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Infection and Immunity Newsletter

March / April 2015

Web Email

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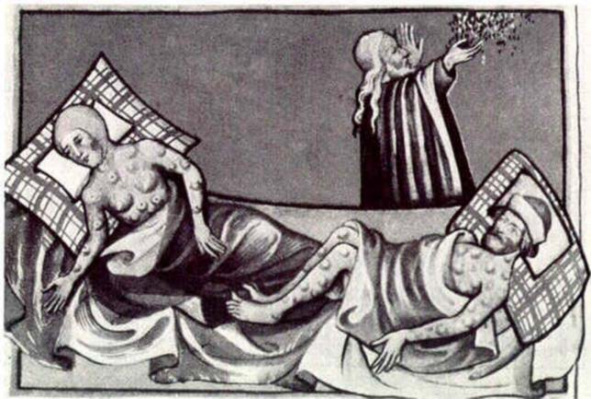
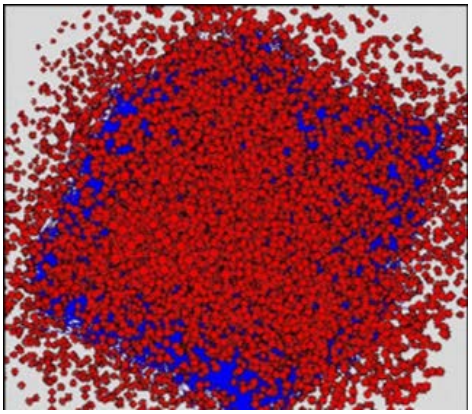


Dysregulated immunity and infection lead to illness and death worldwide. More than half of childhood deaths are due to an infectious cause; disorders of the immune system like allergy and autoimmunity are increasing rapidly in the developed world and the immune system is increasingly being manipulated to allow organ transplantation and to control cancer.



The Theme embraces this diversity of application, incorporating expertise ranging from fundamental studies of the structure of bacteria to population based research tackling the management of antibiotic resistance in general practice. Our key research areas include the pathogenesis of infection, population and human health research and immune regulation.

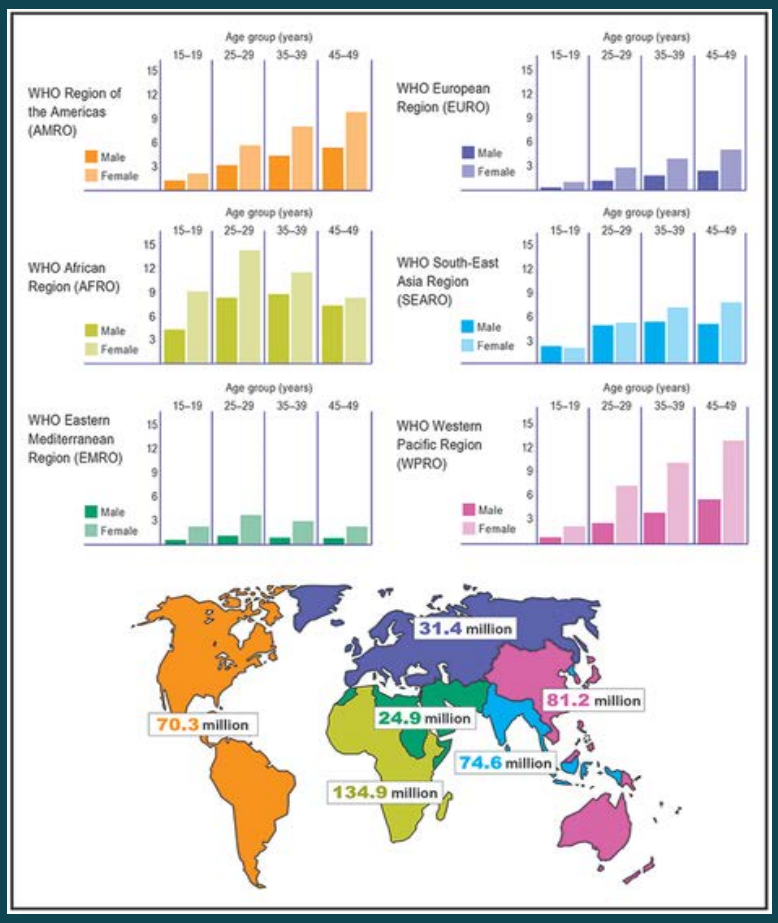
THIS MONTH'S SHOWCASED ARTICLE

Global estimates of prevalent and incident herpes simplex virus type 2 infections in 2012

K. J. Looker, A. S. Magaret, K. M. E. Turner, P. Vickerman, S. L. Gottlieb & L. M. Newman

PLOS ONE. 10(1), p. e114989. Published online 21 January 2015.

This new study is the first update of global herpes simplex virus type 2 estimates, since estimates for 2003 were published in 2008. Approximately 19-million people are newly infected with the virus each year, mainly through sexual transmission. The infection can can cause genital ulcer disease which can, in turn, cause neonatal herpes. Studies have shown that people who are infected with the virus are approximately three times more likely to become infected with HIV, and people with both HIV and herpes are more likely to spread HIV to others. In addition, infection with herpes simplex virus type 2 in people living with HIV often has a more severe presentation and can lead to serious but rare complications such as brain, eye, or lung infections.



Estimates of the number of people (in millions) with prevalent HSV-2 infection in 2012, by age, sex and WHO region.

