THE JENNER INSTITUTE

DEVELOPING INNOVATIVE VACCINES

2011–2014

UNIVERSITY OF OXFORD

THE Pirbright INSTITUTE

Contents

continued

Contents
continued

THE JENNER INSTITUTE
DEVELOPING INNOVATIVE VACCINES

NUFFIELD DEPARTMENT of MEDICINE

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 different species in parallel. A major theme is translational research involving the rapid early-stage development and assessment of new vaccines in clinical trials. The Institute is a partnership between the University of Oxford and The Pirbright Institute, and is the successor to the former Edward Jenner Institute for Vaccine Research. The Institute is supported by the Nuffield Department of Medicine, the Jenner Vaccine Foundation (a UK registered charity), and advised by the Jenner Institute Scientific Advisory Board.

The Institute comprises the research activities of over 25 Jenner Investigators who head leading 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 (TB) and HIV are currently in field trials in the developing world. There has also been substantial progress on livestock vaccines against foot-and-mouth disease, bovine tuberculosis, bluetongue, avian influenza, and other major causes of economic loss.

In the last few years both malaria and tuberculosis vaccine candidates have progressed to phase IIb efficacy testing in Africa, the TB vaccine candidate being the first ever subunit vaccine to reach this milestone. A new foot-and-mouth disease vaccine that can be manufactured without the use of live virus shows considerable promise for allowing safer manufacture of this key livestock vaccine. New vaccines against outbreak pathogens, such as Ebola and Rift Valley Fever, have made rapid progress to field efficacy testing using the vectored vaccine technologies developed by the Institute. The Oxford Vaccine Group, comprising Institute scientists from the University's Department of Paediatrics, made key contributions to the development of the recently licensed meningitis B vaccine, and to the rapid evaluation of H1N1 (swine) influenza vaccines. Finally, new horizons are being explored, with virus-like particle vaccines targeting chronic degenerative diseases such as Parkinson's disease and exciting new T cell-inducing vaccines against cancer entering clinical trials. There have been considerable advances in assessing vaccine efficacy, through controlled human microbial infections with typhoid, paratyphoid and influenza challenge studies, adding to those regularly undertaken for malaria vaccine assessment. Finally, new technologies such as transcriptomics and virus-like particle design add to established platforms for adjuvants and viral vector generation to broaden the suite of approaches available to Jenner Investigators.

The Institute has expanded substantially in the last 10 years with several enlarging groups, strategic recruitments and a broadening base of supportive funders from four continents. The Institute's exceptional capacity to undertake small scale first-in-human trials very rapidly was illustrated by the request from the World Health Organization to undertake, with collaborators, the first trial of a new Ebola vaccine destined for West Africa in the 2014 outbreak. Since then, no less than four new Ebola vaccines have first entered clinical testing in Oxford.

As the Jenner Institute approaches its 10th anniversary in late 2015, the global impact of vaccines and vaccination has never been greater and the scientific opportunities in vaccine development are ever increasing. So much remains to be done. Few other disciplines can offer the blend of ground-breaking science, multi-disciplinary collaboration and potential global impact that is found in vaccinology at its finest. I hope that this report conveys some of the excitement, as well as the sense of privilege, that those of us engaged and inspired by these goals are offered every day.

Adrian Hill
Director of the Jenner Institute

JENNER LOCATIONS

Jenner Laboratories, Old Road Campus Research Building

Pirbright Institute

Clinical Biomanufacturing Facility (CBF)

Wellcome Trust Centre for Human Genetics

Centre for Clinical Vaccinology and Tropical Medicine (CCVTM)

Animal Health and Veterinary Laboratories Agency (AHVLA)

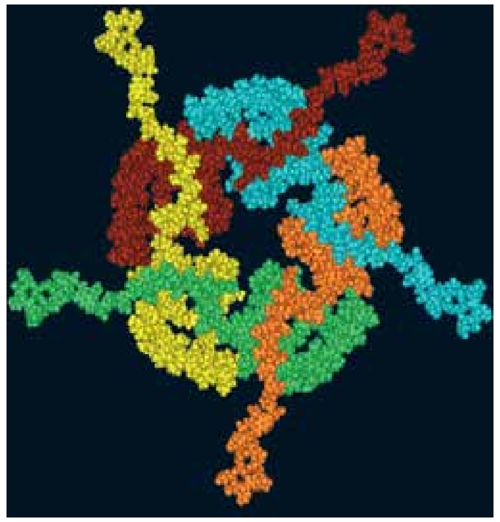
JENNER INVESTIGATORS

MARTIN BACHMANN
Vaccines against chronic diseases

My research group based in the Jenner Institute, University of Oxford is primarily interested in the development of vaccines against chronic, non-communicable diseases. The cores of these vaccines are based on virus-like particles (VLPs) that we use to display antigens of choice. I joined the Jenner Institute in 2012, after spending more than 10 years as Chief Scientific Officer at a biotech company in Zürich (Schlieren). Before this, I completed my PhD with Rolf Zinkernagel in Zürich, then spent 2 years with Pamela Ohashi in Toronto as a Post-Doc before another 2 years as a PI at the Basel Institute for Immunology. I currently divide my time between Oxford, Zürich and Doha.

My research over the last 15 years has focussed on the development of auto-vaccines in order to induce antibody responses against self-molecules involved in chronic diseases. To generate optimal antibody responses, we make use of VLPs (virus like particles) derived from bacteriophages and, more recently, plant viruses. The technology involves the chemical linkage of VLPs to selected antigens, which we would like to neutralise via the induction of specific antibody responses.

Our current goal is to advance the development of 2 specific auto-vaccines, namely a vaccine against Parkinson's disease and a vaccine against psoriasis. At the Jenner Institute, we also actively collaborate with other groups to apply VLP-based approaches to their targets, such as malaria antigens.



▲ Assembly of α-synuclein into pentamers, currently held to be the initiating step of Parkinson's disease (Image: https://www.michaeljfox.org/)

A vaccine against Parkinson's disease

Parkinson's disease (PD) is a progressive and devastating illness caused by a loss of dopamine-producing neurons in the brain. The loss of this neurotransmitter causes neurons to fire abnormally, resulting in patients being less able to direct or control their movement. Currently, there is no therapy with lasting efficacy, posing a significant challenge to the long-term treatment of patients with this neurodegenerative condition.

Overexpression of α-synuclein has been identified as a major cause for the development of Parkinson's disease in humans. It has been noted that as little as a 1.5 or 2-fold up-regulation of α-synuclein can cause familial PD. Lewy bodies (protein clumps consisting mainly of aggregated α-synuclein) are a histological hallmark of the disease. It is unclear whether these large α-synuclein aggregates are responsible for PD pathology, or whether small α-synuclein oligomers may also be toxic and cause disease. Therapies based on antibodies targeted against α-synuclein should, therefore, preferably employ antibodies of broad specificity that are able to recognise soluble oligomeric, as well as aggregated, α-synuclein.

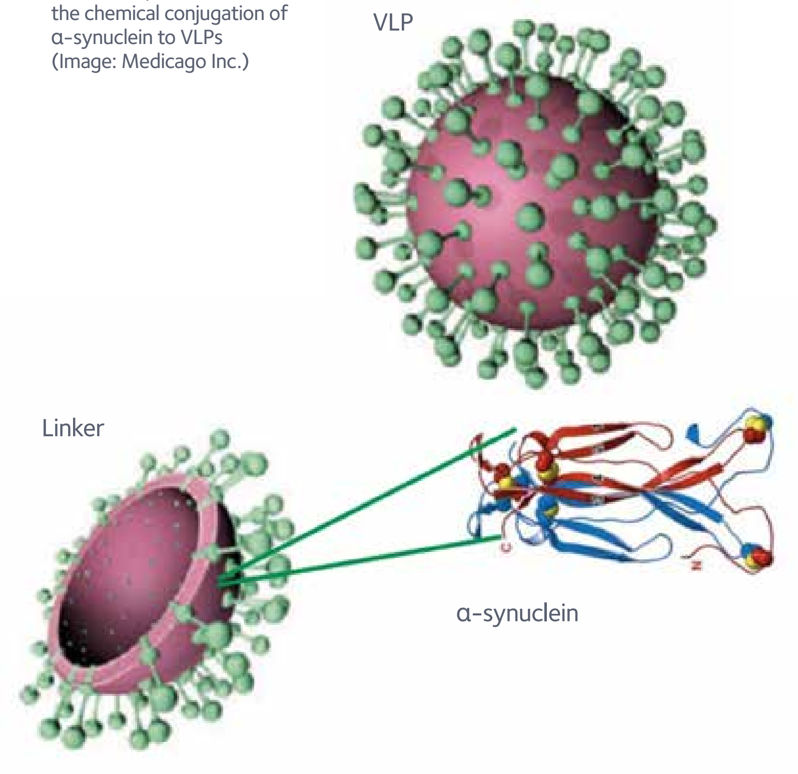
A recently emerging possibility by which intracerebral α-synuclein levels could be reduced is vaccination against the protein for the induction of long-lived antibody-responses. In recent times, mAbs as well as vaccines have reached the stage of preclinical proof-of-concept. However, the vaccine approach faces several difficulties, including generating sufficiently high antibody levels to penetrate the blood-brain barrier at relevant levels, whilst avoiding the possibility of inducing potentially harmful T cell responses. It is, therefore, essential to use a vaccine platform that induces high antibody responses in humans in the absence of relevant target-specific T cell responses. The use of strong adjuvants is particularly counter-indicated in this context, since these "helper-substances" usually enhance antibody responses by increasing potentially dangerous T helper cell responses. The use of next generation VLPs will avoid these issues, as strong antibody responses can be induced in the absence of an adjuvant.

Key publications:

1. Tissot A.C., Maurer P., Nussberger J., Sabat R., Pfister T., Ignatenko S., Volk H., Stocker H., Müller P., Jennings G.T., Wagner F. and M. F. Bachmann 2008. Vaccination against Angiotensin II reduces Day-Time and Early-Morning Ambulatory Blood Pressure: Results of a Randomized Placebo-Controlled Phase IIa Study with CYT006-AngQb. Lancet 371:821-827
2. Schmitz, N., K. Dietmeier, M. Bauer, M. Maudrich, S. Utzinger, S. Muntwiler, P. Saudan, and M.F. Bachmann. 2009. Displaying Fel d1 on virus-like particles prevents reactogenicity despite greatly enhanced immunogenicity: a novel therapy for cat allergy. The J Exp Med 206:1941-1955.
3. Rohn TA, G.T. Jennings, M. Hernandez, P. Grest, M. Beck, Y. Zou, M. Kopf, M.F. Bachmann. 2006. Vaccination against IL-17 suppresses autoimmune arthritis and encephalomyelitis. Eur J Immunol. 36:2857-2867.

▼ Parkinson's disease caused by a loss of dopamine-producing neurons in the brain

▼ Schematic presentation of the chemical conjugation of α-synuclein to VLPs (Image: Medicago Inc.)



We have initiated a new programme for developing a vaccine against PD that employs VLPs to induce strong antibody responses against the disease-causing protein α-synuclein, launched in conjunction with Dr Aadil El-Turabi. Preclinical efficacy will be evaluated in collaboration with the Oxford Parkinson Centre. Provided the vaccine proves efficacious in mouse models of PD, these results will constitute preclinical proof-of-concept and will, upon adequate demonstration of preclinical safety, progress towards clinical trials.

A vaccine against psoriasis

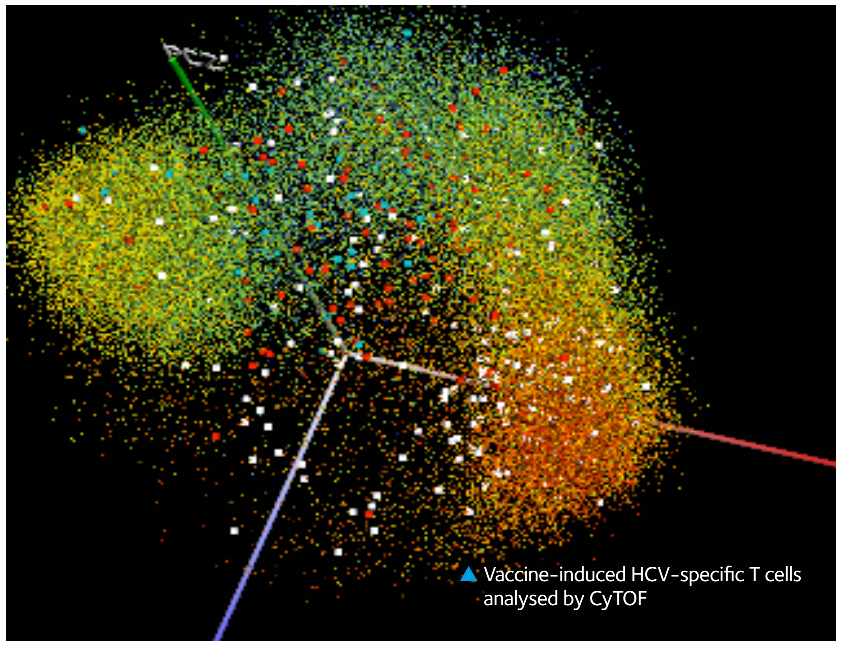
Novel biologics for the treatment of moderate to severe psoriasis have emerged to inhibit the pro-inflammatory cytokine interleukin-17 (IL-17). Monoclonal antibodies (mAbs) targeting IL-17 exhibit superior efficacy over currently licensed biologics, displaying fewer adverse effects in clinical trials. However, the high cost of manufacture and frequent administration of this therapeutic agent inflicts a heavy burden on ever-stretched healthcare budgets. Vaccines based on VLPs displaying antigens of choice on their surface elicit the production of high titre antibodies against those antigens and provide excellent tolerability. As an alternative to mAb-based therapies, VLP-based vaccines represent a new generation of therapeutic strategies, shifting away from costly passive immunisation to active immunisation, instructing the body to produce its own antibodies. This approach will deliver significant cost benefits in terms of manufacture and a more favourable dosing schedule, making them extremely competitive.

The current plan aims to demonstrate that a novel VLP-based vaccine can induce high titre neutralising antibodies for IL-17 as a preclinical proof-of-concept for the proposed active immunisation therapy. If successful, our project will validate the suitability of this approach for autoimmune and inflammatory disorders, creating intellectual property and potential for further commercialisation. More importantly, it will facilitate more affordable therapies for a class of hard-to-treat conditions, favourably impacting on the quality of life of afflicted individuals, and assist in the goal of improving the overall well-being of patients.

ELEANOR BARNES
Hepatitis C vaccines

I am a MRC Senior Clinical Fellow, Professor and an honorary consultant in hepatology at the University of Oxford and the John Radcliffe Hospital. I have spent recent years working on basic T cell immunology at the Peter Medawar Building for Pathogen Research, with a special interest in the immune control of Hepatitis C virus (HCV) infection. Recently, I have been developing T cell vaccines against HCV and am taking these forward into patients with HIV, as part of the FP7 PEACHI consortium. I am also leading the UK-wide MRC-funded consortium STOP-HCV, developing stratified medicine to optimise patient clinical outcomes.

The global burden of HCV infection is immense with 180 million people infected worldwide, and 4 million people newly infected each year. In the UK, 0.4% of the population are infected, with national prevalence rates of 10-30% elsewhere. HCV infection is associated with the development of cirrhosis and hepatocellular cancer, and is the leading cause of liver transplantation in the developed world. HCV epidemics in human immunodeficiency virus (HIV)-infected people in major European cities are a growing problem, with HCV now one of the leading causes of death in HIV-positive people on anti-retroviral therapy. New directly acting antivirals are now available that are associated with cure rates of >90%. However, these can be unaffordable even in developed countries (£30-70,000/person), and will inevitably be associated with the development of drug resistant strains. Therefore, a vaccine to prevent or treat HCV infection targeted to "at risk" populations, or more widely in high prevalence countries, would be of enormous global benefit.



Vaccine-induced HCV-specific T cells analysed by CyTOF

HCV exists globally as seven major genotypes (with 80% amino acid sequence homology between one another), and multiple subtypes that have evolved over thousands of years and which predominate in distinct geographical locations. Significant diversity may be found even within strains of the same subtype, between and within infected hosts. Within the UK, HCV exists predominantly as genotype-1 and subtype-3a infection. The very high prevalence rate of subtype-3a infection (>50%) in the UK is a unique feature of the epidemic.

HCV should be particularly susceptible to a T cell-mediated strategy, since immune-mediated viral eradication occurs spontaneously in 20% of people following primary infection. My group and others have shown that this is crucially dependent on effective T cell immunity and an appropriate host immune genetic background.

HCV vaccine approach

In recent years we have, in collaboration with others, developed highly immunogenic HCV T cell vaccines in experimental medicine studies that include both healthy volunteers and HCV-infected patients. We have used simian and human adenoviral (Ad) vectors derived from rare serotypes, in addition to Modified Vaccinia Ankara (MVA) vectors encoding all non-structural (NS) HCV proteins in heterologous prime/boost regimens. In healthy volunteers, we have shown that these vaccines are highly immunogenic, generating very high levels of functional CD4+ and CD8+ HCV-specific T cells and providing a detailed analysis of T cell function using novel CyTOF technology. Currently, these vaccines are undergoing efficacy testing in intravenous drug-using populations in the USA.

Whilst the development of a highly immunogenic T cell vaccine for HCV represents a major advance in the field, we have also shown that responses are generally attenuated in people with persistent infection and that intra-host and inter-host viral diversity, in combination with host HLA heterogeneity, may present a major challenge to the development of a successful HCV vaccine. Furthermore, recent work from the group evaluating inter-genotypic T cell immunity between HCV genotypes-1 and -3a has shown limited evidence of cross reactivity. This may have consequences for the deployment of HCV vaccines in populations where mixed genotypes circulate.

Since viral variability is an obstacle to vaccine development in several devastating infections, we are developing a generic approach for the design of genetically conserved vaccine immunogens against variable pathogens within the Jenner Institute (HIV, Dengue, and HCV). A computer algorithm has been developed to select conserved viral genomic segments, based on minimum sequence diversity within viral genomic datasets and minimum read lengths for the generation of both CD8+ and CD4+ T cell epitopes. Viral genomic segments that are conserved between genotypes, spanning both structural and NS HCV proteins, have been assimilated into a single immunogen with linker amino acids to prevent the generation of irrelevant epitopes.

