# **I&I NETWORK NEWSLETTER**



# 2022 - ISSUE 3



This University of Bristol-led study, funded and conducted in collaboration with Pfizer Inc., as part of AvonCAP, is the first to compare the number of hospitalisations from respiratory disease infections caused by COVID-19 and non-SARS-CoV-2 infections.

Using data from 135,014 hospitalisations from two large hospitals in Bristol between August 2020 and November 2021, researchers identified 12,557 admissions attributable to acute Lower Respiratory Tract Disease (aLRTD) with

# Increase in respiratory infections predicted

patients admitted with signs or symptoms of respiratory infections including cough, fever,



pleurisy, or a clinical or radiological aLRTD diagnosis. Of these, 12,248 (98%) patients, comprising mainly older adults, consented to participate in the study. Following further analysis, the team show that of the 12,248 aLRTD hospitalisations, 55% were due to infection with no evidence of SARS-CoV-2, while confirmed SARS-CoV-2 infection only accounted for 26% of respiratory infections. The remaining 17% were due to infection with no infective cause.

Finn A 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

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# **EVENTS**

#### Development of animal models to address key paradigms in dengue research

8 September 2022, 13.00 - 14.00, Professor Sylvie Alonso (National University of Singapore), C42 Biomedical Sciences Building (with hybrid option to join virtually)

#### State of the nation & lessons for pandemic preparedness

8 September 2022, 13.00 - 14.00, Dr Susan Hopkins, CBE (Chief Medical Advisor, UK Health Security Agency), online

Immunomodulation Updates 9 September 2022, 9.00 - 16.30, Hallam Conference Centre, 44 Hallam Street, London W1W 6JJ

**Life at Nature Genetics: what we do, how scientific publishing works, and how I got here** 9 September 2022, 12.00 - 13.00, Dr Michael Fletcher (Editor, Nature Genetics journal), OS6 Oakfield House and online

Let's Talk Trials 12 September 2022, 9.00 - 16.00, Business Centre Meeting Room 3, Whitefriars, Bristol, BS1 2NT

NIHR/EPSRC Systems Engineering Innovation hubs for multiple long-term conditions information webinar 12 September 2022, 15.00 - 17.00, online

Sepsis in the Digital Age 13 September 2022, 12.00 - 13.00, online

MRC New Investigator Research Grant (NIRG) information webinar 13 September 2022, 14.00 - 15.30, online

**EBI Global Public Health Strand Final Event** 14 September 2022, 15.00 - 18.00, Room 7G1, 7 Priory Road, Bristol BS8 1TZ

South West Sexual Health Conference 15 September 2022, 9.30 - 16.30, Taunton Racecourse Conference Centre, B3170 Taunton TA3 7BL

**British Association for Lung Research 2022 summer meeting, From bench to breathing: The Ins and Outs of the Lungs – cell science to saturations across the world** 20 September 2022, 9.00 - 17.00, The Spine, Liverpool

UKI2S – Translating complex science into successful global companies 1 September 2022, 13.00 - 14.00, Hassan Mahmudul and Oliver Sexton, C42 Biomedical Sciences, University of Bristol

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

# NEWS

# Feeding dogs raw meat increases antibiotic resistance

Two studies led by a team at the University of Bristol have found dogs who are fed on a diet of raw meat were more

likely to excrete antibiotic-resistant bacteria *Escherichia coli* in their faeces. Previous research has shown

the potential for bacteria to be shared between dogs and their human owners through everyday interaction, leading researchers to suggest that raw feeding is not the safest dietary choice, and that, if chosen, owners should take extra precautions when handling raw meat and be especially careful to clean up after their dog. Both studies, which



used data from different dogs, demonstrate that dogs may excrete resistant bacteria regardless of age

or length of time they are fed raw meat. The environment a dog lives in also played a part; raw feeding was a strong risk factor for dogs living in the countryside, while in citydwelling dogs, risk factors were much more complicated, probably reflecting the variety of lifestyles and exposures among city dogs.

Sealey J *et al.* (2022). Molecular ecology and risk factors for third-generation cephalosporin-resistant Escherichia coli carriage by dogs living in urban and nearby rural settings. *Journal of Antimicrobial Chemotherapy.* 

Mounsey O *et al.* (2022). Evidence that faecal carriage of resistant Escherichia coli by 16 -week-old dogs in the United Kingdom is associated with raw feeding. *One Health.* 

# Animations on using flash glucose monitoring

Two new animations from the National Institute for Health and Care Research (NIHR) Bristol Biomedical Research Centre (BRC) report the views and experiences of young people (from 8 to 17 years old) using flash monitoring for type 1 diabetes.

