I&I NETWORK NEWSLETTER



Elizabeth Blackwell Institute for Health Research

The new **Bristol AMR** interdisciplinary **Research Strand** will build on the Engineering and Physical Sciences Research Council -funded *BristolBridge* network which helped to 'bridge the gaps' between the physical sciences, engineering and biomedical science communities to find new solutions for tackling antimicrobial resistance (AMR).

Supported by the Elizabeth Blackwell Institute for Health Research, Bristol AMR is led by a cross-faculty committee with representatives from the Faculties of Life Sciences, Health Sciences, Science, Engineering, Arts and Social Sciences and Law to forge new links via networking events and to create new collaborative pump-priming AMR projects. The network will further help Bristol's interdisciplinary AMR research community to come together to compete for future large-scale funding, strengthening the University as a UK centre of excellence for interdisciplinary AMR research. It is being co-led by Profs Matthew Avison (School of Cellular and Molecular Medicine) and Adrian Mulholland (School of Chemistry).

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Bristol AMR

The Strand's formation is a recognition of the extraordinary success AMR research has had in winning funding from the UKRI Tackling AMR – A Cross-Council Initiative, a total of £7.4M since 2015. They are also receiving further strategic support from the University to fund two PhD studentships to join the Medical Research Council/Department of Healthfunded project to study AMR in Thailand, plus another share of institutional Global Challenges Research Fund for AMR activities. The Strand hosted its launch event on 14 November 2018. **Read more**

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IMMUNITY

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Uobristol Events

Public health and community-based support initiatives: the work of Health Integration Teams

14 January 2019, 12.30 - 13.45, The Writing Room, City Hall, College Green, BS1 5TR

What are funders looking for in a grant application? Reflections from the NIHR **Research for Patient Benefit panel**

15 January 2019, 12.00 - 13.00, Emma Dures (Associate Professor in Rheumatology and Self-Management, University of the West of England), Tutorial room F, Education & Research Centre, Upper Maudlin Street, Bristol BS2 8AE

T3 Technical Talk Time Seminar series 16 January 2019, 14.00 - 15.00

UHBristol Research Showcase 17 January 2019, 10.00 - 16.00, UHBristol, Upper Maudlin Street

Statistics Clinic 23 January 2019, 14.00 - 15.30, SM3 Mathematics Building

Use low dead space: Driving uptake of safer drug injecting equipment

24 January 2019, 18.00 - 19.30, The Kitchen, The Station, Silver Street, Bristol, BS1 2AG

Above & Beyond (A&B) and Research Capability Funding (RCF) grant writing workshop 5 February 2019, 12.30 - 13.30. Interview Room, Level 3, Education & Research Centre, Upper Maudlin Street, Bristol BS2 8AE

NIHR Bristol BRC's Qualitative Research Network: creating innovation, insight and impact 6 February 2019, 11.30 - 14.00, room OS6, Oakfield House, Oakfield Grove, Bristol, BS8 2BN

Pure drop-in session 6 February 2019, 13.00 - 15.00, Life Sciences foyer

Designing digital interventions to support physical activity for people with longterm conditions 6 February 2019, 13.00 - 14.00, Prof Lucy Yardley (University of Bristol), Room 7G1, 7 Priory Road, BS8 1TZ



An introduction to Open Research





NHS Foundation Trust

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University Hospitals Bristol

Bristol Health Partners

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UoB EVENTS

6 February 2019, 14.00 - 16.00, room 3.13, 35 Berkeley Square BS8 1JA

Above & Beyond (A&B) and Research Capability Funding (RCF) grant writing workshop 12 February 2019, 12.30 - 13.30, Interview Room, Level 3, Education & Research Centre, Upper Maudlin Street, Bristol BS2 8AE

Biomedical Sciences Film club 12 February 2019, 18.15 - 20.00, E29 Biomedical Sciences Building

Above & Beyond (A&B) and Research Capability Funding (RCF) grant writing workshop 13 February 2019, 8.00 - 9.00, Interview Room, Level 3, Education & Research Centre, Upper Maudlin Street, Bristol BS2 8AE

Clinical Research Start-up and Support (CReSS) workshop

19 February 2019, 12.30 - 13.30, Anna Davies (Senior Research Associate, Burns Care Research, University of Bristol), Tutorial room 6, Education & Research Centre, Upper Maudlin Street, Bristol BS2 8AE

Statistics Clinic 20 February 2019, 14.00 - 15.30, SM3 Mathematics Building

T3 Technical Talk Time Seminar series 20 February 2019, 14.00 - 15.00

Statistics Clinic 6 March 2019, 14.00 - 15.30, SM3 Mathematics Building

Biomedical Sciences Film club 12 March 2019, 18.15 - 20.00, E29 Biomedical Sciences Building

OTHER EVENTS

Next steps for combating antimicrobial resistance - funding, prevention and research priorities

6 February 2019, 9.00 - 13.00, Prof Dame Sally Davies (Chief Medical Officer, Department of Health and Social Care); Prof Alan Johnson (Public Health England); Dr Manica Balasegaram (Global Antibiotic Research and Development Partnership). Central London

Pumps and Pipes UK Conference 19 February 2019, 8.00 - 18.00, SPE Aberdeen

NIHR Health Protection Research Unit in Gastrointestinal Infections Annual Conference 2019 13 - 14 March 2019, Public Health England, Colindale, London, NW9 5EQ

SEE THE FULL EVENTS LISTING ON THE I&I WEBSITE

NEWS

Synthetic prototissue capable of synchronised beating

This first chemically programmed approach to producing an artificial tissue could be used to support failing living tissues and to cure specific diseases. The development of synthetic tissue which can mimic the ability of living cells to produce functions such as beating and chemical detoxification has, until now, remained a major synthetic biology challenge. A team, led by Prof Stephen Mann and Dr Pierangelo Gobbo (School of Chemistry) chemically programmed artificial synthetic cells (protocells) to communicate and interact with each other in a highly coordinated way.



