost half are unable to maintain their financial sustainability for the next year. **Read more**

The device, called NoPaS

Jean Golding Institute seedcorn projects announced

The Jean Golding Institute's seed corn scheme for 2022 has supported a number of projects. Among the successful awardees were:

Transferring early disease detection classifiers for wearables on companion animals

Investigators Emily Blackwell, Melanie Hezzell, Andrew Dowsey, Tilo Burghardt, Ranjeet Bhamber and Lucy Vass, will lead a collaboration between Bristol Veterinary School and the Department of Computer Science which will use a newly developed machine learning pipeline for



predicting ill health of cats and dogs using accelerometer data.

Medical Experts as Social Media Influencers of Networks of Practice in the Fight

Against COVID-19

Roberta Bernardi, Edwin Simpson and Oliver Davis will lead a collaboration between the School of Management, Department of Computer Science and Bristol Medical School: Population Health Sciences. This will investigate the influence of medical experts on public debates about COVID-19 on social media and how this may affect public trust in public health.

See the full list of supported projects

Reverse genetics to characterise SARS-CoV-2

A case study from Dr Maia Kavanagh Williamson (pictured), a postdoctoral research associate in the School of Cellular and Molecular Medicine:

In the 12 months following March 2020 the labs of Profs Andrew Davidson and David Matthews, who

recognised the pandemic potential of coronaviruses many years before and had already established facilities for MERS-CoV research at Biosafety Level 3 at the Uni-



versity of Bristol, worked in a large collaboration as part of the COVID-19 Emergency Research Group (UNCOVER). This included establishing

> serological assays to assess immune responses in patients' sera and the establishment of a high through-put system for live SARS-CoV-2

analysis. Thanks to funding from the US Food and Drug Administration and UK Research and Innovation (UKRI) they also developed a SARS-CoV-2 reverse genetics

platform and use it to produce viruses expressing fluorescent reporter genes. Now, as part of the UKRI-funded genotype-to-phenotype (G2P) consortium, they use the reverse genetics platform to generate synthetic copies of the virus carrying specific mutations; these are used to assess the effect of genetic variation identified in the 'variants of concern' on viral characteristics such as the viral transcript profile, growth kinetics and the host cell response.

Read the full article

The Medical Research Council

awarded Prof Abigail Fraser (Bristol Medical School) £157,101 for *B3613: Deep phenotyping of cardiovascular systems physiology in adults born to hypertensive pregnancies*, starting Feb '22 for 5 years.

Dr Josephine Walker (Bristol Medical School) received £89,924 from the Foundation for Innovative New Diagnostics for Cost-effectiveness of implementation of HCV self testing, starting Dec '21 for 25 months.

Prof Jan Frayne (Biochemistry) was awarded £92,970 from

Apollo Health Ventures to

pursue Evaluating effect of FOXO3 activators on HbF levels and ineffective erythropoiesis in β -thalassemia erythroid cells, which started in Aug '21 and will complete in Jan '23.

Dr Laura Rivino has been awarded a Springboard Award from the Academy of Medical Sciences (£99,985 value) to study Correlates of protective immunity and immunopathology for dengue in obesity and normal weight.

PhD student Robert Alexander won **The Aerosol Society Doctoral Student Award 2021** for his work *Determining the loss*

Awards : Part 1

of infectivity of coronavirus in respiratory droplets. This is a collaboration between the School of Cellular and Molecular Medicine (CMM) the Bristol Aerosol Research Group in the School of Chemistry. Robert is affiliated with the Engineering and Physical Sciences Research Council (EPSRC) Centre for Doctoral Training in Aerosol Science.

Dr Jon Tyrell's (CMM) Superbugs project won the **poster award in the 'Education & Engagement' Category** at the British Society of Immunology conference, Edinburgh, 28 Nov - 1 Dec '21.

I&I Early Career Researchers' symposium 2022

The University of Bristol's Infection and Immunity Network hosted its 7th annual Early Career Researchers' symposium in the Life Sciences Building on 16 February 2022.

Over 85 people registered to take part in this live afternoon event, which allows Early Career Researchers (ECRs) the

opportunity to go through an abstract submission process, gets them in front of a captive audience to hone their presentation and communication skills and, most importantly, lets them share their experiences and research with fellow staff and students at the University.

