THE JENNER INSTITUTE
DEVELOPING INNOVATIVE VACCINES

JENNER INSTITUTE NEWS

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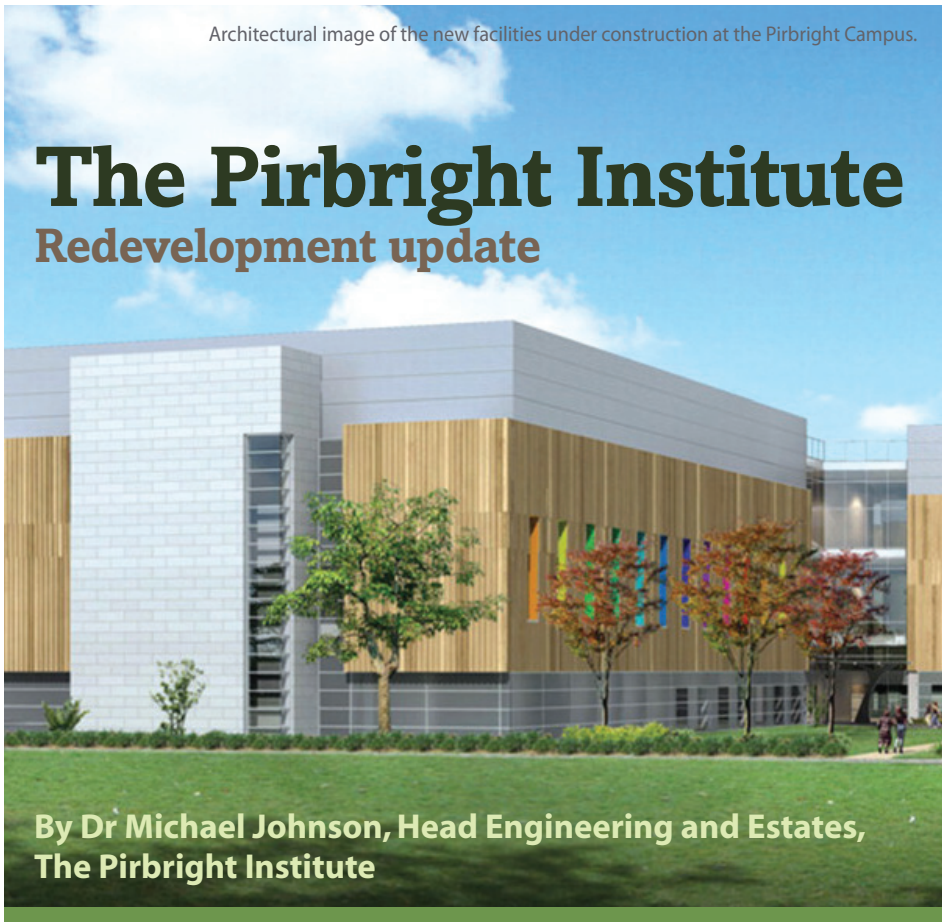
MVA85A efficacy trials: first results in African infants

HIGHLIGHTS

Promising results for new vaccine against Respiratory syncytial virus
Launch of €6m EU-funded programme to develop MRSA vaccine
Vaccinology in Africa – new Master's level course in Ghana

UNIVERSITY OF OXFORD

THE Pirbright INSTITUTE



Architectural image of the new facilities under construction at the Pirbright Campus.

The Pirbright Institute

Redevelopment update

By Dr Michael Johnson, Head Engineering and Estates, The Pirbright Institute

Phase I of the site redevelopment is on time and budget to deliver a £100+ million high-containment laboratory complex for 150 scientists and support staff.

On 04 October 2012 the Institute for Animal Health became The Pirbright Institute (TPI). This continues to be a unique national centre that works to enhance the UK's capability to contain, control, and eliminate virus disease of livestock and viruses that can spread from animals to humans. As a partner in the Jenner Institute, TPI works to develop innovative vaccines against major global diseases, focussing on both diseases of humans and of livestock.

The Institute's main campus at Pirbright is undergoing a renaissance thanks to significant financial investment from the UK government via the Biotechnology and Biological Sciences Research Council (BBSRC). To date, over £250 million has been invested in this transformation, which includes BBSRC National Capability facilities.

Phase one of the redevelopment is on time and on budget to deliver a £100+ million high-containment laboratory complex for 150 scientists and support staff. The building will be handed over from the contractors in early 2014 and is expected to become fully operational by early 2015. New containment level SAPO4 facilities for large animals are already in operation.

Future plans for development include a commercial zone, accommodation, a conference centre, facilities management and social facilities.

Phase two will provide additional laboratory facilities at CL2 as well as CL2 and CL4 facilities for poultry and small mammals. The CL2 building is expected to be completed around the end of 2016 and the CL4 facilities around the end of 2017.

About the Jenner Institute

The Jenner Institute was founded in November 2005 to develop vaccines against major global diseases. Uniquely it focuses both on diseases of humans and livestock and tests new vaccine approaches in parallel in different species. A major theme is translational research involving the rapid early-stage development and assessment of new vaccines in clinical trials.

The Institute comprises the research activities of 28 Jenner Investigators who head research groups spanning human and veterinary vaccine research and development. Together the Institute Investigators comprise one of the largest non-profit sector research and development activities in vaccinology.

Jenner Investigators, through the support of many funders, are developing vaccine candidates against major global infectious diseases. New vaccines against malaria, tuberculosis and HIV are currently in field trials in the developing world. Research is also underway on livestock vaccines against foot and mouth disease, avian influenza, bovine tuberculosis and other major causes of economic loss.

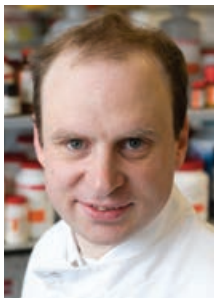
The Institute is a partnership between the University of Oxford and The Pirbright Institute. It is supported by the Jenner Vaccine Foundation, a UK registered charity and advised by a Scientific Advisory Board. The Jenner Vaccine Foundation provides strategic advice to the Institute, elects Jenner Investigators and has funded vaccine research space and facilities.

The leadership of the Institute is undertaken by the Director, Prof Adrian Hill (University of Oxford) and an Executive Committee of representatives from the partnering institutions. ■

New Jenner Vaccine Programme against

Staphylococcus aureus

By Dr David Wyllie, HPA Consultant Microbiologist and Jenner Institute Programme Leader, University of Oxford



Dr David Wyllie, a Programme Leader at the Jenner Institute, has recently been awarded a research grant of 6 million euros by the European Commission to develop a vaccine against *Staphylococcus aureus,* in collaboration with French biotech Imaxio. *S. aureus* is a bacterium which causes a range of serious infections in humans and animals, including wound infections, infection of heart, bones and joints, as well as more common infections of the skin, including abscesses and boils. Dr Wyllie is supported in this work by Drs Pauline van Diemen, Yuko Yamaguchi, and Christine Rollier.

There are many different variants (strains) of *S. aureus*, and highly antibiotic resistant strains (Methicillin-resistant *S. aureus*, MRSA) continue to emerge.

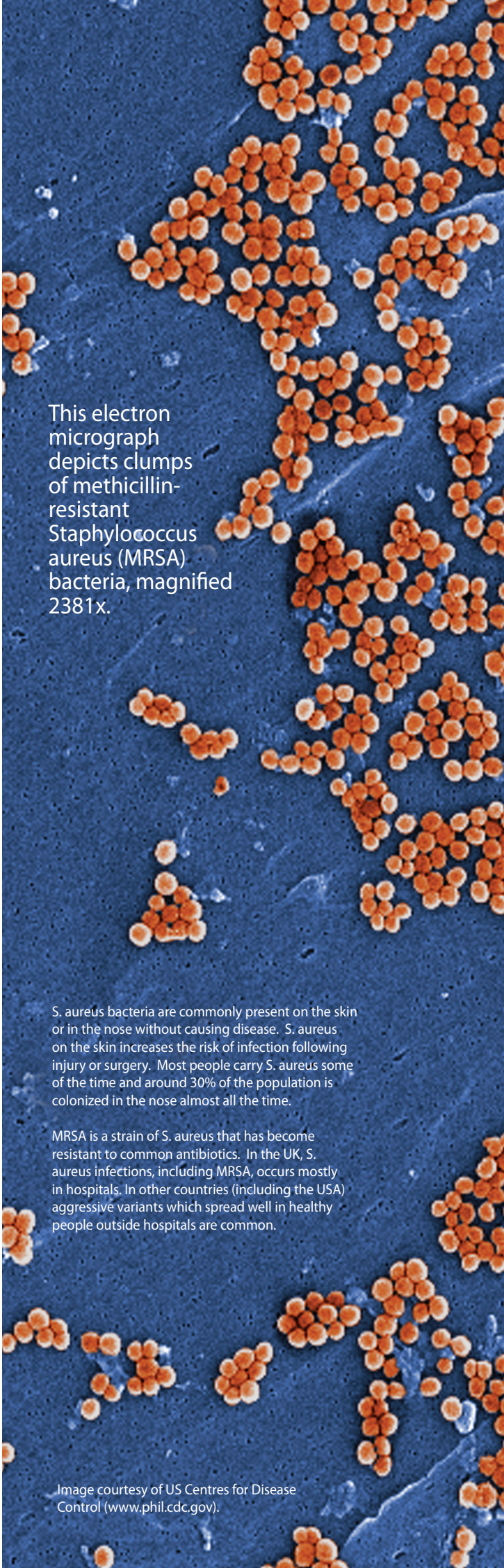
Some MRSA strains spread well in the community and hospitals, such as the USA300 strain common in North America, while other strains only seem to spread well in hospitals, as has been the case in much of Europe.