Image shows a single cluster of artificial cells exhibiting a single beat-like oscillation as the temperature changed. Scale: 50μm. © Dr Pierangelo Gobbo

Read more

Funding successes: Part 1

From the **Medical Research Council** to Prof Helen Lambert (Bristol Medical School, Population Health Sciences) for the *China-UK AMR Partnership Hub*, £1.9M.

From **Innovate UK** to Dr Tristan Cogan (Bristol Veterinary School) for *Novel gene editing CRISPR guided vector technology to replace antibiotic use in farm animal production*, £145, 474 starting 1 Sep 2018 for 19 months.

From the British Small Animal Veterinary Association -Petsavers programme to Dr Melanie Hezzell (Bristol Veterinary School) for Associations between intramyocardial arteriosclerosis and myocardial fibrosis and disease severity in dogs with myxomatous mitral valve disease, £1,000 starting 1 Jan2019 for 8 months.

From the **Juvenile Diabetes Research Foundation** (JDRF) to Dr Kathleen Gillespie (Bristol Medical School, Translational Health Sciences) for *How do Slow Progressors to type 1 diabetes regulate their autoimmune response?*, £291,952 awarded 15 Nov 2018.

From **Genzyme Therapeutics** Limited to Dr Alastair Wilkins (Bristol Medical School, Translational Health Sciences) for *Exploring novel biomarkers to develop personalised therapeutic strategies for multiple sclerosis*, £253,711 starting 1 Dec 2018 for 3 years.

From the **Royal Society** to Prof Emma Raven (School of Chemistry) for *A structural framework for understanding Chagas disease*, £105,254 starting 1 Aug 2018 for 18 months.

From the **Medical Research Council** via the Elizabeth Blackwell Institute for Health Research, to Prof Moin Saleem (Bristol Medical School, Translational Health Sciences), an MRC Confidence in Concept award of £99,250 for the 13 month project *A pathway to full clinical development of the first drug to treat genetic forms of Nephrotic Syndrome* starting 1 Aug 2018. Thirty academics from the University of Bristol have been awarded Turing Fellowships and 10 projects have received funding on the first call launched in August 2018. The Fellows are drawn from a wide range of expertise across all six Faculties. The purpose of the Turing Fellowship is to allow University academic staff to develop collaborations with Turing partners, initiate new research projects and help set the research agenda for the Alan Turing Institute, the national

institute for data science and artificial intelligence.

Fellows include Dr Phillip Hamann, Clinical Lecturer in Rheumatology, and William Browne, Professor of Statistics. Examples of the ten funded projects include Prof Andrew Dowsey (Bristol Veterinary School), Creating an open research data platform from the world's most intensively monitored dairy farm for tackling One Health grand challenges and Dr Danielle Paul (Physiology, Pharmacol-

Turing Fellows announced

ogy and Neuroscience), Applying machine learning techniques to large Cryo-EM data sets. PROOF: Software for the identification of accessory PROteins On Filaments.

A full list of Fellows and projects can be found on the Jean Golding Institute for Data Science website.

Read more

The Alan Turing Institute

Zebrafish could help scientists understand the early stages of diseases such as osteoarthritis after spending time in hypergravity to investigate how their development is affected by increased loading conditions. Two postgraduate students from the Bristol Bone Biologists group, Elizabeth Lawrence (Dynamic Molecular Cell Biology, on the left), and Jessye Aggleton (Anthropology and Archaeology, pictured right), were one of two teams chosen to run

of two teams chosen to run their research with the European Space Agency Academy as part of their annual student hypergravity experiment campaign 'Spin Your Thesis!'.

Zebrafish gravitate to higher levels



The students used a Large Diameter Centrifuge (LDC), which ran for 48 hours, to see whether zebrafish develop normally in altered gravitational fields. The zebrafish larvae have returned to Bristol's Hammond Lab and the students will now study their joints and immune cells. They used hypergravity to simulate increased mechanical loading during a key time in joint development in zebrafish and will be looking at changes to the shape, structure and function of muscles, cartilage and

bone in the larvae to see what impact it has had on their development. The research will help in understanding the importance of mechanical loading and genetics during early life in the onset of diseases such as osteoarthritis.

Incarceration increases viral transmission in drug users

Injecting drug use, through the sharing of needles, syringes and other injecting equipment, is a primary route of transmission for both HIV and hepatitis C virus (HCV), blood-borne infections that cause considerable morbidity and mortality worldwide. New research has found among people who inject drugs, that recent incarceration was associated with an 81% and 62% increase in HIV and HCV acquisition risk, respectively.