Testing HCV vaccines

Moving forward, novel simian Ad vaccines that host conserved HCV genomes have been constructed (Vector Core Facility, Oxford), and immunogenicity will be compared with the current constructs in head-to-head preclinical mouse studies. Also, in collaboration with Okiaros/GlaxoSmithKlein and groups in Switzerland and Germany, we are assessing HCV T cell vaccines in HIV-positive people, and developing genetically adjuvanted HCV vaccines within the EU FP7 funded consortium "PEACHI" (www.peachi.eu/).

Through previous work assessing potent T cell vaccines in persistently HCV-infected people, and seeing first hand the failure to restore adaptive immunity in these patients, the group is interested in the mechanisms underpinning T cell "exhaustion" and aims to develop additional programmes of work that seek to restore immunity in experimental medicine studies in Hepatitis B virus and cancer.

Key publications:

1. Colloca S, Barnes E, Folgori A, Ammendola V, Capone S, Cirillo A, Siani L, Naddeo M, Grazioli F, Esposito ML, Ambrosio M, Sparacino A, Bartiromo M, Meola A, Smith K, Kurioka A, O'Hara GA, Ewer KJ, Anagnostou N, Bliss C, Hill AV, Traboni C, Klenerman P, Cortese R, Nicosia A. Vaccine vectors derived from a large collection of simian adenoviruses induce potent cellular immunity across multiple species. Sci Transl Med. 2012 Jan 4;4(115):115ra2.
2. Barnes E, Folgori A, Capone S, Swadling L, Aston S, Kurioka A, Meyer J, Huddart R, Smith K, Townsend R, Brown A, Antrobus R, Ammendola V, Naddeo M, O'Hara G, Willberg C, Harrison A, Grazioli F, Esposito ML, Siani L, Traboni C, Oo Y, Adams D, Hill A, Colloca S, Nicosia A, Cortese R, Klenerman P. Novel adenovirus-based vaccines induce broad and sustained T cell responses to HCV in man. Sci Transl Med. 2012 Jan 4;4(115):115ra1.
3. Humphreys IS, von Delft A, Brown A, Hibbert L, Collier JD, Foster GR, Rahman M, Christian A, Klenerman P, Barnes E. HCV genotype-3a T cell immunity: specificity, function and impact of therapy. Gut. 2012 Nov;61(11):1589-99.

Key publications:

1. Fenton-May A.E., O. Dibben, T. Emmerich, H. Ding, K. Pfafferott, M.M. Aasa-Chapman, P. Pellegrino, I. Williams, M.S. Cohen, F. Gao, G.M. Shaw, B.H. Hahn, C. Ochsenbauer, J.C. Kappes and P. Borrow. Relative resistance of HIV-1 founder viruses to control by interferon-alpha. Retrovirology, 10: 146, 2013.

2. Stacey, A.R., P. Norris, L. Qin, E.A. Haygreen, E. Taylor, J. Heitman, M. Lebedeva, A. DeCamp, D. Li, D. Grove, S.G. Self and P. Borrow. Induction of a striking systemic cytokine cascade prior to peak viraemia in acute human immunodeficiency virus infection, in contrast to more modest and delayed responses in acute hepatitis B and C virus infections. J. Virol. 83: 3719-3733, 2009.

3. Turnbull, E., M. Wong, X. Wei, S. Wang, N.A. Jones, K.E. Conrod, P. Newton, J. Turner, P. Pellegrino, I. Williams, G.M. Shaw and P. Borrow. Kinetics of expansion of epitope-specific T cell responses during primary HIV infection. J. Immunol. 182: 7131-7145, 2009.

PERSEPHONE BORROW

Understanding the immune response to HIV

I obtained a BA (Hons) degree in Natural Sciences in 1985, and a PhD degree in 1989, both from the University of Cambridge. I then carried out postdoctoral research with Dr Michael Oldstone at The Scripps Research Institute, USA, becoming an Assistant Member (Assistant Professor) there in 1995. In 1997, I moved back to the UK to lead the Viral Immunology Group at the newly-established Edward Jenner Institute for Vaccine Research in Compton. I joined the Nuffield Department of Clinical Medicine (NDM) at the University of Oxford in 2005, where I am currently a Reader and a Jenner Institute Investigator, heading a research team based in the NDM Research Building.

There is an urgent need for vaccines to combat infection with human immunodeficiency virus type 1 (HIV-1), the virus that causes AIDS. There are currently around 35 million people living with HIV/AIDS worldwide, and about 1.5 million people die of AIDS-associated diseases each year. Combination therapy reduces viral load and delays disease progression in those who receive it, but it does not eradicate infection and is associated with many long-term problems; and even in resource-rich countries many infected individuals are not treated effectively. Importantly, the HIV-1 epidemic continues to spread: 2.1 million people became infected with HIV-1 in 2013.

Understanding how T cells help the antibody response

Developing effective HIV-1 vaccines is extremely challenging, due to the variability of the virus and the many strategies it possesses for resisting and evading control by host immune responses. Together with Prof. Andrew McMichael's group, we are working as part of the Centre for HIV/AIDS Vaccine Immunology and Immunogen Discovery (CHAVI-ID) consortium to understand interactions between HIV-1 and the immune response and learn how effective HIV-1 vaccination strategies can be developed.

Most antiviral vaccines confer protection by stimulating neutralising antibody responses, but the 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. In collaboration with Prof. Simon Draper's group, we are also comparing the ability of different vaccination platforms to elicit potent CD4+ Tfh activity and germinal centre B cell responses.

CD8+ (cytotoxic) T cells in HIV vaccines

Other immune responses can also be employed in HIV-1 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 the 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. Mechanisms involved include viral escape from epitope-specific T cell responses, which is facilitated by focussing of the primary HIV-specific T cell response on a limited number of viral epitopes, and decline in T cell functionality following acute infection. By identifying how the specificity of the primary CD8+ T cell response to HIV is determined and how CD8+ T cell control of HIV-1 is evaded, we aim to understand how vaccines can be designed to induce optimally-effective HIV-specific CD8+ T cell responses.

The role of innate immune responses

A third objective is to determine whether innate effector responses can be harnessed to contribute to HIV prophylaxis. We are characterising the innate responses activated in acute HIV-1 infection and addressing their roles in protection and pathogenesis. 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.

VINCENZO CERUNDOLO

Harnessing the immune system to treat cancer, autoimmunity and infection

I work at the Weatherall Institute of Molecular Medicine, Oxford. I studied Medicine at the University of Padua, Italy, specialising in Oncology, and subsequently moved to the UK to work with Professor Alain Townsend on antigen presentation. I now have a personal Chair in Immunology at the University of Oxford and I am Director of the MRC Human Immunology Unit.

The principal aim of my research is to gain a better understanding of the mechanisms that control the cell-cell interplay required for optimal expansion and activation of tumour-specific T cell populations, and to apply this knowledge to the development of better treatment strategies for cancer patients. Research in my laboratory is divided into three complementary areas:

- Analysis of tumour-specific immune responses in melanoma patients and the role of the tumour micro-environment in hampering tumour-specific immune responses
- Structural, kinetic and functional analyses of invariant NKT (iNKT) cell activation
- A clinical trial vaccine programme in melanoma patients

Adjuvants and toll-like receptors enhance immune responses

Over the last three years, we have continued to characterise a range of adjuvants to enhance antigen-specific immune responses. Furthermore, we have identified novel aspects of the human toll-like receptor 7 (hTLR7) biosynthetic pathway, which is important in the innate immune response to infection, demonstrating that hTLR7 is proteolytically processed and that C-terminal fragment selectively accumulates in endocytic compartments. We have shown that hTLR7 processing occurs at neutral pH and is dependent on furin-like proprotein convertases (PCs). Furthermore, hTLR7 processing is required for its functional response to hTLR7 agonists, such as R837 or the influenza virus. Notably, pro-inflammatory and differentiation stimuli increase the expression of furin-like PCs in immune cells, suggesting a positive feedback mechanism for hTLR7 processing during infection. Because self-RNA can activate hTLR7 and trigger autoimmunity under certain conditions, our results identify furin-like PCs as a possible target to attenuate hTLR7-dependent autoimmunity and other immune pathologies.

Key publications:

1. Salio M, Puleston DJ, Mathan TS, Shepherd D, Stranks AJ, Adamopoulou E, Veerapen N, Besra GS, Hollander GA, Simon AK, Cerundolo V. Essential role for autophagy during invariant NKT cell development. Proc Natl Acad Sci USA. 2014. Dec 30; 111(52):E5678-87.
2. Hipp MM, Shepherd D, Booth S, Waithe D, Reis e Sousa C, Cerundolo V. The processed amino-terminal fragment of human TLR7 acts as a chaperone to direct human TLR7 into endosomes. J. Immunol. 2015. Apr 27. pii: 1402703
3. Hipp MM, Shepherd D, Gileadi U, Aichinger MC, Kessler BM, Edelmann M, Essalmani R, Seidah NG, Reis e Sousa C, Cerundolo V. Processing of human TLR7 by furin-like proprotein convertases is required for its accumulation and activity in endosomes. Immunity. 2013 Oct 17;39(4):711-21.

BRYAN CHARLESTON
Foot-and-Mouth Disease and Swine Influenza

I am a Veterinary surgeon with post-graduate training in virology and immunology. I am the current Head of the Livestock Viral Disease Programme at the Pirbright Institute.

Foot-and-mouth disease (FMD)

Experimental studies in collaboration with Prof. Mark Woolhouse (Edinburgh) have determined that the infectious period of foot-and-mouth disease virus (FMDV) in cattle is shorter (mean 1.7 days) than currently realised, and that animals are not infectious until, on average, 0.5 days after clinical signs appear. These results imply that controversial pre-emptive control measures may be unnecessary for FMD and other acute viral infections of livestock and humans. Furthermore, rapid induction of CD4 T cell-independent antibody responses and the formation of virus-antibody immune complexes (IC) have been identified as key events in disease pathogenesis. IC formation triggers productive infection and killing of key immune cells called dendritic cells (DCs), alongside the induction of anti-viral proteins (type-1 interferon) from specialised cells (plasmacytoid DCs): events that correlate with the onset of clinical signs and transmission.

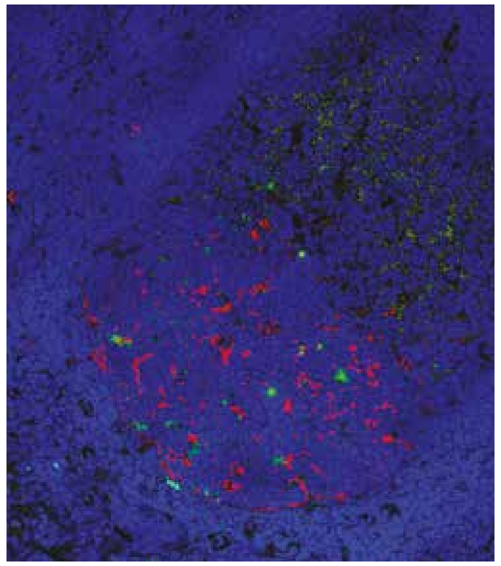
Persistence of non-replicating but infectious virus has been demonstrated in specific regions of lymphoid tissue in the head and neck of cattle, sheep, pigs and African buffalo. These observations have identified a role of this persisting virus in the maintenance of long-term protective antibody responses and generation of virus variation in African buffalo, the natural reservoir of foot-and-mouth disease virus in Africa.

Immunisation is said to be our society's greatest health care achievement. The development and use of vaccines has led to the reduction or eradication of common diseases such as polio and measles. However, pathogens that cause disease and death are still common and so it is important to continue developing new vaccines.

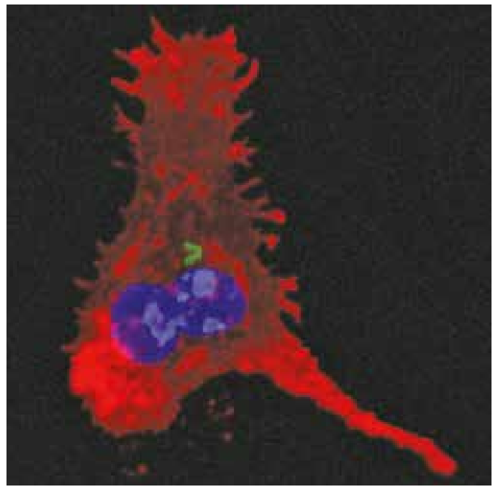
A new FMD vaccine

In collaboration with Prof. Dave Stuart (Oxford) and Prof. Ian Jones (Reading), we have developed a new methodology to produce a vaccine for FMDV. Because the vaccine is all-synthetic, made up of tiny protein shells designed to trigger an optimum immune response, it doesn't rely on growing live infectious virus and is therefore much safer to produce.

▼ Buffalo inoculation



▲ FMDV in lymph node germinal centre



▲ Two fluorescently labelled BCG bacteria (green) inside a cattle dendritic cell

Furthermore, these empty shells have been engineered to be more stable, making the vaccine much easier to store and reducing the need for a cold chain. This is important research, because it represents a big step forward in the global campaign to control FMDV in countries where the disease is endemic, and could significantly reduce the threat to countries currently free of the disease. Crucially, this new approach to making and stabilising vaccines could also impact on how viruses from the same family are fought, including polio.

Improving MVA vaccines

Modified Vaccinia Ankara (MVA) is a highly attenuated virus that is being evaluated as a vaccine delivery system. Whilst MVA is a promising vaccine platform, the development of a vaccine platform that provides strong, long lasting immunity against infectious diseases will benefit the farming industry and improve animal and human health.

After delivery through the skin, this vaccine interacts with DCs, and these in turn initiate and maintain the immune response; it is therefore important for the vaccine not to damage the function of DCs. We have previously reported that bovine DCs are seriously affected by MVA, reducing their capacity to initiate and maintain the immune response. This is because DCs recognise MVA as a foreign invader and produce lethal superoxide ions that kill the vaccine and the cell, making the vaccine ineffective. Our data show that by deleting certain genes from the MVA genome, the toxic effects observed in DC are reduced, in turn increasing the effectiveness of the vaccine.

Swine influenza

Work has just started on a new collaborative long-term study on the transmission of swine influenza. The Biotechnology and Biological Sciences Research Council (BBSRC) Swine Flu Dynamics project is a five-year study which, as well as researching virus transmission, will assess the effectiveness of different control strategies for the disease to improve animal health and help protect the UK economy.

THE Pirbright INSTITUTE

Key publications:

1. Porta C, Kotecha A, Burman A, Jackson T, Ren J, Loureiro S, Jones IM, Fry E, Stuart DI, Charleston B. Rational engineering of recombinant picornavirus capsids to produce safe, protective vaccine antigen. Plos Pathogens;9(3):e1003255.
2. Cubillos-Zapata C, Guzman E, Turner A, Gilbert SC, Prentice H, Hope JC, Charleston B. Differential effects of viral vectors on migratory afferent lymph dendritic cells in vitro predict enhanced immunogenicity in vivo. J Virol. 2011;85(18):9385-94.
3. Charleston B, Bankowski B, Gubbins S, Chase-Topping ME, Schley D, Howey R, Barnett PV, Gibson D, Juleff ND, Woolhouse MEJ. Relationship between clinical symptoms and transmission of an infectious disease and the implications for control. Science 2011;332(6030):726-9.

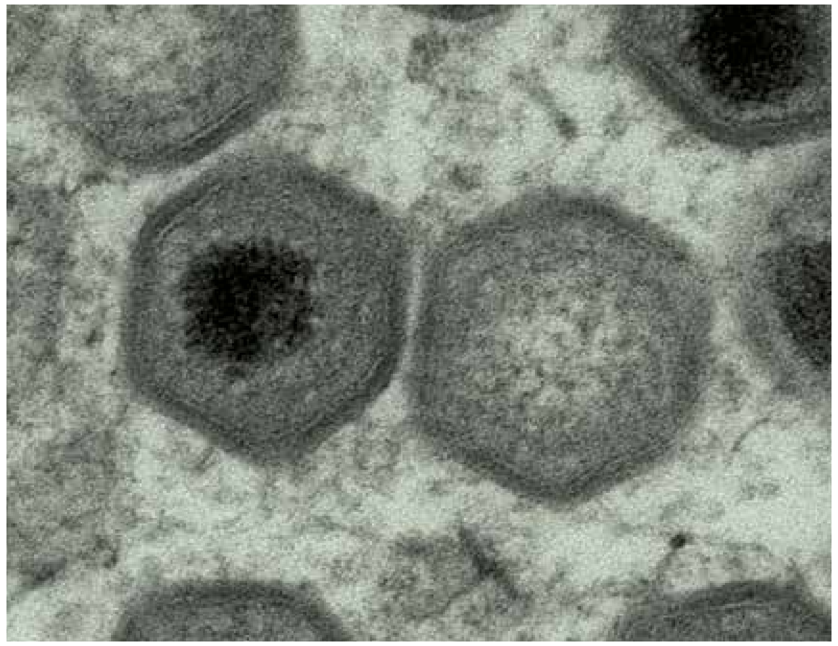
LINDA DIXON
African Swine Fever

I am Head of the African swine fever virus (ASFV) group at The Pirbright Institute. My research interests are directed at understanding how ASFV evades the host response to infection. We are applying the knowledge gained to the development of ASFV vaccines, in collaboration with the Vaccinology group at Pirbright.

African swine fever virus

ASFV is a large DNA virus that causes a haemorrhagic fever resulting in high mortality in pigs. The disease is endemic in many sub-Saharan African countries and Sardinia. Since 2007, ASF has spread from Georgia to the Russian Federation and into neighbouring Eastern European countries. The lack of a vaccine limits options for disease control.

▼ Electron Microscopy image of mature and immature ASF virions in a cytoplasmic virus factory



Attenuated (non-virulent) ASFV strains are known to induce protection against challenge with related virulent viruses. We compared complete genome sequences of a naturally attenuated ASFV isolate, OURT88/3, with virulent viruses and identified a large deletion near the left end of the OURT88/3 genome. This encodes copies of multigene families MGF 360 and MGF 530/505. A further copy of MGF 360 is disrupted near the right genome end. These genes are known to be involved in suppressing the induction of a type I interferon response. Two other genes encoding membrane proteins with adhesion motifs are also disrupted in the OURT88/3 genome. Our previous work has shown that CD8+ cells are required for protection induced by OURT88/3, and that stimulation of lymphocytes from immune pigs correlates with cross-protection by different genotypes of ASFV. To identify a route for rational attenuation of other ASFV strains, we deleted similar MGF 360 and MGF 530/505 from the genome of the virulent Benin 97/1 isolate (BeninΔMGF). This deletion attenuated the Benin 97/1 isolate and induced protection against lethal challenge. Investigation of the cellular and cytokine responses induced by BeninΔMGF have identified some differences compared to those induced by OURT88/3. Future work will determine whether similar gene deletions from the genomes of other ASFV genotypes, including that circulating in Eastern Europe, can also produce candidate attenuated vaccine strains. We will also further investigate the mechanisms of protection induced by BeninΔMGF. In parallel, the effects of deleting other genes involved in inhibiting innate immune responses from virulent and attenuated ASFV strains is being evaluated. These studies currently focus on genes that suppress type I interferon or stress responses.