Herpes simplex virus type 2 (HSV-2) infection causes significant disease globally. Adolescent and adult infection may present as painful genital ulcers. Neonatal infection has high morbidity and mortality. Additionally, HSV-2 likely contributes substantially to the spread of HIV infection. The global burden of HSV-2 infection was last estimated for 2003. Here we present new global estimates for 2012 of the burden of prevalent (existing) and incident (new) HSV-2 infection among females and males aged 15–49 years, using updated methodology to adjust for test performance and estimate by World Health Organization (WHO) region.

EVENTS

Bristol-run events:

Professor David Price: How does the TCR repertoire influence HLA-restricted control of HIV-1?
17 April 2015, 13:00, C42 Medical Sciences Building

One Health Bristol Conference
25 April 2105, Langford

Prof. Sherif El-Khamisy (Lister Research Fellow, Krebs Institute, University of Sheffield)
29 April 2015, 13:00

Festival of Postgraduate Research
30 April, 14:30, Anson Rooms, Richmond Building

Dr Rita Tewari (University of Nottingham)
5 May 2015, 13:00

Dr Angelika Gründling (MRC Centre for Molecular Bacteriology and Infection, Imperial College)
14 May 2015, 13:00

Dr Philippe Bousso (Institut Pasteur)
11 June 2015, 13:00

MRC Integrative Epidemiology Unit: Mendelian Randomization Conference
22 June 2015, 9:00, Victoria Rooms, Bristol

Infection and Immunity Early Career Researchers Event **NOTE THE DATE!!!**
23 June 2015, Life Sciences Building

National events:

BioDynamics Workshop
15 April 2015, 9:00, John McIntyre Conference Centre, The University of Edinburgh

An introduction to infectious disease modelling
21 April 2015, 9:00, Imperial College Paddington Campus, central London

Applied Bioinformatics and Public Health Microbiology
6 May 2015, 9:00, Wellcome Trust Genome Campus, Hinxton

IDRN event - An introduction to infectious disease genomics
18 June 2015, 9:00, venue to be confirmed, central London

Health Services Research Network Symposium
1-2 July 2015, Nottingham

Introduction to Mathematical Models of the Epidemiology and Control of Infectious Diseases
14 September 2015, 9:00, Imperial College London

I and I AWAY DAY

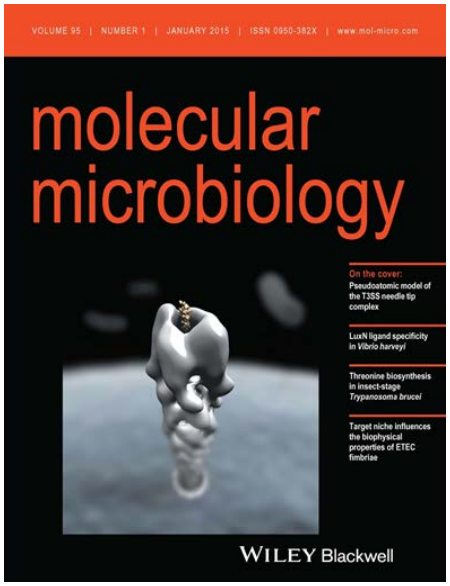
The Infection and Immunity Away Day was held on 14 January 2015 in the Life Sciences Building and ran under the title of *Big Data*. Over 80 people came to listen to talks given by David Wraith, Julian Gough, Katy Turner, Paul Kellam (UCL), Christoph Wuelfing, David Matthews, Jim Spencer and Paul Burton. There was also a demonstration from NanoString Technologies, a biotechnology company which develops products that unlock valuable and clinically actionable genomic information from small amounts of tissue.

Feedback from the day was overwhelmingly positive, with respondents agreeing that their expectations of the day had been met and that the speakers were both interesting and informative. Presentations from the event are now available from the I and I intranet site.

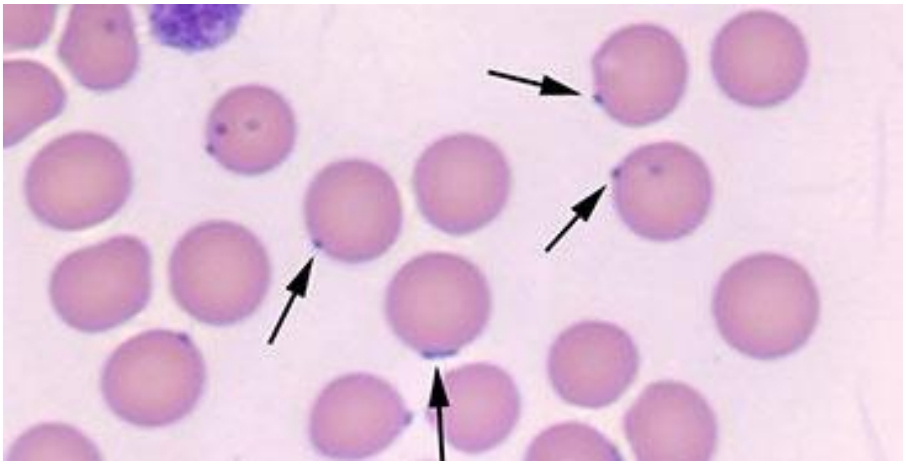
NEWS

- The Art of Science is an annual competition for scientists to submit images that manage to be both aesthetically pleasing and to convey a scientific message or principle. This artwork (by Martin Cheung, the first author of the paper listed below) won the Bristol Art of Science competition in 2013/14, as well as appearing as the cover image for *Molecular Microbiology* 95(1), January 2015.