The study is the first systematic review and metaanalysis to assess whether incarceration history, either recent incarceration or past incarceration, raises the risk of HIV or HCV infection among people who inject drugs (PWID). Findings provided strong evidence that recent incarceration increases HIV and HCV transmission risk.

This work is essential for understanding how the incarceration of PWID, and consequently, international drug policy, can contribute to increasing the burden of HIV and HCV among PWID. Hopefully this work will help guide future evidence-based drug policies and interventions to reduce this risk.

Stone J, Fraser H *et al.* (2018). Incarceration history and risk of HIV and hepatitis C virus acquisition among people who inject drugs: A systematic review and meta-analysis. *The Lancet Infectious Diseases*. Published online 28 October 2018.

Read more

Funding successes: Part 2

From the **Biotechnology and Biological Sciences Research Council**, collaborative grants totalling over £1.6M:

Prof Ian Collinson (School of Biochemistry) for *The bacterial secretosome* (3 years, 2 postdocs)

Prof David Stephens and Dr Laura Vuolo (Research Co-Investigator) for *The role of dynein-2 in building a functional cilium* (4 years, 2 postdocs)

Prof Mark Dillingham for Single molecule DNA repair by homologous recombination in *live bacterial cells* (collaboration with the University of Oxford).

From the **Medical Research Council** to Dr Colin Chu and Prof Andrew Dick (both Bristol Medical School, Translational Health Sciences) an MRC Confidence in Concept award, via the Elizabeth Blackwell Institute, for *Synthetic Ciliary Body Specific Promoter Design for Viral Gene Therapy for Glaucoma using CRISPR-Cas9*. £45,357 starting 1 Nov 2018 for 5 months. An MRC Confidence in Concept award also went to Dr Richard Lee (Bristol Medical School, Translational Health Sciences) of circa £50k for the project Selective Calcineurin Inhibition for the Treatment of Steroid Resistant Diseases.

A **Diabetes UK Fellowship** to Dr Anna Long (Bristol Medical School) £541,651 for an RD Lawrence Fellowship to investigate why some individuals who are at very high risk of developing type 1 diabetes appear to be relatively protected. **Read more**

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Dr Jessica Eddy (pictured) has recently been appointed as the NC3Rs Regional Programme Manager for univer-

sities under the GW4 alliance. Her role is to help us more closely implement 3Rs policies across our research and education agenda. Jess will be working with colleagues across the four universities to provide advice and

NC3Rs Regional Programme Manager

support for ongoing 3Rs initiatives, to assist in identifying new opportunities and to coordinate the sharing of best

practice.



Jess is happy to answer any NC3Rs or 3Rs queries you might have and can also provide advice on PPL applications and NC3Rs grant applications as

well as help with the NC3Rs **Experimental Design Assistant** tool, a web based application to guide animal researchers through the design of their experiments. Do get in touch with her with any questions you might have (jessica.eddy@nc3rs.org.uk) and please visit the NC3Rs page for more information on the organisation and the resources they provide.

Slides presented by Jessica on NC3R can be viewed in OneDrive.

Vet School postgrad on AMR PhD Training Programme

Liz Cresswell (pictured), who is studying for a PhD in Clinical Veterinary Science, is one of 18 students from 16 UK universities who through their research will contribute to the first ever national UKRI -funded cross-council research consortia, which is tackling antimicrobial resistance (AMR) on a global scale. This new PhD Training Programme is designed to help build a strong, active network of early career researchers by bringing together those who study microbiology, genetics and medicine with social scientists, vets, dentists, ecologists, environmental biologists, anthropologists, chemists and biomedical engineers.

Liz's research will focus on AMR in smallholding farms, which is the fastest growing sector of farming. She hopes to be able to identify the issues surrounding AMR in smallholdings and implement ways in which we can control disease and AMR transmission and spread in this population.

Liz will investigate the part smallholder farming may play in the development of antimicrobial resistance and transmission between animals and



compare this to current data being collected on dairy farms and within companion animal populations.

Modification of amino acids

A team in the School of Chemistry has invented a new way to modify amino acids by attaching a ring of carbon atoms at the very centre of the amino acid molecule.

The unusual reaction that introduces this new ring was previously of limited application, but the work showed that introducing new molecular structural features makes it compatible with a

much wider range of chemical structures than pre-



viously suspected. For example, it is now possible to add rings that also carry a whole range of other atoms around their periphery.

The reaction involves the migration of the ring from the nitrogen atom of the amino acid to a carbon atom, and because amino acids exist in two mirror image forms, importantly it retains a memory of the starting mirror image structure in the

> product. The chemistry is also very easy to carry out on large scale, making it potential

ly very valuable for the practical synthesis of new drug molecules. The work has allowed us to turn what was a scientific curiosity into a really practical new way of making an important new group of chemical building blocks. It will provide scientists with a whole new set of modified amino acid molecules for making new medicines or modified proteins, enabling advances in understanding natural biochemical systems or tackling disease.

Leonard D and Clayton J (2018). Asymmetric αarylation of amino acids. Na*ture*. 562, pp 105–109.

