



THE JENNER
INSTITUTE

DEVELOPING INNOVATIVE VACCINES

JENNER INSTITUTE

NEWS

ISSUE 04 / JULY 2012



Targeting Malaria's Achilles Heel

HIGHLIGHTS

New Hepatitis C vaccine shows promise

Bluetongue: Vaccination and future threats

New Vaccine Programme against Meningitis B

Peste des petits ruminants: Prospects for eradication

HIV-1: Aiming for the conserved regions



About the Jenner Institute

The Jenner Institute was founded in November 2005 to develop innovative 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 Institute Investigators, through the support of many funders, are developing new 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 Institute for Animal Health. 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.

David Salisbury appointed Chair of the Jenner Vaccine Foundation



Professor David Salisbury has been appointed the new Chair of the Jenner Vaccine Foundation from January 2012. Prof Salisbury has taken over this role from Prof Sir Brian Greenwood, after the end of his 6 year tenure as Chairman.

Professor David Salisbury is Director of Immunisation at the Department of Health, London, where he is responsible for the national immunisation programme. Professor Salisbury works extensively with the World Health Organization. He was the Chairman of the WHO Strategic Advisory Group of Experts on Vaccines from 2005 to 2010, is Chairman of the European Region Certification Commission for Poliomyelitis Eradication, is a member of the Eastern Mediterranean Commission and the South East Asian Commission. During 2009, Professor Salisbury chaired the WHO H1N1 vaccine group. He is Co-chairman of the Pandemic Influenza Group for the Global Health Security Initiative of G7 countries. He is a Liaison Member of the US Advisory Committee on Immunisation Practices and the US National Vaccine Advisory Committee. He chairs the European Vaccine Advisory Group for the European Centre for Disease Control and the R&D work stream for the Bill & Melinda Gates Foundation Decade of Vaccines initiative. He is a member of the Malaria Advisory Panel for the Gates Foundation and a Science Advisory Council member for the PATH Malaria Vaccine Initiative.

New Jenner Investigators

The Jenner Vaccine Foundation has recently appointed six new Investigators:



Dr Ellie Barnes (University of Oxford): Specialises in Hepatitis C vaccines, both preventative and therapeutic. Her work is featured in this issue, "First trial of a new hepatitis C vaccine shows promise" (p. 14).



Dr Simon Draper (University of Oxford): Focuses on blood-stage malaria vaccines. His work is featured in this issue, "RH5 targeting Malaria's Achilles Heel" (p. 4).



Prof Glyn Hewinson (Animal Health and Veterinary Laboratories Agency): Leads the programme on Bovine Tuberculosis vaccines and diagnostics.



Prof Peter Mertens (Institute for Animal Health): Leads research on Arboviruses, particularly Bluetongue virus and African horse sickness virus at the IAH. His work is featured in this issue, "Bluetongue in the UK and northern Europe: the importance of vaccination and future threats" (p. 8).



Dr Arturo Reyes (University of Oxford): Heads the Malaria Vivax Vaccine Programme at the Jenner Institute Laboratories. This programme will be featured in the next issue.



Dr Martin Vordermeier (Animal Health and Veterinary Laboratories Agency): Collaborates with Prof Hewinson's on Bovine Tuberculosis vaccines and diagnostics.

4 new Investigators are profiled on pages 10-11. Glyn Hewinson and Arturo Reyes will be profiled in the next issue.

Prospects for Global Eradication of PPRV

Michael Baron
(Institute for Animal Health)

Last year saw the final declaration of the complete global eradication of rinderpest, one of the most devastating cattle diseases the world has known. This was the first livestock disease, and only the second viral disease, ever eradicated, and the global benefits of rinderpest eradication are estimated to be in the billions of dollars. However, the 20 years which witnessed the final stages of RPV eradication have seen the continued spread of a close relative, Peste des petits ruminants virus (PPRV) (Fig 1).

As the name implies, PPRV causes disease in sheep and goats, as well as several related species of wild life. The disease spreads easily through contact, and mortality varies from 5% to 85% depending on the strain of virus and the local breeds of sheep/goats. Although sheep/goats have, of themselves, much less economic value than cattle, PPRV's socio-economic impact can be very great, as small ruminants are often the mainstay of the poorest livestock keepers in villages and nomadic communities throughout the developing world. Even a small hit at this level can drive people into total destitution. Scientists and veterinarians in both academic circles and international organisations such as the UN Food and Agriculture Organisation (FAO) and the World Organisation for Animal Health (OIE) have begun working toward not only better control of PPRV, but its ultimate eradication, as has been done to rinderpest, and is hoped to do with another virus in the same group, measles virus.

In March this year the inaugural meeting of the Global PPRV Research Alliance took place at the Wellcome Collection Centre in London. Scientists from laboratories in many countries met, along with representatives from FAO and OIE, to discuss what they are currently doing, and what they see as needing to be done, to promote PPRV control and eventual eradication. Vaccines were discussed, of course, in particular the creation of DIVA vaccines (several very effective live attenuated PPRV vaccines already exist and are in widespread use), and at least four labs are working on possible DIVA vaccines and tests, including a project in my own lab using recombinant



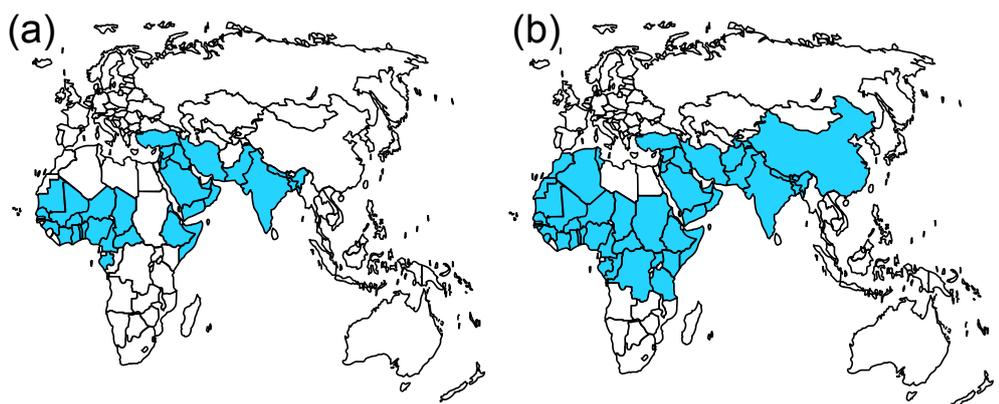
Vaccinating goats against PPRV in Kenya." Courtesy of Dr. Peter Maina Ithondeka, Kenya Veterinary Board.

adenoviruses and fowlpox viruses made in the Jenner vector core facility. What became clear in the meeting was that our understanding of the epidemiology of PPRV is limited, as well as our knowledge of the socio-ecology of the disease and its hosts. There is little effective data on the real incidence of the disease, especially in countries where it is endemic, and we need better knowledge of the role played by wild life in PPRV epidemiology. For effective control, we need to know more about where and how to best apply vaccine (whether DIVA or normal) in order to shut down transmission of disease in countries that have

little effective control of internal or cross-border movement of small ruminants.