The\_FLASH (Glucose Monitoring for Young People with Diabetes) study aims to find out if a sensor worn on the skin of the upper arm can help young people to manage their diabetes better. It is supported by the NIHR Research for Patient Benefit programme.



Prof Jenny Ingram (Bristol Medical School), Dr Rebecca Kandiyali (Warwick University) and the FLASH team created two short, animated videos showcasing how children and young people felt about using the sensor. The videos - aimed at 8–12-year-olds and 13–17year-olds - use quotes provided by children and young people, who took part in the study, to illustrate the impact that flash monitoring had on their everyday lives.

Watch the videos:

- https://youtu.be/ gN4cVU46EvI
- https://youtu.be/ WkEzMMHoNws

Prof Helen Lambert (Bristol Medical School) is among 40 outstanding social scientists who have been conferred to the Academy this autumn.

Prof Lambert's work uses ethnographic, interdisciplinary, and historical approaches to transform understanding of key public health issues including antimicrobial resistance (AMR), infectious diseases including COVID-19 and HIV, gender violence, and suicide preven-

# Fellow of the Academy of Social Sciences

tion. Her longstanding research in India on medical plurality and treatmentseeking focuses on subaltern therapeutic traditions and inequalities in access to care. As UK ESRC Research Champion for AMR (2015-17), she led initiatives to highlight the role of the social sciences in tackling AMR and build crossdisciplinary research capacity. She currently leads STAR-China, a Newton Fundsupported UK-China AMR Partnerships Hub on Strategies to reduce the burden of antibiotic resistance in China, and the social science workstream of ResPharm, a UK-India study on the impact of pharmaceutical waste on AMR in the environment and local community. She has served on WHO's Strategic Technical Advisory Group for AMR and recently completed a two-year secondment to UK **Research and Innovation** (UKRI) as Challenge Leader for UKRI's Global Health portfolio. Read more

# New Clinical co-Leads for the I&I Network

Having completed his threeyear term of office, clinical immunologist Dr Phil Bright has stepped down as co-Lead of the Infection and Immunity Research Network. We are very grateful to Phil for his guidance and commitment during his tenure. We are delighted to confirm that he will remain as a member of the steering group over the coming months to allow the incoming co-Leads to bed in.

The Network warmly welcomes Drs Julia Colston (pictured) and Ed Moran as new clinical co-Leads.

Julia is a Consultant in Infection primarily based at North Bristol NHS Trust (NBT), but she also works through University Hospitals Bristol and Weston NHS Foundation Trust (UHBW), primarily on the Weston site. She is both a



Medical Microbiologist and an Infectious Diseases Consultant and has paired clinical training with academic roles throughout her career. Ed is a Consultant in Infection Disease and is Clinical Lead for Infectious Disease at Southmead Hospital where he and his team deliver clinics in tuberculosis, HIV and general infection. He is very active in research, recruiting to national studies, vaccine trials, and partnering with local researchers to answer questions of interest.

Both Julia and Ed are keen to continue developing an open environment that fosters collaboration and crossfertilisation between scientists and clinicians.

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### Funding successes: Part 1 & other awards

Prof Ann Pullen FRSB (School of Cellular and Molecular

Medicine, pictured) was elected as a Fellow by the Royal Society of Biology's Council. Fellows of the Royal Society of Biology (RSB) have achieved distinction

in the fields of biological research, teaching or the application of biology. Fellowship is the most prestigious grade of RSB membership. teaches to undergraduate students and postgraduate



of Life Sciences.

Dr Lucia Marucci (Dept of Engineering Mathematics) received £63,119 from the Biotechnology and Biological Sciences Research Coun**cil** for *Mind the Gap: AI-Augmented Cell-Free Systems for In-Cell Predictions,* starting June '22 for one year.

The **British Heart Foundation** has awarded Dr Sarah Smith (Bristol Medical School) £192.952 for Validation of novel LincRNAs with preventative roles in adverse cardiac fibrosis, starting Nov '22 for two and a half years.