Study aims to reduce oral antibiotics for ear infections

Middle ear infections (acute otitis media, AOM), are common painful infections in children, for which there are up to three million treatment episodes in England and Wales each year. They are often treated with antibiotics by mouth, which can cause side effects like rashes, diarrhoea and vomiting, and their over-use contributes to the growing global health threat of antibiotic resistance. Researchers from the Universities of Bristol, Southampton, King's College London and Imperial College London, are

collaborating on a new study to investigate alternative treatments, which they hope will reduce unnecessary oral antibiotic use while relieving painful symptoms and reducing healthcare costs.

The Runny Ear Study (REST), funded by the National Institute for Health Research, will focus on children who have middle ear infections with discharge (AOMd), which occur in around 15% of cases, caused by a build-up of pressure in the middle ear which causes the ear drum to burst,

releasing pus. Children with AOMd have more pain, repeat episodes of illness and hearing problems. The team will compare three alternative treatment options: immediate antibiotics by mouth, immediate antibiotic eardrops, which have previously shown to be effective in children with grommets, and 'delayed' oral antibiotics, where parents are advised to wait to see if the child's infection improves without antibiotics.

Effective management of eczema often requires a combination of topical medications, and it can be frustrating for parents trying to liaise with GPs to manage their child's' symptoms. Dr Emma Le Roux (pictured) worked with Action Plans for Children with Eczema (APACHE) to develop a plan for childhood eczema that puts children first.

Using funding from the Elizabeth Blackwell Institute Clinical Primer Scheme, Dr Le

Action plan for childhood eczema

Roux has been working with APACHE to develop a Written Action Plan (WAP) - written, individualised care plans designed to support patient self -management. Initially, this involved contributing towards the quantitative sys-

tematic reviews of the evidence base for WAPs in primary care. This necessitated updating the literature search, screening and extracting data from papers and input into the final paper, which is now published. The project then identified potential pitfalls and ideas in a WAP for eczema for use by parents and clinicians in primary care in a series of interviews and focus groups. Emma led a



qualitative substudy investigating GPs confidence and experience in managing and treating children with eczema, published in 2018. Read more

Biomarker tool to enhance cancer immunotherapy targeting

New immunotherapies which help the immune system to recognise and destroy cancer cells are promising, but some patients don't respond to the new treatments. With the help of an Elizabeth Blackwell Institute Clinical Primer Scheme award, Emily Milodowski (pictured) has been developing a new tool as a step towards being able to identify people who can be helped by these new therapies.

Using flow cytometry, which suspends cells in a stream of fluid and passes them through electronic detection equipment, she has started to look at patterns of coinhibitory receptors on the surface of immune cells such as T lymphocytes to see if these could potentially be used as biomarkers to determine which patients will respond to the treatments for melanoma and which will not.

Using flow cytometry, I am able to study individual immune cells. I can label these cells with different antibodies, tagged with fluorescent markers, and identify the different combinations of receptors found on the surface of each cell. I have designed a new antibody panel to look at the expression of 16 different cell markers simultaneously. Over the course of the sixmonth project, I have been testing how different experimental conditions can affect how co-inhibitory receptors are expressed by Tlymphocytes.



Meet the 2018-19 Vice-Chancellor's Fellows

This year's Vice Chancellor's Fellows include:

Rachel Bennett

Using hydrodynamics and geometry to design bacteriaphobic surfaces



Rachel uses mathematical and physical approaches to understanding important mechanical effects in cells, with a particular interest in the fluid dynamics of swimming microorganisms and nuclear mechanics in cancer cells. Rachel's project will use mathematical and computational modelling to study how different surface geometries can be used to modify the hydrodynamic interactions between swimming bacteria and the surface, with the goal of designing a surface that repels swimming bacteria away from the surface. An important application of these surfaces is to indwelling medical devices to reduce the risk of bacterial infection.

Rebecca Richmond

From clustered behaviours to molecular mechanisms in chronic disease



epidemiology

Rebecca has been awarded the de Pass Vice-Chancellor's Fellowship for future leaders in translational populationbased genetic epidemiology. Her proposed research project aims to highlight the relative importance and interrelationships of several health behaviours for prioritisation in disease prevention strategies and to identify molecular pathways which could serve as therapeutic targets for intervention.

For the full list of Vice Chancellor's Fellows, go to the University's Fellowship pages

Transforming the treatment of diabetes

A team from the University's School of Chemistry, led by Prof Anthony Davis in conjunction with spin-out company Ziylo, have developed an innovative technology platform which could be a key component to enable the next generation of insulin, able to react and adapt to glucose levels in the blood. This could eliminate the risk of hypoglycaemia dangerously low blood sugar levels - leading to better metabolic control for people living with the disease.

The new molecule performs extremely well, binding glucose 100 times more strongly than previous efforts and is almost perfectly selective for its target. It is fully comparable with the natural molecules that bind glucose, despite being many times smaller.



There are good prospects for using the synthetic receptor to help diabetics. Firstly, it could be the key to developing glucose-responsive insulin - insulin which becomes inactive when glucose is not present. Secondly, it could be used in continuous glucose monitors, which would allow diabetics to know their glucose levels at all times.

Tromans R *et al*. (2019). A biomimetic receptor for glucose. *Nature Chemistry*. 11, pp. 52-56.