Fortunately, there are already several projects under way to begin to fill in some of these missing data, and the creation of the GPRA will provide a forum which, it is hoped, can help guide the work being done around the world. There was good agreement at the meeting that PPRV could, and should, be tackled, and agreement in principle by most of those there to cooperate in so doing. ■

Dr Michael Baron is Group Leader, Paramyxo & Bunyavirus at the Institute for Animal Health



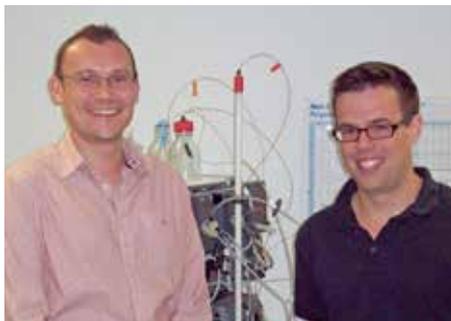
PPRV: a growing threat: outline maps showing countries with at least one PPRV outbreak (a) up to 2000 and (b) up to 2012. Data taken from World Organisation for Animal Health (OIE) statistics, from 1992 onwards.

Targeting Malaria's Achilles Heel



A promising new malaria vaccine developed at the Jenner Institute is showing considerable potential in neutralising multiple strains of the most deadly species of malaria parasite, *Plasmodium falciparum*.

A team of Jenner researchers, led by Simon Draper and Sandy Douglas, have developed a vaccine capable of neutralising all tested strains of the parasite in several animal models. The results were published in *Nature Communications* in December 2011.

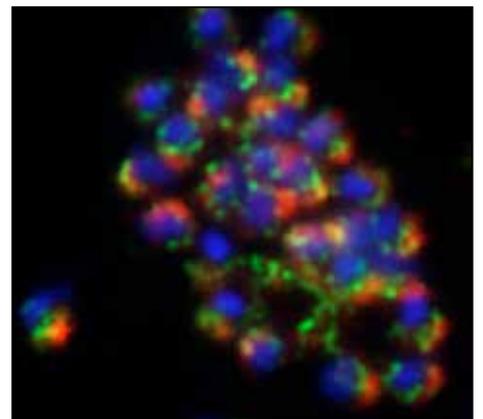


Simon Draper (left) and Sandy Douglas, in front of the Fast Protein Liquid Chromatography (FPLC) apparatus, which is used to analyse and purify mixtures of proteins

The new vaccine primes the immune system to attack a protein called RH5 on the parasite as it moves between red blood cells during the so-called blood-stage of the parasite's life-cycle. This is the stage that causes the clinical symptoms and complications of malaria. It is one of the few moments in its life-cycle when it is exposed to human antibodies and a critical stage for the survival of the parasite because it cannot replicate without invading new red blood cells.

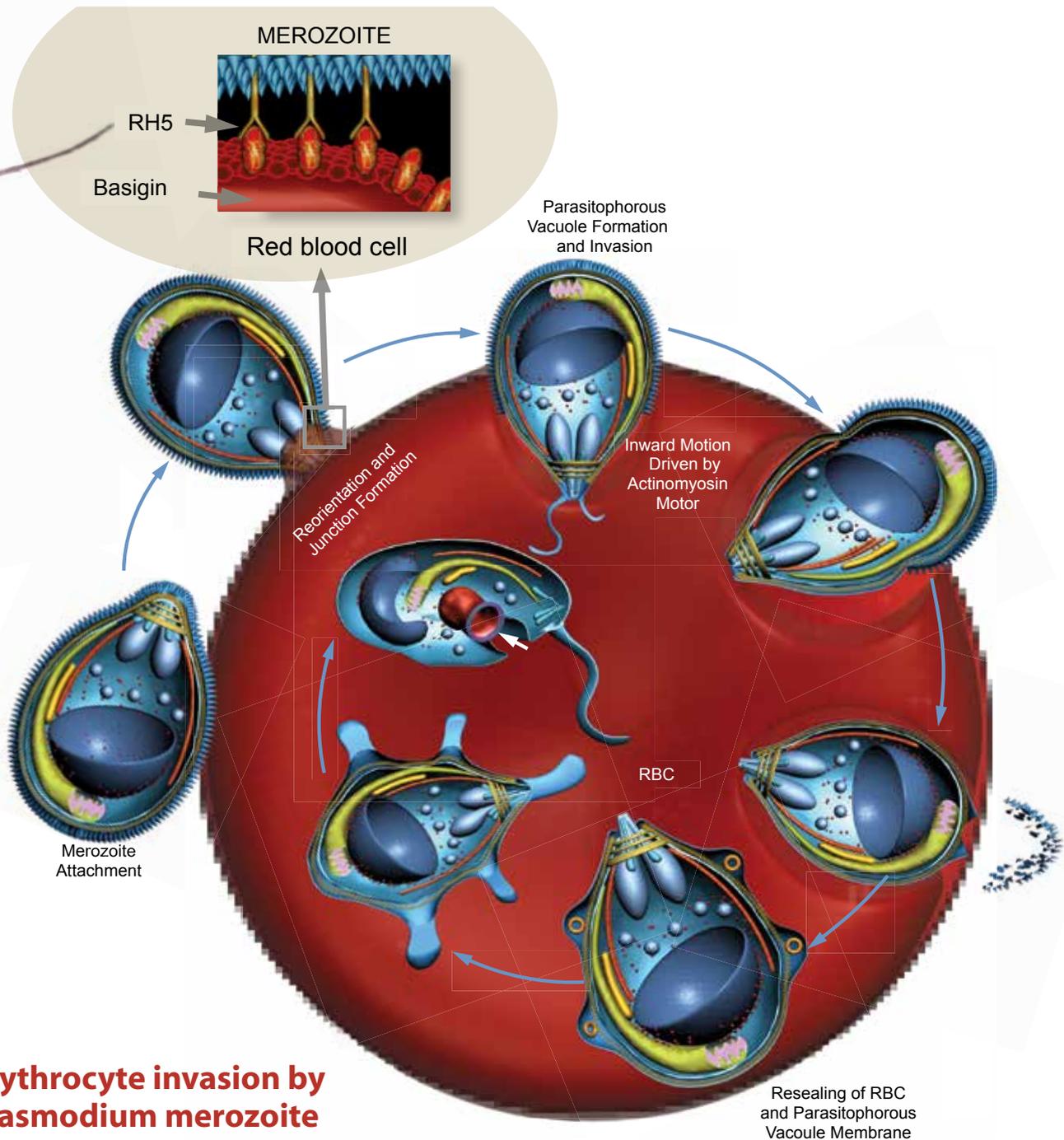
The process of invasion is highly complex, involving multiple interactions between proteins on the surface of the red blood cell and the surface of the parasite. A collaborating team at the Wellcome Trust Sanger Institute in Cambridge recently identified an interaction between RH5 and a receptor on the surface of red blood cells, known as 'basigin'. This particular receptor seems to be essential for the parasite to invade the cells, and appears to be used by every strain of *P. falciparum* tested so far. The work conducted at the Jenner Institute demonstrates that this pathway can be blocked by vaccine-induced antibodies.

Dr Sandy Douglas, first author on the study, says: "It's extremely promising that these antibodies are effective at neutralising multiple strains of malaria parasites, as this seems to overcome one of the major problems which have hampered blood-stage vaccine development. However it is important to stress that this is still early phase research in animals – we're now planning to test the vaccine in clinical trials in humans."