An alternative approach to vaccine design

Another approach for vaccine development is to identify those antigens that induce a protective response and express them from an appropriate viral vector. We have followed two approaches to identify potentially protective antigens. One involves immunising pigs by prime and boost, with pools of DNA and recombinant vaccinia virus vectors expressing individual randomly selected ASFV genes. Cellular and antibody responses to individual antigens were measured and a pool of antigens selected for further study (in collaboration with Biodesign Institute, Arizona State University). A second approach involves identifying those ASFV antigens that are recognised by immune lymphocytes from OURT88/3. A pool of 20 of the most promising antigens from both approaches are being cloned in Adenovirus vectors (Jenner Institute) and will be tested in overlapping pools in immunisation and challenge experiments in pigs.

Key publications:

1. King, K , Chapman, D Argilaguet, JM ; Fishbourne, E., Hutet, E Cariolet, R Hutchings, G, Oura, CAL, Netherton, CL , Moffat, K , Taylor, G , Le Potier, MF , Dixon, LK , Takamatsu, HH 2011 Protection of European domestic pigs from virulent African isolates of African swine fever virus by experimental immunisation. Vaccine 29 4593-4600
2. Chapman, DAG., Tcherepanov, V., Upton C. and Dixon LK. 2008 Comparison of the genome sequences of non-pathogenic and pathogenic African swine fever virus isolates J Gen Virol ; 89: 397-408
3. Charles C. Abrams, Linda K. Dixon Sequential deletion of genes from the African swine fever virus genome using the cre/loxP recombination system 2012 Virology, Volume 433, 142-148

LUCY DORRELL
HIV immunotherapy

I am a Senior Clinical Research Fellow, Associate Professor and Honorary Consultant in HIV medicine. I lead research programmes in HIV immunotherapy and HIV/HCV co-infection, encompassing translational immunology, imaging and vaccine trials. A major focus of my research is the identification of immunological correlates of HIV control.

HIV vaccines used in combination with anti-HIV drugs

Antiretroviral therapy (ART) restores health and life expectancy for HIV-infected individuals but does not provide a cure. New therapies are needed to eliminate the reservoir of CD4+ T cells in lymphoid tissue where HIV persists for years without detection. The goal of my research is to develop innovative vaccination and immunotherapy strategies to enhance immune-mediated killing of cells that harbour HIV, to be used in combination with ART and agents to reverse viral latency.

We have conducted clinical trials of HIV vaccine candidates in HIV-positive subjects treated with ART during chronic and primary infection in the UK and Spain. The vaccines comprised a conserved region immunogen, HIVconsv, delivered by replication-defective chimpanzee adenovirus and MVA vectors. These trials are among the first to evaluate latent HIV reservoirs before and after vaccination. Immunological and virological analyses will be completed in 2015.

Key publications:

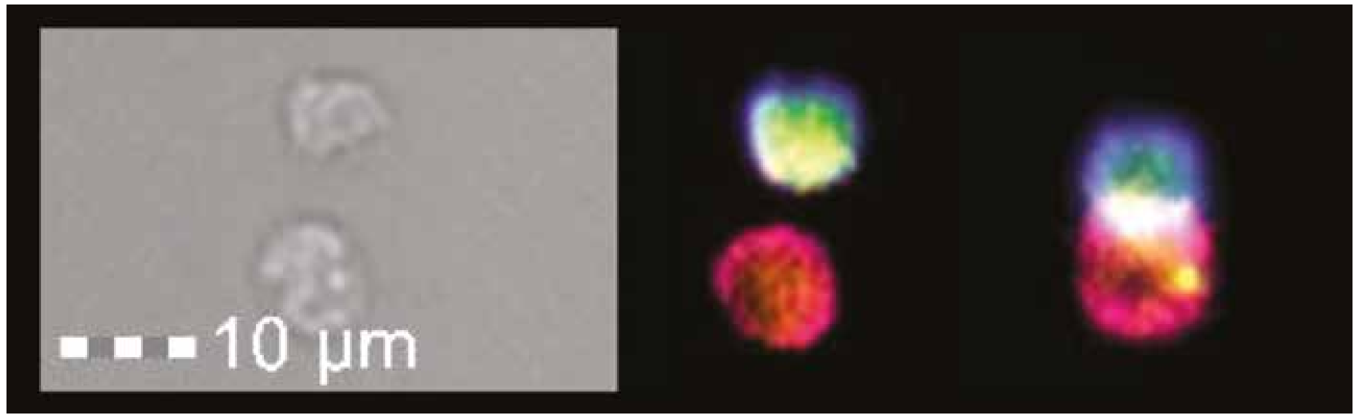
1. Yang H, Wu H, Hancock G, Clutton G, Sande N, Xu X, Yan H, Huang X, Angus B, Kuldanek K, Fidler S, Denny TN, Birks J, McMichael A, Dorrell L. *The antiviral inhibitory capacity of CD8+ T cells predicts the rate of CD4+ cell decline in HIV-1 infection.* J Infect Dis 2012, 206: 552-61.
2. Clutton G, Yang H, Hancock G, Sande N, Holloway C, Angus B, von Delft A, Barnes E, Borrow P, Pellegrino P, Williams I, McMichael A, Dorrell L. *Emergence of a distinct HIV-specific IL-10-producing CD8+ T-cell subset with immunomodulatory functions during chronic HIV-1 infection.* Eur J Immunol. 2013; 43: 2875-85.
3. Hancock G, Yang H, Yorke E, Wainwright E, Bourne V, Frisbee A, Payne TL, Berrong M, Ferrari G, Chopera D, Hanke T, Mothe B, Brander C, McElrath MJ, McMichael A, Goonetilleke N, Tomaras GD, Frahm N, Dorrell L. *HYPERLINK "http://www.ncbi.nlm.nih.gov/pubmed/25723536" Identification of effective subdominant anti-HIV-1 CD8+ T cells within entire post-infection and post-vaccination immune responses.* PLoS Pathog. 2015; 11:e1004658.

ImmTAVs: a novel anti-HIV therapy

HIV is able to gain a foothold because it can rapidly escape evolving adaptive immune responses very early in the course of infection, while simultaneously seeding long-lived CD4+ T cells. In collaboration with Immunocore Ltd., Oxfordshire, we have tested novel agents, engineered immune-mobilising T cell receptors against viruses called 'ImmTAVs' that are designed to clear HIV-infected cells. ImmTAVs are synthetic soluble T cell receptors (TCRs) that recognise HIV epitopes with extraordinarily high affinity and are coupled to a single chain antibody targeting CD3. The ImmTAVs bind specifically to HIV-infected cells via the TCR and harness passing effector T cells via CD3 signalling, resulting in immune-mediated killing of the target cell. We studied patients on long-term ART and observed highly efficient killing of HIV reservoir cells by ImmTAV-redirected CD8+ T cells *ex vivo*. Importantly, ImmTAVs were able to induce killing of cells that expressed very low levels of viral proteins. Our results suggest that ImmTAVs are promising agents that could facilitate clearance of HIV reservoirs. This work has paved the way for a new project on imaging of HIV-immune cell interactions using the first ever containment level 3 high-resolution microscopy facility at the Weatherall Institute of Molecular Medicine, in collaboration with Prof. Christian Eggeling.

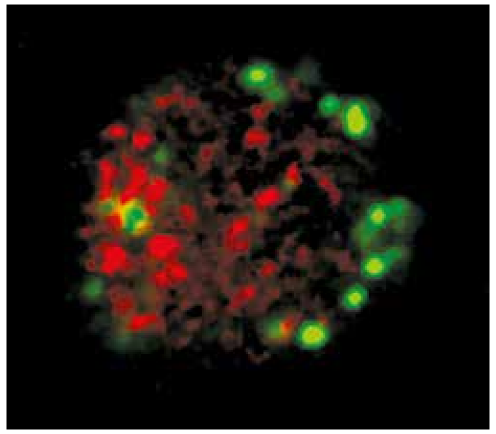
Understanding how HIV vaccines work

Only two HIV vaccines designed to elicit protective T cell responses have reached clinical efficacy testing to date, both with disappointing results. Defining the components of an HIV immunogen that could induce effective CD8+ T cell responses is therefore critical to the development of preventive and therapeutic vaccines. In collaboration with the HIV Vaccine Trials Network (HVTN) and Duke University, USA, we investigated the viral targets of CD8+ T cells that potently inhibit HIV replication *in vitro*, as this is highly predictive of virus control *in vivo*. Rare individuals whom maintain low level viraemia without ART (viraemic controllers) showed broad and potent CD8+ T cell inhibitory activity against diverse HIV strains, in contrast to non-controller subjects. Viral inhibition was strongly correlated with the frequency of CD8+ T cells that targeted epitopes within 26 vulnerable regions in the viral proteome,



▲ Visualisation of ImmTAV-redirected killing of HIV-infected CD4+ T cells

▼ HIV infected cell



which had been identified in an independent study of nearly 1,000 chronically infected individuals. These so-called 'beneficial' regions, while generally conserved and subdominant, would not have been predicted by bioinformatic approaches. Furthermore, vaccines encoding full-length HIV proteins, including the MRK Ad5-Gag/Pol/Nef vaccine tested in the Step trial, rarely induced responses to these regions. This observation suggests that immuno-dominance hierarchies undermine effective anti-HIV CD8+ T cell responses, and provides an explanation for the failure of conventional HIV immunogens to induce effective immune responses. Our research has thus highlighted the need for immunogens based on systematic selection of empirically defined vulnerable regions within the viral proteome, with exclusion of immunodominant decoy epitopes that are irrelevant for HIV control.

PEACHI: preventing HCV and HIV co-infections

As HIV-positive people are living longer, prevention of comorbidities has become a priority. In 2013, we launched PEACHI, an EU FP7-funded project to develop vaccines for the prevention of hepatitis C virus (HCV) and HIV co-infections. The PEACHI consortium brings together expertise in the HIV and HCV fields, with European partners from academia (Oxford, St. James' Hospital Dublin, Kantosspital St. Gallen) and industry (GlaxoSmithKlein and ReiThera) (www.peachi.eu). In 2014 we initiated the first phase I trial to evaluate combined vaccinations with HIV and HCV immunogens, each delivered by replication-defective chimpanzee adenovirus and MVA vectors (PEACHI 04), in healthy volunteers in Oxford. This will be followed by a phase I trial to evaluate the same HCV vaccine candidates in HIV-seropositive HCV-uninfected patients on ART in Ireland and Switzerland (PEACHI 02). In addition, ReiThera has developed next generation viral vectored vaccines employing an HCV immunogen fused to the HLA class II invariant chain. We plan to take these vaccines into a first-in-human trial in 2015. These clinical studies will be complemented by comprehensive immuno-monitoring using established and new laboratory assays, with the goal of identifying possible immune correlates that could be tested in future efficacy trials.

SIMON DRAPER
Blood-Stage Malaria

I am currently a UK Medical Research Council (MRC) Career Development Fellow, Jenner Investigator, Associate Professor and Supernumerary Fellow of Merton College, Oxford. In 2013 I was awarded a Research Prize Fellowship from the Lister Institute of Preventive Medicine.

The development of an effective vaccine against the blood-stage malaria parasite has proved incredibly challenging. The mainstay approach in the field has focussed on inducing antibodies that seek to block red blood cell invasion by the merozoite form of the parasite. This endeavour has been hindered by the antigenic variability of the parasite's proteins, the redundancy of invasion pathways used by the parasite, and the need for extremely high titres of antibody to block this rapid and complex invasion process. Over the last 3 years, my group has sought to tackle these problems by identifying proteins within the merozoite that are conserved, essential and yet highly susceptible to vaccine-induced antibodies. In parallel, we have continued to invest significant time in the development of new and improved vaccine delivery strategies to deliver malaria antigens in a highly immunogenic manner, leading to the induction of high titer antibody responses.

In 2011, we completed a series of three Phase I/IIa clinical trials funded by the UK MRC and the European Malaria Vaccine Development Association (EMVDA). These trials sought to assess the delivery of two candidate antigens from the human malaria parasite *Plasmodium falciparum* (MSP1 and AMA1) using recombinant simian adenovirus (ChAd63) and MVA (modified vaccinia Ankara) viral vectors. These vaccines were shown to be safe and highly immunogenic for T cell, B cell and antibody responses in healthy adult volunteers. However, the induced responses did not protect volunteers following controlled malaria infection delivered by infectious mosquito bites. These studies did, however, provide an opportunity to better understand how vaccine-induced responses can be modulated by exposure to the malaria parasite in a controlled infection setting. This work in malaria-exposed volunteers in Oxford is complemented by similar immunological studies in individuals who are naturally-exposed to malaria in Africa, through our collaboration with the KEMRI-Wellcome Institute in Kilifi, Kenya. This on-going work has a particular interest in antibody effector mechanisms against the blood-stage parasite, including neutralisation as well as antibody Fc interactions with the cellular immune system. Following on from these studies, we have undertaken a series of preclinical experiments to look at the utility of deploying protein-in-adjuvant and viral vectored vaccines in combination with immunisation regimes. This work has led to a fourth Phase Ia clinical trial using the AMA1 antigen, where we have confirmed the superior immunogenicity of the 'adenovirus prime – protein boost' approach in healthy adult volunteers.

Improved vaccine targets

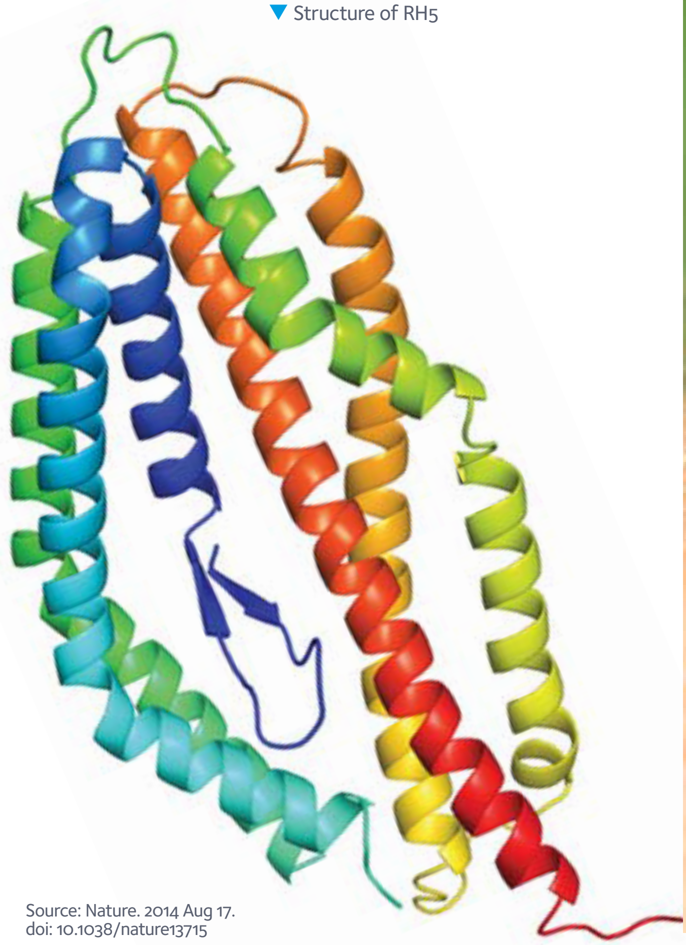
More recently, our preclinical vaccine development work has focussed on the identification of improved antigen targets within the blood-stage merozoite parasite. We have spent significant time establishing new protein vaccine production platforms (based on mammalian and insect cell technologies) that, along with viral vectored delivery, are enabling the generation of a whole new range of vaccines. To date, we have identified the PfRH5 antigen as the first reported target in the *P. falciparum* merozoite that is highly susceptible to broadly-neutralising vaccine-induced antibodies. We have shown that PfRH5 is quantitatively more susceptible to vaccine-induced antibodies than the gold standards in the field (AMA1 and MSP1), with high level protective efficacy in a non-human primate challenge model. With support from the European Commission MultiMalVax programme, as well as the European Vaccine Initiative and UK MRC, we are currently progressing PfRH5 viral vectored vaccines, as well as a protein vaccine made in *Drosophila* S2 cells, to Phase I/IIa clinical trials. These should initiate by mid-2015.

In parallel, we have also progressed a viral vectored vaccine candidate to Phase Ia clinical testing against blood-stage *Plasmodium vivax*. This vaccine targets the PvDBP_RII protein, which is critically essential for red blood cell invasion by this parasite. This is the world's first vaccine trial of a candidate for blood-stage *P. vivax*, and should pave the way to initiate vaccine efficacy studies in the near future.

Future work

Our ongoing work will now seek to make use of the valuable opportunity of having the PfRH5 and PvDBP_RII antigens in clinical testing for the first time. We will begin to explore the human antibody responses to both targets, seeking to generate panels of human monoclonal antibodies from the B cells of vaccinated volunteers. These mAbs can then be used for functional and structural analyses, and should help to guide the design of second-generation improved immunogens. In parallel, at the preclinical stage, we will continue to search for other antigens within the merozoite that are highly susceptible to vaccine-induced antibodies and suitable for inclusion in a combination vaccine with PfRH5. We are also focussing on improving the blood-stage controlled human malaria infection model, which should allow for quicker and easier efficacy testing in Phase IIa clinical trials of new candidate vaccines, including those based on PfRH5.

▼ Structure of RH5



Source: Nature. 2014 Aug 17.
doi: 10.1038/nature13715

Key publications:

1. Douglas, A. D., A. R. Williams, J. J. Illingworth, G. Kamuyu, S. Biswas, A. L. Goodman, D. H. Wyllie, C. Crosnier, K. Miura, G. J. Wright, C. A. Long, F. H. Osier, K. Marsh, A. V. Turner, A. V. Hill, and S. J. Draper. 2011. The blood-stage malaria antigen PfRH5 is susceptible to vaccine-inducible cross-strain neutralizing antibody. Nat Commun 2:601.

