I&I NETWORK NEWSLETTER





This project, supported by a £4.6 million award from the **Biotechnology and Biological** Sciences Research Council under their strategic longer and larger scheme, will study how bacterial defence systems shape the evolution of mobile genetic elements (MGEs) that contribute to the spread of antimicrobial resistance; these segments of DNA can move from one bacterium to another and change key traits of bacteria, including antibiotic resistance and virulence.

Led by Prof Edze Westra at the University of Exeter, the study aims to develop a broader understanding of

2022 - ISSUE 4

Multi-layered bacterial genome defences

multi-layered bacterial genome defence systems, at scales ranging from molecules to populations.

Mark Szczelkun's group



(Biochemistry @Bristol) are part of the team which will use bioinformatic, biophysical and molecular biology approaches to understand how the interactions between genome defence systems protect bacteria against infection. They will combine experimental evolution and mathematical modelling to determine how multilayered defence systems shape

> bacterial genome and MGEs evolution. Knowledge generated through this project has the potential to uncover how combinations of natural genome defence systems could be exploited in the fight against AMR.

This project is a collaboration between 12 investigators based at the Universities of Durham, Bath, Bristol, Exeter, Liverpool, Manchester and St Andrews.

Inside this issue:

Infection and Immunity Events	2	
Infection and Immunity Research and Staff News	3-10	
Funding Opportunities in Infection and Immunity	11-12	Ċ
This Issue's Showcased Article	13	
Contacts	14	

EVENTS

NIHR Pre-Doctoral Fellowship information webinar 8 December 2022, 13.00 - 14.00, online

Science Impact Surgery 8 December 2022, 13.30 - 15.30, Earth Sciences Common Room

LATITUDES network (Library of Assessment Tools and InsTruments Used to assess Data validity in Evidence Synthesis) 13 December 2022, 13.00 - 14.00, online

Engage 2022 Online Conference: Changing Universities 15 December 2022, 9.30 - 16.30, online

NIHR Work and Health Research Development 5 December 2022, 14.00 - 16.00, online

Infection and Immunity Early Career Researchers' Symposium

1 February 2023, Life Sciences Building

Keynotes: Charlotte Odendall (King's College London) Susie Dunachie (Oxford)

REGISTER HERE

E ALL WELCOME

Health-Tech Products : Innovation to Implementation! 15 December 2022, 14.00 - 16.00, University of Bristol campus

Methods in Evidence Synthesis salon 13 January 2023, 12.00 - 13.00, online

Principal Investigator (PI) Essentials 23 January 2023, 9.00 - 13.00, online

Introduction to Policy Engagement 24 January 2023, 14.00 - 16.00, Room 3.34, Physics Building

The Covid Consensus: The Global Assault on Democracy and the Poor - a Critique for the Left 25 January 2023, 16.00 - 17.00, Toby Green and Thomas Fazi, OS6 Oakfield House and online

Joint meeting of the Bristol Heart Institute, Specialist Research Institute and the British Heart Foundation Bristol Accelerator Award

2 February 2023, 9.00 - 17.00, Engineers' House, Clifton Down, Bristol, BS8 3NB

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

NEWS

Tackling respiratory syncytial virus infections in infants

GP practices and NHS Trusts across the West of England will play a vital role in a new respiratory virus study looking into the leading cause of infant hospitalisation. RSV (Respiratory Syncytial Virus) is one of the leading causes of hospitalisation in all infants worldwide and affects 90% of children before the age of two. In recent months, there has been a resurgence of RSV following the easing of COVID-19 public health measures.

MONIE study will take place at ten sites in the region and is a collaboration between Sanofi, its partner AstraZeneca, and



the National Institute for Health and Care Research (NIHR). The study is evaluating the efficacy of nirsevimab, a monoclonal antibody immunisation, in protecting against one of the leading causes of infant hospitalisation worldwide. RSV often causes only mild illnesses, like a cold. However, for some babies, it leads to more severe lung problems such as bronchiolitis and pneumonia.

More than 20,000 infants across three countries (United Kingdom, France and Germany) will take part in the study, from August 2022 to March 2023. Dr Anu Goenka, is Principal Investigator for the study at University Hospitals Bristol and Weston NHS Foundation Trust.