The programme consisted of 8 oral and 15 poster presentations (following an abstract submission process) given by ECRs from three faculties and six schools across the University, as well as talks by two invited keynote speakers:

- Dr Alex McCarthy (Lecturer in Innate Immunity, Imperial College London, pictured below delivering his talk)
- Prof Laura Bowater Professor of Microbiology Education and Engage-

ment, University of East Anglia)

The full programme, including poster presenters, are



listed on the press release.

We are delighted to have offered prizes to the follow-ing:

 Best oral presentation

 (1st place): Chinelo Etiaba
 (undergraduate student,
 School of Cellular and Molecular Medicine [CMM])
 for Hemozoin, a by



product of malaria infection, suppresses the neutrophil oxidative burst. Chinelo received a £50 Amazon voucher kindly donated by Qiagen.

 Best oral presentation (joint 2nd place, a £30) cash prize for each):

- Julia Crunden

 (Postdoctoral Research Associate, CMM)
 for The role and interaction networks of
 Hsp90 in the fungal pathogens of humans, Candida glabrata and Candida albicans, and
- Henry Oswin (PhD student, Chemistry) for An investigation of the airborne stability of Group A Streptococcus
- Best poster presentation (1st place, £30): Rachael Barr (EBI Clinical Primer, CMM) for Understanding the antibody response to Group A Streptococcus by exposure risk
 - Best poster presentation (2nd place): Max Erd-

mann (PhD student, CMM) for Establishment of versatile transient dual-reporter replicon systems for SARS-CoV-2, who received a £30 cash prize

• Best poster presentation (3rd place, £20): Michaela Gregorova (PhD student, CMM) for *Immune cell responses to dengue virus infection in obese/ overweight versus nonobese children and young adults*

Brigstow Institute seedcorn Experimental Partnerships

The University of Bristol's Brigstow Institute has announced their latest round of successful seedcorn awardees. They include the project-

Improving Access to Oral Health Services for Adult Survivors of Child Sex Abuse (CSA)

Health professionals are often unknowingly work in close contact with survivors of CSA. The proximity and intimacy required in dental care alongside the differential in power dynamics can lead to potentially triggering unwanted memories or a



traumatic response which results in patients avoiding dental visits. This research will work with adult survivors of child sex abuse to understand experiences of dental care and how we can improve access to dental services.

The project involves Nilufar Ahmed, Patricia Neville and Angela Hague (Bristol Dental School) and Viv Gordon (Viv Gordon Company).

See the full list of supported projects

Inappropriate testing for Sexually Transmitted Infections (STIs) has been a growing concern in recent years, and in 2020, Sexual Health Improvement Programme (SHIP) Health Integration Team (HIT)

directors Emma Harding-Esch, Paddy Horner and Katy Turner,



along with Peter Muir at the UK Health Security Agency, co -supervised a London School of Hygiene & Tropical Medicine MSc summer project entitled Online Tests for Sexually Transmitted Infections -Friend or Foe? A Scoping Review and Analysis of Providers.

In March 2021, following on from this project, the British Association for Sexual Health and HIV (BASHH) released a

position statement "to alert the relevant regulatory and advisory bodies to the testing and treatment practices of some STI service providers which are inconsistent

with national guidance".

BASHH's Bacterial Special Interest Group (BSIG), which Drs Harding-Esch and Horner are members of, has been leading a programme of work to take this forward and effect long-

Safe STI tests

term change in online STI provision to ensure appropriate patient care. Progress to date was presented at a BASHH webinar on 2 Feb '22. On 3 Feb '22 *The Telegraph* published an article highlighting that "sexual health experts have called for tighter regulation of companies offering self-testing for STIs over concerns of a lack of follow-up and unmonitored prescribing of antibiotics."

It is hoped that through the programme of work and this level of coverage, patients will be able to make informed choices about where to test and know what level of service to expect.