2 Sheehy, S. H., C. J. Duncan, S. C. Elias, P. Choudhary, S. Biswas, F. D. Halstead, K. A. Collins, N. J. Edwards, A. D. Douglas, N. A. Anagnostou, K. J. Ewer, T. Havelock, T. Mahungu, C. M. Bliss, K. Miura, I. D. Poulton, P. J. Lillie, R. D. Antrobus, E. Berrie, S. Moyle, K. Gantlett, S. Colloca, R. Cortese, C. A. Long, R. E. Sinden, S. C. Gilbert, A. M. Lawrie, T. Doherty, S. N. Faust, A. Nicosia, A. V. Hill, and S. J. Draper. 2012. ChAd63-MVA-vectored Blood-stage Malaria Vaccines Targeting MSP1 and AMA1: Assessment of Efficacy Against Mosquito Bite Challenge in Humans. Mol Ther 20:2355-2368.

2 Wright, K. E., K. A. Hjerrild, J. Bartlett, A. D. Douglas, J. Jin, R. E. Brown, J. J. Illingworth, R. Ashfield, S. B. Clemmensen, W. A. de Jongh, S. J. Draper, and M. K. Higgins. 2014. Structure of malaria invasion protein RH5 with erythrocyte basigin and blocking antibodies. *Nature* 515: 427-430.

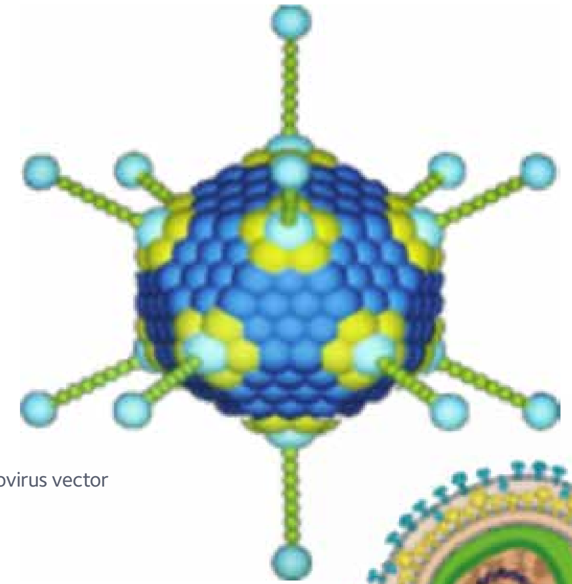
SARAH GILBERT

Targeting Influenza and Rift Valley Fever with viral vector vaccines

I moved to the University of Oxford in 1994, following a BSc in Biological Sciences at the University of East Anglia and a PhD in Biochemistry from the University of Hull, plus post-doctoral work in academia and industry. My main research interest is in the use of recombinant viral vectors as vaccines. I lead the Jenner Institute human influenza vaccine programme and collaborate on the development of a number of veterinary vaccines.

New vaccines for Influenza

The main activity of my group in the last three years has been to conduct clinical trials of new influenza vaccines, which are designed to work in a different way to existing influenza vaccines and either replace or complement them. Current influenza vaccines are capable of inducing immunity to the proteins on the surface of the influenza virus, but since they constantly change from year to year, the composition of the vaccine has to be changed frequently and vaccination must be given annually. Even when the vaccine is a very good match for the influenza strains that are circulating shortly after the vaccine is given, the vaccines are not particularly effective in people aged over 65 years, which is the major target group for vaccination against influenza.



▲ Adenovirus vector

▶ MVA vector

Viral vectored vaccines

My group has been using viral vectored vaccines to induce immune responses against internal regions of the influenza virus as these are not subject to frequent change. If we can induce a protective immune response against them, we can induce T cells that can recognise and kill virus-infected cells early on in the course of infection so that the virus can be prevented from spreading through the body before any illness occurs. We know that this happens when people have been infected by the influenza virus and then recover, but existing vaccines do not enhance the T cell response to influenza in adults.

In our first clinical trial, we demonstrated that we could achieve a significant boosting of T cell responses to conserved influenza antigens with a single dose of our vaccine, MVA-NP+M1. We went on to show that this vaccine is also highly immunogenic in older adults, and may be a better way of immunising older people who do not respond well to existing vaccines. In a proof-of-concept 'influenza challenge' study, in which healthy young volunteers were deliberately infected with influenza virus, we saw that fewer vaccinated than unvaccinated volunteers became ill with symptoms of influenza.

We have also found that if we give our influenza vaccine, MVA-NP+M1, at the same time as the licensed trivalent inactivated vaccine (TIV) which is normally given to adults, it not only boosts T cell responses to influenza but also increases the antibody response to the TIV vaccine. This is expected to considerably improve the efficacy of TIV in older adults, and we hope to conduct a much larger study of this approach starting in 2015.

Key publications:

1. Berthoud, TK, Hamill, M, Lillie, PJ, et al., *Potent CD8+ T-cell immunogenicity in humans of a novel heterosubtypic influenza A vaccine*, MVA-NP+M1. Clin Infect Dis, 2011. 52(1): p. 1-7.
2. Lillie, PJ, Berthoud, TK, Powell, TJ, et al., *Preliminary assessment of the efficacy of a T-cell-based influenza vaccine*, MVA-NP+M1, in humans. Clin Infect Dis, 2012. 55(1): p. 19-25.
3. Antrobus, RD, Coughlan, L, Berthoud, TK, et al., *Clinical assessment of a novel recombinant simian adenovirus ChAdOx1 as a vectored vaccine expressing conserved Influenza A antigens.* Mol Ther, 2014. 22(3): p. 668-74.

A novel viral vector vaccine with increased potency

Work on viral vectors at the Jenner Institute has led to the development of a new simian adenovirus vector ChAdOx1. We know that replication-deficient adenoviruses are potent vaccine vectors when tested in animals, but if we use a human adenovirus to make a vaccine vector to use in humans, the response is reduced because of naturally-acquired human immunity to the adenovirus vector. This problem is avoided if we use an adenovirus normally found in chimpanzees to make a vaccine vector. Following the initial development of ChAdOx1 in the lab, we introduced two conserved antigens from influenza and made a vaccine that has now been tested in clinical trials. As with MVA-NP+M1, the new vaccine boosts T cell responses to influenza and, when both vaccines are used one after the other, the response is even stronger. We are now continuing with a clinical trial using both novel vaccines with the aim of determining the optimum approach to vaccination.

Rift Valley Fever

Work led by George Warimwe using adenoviral vectors to vaccinate sheep, goats, and cattle against Rift Valley Fever virus is showing great promise. A single immunisation induces high titre antibodies, and the vaccine that is being developed could be used in humans as well as livestock – perhaps the ultimate example of a One Health vaccine. This vaccine programme is developing rapidly, with plans to vaccinate camels in the next few months, since they can be infected with Rift Valley Fever virus and have been implicated in spreading the virus following an outbreak.

TOMÁŠ HANKE
HIV-1 vaccine development

I completed my PhD at The University of St Andrews, UK. In 1994, I took up a post-doctoral position in the lab of Prof. Sir Andrew McMichael at the University of Oxford. With the establishment of the Medical Research Council (MRC) Human Immunology Unit in 1998, I started my own group and, five years later, obtained an MRC Career Scientist position. In 2011, my laboratory relocated to the Jenner Institute, where I lead the HIV-1 Vaccine Development Programme.

The HIV-1 vaccine development programme

In collaboration with other experts in the field, we explore novel approaches and emerging technologies to induce protective T cell and neutralising antibody responses. The vaccine development programme covers conception, construction and stepwise improvements of new vaccine candidates in an iterative process from mouse to non-human primate models, followed by clinical studies in humans.

Designing an effective vaccine against HIV-1 is far from straightforward. The HIV-1 virus is highly mutable and thus highly variable, and evolves to evade the adaptive arms of the immune system. Furthermore, during HIV-1 infection, immune responses are dominated by those targeting the most variable parts of proteins. These variable regions serve as decoys, which attract most of the attention of the immune response, but easily change under their selective pressure. Mutated, unrecognised viruses then rapidly overgrow the targeted strains and replace them.

Scientists have employed a range of innovative solutions to combat these challenges. After being initially ignored, the problem of variability was tackled by creating immunogen cocktails from different HIV-1 isolates or amino acid average sequences. Efforts to make use of the growing HIV-1 sequence database and the advent of increasing computing power has led Dr Bette Korber's team at the Los Alamos National Laboratory, USA, to develop mosaic proteins. As artificial proteins assembled from all HIV-1 sequence variants in the database, these immunogens are computed over every HIV-1 protein to maximise the perfect match by vaccines of all the potential killer T cell epitopes present in every circulating HIV-1 isolate.

We are studying the potential impact of vaccine-induced T cells targeting the most functionally conserved regions of the HIV-1 proteome. This approach should generate effectors that kill the virus-infected cells soon enough after transmission to slow HIV-1 replication and prevent damage to the immune system. In general, focusing both T cells and antibodies on functionally conserved regions is a very attractive strategy, and possibly the most effective method for tackling pathogen variability.

HIV-1 clinical trials

Successful vaccine development requires systematic and iterative clinical trials using humans. We have pioneered clinical tests of HIV-1 vaccines that focus T cell responses on the most conserved regions of the HIV-1 proteome. The first generation of the conserved T cell immunogen, delivered by a combination of plasmid DNA, simian (chimpanzee) adenovirus (ChAdV) and modified vaccinia Ankara (MVA) in trial HIV-CORE 002, demonstrated safety and highly promising immunogenicity in terms of the magnitude, persistence, breadth and functionality of vaccine-elicited T cell responses.

These promising initial observations are being incorporated into a broader programme that consists of six prophylactic and therapeutic trials of human adults in Europe and Africa, with the results set to emerge over the next one to two years. Recently, we collaborated with Dr Korber to design second generation conserved region vaccines. Based on the mosaic proteins designed to enhance the T cell epitope match with global HIV variants, these vaccines are currently being prepared for clinical tests. We aim to assess T cell induction by the second generation vaccines in a small first-in-man bridging trial in Oxford, recruiting healthy, HIV-1-uninfected humans. The data from the on-going programme and the bridging study will help define the future developmental path for the conserved region strategy.

Dual protection against HIV-1 and TB

According to the UNAIDS 2013 global report, over 700 children are newly infected with HIV-1 every day, with the majority acquiring the virus from their mothers. With only 57% access to appropriate anti-retroviral drugs in 2012, there is an urgent need for both effective HIV-1 vaccines that decrease infection rates in mothers, and paediatric vaccines that protect infants against breast milk HIV-1 transmission. In 2007, we worked to develop a dual vaccine to protect newborns against both TB and HIV-1 infections. We proposed that the insertion of an HIV-1-derived immunogen into the scheduled BCG vaccine for TB, delivered soon after birth, could provoke HIV-1-specific responses, and thus potentially decrease mother-to-child HIV-1 transmission through breastfeeding. In 2010, I led randomised clinical trials that involved administering a candidate HIV-1 vaccine to 20-week-old infants born to HIV-1-negative mothers in The Gambia, and HIV-1-positive mothers in Kenya. Promisingly, and similarly to the other published infant trials, the study demonstrated that it is feasible to test candidate HIV-1 vaccines in high-risk African infants. Furthermore, the results supported the use of MVA as a boosting vector within heterologous prime-boost vaccine strategies in the under-1-year age group.

Images: EDCTP

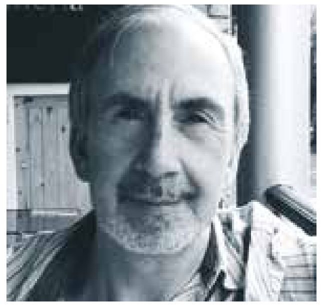
Key collaborators

Our key collaborators are: Prof. Lucy Dorrell, Prof. Sir Andrew McMichael and Dr Benedikt Kessler, University of Oxford; Prof. Walter Jaoko, University of Nairobi, Kenya; Dr Bette Korber, Los Alamos National Laboratory, USA; The International AIDS Vaccine Initiative; Dr Katie Flanagan, formerly MRC Laboratories, The Gambia; Prof. Grace John-Stewart, University of Washington, USA; Prof. Marie Reilly, Karolinska Institute, Sweden; Prof. Sir Mark Pepys, University College London; Prof. Christian Brander and Dr Beatriz Mothe, Irsicaixa AIDS Research Institute HIVACAT, Spain; Dr Sarah Fidler, Imperial College London and Dr Joan Joseph, Hospital Clinic Barcelona, Spain.

Key publications:

1. Hanke T. Conserved immunogens in prime-boost strategies for the next-generation HIV-1 vaccines. *Expert Opin.* Biol. Ther. 14: 601-616 (2014).
2. Borthwick B, Ahmed T, Ondondo B, Hayes P, Rose A, Ibrahimsa U, Hayton E-J, Black A, Bridgeman A, Rosario M, Hill AVS, Berrie E, Moyle S, Frahm N, Cox J, Colloca S, Nicosia A, Gilmour J, McMichael AJ, Dorrell L and Hanke T. Vaccine-elicited human T cells recognizing conserved protein regions inhibit HIV-1. *Mol Ther* 22:464-475 (2014).
3. Njuguna IN, Ambler G, Reilly M, Ondondo B, Kanyugo M, Lohman-Payne B, Gichuhi C, Borthwick N, Black A, Mehedi S-R, Maleche-Obimbo E, Chohan B, John-Stewart GC, Jaoko W and Hanke T. PedVacc 002: A phase I randomized clinical trial of MVA. HIVA vaccine administered to infants born to human immunodeficiency virus type 1-infected mothers in Nairobi. *Vaccine* 2014 Oct 7;32(44):5801-8.

GLYN HEWINSON
Bovine tuberculosis vaccine programme



I trained as a microbiologist at Bristol University and then at the University of Oxford. I lead the Bovine Tuberculosis (BTB) research programme at the Animal and Plant Health Agency overseeing the development of TB vaccines for both cattle and badgers. My interests range from the fundamental understanding of host and pathogen responses to TB infection, to the implementation of field trials for vaccines and diagnostic tests. I am a named OIE expert on bovine tuberculosis, a visiting professor at Imperial College London, Chair of the Acid Fast Club, section Editor of Tuberculosis and recently elected chair of the Global Research Alliance for Bovine Tuberculosis (GRABTB).

Development of TB vaccines for Cattle

Bovine TB is currently one of the greatest challenges that the farming industry faces in the UK, especially in the southwest of England and Wales. The most cost-effective control measure for infectious disease is vaccination, and used alongside existing bovine TB control measures, vaccination could reduce disease severity and prevalence. The development of vaccines for cattle forms part of the Government's comprehensive eradication strategy for bovine TB.

The development of an effective vaccination strategy for TB is compromised in humans and cattle by two major problems. The first is that the protection conferred by the only currently available vaccine, BCG, is variable at both the individual and population level and host responses to vaccination are unpredictable. Thus one arm of our vaccination programme is to exploit this variability in cattle to identify correlates of protective immunity and in doing so identify the underlying reasons for the variability in protective efficacy of BCG. The comparison of transcriptome and RNAseq profiles of vaccinated cattle that are protected from infection with those that are not protected is helping us to identify useful immune markers that predict the outcome of vaccination (for more details please see the section from my colleague Martin Vordermeier). Along with Adrian Hill and John Fazakerley, I am joint holder of the Wellcome Trust Strategic Award that supports the Transcriptomics Core Facility at the Jenner Institute and this facility helps underpin the collaborative work on TB between myself, Helen McShane and Martin Vordermeier.

Diagnosis of TB

The second problem that we face is that since BCG is not 100% effective, a diagnostic test is required to differentiate vaccinated from infected individuals (a so called DIVA test) so that disease control programmes may continue in the face of vaccination. Unfortunately BCG vaccination interferes with the statutory diagnostic skin (tuberculin or PPD) test. This problem has been, to a certain extent, alleviated for humans in prosperous countries by the development of blood-based DIVA diagnostic tests that predict the outcome of vaccination, but these are expensive and inappropriate for the developing world and as cost-effective livestock tests. Cost benefit analysis of cattle vaccination suggests that the optimal combination of vaccine and diagnostic test would be either a vaccine with an associated skin test DIVA that could replace the existing comparative tuberculin skin test, or a vaccine that does not sensitise vaccinated animals to the current tuberculin skin test. At present our research programme aims to addresses both these problems.

Key publications:

1. Dean G, Whelan A, Clifford D, Salguero FJ, Xing Z, Gilbert S, McShane H, Hewinson RG, Vordermeier M, Villarreal-Ramos B. *Comparison of the immunogenicity and protection against bovine tuberculosis following immunization by BCG-priming and boosting with adenovirus or protein based vaccines.* Vaccine. 2014 Mar 5;32(11):1304-10.
2. Whelan AO, Coad M, Upadhyay BL, Clifford DJ, Hewinson RG, Vordermeier HM. *Lack of correlation between BCG-induced tuberculin skin test sensitisation and protective immunity in cattle.* Vaccine. 2011 Jul 26;29(33):5453-8.
3. Buddle BM, Wedlock DN, Denis M, Vordermeier HM, Hewinson RG. *Update on vaccination of cattle and wildlife populations against tuberculosis.* Vet Microbiol. 2011 Jul 5;151(1-2):14-22.

Testing vaccine efficacy in field trials

One of the difficulties we encounter in developing vaccines against bovine tuberculosis is deciding when vaccines are ready to enter clinical field trials. The stringent challenge model used to assess the efficacy of TB vaccines in cattle consists of an endobronchial challenge with a single dose of approximately 1,000 cfu of *M. bovis* grown in artificial culture media. In the field, vaccination must protect against natural challenge comprising of multiple exposures to *M. bovis* that may express different antigens than those expressed in artificial culture of varying dose over the lifetime of the animal. For this reason we have developed a natural transmission model for bovine TB that allows us to test vaccine efficacy in a natural transmission setting. The recent award of a 5 year grant funded under the ZELS (Zoonoses and Emerging Livestock Systems) research initiative (www.bbsrc.ac.uk/funding/opportunities/2012/zoonoses-emerging-livestock-systems.aspx) will allow us to maintain and develop this model.

ADRIAN HILL
Pre-erythrocytic malaria

I trained initially at Trinity College Dublin, qualified in Medicine from Oxford in 1982 and was awarded a DPhil for population genetic studies of the thalassaemias in Oceania in 1986. In 2005, I was appointed Director of the Jenner Institute, an initiative aimed at accelerating public sector vaccine development for a variety of infectious diseases, spanning human and veterinary vaccinology. I am also Professor of Human Genetics at the University of Oxford, a Fellow of the UK Academy of Medical Sciences and of the Royal College of Physicians, and both a National Institute of Health Research and Wellcome Trust Senior Investigator.