  Cheung, M., Shen, D., Makino, F., Kato, T., Roehrich, A. D., Martinez-Argudo, I., Walker, M. L., Murillo, I., Liu, X., Pain, M., Brown, J., Frazer, G., Mantell, J., Mina, P., Todd, T., Sessions, R. B., Namba, K. & Blocker, A. J. (2014). Three-dimensional electron microscopy reconstruction and cysteine-mediated crosslinking provide a model of the T3SS needle tip complex. *Molecular Microbiology* 95(1), p. 31-50.



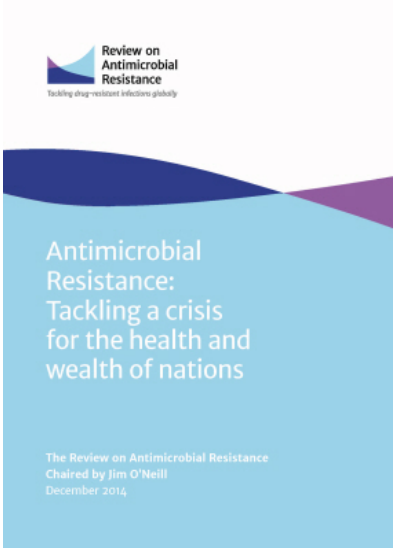
- A study led by Dr Séverine Tasker with colleagues at Bristol and the University of Zürich has advanced the knowledge of immunity of relatively unknown blood borne pathogens, haemoplasma.



Blood smear showing haemoplasma organisms (examples are arrowed) attached to the surface of red blood cells

Haemoplasma bacteria are found in a wide range of mammals including domestic and wild cats, and can cause severe anaemia. Information about the immune responses that occur in animals following haemoplasma infection is relatively unknown, largely due to the fact that researchers struggle to study these bacteria as they are unable to grow them in the laboratory. Antibiotics do not consistently clear infection and without correct treatment the anaemia can be fatal. Recently haemoplasma associated anaemia has been reported in a human too. The aim of the study was to determine whether cats who had previously recovered from *Mycoplasma haemofelis* infection were protected from re-infection. The researchers found that they were, representing a significant advancement in scientists' knowledge of immunity for haemoplasma infections. The exact methods of protective immunity could not be clearly identified despite extensive investigations, but the study's results suggest that a vaccine, using a weakened form of the bacteria, may offer protection against haemoplasma infection. The study recommends future research should explore whether the bacterial animal infection could be transmitted to humans and how the immune system targets the pathogen.

Hicks, C. E. A., Willi, B., Novacco, M., Meli, M. L., Stokes, C. R., Helps, C. R., Hofmann-Lehmann, R. & Tasker, S. (2014). Protective immunity against infection with *Mycoplasma haemofelis*. *Clinical and Vaccine Immunology*. Published online 19 November 2014.



- A review to address the growing global problem of drug-resistant infections, hosted and funded by the Wellcome Trust, has now been published. Increasingly bacteria, parasites, viruses and other disease-causing micro-organisms are becoming resistant to the drugs we have

available. However, no new classes of antibiotic drugs have come on the market for more than 25 years, and the drugs we do have are over-prescribed. This international review explored the economic issues surrounding antimicrobial resistance, including how to incentivise the drug pipeline so that new drugs are developed, but also focussed on our relationship with existing antimicrobials and how they can be used to better to treat illness. Led by economist Jim O'Neill, with backing from the Department of Health and HM Treasury, the commission was based on scenarios modelled by researchers Rand Europe and auditors KPMG. They found that drug resistant E. coli, malaria and tuberculosis (TB) would have the biggest impact. In Europe and the United States, antimicrobial resistance causes at least 50,000 deaths each year; if left unchecked, deaths would rise more than 10-fold by 2050.

ELIZABETH BLACKWELL INSTITUTE FUNDING SCHEMES

EBI Workshops Funding

Support for interdisciplinary workshops in health research at a new or emerging interface between two or more disciplines. Applications are reviewed on a rolling basis.

EBI Catalyst Fund

Pump priming awards can support the most promising and ambitious ideas across the widest interdisciplinary boundaries. These projects will be identified largely through the running of workshops to explore new possibilities and identify the big questions. Applications are reviewed on a rolling basis.

EBI Senior Fellowships

To enable University of Bristol academic staff to work on a new or emerging activity at the interface between two or more disciplines and which addresses innovations in health research. Closing date: 20 March 2015.