Apart from the illness and mortality caused by *S. aureus* infections, they are also very expensive to treat: estimates differ, but one recent European estimate suggested European costs of about €380 million per annum attributable to *S. aureus*.

The spread of antibiotic resistant strains, together with the requirement to use expensive and prolonged antibiotic therapy, sometimes combined with surgery, to treat *S. aureus* infections, makes a vaccine attractive.

Unfortunately, recent candidate vaccines, either using the capsule of the organism, or by using an iron uptake protein (IsdB), have not proven effective in large Phase III studies. One possible explanation for the latter failure concerns the recently discovered T cell based protection against invasive bacterial diseases, including *S. aureus*.

Our work is using viral vectored vaccines (including adenoviruses and Modified Vaccinia Ankara) to generate protective responses against *S. aureus*. Novel, protective antigens have been identified and we are looking to expand our programme of work in the near future. ■



This electron micrograph depicts clumps of methicillin-resistant Staphylococcus aureus (MRSA) bacteria, magnified 2381x.

S. aureus bacteria are commonly present on the skin or in the nose without causing disease. S. aureus on the skin increases the risk of infection following injury or surgery. Most people carry S. aureus some of the time and around 30% of the population is colonized in the nose almost all the time.

MRSA is a strain of S. aureus that has become resistant to common antibiotics. In the UK, S. aureus infections, including MRSA, occurs mostly in hospitals. In other countries (including the USA) aggressive variants which spread well in healthy people outside hospitals are common.

Image courtesy of US Centres for Disease Control (www.phil.cdc.gov).

MVA85A efficacy trials: first results in African infants

By Sam Vermaak, TB Vaccine Programme Coordinator, The Jenner Institute, University of Oxford.

The results of the first tuberculosis vaccine infant efficacy trial since the 1960s, MVA85A, a candidate vaccine developed by Jenner Investigator Prof Helen McShane, created global media interest on 4th February 2013. Unfortunately boosting BCG with MVA85A did not prove more efficacious against TB disease than BCG vaccination alone, but many lessons have been learnt and useful data generated for the TB field.

While the existing BCG vaccine protects against disseminated TB in young children, protection against pulmonary TB, the biggest killer, is very variable. Drug resistant strains are also on the rise, so a more effective vaccine is crucial to eradicating this disease.

From July 2009, 2797 BCG-vaccinated South African infants were enrolled into TB020, a Phase IIb double-blind, placebo-controlled efficacy trial, receiving either an MVA85A or a placebo booster vaccination at 4-6 months of age. The infants were followed up every 3 months, for up to 37 months. The primary outcome of the study, safety, was met. Unfortunately, the secondary outcome of efficacy, either against disease or infection, was not seen, with efficacy against TB disease at a non-significant 17.3% above BCG alone (95% CI -31.9 to 48.2).

TB is a major global health problem, with an estimated 8.7 million cases and 1.4 million deaths in 2011.

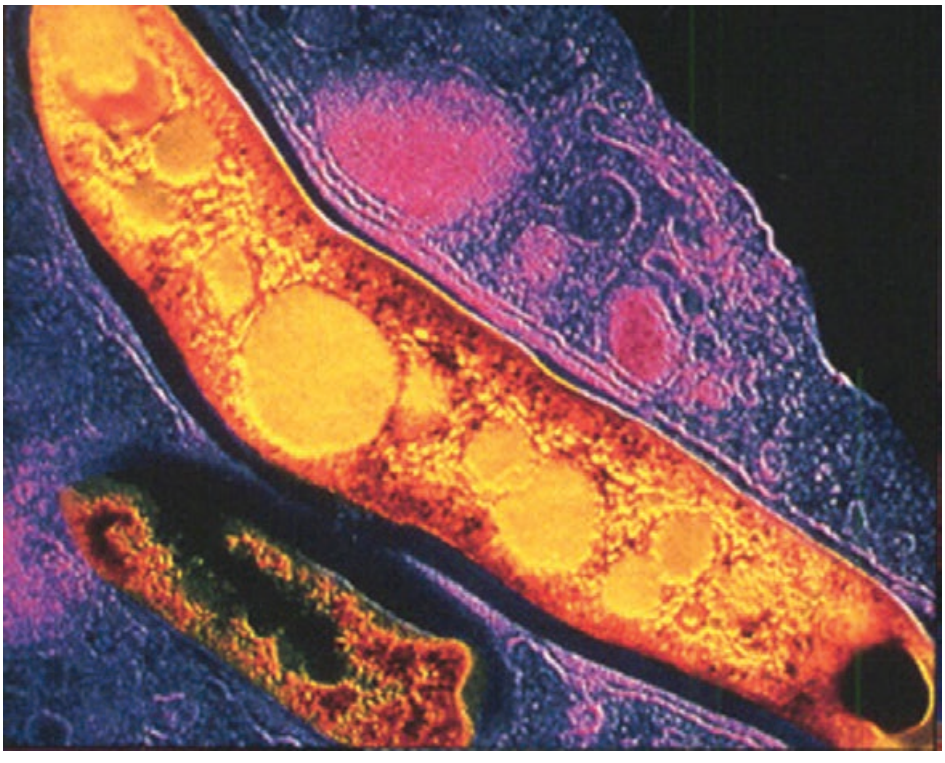
A SATVI researcher works on the MVA85A trial in SATVI's University of Cape Town laboratory. (image courtesy of Aeras/SATVI)

However, despite this disappointing outcome, the study was extremely useful for the TB field and helps point the way for future research. Firstly, when the trial began many people had concerns about the safety of giving TB vaccines to infants. TB020 has finally laid this fear to rest – and proved that TB vaccine efficacy trials are an achievable goal. Secondly, the size and cost of the trial has highlighted how important it is for TB researchers to find a correlate of protection for TB, i.e. a measurable immune response in the lab that corresponds to protection against TB disease in real life. Equally important was the creation of a challenge model for TB, so that candidate vaccines can be tested for efficacy in much smaller and cheaper challenge trials before promising vaccines go on to the more expensive large-scale efficacy trials in target countries. The TB vaccine group at the Jenner will be working on the correlate samples generated during this trial which will undoubtedly yield further immunological insights. Additionally, other administration routes such as aerosol, delivery which the Jenner TB team is already investigating and which yields far higher immune responses to vaccination, may give improved results against respiratory diseases such as TB, and this needs to be further explored.

Infant immune systems are challenging to activate, and very difficult to predict. The good news for MVA85A is that Phase I trials in adults in South Africa have shown immune responses to MVA85A up to ten times higher than those seen in infants.

Hopefully this means that the 17% efficacy in TB020, although not statistically significant, would indicate that with the larger immune responses in adults there may be higher efficacy as well. A Phase IIb efficacy trial of MVA85A in HIV-infected adults, 'TB021', is currently in progress in South Africa and Senegal to test this hypothesis. The results, expected in 2016, will add to those from TB020 and will further aid the TB vaccine field towards finding an efficacious vaccine and eliminating TB once and for all. ■

The good news: Adults have immune responses to MVA85A that are up to ten times higher than those we see in infants.



One of the first infants enrolled in the MVA85A trial in Worcester, South Africa, in July 2009. (Image courtesy of Aeras/SATVI)

A microscopic view of the bacterium that causes tuberculosis, Mycobacterium tuberculosis (Image source: Microbe Wiki).

Vaccinology in Africa – a five-day Master's level course

2nd - 6th September 2013, Noguchi Institute, Accra, Ghana

The University of Ghana in Accra

Jointly organised by the Jenner Institute and the Fondation Mérieux, the course will be covering the main aspects of vaccinology, the vaccine development process, biomanufacturing and well as regulatory and ethical issues.

The faculty will be high-profile lecturers drawn from the Oxford Vaccinology Programme, the Fondation Mérieux's Advanced Course of Vaccinology (ADVAC) and West African vaccine experts. The course resonates with the 'One Health' agenda - highlighting human and veterinary links and synergies from scientific, technological and regulatory perspectives.

The course is aimed at students, researchers and professionals resident in Africa. Delegate numbers will be limited to 30 participants. ■

The course is supported by the Jenner Vaccine Foundation, the Fondation Mérieux and GSK.

PRELIMINARY PROGRAMME

Principles of Vaccinology
- Overview of human and veterinary vaccinology
- Vaccine immunology
- Recent advances in molecular immunology & pathogen genomics
- Immunogenicity & correlates of protection
- The vaccine development pathway - from bench to market
- Ethical issues in vaccine development & deployment

Vaccine Biomanufacturing
- Current vaccines and their manufacturing requirements
- The vaccine biomanufacturing process
- GMP principles applied to vaccine production
- Introduction to Quality Assurance and testing methods

Vaccine Development and Clinical Trials
- The phases of vaccine testing - Phase I to IV
- Vaccine immunogenicity & correlates of protection in field trials
- Veterinary vaccine development
- Introduction to Good Clinical Practice.