A vaccine for pre-erythrocytic malaria

My group's work has focused on the development of a vaccine against *Plasmodium falciparum* malaria, specifically against the early sporozoite and liver stages of this parasite. We designed and developed vaccine candidates that, uniquely, show efficacy in clinical trials associated with the induction of cellular immunity, in particular CD8+ T cells. This has been achieved by the iterative development of so-called heterologous prime-boost regimes, where one viral vector is used to prime the immune response and another as a booster immunisation. This leads to the induction of exceptional levels of CD8+ T cells in animals and humans, and has demonstrated high levels of immunogenicity and protection of human vaccines against infection using a liver-stage malarial protein, known as TRAP, expressed from particular recombinant viral vectors. These viruses act as highly efficient delivery mechanisms to target genes encoding malarial protein(s) into human cells, via natural cellular infection pathways; the foreign protein, in this case *P. falciparum* TRAP, is expressed inside the infected cells leading to the generation of a powerful cellular immune response. The optimal immunisation regime uses adenoviruses as priming agents and MVA (modified Vaccinia Ankara) as a boosting agent, and we discovered that simian adenovirus vectors are excellent priming vaccines clinically, probably as there is no pre-existing immunity to these chimpanzee vectors in humans, thereby avoiding any neutralisation of the adenovirus vaccine.

Partial efficacy with the *P. falciparum* TRAP-vectored vaccines was initially demonstrated through the use of a standardised controlled human malaria infection model. This entails volunteers agreeing not just to be immunised with new vaccines but to undergo a controlled infection with mosquito bites to allow the vaccine's efficacy to be assessed. Oxford is one of the leading centres globally for this "challenge model" with over 20 such studies conducted.

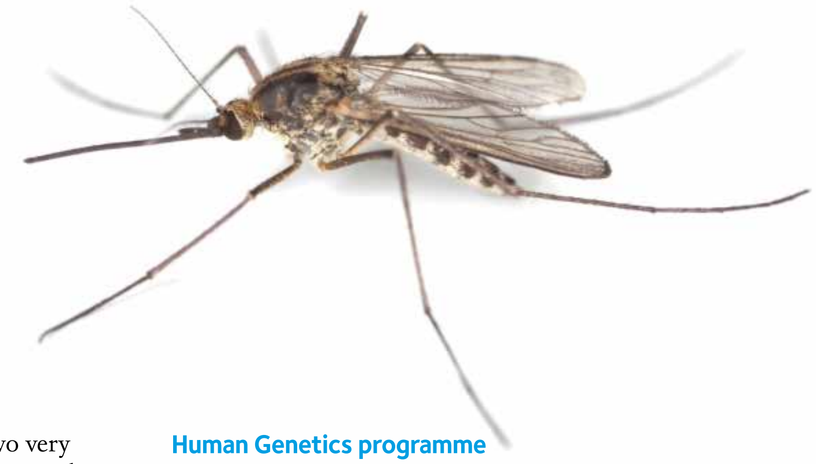
In the last 3 years, African field trials in adults, children and infants have been completed using Chimpanzee Adenovirus (ChAd) strain 63 encoding the ME-TRAP antigen as an initial priming vaccination, and MVA-ME-TRAP as the secondary boost. Data has demonstrated good safety and immunogenicity profiles of this vaccination regime for malaria in all populations tested, now totalling over 1000 vaccinees. In a recent efficacy trial in Kenyan adults, 67% efficacy was found against malaria infection in a short two month trial using new PCR-based monitoring techniques.

New malaria vaccine approaches

Complete protection of humans against infection has yet to be achieved, so we have taken a number of approaches to increase the effectiveness of malaria vaccines. We have generated new simian adenovirus vectors (called ChAdOx1 and ChAdOx2), and also improved the effectiveness of existing adenovirus and MVA viral vectors by the addition of a 'molecular adjuvant' related to the CD74 invariant chain, which increases the presentation of foreign proteins to the immune system leading to an enhanced immune response. This work was funded by a major grant from the Bill and Melinda Gates Foundation, addressing one of the Grand Challenges in Global Health. We have carried out an extensive screen for new liver-stage antigens (proteins) which would either make effective vaccines on their own, or could be combined with other antigens, including TRAP. This screen has identified two very promising candidates, known as LSA1 and LSAP2, which confer complete protection against infection in a novel rodent model for malaria, which was developed in collaboration with Leiden University.

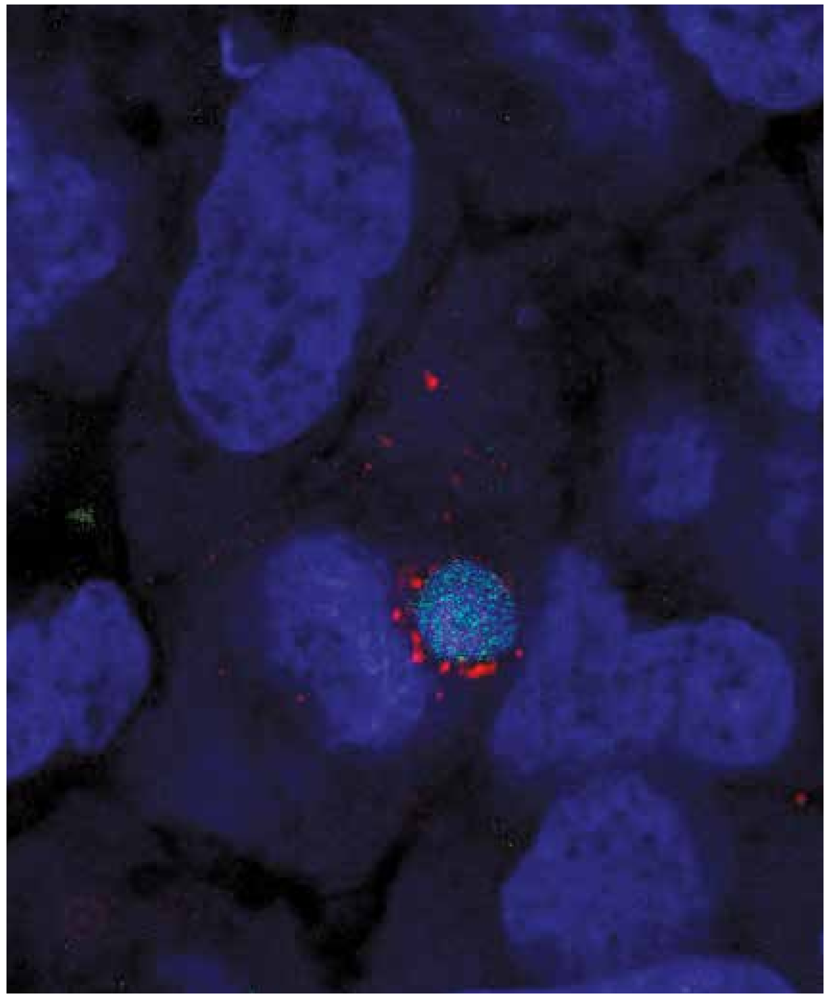
As a complementary approach to virally vectored vaccines, we have developed a virus-like-particle vaccine by fusing a segment of the *P. falciparum* circumsporozoite protein to the Hepatitis B surface antigen protein, which spontaneously forms particles containing numerous copies of the protein and is used as a vaccine against the HepB virus. This malaria vaccine, called R21, is similar to the RTS,S vaccine produced by GSK which protects up to 50% of individuals in a vaccinated population. One hypothesis being tested is that R21 will generate a greater malaria-specific immune response as it contains a higher proportion of the circumsporozoite protein relative to hepatitis protein.

It has proved extremely challenging to produce a completely effective vaccine against malaria, as *Plasmodium* is a complex parasite with several different life stages in mosquito and human hosts; many of its genes are highly polymorphic and there is redundancy in many of its functions, meaning that if one protein is targeted by a vaccine, others can take its place. It is therefore possible that in order to protect 100% of a population we will need to combine different vaccines, probably against different stages of the parasite's life cycle. We are coordinating a European consortium (MultiMalVax), which has received funding to test a combination of vaccines, either viral vectors expressing antigens from different life stages, or viral vectors in combination with the R21 virus-like-particle. Very encouraging clinical data has already been obtained from a challenge trial in UK adults testing this approach, combining GSK's RTS,S vaccine and viral vectors containing ME-TRAP.



Human Genetics programme

Our human genetics programme studies genetic susceptibility to a range of bacterial infectious diseases and also genetic factors impacting on vaccine responses. The group, located at the Wellcome Trust Centre for Human Genetics on the Old Road Campus, has studied genetic susceptibility to infectious diseases in populations from five continents with the largest studies focused on sub-Saharan Africa. We have a particular interest in major bacterial diseases in Africa such as tuberculosis, bacteraemia and non-typhoidal Salmonella, but also study sepsis, pneumococcal disease and respiratory infections in Europeans, and Group A streptococcal infections in Melanesia. The group uses candidate gene analyses and genome-wide association studies, including newer exomic approaches, to map and identify susceptibility genes.



▶ *P. Falciparum* infected liver cell with anti-parasite antibodies stained red

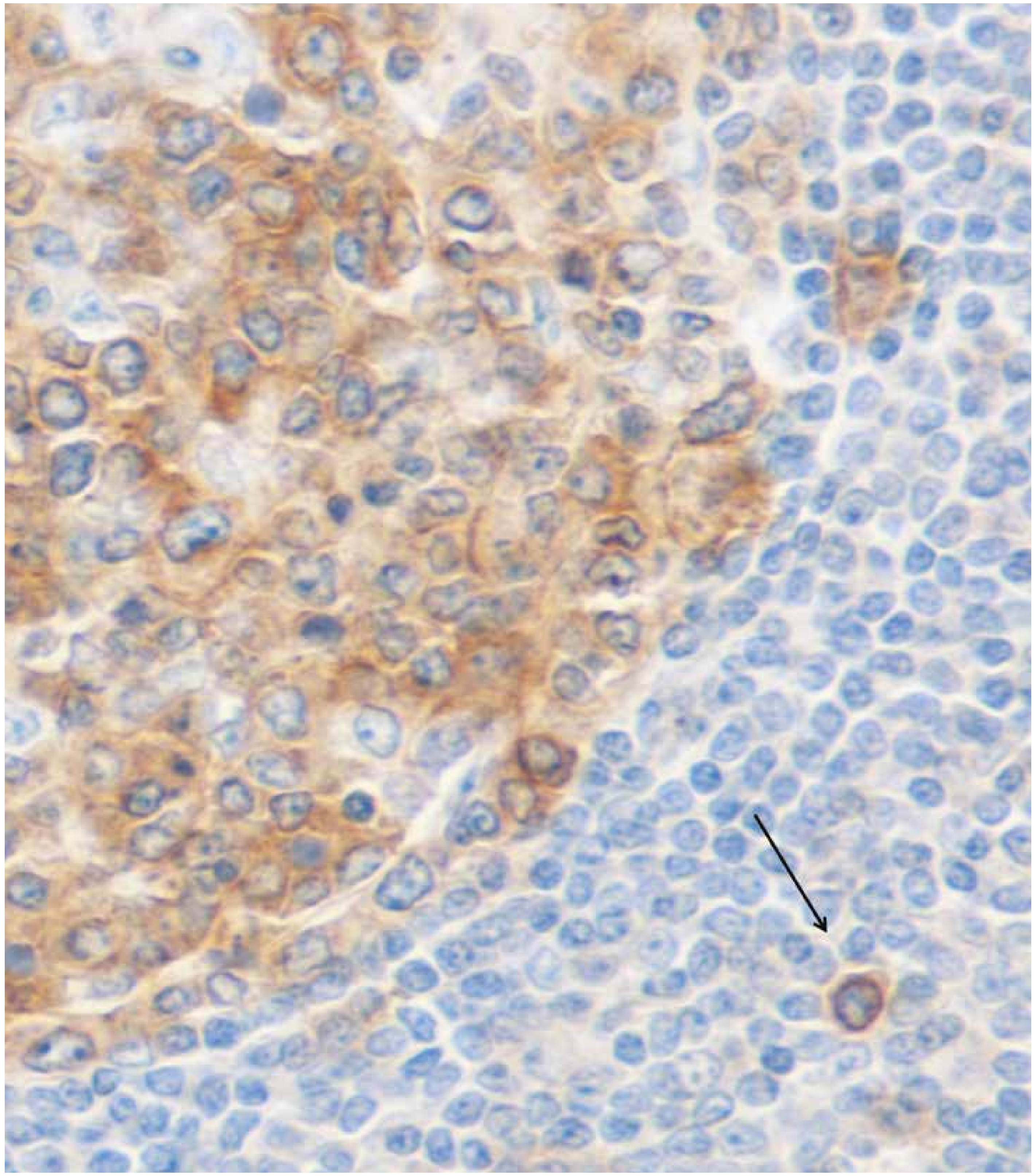
Key publications:

1. C. Ogwang, D. Kimani, N. J. Edwards, et al. (2015). Prime-boost vaccination with chimpanzee adenovirus and modified vaccinia Ankara encoding TRAP provides partial protection against Plasmodium falciparum infection in Kenyan adults. Sci Transl Med 7, 286re5.
2. Hodgson SH, Ewer KJ, Bliss CM, et al. (2015). Evaluation of the efficacy of ChAd63-MVA vectored vaccines expressing circumsporozoite protein and ME-TRAP against controlled human malaria infection in malaria-naive individuals. J Infect Dis Apr 1;211(7):1076-86.
3. Ewer KJ, O'Hara GA, Duncan CJ, et al. (2013). Protective CD8+ T-cell immunity to human malaria induced by chimpanzee adenovirus-MVA immunisation. Nat Commun; 4:2836.

Key publications:

1. Bolinger B, Sims S, O'Hara G, de Lara C, Tchilian E, Firner S, Engeler D, Ludewig B, Klenerman P. 2013 A new model for CD8+ T cell memory inflation based upon a recombinant adenoviral vector. J Immunol. 190, 4162-74.
2. Fergusson JR, Smith KE, Fleming VM, Rajoriya N, Newell EW, Simmons R, Marchi E, Björkander S, Kang YH, Swadling L, Kurioka A, Sahgal N, Lockstone H, Baban D, Freeman GJ, Sverremark-Ekström E, Davis MM, Davenport MP, Venturi V, Ussher JE, Willberg CB, Klenerman P. 2014. CD161 defines a transcriptional and functional phenotype across distinct human T cell lineages. Cell Rep. 9, 1075-88.
3. Barnes E, Folgori A, Capone S, Swadling L, Aston S, Kurioka A, Meyer J, Huddart R, Smith K, Townsend R, Brown A, Antrobus R, Ammendola V, Naddeo M, O'Hara G, Willberg C, Harrison A, Grazioli F, Esposito ML, Siani L, Traboni C, Oo Y, Adams D, Hill A, Colloca S, Nicosia A, Cortese R,Klenerman P. 2012. Novel adenovirus-based vaccines induce broad and sustained T cell responses to HCV in man. Sci Transl Med., 4, 115ra1.

▼ Immunohistochemical analysis of human tonsil showing germinal centre formation (Image: Alba Llibre and Chris Willberg)



PAUL KLENERMAN

Vaccines for Hepatitis C Virus and Respiratory Syncytial Virus

I trained in infectious diseases in Cambridge, Oxford and London. My PhD, on the human immunodeficiency virus (HIV), was gained from the University of Oxford with Andrew McMichael and Rodney Phillips, after which I moved to work with Rolf Zinkernagel and Hans Hengartner in Zurich on models of persistent virus infection. Since 2000, I have held a Wellcome Trust Senior Clinical Fellowship in Oxford.

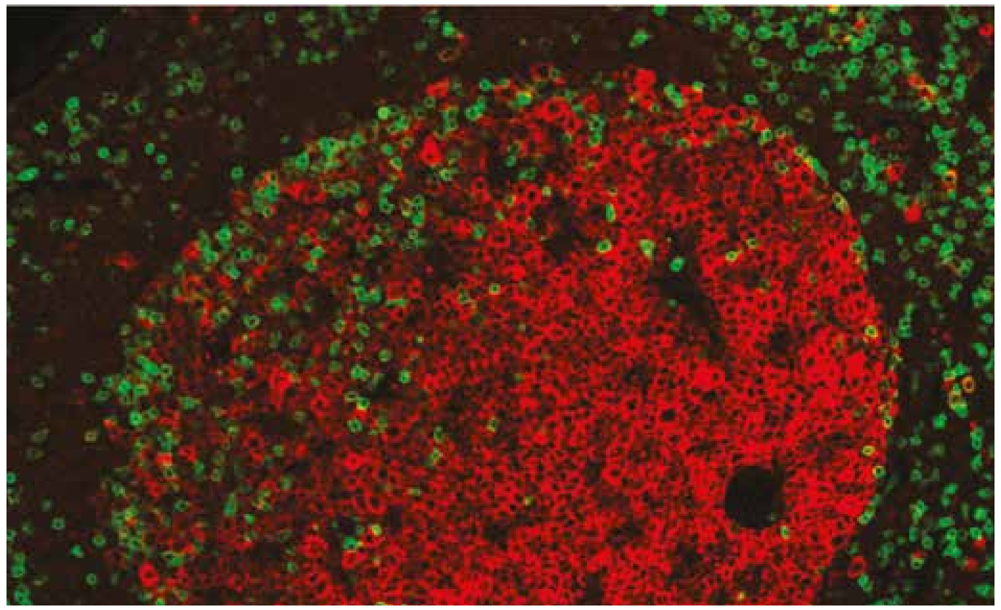
My group has been involved in studies of T cell responses to viruses, and our work over the last 3 years has focused on two areas – hepatitis C virus (HCV) and respiratory syncytial virus (RSV).

Hepatitis C virus

HCV is a major cause of liver disease globally and no vaccine is currently licensed. Some HCV-infected people clear the virus spontaneously, i.e. through effective innate and adaptive immunity. The relevant immunity appears to be mediated by T cells, and by generating a vaccine that induces T cells it has been shown in proof-of-concept preclinical studies that this can accelerate immune control. We collaborated with Okairos to test T cell vaccines for HCV. The first of these trials (HCV001) using two different adenoviral constructs, one based on a newly described adenovirus (ChAd3), showed good immunogenicity. Ellie Barnes has taken this work forward in further trials using these vectors as immunotherapy (in patients already infected with HCV) and also with an improved boosting regimen with a modified vaccinia virus (MVA) vaccine, in HCV003. This latter strategy appears to produce the highest levels of immune response and has been taken into Phase II trials by Okairos in the US.