Awards: Part 2

John Smith was an anaesthetist with an interest in the management of difficult airways and became a national pioneer in the use of fibreoptic laryngoscopes. In recognition of his contributions, the John Smith airway award for publications in airway management are awarded annually at the winter conference of the Association of Anaesthetists. One of this year's winners was a paper published in October 2020 in Anaesthesia: Brown J et al., A quantitative evaluation of aerosol generation during tracheal intubation and extubation. The paper included authors Profs Tony Pickering (Physiology, Pharmacology and Neuroscience) and Jonathan Reid (Chemistry) as members of University's AER-ATOR study team. The study found that anaesthetic procedures produce less aerosol generation than believed, meaning that medical procedures would not spread SARS-CoV-2 as much as previously thought.

Lung Health @30. Understanding the origins of chronic lung disease and the impact of COVID-19 has been supported by **Southmead Hospital Charity**. Dr James Dodd (Bristol Medical School) received £191,526 for the project which will start in Oct '22 for three years.

Dr Amy Ward (Cellular and Molecular Medicine [CMM]) received £20,609 from **Wellcome** for The role of IL-27 during ocular inflammation, starting Jun '22 for four months. Dr Alice Halliday (CMM) received £19,116 from **Wellcome** for Understanding respiratory pathogen antigenicity and immunodominance for the rational design of mucosal vaccines, Apr-Aug '22.

Smoking, platelet activity and heart attacks

Smoking cigarettes may increase the risk of a heart attack by activating a gene that affects blood clotting.

The team demonstrated that activity of a gene, known as F2RL3, can be enhanced by smoking and that this gene, which is expressed on blood platelets, can in turn increase the risk of clotting events that lead to a heart attack.

A mechanism used by cells to control gene expression, known as DNA methylation, is a reversible process that changes the properties of DNA molecules (without changes being made to the DNA sequence itself). Cigarette smoking appears to cause changes to DNA methylation at lots of sites across



the genome, which could be one way that smoking predisposes to adverse health outcomes such as heart disease. Researchers discovered this was the case with the F2RL3 gene, whose protein (PAR4) is involved in activating platelets, the blood cells that help form blood clots. Through analysing smoking-related changes seen in this gene, the scientists were able to see that reductions in DNA methylation at F2RL3 could contribute to the increased risk of a heart attack in smokers by changing the activity of platelets.

Corbin LJ et al. (2022). Epigenetic regulation of F2RL3 associates with myocardial infarction and platelet function. Circulation Research.

The University of Bristol launched a research project which promises to address the common drivers of both obesity and under-nutrition in China and Southeast Asia on 15 December 2021.

Malnutrition is the leading cause of disease and mortality globally in Southeast Asia and carries substantial social and economic burdens. The multination project: Systems Actions to Malnutrition in All Its Forms in Chinese and Southeast Asian Cities – Developing

Tackling the global malnutrition crisis

Double Duty, Population-Level Interventions (SYSTAM CHINA-SEACS) is funded by the Medical Research Council in the UK and will be led by Dr Bai Li (School for Policy Studies).

Through this world-first initiative, Dr Li plans to demonstrate that by developing systemic solutions to tackle under nutrition, governments and policy-makers can also prevent obesity and non-

communicable diseases (NCDs) such as cancer, diabetes and

stroke.

This approach is known as double-duty, and involves identifying interventions, programmes and policies that can simultaneously reduce the burden of both undernutrition (including wasting, stunting and micronutrient deficiency or insufficiency) and overweight, obesity or diet-related NCDs. The study will be piloted in the Chinese city of Fang Cheng Gang.

Read the full press release

Dr Melanie Hezzell (Bristol Veterinary School) was awarded £9,953 from **Petsavers** for *Do measurements of circulating fibrosis markers change with disease progression in canine myxomatous mitral valve disease?*, starting May '22 for two years; and a further £2,750 from **Langford Trust** for *Remodelling in Canine Myxomatous Mitral Valve Disease* which started in Jan '22 for four years.