Fluorescent photo of the vaccine-induced antibodies binding to parasites in a malaria-infected red blood cell. The blue areas are the *Plasmodium* parasites. The green areas are where antibodies have bound to RH5

The efforts of scientists to develop a vaccine against malaria's blood-stage have long been frustrated by the extreme genetic diversity of the parasites' antigens which are constantly evolving to evade the body's immune system. "The RH5 antigen doesn't show this diversity, making it a particularly good target for a vaccine to exploit," explains Prof Adrian Hill, Director of the Jenner Institute. The researchers believe the low genetic diversity is due to the fact that humans have very low or undetectable levels of antibodies against RH5, even people who have been naturally and repeatedly exposed to malaria. Such low levels of antibody would be insufficient to kill the parasites, and so would not exert a selective pressure for the antigen to evolve towards greater variability.



Erythrocyte invasion by plasmodium merozoite

Courtesy of Qiagen

Being an essential pathway for the parasite's replication, with a low genetic diversity and accessible to the immune system, the RH5 antigen appears as an attractive "Achilles heel" for the researchers to target.

In October 2011, scientists working with GlaxoSmithKline (GSK) Biologicals, the PATH Malaria Vaccine Initiative and the Bill and Melinda Gates Foundation tested RTS,S for the first time in children at 11 sites in Africa. The results appeared to be encouraging: RTS,S seems to cut the risk of infection with malaria by 56%, and

reduced severe cases of the disease by 47%. However, many scientists believe that a much more powerful vaccine is needed in order to combat malaria effectively. Existing vaccines against other childhood infections such as measles and rotavirus typically protect more than 70% of children against disease, and frequently more than 90%.

Simon Draper has suggested that the RH5 vaccine could be used to complement RTS,S, which stops *P. falciparum* from entering the liver, during the pre-erythrocytic, or liver-stage, of the parasite's life-cycle in the human body.

"Ultimately we don't know until we test our vaccine in humans whether it will be more efficacious than RTS,S, but these preclinical data on RH5 are some of the most exciting in the field at the moment," Draper adds.

The team is now in the process of developing clinical grade vaccine material that could be taken forward into GMP manufacture, and hope to begin clinical trials within the next two to three years. ■

Oxford Vaccinology Programme

3 years on

Launched in 2009, with the aim of strengthening the knowledge base about vaccines, the three courses in the Oxford Vaccinology Programme have so far attracted 150 participants. Those attending have come from as far afield as India, Canada, Malaysia, Kenya and Uganda.

The programme provides specialist teaching in both veterinary and human vaccinology, drawing on the experience of Oxford University, through the Jenner Institute based in Oxford, the Institute for Animal Health (IAH) 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.

- **Human and Veterinary Vaccinology**
– next course 26th-30th November 2012
- **Clinical Vaccine Development**
– next 2-day course in April 2013
- **Vaccine Biomanufacturing**
– next 2-day course in April 2013

We are very fortunate to have gained the support of a number of leading experts who teach on the programme, including Prof David Salisbury (Director of Immunisation, UK Department of Health), Dr Jerold Sadoff (Chief Medical Officer of Crucell), Dr Daniel Vellom (Senior Director, Global Technology and Innovation, Sanofi Pasteur) and Dr Alain Pralong (Vice President, New Product Introduction and Industrialisation, GlaxoSmithKline Biologicals).

This programme has proven to be a good example of an initiative launched by the Jenner Institute which has brought together experts from industry and academia to share their knowledge and expertise about vaccine development.

What people have said about the programme:

"Great course. Lots of relevant topics covered. Excellent talks!"

Mariana De Niz Hidalgo, London School of Hygiene and Tropical Medicine

"Good course for learning all aspects of vaccine development."

Mercedes Fabra, Product Manager Unit Immunology and Vaccines, Laboratorios Leti S.L.

"Really liked the variety of topics, speakers and perspectives. Great baseline and point of reference."

Tracey Schmitt, Vice President, Corporate Communications, Emergent BioSolutions, Inc.

"Very good outline with lots of info to make you think. Very applicable to work"

Fionnadh Carroll, Research Assistant, Jenner Institute, University of Oxford

"The course balance was very good and covered most aspects.....from the lab bench to regulatory affairs."

George Newlands, Senior Research Scientist, Inocul8

The courses are open to anyone with a relevant background and participants have come from a large number of different companies and organizations including:

Baxter BioScience, Baxter Innovations GmbH, Boehringer Ingelheim Animal Health GmbH, Division of Public Health and Primary Health Care (Oxford), Drug Delivery Solutions, European Medicines Agency (EMA), Emergent BioSolutions Inc, Federal Ministry of Animal Resources and Fisheries, Genecom, Glide Pharma, ICON Clinical Research, IDT Biologika GmbH, Imaxio, Inocul8, Irsicaixa, London School of Hygiene and Tropical Medicine, Medicago R&D, MHRA, Moredun Research Institute, Novartis, PATH Malaria Vaccine Initiative (MVI), Pfizer Ltd, Sagittarius IP, Solvay Biologicals, Solvay Pharmaceuticals Inc, Statens Serum Institut, Subiaco Associates Ltd, Vaccibody AS, Veterinary Laboratories Agency, World Health Organisation, Wyeth. ■



For further information:

Website:
www.conted.ox.ac.uk/vaccinology

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Going overseas

Teaching vaccinology in Tanzania

Sarah Gilbert (University of Oxford)

After 20 years experience in vaccine development and a wide range of teaching involvement, Jenner Investigator Professor Sarah Gilbert was invited to join the faculty of a training workshop for African scientists at Sokoine University of Agriculture (SUA), in Morogoro, Tanzania.

Last year, I was privileged to be invited to join the faculty of a training workshop for African scientists, “One Health: Understanding Human and Veterinary Diseases from Molecular Cell Biology to Successful Interventions”, which was to be my first experience of teaching vaccinology overseas. The students were 24 early-career researchers from eight African countries (Burkina Faso, Egypt, Ethiopia, Kenya, Tanzania, Uganda, South Africa and Zambia), selected from among 270 applicants.

International faculty from the University of Oxford, the Institute for Animal Health, SCYNEXIS (USA), the Southern African Centre for Infectious Disease Surveillance (SACIDS), and SUA participated.



Group work on vaccine design

The goal of the course was to share experience about molecular and cell biology techniques that underpin infectious disease research, surveillance, and intervention strategies such as vaccines, with a particular focus on synergies in human and livestock disease research. The week was organized as a series of lectures, group discussions, and case studies. Lectures ranged from basic concepts in cell biology and immunology, to the realities of field data collection in rural Africa, and the transformative impact of new mobile technologies on disease surveillance.



Students on One Health Course

The major part of the week was dedicated to four longer case studies, which gave students first-hand accounts of how theory and methods are applied in practice. The case study which I was given to lead, focussed on vaccines, discussing the current status of vaccine development for malaria and other challenging diseases. The students worked in small groups to “design” a vaccine against Rift Valley Fever (RVF). This required application of many of the concepts raised in lectures, from virus biology and the differences between T cell vs. antibody-mediated immune response to trial design and the economics of vaccine production.