Learn more about the study and see if your baby is eligible

The ground-breaking HAR-

Recognition for pandemic modelling work

Drs Ellen Brooks Pollock OBE (Bristol Medical School), Leon Danon and Robert Challen (both Engineering Mathematics) have been awarded the prestigious Weldon Memorial Prize along with other members of the SPI-M-O group, which reports to the Scientific Advisory Group for Emergencies (SAGE).

Additionally, Drs Leon Danon, Robert Challen, Amy Thomas (Bristol Medical School) and Emily Nixon (Biological Sciences) were awarded the SPI-M-O (Scientific Pandemic Influenza Group on Modelling group) Award for Modelling and Data



Support (SAMDS) which recognises those who have made an exceptional contribution to the work of the group outside of their usual work activity.

The Weldon Memorial Prize is awarded annually by the University of Oxford for "noteworthy contributions in the development of mathematical or statistical methods applied to problems in biology". This is the first time in its history that the prize, which has been awarded since 1911, has been given to a group rather than an individual.

Read more

Image L-R: Robert, Ellen, Leon, Emily & Amy

First clinical trial of lab-grown blood transfusion

The manufactured blood cells were grown from stem cells from donors and then transfused into volunteers in the RESTORE randomised controlled clinical trial.

This is the first time in the world that red blood cells that have been grown in a laboratory have been given to another person as part of a trial into blood transfusion. If proved safe and effective, manufactured blood cells could in time revolutionise treatments for people with blood disorders such as sickle cell and rare blood types. It can be difficult to find enough well-matched donated blood for some people with these disorders. The RESTORE trial is a joint research initiative by NHS Blood and Transplant and the University of Bristol, working with the University of Cambridge, Guy's and St Thomas' NHS Foundation Trust. NIHR Cambridge Clinical Research Facility, and Cambridge University Hospitals NHS Foundation Trust. The trial is studying the lifespan of the lab grown cells compared with infusions of standard red blood cells from the same donor. The lab -grown blood cells are all fresh, so the trial team expect them to perform better than a similar transfusion of standard donated red cells, which contains cells of varying ages.

Watch the video

Image: microscope image of a RE-STORE lab-grown young red blood cells

Dr Bryan Bzdek (Chemistry) was awarded £100,000 by the Leverhulme Trust. Philip Leverhulme Prizes are designed to recognise and facilitate the work of outstanding research scholars of proven achievement, who have made and

are continuing to make original and significant contributions to knowledge in their particular field.

Dr Bzdek and his research group explore the physical and analytical chemistry of aerosols, with particular focus on major global challenges in atmospheric science and disease transmission. These expertise have proven vital during the COVID-19 pandemic and ongoing climate crisis. His group has made pioneering contributions to identify the surface composition of microscopic droplets, furthering

understanding of how cloud droplets form in the atmosphere.

They have also been at the forefront of charac-

terising respiratory aerosols generated by singing, playing musical instruments, exercising, and performing medical procedures, which led directly to changes in UK Government Guidance during the pandem-

Philip Leverhulme Prize award

ic as well as changes in NHS guidelines for aerosol generating medical procedures.

The prize funds will help the group advance an exciting collaborative project using a novel combination of unique aerosol and spectroscopy tools to explore light-induced chemistry in aerosols. Unravelling these processes is crucial to assessing aerosol climate and health impacts. Light-induced processes driving chemical and biological phenomena in aerosols have been largely ignored but can play key roles in pollutant transformation, reaction rates and products, as well as pathogen survival.



Prize at West Country Chest Society conference

Robyn Heath, Senior Clinical Research Practitioner (University Hospitals Bristol and Weston NHS Foundation Trust [UHBW], pictured) with the AvonCAP Study Research Team, recently won a prize at

AvonCAP study is looking at how respiratory disease may change due to the COVID-19 pandemic, including whether it makes other lung infections more or less likely. Alongside

on 30 September 2022. The

the West Country Chest Society Annual Meeting.

Robyn's presentation was about the changes in incidence and severity of pneumococcal

pleural disease between 2006 to 2018 and won 1st place at the event which took place



COVID-19, the

Doctors in training and allied healthcare professionals based in the Southwest firstly had to construct an abstract to be short listed for a poster presentation, and then the 3 best submissions were selected for a 10-minute presentation. Robyn, along with Dr Catherine Hyams (Bristol Medical School), Prof Adam Finn (School of Cellular and Molecular Medicine), and others from UHBW, North Bristol Trust, the University of Bristol, **Royal United Hospitals Bath** and the UK Health Security Agency, collected the data and was one of the three selected for a 10-minute presentation.