Respiratory syncytial virus

RSV is a major cause of respiratory disease in infants and is increasingly recognised as a problem in the elderly, potentially on a scale similar to influenza. No vaccine exists, partly as a result of failed vaccine trials in the past, where there was enhanced immune-mediated pathology in infants. Improved immunogenicity for B and T cells based on adenoviral and MVA vectors is being assessed in a Phase I trial with Andrew Pollard's group. This trial has been completed in healthy young adults and it is hoped that it will soon move on to paediatric populations, as well as older adults.



▲ Germinal centre analysis by immunofluoresence showing B cells (red) and follicular T cells (green) (Image: Alba Llibre and Chris Willberg)

MARTIN MAIDEN
Understanding and controlling meningococcus infection

I originally trained as a microbiologist at the University of Reading, followed by a molecular genetics and biochemistry PhD at the University of Cambridge, after which I worked at the National Institute for Biological Standardisation and control for 9 years on various aspects of bacterial vaccines. I moved to the University of Oxford as a Wellcome Trust Senior Fellow in 1997 and, since 2004, have been Professor of Molecular Epidemiology and a Fellow of Hertford College. In 2010, I was elected a Fellow of the Royal College of Pathologists.

Vaccines against meningococcus

We are interested in the design and implementation of vaccines against the encapsulated bacterium *Neisseria meningitidis*, otherwise known as the meningococcus, a much feared cause of both meningitis and septicaemia worldwide. We use an explicitly multidisciplinary and collaborative approach, based on understanding the ecology and evolution of this enigmatic pathogen which, paradoxically for such a notorious cause of severe disease, is found to harmlessly colonise the upper respiratory tract of many people.

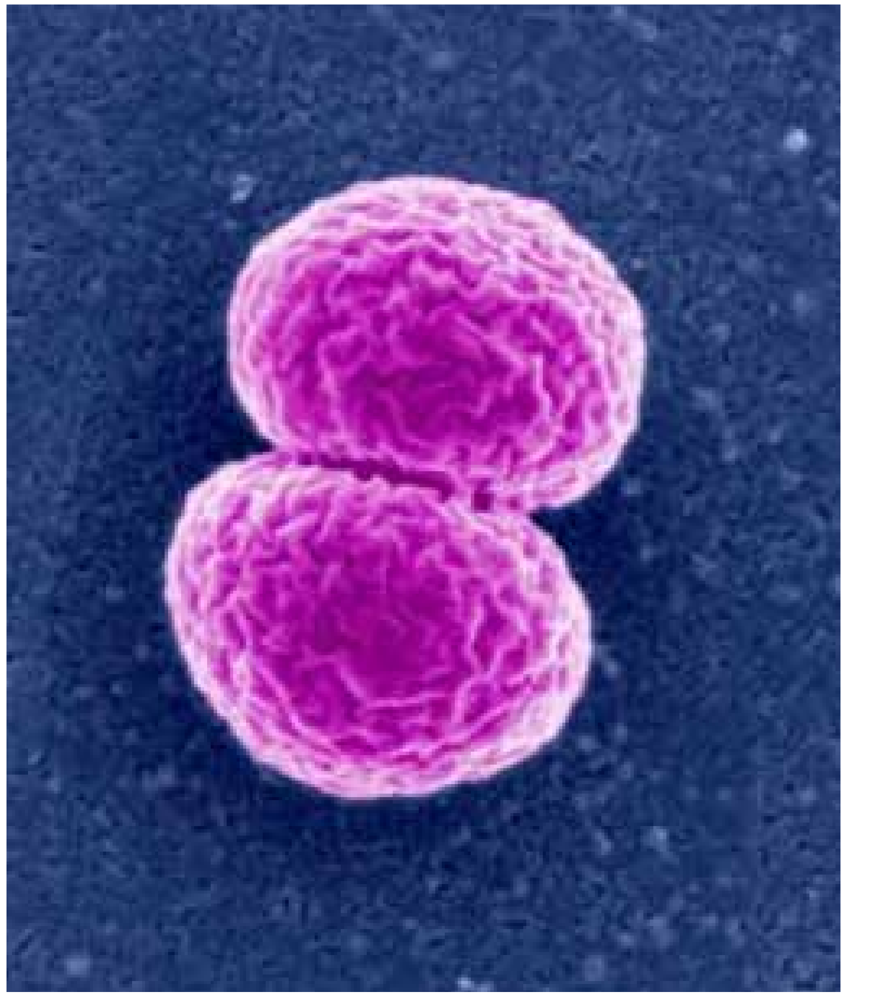
Disease is usually caused by only 6 of the 12 capsular 'groups', the genetics of which we recently defined at the genomic level. When combined with protein antigens to create protein-polysaccharide conjugates, these form the basis of highly effective vaccines and we made a major contribution to the field by helping to demonstrate that this is due to their ability to elicit 'herd immunity' (also called herd protection or population immunity) in both Europe and Africa. Unfortunately, a variety of reasons have conspired to prevent the development of such conjugate polysaccharide vaccines against the serogroup B meningococcus, which has led to various attempts to generate vaccines based on the highly variable surface proteins of the meningococcus. We have worked to catalogue and understand the diversity of these antigens for a quarter of a century, looking into means of exploiting structured and stable repertoires evident in this diversity in vaccine design. Our latest work in this area includes working on the Meningitis Research Foundation 'Meningococcus Genome Library' (MRF-MGL)

▼ The Maiden lab

Understanding meningococcal diversity

We are involved in a ground-breaking initiative to make the latest genomic data on meningococcal genomes from England and Wales available on-line in near real time (http://www.meningitis.org/current-projects/genome). We also work to curate and maintain catalogues of diversity in vaccines, such as the newly licenced Novartis vaccine Bexsero© (http://PubMLST.org/neisseria). We have developed easy to use, publicly available tools for the resolution of epidemics caused by highly variable pathogens such as the meningococcus. Our own approach to the development of a novel meningitis vaccine, MenPF, is based on two major outer membrane proteins, PorA and FetA, and comprises a carefully composed combination of variants of these proteins. MenPF1, a first generation realisation of this concept, has recently completed a successful phase I trial in collaboration with Prof. Ian Feavers (National Institute for Biological Standards and Control), Prof. Jeremy Derrick (University of Manchester) and Prof. Andrew Pollard (Department of Paediatrics, Oxford). At the time of writing, we are embarking on a major survey of meningococcal carriage in the UK (UKMenCar4) that will sample 18,000 teenagers to generate a large dataset of carried meningococci collected at the present time, a period of very low meningococcal disease incidence. This data will complement the disease isolate data from the MRF-MGL and the carriage surveys conducted by us at the time of the introduction of the meningococcal C conjugate polysaccharides 15 years ago, a period of high meningococcal disease incidence. The data generated will provide unparalleled opportunities in understanding the highly variable and inherently unpredictable epidemiology of meningococcal disease, and hopefully lead to novel approaches to vaccination.

▼ *N. meningitidis* bacteria

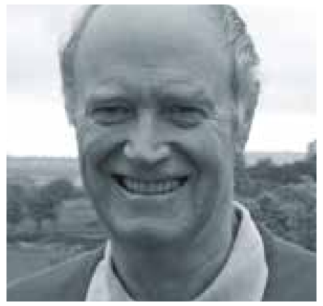


Key publications:

1. Maiden, M. C. J., Bygraves, J. A., Feil, E. et al. (1998). Multilocus sequence typing: a portable approach to the identification of clones within populations of pathogenic microorganisms. *Proc Natl Acad Sci USA* 95, 3140-3145.
2. Maiden, M. C., Ibarz-Pavon, A. B., Urwin, R. et al. (2008). Impact of meningococcal serogroup C conjugate vaccines on carriage and herd immunity. *J Infect Dis* 197, 737-743.
3. Daugla, D., Gami, J., Gamougam, K. et al. (2013). Effect of a serogroup A meningococcal conjugate vaccine (PsA-TT) on serogroup A meningococcal meningitis and carriage in Chad: a community trial. *Lancet* 383, 40-47.

SIR ANDREW McMICHAEL

HIV vaccine immunogen discovery



I was Director of the MRC Human Immunology Unit from 1998–2010, Director of the Weatherall Institute of Molecular Medicine from 2000–2012 and I am currently Professor of Molecular Medicine. I have worked on T cell immunity to viruses, particularly influenza and HIV, showing how HLA molecules present influenza virus and HIV peptide epitopes and how HIV-1 escapes T cell recognition. I am very active in HIV-1 vaccine development and have worked with the Jenner Institute since it moved to Oxford.

My team works closely with Dr Persephone Borrow, and is supported by the NIH Center for HIV AIDS Vaccine Immunology – Immunogen Discovery (CHAVI-ID) and by the Medical Research Council. We are working on the design of HIV-1 specific vaccines that stimulate T cell and innate Immunity.

We have four main projects:

1 Identification of ligands for the stimulatory killer cell immunoglobulin-like receptors (KIR) on natural killer (NK) cells and T cells. The ligand for KIR3DS1 is elusive. We have expressed soluble KIR3DS1 protein and are searching for its ligands using HLA (human leukocyte antigen) arrays, peptide-HLA tetramers, virus infected cells and yeast cells expressing HLA class I molecules with random peptides. So far no ligand has been identified. It is possible that there is no specific ligand in most cells, but that NK cells bearing KIR3DS1 are slightly more activated than those bearing the inhibitory allelic forms (KIR3DL1).

2 Investigating the epitope specificity of HIV-1 envelope-specific CD4 T cells. We have shown that HIV-1 unexposed and uninfected donors have naïve and memory T cells in their blood that are HIV-1-specific. We are exploring the hypothesis that the latter are primed by cross-reactive antigens, including bacteria of the gut and skin microbiome.

3 Optimisation of a conserved vaccine to stimulate cytotoxic CD8 T cells that are specific for conserved epitopes of HIV-1. In collaboration with Tomáš Hanke (Jenner Institute) and Bette Korber (Los Alamos National Laboratory), we have designed a second generation conserved region HIV-1 vaccine that is a two stranded mosaic. This has better coverage of HIV-1 variability than the HIVconsv vaccine, which has shown excellent immunogenicity in a phase one trial. The new vaccine perfectly matches more than 80% of all conserved nonamer epitopes present in all the major clades of HIV-1. This vaccine is currently in preclinical development and will be used for prophylactic and therapeutic immunisations. It should enable the recipients to make T cell responses that are much less likely to select virus escape mutants than the natural primary T cell responses in acute HIV-1 infection.

4 Searching for HLA class II and HLA-E-restricted HIV-1-specific CD8 T cells. These T cells have been shown by Picker et al. to be associated with T cell responses that can eradicate Simian Immunodeficiency Virus infection in rhesus monkeys. If these unusual T cells can be shown to exist in humans, vaccines could be designed to stimulate them.

Our group, together with that of Dr Persephone Borrow in Oxford, leads the T cell and innate cell programmes of the CHAVI-ID consortium, under the overall direction of Dr Bart Haynes at Duke University.

Key publications:

1. Campion, S.L., T.M. Brodie, W. Fischer, B.T. Korber, A. Rossetti, N. Goonetilleke, A.J. McMichael, and F. Sallusto. 2014. Proteome-wide analysis of HIV-specific naive and memory CD4+ T cells in unexposed blood donors. *The Journal of Experimental Medicine* 211:1273-1280.
2. 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, C.C. B, 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. *The Journal of Clinical Investigation* 123:380-393.
3. Wilkinson, T.M., C.K. Li, C.S. Chui, A.K. Huang, M. Perkins, J.C. Liebner, R. Lambkin-Williams, A. Gilbert, J. Oxford, B. Nicholas, K.J. Staples, T. Dong, D.C. Douek, A.J. McMichael, and X.N. Xu. 2012. Preexisting influenza-specific CD4+ T cells correlate with disease protection against influenza challenge in humans. *Nature Medicine* 18:274-280.

HELEN McSHANE
Tuberculosis vaccine programme

I have lead a TB vaccine research group at the University of Oxford since 2001. My research interests include TB immunology, preclinical animal models, translational clinical trials, human mycobacterial challenge models and mucosal immunisation. I have published over 100 research articles and have an H-index of 30. I was appointed Professor of Vaccinology at the University of Oxford in 2010. I am a member of the University Council, the Wellcome Trust Clinical Interview Committee and the GLOBVAC Board. I am also an honorary consultant physician in HIV/GU medicine, and the Academic Foundation Programme lead for academic junior doctor supervision.

▼ TB Group

Tuberculosis (TB), a disease caused by *Mycobacterium tuberculosis* (*M.tb*), has been around since the Pharaohs, and remains a very significant cause of disease and death throughout the world in the 21st Century. In 2012, there were 8.6 million new cases of TB and 1.3 million deaths. The emergence of drug resistant strains of *M.tb* and the geographical overlap with the HIV epidemic have compounded the challenges facing our ability to control TB worldwide, and there is an urgent need for improved tools for TB control. The most cost-effective way to control any infectious disease epidemic is with an effective vaccine. The only licensed vaccine against TB is an attenuated strain of *Mycobacterium bovis*, Bacille Calmette Guerin (BCG). When administered at birth, BCG confers consistent and reproducible protection against disseminated disease, particularly TB meningitis, in the first ten years of life. However, the protection conferred against lung disease is much more variable and is lowest in TB high burden countries. We therefore need a more effective vaccine.

Towards an improved TB vaccine

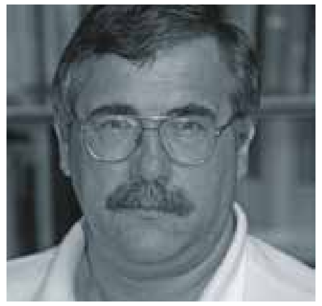
Strategies to develop an improved TB vaccine regimen include replacing BCG with a recombinant strain of BCG, or attenuated strain of *M.tb*; and/or developing a subunit booster vaccine, where only one or a few proteins from *M.tb* are used, to be administered after BCG either in infancy or in adolescence. I lead a research group developing subunit booster vaccines. One of the vaccines that we developed was the first new TB vaccine to enter into clinical trials, MVA85A, a recombinant strain of modified vaccinia Ankara expressing the mycobacterial antigen 85A. This vaccine has been evaluated in many phase I and IIa clinical trials in the UK and several countries in Africa, and was the first vaccine to enter into phase IIb efficacy testing in BCG-vaccinated South African infants in 2009. An efficacy trial in HIV-infected adults is ongoing. Current work in the group includes identifying methods of optimising the immunogenicity of new TB vaccines. One promising strategy is to administer the vaccine directly into the airways, which is the route by which M.tb enters the body. Data from our first phase I study using this route are very promising, and we have just commenced our second clinical trial to evaluate this route of immunisation further. Other ongoing trials include combination studies where recombinant adenoviral vectors, which are potent at inducing CD8+ T cells, are combined with MVA vectors, which are potent at inducing CD4+ T cells. Current opinion is that an optimal new TB vaccine would induce both T cell subsets. Other areas of work include developing a human mycobacterial challenge model with which to test new vaccine candidates, and new methods of immuno-monitoring in TB vaccine trials including functional mycobacterial growth inhibition assays. Ongoing overseas trials in Uganda will evaluate the effect of helminth co-infection on TB vaccine immunogenicity, and in South Africa will evaluate safety of new TB vaccines in BCG-naïve infants.

Key publications:

1. Satti I, Meyer J, Harris SA, Manjaly-Thomas ZR, Griffiths K, Antrobus RD, Rowland R, Lopez Ramon R, Smith M, Sheehan S, Bettinson H, McShane H. Safety and immunogenicity of a candidate TB vaccine, MVA85A, delivered by aerosol in BCG-vaccinated healthy adults. Lancet Infect Dis. 2014 Oct;14(10):939-46.
2. Tameris MD, Hatherill M, Landry BS, Scriba TJ, Snowden MA, Lockhart S, Shea JE, McClain JB, Hussey GD, Hanekom WA, Mahomed H, McShane H; MVA85A 020 Trial Study Team. Safety and efficacy of MVA85A, a new tuberculosis vaccine, in infants previously vaccinated with BCG: a randomised, placebo-controlled phase 2b trial. Lancet. 2013 Mar 23;381(9871):1021-8.
3. McShane H, Pathan AA, Sander CR, Keating SM, Gilbert SC, Huygen K, Fletcher HA, Hill AVSH. Recombinant modified vaccinia virus Ankara expressing antigen 85A boosts BCG primed and naturally acquired anti-mycobacterial immunity in humans. Nature Medicine 2004. 10(11):1240-4.

PETER MERTENS

Bluetongue and African horse sickness viruses



I am Head of the Vector-borne Viral Diseases Programme and a research leader in the Arbovirus Molecular Research Group at the Pirbright Institute, where I have worked for 33 years. My major research interests concern the identification, structure and replication of the orbiviruses, as well as the development of diagnostic assays and vaccines against them, particularly Bluetongue and African horse sickness viruses (BTV and AHSV). I am a visiting Professor at the University of Glasgow and at the University of Minas Gerais, Belo Horizonte, in Brazil. I am also an OIE (World Organisation for Animal Health) expert on BTV.

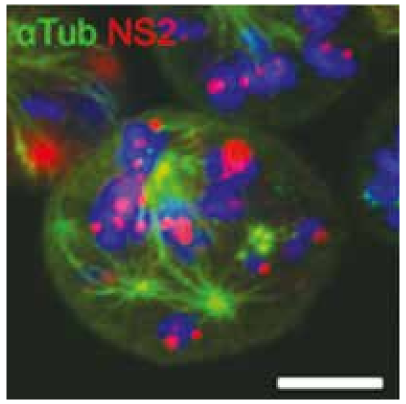
Phylogenetic studies of Bluetongue virus (BTV) and related orbiviruses

The Arbovirus Molecular Research Group has established, continues to maintain and is expanding a reference collection of bluetongue and other related orbivirus isolates from around the world (http://www.reoviridae.org/dsRNA_virus_proteins/ReoID/virus-nos-by-country.htm). This has provided a basis for full genome sequencing studies and phylogenetic analyses that have revealed the extent of serological and geographic variation within the Bluetongue virus genome and antigens. The collection has provided virus isolates for other research groups, and vaccine production companies.