In the final case study John Anderson (IAH) told the encouraging story of how the devastating cattle disease Rinderpest was eradicated. After smallpox, Rinderpest is only the second disease in history to be completely eradicated. Anderson highlighted as key factors in this success the development of appropriate diagnostic assays, technology transfer, and training of local scientists. The students were asked to consider whether other diseases could be eradicated too, and Human African Trypanosomiasis, Rift Valley Fever, Foot and Mouth Disease and Tuberculosis were used as examples. After scoring these diseases against eight biological characteristics considered important in the eradication of smallpox and Rinderpest, each group concluded that the prospect of eradicating them was slim. It was, however, a valuable exercise in looking at the wider, long-

term perspective. This resonated with the students’ expressed wish to engage in research with an impact on Africa’s disease burden.

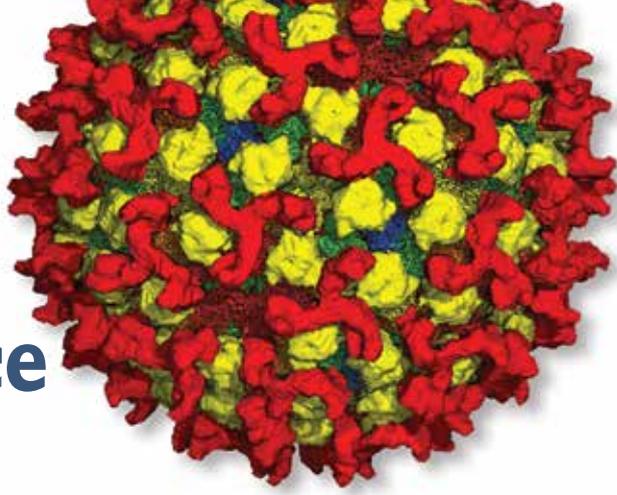
In conversation, many students voiced their frustration over the lack of modern equipment in their laboratories, which they feel leaves them at a disadvantage in the global competition with scientists from the “North.” However, as John Anderson underlined, cutting-edge technology is not always required to succeed; dedicated individuals working together toward a common goal, using what he called “appropriate” technology, can have a major impact.

Meal times offered plenty of time for informal discussions. We even learned about a novel approach to diagnostics: We attended a training session for giant African pouched rats (www.apopo.org) that detect TB in clinical samples by smell! This rounded off a mutually stimulating workshop, which left students and faculty alike with new knowledge, personal contacts, and the feeling that, as scientists, we have a possibility to make a positive difference.

The course was organised by Professor Keith Gull (a Jenner Foundation Trustee) and Dr Eva Gluenz on behalf of the American Society for Cell Biology and supported by a grant from Carnegie Corporation of New York, with additional support from the Jenner Vaccine Foundation. A longer report about the course can be found in the ASCB Newsletter, October 2011: www.ascb.org/files/1110IAC.pdf ■

Bluetongue in the UK and northern Europe: the importance of vaccination and future threats

Peter Mertens, Jenner Investigator



The *Culicoides* midge, the vector that carry the virus, usually breed on animal dung and moist soils, either bare or covered in short grass

The first recorded outbreak of bluetongue (BT) in northern Europe started in sheep in the Maastricht region of the Netherlands during July/August 2006, linked to record summer temperatures in Europe that year. The Institute for Animal Health (IAH), identified bluetongue virus type 8 (BTV-8) from sub-Saharan Africa, although how this virus arrived in northern Europe is still uncertain. During 2006 the virus spread (mainly in cattle) to a small number of animals on approximately 2000 farms across the Netherlands, Belgium, Luxembourg, Germany and north east France, although there were some fatalities. The outbreak subsided as adult biting midges which transmit the virus disappeared during the winter of 2006/7. However, it re-emerged in summer 2007 with massively increased intensity, involving over 50,000 farms across the region, killing thousands of animals (mainly sheep), including an estimated 25-30% of the entire sheep population of Belgium.

During August 2007 wind-borne midges from mainland Europe, initiated infection of ~200 animals in south-east England. Modelling indicated that re-emergence of the disease during the summer of 2008 would cause catastrophic BT outbreaks in the UK's (estimated) 30 million cattle and

30 million sheep. Although BTV-8 vaccines developed for use in endemic regions of sub-Saharan Africa, were commercially available, they contained live-attenuated viruses that caused severe clinical disease in naïve European sheep. Vaccine derived outbreaks had already occurred in southern Europe.

In order to secure production, Defra placed an order for 22.5 million doses of a new and safer 'inactivated' BTV-8 vaccine, which was deployed by UK farmers and veterinarians through a voluntary 'Joint-Action-against-Bluetongue' (JAB) vaccination-campaign, prior to re-emergence of midges in May 2008. Over 90% cover was achieved in and around affected premises, entirely eliminating further insect-transmission during 2008, making the UK the only country in Europe to achieve disease control that year, saving over £400m during 2008 alone. Inactivated vaccines were subsequently used to eradicate BTV-1 and BTV-8 from northern Europe. As an example France went from 38,000 affected premises in 2008 (when vaccination started), to 83 in 2009, then 1 in 2010.

These vaccines, which contain unpurified chemically-inactivated infected-cell-culture materials, are BTV-serotype specific, generating antibodies to all of the virus proteins. This has hindered development of serological tests to distinguish 'infected' from 'vaccinated' animals (DIVA test). Consequently surveillance has relied on diagnostic RT-PCR assays, to detect viral RNA in blood/tissue samples. Work is ongoing at IAH (with partners across Europe) to develop better next-generation DIVA-compatible BTV and African horse sickness virus vaccines, and explore the possibility of cross-protective vaccines against the 26 known BTV types.

Vaccination against BTV has now stopped in northern Europe. With an estimated annual turnover of ~20%, we will soon return to a fully naïve livestock

population. There are many other viral diseases transmitted to animals and humans by midges, mosquitoes and flies and ticks, that may also respond to 'climate change' and increases in international trade. We have already seen the arrival of West Nile, Chikungunya, Toscana, Dengue and Crimean Congo viruses as well as ten BTV serotypes in Southern Europe, as well as Liao ning virus in Belarus. The recent arrival of Schmallenberg virus in northern Europe during 2011 (five years after BTV-8) confirms that these risks are not limited to the Mediterranean region. We must therefore expect further arboviral disease incursions, threatening both the animal and human populations of Europe, including the UK. Further changes in our climate and increases in international trade would increase these risks and consequently the demand for safe, inexpensive and effective vaccines. ■



Prof. Peter Mertens is Research Leader within the Arbovirus Molecular Research Group and Head of the Institute's Vector-borne Viral Diseases Programme. Prof Mertens' group was responsible

for development of the diagnostic assays and molecular epidemiology systems that were used to identify and track virus movements during recent bluetongue outbreaks in Europe, contributing to the eradication of the bluetongue virus from the UK in 2008. He is currently working on next generation vaccines for bluetongue and African horse sickness viruses.

Above: The bluetongue virus particle, reconstructed by X-ray crystallography and cryo-electron microscopy

TRIAL UPDATE

Human Tuberculosis: MVA85A Clinical Trial Update

By Helen McShane, Professor of Vaccinology and Wellcome Trust Senior Clinical Fellow, Leader of the Jenner Institute Human TB Vaccine Programme

Tuberculosis (TB) is a contagious airborne disease that disproportionately affects the developing world and those living in poverty. In 2010 there were 8.8 million new TB cases and 1.4 million deaths from the disease. Up to one third of the world's population is latently infected, each with a 10% risk of developing active TB in their lifetime. Drug-resistant strains are on the rise, so an effective and affordable vaccine is a global public health priority.