Vaccine Development in Developing Countries
- Pre-clinical development & Phase I trials in developing countries
- Biomanufacturing in BRIC & other countries
- Large scale field trials of vaccine efficacy
- Financing challenges in vaccine provision for global health

The Noguchi Memorial Institute for Medical Research, Accra

How to apply:
Participation is competitive and places are allocated based on individual applications. 15 places are available which will cover the course fee, accommodation and meals during the course. A further 15 bursaries are available for those living further afield which will also include travel expenses.

To download an application form, please visit: www.jenner.ac.uk/vaccinology-in-africa

Application deadline is 1st June 2013

Going overseas

Teaching vaccinology in Uganda and South Africa

By Dr Simon Draper, Group Leader, Blood-stage Malaria Vaccines, The Jenner Institute

Over the last few years, I have been privileged to be invited to teach on a number of training courses for African graduate students and early-career researchers.

Immunology in the Tropics

Immunology in the Tropics is funded by a capacity-building grant from the Wellcome Trust and run by Dr Steve Cose, through the Makerere University and Uganda Virus Research Institute (UVRI) Research Training Programme. Training is organised into modules that run every March and September, at the UK MRC unit in Entebbe, Uganda. The modules cover basic immunology, immunology of TB and HIV, evolution of the immune system, as well as malaria and helminth immunology. I have been fortunate to teach on the malaria immunology module for the last three years.

The course attracts applicants from across East and West Africa, and about 25 students are selected each course. Students are often studying for a Masters or PhD degree at African Universities and research institutes. Invited speakers are tasked with providing lectures on their subject areas, as well as leading discussion sessions and journal clubs. In addition, all speakers are requested to give a seminar on their latest work which is open to the whole campus, which the MRC shares with the UVRI and the American CDC (Centers for Disease Control). Practical sessions are also held, including a one-day training course in flow cytometry.

Symposium on Infectious Diseases in Africa

The second course which I have been fortunate to teach on is run every 18 months at the University of Cape Town in South Africa. *Symposium on Infectious Diseases in Africa* is a two week residential course on the latest advances in immunology and vaccines for HIV, TB and malaria, organised by Dr Clive Gray (University of Cape Town) and Dr Guido Ferrari (Duke University).

Participants in the Immunology in the Tropics course held in March this year at the UK MRC unit in Entebbe, Uganda (Photo courtesy of Paul Ogongo).

As with the course in Uganda, the Cape Town course is largely over-subscribed, and students are attracted from all over the continent.

First week is spent teaching through lectures, seminars, journal clubs, small group discussions and Q&A sessions. Other exercises include grant writing sessions, whereby the students design, justify and present grant proposals to the Faculty, who provide advice and feedback. These can become quite competitive for the students, despite the lack of any grant money as a reward! Second week of the course is training in flow cytometry in the University labs led by experts in the field.

Both courses are hugely valuable for the students who all, without exception, appear very appreciative of the opportunity. This is reflected in their enthusiasm for all aspects of the course, and the degree to which they engage and ask many questions. For those of us teaching, the days can be long and demanding but highly rewarding.

Many students wish to continue discussing the science after sessions, and are especially driven to understand the immunology of infectious diseases which are endemic in their home countries. Many place much hope in the development of new vaccines, and duly wish to make their own contribution through their future research in Africa. ■

For more information on the courses, please visit:

Immunology in the Tropics (Uganda): www.muii.org.ug/index.html

Symposium on Infectious Diseases in Africa (South Africa): www.iidmm.uct.ac.za/

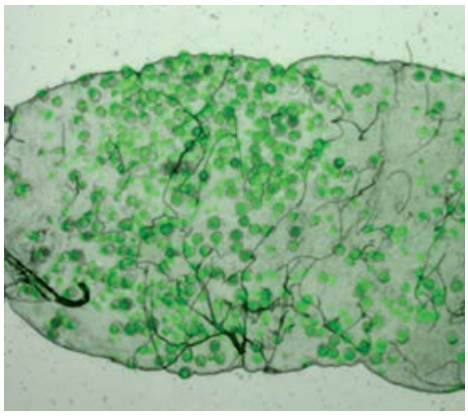
New Jenner Vaccine Programme against *Plasmodium vivax* malaria

Plasmodium vivax is the world's most widely distributed malaria parasite and a potential cause of morbidity and mortality for approx. 2.85 billion people living mainly in South East Asia and Latin America. Despite being responsible for nearly 40% of the malaria cases in the world, P. vivax receives little funding and very few vaccines have been assessed in humans.

A new programme aims to develop a vaccine to prevent malaria caused by Plasmodium vivax has been launched by Jenner Investigator Dr Arturo Reyes-Sandoval with the support of the Wellcome Trust and a team composed of Amar Lall, Joshua Blight, Erwan Atcheson, Ahmed Salman, Heather West and Fernando Reis.

The programme will follow the Jenner Institute's strategy applied to the development of a vaccine against the P. falciparum parasite. This strategy consists on the use of recombinant Modified Vaccinia Ankara (MVA) and Chimpanzee Adenoviruses (ChAd63) expressing the sporozoite antigens known as circumsporozoite protein (CSP) and thrombospondin-related adhesion protein (TRAP). Both are considered pre-erythrocytic antigens that can be targeted as soon as the parasite is injected into a human being by a mosquito and sets for the liver, a phase that can take several days. During this phase antibodies and cytotoxic lymphocytes can target the sporozoite and the infected hepatocytes to stop further development of the parasite in blood and prevent typical malaria symptoms and severe pathology. This research is aiming to develop a product that can be suitable for human clinical trials in approx. 3-4 years.

Dr. Reyes-Sandoval's group is also collaborating with scientists at the Leiden Malaria Research Group in the Netherlands (Dr. Chris Janse and Dr. Shahid Kahn) and at the Wellcome Trust Sanger Institute (Dr. Oliver Billker) to develop novel approaches to test new vaccine candidates in pre-clinical models. The aim of this project is to construct transgenic parasites to infect small pre-clinical models which express the human malaria parasite antigens. This work could potentially permit an early and rapid assessment of new vaccine candidates for P. vivax malaria, without the requirement of expensive clinical trials and avoiding difficulties in obtaining P. vivax parasite isolates available only in countries where this type of malaria is endemic. ■



Photomicrograph showing the midgut of an Anopheles mosquito infected with a transgenic Plasmodium parasite expressing green fluorescent protein (GFP). When a mosquito ingests blood of a malaria-infected host, the parasite's gametes fertilize and the resulting zygotes (ookinetes) travel to the midgut epithelium where they form structures known as oocysts (the green spheres in the micrograph).

A Phase IIb trial to test safety and efficacy of a malaria vaccine in Burkinabe children and infants

By Rachel Roberts, Malaria Vaccine Programme Coordinator, Jenner Institute, University of Oxford

FIELD TRIAL UPDATE

Dr Mohammed Afolabi immunizing a participant in the "VAC 042" infant vaccination trial, Medical Research Council Unit, The Gambia.

Malaria is the preeminent tropical infectious disease globally, with most cases occurring in Africa. It is fatal predominantly in children under the age of five years, with over 90% of cases due to the parasite species, Plasmodium falciparum. The development of a vaccine against malaria is of paramount importance to reduce the burden of this devastating disease.

A prime-boost vaccination regimen with ChAd63 ME-TRAP, followed eight weeks later by MVA ME-TRAP, has shown durable partial efficacy in a P. falciparum malaria challenge study in UK adults. Testing of this promising vaccination strategy in adults living in malaria-endemic areas has recently taken place in The Gambia, Kenya and Senegal.

Age de-escalation along with dose optimisation was the next objective in progressing towards vaccinating the population who would benefit most from a malaria vaccine, i.e. young children. The prime boost regimen was then administered to 24 Gambian children (aged 5-12 months), followed by 24 ten week old infants. The vaccines continued to elicit promising immune responses in these younger children while showing a good safety profile.

Plans were then developed to scale up the vaccine trials with the aim of assessing the protective effect of ChAd63 ME-TRAP / MVA ME-TRAP prime-boost immunisation, in 5-17 month old infants and children living in a malaria-endemic area (Burkina Faso).