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Bacterial defences against antibiotic resistance

Antibiotic resistance- the ability of bacteria to defend against antibiotic attack, and the spread of these resistance mechanisms- is a global public health concern. A form of resistance caused by a family of bacterial proteins, the Verona Imipenemase (VIM) betalactamases, is of acute clinical concern because it can inactivate antibiotics (penicillins and related agents) that comprise over half of the global antibacterial market. A team have uncovered near-atomic level structural detail of VIM proteins, which helps explain how the products of one family of resistance genes recog-



nise penicillin-type antibiotics and suggests routes to blocking this resistance in future treatments.

Salimraj R *et al.* (2018). Crystal Structures of VIM-1 Complexes Explain Active Site Heterogeneity in VIM-Class Metallo-β-Lactamases. *The FEBS Journal*. Published online 2 November 2018.

Image: Antibiotic (green) bound to the VIM enzyme (solid surface) © Eilis Braggington and Yuiko Takebayashi

A groundbreaking 'living laboratory' for livestock will be established at the Bristol Veterinary School thanks to a £1 million donation from the John Oldacre Foundation. The John Oldacre Centre for Sustainability and Welfare in Dairy Production will tackle the global challenge of ethical food security and train the next generation of vets and agriculturalists to help address the major issues facing agriculture.

Based within Wyndhurst Farm, the University of Bristol's commercially run dairy unit at Langford, the Centre will be equipped with the latest data collec-

A living laboratory for livestock

tion devices such as motion detection, GPS tracking and thermographic sensors to gather data that will identify and support changes in agricultural practices.

The Centre will bring together colleagues from engineering, data and behavioural sciences to use technology, such as motion sensing, to identify small behavioural and physiological changes at the beginning of a disease, such as mastitis. The Vet School is already working with colleagues in Life Sciences, using thermography as a novel way of predicting disease, which can reveal, very quickly, which cow is ill. The earlier a disease can be detected, the easier it is to treat effectively.

As well as being a research resource, the Centre will teach undergraduate and

> postgraduate students in animal production and livestock research, understanding and communicating data, and engagement with the wider farming community.



New membrane chain: combating antibiotic resistance

Dr Sara Alvira-de-Celis (pictured) has used the Elizabeth Blackwell Institute Bridging Funds for Research Fellows scheme to continue her work which will help us to understand the way that bacteria generate and express proteins in their membranes, a critical avenue to explore for novel antibiotics



with new mechanisms of action.

Sara is emphatic that a completely new mechanism need to be uncovered, so that new treatments don't become quickly superseded by the target bacteria's evolutionary defences.

Current research in to antibiotics still largely looks into modifications of existing antibiotic families. It is imperative that alternative approaches such as novel mechanisms, gene therapies, bacteriophages or vaccines are investigated to fight this health problem

Her own approach involves unravelling the basic processes that bacteria use for survival. which can be used to generate novel antibiotics that work in different ways to the existing ones. She is identifying, to atomic resolution, the mechanisms which take proteins from one area of the cell to the cell membranes, and the changes they need to go through on the way. The information generated could be used to develop drugs to disrupt these critical procedure within the bacteria, and thereby help the infected body's immune system to kill them.

Read more

SHIP submits to Health and Social Care Committee

The Sexual Health Improvement Programme (SHIP) Health Integration Team (HIT), supported by Bristol Health Partners, has submitted written evidence to the Health and Social Care Committee inquiry into sexual health.

On Friday 21 September 2018, SHIP convened an open meeting in Bristol on preparing sexual health services for the challenge of antibiotic resistant (AMR) bacteria, cohosted by SHIP and British Association of Sexual Health and HIV (BASHH).

Around 50 clinicians, health professionals, Public Health England employees, academics, laboratory staff, industry representatives attended, mostly from the South West area, but also participants from Plymouth, Brighton, London and Cambridge and Wales.

The written evidence gives a brief summary of key areas discussed during the meeting and highlight challenges and potential solutions for sexual health services relating to their theme of improving STI testing and responding to antimicrobial resistant (AMR) infections.

Bristol Health Partners

Read SHIP's written evidence submission.

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Human papilloma virus: 10 years of vaccination

Prof Adam Finn presented at an anniversary event in Portugal celebrating 10 years of the integration of the human papilloma virus (HPV) vaccine into the country's Na-

tional Vaccination Program. The event, held in Lisbon on 5 November 2018, looked at how successful the programme has been in Europe and challenges for the future.

The commemoration

was an important date for Public Health as it celebrated the 10th anniversary of the first vaccine specifically aimed at combating cancer diseases, namely cervical can-



cer. Considering the relevance of HPV vaccination and the fact that adherence to it, in Portugal, is an example of worldwide success, it is important to continue to advo-

> cate for the vaccine. The event was attended by Portugal's Minister of Health and the Secretary of State for Health.

Watch Adam's excellent presentation

HPRU in Evaluation of Interventions Blog: HPV

Researchers from the Centre for Academic Primary Care and Population Health Sciences, Bristol Medical School, with colleagues from Queens University Belfast, Ulster University, and Southampton University, have published an editorial in the British Journal of General Practice (BJGP) in response to Public Health England's (PHE) recommendation to roll out a targeted Human papillomavirus (HPV) vaccination programme for men who have sex with men (MSM) through genitourinary medicine (GUM) and HIV clinics across England.

The editorial argues that although this announcement is a positive step, it would be more effective to follow more recent recommendations to introduce gender neutral HPV vaccination to achieve total elimination of HPV, rather than a reduction. The PHE proposal means MSM who do not attend sexual health clinics, unvaccinated women and heterosexual men who have sex abroad would continue to suffer from HPV-related genital warts and cancers.