Ann is an immunologist who

# Pfizer and AZ vaccines protection against severe COVID

Researchers from Bristol Medical School, Oxford University and the London School of Hygiene and Tropical Medicine sought to investigate how quickly vaccine effectiveness waned over time in adults without prior SARS-CoV-2 infection and who received two doses of BNT162b2 (Pfizer-BioNTech) or ChAdOx1 (AstraZeneca) COVID-19 vaccine compared with unvaccinated individuals.

Rates of COVID-19 hospital admission and COVID-19 death were substantially lower among vaccinated than unvaccinated adults up to six months after their second dose. Vaccine effectiveness against these events was found to be at least 80% for BNT162b2, and at least 75%



for ChAdOx1. However, waning vaccine effectiveness against infection with SARS-CoV-2 meant that rates in vaccinated individuals were similar to or higher than in unvaccinated individuals by six months after the second dose. Although they found that protection against severe COVID-19 provided by two doses of vaccine wanes over time, the very high initial protection means that, despite waning, protection remains high six months after the second dose. This finding was consistent across all adults, including older adults and those who are at risk of severe COVID-19.

Horne E *et al.* (2022). Waning effectiveness of BNT162b2 and ChAdOx1 covid-19 vaccines over six months since second dose: OpenSAFELY cohort study using linked electronic health records. *The BMJ Open*.

# **Bristol Centre for Engineering Biology funded projects**

Launched in January 2022, the Bristol Centre for Engineering Biology (BrisEngBio) will build on Bristol's success in synthetic biology and accelerate translation of its pioneering research to address global challenges and boost the UK's bioeconomy. By applying engineering principles to living systems, engineering biology aims to solve some of the world's most pressing challenges in health, food security, and the environment. BrisEngBio brings together scientists from a wide range of disciplines – from biology and chemistry to data science and systems engineering.

The Centre has funded four Discovery and eight Proof of Concept Projects to facilitate the translation of discovery synthetic biology research into new therapeutics, diagnostics and materials. More details about these projects will be available soon, but some of the funded projects include:

#### Discovery:

Ribosome engineering and CRISPR tools for optimising antimicrobial natural-product production, PI: Dr Paul Curnow (School of Biochemistry)

#### Proof of concept:

MEGAcryoFFAR: Megabody in vitro selection, evolution and engineering for cryo-EM structure analysis of FFAR1-bound lung fibrosis drugs to treat long COVID, PI: Prof Christiane Berger-Schaffitzel (School of Biochemistry), Co-I: Adrian Mulholland, Christopher Woods, Rich Pitts.

A versatile toolkit to functionalise magnetic nanoparticles for labelling and capture of bacteria, PI: Prof Jim Spencer (School of Cellular and Molecular Medicine), Co-Is: Tomasso Garfagnini, Carmen Galan, Annela Seddon.

# Next generation of research leaders

Dr Emma Anderson, Dr Rachel James, Dr Peter Dunne and Dr Sinead English have been selected for their work on dementia, climate change,

respecting trans and non-binary identities and nutrition and immunity in pregnancy, respectively.

#### Dr Sinead Eng-

lish (pictured) of the School of Biological Sciences is aiming to understand consequences for mothers and offspring of mounting an immune response in pregnancy, and how these depend on maternal nutritional state. She explained: "Pregnancy is a critical period determining health outcomes for mothers and



disease through to lack of access to nutrition. My project will take an innovative approach, bringing insights from evolutionary biology, to understand how these challenges interact to determine maternal and child health. My team will tackle these questions using mathematical models, experiments on unusual model insects - flies and cockroaches which give birth to live young, and analyses of cross-cultural cohort studies, including the Avon Longitudinal Study of Parents and Children (UK) and from the Early Nutrition and Immune Development trial (The Gambia)."

Read about the other awards

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# Ventilation to prevent spread of COVID-19 indoors

A review of 18 existing studies led by the University of Bristol and the UK Health Security Agency (UKHSA) indi-

cates that airborne transmission of the SARS-CoV-2 virus from an infectious individual to others located more

than two metres away can happen in different indoor non-healthcare settings. They reviewed studies on the subject published between Jan 2020 - Jan 2022, focusing



on observational studies of COVID outbreaks around the world. These outbreaks happened within various commu-

> nity settings including flats in apartment blocks, quarantine hotels, restaurants, buses, a food processing factory, a

courtroom, a fitness facility, and during singing events. The concluded that long distance airborne transmission was likely to have occurred for some or all transmission

events in 16 out of 18 studies. It was unclear in the other two studies. Researchers stress that the evidence from these studies was deemed to be of very low certainty, and say continued investigation into the potential for long distance airborne transmission of SARS-CoV-2 is needed.