Following the success of a lead-in Phase I safety evaluation of 30 participants, the scene is set in the spring of 2013 to vaccinate seven hundred 5-17 month old infants and children in a double-blinded, randomized controlled study, with a planned 2 year follow-up period. ■

Towards a Universal Influenza Vaccine

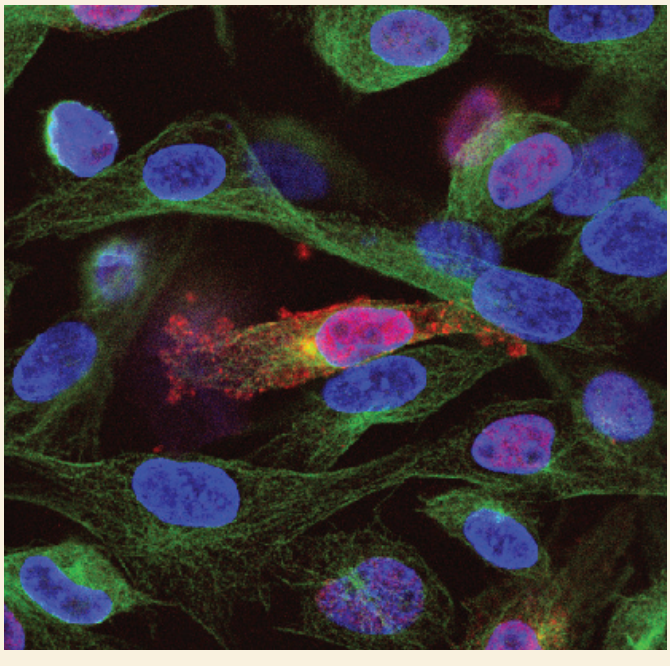
By Dr Colin Butter, Avian Viral Immunology Group, The Pirbright Institute

Avian influenza virus threatens food security and, as the potential source of a pandemic virus, human health.

Conventional antibody-inducing flu vaccines target the viral surface proteins hemagglutininn (HA) and neuraminidase (NA), which are highly variable between strains of virus, requiring a close antigenic match of field virus and vaccine. Additionally, new viruses constantly evolve which escape vaccine protection and necessitate reformulation of field vaccines to better match these emerging strains. **A more sustainable strategy is the development of heterosubtypic immunity by a universal vaccine that could protect animals and humans from all types of influenza virus.**

Recent progress has been made by Jenner researchers at The Pirbright Institute and Oxford University, with research published in the journal Vaccine demonstrating immunogenicity of two well-understood human viral vectors, Adenovirus 5 and Modified Vaccinia Ankara, carrying the NP and M1 genes of a human H3N2 influenza virus. This combination gave partial protection in chickens to challenge with a distantly related H7N7 avian virus.

NP and M1 are "internal" proteins, not present on the outside of the virus and relatively highly conserved, accounting for vaccine cross-protection between viral strains. The research, led by Colin Butter at The Pirbright Institute and Sarah Gilbert at the University of Oxford, is now aiming to improve the efficacy of this approach and develop a vaccine that would be fully effective against a wide variety of influenza viruses whilst not promoting antigenic variation. ■



Electron micrograph of Flu virus infecting chicken cells. Expression of the nucleoprotein of influenza virus (red) starts in the nucleus, spreading to the cytoplasm and eventually being released from the cell. Nuclei are blue with tubulin, showing the cytoskeleton, in green.

Image source: Karen Staines, The Pirbright Institute

Challenging typhoid disease

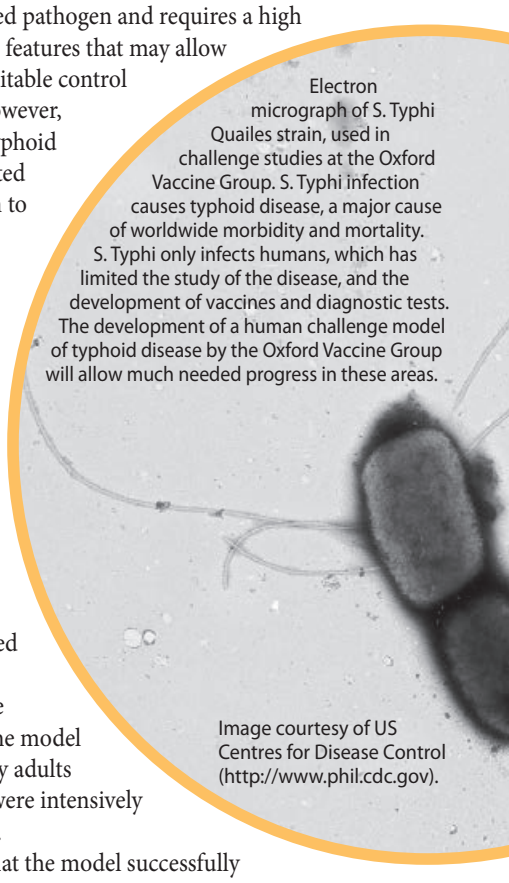
By Dr Claire Waddington, Oxford Vaccine Group, Department of Paediatrics, University of Oxford

The Typhoid research team, Oxford Vaccine Group

The Oxford Vaccine Group, headed by Prof Andrew Pollard (Jenner Investigator), has successfully developed a controlled human infection model of typhoid disease and is now using this to develop vaccines and diagnostic tests. Typhoid disease is caused by infection with the bacterium S. Typhi, and worldwide causes significant mortality and morbidity in disease endemic countries and travellers.

S. Typhi is a human restricted pathogen and requires a high innoculum to cause disease, features that may allow its eventual eradication if suitable control measures were available. However, although vaccines against typhoid disease exist, they have limited efficacy and cannot be given to young children.

Novel vaccine development has been attempted, but has been held back by a poor understanding of the protective immune response to S. Typhi infection. Clinical management and field trials are hindered by the lack of reliable diagnostic tests. The Oxford Vaccine Group developed a controlled human infection model of typhoid disease to overcome some of these difficulties. The model was established in 40 healthy adults who ingested S. Typhi and were intensively followed up over two weeks.



Electron micrograph of S. Typhi Quailes strain, used in challenge studies at the Oxford Vaccine Group. S. Typhi infection causes typhoid disease, a major cause of worldwide morbidity and mortality. S. Typhi only infects humans, which has limited the study of the disease, and the development of vaccines and diagnostic tests. The development of a human challenge model of typhoid disease by the Oxford Vaccine Group will allow much needed progress in these areas.

Image courtesy of US Centres for Disease Control (http://www.phil.cdc.gov).

We were able to show that the model successfully replicated naturally occurring disease and was extremely safe. Participants were also very positive about their experience. We then validated the model as a way to appraise vaccines by demonstrating protective efficacy of the licenced Ty21a vaccine against challenge. The model has since been used to investigate novel vaccines, the nature of immune protection and to develop diagnostic tests. These studies might ultimately contribute to typhoid eradication worldwide. ■

Jenner Investigator Profiles

Andrew McMichael

I qualified in Medicine in 1968 and worked for a PhD on B cell memory with Ita Askonas and Alan Williamson at the MRC National Institute for Medical Research, Mill Hill, between 1971 and 1974. Then I went to work with Hugh McDevitt in Stanford for two and a half years before coming to Oxford in 1977. I moved to the Weatherall Institute of Molecular Medicine when it was first built in 1989 and succeeded David Weatherall as Director from 2000-2012. I founded the MRC Human Immunology Unit in 1998 and was its Honorary Director until 2010.

My research has focused on human immune responses, particularly CD8 T cell responses to influenza virus and HIV-1. I first showed CD8 T cell responses in humans were HLA restricted in 1977, then showed that T cell responses to influenza virus were associated with rapid clearance of nasal virus in 1983. In 1986, Alain Townsend in my group showed that CD8 T cell recognized short peptides, derived from virus proteins, presented by MHC molecules. Different HLA types presented different peptides. We applied this to HIV shortly afterwards and then showed that CD8 T cells selected mutant epitopes as virus escaped, indicating the very strong antiviral pressure exerted by these immune cells. In 2003, in collaboration with Mark Davis at Stanford we introduced HLA-tetramers for the study and quantitation of antiviral T cell responses.

Since 2000 I have been working with Tomas Hanke on the design of vaccines that stimulate anti-HIV CD8 T cell responses. We are currently testing a vaccine we designed together, that just elicits T cell responses to the least variable parts of the virus. This should be more effective because it will be hard for virus to escape. These phase I clinical trials are being conducted at the Jenner Institute. I am also one of the leaders of the NIH funded consortium, Center for HIV AIDS Vaccine Immunology – Immunogen Discovery, that is developing more advanced approaches to HIV vaccine design. HIV vaccine discovery is now the main focus of my research.

Key Publications:

McMichael, A.J., A. Ting, H.J. Zweerink, and B.A. Askonas. 1977. HLA restriction of cell-mediated lysis of influenza virus-infected human cells. *Nature* 270:524-526.

McMichael, A.J., F.M. Gotch, G.R. Noble, and P.A. Beare. 1983. Cytotoxic T-cell immunity to influenza. *N Engl J Med* 309:13-17.

Townsend, A.R., J. Rothbard, F.M. Gotch, G. Bahadur, D. Wraith, and A.J. McMichael. 1986. The epitopes of influenza nucleoprotein recognized by cytotoxic T lymphocytes can be defined with short synthetic peptides. *Cell* 44:959-968.

Phillips, R.E., S. Rowland-Jones, D.F. Nixon, F.M. Gotch, J.P. Edwards, A.O Ogunlesi, J.G. Elvin, J.A. Rothbard, C.R. Bangham, C.R. Rizza, and McMichael, A.J. 1991. Human immunodeficiency virus genetic variation that can escape cytotoxic T cell recognition. *Nature* 354:453-459.