MVA85A, a candidate TB vaccine developed by Jenner Investigator Prof Helen McShane, has already been shown to be safe in Phase I and IIa trials in the UK, South Africa, Senegal and The Gambia. MVA85A acts as a booster vaccine to BCG, which is routinely given to infants in endemic countries. While BCG confers some protection against severe disease in childhood, unfortunately, it is less effective against pulmonary (lung) TB, particularly in adolescents and adults. MVA85A has been shown to significantly enhance the BCG-induced immune response, and can improve BCG-induced protection in preclinical models. It is important to find out next whether this immune response leads to improved protection against TB disease and, for TB, this requires large scale Phase IIb efficacy trials.

Our first MVA85A efficacy trial started in July 2009 with a double-blind, placebo-controlled efficacy trial in South Africa, which has some of the highest TB disease rates in the world. 2797 BCG-vaccinated infants have received either an MVA85A booster or a placebo at 4-6 months of age, and are being followed for at least 18 months to compare TB infection and disease rates after MVA85A versus after placebo. Working with the South African Tuberculosis Vaccine Initiative (SATVI), this trial is sponsored by Aeras and funded by Aeras, the Wellcome Trust, and the Oxford Emergent Tuberculosis Consortium (OETC). The trial is due to complete in

September 2012 with unblinded data expected in early 2013.

TB is a leading cause of death among HIV-infected individuals, who are 20-40 times more likely to develop active TB than HIV-uninfected peers, making them an important target population for any TB vaccine. MVA85A has now entered a second Phase IIb efficacy trial vaccinating HIV-infected adults in South Africa and Senegal. Vaccination started in August 2011 and, with 1400 adults to immunise (randomised to receive either MVA85A or a placebo), enrolment is projected to finish in 2013. Each individual will be followed for at least 2 years. This trial is also sponsored by Aeras, and funded by EDCTP, Aeras and OETC.

In addition to efficacy trials, a key area of research interest is developing an alternative method of delivery of MVA85A vaccine. Currently MVA85A is given by intradermal needle injection, however, there would be substantial benefits to being able to deliver MVA85A as an aerosol using an inhaler. Inhalation removes the issues involved with safe and appropriate needle-disposal, as well as the potential for HIV cross-contamination. Additionally inhaler-delivery is far simpler and could be carried out by a community health worker in developing countries, and the inhalers can be cleaned and re-used safely, saving on costs of vaccine delivery. Aerosol delivery is also usually less painful and better tolerated by subjects than injection. Finally, as Mycobacterium tuberculosis enters through the lungs, inhalation of MVA85A into the lungs could result in a more organ-specific immune response. A phase I trial comparing needle and inhaler delivery of vaccination in healthy UK adults began in November 2011 and is the first inhalation trial of an unlicensed vaccine.

Across the rest of the MVA85A clinical trial portfolio we are performing trials to compare intradermal injection to intramuscular injection, which involves obtaining a long-term



In April 2011 the final infant was vaccinated in our Phase IIb efficacy trial of MVA85A in South African infants. 2797 infants were vaccinated in total, with either MVA85A or placebo. Unblinded results are expected early 2013.



The adult efficacy trial team – a collaboration with members from the UK, South Africa, Senegal, The Gambia, Belgium and the USA.

blood sample from our previous vaccinees in South Africa to investigate long-term immunogenicity to MVA85A, and a trial starting soon that will be giving MVA85A to HIV-exposed infants in South Africa (in whom BCG is contra-indicated) in the hope of reducing TB disease in this at-risk population. The TB group works closely with many excellent collaborators around the world, elucidating questions about how TB infects and affects humans, developing challenge models that could eventually negate the need for expensive efficacy trials for TB, performing clinical trials with the candidate vaccine MVA85A, and working towards developing the first new TB vaccine in 80 years. ■

Jenner Investigator Profiles >>>>

Dr Simon Draper



I undertook a degree in Biochemistry at Trinity College, Oxford University, and then worked at the Institute for Hormone and Fertility Research in Hamburg, Germany, and at the Weatherall Institute of Molecular Medicine in Oxford. I subsequently joined Prof Adrian Hill's research group to undertake my DPhil. I have since stayed on at the Jenner Institute, first as a Junior Research Fellow of Merton College,

and subsequently as a MRC Career Development Fellow and University Research Lecturer. The aim of my work is to develop and translate new vaccine candidates for malaria into proof-of-concept human clinical studies. My group has a particular interest in optimising antibody and B cell induction by subunit vaccines, as well as better understanding vaccine-induced immunity to the blood-stage of malaria infection.

In recent years, we have developed simian adenovirus (ChAd63) and MVA viral vectored vaccines targeting two major candidate antigens from the human malaria parasite *Plasmodium falciparum* and one from *P. vivax*, and have translated these candidates into Phase I/IIa clinical vaccine trials. The aims of this work are to assess the safety, immunogenicity and protective efficacy of these new vaccines in human volunteers. These studies provide an opportunity to better understand how vaccine-induced responses can protect against malaria infection in humans, and also how exposure to the parasite can modulate humoral and cellular immunity. This work is also complemented by studies in naturally-exposed individuals through our collaboration with the KEMRI-Wellcome Institute in Kilifi, Kenya.

My research group is also investigating the utility of deploying protein-in-adjuvant and viral vectored vaccines in combination immunisation regimes, alongside research focusing on novel vaccine adjuvants. We are now utilising these new vaccine delivery platforms that we have developed to screen blood- and mosquito-stage antigens for effective antibody induction. In 2002, the genome sequence of *P. falciparum* was reported, highlighting the existence of over 5,000 genes. However, despite this genomic success, no systematic analysis of the utility and efficacy of so many potential vaccine candidate antigens has been reported. This work is aiming to define new antibody target combinations that may prove to be more successful in inducing protective efficacy against malaria by subunit vaccination in humans.

Key Publications:

S. H. Sheehy, C. J. Duncan, S. C. Elias, S. Biswas, K. A. Collins, G. A. O'Hara, F. D. Halstead, K. J. Ewer, T. Mahungu, A. J. Spencer, K. Miura, I. D. Poulton, M. D. Dicks, N. J. Edwards, E. Berrie, S. Moyle, S. Colloca, R. Cortese, K. Gantlett, C. A. Long, A. M. Lawrie, S. C. Gilbert, T. Doherty, A. Nicosia, A. V. Hill, & S. J. Draper. Phase I Clinical Evaluation of the Safety and Immunogenicity of the *Plasmodium falciparum* Blood-Stage Antigen AMA1 in ChAd63 and MVA Vaccine Vectors. *PLoS One*. 7, e31208 (2012).

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Prof Peter Mertens



Peter Mertens studied Virology at Warwick and Oxford Universities, then moved to the University of Guelph in Canada in 1979. After completing his post-doctoral fellowship there, he returned to the UK in 1981. He has since worked on the Arboviruses, particularly

Bluetongue virus and African horse sickness virus, at the UK's Institute for Animal Health, Pirbright Laboratory, (for almost 31 years). He is currently Research Leader within the Arbovirus Molecular Research Group and Head of the Institute's Vector-borne Viral Diseases Programme.