HPV is one of the mostly common sexually transmitted infections globally. Most people who contract HPV have no symptoms. Certain HPV subtypes are associated with anogenital and oral cancers in men and women, and many strains of the virus cause genital warts. The incidence of HPV-related cancers, particularly oropharyngeal cancers, has risen in recent decades. Preventive measures to reduce the burden of HPVrelated diseases include safe sex practices, regular cervical smears for women, and HPV vaccination programmes. However, the optimal approach for the reduction and prevention of HPV-related diseases is yet to be determined.

Read the editorial by Merriel S *et al.* (2018). Jabs for the boys: time to deliver on HPV vaccination recommendations. *British Journal of General Practice*. 68(674), pp406-407.

Creating rings in natural antibiotic synthesis

Mupirocin is an antibiotic widely used as a topical treatment for bacterial skin infections. It is produced commercially using the microorganism *Pseudomonas fluorescens,* which has developed complex biosynthetic machinery to produce the final molecule assembled on the tetrasubstituted six-membered ring essential for antibiotic activity. selectively this sixmembered ring from a complex linear starting material. The shows that the enzyme MupW is responsible for a chemically challenging transformation to give a new intermediate which a second enzyme, MupZ, then converts to the six-membered ring. Without MupZ (which itself forms beautiful hexagonal crystals, shown in the

A team at BrisSynBio has revealed an enzymatic reaction cascade that generates



image), a fivemembered ring is produced which has no antibiotic activity.

This reaction cascade would be difficult to achieve using existing synthetic methodology and the team is now investigating these biocatalysts to prepare more stable analogues of the active component of the antibiotic mupirocin.

Wang L *et al.* (2018). A Rieske oxygenase/epoxide hydrolase-catalysed reaction cascade creates oxygen heterocycles in mupirocin biosynthesis. *Nature Catalysis*. 1, pp. 968-976.

Image: Interdisciplinary studies reveal how nature creates a globally used antibiotic

Future technology for contactless medical procedures

Advancements in acoustic tweezers from Prof Bruce Drinkwater (Department of Mechanical Engineering) and his colleague Dr Asier Marzo (Universidad Publica De Navarra, Spain) are driving the technology towards this futuristic-sounding reality.

Sound exerts a small acoustic force and by turning up the volume of ultrasonic waves, too high pitched for humans to hear, scientists create a sound field strong enough to move small objects. The team have enabled the efficient generation of sound fields complex enough to trap multiple objects at the target locations by applying a novel algorithm that controls

an array of 256 small loudspeakers, which will allow the creation of intricate, tweezerlike, acoustic fields. Ultrasound is routinely used in pregnancy scans and kidney stone treatment as it can safely and non-invasively pen-



etrate biological tissue.

Marzo A and Drinkwater BW (2018). Holographic Acoustic Tweezers. Proceedings of the National Academy of Sciences. Published online 17 December 2018.

Testing for wet age-related macular degeneration at home

The MONARCH study aims to investigate if patients with wet age-related macular degeneration (AMD) could test their vision at home rather than attend a hospital appointment. The condition develops when abnormal blood vessels form underneath the macula stops functioning as well as it used to. Patients experience blurred distorted vision, difficulty seeing in dim lighting and problems reading. Current treatment is a series of

monthly injections which reduce the growth of new vessels which limit vision loss. Following treatment, patients attend regular hospital checkups where clinical staff monitor the macula by taking photographs and doing vision tests, checking whether any follow-up treatment is needed.

About 30% of patients will require follow-up treatment; however, these check-up appointments put a huge strain on already-stretched resources, and limit the capacity for seeing new patients who, if not seen urgently, are at high risk of losing their vision. The study aims to find out whether monitoring vision by patients themselves at home could potentially alleviate some of the burden of AMD on the NHS, as well as be more convenient for patients, without compromising their safety or wellbeing.

Read more

Vitamica completes initial seed funding round

Vitamica, a University of Bristol spin-out company, has closed its initial seed funding round. This is a major milestone for the company which is developing a rapid diagnostic to determine the susceptibility of bacteria to antibiotics.

The investment will support further development of the prototype instrument and the expansion of validation trials.

Vitamica is working in an area of global importance: slowing the rise of antimicrobial resistance (AMR) among infectious bacteria. Among the tools required by healthcare professionals to help slow the spread of AMR are rapid diagnostic tests that will show which antibiotics are effective against a patient's infection. This challenge is being addressed by Vitamica with its innovative rapid test technology.

Research led by Dr Massimo Antognozzi (School of Physics) has shown that measuring tiny internal movements within bacteria could help doctors prescribe antibiotics more effectively in future. These internal vibrations cease when microbes are killed by antibiotics, giving rise to the possibility of a new diagnostic test to help guide prescribing decisions. With the support of a grant from Innovate UK, the company is making good progress with laboratory tests to study the interaction between com-

> monly used antibiotics and a range of bacteria.

Image: Vitamica's innovative microscope that measures the susceptibility of bacteria to antibiotics in under one hour.



Tube travel linked to the spread of flu-like illnesses

Despite the commuter cold being a widely accepted concept, it's never been proven that public transport contributes to the spread of airborne infections. Now new research on the London underground commute has proven a link does exist.