Paper: Duval D et al. (2022). Long distance airborne transmission of SARS-CoV-2: rapid systematic review. BMJ Editorial: Dancer SJ (2022). Airborne SARS-CoV-2. BMJ.

Prof Ingeborg Hers (School of Physiology, Pharmacology and Neuroscience) received £52, 500 from Bio-Techne / Tocris Cookson Ltd for Generation of novel PROTAC tools for targeting protein kinase degradation in human platelets, starting Sep 2022 for four vears.

Wellcome has awarded £15,290 to Dr Ore Francis

(Bristol Veterinary School, pictured right) to pursue Further development of standardised virus pseudotype assay to



quantify SARS-CoV-2 neutralising antibodies in saliva and

serum; this is an extension of his original funding until October 2022.

An award of £44,917 was made to Prof Peter Vickerman (Bristol Medical School) from the World Health Organiza**tion** for his project looking at Hepatitis C which started in June 2022 and is expected to complete in Feb 2023.

The Southmead Hospital **Charity** awarded Dr **Barney** Hole (Bristol Medical School) £18,600 for How many UK adults developed kidney failure since the year 2000?, begun in May 2022

and completing in Dec 2022.

# Funding successes: Part 2

Dr Borko Amulic (School of Cellular and Molecular Medicine) received £8,778 from the Medical Research Council for Regulation of neurophil functions by cell proteins, started in June 2022 and completing in Aug 2023.

Dr Jo Kesten (Bristol Medical School, pictured right) was awarded £46,628 from University Hospitals Bristol and Weston NHS Foundation Trust for Self testing HIV and STI vend-

ing machines, which began in April 2022 and will run until March 2023.



# **WAAVP-Network for Africa**

Through his role with the World Association for the Advancement of Veterinary Parasitology (WAAVP), Prof Richard Wall (School of Biological This will be supported by the Bill and Melinda Gates Foundation over a 5-year period. The first meeting of the steering group took place in June

2022 in Kampala,

Sciences) is working with the Bill & Melinda Gates Foundation (BMGF) to establish the 'WAAVP-Network for Africa', as a sustainable network of pan-African scien-

tists, researchers, farmers, and policy makers to address critical challenges in veterinary parasitology in Africa.



Richard has commented "This much-needed initiative will provide the collaborative, multidisciplinary ap-

proach essential for tackling parasitic disease in livestock, companion animals and, in the case of zoonotic disease, humans. It will help to reduce animal suffering and contribute to improved food security in Africa."

Richard is a veterinary entomologist working on a wide range of ectoparasite systems, whose current projects look primarily at ticks and tickborne pathogens and the environmental impacts of veterinary anti-parasitic treatments.



# Infectivity of airborne SARS-CoV-2

The SARS-CoV-2 virus can lose 90% of infectivity when in aerosol particles within 20 minutes, according to new University of Bristol findings. The study is the first to inves-

tigate the decrease in infectivity of SARS-CoV-2 in aerosol particles over periods from seconds to a few

minutes. The aim of the study was to explore the process that could change viral infectivity over short timescales following exhalation. Using a novel instrument



generated airborne particles and examine how temperature and humidity drive changes in infectivity, from timescales span-

ning five seconds to 20 minutes. The same experiment was carried out comparing four different SARS-CoV-2 variants, including Alpha and Beta. Results from the team's experiments found a significant loss in infectivity within the first ten minutes of aerosol particle generation that is strongly dependent on the environmental relative humidity, but not temperature. This effect did not alter across the different SARS-CoV-2 variants.

Reid JP, Davidson AD *et al*. (2022). The dynamics of SARS-CoV-2 infectivity with changes in aerosol microenvironment. *PNAS*.

Image: SARS-CoV-2 laboratory generated airborne particles using CELEBS

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The University of Bristol has launched Bristol Innovations, a new initiative that will combine its far-reaching research expertise with the industry know-how of global partners, leading to progressive sectorwide and multidisciplinary discoveries.