Care improves prescribing of cardiovascular medications

People at risk of heart disease are more likely to be prescribed relevant medications if they see the same GP over time (known as continuity of care) but not more likely to take their medications (known as adherence), according to researchers at the University of Bristol.

They found strong evidence that prescription of clinically relevant medications such as statins (used to lower cholesterol), anticoagulants and antiplatelet agents (both used as blood thinners) and antihypertensives (for lowering blood pressure) increased with greater continuity of care. These medicines are widely used and if prescribed appropriately and taken cor-



rectly by patients, can help reduce the risk of heart disease and strokes.

This is the first time that the association between continuity of care, prescribing and adherence to medications has been described. Although we cannot prove a causal association, findings suggest that prescribing of important cardiovascular medications may be positively influenced by improved continuity of primary care. Peter Tammes, lead author

Tammes P *et al.* (2022). Association between continuity of primary care and both prescribing and adherence of common cardiovascular medications: a cohort study among patients in England. *BMJ Open*.

Page 5

Risk of blood clots remains for 49 weeks after COVID-19

COVID-19 infection increases the risk of potentially lifethreatening blood clots for at least 49 weeks.

Recent findings suggest that the COVID-19 pandemic may have led to an additional 10,500 cases of heart attacks, strokes and other blood clot complications such as deep vein thrombosis in England and Wales in 2020 alone, although the excess risk to individuals remains small and reduces over time.

The research – involving a large team of researchers led by the Universities of Bristol,



Cambridge, and Edinburgh, and Swansea University – shows that people with only mild or moderate disease were also affected. The authors suggest that preventive strategies, such as giving high

> -risk patients medication to lower blood pressure, could help reduce cases of serious clots.

Sterne JAC *et al.* (2022). Association of COVID-19 with major arterial and venous thrombotic diseases: a population-

wide cohort study of 48 million adults in England and Wales. *Circulation*.

British Society for Oral and Dental Research prize

The President's Prize, awarded by the British Society for Oral and Dental Research, is made annually to an earlycareer researcher who has

made a significant contribution to basic, translational or clinical dental research. This year's prize

was awarded to Dr Cher Farrugia for her work on two translational microbiology projects focusing on the standardisation of antimicrobial testing, and on the link between periodontal/gum disease and cardiovascular disease. Her work on antimicrobial testing of dental devices and materials stemmed from a lack of testing standardisation. Following international collab-

PER

oration, it culminated in a paper which summarised current testing techniques and their limitations. Proposals from this study have been referenced in a

new International Standards organisation document, ISO/ DIS 3990 Dentistry - Evaluation of antibacterial activity of dental restorative materials, luting cements, fissure sealants and orthodontic bonding or luting materials. The work aims to increase clinical relevance of antimicrobial testing, as well as facilitating comparisons of tests carried out in different centres and laboratories when a new or modified material is being developed.

Research on the link between periodontal disease and cardiovascular disease focused on the role of anaerobes, which are frequently associated with gum disease and have been shown to play a role in the link between oral health and general health.

Image: Dr Farrugia being presented with the award on 15 September 2022 during this year's International Association for Dental Research meeting (PER-IADR Oral Health Research Congress) in Marseille, France

Page 6

New trial to assess rapid testing in primary care

A new randomised controlled clinical trial, led by the University of Bristol, will investigate whether rapid microbiological 'point-of-care' tests for respiratory infections could reduce antibiotic prescribing in primary care, thanks to funding of £1.6 million by the National Institute for Health and Care Research (NIHR).

2022 -

ISSUE 4

The tests, which are carried out in GP surgeries rather than sent to a laboratory, detect the presence of viruses and some bacteria, with results available on the same day. Every year, millions of people in the UK seek help for respiratory infections such as coughs, colds, chest infections, sore throats and ear-



aches. On average, GPs and nurses give antibiotics to half of these patients. This is more than is necessary because most respiratory infections are caused by viruses, including COVID-19, but antibiotics only work on bacteria. This is needlessly contributing to antimicrobial resistance, but since clinicians don't always know who needs them, they are often given 'just in case'.