EBI Bridging Funds for Senior Fellows

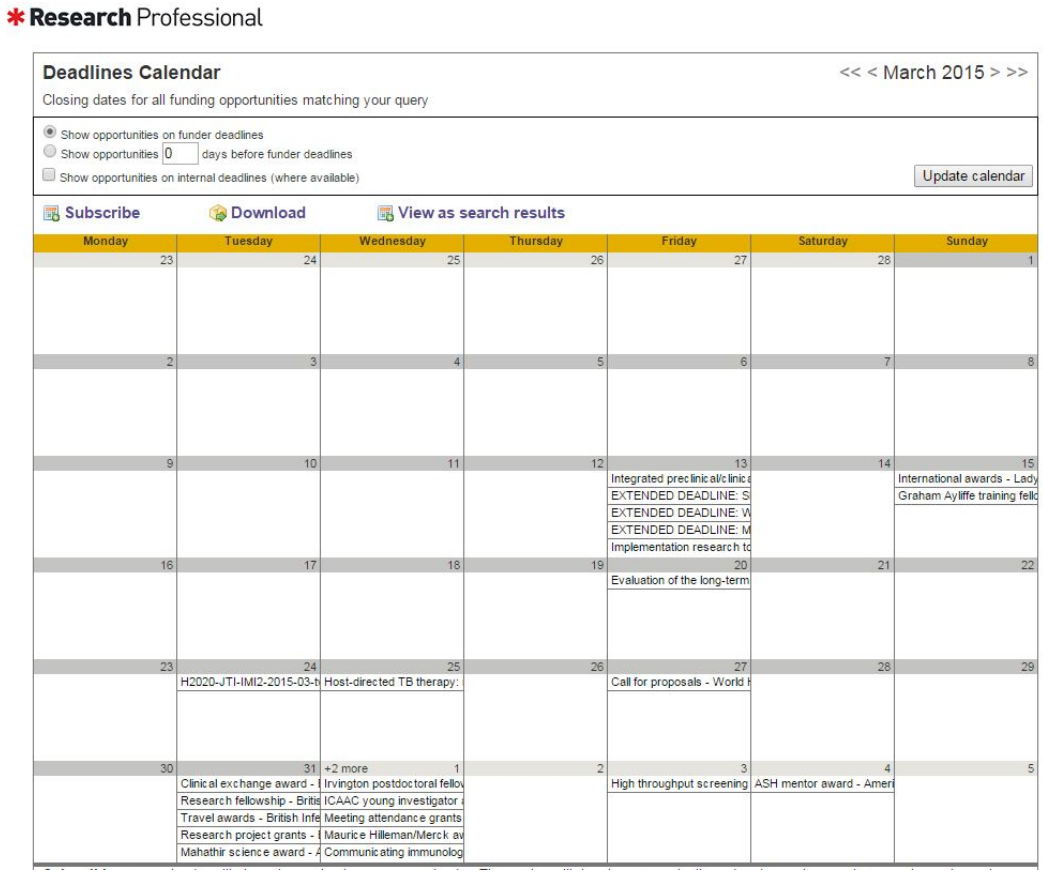
To support a small number of academic staff at UoB who currently hold an externally funded research fellowship. Closing date for nominations: 7 April 2015. Application deadline: 5 May 2015.

EBI Identifying Candidates for Wellcome Trust Investigator Awards

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. Closing date for nominations: 7 April 2015. Application deadline: 27 April 2015.

FUNDING OPPORTUNITIES

A **calendar** of potential **funding opportunities** for Infection and Immunity has been set up via Research Professional. This calendar, which will automatically update with new opportunities as they arise, specifies title, submission deadline and links for each opportunity. This calendar is accessible via their **website** and will be updated automatically according to specified search criteria (immunisation programmes & vaccination; autoimmune diseases; infectious diseases; immunology; immunological & bioassay methods). Other subjects can be added by request- please email the theme with suggestions and/or comments.



Bayer

Grants for Targets

Aims to encourage research on novel targets and disease-related biomarkers in the fields of, amongst others, haematology. Different types of grants are awarded depending on the specifics of the target and its development phase: support grants between €5,000 and €10,000 to advance research on targets that are at a very early stage of discovery; focus grants between €10,000 and €125,000 for more mature ideas, such as addressing specific aspects of a target as a first step towards transferring it to the drug discovery process.

Award amount: €125,000 Deadline: 31-Mar-15

Laerdal Foundation for Acute Medicine

Centre Support

Aims to support a three year research centre in practically-oriented research and development in acute medicine. Research proposals should be of particular value of strengthening at least one of the factors in Utsteins formula of survival.

Award amount: NOK3,000,000 Deadline: 01-Apr-15

Sparks

Project Grant

Support research into rare diseases and premature birth which will maximise the benefit for the health of children and pregnant women. Will encourage projects where there is a strong partnership of basic scientists with clinical academics/consultants and a clear route to potential clinical application.

Award amount: not specified Deadline: 10-Apr-15

Sparks

Innovation Grant

Support research into rare diseases and premature birth which will maximise the benefit for the health of children and pregnant women. Will encourage projects where there is a strong partnership of basic scientists with clinical academics/consultants and a clear route to potential clinical application.

Award amount: not specified Deadline: 10-Apr-15

European and Developing Countries Clinical Trials Partnership

Strategic projects with major co-funding

Supports strategically important, large-scale research projects with the potential to achieve rapid advances in the field of poverty-related diseases. Proposals should focus on clinical trials, related clinical research or capacity building efforts on poverty-related diseases in sub-Saharan Africa.

Award amount: €10,000,000 Deadline: 16-Apr-15

Wellcome Trust

Research Career Development Fellowships in Basic Biomedical Science

Enable postdoctoral scientists to become independent research scientists and undertake research at an institution in the Republic of Ireland. Scientists must work across the remits of specific funding streams, including cellular, developmental and physiological sciences; genetic and molecular sciences; infection and immunobiology; neuroscience and mental health; population health.

Award Amount: not specified Deadline: 17-Apr-15

Medical Research Foundation

Respiratory Diseases Funding for Mid-Career Researchers: Inflammatory, Interstitial and Fibrotic Lung Diseases

The call is for research into the disease mechanisms underlying inflammatory, interstitial and fibrotic lung diseases, including mesothelioma, but also looking at work leading to better diagnosis or modification of disease progression/outcomes. The description states that it is aimed at mid-career researchers, in fact it's more suited to early career researchers as the eligibility criteria state applicants must have between 3 and 6 years postdoctoral experience.

If you are interested in applying, please contact Hazel Phillips in RED in the first instance.