Prof Mertens' group was responsible for development of the diagnostic assays and molecular epidemiology systems, that were used to identify and track virus movements during recent bluetongue outbreaks in Europe, contributing to the eradication of the bluetongue virus from the UK in 2008. He also played a central role in determination of the atomic structure of the bluetongue virus core particle, in collaboration with David Stuart's group, still the largest single molecular structure determined to date.

Professor Mertens has written over 180 scientific papers on these viruses has supervised over 20 PhD students and is currently a Visiting Professor within the Department of Veterinary Medicine, at the University of Glasgow, as well as a Fellow of the Society of Biology and Fellow of the Higher Education Academy. He is co-chair of the Retroviridae study Group for the International Committee on Taxonomy of Viruses (ICTV) and a member of the Bluetongue Committee for the United States Animal Health Association (USAHA), and is currently working on next generation vaccines for bluetongue and African horse sickness viruses.

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Dr Ellie Barnes



I trained in medicine at St Bartholomew's Hospital, London and thereafter specialized in liver medicine. My PhD was in T cell immunity to hepatitis C virus (HCV) in the context of therapy. I have been supported by the MRC throughout, more recently as a Clinician Scientist at the Peter Medawar Building. The OxNIHR BRC has

provided essential support in establishing the infrastructure and a small team of excellent research nurses that support our work.

For 20 years the academic community has sought to understand why some people clear HCV spontaneously and other do not. Whilst there is much still to be learnt, it is clear that effective T cell immunity and an appropriate host genetic background are key. Over recent years I have been working to establish a prophylactic and therapeutic HCV T cell vaccine. It has given me real pleasure to move the basic lab work forward into healthy volunteer and patient populations. The learning curve has been steep, and the support and integration with the Jenner has been absolutely instrumental in this.

We have developed a highly immunogenic T cell vaccine for HCV based upon simian adenoviral and MVA vectors that encode the entire non-structural region of the HCV protein. Vaccine induced T cell responses are attenuated in chronic HCV infection, and I am currently exploring in detail the reasons for this. A major challenge for HCV vaccine development is significant viral diversity within and between hosts –though parts of the viral genome are relatively conserved making these excellent T cell targets. In the UK 50% of people are infected with genotype-1 and the rest with subtype-3a infection. I have therefore developed a program of work defining cross-reactive protective immunity between these strains. Within the Jenner Institute we are planning to develop generic strategies to tackle diversity against a number of devastating diseases.

My other interests include coagulation in liver disease, IgG4 related systemic disease –an enigmatic mimic of biliary and pancreatic cancer, and the detection of liver fibrosis using MRI technologies.

Key Publications:

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Dr Martin Vordermeier



Martin Vordermeier studied biology at the Universities of Stuttgart and Tuebingen (Germany) and obtained his doctorate in Microbiology in 1987 (Tuebingen) studying the interaction of bacterial compounds with B cells. He undertook post-doctoral training in Adelaide (Australia) investigating T cell responses in a murine Salmonella

infection model. Since 1990 he has worked on tuberculosis, initially on human tuberculosis until 1997 in the MRC TB and Related Infections Unit at Hammersmith Hospital, London, and since 1997 on bovine tuberculosis of ruminants at the Animal Health and Veterinary Laboratories Agency.

His current research interests are aimed at the investigation of immune responses against mycobacterial infections to support the development of vaccines and diagnostic reagents against bovine tuberculosis in cattle. His team are applying and testing a range of vaccine strategies including heterologous prime-boost approaches using virally vectored recombinant adenoviruses and Modified Vaccinia Virus Ankara-based vector systems. Part of this work is being undertaken in collaboration with the groups of Adrian Hill and Helen McShane at the Jenner Institute. For example, his team recently tested polyvalent virally vectored subunit vaccines for their protective efficacy in cattle and also compared the effects of mucosal and systemic delivery of recombinant adenoviral vaccines their immunogenicity in calves.

Supporting these objectives, his group is also engaged in the definition of immunological surrogates/predictors of protective and pathological immune responses through biomarker studies using, for example, genome-wide expression analysis of vaccine or infection-induced host responses. They recently identified a number of biomarkers that could support the ante-mortem diagnosis of bovine tuberculosis including Interleukin-22 and granzyme A. He is also interested in bovine TB in cattle in Africa, in particular the differences in the susceptibility to bovine tuberculosis between endogenous and exotic breeds in East Africa.

Key Publications:

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New Jenner Vaccine Programme against Meningitis B

A new programme has been launched by Jenner Investigator Prof Andrew Pollard and 3 post-doctoral scientists, Leanne Marsay, Christina Dold and grant holder Christine Rollier, to develop a vaccine against *Neisseria meningitidis*, a bacterium that can cause meningitis and other forms of meningococcal disease. There are several subtypes of *Neisseria meningitidis*, often referred to as meningococci, which are classified according to the antigenic structure of their polysaccharide capsule. Six of these (A, B, C, W135, X, and Y) are able to cause epidemics. The new programme aims to develop a vaccine against serotype B, which is responsible for the majority of meningitis cases in the UK.

Meningococcal meningitis is a bacterial form of meningitis, a serious infection of the thin lining that surrounds the brain and spinal cord. It is estimated that there are 1.2 million cases of meningococcal disease each year. Although the majority of cases occur in the developing world, disease rates in Europe remain at one to six cases per 100,000, with a fatality rate of around 8%. Invasive meningococcal disease can result in severe morbidity and sequelae such as hearing and speech impairment, loss of limbs and a detrimental impact upon future

quality of life and socioeconomic status.

Effective vaccination is considered to be the only strategy for the control of meningococcal disease. However, unlike other meningococcal serogroups (e.g. A, C, W135 and Y), the polysaccharide on the serogroup B capsule cannot be used in a vaccine, mainly because it is poorly immunogenic in humans. The major hurdle for licensure of MenB vaccines is induction of bactericidal antibodies (antibodies which bind complement factors and kill *N. meningitidis*), which are believed to be the correlate of protection. Since the polysaccharide capsule of these bacteria is poorly immunogenic, the search for comprehensive protection against MenB disease necessarily focuses on subcapsular protein antigens. To overcome this problem, we are using adenoviral vectors to display antigens from MenB.



The people behind the *N. meningitidis* Vaccine Programme, from left: Prof Andrew Pollard, Dr Christine Rollier, Dr Christina Dold, Dr Leanne Marsay (seated)

Our work links, for the first time, two lines of research; expertise in design and development of meningitis B vaccines from the Oxford Vaccine Group, with the extensive experience in using the vaccine technology based on Adenoviruses at the Jenner Institute Laboratories. We currently have 2 research programmes on this strategy, funded by the charities Meningitis UK and Action Medical Research. ■

Leanne Marsay, Christina Dold, Christine Rollier and Andrew J Pollard, Oxford Vaccine Group and Jenner Institute.

Vaccines targeting conserved regions of HIV-1: Encouraging signs in first trials

Prof Tomáš Hanke, Jenner Institute Laboratories, University of Oxford



HIV-1 infection/AIDS continues to be a major global health challenge. Despite improving efficacy of antiretroviral drugs, the best hope for a profound fall in the incidence of HIV-1 infection remains the development of an a safe, effective, affordable and accessible vaccine.