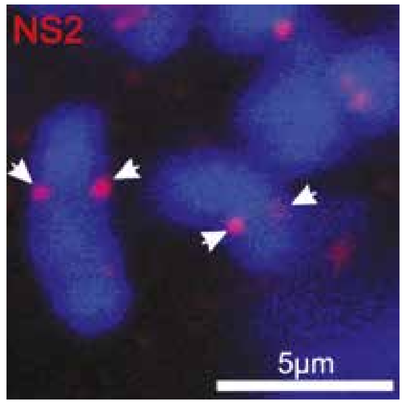
These sequence analyses have allowed us to develop and update a suite of novel diagnostic and typing assays that are more sensitive, more rapid and more reliable than the conventional serological assays, and which now represent the primary basis for Bluetongue virus serotype detection and identification around the world. As part of these studies, we actively track the movement and can identify the origins of individual virus lineages that threaten or emerge in Europe or elsewhere, showing that new strains of the virus have entered Europe (usually in the Mediterranean region) every year since 1998. This database has played a vital role in the identification of two novel serotypes of BTV (BTV-25 from Switzerland and BTV-26 from Kuwait). We have also recently established reverse genetics technologies for Bluetongue viruses that have allowed us to identify the individual viral genes of BTV-26 that restrict its infection or replication in cells of *Culicoides* vector species (biting midges).

In 2014, a novel virulent strain of BTV-4 was identified that emerged in Greece and Bulgaria, causing severe disease in local breeds of sheep. Full genome analyses showed that this virus is related to earlier strains that were circulating in the eastern Mediterranean region, particularly in North Africa. Genome segment exchange / re-assortment has generated a novel combination of the ten viral genes, potentially leading to its enhanced transmission and virulence characteristics.

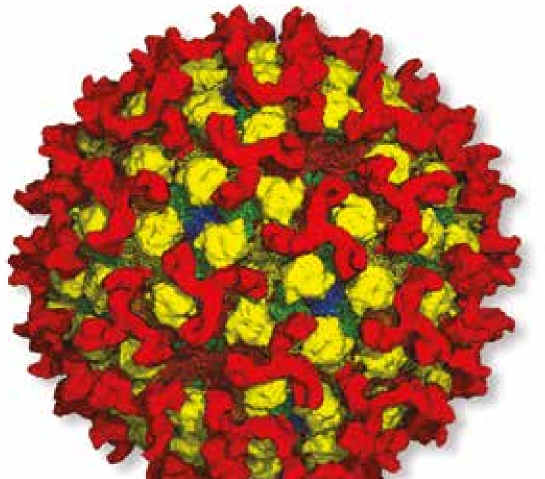
▼ Mitotic BHK-21 cells infected with Bluetongue virus type 16 had multiple, disorganised and asymmetric spindles (alpha tubulin labelling in green) that were disassociated from the condensed chromosomes (blue)



▼ Non-structural protein NS2 (red / arrows) was observed associated with the condensed chromosomes (blue) in locations suggestive of the kinetochores (Shaw et al 2013)



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



Vaccine development for BTV and AHSV

Studies of BTV and AHSV outer capsid protein VP2 (which is involved in cell attachment and interaction with neutralising antibodies) expressed by bacteria, plants, baculoviruses or modified Vaccinia Ankara have led to the development of subunit vaccine candidates. Unlike the previous live or inactivated vaccines, these are compatible with assays to distinguish vaccinated from infected animals (DIVA compatible). In particular, the modified Vaccinia Ankara strains expressing VP2 from different AHSV serotypes appear to be effective vaccine candidates.

Intracellular studies of BTV replication have shown that infection can cause cell cycle arrest in mammalian cells (BHK 21 cells), linked to the disruption of spindle formation during mitosis. Fluorescence microscopy studies have implicated BTV protein NS2 in this mechanism, and may provide a partial explanation for the anti-tumour activity previously reported for BTV.

Other orbiviruses

We have extended our full genome sequencing studies to include all of the 22 known *Orbivirus* species, including several other significant pathogens of livestock (such as palyam viruses, equine encephalosis virus, Peruvian horse sickness virus and epizootic haemorrhagic disease viruses). These studies have not only provided information concerning potential protective antigens against these viruses, but also provide a basis for virus identification and diagnostic assay development, and have identified seven additional species of *Orbivirus*.

▼ *Culicoides imicola*, the most common biting insect that transmits AHSV. Image: Steven Archibald, Pirbright Institute

Key publications:

1. Andrew E Shaw, Anke Brüning-Richardson, Ewan E Morrison, Jacquelyn Bond, Jennifer Simpson, Natalie Ross-Smith, Oya Alpar, Peter P.C. Mertens and Paul Monaghan (2013) Bluetongue virus infection induces aberrant mitosis in mammalian cells. Virol J. 2013 Oct 28;10(1):319.
2. Sushila Maan, Narender S. Maan, Kyriaki Nomikou, Eva Veronesi, Katarzyna Bachanek-Bankowska, Manjunatha N. Belaganahalli, Houssam Attoui and Peter P.C. Mertens (2011) Complete genome characterisation of a novel 26th bluetongue virus serotype from Kuwait. PLoS ONE 6(10): e26147.
3. Maan N.S., Maan, S., Johnson D.J., Ostlund, E.N., Nomikou, K., & Mertens P.P.C (2012). Identification and differentiation of the twenty six Bluetongue virus serotypes by RT–PCR amplification of the serotype-specific genome segment 2. PLoS One. 2012;7(2):e32601.

RICHARD MOXON
Meningococcus and *Haemophilus influenzae*

Key publications:

1. Genome sequencing of disease and carriage isolates of nontypeable Haemophilus influenzae identifies discrete population structure. De Chiara M, Hood D, Muzzi A, Pickard DJ, Perkins T, Pizza M, Dougan G, Rappuoli R, Moxon ER, Soriani M, Donati C. Proc Natl Acad Sci U S A. 2014. 111(14):5439-44.
2. The role of host and microbial factors in the pathogenesis of pneumococcal bacteraemia arising from a single bacterial cell bottleneck. Gerlini A, Colomba L, Furi L, Braccini T, Manso AS, Pammolli A, Wang B, Vivi A, Tassini M, van Rooijen N, Pozzi G, Ricci S, Andrew PW, Koedel U, Moxon ER, Oggioni MR. PLoS Pathog. 2014. 10(3):e1004026.
3. The next decade of vaccines: societal and scientific challenges. Moxon ER, Siegrist CA. Lancet. 2011. 378(9788):348-59.

I was Action Research Professor of Paediatrics from 1984-2008, Head of the Molecular Infectious Diseases Group in the Weatherall Institute of Medicine (1988-2008), founded the Oxford Vaccine Group in 1994 and was the principal investigator and lead scientist for funding and establishing the Centre for Clinical Vaccinology and Tropical Medicine [CCVTM] (1999 – 2008). I am currently an Emeritus Professor of Paediatrics in the Medical Sciences Division, a member of the Scientific Council for Institut Pasteur and the Advisory Boards of the Hilleman Foundation, Novartis Vaccines and GlycoVaxyn. My research has been on the molecular basis of bacterial infections of childhood, especially meningitis and septicaemia caused by *Haemophilus influenzae* type b and the meningococcus, with a major interest in their prevention by immunisation.

I remain active in original research on bacterial pathogens with emphasis on how this knowledge can facilitate prevention of bacterial infections in childhood through immunisation. In the past three years, my research has included:

1 The development of a model of otitis media caused by capsule-deficient *H. influenzae* (Hi). Scientists at Harwell have identified a mutant mouse line (Junbo) that is susceptible to nasopharyngeal colonisation and ascending bacterial infection with Hi resulting in otitis media. This has opened the door to investigations of the pathogenesis, treatment and prevention of this important infection of childhood. In collaboration with Derek Hood and other Harwell Scientists, we have demonstrated the importance of a profound population bottleneck during the establishment of otitis media and the feasibility of the model to investigate the protective effect of candidate Hi antigens, identified through whole genome sequencing.

2 Subsequent to the licensure of a vaccine against the B strain of meningococcus (MenB), I am collaborating with the research group of Martin Maiden (Zoology Department) to use whole genome sequences of large collections of MenB carriage and disease isolates to describe their genetic diversity, especially with respect to variations in the vaccine antigens over time, before and after the introduction of Bexsero into the UK routine immunisation programme.

3 In conjunction with Professor Andrew Pollard and the Oxford Vaccine Group, we have evaluated the adjuvant effect of a modified lipopolysaccharide in native outer membrane vesicles (nOMVs) on immune responses to vaccination with the recombinant meningococcal protein, rPorA, tetanus toxoid, or meningococcal serogroup C capsular polysaccharide. These results highlight the potential importance of considering not just the antigens that result in priming and boosting B cell responses, but the pathogen-specific molecular determinants that underpin interactions with the innate immune response in obtaining optimal protection and long-lasting immunity following immunisation.

4 In collaboration with Marco Oggioni of Leicester University, I am investigating the pathogenesis of pneumococcal bacteremia (in a mouse model) to better understand the early phases in the infection. Previous research in the past 2 years has shown that pneumococcal bacteremia, initiated following challenge with millions of bacteria, is founded by a single surviving bacterial clone. Further, we have identified adaptive mutations in *ex vivo* organisms obtained from blood during the bacteremic phase. Our future research aims to identify the details of the profound population bottleneck of pneumococci, the role of host factors in clearance and the host-adaptive mechanisms of the pathogen.

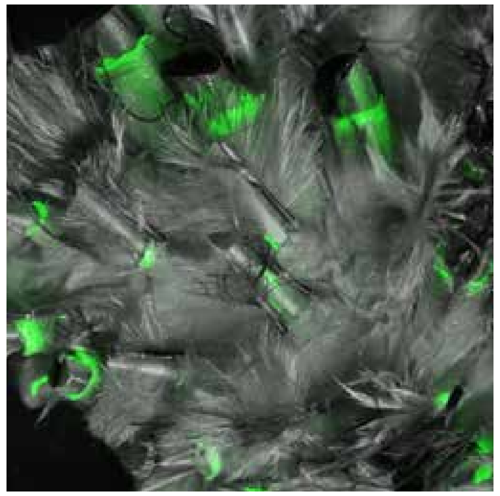
In my capacity as a scientific adviser to Novartis Vaccines, I have been deeply involved with the research leading up to the licensure of the MenB vaccine (Bexsero) and the subsequent post-licensure events leading to the recommendation that the vaccine, if cost-effective, should be introduced into the routine infant immunisation programme in the UK. As a member of the Scientific Council of Institut Pasteur, I am active in supporting a new initiative that aims to bring about a major programme in vaccinology spear-headed by the Director General, Christian Brechot. I continue to be active in teaching for example as a member of the faculty of the annual Advanced Course In Vaccinology (held in Annecy, France), where I lecture and participate in workshops and discussion groups.

VENUGOPAL NAIR OBE

Avian viral diseases programme

I obtained my veterinary qualification and doctorate degree in Veterinary Medicine from India. I have over 25 years experience in veterinary virology and avian diseases, have published more than 120 scientific publications and book chapters, and also served as one of the Associate Editors of the 13th Edition of *Diseases of Poultry*. In recognition of my contributions to Avian Medicine, I was inducted to the World Veterinary Poultry Association Hall of Honour in 2013. I also hold honorary Visiting Professorships at Imperial College London and The University of Liverpool, and I am an Adjunct Fellow at Linacre College, Oxford.

I am head of the Avian Viral Diseases programme at the Pirbright Institute (http://www.pirbright.ac.uk/ISPG/AVD.aspx), studying the pathogenesis and control of avian viral diseases, where vaccination is the major method of control. Despite the success of vaccination as the cornerstone of disease prevention, vaccine-based control methods continue to pose immense challenges. The research objectives of the programme are centred around studies identifying (a) viral determinants of pathogenicity, (b) virus-host molecular interactions, and (c) host immune responses to viral infections and vaccines, using representative disease models in the natural avian target hosts.



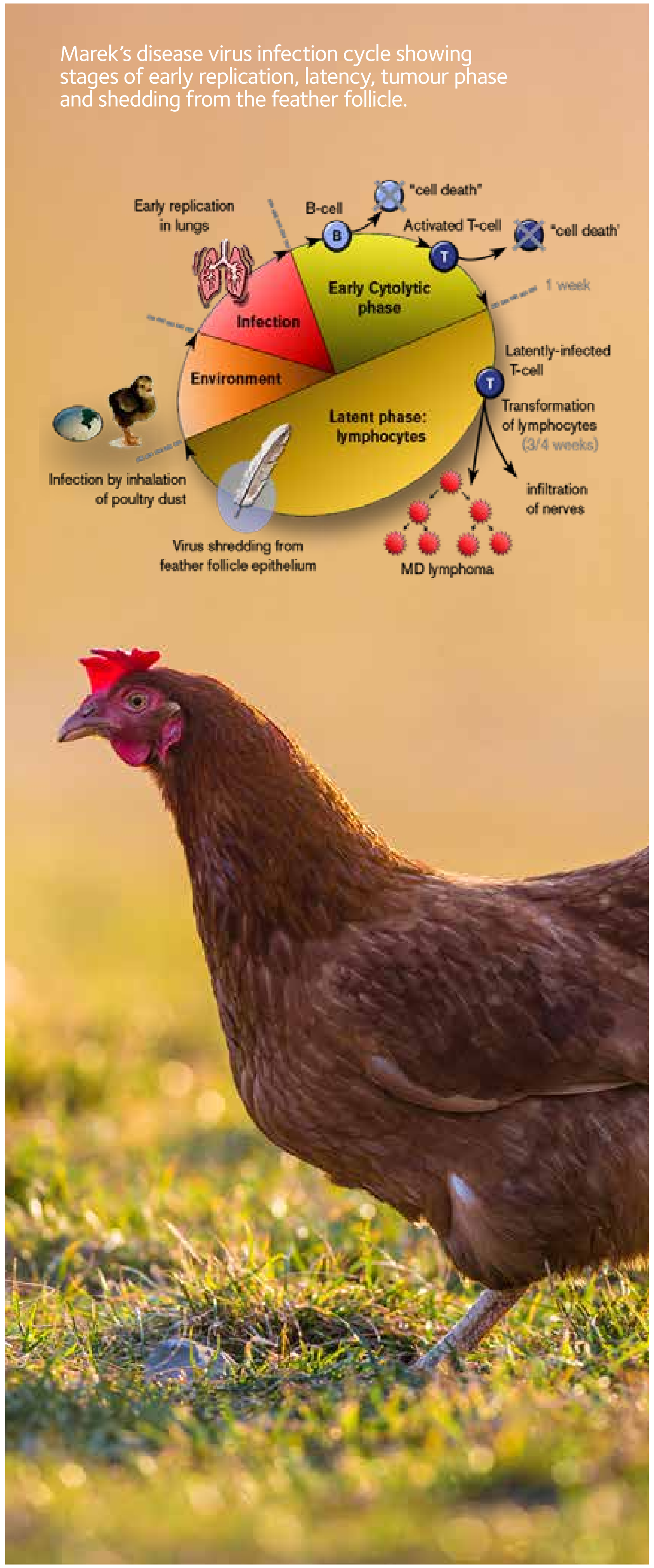
▲ Section of the skin from infected birds showing replication of Marek's disease virus expressing EGFP

Marek's Disease

My laboratory (www.research.pirbright.ac.uk/viraloncogenesis/) currently focuses on Marek's disease (MD), a highly contagious neoplastic disease of poultry caused by the Marek's disease virus (MDV). My group is one of the two World Reference Laboratories on MD for the World Organisation for Animal Health (OIE). As a major disease of poultry, causing estimated annual economic losses of up to $2,000 million to the poultry industry worldwide, understanding the molecular determinants and mechanisms of the disease is crucial to develop novel control strategies. We have identified a number of major viral determinants directly associated with the induction of T cell lymphomas utilising:
a) highly efficient reverse genetics systems with bacterial artificial chromosome (BAC) clones of the full-length genomes of a number of pathogenic and vaccine strains of MDV; and b) excellent models of the disease in genetically-defined susceptible chicken hosts. These include the major virus-encoded oncogene Meq, a basic leucine zipper-containing transcription factor, as well as miR-M4, a virus-encoded homologue of the oncogenic microRNA gga-miR-155. For further elucidation of the molecular pathways of oncogenesis, we are currently examining the global Meq "interactome" (the set of proteins that interact with Meq), and miR-M4 "targetome" in transformed tumour cells. More recently, we have also determined the global changes in DNA methylation in MDV-induced lymphomas, in order to demonstrate that these epigenetic changes also contribute to oncogenicity.

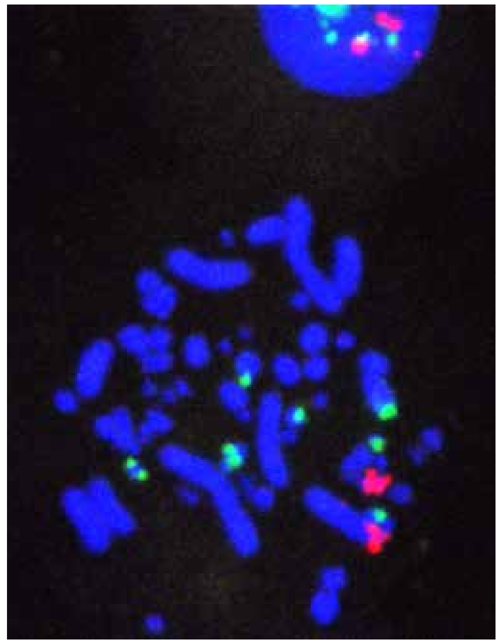
Key publications:

1. Andrew C. Brown, Venugopal Nair and Martin J. Allday (2012). Epigenetic regulation of the latency-associated region of Marek's disease virus (MDV) in tumour-derived T-cell lines and primary lymphoma. Journal of Virology 86 (3): 1683-95.
2. Yongqing Li, Kolli Reddy, Scott M, Reid, William J, Cox, Ian H, Brown, Paul Britton, Venugopal Nair and Munir Iqbal (2011) Recombinant herpesvirus of turkeys as a vector-based vaccine against highly pathogenic H7N1 avian influenza and Marek's disease. Vaccine 29(46):8257-66.
3. Yuguang Zhao, Lawrence Petherbridge, Lorraine P Smith, Yongxiu Yao, Hongtao Xu, Sue Baigent & Venugopal Nair (2011). Critical role of a single virus-encoded microRNA in the induction of Marek's disease lymphomas. PLoS Pathogens 7 e1001305.



Marek's disease virus infection cycle showing stages of early replication, latency, tumour phase and shedding from the feather follicle.