PhD students Matt Tarnowski (Biological Sciences) and Harry Thompson (Biochemistry) are embarking on a short project attempting to develop a high sensitivity biosensor to identify individual species of bacteria in river water samples. As avid wild swimmers,

Harry and Matt (pictured) are hopeful that this could be a useful tool in clarifying the safety of water to swim in. Ideally, the biosensor

would enable the rapid identification of microbial species in rivers and other waterways used for swimming/ recreation. You can find out more about the project_on the Bristol BioDesign Institute blog, where they will be writing regular updates on their progress. Matt and Harry received PhD funding from

Awards: Part 3

the EPSRC/BBSRC Centre for Doctoral Training in Synthetic

> Biology (SynBio CDT), and the University of Bristol. Funding for this research project is provided by the **SynBio**

CDT Innovation Award.

Drs Laura Rivino, Gareth Jones and Chris Williams gained Fellowships of the Higher Education Academy. Fellowship demonstrates a personal and institutional commitment to professionalism in learning and teaching in higher education.

2021 Clinical Primer awardees

This funding scheme, supported by the Elizabeth Blackwell Institute, offers doctors, veterinarians and dentists at the early stage of their clinical career the chance to experience working as a researcher for the first time.

Among the latest round of successful awards were: Eleanor Best, Natural Product Antibiotic Drug Discovery: Exploring deep sea microorganisms and associated metabolites as potential sources for the development of novel antimicrobial agents. Eleanor will work with Prof Paul Race

(Biochemistry) looking at natural product antibiotic drug discovery. Antibiotic resistance presents a huge threat to global health and could cause up to 10 million deaths by 2050 if nothing is done. Over the next 6 months, she will study previously undiscovered deep sea sponges and culturing the bacteria living inside them to hopefully uncover new species of antibiotic producing bacteria. She will then test their antimicrobial activity against resistant pathogens to hopefully lead to the development of novel antimicrobial agents effective against the most resistant

bacteria, and help develop a solution to the growing antimicrobial resistance crisis.

Frances Edwards, Exploring genetic mechanisms underpinning diagnostic uncertainties in susceptibility to piperacillin/tazobactam. Frances will look at antibiotic resistant strains of E. coli bacteria, and aim to understand the genetics behind why some are less susceptible to Tazocin (one of the most commonly prescribed antibiotics in hospitals). This will help us improve the treatment of patients with serious drug resistant infections.

Decolonising the immunology curriculum

By Drs Bronwen Burton (Cellular and Molecular Medicine) and Caroline McKinnon (Biochemistry): Decolonising the immunology curriculum: starting to interrogate structural inequalities in science. Conversations about racism and antiracism have been growing in recent years, amplified by the Black Lives Matter and 'Why is my curriculum white?' movements, the **Rhodes Must Fall campaign** and the toppling of the Colston statue in Bristol. Universities are responding by committing to decolonising their curricula to address the damaging legacies of colonialism.

Examples of cultural bias in science:

- BAME researchers and women are less likely to receive funding or receive lower awards: data from multiple funding bodies
- BAME researchers in STEM are more likely to be on a fixed-term contract and are less likely to be professors, reflecting wider patterns across all academic disciplines

• Bias towards the Global North and men is seen in the composition of editorial boards in science and medicine; women are even underrepresented in the editorial boards of women's health journals

The authors discuss what they have learnt as they work to diversify the biomedical curricula at the University of Bristol, supported by a British Society for Immunology Equality, Diversity and Inclusion activity grant. Dr Amy Thomas (Bristol Medical School) was awarded an 'Unsung COVID Heroes' award from WISE, an organisation that promotes women in science, maths and engineering for her work during the COVID-19 pandemic.

After identifying very early into the pandemic that collecting samples from children was challenging, Amy proceeded to design and validate a simple saliva spit test to roll out to schools across Bristol. The antibody test is still contributing to national decision-making for outbreak



control and has already been used in more than twenty outbreaks in Bristol. Her work remarkable in that it was conducted shortly after her

Unsung COVID hero

PhD studies in an unrelated field. She used her initiative to source laboratory space, prepandemic saliva samples (from researchers in Portugal) and set up a pop-up clinic in the car park of a local hospital to collect saliva samples. The project secured £1.8 million in funding.

Amy received her award from Princess Anne at a ceremony held at Windsor Castle ceremony earlier this month (see photo).

Prof Robin Shattock at Imperial College London and collaborators, including Prof Imre Berger (Biochemistry), have been awarded an extension to the Engineering and Physical Sciences Research Council Future Vaccine Manufacturing Hub that aims to optimise the design, development and delivery of vaccines. The initial award started in Dec '17 with an £11.5 million grant.