Altman, J.D., P.A. Moss, P.J. Goulder, D.H. Barouch, M.G. McHeyzer-Williams, J.I. Bell, A.J. McMichael, and M.M. Davis. 1996. Phenotypic analysis of antigen-specific T lymphocytes. *Science* 274:94-96.

Goonetilleke, N., M.K. Liu, J.F. Salazar-Gonzalez, G. Ferrari, E. Giorgi, V.V. Ganusov, B.F. Keele, G.H. Learn, E.L. Turnbull, M.G. Salazar, K.J. Weinhold, S. Moore, N. Letvin, B.F. Haynes, M.S. Cohen, P. Hraber, T. Bhattacharya, P. Borrow, A.S. Perelson, B.H. Hahn, G.M. Shaw, B.T. Korber, and A.J. McMichael. 2009. The first T cell response to transmitted/founder virus contributes to the control of acute viremia in HIV-1 infection. *J Exp Med* 206:1253-1272.

Liu, M.K., N. Hawkins, A.J. Ritchie, V.V. Ganusov, V. Whale, S. Brackenridge, H. Li, J.W. Pavlicek, F. Cai, M. Rose-Abrahams, F. Treurnicht, P. Hraber, C. Riou, C. Gray, G. Ferrari, R. Tanner, L.H. Ping, J.A. Anderson, R. Swanstrom, M. Cohen, S.S. Karim, B. Haynes, P. Borrow, A.S. Perelson, G.M. Shaw, B.H. Hahn, C. Williamson, B.T. Korber, F. Gao, S. Self, A. McMichael, and N. Goonetilleke. 2013. Vertical T cell immunodominance and epitope entropy determine HIV-1 escape. *J Clin Invest* 123:380-393.

Arturo Reyes-Sandoval

I undertook a degree in Microbiology at the National Polytechnic Institute (IPN) in Mexico City where I also completed an MSc in Cytopathology and a PhD in Molecular Medicine. My PhD research training was at the Wistar Institute and the University of Pennsylvania with Professor Hildegund Ertl, developing new recombinant adenovirus from chimpanzee isolates as an alternative to the human serotypes, in order to make more effective vaccines.

My interest in vaccinology started in 1999 when I joined a research group working on the frontiers of gene replacement therapy and vaccine development at the Wistar Institute and the University of Pennsylvania in Philadelphia. It was this decade when the field of gene therapy developed a system that unintentionally would become an important tool and the cornerstone of one of the leading vaccination strategies of our days: the chimpanzee adenoviral vectors. My initial contributions lead to the development of various vaccine candidates, including rabies, papillomavirus and HIV. My interest in further expanding the application of these vaccines took me to Professor Adrian Hill's laboratory and in 2008 I published the first report of a malaria vaccine using chimpanzee adenoviruses. My research has since focused on establishing the optimal vaccination regimen in mice and nonhuman primates, crucial for the design and application of this system in human trials for malaria. The use of chimpanzee adenoviruses has evolved very rapidly, becoming the core of the vaccine research and development at the Jenner Institute.

In 2012, I became a Wellcome Trust Career Development Fellow and a University Research Lecturer. My group now focuses on the development of a vaccine against the neglected form of malaria caused by Plasmodium vivax, which is prevalent mainly in Latin America and South East Asia. I am also involved in projects to develop a vaccine against Dengue and Chagas disease.

Key Publications:

Reyes-Sandoval A, Rollier CS, Milicic A, Bauza K, Cottingham MG, Tang CK, Dicks MD, Wang D, Longley RJ, Wyllie DH, Hill AV. Mixed Vector Immunization With Recombinant Adenovirus and MVA Can Improve Vaccine Efficacy While Decreasing Antivector Immunity. Mol. Ther. 20(8): 1633-47. 2012

O'Hara GA, Duncan CJ, Ewer KJ, Collins KA, Elias SC, Halstead FD, Goodman AL, Edwards NJ, Reyes-Sandoval A, Bird P, Rowland R, Sheehy SH, Poulton ID, Hutchings C, Todryk S, Andrews L, Folgori A, Berrie E, Moyle S, Nicosia A, Colloca S, Cortese R, Siani L, Lawrie AM, Gilbert SC, Hill AV. Clinical assessment of a recombinant simian adenovirus ChAd63: a potent new vaccine vector. J. Infect. Dis. 205(5): 772-781. 2012.

Reyes-Sandoval, A; Wyllie, D.H; Bauza, K; Milicic, A; Forbes, E.K; Rollier, C.S. and A.V.S. Hill. CD8+ T Effector Memory Cells protect against Liver-Stage Malaria. Journal of Immunology. 187(3):1347-57. 2011.

Capone, S*; Reyes-Sandoval, A*; Naddeo, M; Siani, L; Ammendola, V; Rollier, C.S; Nicosia, A; Colloca, S; Cortese, R. Folgori, A. and Hill, A.V. Immunogenicity in macaques of prime-boost regimes using the simian adenoviral vector AdCh63 and the poxvirus MVA expressing the pre-erythrocytic antigen ME.TRAP from *P. falciparum*. Vaccine 29(2):256-65. 2010.

Reyes-Sandoval A, Berthoud T, Alder N, Siani L, Gilbert SC, Nicosia A, Colloca S, Cortese R, Hill AV. Prime-boost immunization with adenoviral and modified vaccinia virus ankara vectors enhances the durability and polyfunctionality of protective malaria CD8+ T-cell responses. Infection and Immunity. 78(1):145-53. 2010.

Reyes-Sandoval, A., Sridhar, S., Berthoud, T., Moore, A.C., Harty, J.T., Gilbert, S.C., Gao, G.P., Ertl, H.C.J., Wilson, J.M. and A.V.S. Hill. Single dose immunogenicity and protective efficacy of simian adenoviral vectors against P. berghei. European Journal of Immunology. 38(3):732-41. 2008.

Tatsis N*, Fitzgerald JC*, Reyes-Sandoval A*, Harris-McCoy KC, Hensley SE, Zhou D, Lin SW, Bian A, Xiang ZQ, Iparraguirre A, Lopez-Camacho C, Wherry EJ, Ertl HC. Adenoviral vectors persist in vivo and maintain activated CD8+ T cells: implications for their use as vaccines. Blood. 110(6):1916-23. 2007.

Persephone Borrow

I undertook an undergraduate and a PhD degree at the University of Cambridge, followed by postdoctoral research with Dr Michael Oldstone at The Scripps Research Institute, where I became an Assistant Professor. In 1997 I became leader of the Viral Immunology group at the newly-established Edward Jenner Institute for Vaccine Research; and in 2005 I joined the University of Oxford, where I am currently a Reader and a Jenner Institute Investigator. Here, my group is carrying out basic research on innate and T cell-mediated immune responses and their subversion by viruses to inform the design of vaccines for persistent virus infections.

Much of our current work is focused on immune responses in human immunodeficiency virus type 1 (HIV-1) infection. Together with Prof Andrew McMichael's group, we are working as part of the Centre for HIV/AIDS Vaccine Immunology and Immunogen Discovery to understand how effective HIV vaccination strategies can be developed.

Most antiviral vaccines confer protection via stimulation of neutralising antibody responses, but induction of antibodies with broad neutralising activity against the many circulating HIV-1 strains is extremely challenging. One of our aims is to understand the role played by CD4+ follicular helper T (TFH) cells in promoting the generation of HIV-1 broadly-neutralising antibodies.

Other immune responses can also be employed in HIV vaccine design. Having previously shown that virus-specific CD8+ T cell responses are rapidly induced in primary HIV-1 infection and make an important contribution to control of virus replication, other work in the group is addressing why the CD8+ T cell response in most infected individuals fails to contain HIV replication more completely. By identifying how CD8+ T cell control of HIV is evaded we aim to understand how vaccines can be designed to induce optimally-effective HIV-specific CD8+ T cell responses.

A third objective is to determine whether innate effector responses can be harnessed to contribute to HIV prophylaxis. Recent results show that type 1 interferons play an important role in restricting HIV-1 replication very early after transmission, and we are now addressing the interferon-stimulated genes that mediate this activity. Natural killer (NK) cells also exert antiviral activity against HIV. Other studies aim to identify the ligands on HIV-infected cells recognised by NK cells and explore the feasibility of developing vaccine immunogens that enhance NK cell control of HIV.

Key Publications:

Chronic HIV infection affects the expression of the 2 transcription factors required for CD8 T-cell differentiation into cytolytic effectors. Ribeiro-dos-Santos P, Turnbull EL, Monteiro M, Legrand A, Conrod K, Baalwa J, Pellegrino P, Shaw GM, Williams I, Borrow P, Rocha B. Blood. 2012 May 24;119(21):4928-38.

Escape is a more common mechanism than avidity reduction for evasion of CD8+ T cell responses in primary human immunodeficiency virus type 1 infection. Turnbull EL, Baalwa J, Conrod KE, Wang S, Wei X, Wong M, Turner J, Pellegrino P, Williams I, Shaw GM, Borrow P. Retrovirology. 2011 Jun 2;8:41.