Award Amount: £300,000 Deadline: 06-May-15

National Institute for Health Research

Health Technology Assessment commissioned call for infection research - Antibiotics for acute otitis media with discharge

Eardrum perforation due to AOM may resolve spontaneously, but antibiotics in the form of medicine or drops are widely prescribed. However, the best mode of delivery, orally or topically, is not known. It would be very helpful to parents and the NHS to know what the best clinical approach is in order to help guide prescribing practice for this condition. A simple randomised controlled trial to determine the best way of treating AOM with discharge is proposed.

Award Amount: not specified Deadline: 12-May-15

Bill and Melinda Gates Foundation

Grand challenges explorations grants

Support early-stage research projects and innovative ideas that could lead to new vaccines, diagnostics, drugs and other technologies targeting diseases.

Award Amount: US$1,100,000 Deadline: 12-May-15

Cancer Research UK

Cancer Immunology Project Awards

Aim to to catalyse research and build the UK's research base in cancer immunology by funding immunologists in non-cancer fields. Proposals may address any area of immunological research including any of the following key areas: cellular and molecular immunology; inflammation, allergy, transplantation and auto immunity; the immune response to infection; the interaction of immune cells with tissues; immunity and disease susceptibility or resistance.

Award Amount: £300,000 Deadline: 18-May-15

Medical Research Council

Research grants – infections and immunity

Suitable for focused research projects that may be short- or long-term in nature. In addition, they can be used to support method development and continuation of research facilities and may involve more than one research group or institution.

Award amount: £1M Deadline: 20-May-15

Medical Research Council

Partnership Grants - infections and immunity

Provide core funds to support partnerships between diverse groupings of researchers, and can be used for infrastructure support, platform activities and for bringing together managed consortia or multidisciplinary collaborations.

Award amount: not specified Deadline: 20-May-15

Medical Research Council

Programme Grants - infections and immunity

Provide large and long-term renewable funding. A programme is defined as a co-ordinated and coherent group of related projects that may be developed to address an interrelated set of questions across a broad scientific area.

Award amount: not specified Deadline: 20-May-15

Medical Research Council

Population and Systems Medicine

Suitable for focused research projects that may be short- or long-term in nature. In addition, they can be used to support method development and continuation of research facilities and may involve more than one research group or institution.

Award amount: £1,000,000 Deadline: 27-May-15, 30 Sep-15

Medical Research Council

New Investigator Research Grant- Population and Systems Medicine

Provide support for clinical and non-clinical researchers while they are establishing themselves as independent principal investigators. For those who already have an institutional post, it provides funding and protected time with which to establish an independent research career. The grant is also a potential source of research funding for fellows whose awards only cover a personal salary or limited research funds.

Award amount: not specified Deadline: 27-May-15, 30 Sep-15

Medical Research Council

Partnership Grant

Provides core funds to support partnerships between diverse groupings of researchers, and can be used for infrastructure support, platform activities and for bringing together managed consortia or multidisciplinary collaborations.

Award amount: not specified Deadline: 27-May-15, 30-Sep-15

Medical Research Council - Thailand

Joint Health Research Call

The major and rising causes of death among Thai citizens are non-communicable diseases. The prevalence rate of communicable (infectious) diseases, which used to be significant health problems have been declining, however drug-resistant and re-emerging infectious diseases are a growing challenge for disease control and prevention in Thailand. This call will look into dengue, malaria, outbreak prediction, and emerging infectious diseases.

Award amount: £444,000 Deadline: 02-Jun-15

Infection Prevention Society

Postdoctoral Grant

Supports research on any aspect of infection prevention and control. The grant is worth £3,000 per year for two years.

Award amount: £6,000 Deadline: 03-Jun-15

Infection Prevention Society

Collaborative Small Projects Grant

Enables a team of up to five researchers to conduct research on any aspect of infection prevention and control.

Award amount: £5,000 Deadline: 03-Jun-15

National Institute of Diabetes and Digestive and Kidney Diseases

Lymphatics in health and disease in the digestive, urinary, cardiovascular and pulmonary systems (R01)

Supports research into aspects of lymphatic vessel physiology and pathophysiology related to health and disease of digestive system and urinary tract organs, and cardiovascular and pulmonary systems, in resolution of thromboembolic events and inflammation and immune responses as they relate to these diseases. Studies to understand the factors that control local lymphatic vessel functional anatomy and physiology during health or disease in these organs or systems, and the mechanisms by which alterations of lymphatic vessel function affect organ function are of interest. Studies with a major focus on immune mechanisms will not be considered responsive.

Award amount: US$1,250,000 Deadline: 05-Jun-15

National Institute of Allergy and Infectious Diseases

Investigations on primary immunodeficiency diseases (R01)

Supports innovative investigations in primary immunodeficiency diseases. Of particular interest are the detection of primary immunodeficiency diseases, the identification of the molecular basis of these diseases and the design and pre-clinical development of innovative therapies for these diseases. Clinical trials will not be supported.

Award amount: not specified Deadline: 05-Jun-15

Lupus Research Institute

Distinguished Innovator Awards

Provide support to conduct novel research into the fundamental causes of lupus and so provide new directions toward a cure or prevention.

Award amount: US$1,000,000 Deadline: 25-Jun-15

National Institute of Allergy and Infectious Diseases
Molecular mechanisms of combination adjuvants (U01)
Encourages studies of the mechanism of action of a combination of two or more vaccine adjuvants (combination adjuvant). Adjuvants that are used in these studies must already have shown immune boosting activity when used individually in licensed or unlicensed vaccines.