The biggest challenge in developing such a vaccine is the enormous ability of the AIDS virus to change. This means that every time the body or vaccine launches a protective response, HIV-1 changes, becomes invisible to these responses and escapes. The good news is that there is a limit to HIV-1 variation, because even HIV-1 has to keep small important parts of its proteins more or less constant in order to survive. And it is these conserved regions, HIV's weak point, that we target with vaccines.

This approach has another advantage: there are regional subtypes of HIV-1 viruses, which differ in up to 30% of amino acid sequences, but all share these common essential protein regions. Therefore if our vaccines work, they can be deployed in Africa, Asia, Europe or

America. The other strength of our vaccine approach comes from a potent combination of different vaccine types such as plasmid DNA, non-replicating poxvirus and non-replicating adenovirus of chimp origin, the last of which avoids inhibitory pre-existing anti-adenovirus responses in vaccine recipients. Similar regimens have been pioneered for other diseases by Jenner Institute investigators.

As a collaborative effort led by Tomáš Hanke, Lucy Dorrell and Andrew McMichael, these three candidate HIV-1 vaccines entered two HIV-CORE (COnserved REGions) trials in Oxford funded by the Medical Research Council UK. Trial HIV-CORE002, which assesses immunogenicity of these three vaccines in healthy, HIV-1 uninfected volunteers, started in March 2011, completed recruitment in January 2012 and the last volunteers/last visit is scheduled for August 2012.

So far, the tested vaccine combinations have been well tolerated and showed a 10-fold higher induction of HIV-1-specific responses compared to the 2007 STEP study prematurely terminated for futility. However, only efficacy trials in volunteers of high risk of HIV-1 infection will determine whether or not these vaccine-elicited immune responses can control HIV-1 infection. ■

Immune control of HIV: the importance of studying the 99%

Lucy Dorrell, Jenner Investigator (University of Oxford)



The lack of a clear indicator of immune protection against HIV and AIDS is a major obstacle to the development of an effective vaccine. Recently, exhaustive analyses of the results of two large efficacy trials, Rv144 and Step, have begun to yield clues to the attributes of immune responses that are associated with protection against infection or early control of viral replication. How to translate this knowledge into designing an effective vaccine is a formidable challenge.

Another fruitful approach has been to study immune responses in rare individuals who show complete suppression of HIV without antiretroviral therapy from an early stage of infection, known as HIV controllers. Less than 1% of people with HIV infection can be classified as controllers. In laboratory assays they show similar numbers of HIV-specific T cells to typical patients with progressive HIV disease, but more significantly stronger antiviral inhibitory activity, which supports the notion that qualitative aspects of HIV-specific immunity are key to the outcome of infection. However, these observations come from studies of patients with established infection. It is not clear yet whether the presence of fully functional HIV-specific T cells is the cause or consequence of suppressed viral replication. Furthermore, the rate of progression to AIDS varies considerably among the vast majority of patients with detectable viraemia; whether this can be explained by variation in specific functional aspects of their immune response to HIV is unresolved.

My group is working on answering these questions by sampling CD8+ T cells from a diverse group of patients and assessing their capacity to block HIV replication directly in culture.

We found that among patients in Oxford who had been infected for an average of 5 years, the level of CD8+ T cell antiviral activity was strongly associated with the rate at which their CD4+ cell count had fallen since diagnosis (the best surrogate marker of disease progression). We confirmed these initial results in a second cohort of patients from China who were known to have recently seroconverted (average 6 months previously) and found that the antiviral inhibitory capacity of their CD8+ T cells was strongly predictive of the rate of CD4+ cell loss in the first three years of HIV infection. Potent CD8+ T cell antiviral function was associated with a significantly longer time to reach a CD4 cell count of less than 350 cells per microlitre, the threshold at which antiretroviral therapy is usually started, and was also inversely

correlated with viral load set-point (level of viraemia established after acute infection).

The antiviral inhibitory capacity of CD8+ T cells provides a composite measure of HIV-specific immunity and so could be used as a benchmark of effective immunity in the early clinical testing of new HIV vaccine candidates. We are investigating this in ongoing phase I trials of our HIVconsv vaccines in Oxford (see page 12). In addition, our findings suggest that it should be further evaluated as a prognostic marker for patients when they are diagnosed with HIV infection. ■



Electron micrograph picture of an HIV-infected CD4+ cell

Reference:

H. Yang, H. Wu, G. Hancock, G. Clutton, N. Sande, X. Xu, H. Yan, X. Huang, B. Angus, K. Kuldaneek, S. Fidler, T. N. Denny, J. Birks, A. McMichael, L. Dorrell *The antiviral inhibitory capacity of CD8+ T cells predicts the rate of CD4+ cell decline in HIV-1 infection* J Infect Dis 2012, in press.

First trial of a new hepatitis C vaccine shows promise

Jenner Investigators Paul Klenerman and Ellie Barnes (University of Oxford)

A new vaccine against the chronic liver disease hepatitis C has shown promising results in a first clinical trial in humans, directed by Prof Paul Klenerman and Dr Ellie Barnes.

The vaccine generated immune responses similar to those seen in the minority of people who are naturally able to clear any infection with the hepatitis C virus. These findings suggest it might be possible to develop a vaccine that will be broadly effective against hepatitis C and offer lasting protection.

The researchers are hopeful that in time, this work could lead to a vaccine that protects those at risk from the disease or helps in treating those with hepatitis C infections. They caution that many more studies over a number of years would be needed in developing such a vaccine.

“It’s possible to prime very high levels of T cell responses that target multiple parts of the virus and which last for at least a year,” says Ellie Barnes.

“The immune responses we’ve seen are exciting and we are beginning the next stage of trials”, adds Paul Klenerman.

The study is published in the journal *Science Translational Medicine*. It was funded by the European Commission along with support from the UK Medical Research Council, the Wellcome Trust, the Oxford Biomedical Research Centre, and the Oxford Martin School at the University of Oxford.

Hepatitis C is caused by a virus transmitted through the blood, with infection typically remaining hidden for many years. Many people do not know they are infected because they do not show any symptoms. It is estimated that about 250,000 people are infected with hepatitis C in England and Wales, and the disease is now the leading reason in the West for liver transplants.

The course of hepatitis C infection is unpredictable. In a number of people, infection with hepatitis C leads to gradual damage to the liver than can eventually lead to cirrhosis. Some people’s immune responses, however, are sufficient to clear the virus soon after infection, which gives hope that a vaccine might be possible. However,



Rachel Townsend, postdoctoral scientist working on the Hepatitis C Vaccine Programme

hepatitis C is a virus that constantly changes its make-up, like HIV. This makes it a very difficult target for designing a vaccine.

The Oxford researchers, in collaboration with Italian biotech Okairros and colleagues at the University of Birmingham, have used a new approach to stimulate a different arm of the body’s immune system from previous attempts at a vaccine. This vaccine is designed to generate a T cell response to the more constant internal parts of the hepatitis C virus, rather than looking to prime an antibody attack on the ever-changing outer coat of the virus.