Evidence of dysregulation of dendritic cells in primary HIV infection. Sabado RL, O'Brien M, Subedi A, Qin L, Hu N, Taylor E, Dibben O, Stacey A, Fellay J, Shianna KV, Siegal F, Shodell M, Shah K, Larsson M, Lifson J, Nadas A, Marmor M, Hutt R, Margolis D, Garmon D, Markowitz M, Valentine F, Borrow P, Bhardwaj N. Blood. 2010 Nov 11;116(19):3839-52.

The immune response during acute HIV-1 infection: clues for vaccine development. McMichael AJ, Borrow P, Tomaras GD, Goonetilleke N, Haynes BF. Nat Rev Immunol. 2010 Jan;10(1):11-23.

Kinetics of expansion of epitope-specific T cell responses during primary HIV-1 infection. Turnbull EL, Wong M, Wang S, Wei X, Jones NA, Conrod KE, Aldam D, Turner J, Pellegrino P, Keele BF, Williams I, Shaw GM, Borrow P. J Immunol. 2009 Jun 1;182(11):7131-45.

Induction of a striking systemic cytokine cascade prior to peak viremia in acute human immunodeficiency virus type 1 infection, in contrast to more modest and delayed responses in acute hepatitis B and C virus infections. Stacey AR, Norris PJ, Qin L, Haygreen EA, Taylor E, Heitman J, Lebedeva M, DeCamp A, Li D, Grove D, Self SG, Borrow P. J Virol. 2009 Apr;83(8):3719-33.

Determinants of human immunodeficiency virus type 1 escape from the primary CD8+ cytotoxic T lymphocyte response. Jones NA, Wei X, Flower DR, Wong M, Michor F, Saag MS, Hahn BH, Nowak MA, Shaw GM, Borrow P. J Exp Med. 2004 Nov 15;200(10):1243-56. Association of strong virus-specific CD4 T cell responses with efficient natural control of primary HIV-1 infection. Gloster SE, Newton P, Cornforth D, Lifson JD, Williams I, Shaw GM, Borrow P. AIDS. 2004 Mar 26;18(5):749-55.

Antiviral pressure exerted by HIV-1-specific cytotoxic T lymphocytes (CTLs) during primary infection demonstrated by rapid selection of CTL escape virus. Borrow P, Lewicki H, Wei X, Horwitz MS, Peffer N, Meyers H, Nelson JA, Gairin JE, Hahn BH, Oldstone MB, Shaw GM. Nat Med. 1997 Feb;3(2):205-11.

Sarah Rowland-Jones

I trained in medicine, first in Cambridge and then at clinical school in Oxford, before embarking on post-graduate training in general medicine and infectious diseases. I came to research relatively late in my medical career, embarking on a PhD with Professor Andrew McMichael, looking at the cytotoxic T-cell response to HIV-1 infection and how viral variation can lead to the emergence of mutants that evade the response. My research group grew during a series of MRC fellowships (Clinical training, Clinician scientist and Senior fellowship) and we have worked with clinicians and epidemiologists around the world to study cellular immune responses to HIV and other viral infections in diverse patient cohorts in Africa and Asia. The main question we have attempted to address is which immune responses (that could be induced with candidate vaccines) would confer protective immunity against HIV infection. An increasing interest in tropical medicine and global health led me first to becoming Director of the Oxford Centre for Tropical Medicine and subsequently to a move to West Africa, where for several years I was Research Director of the MRC Laboratories in The Gambia. Whilst in The Gambia, through our studies in the Sukuta Infant Immunology field site, I became particularly interested in studying how the infant immune system responds to vaccines given in early life and how this is affected by intercurrent infections and other vaccines given at the same time. Back in Oxford, my group continues to study the immunology of HIV-1 and HIV-2 infection, working with teams in China, West Africa, Kenya and Zimbabwe.

Key Publications:

Rowland-Jones, S.L., Sutton, J., Ariyoshi, K., Dong, T., Gotch, F., McAdam, S., Whitby, D., Sabally, S., Takiguchi, M., Schultz, T., McMichael, A., Whittle, H.: HIV-specific cytotoxic T-cells in HIV-exposed but uninfected Gambian women. *Nature Medicine* (1995) 1: 59 - 64

Kaul, R., Dong, T., Plummer, F.A., Kimani, J., Rostron, T., Kiama, P., Njagi, E., Chakraborty, R., Irungu, E., Farah, B., Oyugi, J., MacDonald, K.S., Bwayo, J.J., McMichael, A.J. and Rowland-Jones, S.L.: HIV-specific CD8+ lymphocyte responses correlate with resistance to HIV infection, and target different epitopes in seronegative and infected subjects. J. Clin. *Investigation* (2001) 107: 1303-1310

Appay, V., Dunbar, P.R., Callan, M., Klenerman, P., Gillespie, G.M.A., Ogg, G.S., King, A., Papagno, L., Lechner, F., Spina, C.A., Havlir, D.V., Richman, D.D., Gruener, N., Pape, G., Waters, A., Easterbrook, P., McMichael, A.J., and Rowland-Jones, S.L.: Virus-specific CD8+ T cells differ in maturation state in different persistent virus infections. *Nature Medicine* (2002) 8: 379-385

Dong, T., Stewart-Jones, G., Chen, N., Xu, X., Papagno, L., Appay, V., Weekes, M., Conlon, C., Spina, C., Little, S., Screaton, G., Richman, D.R., Easterbrook, P., McMichael, A.J., Jones, E.Y. and Rowland-Jones, S.L. HIV-specific cytotoxic T cells from long-term survivors select a unique T-cell receptor *J. Exp. Medicine* (2004) 200: 1547-1557

Luhn, K., Simmons, C.P., Moran, E., Dung, N.T.P., Chau, T.N.B., Thao, L.T.T., Ngoc, T.V., Dung, N.M., Wills, B., Farrar, J., McMichael, A.J., Dong, T and Rowland-Jones, S.L. Increased frequencies of CD4+CD25high regulatory T-cells in acute dengue infection *Journal of Experimental Medicine* (2007) 204: 979-985

Leligdowicz, A., Yindom, L-M., Onyango, C., Sarge-Njie, R., Alabi, A., Cotten, M., Vincent, T., da Costa, C, Aaby, P., Jaye, A., Dong, T., McMichael, A.J., Whittle, H.C. and Rowland-Jones, S.L. Robust gag-specific T-cell responses characterize viraemia control in HIV-2 infection *Journal of Clinical Investigation* (2007) 117: 3067-74

John-Stewart, G.C., Mbori-Ngacha, D., Lohman-Payne, B., Farquhar, C., Richardson, B., Emery, S., Otieno, P., Obimbo, E., Dong, T., Slyker, J., Nduati, R., Overbaugh, J. and Rowland-Jones, S.L. HIV-1 specific CTLs and Breastmilk HIV-1 transmission *Journal of Infectious Diseases* (2009) 199: 889-98

Dong, T., Zhang, Y., Xu, K.Y., Yan, H., James, I., Peng, Y., Blais, M-E, Gaudieri, S., Xinyue Chen, X., Lun, W.H., Wu, H., Zhao, C.H., Rostron, T., Li, N., Mao, Y., Mallal, S., Xu, X., McMichael, A., John, M. and Rowland-Jones, S.L. Extensive HLA-driven viral diversity detected following a single-source HIV-1 outbreak in rural China *Blood* (2011) 118: 98-106

One Health approach to the development of a vaccine against RSV infection in children

By Dr Geraldine Taylor, Respiratory Syncytial Virus Research Leader, The Pirbright Institute

A new vaccine against respiratory syncytial virus (RSV), the most common cause of severe respiratory infections in infants and young children, has shown promising results in pre-clinical studies in calves, a natural host of bovine (B)RSV.

Annual epidemics of RSV disease occur during the winter and early spring and most severe disease is seen in infants less than 6 months of age. In the UK, the annual incidence of hospital admissions due to RSV in children less than 1 year old is 2 to 3%. Nearly all children have been infected with RSV by 2 years of age and the virus readily reinfects throughout life, even with closely related virus strains. In fact, the burden of RSV disease in the elderly is comparable to that of seasonal influenza, while the economic impact of RSV disease in adults is even greater.

There is a need for a safe and effective RSV vaccine not only to protect infants, but also to boost immunity in adults and the elderly, thereby reducing circulation of RSV in the community.

There is currently no effective RSV vaccine or anti-viral therapy and vaccine development has been hampered by the experience with a formalin-inactivated RSV vaccine that was evaluated in infants and young children in the 1960s. The vaccine failed to protect against RSV infection and vaccinated infants developed more severe disease following natural exposure than unvaccinated infants.

RSV is a major cause of respiratory disease in infants throughout the world, causing severe disease in an estimated 34 million children under the age of 5 years, every year (Nair et al., 2010).

Ideally, an RSV vaccine should induce rapid, protective antibody and cell-mediated immune responses and not prime for enhanced disease in very young infants, and should also be able to boost immune responses in those whose immunity has declined. To this end, researchers at The Pirbright Institute, in collaboration with Okairos, an Italian biotech company, have used a new approach to stimulate both an antibody and a T-cell response.