Award amount: US$1,750,000 Deadline: 09-Jul-15

Myositis Association
Research Fellowships
Designed to help promising postdoctoral investigators to pursue research into any other form of myositis or immune myopathy.

Award amount: US$100,000 Deadline: 15-Jul-15 (anticipated)

Myositis Association
Programme Grants
Seed monies for new or innovative research projects in the hope that they will develop sufficiently to attract funding from other sources and will be awarded for one or two years; or for established projects.

Award amount: US$100,000 Deadline: 15-Jul-15 (anticipated)

National Institute for Health Research
PHR commissioned funding opportunities - Public communication for anti-microbial resistance (15/50)
The effectiveness of antibiotics is currently seriously jeopardised by the emergence and spread of microbes that are resistant to affordable and effective "first-line" antibiotics, rendering the drugs concerned ineffective for the treatment of the infection. There is a pressing need to address the issue of antimicrobial resistance (AMR) and the problem continues to grow.

Award amount: not specified Deadline: 03-Sep-15

Cancer and Polio Research Fund
Research Grants
Support research into cancers, with particular reference to the causes, development and treatment of these diseases, or research into polio and other crippling diseases.

Award amount: not specified Deadline: 15-Oct-15

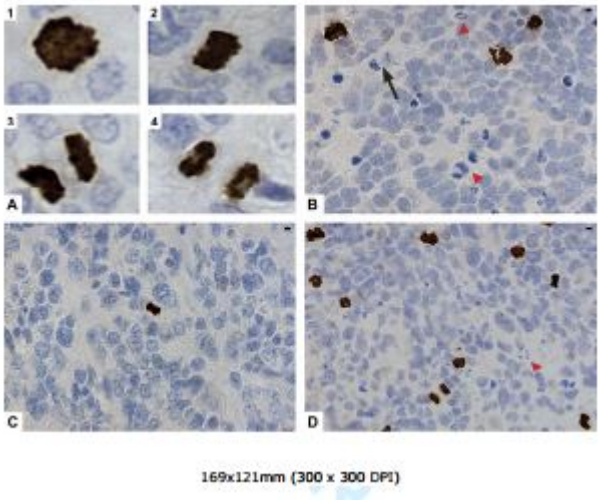
Royal Society
Research Professorships
Enable world-class scientists to be relieved from teaching and administration duties in order to focus on research.

Award amount: £1,115,000 Deadline: 03-Nov-15

PUBLICATIONS

Lucas, P. J., Cabral, C., Hay, A. D. & Horwood, J. (2015). A systematic review of parent and clinician views and perceptions that influence prescribing decisions in relation to acute childhood infections in primary care. *Scandinavian Journal of Primary Health Care*. p. 1-10.

Ramani, P., Taylor, S., Miller, E., Sowa-Avugrah, E. & May, M. (2015). High phosphohistone H3 expression correlates with adverse clinical, biological and pathological factors in neuroblastomas. *The Journal of Histochemistry and Cytochemistry*. Published online 14 February 2015.



169x121mm (300 x 300 DPI)

Image caption: Immunohistochemical expression of pHH3 in neurblastomas (NBs) (A) pHH3 stained the mitotic figures in the prophase (1) metaphase (2), anaphase (3) and telophase (4), (B) pHH3 did not stain neutrophils (black arrow) or karyorrhectic debris (red arrow heads), (C) Low pHH3 proliferation index (pHH3-PI) in a non-MYCN amplified NB with low mitosis karyorrhexis index (MKI) (D) High pHH3-PI in a MYCN-amplified NB with high MKI (red arrow head points to karyorrhectic debris). Scale bar - 3.17 µm.

Perdu, C., Huber, P., Bouillot, S., Blocker, A., Elsen, S., Attrée, I. & Faudry, E. (2015). ExsB is required for correct assembly of Pseudomonas aeruginosa type III secretion apparatus in the bacterial membrane and full virulence in vivo. *Infection and Immunity*. Published online 17 February 2015.

Xu, Y., Balasubramaniam, B., Copland, D. A., Liu, J., Armitage, M. J. & Dick, A. D. (2015). Activated adult microglia influence retinal progenitor cell proliferation and differentiation toward recoverin-expressing neuron-like cells in a co-culture model. *Graefe's archive for clinical and experimental ophthalmology*. Published online 14 February 2015.

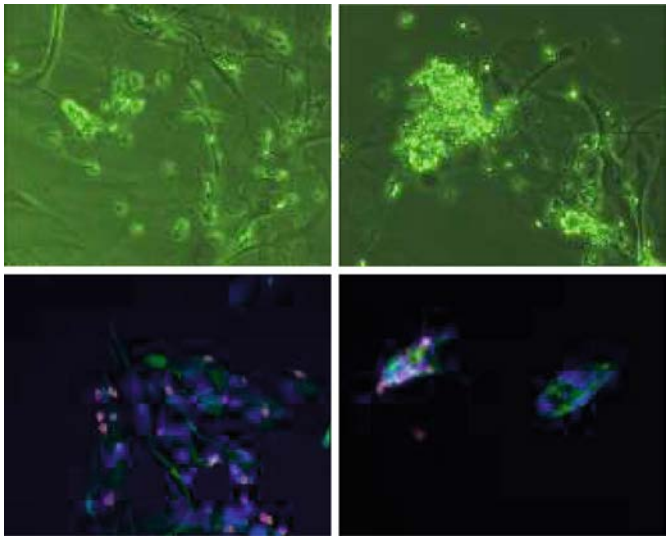


Image caption: Impact of activated microglia on the differentiation of retinal progenitor cells (neurospheres). Neurospheres were co-cultured with activated microglia or control for 14 days. b and d show cell morphology and immune reactivity of the cocultures using activated microglia; a and c show data of the controls.