By comparing Oyster card route information and Public Health England data on flu-like illnesses, Dr Lara Goscé (Department of Civil Engineering) and Dr Anders Johansson (Department of Engineering Mathematics) discovered higher rates of airborne infections in Londoners that have longer tube journeys through busier terminals.

Higher rates can be observed in boroughs served by a small number of underground lines: passengers starting their journey in these boroughs usually have to change lines once or more in crowded junctions such as King's Cross in order to reach their final destination. On the other hand, lower influenza-like rates are found in boroughs where either the population does not use public transport as the main form of transport to commute to work; or boroughs served by more underground lines, which guarantee faster trips with less stops and contacts with fewer people.

Looking to the future, the group want to draw a clearer map of the spread of coldlike infections in a metropolitan environment, and so plan to combine individual level infection data with existing studies from households and schools.

Goscé & Johansson (2018). Analysing the link between public transport use and airborne transmission: mobility and contagion in the London underground. *Environmental Health*. 17(1), p84.

Partnership with Max Planck Society

The University of Bristol has partnered with the Max Planck Society in Germany to establish an innovative new Max Planck Centre for Minimal Biology in Bristol. The Centre will pursue gamechanging research in the emerging field of minimal biology to address some of the most complex challenges in fundamental science. This could lead to transformative applications in biotechnology and medicine.

As an emerging field of sci-

ence, the applications in minimal biology are wide-ranging and pave the way for new therapies that could see artificial cells programmed with specific properties to rescue diseased cells and tissue, and the engineering of bacterial and mammalian cells to improve the production of pharmaceuticals.

Training the next generation of scientists to work between the physical and life sciences will be a core mission of the new Centre, which is expected to become fully operational in 2019. The Centre will focus on several key areas, including: synthetic nanoscale biology, implementing custom -designed functionalities in proto- and living cells, tissues and ultimately organisms; protein design in living cells, whereby completely new proteins will be designed from scratch to operate alongside natural proteins; and biomedical genome intervention by engineering synthetic, virusderived, programmable nanodevices. **Read more**

JANUARY - FEBRUARY 2019

Dr Ellen Brooks Pollock

(Bristol Veterinary School, Lecturer in Infectious Disease Mathematical Modelling) contributed to the Institute of Mathematics & its applications blog, commemorating World Aids Day on 1 December 2018. In it she describes



the important role disease modelling has played in fighting the human immunodeficiency virus

Disease modelling to combat HIV-AIDS

(HIV) that eventually leads to acquired immunodeficiency syndrome (AIDS).

The HIV-AIDS epidemic is without doubt one of the biggest health disasters of recent times, responsible for over 35 million deaths worldwide. Thirty years ago, HIV was considered a disease of gay men and drug users. Since then, infection has changed from a death sentence to a manageable condition that, with the right treatment, hardly alters life expectancy. Tackling HIV-AIDS has required multi-disciplinary effort, and mathematical modelling played a central role. AIDS presented new challenges for modelling, as a disease with a long and variable latency that took years or decades to progress. The AIDS epidemic was a wake-up call for public health and a defining event for disease modelling of all types.

Read the full article

Life sciences is a sector that operates at the cutting-edge of technological developments and on December 7th 2018 the second Life Sciences Sector Deal was announced. The Great West region, including the University of Bristol, was recognised in the report for its flourishing life science industry, due to its collaboration be-

tween more established technology and digital businesses.

The deal announced a £1.3bn industrygovernment investment in the UK economy and a

new partnership driving early disease detection, with global biopharmaceutical company UCB investing around £1bn in research and development, including in a new state-ofthe-art facility.

This builds on the government's Life Sciences Industrial Strategy published in December 2017, which recog-

Life Sciences Sector Deal

nised the importance of regional clusters and followed intense collaboration between life sciences organisations and the GW4 Alliance, and GW4's regional strengths such as convergence with AI, high performance computing, quantum technologies and world-leading academic expertise. Places continues to

> be one of five key commitments within the deal, which this time round has a strong focus on technology and digital innovation.

Read more



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ELIZABETH BLACKWELL FUNDING

EBI Identifying Candidates for Wellcome Trust Investigator Awards

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

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

EBI Workshop Support

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

Returning Carers Scheme

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

The deadline for applications is 30 April and 31 October each year.

EBI Bridging Funds for Research Fellows

This scheme is designed to support a small number of academic staff at the University of Bristol who currently hold an externally funded research fellowship. Applications accepted on a **rolling** basis.

The Elizabeth Blackwell Institute for Health Research is officially a member of Equality, Diversity and Inclusion in Science and Health, or EDIS, an initiative set up by the Wellcome Trust, the Crick Institute and GSK.

Rachael Gooberman-Hill, Director of the EBI, attended the interim Board meeting on 12 December 2018 as a University of Bristol representative.

Find out more about EDIS

FUNDING OPPORTUNITIES

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

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

Research Professional provides access to an extensive database of funding opportunities, and can send out tailored alerts based on keywords that <u>you</u> input, ensuring that the funding alerts you receive are the ones you want to hear about. UoB staff and students have **FREE** online access to the database from any device – once you've registered then you can view upcoming funding opportunities from home or away, not just while on the University network.