They have used a replication-defective chimpanzee adenovirus (ChAd) vector, which is not neutralized by pre-existing immunity in humans, and an attenuated poxvirus vector, Modified Vaccinia Ankara (MVA), expressing a string of conserved RSV proteins, and evaluated the ability of the vaccine to protect calves against bovine (B)RSV. BRSV, which is the most important cause of respiratory disease in young calves, is closely related to human RSV, and the epidemiology and pathogenesis of disease caused by these viruses are similar. Pre-clinical studies, especially trials in calves at Compton, showed excellent safety, immunogenicity and efficacy.

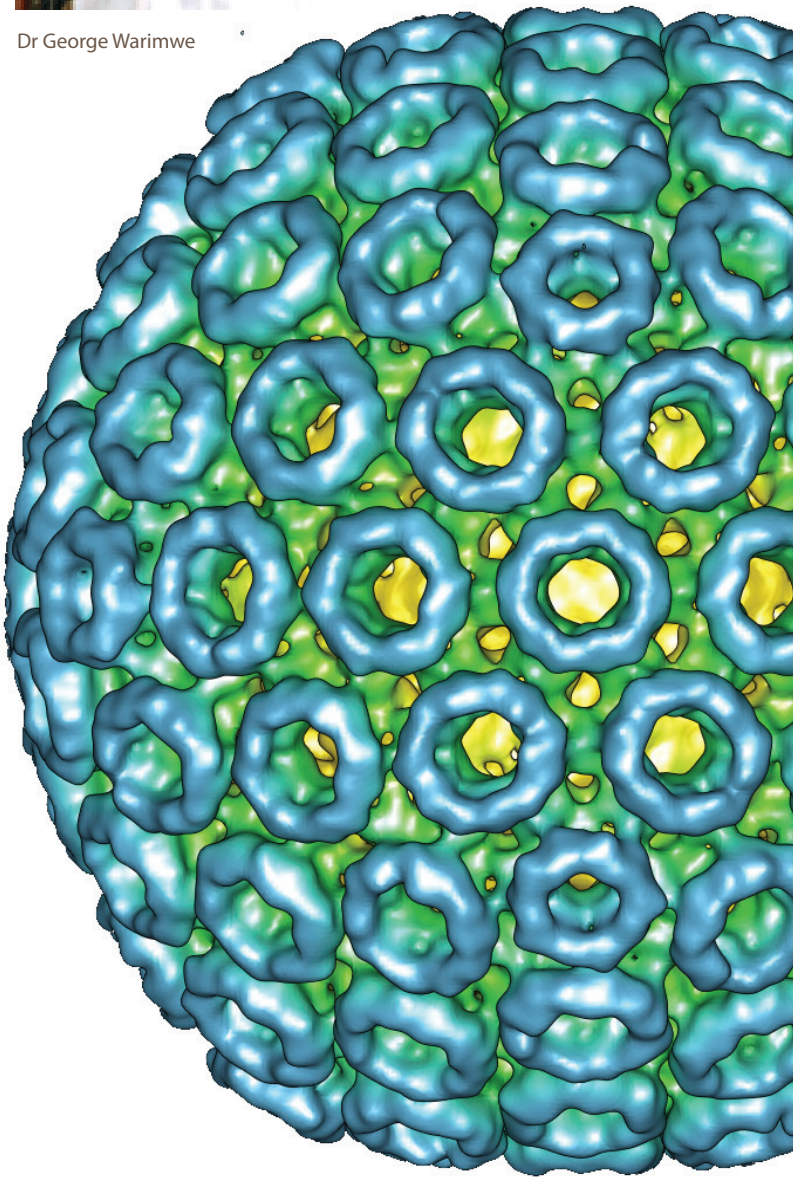
The vaccine is soon to go into a Phase I clinical trial involving 40 healthy adult volunteers in the UK. The exploitation of BRSV infection in the natural host, calves, to evaluate an RSV vaccine being developed for use in man, highlights the value of the One Health approach of uniting research in veterinary and human medicine in the development of vaccines. ■

One Health: Development of a Rift Valley Fever vaccine that can be used in both humans and livestock

By Dr George Warimwe, Veterinary Surgeon and Wellcome Trust Training Fellow in Public Health and Tropical Medicine, Jenner Institute, University of Oxford

Rift Valley Fever (RVF) is one of numerous diseases that are transmitted between animals and humans, the so-called zoonoses. It is caused by a mosquito-borne virus that was first isolated from sheep on a Kenyan farm in 1930 and has since spread throughout much of sub-Saharan Africa and parts of the Middle East, causing extensive outbreaks that constrain both livestock production and human health.

Dr George Warimwe



Graphic illustration of the Rift Valley Fever virus (Courtesy of Dr Juha Huiskonen, Division of Structural Biology, University of Oxford)

The RVF virus can infect a wide range of domestic and wild animals but its effects are most pronounced in sheep where almost 100% mortality and abortion rates occur in newborn lambs and pregnant ewes, respectively. RVF in humans primarily occurs following close contact with infected animal tissue and body fluids and presents as a mild febrile illness that sometimes progresses to the more severe manifestations of encephalitis and haemorrhagic diathesis that are frequently fatal.

Fortunately, a safe and effective live-attenuated vaccine called Clone 13 is available for livestock use and there are ongoing efforts to develop new subunit livestock vaccines based on the viral antigenic targets of neutralizing antibodies, Gn and Gc.

There is currently no licensed RVF vaccine for use in humans and neither Clone 13 nor the vast majority of subunit vaccines under development are likely to be licensed for human use due to safety concerns.

The Jenner Institute RVF vaccine development programme aims to address this by exploiting a viral vectored vaccine design strategy based on the inclusion of the Gn and Gc antigens into a non-replicating chimpanzee Adenovirus vaccine vector, ChAdOx1. Previous studies at the Jenner Institute have already established the safety of the ChAdOx1 vector for use in humans and livestock, meaning that the developed ChAdOx1-GnGc RVF vaccine could be used in both humans and livestock.

Preliminary results from ongoing pre-clinical studies of ChAdOx1-GnGc indicate that the vaccine induces very high titers of RVF virus neutralizing antibodies, a well-established biomarker of vaccine efficacy. Data obtained from these studies will help inform clinical development of a product for use in both humans and livestock.

This work exemplifies The Jenner Institute's endorsement of a 'One Health' approach to zoonotic disease control and involves collaborations with two Kenyan institutes: the International Livestock Research Institute (ILRI) and the Kenya Agricultural Research Institute. The programme is funded through a Wellcome Trust Fellowship in Public Health and Tropical Medicine to Dr. Warimwe. ■

The Cambridge Challenge Meeting 2013

Tom Darton and Christoph Blohmke, Oxford Vaccine Group, University of Oxford

Jesus College, Cambridge

An international meeting of investigators, researchers, regulators, bioethicists and representatives from the pharmaceutical industries was held at Jesus College, Cambridge in January 2013, supported by the Wellcome Trust, British Society for Immunology and the Jenner Institute. Prof Andrew Pollard, Jenner Investigator and Director of the Oxford Vaccine Group, and Prof Adrian Hill, Director of the Jenner Institute, were among the co-organisers of the meeting. Tom Darton and Christoph Blohmke (Oxford Vaccine Group) have provided this report.