PhD student Lynden Rooms (Biochemistry) has received a Wellcome Translational Partnership award which will start this Summer. The funding will enable him to continue his hunt for novel antimicrobials that target folate biosynthesis.

Dr Laura Rivino has been awarded a Royal Society research grant to set up a Met-Flow to study the metabolic profiles of CD4+ and CD8+ Tcells in overweight/obese versus normal weight patients in dengue virus infection. This is a collaboration with Dr Andrew Herman, Director of Flow Cytometry in the Faculty of Life Sciences, who will set up the flow cytometry-based method which captures the metabolic state of immune cells by targeting key proteins and rate-limiting enzymes across multiple pathways.

Awards: Part 4

Dr Anna Long (Bristol Medical School) received £130,564 from **Diabetes UK** for *Does ZnT8 autoimmunity more accurately reflect beta cell destruction compared with other islet autoantibodies?*, starting Jan '22 for two years.

Applying machine learning to accelerate SCFI-based antimicrobial susceptibility test was supported by a £14,016 award from the **Biotechnology and Biological Sciences Research Council**. The project, led by Dr Massimo Antognozzi (Physics) started in Jan '22 and will continue for 14 months.

Link between high blood pressure and diabetes

An international collaboration between the Universities of Auckland and Bristol has discovered why so many patients suffering with hypertension also have diabetes. sory organ, the carotid body, located in the neck.

The University of Bristol group used a high-throughput genomics technique, RNA se-

Non-specific lipid-transfer protein 1 (LP -1) is released from the wall of the gut after

eating and acts to stimulate insulin from the pancreas to control blood sugar levels. This was known but what has now been unearthed is that Glucagon-like peptide 1 (GLP-1) also stimulates a small sen-



quencing, to read all the messages of the expressed genes in the carotid body in rats with and without high blood pressure. This led to

the finding that the receptor that senses GLP-1 is located in the carotid body, but less so in hypertensive rats.

The carotid body is the convergent point where GLP-1 acts to control both blood sugar and blood pressure simultaneously; this is co-ordinated by the nervous system which is instructed by the carotid body. People with hypertension and/ or diabetes are at high risk of life-threatening cardiovascular disease. Even when receiving medication, a large number of patients will remain at high risk. This is because most medications only treat symptoms and not causes of high blood pressure and high sugar.

Pauza AG *et al.* (2022). GLP1R Attenuates Sympathetic Response to High Glucose via Carotid Body Inhibition. *Circulation Research*.

Tackling the spread of disease

An international research team, led by the University of Bristol, has developed a statis-

tical approach, spacetime statistical inference, to quantify and separate the different sources of increasing sea levels. A European Research Council grant will allow this approach to be used to develop a software

tool which can address farreaching space-time, or fourdimensional, problems such as the transmission of vectorborne diseases and viruses, air pollution patterns, traffic flow, and crime trends. The grant will allow the re-



search team to capitalise on further progress made by the GlobalMass project, widening its applications and growing the number of potential users. Work will focus on the creation of a new software tool, called 4DM, which can handle

> big data and recurring process problems. The tool has the potential to transform many disciplines, not just in Earth and environmental sciences but also in areas such as public health and national security, and has the potential to attract

huge commercial interest, for example in extreme weather risk assessment for insurance and reinsurance.

Read the full press release

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Superior Covid protection from better face masks

New research from the universities of Surrey and Bristol and ESPCI Paris has shown that FFP2 (filtering facepiece)

respirator masks are five times more efficient at filtering particles which carry the Covid-19 virus than cloth masks.

The research details how the team conducted confocal microscopy to take three dimensional images of woven fabric which was then used to perform Lattice Boltzmann simulations of the air flow through it. The findings enabled the team to calculate the



For particles with a diameter of $1.5\mu m$, the typical size of Covid-bearing particles, the team estimated woven fabric is only 2.5 to 10%,

because most of the air flow

is channelled through rela-

tively large gaps between the fabric's yarns. Multiple layers of fabric improve efficiency in a roughly linear fashion, meaning triple-layer cloth masks are up to 30% efficient, but this is still poor in comparison with the material used for FFP2 masks, which is typically more than 90% efficient.