You can search for funding information by discipline, sponsor, database searches, by recent calls or by upcoming deadlines. If you register for the site and log in, you'll be able to:

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

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

National Institute of Allergy and Infectious Diseases, USA

Fc-dependent mechanisms of antibody-mediated killing

Closing date: 1-Feb-19

Award amount: USD 1.5 million

This supports research that addresses knowledge gaps in the mechanisms of Fc-dependent, antibody-mediated killing of infected or aberrant cells, or antibody-mediated therapeutic ablation of cells implicated in immune pathologies, including autoimmune and allergic diseases. Targets of therapeutic Fc-dependent, antibody-mediated killing include pathogen-infected cells, malignant cells and host cells implicated in immune pathologies such as autoimmune and allergic disease. Projects should focus on either or both antibody dependent cellular cytotoxicity and antibodydependent cell-mediated phagocytosis.

National Institute of General Medical Sciences, USA Modelling of infectious disease agent study research projects

Closing date: 5-Feb-19

Award amount: unspecified

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This supports innovative research that will develop and apply computational tools and methods for modelling interactions between infectious agents and their hosts, disease spread, prediction systems and response strategies. Areas of interest include infectious disease research and computational, mathematical and statistical model research. The models should be useful to researchers, policy makers, or public health workers who want to better understand and respond to infectious diseases.

British Society for Antimicrobial Chemotherapy

Travel grants – European Congress of Clinical Microbiology and Infectious Diseases

Closing date: 28-Feb-19

Award amount: £1,000

Travel grants to attend the European Congress of Clinical Microbiology and Infectious Diseases. These enable members to give oral or poster presentations at ECCMID, to be held in Amsterdam, Netherlands between 13 and 16 April 2018. BSAC members worldwide may apply.

European Society for Paediatric Infectious Diseases

Postgraduate teaching visits to resource-poor countries

Closing date: 1-Mar-19

Award amount: €1,500

This enables ESPID members to conduct teaching and training activities in resource-poor countries, contributing to an established programme of postgraduate medical or scientific education directly related to paediatric infectious diseases.

Healthcare Infection Society

Mike Emmerson early-career research award in the field of healthcare acquired infection

Closing date: 1-Mar-19

Award amount: £10,000

This encourages trainees to work on the subject of healthcare acquired infection, including both hospital and community settings.

British Infection Association

Research fellowship

Closing date: 31-Mar-19

Award amount: £70,000

This supports infection-related research in an academic centre in the UK, or appropriate UKlinked centre overseas. Applicants must be UK- or Ireland-based clinically qualified trainees in infection or infection-related specialities, who are not in a consultant level post, or UK-based non-clinical postdoctoral scientists within four years of the award of their PhD who are not in a tenured academic or top-grade scientist post.

THIS ISSUE'S FEATURED ARTICLE

High response and re-infection rates among people who inject drugs treated for hepatitis C in a community needle and syringe programme

Schulkind J, Stephens B, Ahmad F, Johnston L, Hutchinson S, Thain D, Ward Z, Vickerman P, Hickman M, Dillon J. *Journal of Viral Hepatitis*. First published online 13 November 2018.

To achieve WHO hepatitis C virus (HCV) elimination targets by 2030, mathematical models suggest there needs to be significant scale-up of treatment among people who inject drugs (PWID). We tested whether people who actively inject drugs can be recruited and treated successfully through a community needle and syringe programme (NSP), and assessed rates of re-infection. 105 HCV RNA positive participants were enrolled prospectively. Participants were recruited from the largest NSP in Dundee over 42 months. 94/105 individuals commenced treatment. Genotype 1 (G1) individuals (n = 37) were treated with peg-interferon + ribavirin + Simepravir/Telaprevir. Genotype 2/3 (G2/3) (n = 57) received peg-interferon + ribavirin. Weekly study visits took place within the NSP. Mean age of participants was 34.0 years (SD 6.9), 71.3% (61/94) were male. One in five (20/94) participants were homeless. 68.1% (64/94) were on OST (opiate substitution therapy) at enrolment; participants injected median 6.5 times/wk. In terms of clinical outcomes, >80% treatment adherence was 71.3% (67/94). There was no difference in SVR-12 rates by genotype: 81.0% (30/37) for G1 and 82.5% (47/55) for G2/3. At 18 months post-treatment, 15/77 participants were re-infected, followed up over 69.8 person-years, yielding a re-infection rate of 21.5/100 person-years (95% CI 13.00-35.65). This trial demonstrates that HCV treatment can be delivered successfully to the target population of treatment as prevention strategies. We report higher rates of re-infection than existing estimates among PWID. Scale-up of HCV treatment should be pursued alongside a comprehensive programme of harm reduction interventions to help minimize re-infection and reduce HCV transmission.



Flow diagram of study outcomes at 3-mo, 6-mo and 18-mo follow-up

CONTACTS

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

Co-Chair: Ruth Massey Reader



Co-Chair: Adam Finn Prof of Paediatrics



- Borko Amulic Lecturer in Immunology
- Philip Bright - Clinical Immunologist
- Andrew Davidson Senior Lecturer in Virology
- Hannah Fraser Senior RA in Infectious Disease Mathematical Modelling
- Wendy Gibson Professor of Protozoology
- Kathleen Gillespie Reader in Molecular Medicine, Head of the Diabetes and
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