Collin, S. M., Tilling, K., Joinson, C., Rimes, K. A., Pearson, R. M., Hughes, R. A., Sterne, J. A. C. & Crawley, E. (2015). Maternal and childhood psychological factors predict chronic disabling fatigue at age 13 years. *The Journal of Adolescent Health*. 56(2), p. 181-7.

Dixon, P., Davies, P., Hollingworth, W., Stoddart, M. & MacGowan, A. (2015). A systematic review of matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry compared to routine microbiological methods for the time taken to identify microbial organisms from positive blood cultures. *European Journal of Clinical Microbiology & Infectious Diseases*. Published online 27 January 2015.

Hill, E. V., Ng, T. H. S., Burton, B. R., Oakley, C. M., Malik, K. & Wraith, D. C. (2015). Glycogen synthase kinase-3 controls IL-10 expression in CD4(+) effector T-cell subsets through epigenetic modification of the IL-10 promoter. *European Journal of Immunology*. Published online 17 February 2015.

Yazid, S., Gardner, P. J., Carvalho, L., Chu, C. J., Flower, R. J., Solito, E., Lee, R. W. J., Ali, R. R. & Dick, A. D. (2015). Annexin-A1 restricts Th17 cells and attenuates the severity of autoimmune disease. *Journal of Autoimmunity*. 22 Jan 2015.

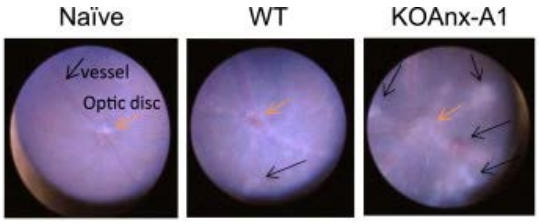


Image caption: Anx-A1$^{-/-}$ mice exhibit severe retinal inflammation during EAU associated with loss of visual function when compared to WT animals. Mice were challenged with uveitogenic RBP$_{1-20}$ peptide (500 µg) emulsion with CFA plus a Pertussis toxin i.p. injection (0.4 µg)

Carambia, A., Freund, B., Schwinge, D., Bruns, O. T., Salmen, S. C., Ittrich, H., Reimer, R., Heine, M., Huber, S., Waurisch, C., Eychmüller, A., Wraith, D. C., Korn, T., Nielsen, P., Weller, H., Schramm, C., Lüth, S., Lohse, A. W., Heeren, J. & Herkel, J. (2015). Nanoparticle-based autoantigen delivery to Treg-inducing liver sinusoidal endothelial cells enables control of autoimmunity in mice. *Journal of Hepatology*. Published online 21 January 2015.

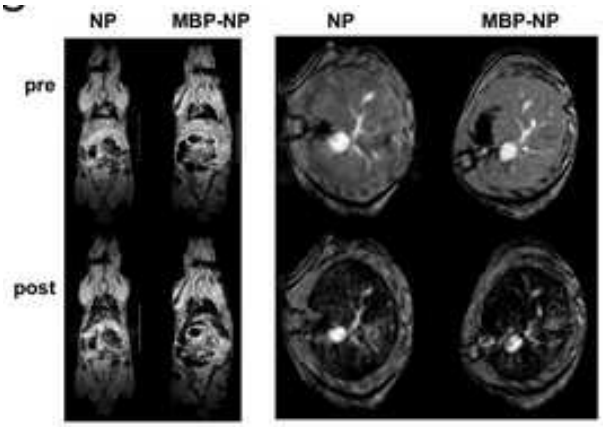


Image caption: Selective delivery of MBP peptide antigens to Treg-inducing LSECs in vivo by nanoparticles. Representative coronal (left) and transversal (right) MR images of mice before and after injection of unloaded NPs or MBP-NPs.

Rasmussen, L. D., Helleberg, M., May, M., Afzal, S., Kronborg, G., Larsen, C. S., Pedersen, C., Gerstoft, J., Nordestgaard, B. G. & Obel, N. (2015). Myocardial infarction among Danish HIV-infected individuals: Population attributable fractions associated with smoking. *Clinical Infectious Diseases*. Published online 16 January 2015.

Looker, K. J., Wallace, L. A. & Turner, K. M. (2015). Impact and cost-effectiveness of chlamydia testing in Scotland: a mathematical modelling study. *Theoretical Biology and Medical Modelling*. 12(2). p. 2.

Brittan, J. L. & Nobbs, A. H. (2015). Group B Streptococcus pili mediate adherence to salivary glycoproteins. *Microbes and Infection*. Published online 6 January 2015.

Hicks, C. A. E., Willi, B., Riond, B., Novacco, M., Meli, M. L., Stokes, C. R., Helps, C. R., Hofmann-Lehmann, R. & Tasker, S. (2015). Protective Immunity against Infection with *Mycoplasma haemofelis*. *Clinical and Vaccine Immunology*. 22(1), p. 108-118.