RAPID-TEST is a large randomised controlled clinical trial that will investigate whether point-of-care tests really do reduce antibiotic prescribing in general practice, and how. The project is part of a longstanding collaboration between the University of Bristol and the Bristol, North Somerset and South Gloucestershire NHS Integrated Care Board.

UK-Slovenia Researcher Mobility launch

Professor of Bacteriology Jim Spencer (School of Cellular and Molecular Medicine, pictured) presented at the Slovenian Research Agency, UK-Slovenia Researcher Mobility scheme launch event in October 2022. The UK and Slovene researchers together are finding new ways to tackle the growing problem of antimicrobial resistance and keep our antibiotics working.

The Science & Innovation Department at the British Embassy in Ljubljana aims to promote science and innovation co-operation between the UK and the Republic of Slovenia and to facilitate technology transfer and innovation. Read the introductory



brief, UK Science and Innovation Network Country Snapshot - Slovenia.

SIN Slovenia works to the following global objectives:

- influences science and innovation policies of the Slovene governments, industry and academia to benefit the UK
- improves UK policy based on international experience and emerging opportunities and challenges with Slovenia
- stimulates strategic science collaborations with Slovenia to benefit the UK and delivers wider policy goals
- harnesses Slovenia's international technology partnerships and investment to grow UK innovation capability.

Halo Therapeutics won the BioSeed 'One to Watch Award in Therapeutics' at the OBN Awards event held 17

November 2022 in London. The awards celebrate innovation and achievement in life sciences, and offer twelve award categories which en-

compass biotech, medtech and digital health sectors, as well as dealmakers, CRO's and innovative industry supporters. The awards recog-



17 citing innovation, novel and exciting approaches to unmet clinical needs, outstanding company

of development, recognising

inspirational leadership, ex-

progression and the delivery of real-life, tangible results.

Halo Therapeutics is a University of Bristol

spin-out company founded by Imre Berger (CSO, pictured centre) and Christiane Berger -Schaffitzel (CTO) in the

Halo Therapeutics wins award nise companies at all stages School of Biochemistry at the

University of Bristol, and Dan Fitzgerald CEO and Peter Pack NED. The company is advancing a pipeline of novel and proprietary pan-coronavirus antiviral therapeutics by applying expertise in structural biology, virology, and computational chemistry. Founded in December 2020 and based in Bristol, their vision is to roll out a class of small molecule pan-coronavirus therapeutics targeting the central axis of disease pathology: lipid regulation.

A person's blood type is determined by the presence or absence of proteins present on the surface of red blood cells. Although ABO or Rh are most well-known, there are many other important blood groups. Where mismatch exists between one person's blood and that of another, the possibility of alloimmunisation (when a person generates an antibody against a blood group antigen that they do not carry) arises. The presence of alloantibodies can have clinical consequences in transfusion or pregnancy by triggering an attack by the immune system.

Researchers from Bris-

Discovery of Er Blood Group System

tol's School of Biochemistry and the International Blood Group Reference Laboratory spearheaded an international collaboration which sought to investigate a 30year mystery surrounding the basis of three known, but genetically uncharacterised, antigens that did not fit into any known blood group system.

In the study, individuals with alloantibodies against a collection of antigens termed Er were investigated. Specific changes were identified in the gene coding for the Piezo1 protein, which would result in the production of an altered protein on the cell surface of these individuals. Using a combination of cutting-edge DNA sequencing and gene-editing techniques, the team were able to conclusively show that Piezo1, a protein of widespread biological interest, is the carrier for these sites (and more) and, in so doing, establish Er as a new blood group system.

Crew VK *et al.* (2022). Missense mutations in PIEZO1, encoding the Piezo1 mechanosensor protein, define the Er red blood cell antigens. *American Society of Hematology*.

Page 8

Doctoral prize winners 2022

Each year the University of Bristol picks six outstanding theses - one from each faculty - from hundreds of submissions by doctoral researchers in the last year. This year's winners each receive £500 and a special certificate. They include:

Health Sciences - Dr Claire Williams

The natural history of the autoimmune response to zinc transporter 8 (ZnT8) in type 1 diabetes

Claire studied one of the lesser-known early signs of type 1 diabetes, the body's immune response to zinc transporter 8 (ZnT8). She developed ways to understand which immune cells recognise ZnT8 and how they bind to it. She also developed a cheaper and better way of detecting those cells. The work was supported by a studentship from Diabetes UK. Another grant from the charity is allowing her to expand her work as a Post-doctoral Research Associate at Bristol.