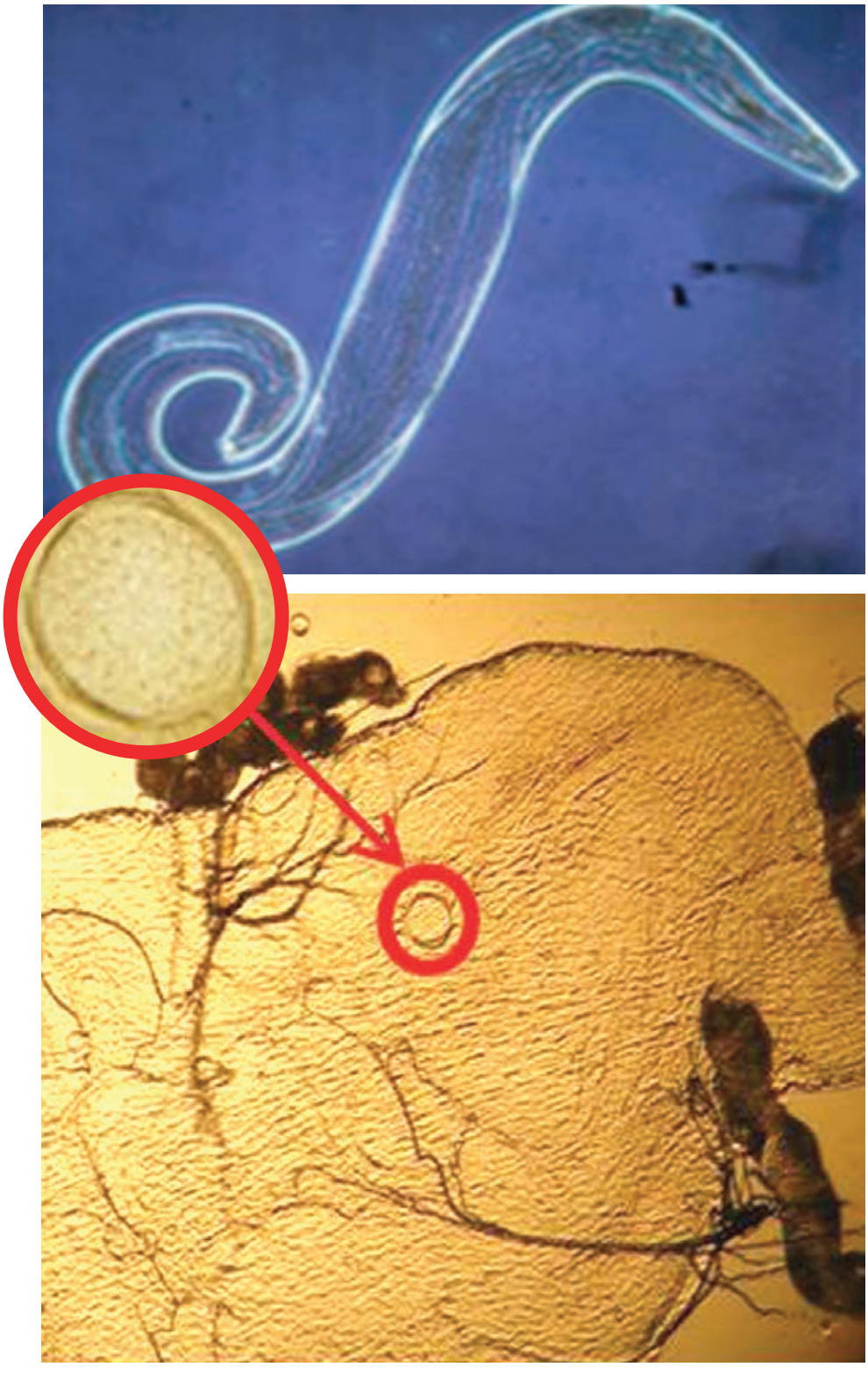
With much reason, challenge studies have been on uncertain ground ever since James Phipps had his sleeve rolled up by Edward Jenner in 1796. Deliberate exposure of fellow humans to known or putative infectious material is contrary to most people's understanding of what medical research is for. For many, these attitudes have been cemented by revelations of unethical practices during several decades of the last century, so that the substantial discoveries made in performing such studies, including vaccination, are often forgotten. Controlled human infection (CHI) studies are emerging from this legacy however, and are fast becoming a more popular and accepted method for resolving otherwise unanswerable questions.

An international meeting of investigators, researchers, regulators, bioethicists and representatives from the pharmaceutical industries was held at Jesus College, Cambridge in January 2013. Almost the only common ground amongst this apparently disparate gathering was the belief that controlled human infection studies still have some place on the infectious diseases research agenda. However, as the meeting progressed it was clear that these patches of common ground were larger than at first appeared. The diversity of organisms currently being used for CHI ranges from RSV to hookworms and is exceeded still by the breadth of research questions that these models are being used to answer; from elucidating mechanisms of pathogenesis to testing of methods to prevent aerosol transmission of respiratory viruses.

Many of the reasons for the renaissance in CHI activity are in response to non-academic enquiry too. A common theme across the diverse range of infections discussed, was a requirement to increase the pace and efficiency of novel vaccine development. CHI models offer a setting for confirming apparent vaccine efficacy prior to the massive financial outlay required in performing phase 3 field-trials. As well as offering a mechanism for reassuring investors and regulatory authorities, the scant availability of field-trial locations of sufficient size and background infection incidence so as to accurately assess the efficacy of, for example, a tuberculosis vaccine, mandates that only the most 'prime' vaccine candidates may be tested on such a large scale. Down selection of these candidates using a human model seems a more rational method for doing this.

The meeting highlighted several issues common to many CHI studies; those of payment or reimbursement of participants, participant safety and infection containment, and the potential 'privatisation' of CHI models by spinout companies. A recurring theme was the huge number of participants who had been challenged safely in various models and in various settings to-date (notably at the University of Maryland, at the now Center

Plasmodium falciparum, one of the species of Plasmodium that cause malaria in humans. It is transmitted by the female Anopheles mosquito. Malaria caused by this species is the most dangerous form of malaria, with the highest rates of complications and mortality.



Dissected midgut of Anopheles gambiae mosquito infected with cultured 3D7 parasites, showing oocyst (inset showing oocyst magnification)

for Vaccine Development, and at Salisbury in the UK at the Common Cold Research Unit), which is likely to exceed 40,000.

The overarching question arising from the meeting was how to take the field of CHI studies forward. A potential path has been blazed in the malaria field, in which the construction of consensus documents and the widened availability of a challenge strain have allowed new centres to get involved in this type of research. Aside from standardisation and therefore, hopefully, more widespread acceptance of CHI as a valid research method, the field is likely to continue pushing at the boundaries. Enrolment of patients with underlying co-morbidities and the establishment of CHI models in areas endemic for many of the infections being studied are exciting new prospects.

James Phipps attended the funeral of Edward Jenner in 1823. While he was certainly lucky that vaccination had worked, there was mutual gratitude for his participation (albeit in the absence of consent) from Jenner in the form of a free lease to a house following Phipps' marriage. CHI studies will continue to challenge our concepts of medical research and the role of the physician; respect and gratitude to our participants for taking part in this type of research clearly must also endure. ■

OXFORD VACCINOLOGY PROGRAMME
Courses in 2013

The Oxford Vaccinology Programme offers training opportunities in vaccinology through a five-day Human and Veterinary Vaccinology course and a three-day course on Clinical Vaccine Development.

For those from business, academic, clinical and veterinary backgrounds, including research scientists, programme managers, clinical trial co-ordinators, nurses, physicians and veterinarians. The courses will be accessible to people already working in the field or to those who wish to enter the field.

Upcoming courses:

- **Clinical Vaccine Development and Biomanufacturing**
  (16 - 18 October 2013)
- **Human and Veterinary Vaccinology**
  (18 – 22 November 2013)

The Programme provides state-of-the-art teaching in both veterinary and human vaccinology, drawing on the experience of the Jenner Institute, University of Oxford, The Pirbright Institute and our partners in industry to provide training in areas related to vaccine design and construction, including: immunology and molecular biology; manufacturing; clinical trial design; immunomonitoring; regulatory strategy; post-marketing surveillance; vaccine financing; and the ethics of vaccination.

For further information:
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Jenner Investigators - May 2013:

JENNER INVESTIGATORS		AFFILIATION	PRINCIPAL AREAS OF INTEREST
Dr	Ellie Barnes	OXFORD	Hepatitis C vaccines
Dr	Paul Barnett	TPI	Foot-and-mouth disease vaccines
Dr	Persephone Borrow	OXFORD	HIV immunity
Prof	Vincenzo Cerundolo	OXFORD	Cancer vaccines
Dr	Bryan Charleston	TPI	FMDV vaccines
Dr	Lucy Dorrell	OXFORD	HIV vaccines
Dr	Simon Draper	OXFORD	Malaria vaccines
Prof	Sarah Gilbert	OXFORD	Influenza & malaria vaccines
Prof	Tomáš Hanke	OXFORD	HIV vaccines
Prof	Glyn Hewinson	AHVLA	Bovine TB vaccines
Prof	Adrian Hill	OXFORD	Malaria vaccines
Prof	Paul Klenerman	OXFORD	Hepatitis C vaccines
Prof	Martin Maiden	OXFORD	Meningitis vaccines
Prof	Andrew McMichael	OXFORD	HIV immunity & vaccines
Prof	Helen McShane	OXFORD	TB vaccines
Prof	Peter Mertens	TPI	Arborovirus vaccines
Prof	Richard Moxon	OXFORD	Paediatric vaccines
Prof	Venugopal Nair	TPI	Poultry vaccines
Dr	Satya Parida	TPI	FMDV vaccines
Prof	David Paton	TPI	FMDV vaccines & diagnostics
Prof	Brian Perry	TPI	Veterinary epidemiology & control
Prof	Andrew Pollard	OXFORD	Paediatric vaccines
Dr	Arturo Reyes-Sandoval	OXFORD	Malaria Vivax & dengue vaccines
Prof	Sarah Rowland-Jones	OXFORD	HIV immunity
Prof	Quentin Sattentau	OXFORD	HIV vaccines
Dr	Adrian Smith	OXFORD	Coccidiosis immunity
Dr	Geraldine Taylor	TPI	Respiratory syncytial virus vaccines
Dr	Martin Vordermeier	AHVLA	Bovine TB vaccines

Oxford: University of Oxford, TPI: The Pirbright Institute, AHVLA: Animal Health and Veterinary Laboratories Agency

Call for volunteers to participate in clinical trials

The Centre for Clinical Vaccinology and Tropical Medicine (CCVTM) on the Headington campus of the University of Oxford conducts clinical trials on diseases of global importance and impact. If you would like to learn more about the clinical trial process, what it entails and how to volunteer to participate, please contact the Volunteer Coordinator via email or telephone.

Email: VaccineTrials@well.ox.ac.uk
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Web: www.jenner.ac.uk/clinicaltrials

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