Bristol Innovations is a virtual network designed to increase opportunities for University academics, researchers and entrepreneurial students to collaborate with third party stakeholders to translate research for real-world purposes. It launches at a time when the UK government has pledged to turn the UK into a global innovation hub.



Supported by the Bristol Grid – a University of Bristol digital hub for entrepreneurial activities – the network will enhance the University's efforts

#### **Bristol Innovations**

to apply its knowledge and expertise for the benefit of millions of people across the world. This includes working with industry partners to identify and respond to social and economic needs; exploring new spin-out and start-up opportunities; investing in more resources for business development; offering more consultancy and licencing opportunities; and working with third parties through knowledge exchange, public engagement and research commercialisation.

### Newborn illness and mortality throughout childhood

New evidence has found a link between poor health as a newborn and mortality up to the age of ten. The new report from England's National Child Mortality Database (NCMD), led by the University of Bristol, shows of the 4,829 children aged ten and under who died in England between 2019 and 2021, 72 per cent were found to have required additional care in the neonatal period.

The report shows the dramatic impact of perinatal events – being born prematurely, or suffering an injury or infection shortly after birth – on mortality in the first year of life, where 83 per cent of deaths were linked to additional care requirements after birth. But more surprisingly, it shows for the first time how that risk persists throughout childhood; although they only



make up 15% of the population, these children account for 38% of deaths aged 1 to 4 years, and 27% of deaths aged five to nine years.

The publication also examines

the factors that could be changed to improve the situation, and presents recommendations for policymakers and health officials. Smoking during pregnancy, lack of involve-

ment from appropriate services and maternal obesity were the three most prominent modifiable factors identified by child death review, and the report authors have called for current interventions to be strengthened and new measures to be deployed to tackle these issues.

Odd D *et al.* (2022). The contribution of newborn health to child mortality across England. National Child Mortality Database.

# New DNA repair-kit fixes hereditary disease in cells

Genetic mutations which cause a debilitating hereditary kidney disease affecting children and young adults have been fixed in patientcialised kidney cells and essential for kidney function. Faulty podocin, however, remains stuck inside the cell and never makes it to the sur-

derived kidney cells using a potentially gamechanging DNA repair-kit. In this new study, the international team describe how they creat-

ed a DNA repair vehicle to genetically fix faulty podocin, a common genetic cause of inheritable Steroid Resistant Nephrotic Syndrome (SRNS). Podocin is a protein normally located on the surface of spe-



face, terminally damaging the podocytes. Since the disease cannot be cured with medications, gene therapy which repairs the ge-

netic mutations causing the faulty podocin offers hope for patients.

Typically, human viruses have been utilised in gene therapy applications to carry out genetic repairs; they are used as a 'Trojan Horse' to enter cells carrying the errors. However, they are restricted in space, which means they can't carry much cargo; namely, the DNA repair kit. The team reengineered a harmless insect baculovirus which can carry much more.

Aulicino F *et al*. Highly efficient CRISPR-mediated large DNA docking and multiplexed prime editing using a single baculovirus. *Nucleic Acids Research*.

Image: Patient-derived podocyte kidney cells repaired with baculovirus-vectored approach. Podocin (coloured in green) is restored to the cell surface as in healthy podocytes.

# Pinpointing those most at risk of Long COVID

A national study suggests that those at greatest risk of long COVID are women, those aged 50-60, people with poor pre-pandemic mental health and those in poor general health, such as anyone with asthma or who is overweight.

Around two million people in the UK are affected by long COVID (ONS data, 1 May 2022), enduring symptoms for 12 weeks or more after they've been infected. Whilst the syndrome has been widely reported, the frequency and risk factors for the condition are not well understood. In order to develop new treatments, Children of the 90s –



along with nine other population-based cohort studies – has helped researchers to understand what causes some people to suffer the condition more than others. In parallel, researchers also utilised data from electronic health records collected by Spring 2021 for 1.1 million individuals diagnosed with COVID-19. The research is part of the UKRI-NIHR funded multi-institution CONVALESCENCE study, which is run by University College London and is the first of its kind to look at long COVID.

Thompson EJ *et al.* (2022). Long COVID burden and risk factors in 10 UK longitudinal studies and electronic health records. *Nature Communications.* 

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# **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

#### European Society of Clinical Microbiology and Infectious Diseases

Young investigator awards for research in clinical microbiology and infectious diseases

Closing date: 12 October 2022 Award amount: €5,000

These acknowledge excellence in research and stimulate further research at the highest scientific level. Research must be based on laboratory investigations, clinical trials or studies, animal studies or a combination thereof. Only self-nominations are accepted. Applicants must have a valid ESCMID membership.