“The outside shell of the hepatitis C virus is very variable but the inside of the virus is much more stable. That’s where the engine of the virus is, where we may be able to successfully target many of the crucial pieces of machinery,” explains Professor Klenerman. “But we need T cells and not antibodies to be able to react to the inner components of the virus.”

The Oxford team carried out a first clinical trial in humans with the new vaccine. The phase 1 study of this trial was done primarily to gain safety data on the vaccine. It also recorded what kind of immune response was generated. In total,

41 healthy adults participated in the study. The vaccine appeared safe in this group and there were no significant adverse effects reported.

From this study, the researchers found that the vaccine could stimulate a large T cell response against hepatitis C that lasted for at least a year (the length of the study). The immune response was of a similar type and size to that reported in people who naturally clear the virus from their bodies after infection.

The Oxford team is now carrying out a new trial to see if the vaccine can help treat those already infected with hepatitis C, as well as continuing to improve the vaccine in order to obtain better immune responses: “Boosting the immune response in people already infected might help to clear the virus especially in combination with other drugs that lower the amount of virus around” says Ellie Barnes.

A US team is also looking to carry out a larger trial in at-risk groups to see if the vaccine can offer any protection against infection with hepatitis C. ■

Introduction to *'The Challenge'*: Mark is unemployed. His mother, Maureen, works in a primary school local to the Churchill Hospital. When, out of boredom, Mark decides to join the army, Maureen's response is to become a volunteer in the malaria trials at the hospital – a way of facing her own 'challenge'. In doing so, she has unwittingly ensured that her son's fate is entwined in hers.

The Challenge is published in 'Bio-Punk: An Anthology of Bio-engineered Futures', ed. Ra Page, Comma Press, May 2012.



The Challenge

by Jane Feather

A year ago, I was contacted by Ra Page, editorial director of a dynamic publishing house in Manchester, Comma Press. He was running a project designed to put writers in touch with leading scientists in their field with a view to publishing an anthology of stories. Would I like to be involved? I agreed on the spot.

My formal education in the sciences was desultory. So, when I was sent a list of the 37 bio-medical areas of research from which to choose, I was blinded by ignorance. I more or less stuck a pin in the map, and chose 'Infectious challenge of human subjects'. And so I found myself, a few months later, travelling from Devon to the Jenner Institute to meet up with Dr Sarah Gilbert, my scientific mentor on the subject.

Sarah's office was light and functional, much like that of a manager in any institution, and I realised that I'd been expecting, even from the ambience of the place, more of a *difference*. Where were the men and women in white coats, the long benches of petri dishes? Patiently Sarah outlined for me the work of the institute and her own expertise in developing new vaccines against 'flu and malaria. The work I learned is painstaking and un-showy, incongruously so, it seemed to me, given the dramatic potential it carries to improve and protect the health and, by extension, the social and economic wellbeing of millions around the world. I couldn't help but feel, in terms of usefulness to society, the enormity of the gap between us.

And then Sarah began to describe the physical detail of 'the challenge': the moment in which an ordinary plastic cup, fitted with a gauze cover and containing live mosquitoes, is placed against the volunteer's arm. I was fascinated to discover that in the midst of such sophisticated, world-leading research, there lay an experiment that depended on such a crude procedure.

I came away from our talk imagining that I was going to need to do a great deal more research, kicking myself for not being equipped to ask

more apposite questions. It was on the bus back, coincidentally, that I noticed a young couple: a boy-soldier in a beret and combats sitting with his girlfriend, their hands clenched together. They seemed unfeasibly, poignantly young. The boy reminded me of the young recruits I'd seen recently in a documentary programme about the build-up towards deployment in Afghanistan.

By the time I got home I'd decided that I'd approach my story from the volunteer's point of view. I emailed Sarah for more practical information and she put me in touch with someone in the department who'd been a volunteer herself, who, in turn, proved incredibly helpful in answering my questions about arrangements and motivations. I included my own experience of Oxford that day and the boy-soldier I'd seen on the bus: my volunteer would be his mother. With these two elements in place – the mother's participation in the trial and the son's in the war in Afghanistan - I prodded and pushed my story into place.

It would never have been written had I not had that glimpse into Sarah's work at the Institute. That encounter has only deepened my admiration for scientists like her, who are making a real and tangible difference. But there is another group of people, whom I had barely thought about before: the volunteers. Although the volunteer in my story is an entirely fictional one, I hope perhaps that, through her, some thought and recognition might be accounted to the countless anonymous volunteers who for minimal reward put themselves forward so heroically for the greater good. ■

Keystone Symposium: Immunological Mechanisms of Vaccination

13-18th December 2012, Fairmont Château Laurier, Ottawa, Canada



Keystone Symposia conferences are known for their collegial environments that foster interdisciplinary cross-talk and spark valuable new scientific collaborations.

DEADLINES:

Global Health Travel Award Deadline: Jul 17, 2012

Scholarship Deadline: Aug 13, 2012

Abstract Deadline: Aug 13, 2012

Late Abstract Deadline: Sep 13, 2012

Early Registration Deadline: Oct 11, 2012

This meeting is part of the Keystone Symposia Global Health Series supported by the Bill & Melinda Gates Foundation. It will be held juxtaposed with the Annual Grand Challenges in Global Health meeting; the final day of that meeting being the opening day of the Keystone Symposia.

The meeting will bring together an interdisciplinary group of scientists in vaccinology, immunology and pathogen biology, to address recent advances in these fields and their potential for accelerating vaccine design and development. As many of the relatively easy vaccines have already been made, vaccinology is now tackling more difficult diseases, often caused by complex and genetically variable pathogens. A better understanding of the immunological mechanisms underpinning existing and novel vaccines is therefore required. Fortunately, research efforts to uncover new molecular and cellular techniques offer exceptional opportunities for improved vaccine design.

The meeting is co-organised by Dan Barouch (Harvard Medical School), John Harty (University of Iowa), Tania Watts (University of Toronto) and Adrian Hill (Jenner Institute/University of Oxford).

Jenner Investigators - July 2012:

JENNER INVESTIGATORS	AFFILIATION	PRINCIPAL AREAS OF INTEREST
Dr Ellie Barnes	OXFORD	Hepatitis C vaccines
Dr Paul Barnett	IAH	Foot-and-mouth disease vaccines
Dr Persephone Borrow	OXFORD	HIV immunity
Prof Vincenzo Cerundolo	OXFORD	Cancer vaccines
Dr Bryan Charleston	IAH	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	IAH	Arbovirus vaccines
Prof Richard Moxon	OXFORD	Paediatric vaccines
Prof Venugopal Nair	IAH	Poultry vaccines
Dr Satya Parida	IAH	FMDV vaccines
Prof David Paton	IAH	FMDV vaccines & diagnostics
Prof Brian Perry	IAH	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	IAH	Respiratory syncytial virus vaccines
Dr Martin Vordermeier	AHVLA	Bovine TB vaccines

Oxford: University of Oxford, IAH: Institute for Animal Health, AHVLA: Animal Health and Veterinary Laboratories Agency

Call for Volunteers to Participate in Clinical Trials

The Centre for Clinical Vaccinology and Tropical Medicine (CCVTM) adjacent to the Old Road 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

Tel: +44 (0)1865 857406

Web: www.jenner.ac.uk



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