Sear R et al. (2022). Modeling the filtration efficiency of a woven fabric: The role of multiple lengthscales. *Physics of Fluids*.

A study has shown how SARS-CoV-2 may contribute to severe microvascular damage seen in severely-ill COVID-19 patients by transforming human heart vascular cells into inflammatory cells, without infecting them. The research indicates blocking antibodies could represent a new treatment to alleviate cardiovascular complications.

The team exposed human heart pericytes to SARS-CoV-2 Alpha and Delta variants, along with the original Wuhan virus, and found they were not infected. They then challenged the pericytes with the spike protein alone, without the virus. The spike protein

Cardiac damage in SARS-CoV-2 patients

made pericytes unable to interact with their companion endothelial cells and induced them to secrete inflammatory



cytokines, suggesting the spike protein is harmful to human cardiac cells. Interestingly, the team found that antibodies blocking CD147 - a receptor for the spike protein – protected heart pericytes from damage.

Finally, they identified the presence of the SARS-CoV-2 spike protein in blood samples obtained from COVID-19 patients, which opens the possibility that spike protein particles travelling through the circulation can reach a site distant from the respiratory system and cause systemic damage.

Avolio E *et al.* (2022). The SARS -CoV-2 Spike protein disrupts human cardiac pericytes function through CD147 receptormediated signalling: a potential non-infective mechanism of COVID-19 microvascular disease. *Clinical Science*.

Evotec collaboration for treatment of kidney diseases

A new collaboration to help patients with nephrotic syndrome was announced on 2 March 2022 by the University of Bristol and Evotec SE.

Under the collaboration, Evotec will receive access to longitudinal samples from an international patient cohort, collected under a Medical Research Council funded global challenges project, which includes several hundreds of patients from Asia, India and Africa linked to anonymised clinical records. Currently, diagnosis of nephrotic syndrome, which is a group of symptoms like proteinuria and oedema that indicate kidneys are not working properly, remains challenging and current treatment regimens are mostly symptomatic. Evotec will analyse the sam-



ples using its proprietary multi -omics platform EVOpanOmics. Expert teams at Evotec and Bristol will leverage Evotec's data analytics and prediction platform EVOpan-Hunter to jointly identify key drivers of nephrotic syndrome disease progression and potential molecular targets for intervention as well as molecular markers for diagnosis.

Molecular patient data combined with clinical data is instrumental for the identification and validation of diseaserelevant molecular mechanisms and targets. Stratification of patients according to disease-associated molecular mechanisms re-classify certain subtypes of the disease, i.e. steroid sensitive and steroid resistant nephrotic syndrome and deliver new starting points for the discovery of novel targeted therapies.

Awards: Part 5 and engagement

Dr Mark Naven and Prof Paul Martin (Biochemistry) have won a Biotechnology and Biological Sciences Research Council international partnering grant to investigate the circadian regulation of wound repair with colleagues in Australia.

Dr Ore Francis (Cellular and Molecular Medicine) was awarded £14,998 from a **University of Bristol internal funding call** for *Further development of standardised virus pseudotype assay to quantify SARS-CoV-2 neutralising anti-* bodies in saliva and serum, which started in Jan '22 and will finish in Apr this year.

Wellcome awarded Dr Barbara Caddick (Bristol Medical School) £11,360 to pursue An historical exploration of antibiotic use in Primary Health, starting Jan '22 for 9 months.

Identifying new molecular pathways and therapeutic targets in diabetic nephropathy

| Reduce inflections and outbreaks through improved ingleme and infrastructure; restrict use in agriculture | | |
|--|--|--|
| | Improve diagnostics New methods to identify resistant bacteria can make treatment more effective, and reduce outbreaks | |
| P | Identify new targets Some cellular pathways are harder for bacteria to bypass or modify, making them ideal targets for new antibiotics | |
| % | Combination therapies Traditional antibiotics can be combined with molecules that block resistance mechanisms | |

has been supported by a £983,305 award from the Medical Research Council. Principal Investigator Prof Richard Coward (Bristol Medical School) is leading the project which is expected to run Mar '22 - Feb '26.