Life Sciences - Dr James Daly Molecular Insights into the Role of Endosomal Recycling in Health and Disease Our bodies are recycling important biomolecules (like proteins and lipids), reducing demand for raw materials and limiting the build-up of toxins. James' PhD focussed on endosomes, which act as waste management and recycling stations inside cells. He suggested a model for how a protein complex that regulates this sorting process protects against neurodegenerative diseases. Thanks to a Wellcome Early Career Award, he is further exploring the role of Neuropilin receptors in viral infection with Michael Malim at King's College London.

Finding solutions for a healthier future

Climate change is one of the biggest health threats facing humanity; it is already affecting our health, and these impacts are likely to increase. A series of short films developed by the University of Bristol's Elizabeth Blackwell Institute for Health **Research and Cabot Institute** for the Environment explain how the health of our planet is linked to human health, and how research at Bristol will help us to understand these complex and interwoven issues.

The Climate Change and Health research programme

is a new collaboration between the two institutes looking into the intersection between climate change and health. The programme



brings together experts from different disciplines to understand and address the health impacts of a changing climate. The films set out some of these complex challenges and explain why it's urgent we act now; how University of Bristol researchers are working together to understand and address the issues; and what we can achieve by investing in this area of research.

Climate change will impact health in multiple ways, including mental health; changes in disease patterns; impacts on water, food and nutrition; health consequences of extreme weather events; implications for health; and inequalities of strategies to reduce greenhouse gas emissions and to support wider adaptation. Watch the films

Page 10

Eighteen University of Bristol academics have been named on Clarivate's Highly Cited Researchers 2022 list.

The annual list recognises in-

fluential researchers worldwide, who have published multiple papers frequently cited by their peers during the last decade.



The full list of names has been taken from papers ranked in the top 1% of most cited works for their field and publication year in the Web of Science citation index.

Among the academics on this year's list are:

- Professor Jonathan
 Sterne (pictured left),
 Professor of Medical Statistics and Epidemiology,
 Bristol Medical School
- Professor Peter Vickerman (pictured right), Professor of Infectious Disease Modelling, Bristol Medical School

 Professor Matthew Hickman (pictured below), Professor in Public Health and Epidemiology, Bristol Medical School





Highly Cited researchers 2022

Antimicrobial Use in Livestock Farming

Dr Maria Paula Escobar-Tello (Bristol Veterinary School) was one of the co-editors of an ebook entitled Interdisciplinary Approaches to Antimicrobial Use in Livestock Farming, published by Frontiers in Veterinary Science in September 2022.

The call for contributions to the book sought to create bridges between the fields of qualitative veterinary research and social sciences, with the objective of offering a true interdisciplinary dialogue. Proposals that grasped both individual, collective and structural components of antimicrobial use (AMU) were welcomed, and possible topics included:

 Knowledge, practices and technologies of animal disease management



🐉 frontiers Research Topics

 Labour conditions, professional and business models of animal health actors (farmers, veterinarians, livestock technicians)

- Economic and commercial strategies of stakeholders of the drug- and food-supply chains (pharmaceutical companies, agricultural cooperatives, feed mills, processors, retailers, etc.)
- Scientific and/or political controversies on antimicrobial resistance
- AMR policy (including One Health approaches) and regulation of the veterinary drug market
- Antimicrobial stewardship

More information and read the publication

Producing antibiotics and anti-fungals faster

Polyketides are natural products found in a variety of places, including bacteria, sea sponges and sediments. The compounds are often only present in tiny quantities, but they have powerful medicinal properties which the pharmaceutical industry has used to develop a wide range of medicines. Around a fifth of all pharmaceuticals are derived from polyketides.

The research team, based in the School of Chemistry at the University of Bristol, worked on a polyketide called Bahamaolide A, which acquired its name as it originates from bacteria cultured from a marine sediment at North Cat Cay in the Bahamas.



Using existing methods, it would normally take more than 20 different steps to construct it in a laboratory. The researchers found a new, improved way to combine the building blocks for the molecule so it could be made in just 14 steps.

The breakthrough marks the culmination of a five-year research project, which has finally cracked how to reconstruct in a laboratory this particularly complex molecule.