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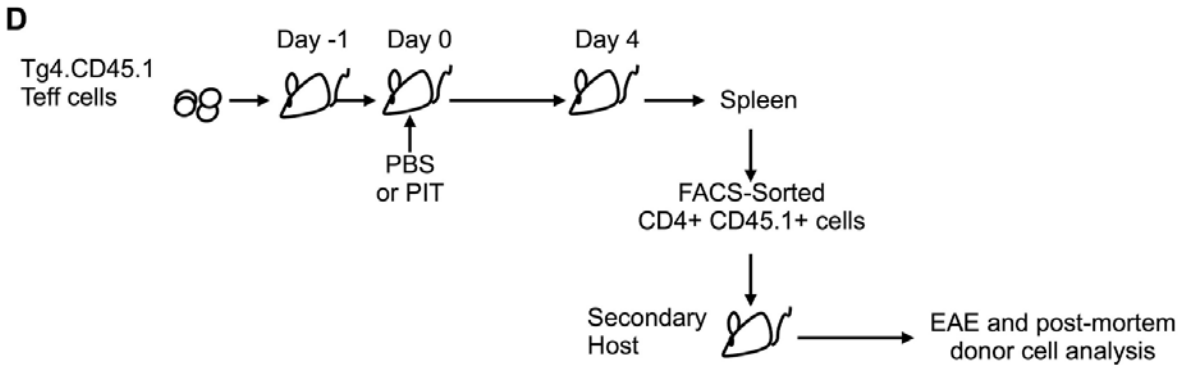

Image caption: B10.PLxC57BL/6 mice received PBS/PIT 1 day after transfer of Tg4 Teff cells. 4 days later CD4+ Tg4 donor cells were FACS-sorted and 2 × 106 were transferred into secondary hosts that were not exposed to PIT (PTX was given on the same day).

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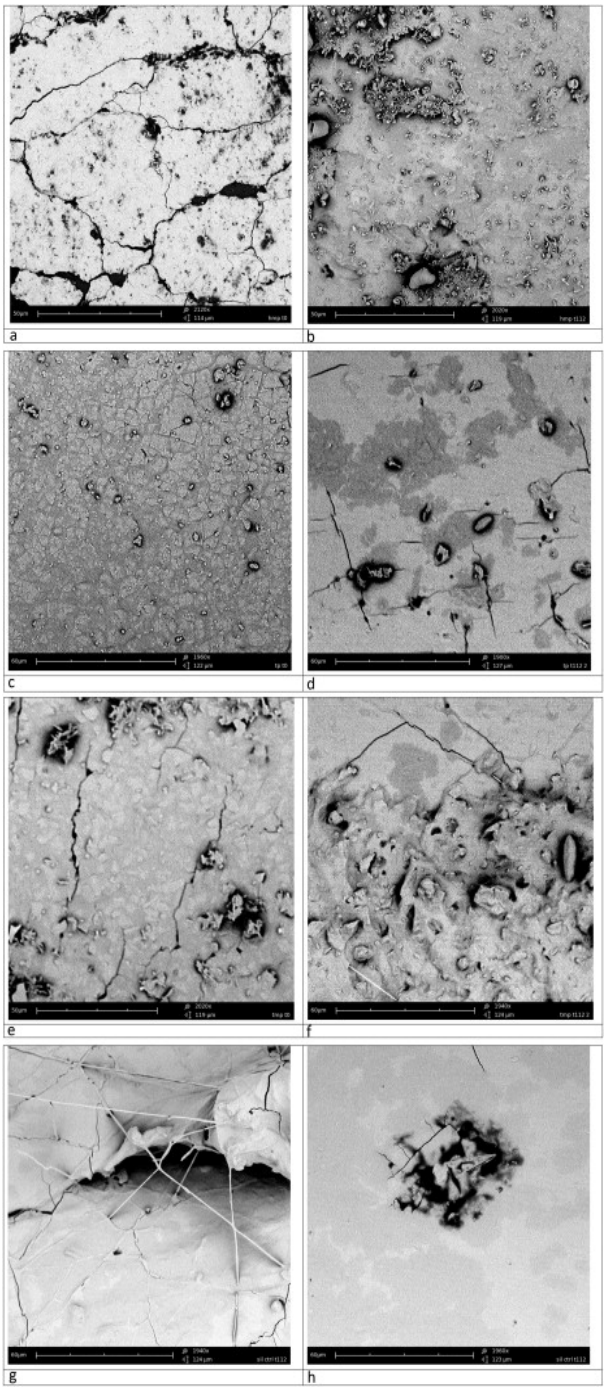

Image caption: SEM images of specimens coated with Chlorhexidine (CHX)- nanoparticles (NPs) are shown. The NPs formed a dense aggregated coating on the silicone surface. After 112 days' immersion in artificial saliva, there was some an indication that areas of NPs were still present, particularly with the CHX-hexametaphosphate (HMP) precipitate, but that the coverage was less than at the outset. The scans show body silicone coated with CHX-HMP immediately after coating (a) and after 112 days' immersion in artificial saliva (b), CHX-TP (triphosphate) immediately after coating (c) and after 112 days' immersion in artificial saliva (d), and CHX-TMP (trimetaphosphate) immediately after coating (e) and after 112 days' immersion in artificial saliva (f). Also shown, two views of uncoated body silicone after 112 days' immersion in artificial saliva.

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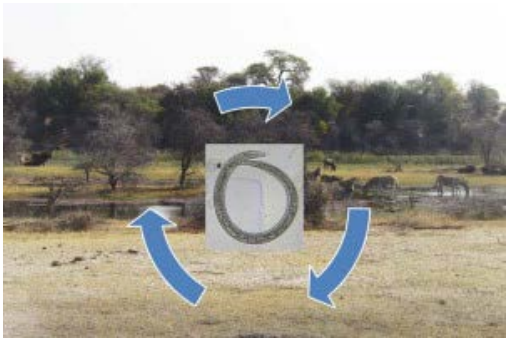

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