Profs Kristen Reyher (Bristol Veterinary School) and

Matthew Avison

(Cellular and Molecular Medicine) were interviewed about antibiotic resistance on BBC Radio Bristol; listen to the excerpts: clip 1 and clip 2.

SARS-CoV-2 plays hide and seek in immune system

People suffering from COVID-19 could have several different SARS-CoV-2 variants hidden away from the immune system in different parts of the body.

New research by an international team led by Prof Imre Berger at the University of Bristol and Prof Joachim Spatz at the Max Planck Institute for Medical Research in Heidelberg, both Directors of the Max Planck Bristol Centre of Minimal Biology, show how the virus can evolve distinctly in different cell types, and adapt its immunity, in the same infected host. They used cutting-edge synthetic biology techniques, state-of-the-art imaging and cloud computing to decipher viral mechanisms at work. They demonstrated that upon binding of a fatty



acid, the virus' spike protein changed their shape, which effectively cloaks the virus from the immune system.

Results showed that one can have several different virus variants in one's body. Some of these variants may use kidney or spleen cells as their niche to hide, while the body is busy defending against the dominant virus type. This could make it difficult for the infected patients to get rid of SARS-CoV-2 entirely.

Gupta K *et al.* (2022). Structural insights in cell-type specific evolution of intra-host diversity by SARS-CoV-2. *Nature Communications.*

Staufer O *et al.* (2022). Synthetic virions reveal fatty acidcoupled adaptive immunogenicity of SARS-CoV-2 spike glycoprotein. Nature Communications. Image © O Staufer and MPI for Medical Research, Germany

Aspirin may improve 3-month survival for COVID critically ill

People who become seriously ill with COVID-19 are at risk of developing blood clots that can block their blood vessels and lead to potentially fatal organ damage. Researchers want to know if this process could be prevented by treating patients with bloodthinning antiplatelet drugs. The study found that using antiplatelet drugs, such as aspirin, to treat patients who are seriously ill with COVID-19 does not seem to alter the short-term need for life support. However, they did find

signs that patients given these drugs were more likely to survive in the following three months.



The clinical trial, called REMAP -CAP, involved 1,557 patients critically ill with COVID-19 in 105 hospitals in Canada, France, Germany, India, Italy, Nepal, Netherlands and the UK during 2020 and 2021. They found that those were treated with antiplatelet drugs were more likely to survive over this longer time (70.5% versus 67.3%).

Bradbury C *et al.* (2022). Effect of Antiplatelet Therapy on Survival and Organ Support–Free Days in Critically III Patients With COVID-19A Randomized Clinical Trial. *The Journal of the American Medical Association* (JAMA).

ELIZABETH BLACKWELL FUNDING

Nurturing Research. Improving Health.



The Prudence Trust/Elizabeth Blackwell Institute Fellowship in mental health

With support from the Prudence Trust, funding is available for a for a researcher with substantial experience in the area of mental health in young people.

Closing date: 26 April 2022

Elizabeth Blackwell Institute support scheme for academic training 2022

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

Closing date: 31 August 2022

Elizabeth Blackwell Institute academic bridging funding scheme 2022

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

Closing date: 31 August 2022

Public Engagement seed funds

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

Workshop support

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

Returning Carers Scheme

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

FUNDING OPPORTUNITIES

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

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

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

* Research Professional

British Society for Immunology Travel awards

Closing date: 1 May 2022

Award amount: £1,000

These enable members to attend scientific meetings or visit laboratories for specific short-term activities, such as collaborative research or to learn new techniques. Awards are worth £500 for travel within the UK, £700 for European travel and £1,000 for intercontinental travel.