Aiken SG *et al*. (2022). Iterative synthesis of 1,3polyboronic esters with high stereocontrol and application to the synthesis of bahamaolide A. *Nature Chemistry*.

Respiratory disease in Bristol during the pandemic

The emergence of COVID-19 and public health measures implemented to reduce SARS-CoV-2 infections have both affected acute lower respiratory tract disease (aLRTD) epidemiology and incidence trends. The severity of COVID-19 and non-SARS-CoV-2 aL-RTD during this period have not been compared in detail.

The research team conducted a prospective cohort study of adults age ≥18 years admitted to either of two acute care hospitals in Bristol from August 2020 to November 2021. 12,557 adult aLRTD hospitalisations occurred: 10,087 were associated with infection (pneumonia or nonpneumonic lower respiratory tract infection, 2161 with no infective cause, with 306 providing a minimal surveillance dataset. Confirmed SARS-CoV-2 infection accounted for 32% of respiratory infections.

Data showed that while COVID-19 disease was a large component of total aLRTD during this pandemic period, non- SARS-CoV-2 infection still caused the majority of respiratory infection hospitalisations. COVID-19 disease showed significant temporal fluctuations in frequency, which were less apparent in non-SARS-CoV-2 infection. Despite public health interventions to reduce respiratory infection, disease incidence remains high.

Hyams C et al. (2022). Incidence of community acquired lower respiratory tract disease in Bristol, UK during the COVID-19 pandemic: A prospective cohort study. The Lancet Regional Health - Europe.

Page 12

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

Cancer Research UK

Cancer immunology project awards

Closing date: 19 January 2023 Award amount: £300,000

These aim to catalyse research and build the UK's research base in cancer immunology by funding immunologists from non-cancer fields. Proposals should address any area of immunological research, providing the cancer relevance is clearly articulated in the proposal, including the following key areas: cellular and molecular immunology; inflammation, allergy, transplantation and autoimmunity; immune response to infection.

CARB-X

Closing date: 30 January 2023

Award amount: £300,000

This supports research into the development of oral therapeutics, vaccines for neonatal sepsis, and gonorrhea products.

British Infection Association Travel awards

Closing date: 30 January 2023

Award amount: £300,000

These support travel to major national or international meetings, in particular to the American Society for Microbiology, the Interscience Conference of Antimicrobial Agents and Chemotherapy, the Infectious Diseases Society of America and the European Congress of Clinical Microbiology and Infectious Diseases meetings, and enable to present original research where an abstract has already been accepted.

British Infection Association Early Career Research grant

Closing date: 31 January 2023

Award amount: £300,000

These awards flexibly provide consumables and/or salary costs for trainees pre-PhD undertaking an infection-related research project in an academic centre in the UK or Ireland. The scheme prioritises those without research salary support to generate preliminary data with the intention of taking the work forward towards a higher degree. It is expected that this would enable the successful candidate to take time out of their clinical training, for example as a block of up to 3 months or spread part-time over part/all of the award period in preparation for a fellowship application.

National Institutes of Health, USA

Enhancement or Sustainment of Data Science Tools for Infectious and Immune-Mediated diseases (U24 Clinical Trial Not Allowed)

Closing date: 17 February 2023

Award amount: USD \$600,000

The purpose of this Funding Opportunity Announcement (FOA) is to solicit applications for the enhancement and/or sustainment of high-value data science research software to improve the acquisition, management, analysis, visualization, and dissemination of data and knowledge across the immune-mediated, and infectious-disease research continuum, aligned with the research mission of NIAID. This includes infectious diseases, emerging infections, or immune-mediated diseases that include allergy, autoimmunity, or immune reactions associated with transplantation.

Horizon Europe: Global Challenges and European Industrial Competitiveness HORIZON-HLTH-2023-DISEASE-03 - tackling diseases

Closing date: 13 April 2023

Award amount: €8 million

This supports proposals that set out a credible pathway to contributing to tackling diseases and reducing disease burden. Funding is available under the following topics: novel approaches for palliative and end-of life care for non-cancer patients; interventions in city environments to reduce risk of non-communicable disease; pandemic preparedness and response, broad spectrum anti-viral therapeutics for infectious diseases with epidemic potential; pandemic preparedness and response, sustaining established coordination mechanisms for European adaptive platform trials and for cohort networks; towards structuring brain health research in Europe; relationship between infections and noncommunicable diseases; pandemic preparedness and response, understanding vaccine induced-immunity; pandemic preparedness and response: Immunogenicity of viral proteins of viruses with epidemic and pandemic potential.