**Biotechnology and Biological Sciences Research Council** UKRI-Defra one health approach to vector borne diseases

Closing date: 27 October 2022 Award amount: £1,250,000

This aims to forecast, understand, mitigate and avoid vector (arthropod) borne disease (VBD) threats to the UK, in response to climate, environmental and land-use changes both now and in the future. Projects must take a one health approach encompassing both multidisciplinary research and multisectoral policy. The programme has two components as follows:

- research consortia grants, supporting interdisciplinary consortia in undertaking projects with a full economic cost of up to £1.25 million;
- VBD data hub, which supports the development of shared data infrastructure that brings together, and where suitable, links VBD and associated data, with funding worth up to £625,000.

#### **Versus Arthritis**

#### Priorities 2023: Accelerating diagnosis and treatment

Closing date: 9 November 2022

Award amount: £800,000

This call for applications for research funding focusses on two of the priority areas:

- *Early detection and prevention*: spotting the biological signatures of arthritis early to maximise the opportunities for timely intervention and preventing it from getting worse.
- *Targeted treatments*: taking the guesswork out of treatment by increasing effective, reliable and timely drug and non-drug solutions to reduce, manage or cure disease.

#### **National Science Foundation**

Ecology and evolution of infectious diseases

Closing date: 16 November 2022 Award amount: USD 2,500,000

This 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. Research may be on zoonotic, environmentally-borne, vector-borne, or enteric pathogens of either terrestrial or aquatic systems and organisms, at any scale from specific pathogens to inclusive environmental systems. 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.

#### **European Society for Paediatric Infectious Diseases**

Fellowship awards

Closing date: 1 December 2022 Award amount: €100,000

These support basic or clinical research that utilises advanced techniques and methods to improve the health of children through the prevention or management of infectious diseases. Fellowships can take place outside or within the applicant's institution and country. You must be a ESPID member to apply.

International Union of Immunological Societies Menarini prize for an outstanding woman immunologist

Closing date: 1 January 2023

Award amount: USD 40,000

This recognises women immunologists and their research accomplishments.

# THIS ISSUE'S FEATURED ARTICLE

#### ESCPE-1 mediates retrograde endosomal sorting of the SARS-CoV-2 host factor Neuropilin-1

Simonetti B, Daly JL et al. (2022). PNAS.

#### Novel host cell pathway hijacked during COVID-19 infection

An international team of scientists, led by the University of Bristol, has been investigating how the SARS-CoV-2 virus manipulates host proteins to penetrate into human cells. After identifying Neuropilin-1 (NRP1) as a host factor for SARS-CoV-2 infection, new findings describe how the coronavirus subverts a host cell pathway in order to infect human cells.

NRP1 is a dynamic receptor that senses the microscopic cellular environment through the recognition of proteins containing specific neuropilin-binding sequences (ligands). By mimicking this neuropilin-binding sequence, SARS-CoV-2 is able to subvert this receptor to enhance its entry and infection of human cells.



DAPI GFP-Nrp1 aSNX1 aCI-MPR



The function of this pathway is still not completely clear, but the team found that using gene editing to remove ESCPE-1 from human cells effectively blocked SARS-CoV-2 infection by around 50%, suggesting that this process is beneficially hijacked by the virus during the infection process.

This study represents an advance in the understanding of the pandemic coronavirus, and how it subverts host biology in order to infect cells. The identification of this pathway used by SARS-CoV-2 opens avenues for designing therapeutic interventions that can prevent ESCPE-1 and NRP1 from associating with the Spike protein to reduce infection.

Image: A proteomic screen for ESCPE-1 retrograde cargoes identifies NRP1. ((E and F) HeLa cells expressing GFP-Nrp1 were costained with anti-SNX6 and anti-TGN46 antibodies (E) or anti-SNX1 and anti-CI-MPR antibodies (F).

Watch the video explaining the research findings

# 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
- 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
- Sandra Spencer Research Development Associate for the Faculty of Life Sciences
- Peter Vickerman Professor of Infectious Disease Modelling
- Linda Woolridge Chair in Translational Immunology
- Catherine Brown Network Administrator

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

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

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