Medical Research Council

Research grants - infection and immunity

Closing date: 11 May 2022

Award amount: unspecified

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

Medical Research Council

Build on existing COVID-19 infrastructure, partnerships and resources

Closing date: 11 May 2022

Award amount: unspecified

This supports newly established infrastructure, partnerships and resources to continue to build and develop sustaining high-value collaborative activities and capabilities arising from the COVID-19 pandemic response. Proposals should demonstrate:

- significant novelty in infrastructure, partnerships and resources through previous COVID-19 funding that can be developed with a new award
- how further funding would enable collaborative activities or capabilities to add value to high-quality scientific programmes underpinning understanding and management of infectious disease, human immunology or preparedness for future outbreaks

National Institute of Allergy and Infectious Diseases, US

Host immunity and novel immunisation strategies for *Clostridioides difficile* infection (U19 clinical trial not allowed)

Closing date: 20 May 2022 Award amount: USD 1 million

Supports the formation of co-operative research centres to pursue vaccine development through multidisciplinary investigations into the host immune response to *C. difficile* infection.

European Society for Paediatric Infectious Diseases

Collaborative research meeting award scheme

Closing date: 1 June 2022

Award amount: €5,000

Supports research meetings that aid the initiation or development of interdisciplinary research projects and networks in paediatric infectious diseases; applicants must be ESPID members. Workshops must be held in a European location and participation and open to ESPID members.

Healthcare Infection Society

Small research grants

Closing date: 1 September 2022 Award amount: £10,000

These support small-scale research projects within the scope of infection prevention and control and nosocomial infections, or possibly the costs associated with the visit of an overseas research fellow.

National Science Foundation

Ecology and evolution of infectious diseases

Closing date: 16 November 2022

Award amount: USD 2.5 million

Supports collaborative research on the ecological, evolutionary and social drivers that influence infectious diseases and increase quantitative or computational understanding of pathogen transmission dynamics. Proposals should focus on understanding the determinants and interactions of transmission of diseases to humans, non-human animals, plants or other species. Proposals for research on disease systems of public health concern to developing countries are strongly encouraged, as are disease systems of concern in agricultural systems. Projects must involve scientists from the US in collaboration with scientists from the UK, Israel or China.

THIS ISSUE'S FEATURED ARTICLE

Association of COVID-19 vaccines ChAdOx1 and BNT162b2 with major venous, arterial, or thrombocytopenic events: A population-based cohort study of 46 million adults in England Whitely WN, Ip S, Cooper JA, Bolton T, Keene S *et al.* (2022). *PLOS Medicine*.

Why was this study done?

- ⇒ Cases of venous and arterial thromboses in unusual locations, such as the cerebral veins, and with low platelet levels, have been reported after vaccination with ChAdOx1-S COVID-19 vaccine.
- ⇒ Case finding efforts in vaccinated people may lead to overestimation of risk associated with vaccines, if diagnostic thresholds vary between vaccinated and unvaccinated people.
- ⇒ Effects of vaccination on rates of common venous and arterial events—such as stroke, myocardial infarction (MI), deep vein thrombosis (DVT), and pulmonary embolism (PE)—are difficult to measure based on case reports. Population-level data may give better estimates.



adjusting for potential confounding factors.

What did the researchers do and find

⇒ We used nationally collated data from electronic health records on 46 million adults, of whom 21 million were vaccinated during the study, and compared the incidence of venous and arterial events before and after the first vaccination with ChA-dOx1-S and BNT162b2 COVID-19 vaccines.
 ⇒ Overall rates of major arterial and venous events were lower after vaccination with both ChAdOx1-S and BNT162b2, after

⇒ In people <70 years, rates of hospitalisation due to intracranial venous thrombosis (ICVT) or due to thrombocytopenia were higher after vaccination with ChAdOx1-S but not BNT162b2, although the absolute increase in the risk of these events was very small.</p>

What do these findings mean

- ⇒ In adults ≥70 years, a first vaccination with either ChAdOx1-S and BNT162b2 was not associated with an increase in rates major arterial or venous thrombotic events.
- ⇒ In adults <70 years, the small increased risks of ICVT and hospitalisation with thrombocytopenia after first vaccination with ChAdOx1-S are likely to be outweighed by the vaccines' effect in reducing COVID-19 mortality and morbidity.
- \Rightarrow The main limitations of the study were its reliance on the accuracy of coded electronic health records, and the potential for residual confounding.

Read the University of Bristol press release

CONTACTS

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

Co-Chair: Philip Bright Clinical Immunologist



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



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

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

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

e: infection-immunity@bristol.ac.uk

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

@Bristollandl

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