THIS ISSUE'S FEATURED ARTICLE

The free fatty acid–binding pocket is a conserved hallmark in pathogenic β-coronavirus spike proteins from SARS-CoV to Omicron

Toelzer C, Gupta K, Yadav SKN, Hodgson L et al. (2022). Science Advances.

In this new study, an international team, led by Bristol, scrutinised the spike glycoproteins decorating all coronaviruses. They reveal that a tailor-made pocket feature in the SARS-CoV-2 spike protein, first discovered in 2020, is present in all deadly coronaviruses, including MERS and Omicron. In striking contrast, the pocket feature is not present in coronaviruses which cause mild infection with cold-like symptoms.

The team say their findings suggest that the pocket, which binds a small molecule, linoleic acid—an essential fatty acid indispensable for many cellular functions including inflammation and maintaining cell membranes in the lungs so that we can breathe properly—could now be exploited to treat all deadly coronaviruses, at the same time rendering them vulnerable to a linoleic acid-based treat-



ment targeting this pocket.

Abstract: As coronavirus disease 2019 (COVID-19) persists, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern (VOCs) emerge, accumulating spike (S) glycoprotein mutations. S receptor binding domain (RBD) comprises a free fatty acid (FFA)–binding pocket. FFA binding stabilizes a locked S conformation, interfering with virus infectivity. We provide evidence that the pocket is conserved in pathogenic β -coronaviruses (β -CoVs) infecting humans. SARS-CoV, MERS-CoV, SARS-CoV-2, and VOCs bind the essential FFA linoleic acid (LA), while binding is abolished by one mutation in common cold–causing HCoV-HKU1. In the SARS-CoV S structure, LA stabilizes the locked conformation, while the open, infectious conformation is devoid of

LA. Electron tomography of SARS-CoV-2–infected cells reveals that LA treatment inhibits viral replication, resulting in fewer deformed virions. Our results establish FFA binding as a hallmark of pathogenic β -CoV infection and replication, setting the stage for FFA-based antiviral strategies to overcome COVID-19.

Image: Spike glycoprotein structure of SARS-CoV, the coronavirus causing the 2002 outbreak. When linoleic acid is bound, the structure is locked in a non-infectious form. The cryo-EM density, calculated by cloud computing, is shown (left) along with the protein structure (middle). Linoleic acid molecules are coloured in orange. A zoom-in of the pocket (boxed), conserved in all deadly coronaviruses, is shown.

© Christiane Schaffitzel and Christine Toelzer, University of Bristol

CONTACTS

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

Co-Chair (non-clinical): Co-Chairs (clinical):

Angela Nobbs - Senior Lecturer in Oral Microbiology Julia Colston - Consultant in Infection Ed Moran - Consultant in Infectious Diseases

- Borko Amulic Senior Research Fellow in Immunology
- Matthew Avison Professor of Molecular Bacteriology
- Charles Beck Consultant Epidemiologist & Head of Team, Field Service South West, National Infection Service, UK Health Security Agency
- Philip Bright Clinical Immunologist, North Bristol NHS Trust
- 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 Associate Professor in Cardiology
- Anna Long Senior Research Associate (Diabetes UK RD Lawrence Fellow)
- Jamie Mann Senior Lecturer in Vaccinology & Immunotherapy
- Adrian Mulholland Professor of Chemistry
- Laura Peachey Lecturer in Veterinary Parasitology
- Annela Seddon Director of the Bristol Centre for Functional Nanomaterials
- Luca Shytaj Lecturer in Virology
- Sandra Spencer Research Development Associate for the Faculty of Life Sciences
- Peter Vickerman Professor of Infectious Disease Modelling
- Richard Wall Professor of Zoology
- Linda Woolridge Chair in Translational Immunology
- Catherine Brown Network Administrator

The content of this newsletter is not the intellectual property of the Network, but rather an amalgamation of information obtained through a variety of sources including our community members; research groups such as 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



Subscribe to the Elizabeth Blackwell Institute newsletter Subscribe to the Infection and Immunity mailing list