▼ Fluorescent *in situ* hybridization (FISH) on chromosome spreads of Marek's disease virus-transformed lymphoma cells showing integrated viral genomes (green). Probes specific for chromosome 18 are shown in red.



Vaccines for Marek's Disease

MD is a good natural model for virus-induced lymphomas, and is the first example of a cancer that can be prevented by vaccination. Although vaccines have been immensely successful in preventing the disease during the last 40 years, the current trend of continuing virulence of MDV strains is threatening the sustainability of the vaccination strategy. Our recent studies suggest that the inability of the current vaccines to prevent virus replication and transmission (as opposed to preventing disease) is contributing to this increased virulence, which is caused by viral mutation. Novel strategies that can reduce virus transmission are required to stop this current trend. Recombinant vaccine vectors, such as herpesvirus of turkeys (HVT), expressing MDV proteins are now widely deployed as an alternative vaccination strategy, which can prevent not only disease but also transmission between birds, and so control the viral evolution that leads to increased virulence. BAC clones of the genomes of HVT and other vaccine strains also provide us with the opportunity to develop novel recombinant vectors.

Key publications:

1. Oh Y, Fleming L, Statham B, Hamblin P, Barnett P, Satya Parida. (2012) Interferon-γ Induced by In Vitro Re-Stimulation of CD4+ T-Cells Correlates with *In Vivo* FMD Vaccine Induced Protection of Cattle against Disease and Persistent Infection. PLoS ONE 7(9): e44365.
2. Pope RA, Parida S*, Bailey D, Brownlie J, Barrett T, Ashley C. Banyard*. (2013) Early Events following Experimental Infection with Peste-Des-Petits Ruminants Virus Suggest Immune Cell Targeting. PLoS ONE 8(2): e55830. (*corresponding author)
3. Muniraju, M., Munir, M., Parthiban, A.R., Banyard, A.C., Bao, J., Wang, Z., Ayebazibwe, C., Ayelet, G., El Harrak, M., Mahapatra, M., Libeau, G., Batten, C., Parida, S., 2014. Molecular evolution of peste des petits ruminants virus. Emerging Infectious Diseases 20, 2023-2033.

▼ Oro-pharyngeal sample collection in cattle in field at Lao PDR

SATYA PARIDA

Vaccines for Foot-and-Mouth Disease (FMD) and Peste des Petits Ruminants (PPR)

I lead the Vaccine Differentiation Group in the Livestock Viral Disease Programme at The Pirbright Institute, UK, which carries out applied research that will help to control foot-and-mouth disease (FMD) and peste des petits ruminants (PPR). I am an adjunct Professor to Murdoch University, Australia, and an Investigator at the Jenner Institute, University of Oxford. I recently joined the National Institute of Animal Biotechnology (NIAB), Hyderabad, India, as a Visiting Faculty in the infectious disease programme.

Ongoing work on foot-and-mouth disease and peste des petits ruminants

My group is focussed on the development and validation of marker vaccines and associated diagnostics for FMD and PPR, with three lines of investigation: (1) improving our understanding of the aspects of the immune response that are important in the protection of vaccinated animals against acute and persistent infection; (2) developing alternative means of detecting infection in vaccinated animals; and (3) developing and evaluating improved marker vaccines (DIVA vaccines) for FMD and PPR. Marker vaccines allow differentiation between infected and vaccinated subjects, which is particularly important for the control of disease epidemics affecting livestock.

During the last four years, our work has focussed on these areas:

FMD vaccine development

1 Determining the immunogenic potential of 2 recombinant viral vector vaccines (rSeV/FMD and rAdV/FMD), and obtaining data on the ability of these vaccine candidates to block FMDV (foot-and-mouth disease virus) infection through the intranasal route. Both vaccines were immunogenic in a homologous prime-boost parenteral vaccination strategy, and protected cattle against virulent FMDV challenge delivered using a nebuliser and mask. Intranasal vaccination of cattle with one vaccine alone (rSeV/FMD), but not the other, also provided full protection against FMDV challenge.

2 Improving existing inactivated FMD vaccines: 8 new adjuvants, Abisco300, CPG, ISA206, Poly I:C, Imiquimod, MPLA, liposome and ISA70, were tested with FMD antigen + ISA206 in cattle. Two of them improved the immunogenicity of the existing vaccine and provided complete protection upon challenge with virulent FMD virus.

3 The widest diversity of FMD viruses circulates in East Africa, with four serotypes found in livestock, and few tailor-made vaccine strains are currently available. We have serologically characterised field isolates and vaccine strains for serotypes A and O. The genes encoding the virion proteins of these viruses have been sequenced, and the serological and genetic data have been synthesised to determine genetic determinants of their antigenic phenotypes. Collaborating with Glasgow University, we are currently involved in developing a sequence-based method for determining antigenic similarity, and using this to develop a method for vaccine strain selection for emerging foot-and-mouth disease virus outbreaks in enzootic countries, through analysis of the antigenic characteristics of recently circulating viruses.

4 We have developed and validated confirmatory antibody tests against non-structural proteins that could differentiate infection in vaccinated animals (DIVA). Also we have developed a mucosal antibody test (IgA) for O, A, and Asia1 serotypes that could detect persistently FMDV virus infected ruminants.

PPR vaccine development

5 Development of a recombinant PPR marker vaccine: Reverse genetic techniques have been established for the PPR virus, and a live attenuated recombinant marker vaccine for PPR Nigeria 75/1 has been developed and evaluated in goats, which provides complete protection.

6 For the first time, we have sequenced the complete genome of Lineage III PPR virus and the complete genome of 6 other PPR viruses. Using these full genome sequences, we have studied the evolution and worldwide emergence of the PPR virus.

BRIAN PERRY OBE

Global disease control and health initiatives

I am a veterinarian and epidemiologist specialised in assessing the impacts of livestock diseases and their control in developing country settings, where I have widespread experience in many countries of Africa, Asia and Latin America. In recent years, I have led many independent evaluations of public funding investments in agricultural and health development programmes by international and bilateral agencies. I hold honorary and visiting Professorships at the Universities of Oxford, Edinburgh and Pretoria, and Chair the Scientific Advisory Board of the Wellcome Trust-funded One Health research consortium 'Afrique One'.

Foot-and-mouth disease research

Following many years of exploring the contributions of foot-and-mouth disease (FMD) control to development and poverty reduction, I convened a global consultation in India in 2007 on the need for research into the better control of FMD in endemic settings of the world. Following on from this, I embarked on a two year process of leading the design of research to address FMD in endemic settings, and seeking funding for its support. Many of the concepts presented have now been funded by the Wellcome Trust and others, including a new strategic award obtained by the Jenner Institute.

Human resource and institutional capacity building in the health sciences

Afrique One.

Since 2009, I have been Chairman of the Scientific Advisory Board of Afrique One, an Africa-wide consortium of eleven universities and research institutions undertaking research on zoonotic diseases at the human, animal and environmental interface in Africa. This is supported by funding from the Wellcome Trust under its African Institutions Initiative.

Zoonosis and Emerging Livestock Systems Initiative (ZELS).

In 2013, I was invited to Chair the Development Relevance Panel Review Committee in the evaluation of research proposals submitted to the Biotechnology and Biological Sciences Research Council (BBSRC), for the £19 million investment in the Zoonosis and Emerging Livestock Systems Initiative (ZELS) by the Department for International Development (DFID).

Strategic analytical contributions to global opportunities in livestock research and development and animal health

Livestock disease control and processes of poverty reduction.

It is now 10 years since I led a DFID initiative to develop a prioritisation of research needs and opportunities for the better control of livestock diseases affecting poorer sectors of society in Africa and Asia. I have continued to play an active research role in this field, updating earlier work on disease impacts and exploring other mechanisms for contributions of disease control to economic growth.

Global livestock disease dynamics.

I was invited by the Food and Agriculture Organisation (FAO) to be the team member responsible for animal health in the development of the FAO's annual publication on livestock entitled "The State of Food and Agriculture"; the special edition was entitled "Livestock in the Balance". From this work, a publication emerged in the Proceedings of the National Academy of Science entitled "Current drivers and future directions of global livestock disease dynamics".

Global livestock research imperatives and responses by the Centres of the Consultative Group on International Agricultural Research (CGIAR).

In 2013, I was invited by the Independent Science and Partnership Council (ISPC) of the CGIAR to develop a strategic overview of the current priorities for global livestock research, the comparative advantage of the CGIAR, and the responses made by the 15 research centres through the formation of the CGIAR Research Programmes (CRPs), designed to build and enhance partnerships between centres and disciplines and to be largely undertaken in the context of specified ecoregions. The final report was published as a white paper in early 2014 and appears on the ISPC website. As part of the Sustainable Livestock Initiative, I have also been invited to organise, operate and facilitate international panel discussions involving multiple stakeholders.

Leadership of independent evaluations of public funding investments in agriculture and health

Since 2009, I have led nine independent evaluations of the effectiveness and impact of public funding investments in agriculture and health in different countries and regions of the world.

These have included the global real-time evaluation of the FAO's programmes in highly pathogenic avian influenza, the performance of the United Nation's programmes in agriculture in Ethiopia and, in late 2013, I participated in an evaluation of the decentralisation process of the FAO in Asia and the Pacific, in which I led the review of all of the FAO's work on animal health and production in the region.

Other activities

I have been involved in assessing the impact of the World Bank's investment in avian flu control in Nigeria. In a different field, I have undertaken a study of the effect of changing trade agreements on the benefits to different stakeholders engaged in the export of fresh flowers from Kenya and Ethiopia, in particular to Norwegian markets.

Key publications:

1. Perry, B.D., Morton, J., Stur, W. (2014). A strategic overview of livestock research undertaken by the Consultative Group for International Agricultural Research (CGIAR) Consortium, 64 pp. http://www.sciencecouncil.cgiar.org/system/files_force/ISPC_WhitePaper_StrategicReviewLivestock.pdf?download=1
2. Perry, B.D., Grace, D., Sones, K.R. (2011). Current drivers and future directions of global livestock disease dynamics. Proceedings of the National Academy of Science www.pnas.org/cgi/doi/10.1073/pnas.1012953108
3. Perry, B.D., Romero, J., Lora, E. (2012). Evaluación independiente del Proyecto Regional Integrado para el Control Progresivo de la Fiebre Aftosa en Bolivia, Colombia, Ecuador, Perú y Venezuela. FAO Office of Evaluation, FAO, Rome, 55 pp. + anexos. http://www.fao.org/fileadmin/user_upload/oed/docs/GCPRLA178SPA_172ITA_2012_ER.zip

ANDREW POLLARD
The Oxford Vaccine Group (OVG)

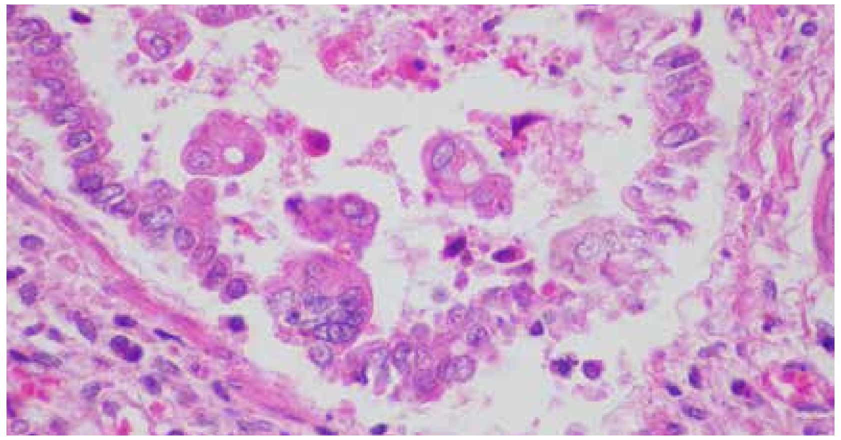
I am Professor of Paediatric Infection and Immunity, and Director of the Oxford Vaccine Group (since 2001), in the Department of Paediatrics and my research focusses on preclinical design and development, clinical testing and laboratory evaluation of vaccines. I studied medicine at St Bartholomew's Hospital Medical School and trained in paediatrics and infectious Disease in Birmingham, London and Vancouver. I obtained my PhD at Imperial College studying development of immunity to *Neisseria meningitidis* after infection. Today I also lead the Children's network for the National Institute for Health Research's Thames Valley Clinical Research Network and I am the clinical co-director for Children in the Thames Valley Academic Health Science Network. I chair the Department of Health's Joint Committee on Vaccination and Immunisation and the European Medicine's Agency Scientific Advisory Group on vaccines.

My research group, the Oxford Vaccine Group (OVG), includes over 70 clinical trials and scientific staff, who enrolled more than 10,000 participants to research studies and published over 100 scientific papers in the past 5 years. Studies conducted by the group have impacted on the licensing or deployment of many of the vaccines currently recommended for use in the paediatric immunisation schedule, and were also instrumental in providing safety data allowing the use of the Influenza A H1N1 'swine flu' vaccines in response to the recent pandemic and the evaluation of vaccines in response to the Ebola outbreak in 2014.

Meningitis and encephalitis

I have been investigating immunity to meningococcal disease following infection and vaccination for 20 years, bringing this focus to the work of the Oxford Vaccine Group since 2001. *Neisseria meningitidis* causes approximately 500,000 cases of invasive meningococcal disease (meningitis and septicaemia) every year. OVG has had a broad programme of meningitis vaccine development and evaluation, spanning from preclinical development to clinical trials and post-licensure studies.

▼ Respiratory syncytial virus (RSV) infection usually produces widespread bronchiolitis and interstitial pneumonia which may sometimes be associated with giant cells. This image shows a non-specific interstitial pneumonia pattern with no giant cells present.



Highlights include:

- Leadership of phase II and III clinical trials supporting development and evaluation of capsular group B meningococcal vaccines and quadrivalent capsular group A, C, W and Y meningococcal vaccines.
- Delivery of a large European project to identify genetic factors underlying the reactogenicity and immunogenicity of a recently licensed MenB vaccine.
- Key studies in the development of pneumococcal conjugate vaccines for the UK programme.
- Study of the impact of smoking in different age-groups on meningococcal disease.
- Investigation of capsular group X meningococcal serological responses in Africa and preclinical characterisation of the structure and vaccine potential of the X polysaccharide.
- Improvement of the outer membrane vesicle components of MenB vaccines through several research projects, one of which has included the creation of a proof-of-concept vaccine characterised in preclinical models, which was recently evaluated in a first-in-man phase I clinical trial.
- Creation of a novel capsular group B meningococcal (MenB) vaccine, which will enter phase I clinical trials in 2015.

In 40-50% of meningitis and encephalitis cases the cause is unknown. We are now undertaking the largest prospective study of paediatric meningitis and encephalitis in Europe to identify the causes of these infections, develop better diagnostics and describe outcomes, and plan to initiate a clinical trial of intravenous immunoglobulin for the treatment of encephalitis in early 2015 funded by the National Institute for Health Research.

Respiratory Syncytial Virus

Respiratory Syncytial Virus (RSV) is the single greatest burden to paediatric hospital resources every winter in industrialised nations. Two thirds of infants have an RSV infection in the first year of life, with 2-3% requiring admission to hospital, and approximately 6% of these needing management on dedicated paediatric intensive care units (PICU). Worldwide, RSV disease in children under the age of 5 years accounts for 33.8 million lower respiratory infections, 3.4 million hospitalisations and 66,000-199,000 deaths annually, second only to malaria in all-cause post-neonatal infant mortality. Estimates in the elderly population suggest that RSV causes a burden of death and disease comparable to seasonal flu.

Despite decades of research effort, there remains no licensed RSV vaccine to mitigate the enormous human and financial cost of the worldwide annual RSV epidemic. OVG are currently conducting a phase 1 adult study of a novel RSV vaccine, using viral vectors to deliver key RSV protein antigens.

Enteric Fever

Enteric fever, the systemic illness caused by bacteria including *Salmonella typhi* and *Paratyphi A*, continues to be a major cause of illness and death globally, particularly in children living in impoverished surroundings.

In 2009, a programme to accelerate the progress being made in the control of enteric fever was initiated, with major funding provided by the Wellcome Trust. Our central aim was to design, initiate and utilise a human model of typhoid infection to make major advances in our understanding of host-pathogen interactions and the development of protective immune responses. While providing novel insights into *S. typhi* pathogenesis, we have also directly applied the model to assess and validate novel diagnostics and vaccines. Experience gained in performing human challenge studies has led to the field introduction and testing of novel approaches to typhoid diagnostics and interventions.

Since completion in 2012 of the largest single randomised control trial using human challenge to assess vaccine efficacy, the enteric fever programme has expanded to encompass the development of a paratyphoid challenge model, work exploring immunobiological responses following re-challenge, and funding aimed to introduce a new generation of diagnostics and vaccines to those most at need.

B cells and antibodies

While the kinetics of antibody responses following immunisation against pneumococcus, meningococcus and *H. influenzae* type b capsular polysaccharides have been studied extensively, little is known about the specific B cell responses that underlie the production of antibody. We have investigated B cell responses using various approaches to explore the mechanisms of protection through use of both plain polysaccharide and protein-polysaccharide conjugate vaccines.

Our work focuses on the effect of capsular antigens on the frequencies of antigen-specific IgM-memory B cells, innate B1 cells and plasma cells. Maturation of the B cell response at the molecular level is being studied using high-throughput sequencing technology and novel bioinformatics algorithms in order to investigate B-cell receptor repertoire following vaccines against meningococci, *H. influenzae, S. pneumoniae* and Hepatitis B. These methods have the potential to identify antigen specific B-cell sequences and determine patterns of B-cell subset activation.

Childhood infections in Nepal

In 2013, GAVI (Global Alliance for Vaccines and Immunisation) funded a 4-year programme of research to investigate the impact of the introduction of pneumococcal conjugate vaccines in the Nepal infant immunisation schedule. This programme of research, led by OVG, is being undertaken jointly with the International Vaccine Access Centre (IVAC) at Johns Hopkins School of Public Health and the Agence de Médecine Préventive (AMP), and continues a collaboration with Patan Hospital Department of Paediatrics that commenced in 2005. This collaboration has allowed the epidemiology of bacterial pneumonia and meningitis to be defined in Nepali children funded by PneumoADIP and WHO, together with large-scale studies of the carriage of *Haemophilus influenzae* type b and *Streptococcus pneumoniae*, which are the most important causative pathogens. In addition, a recently completed clinical trial of 10-valent pneumococcal conjugate vaccine (PCV10) has supported the planned introduction of this vaccine in Nepal in 2014/15.

Key publications:

1. Gossger N, Snape MD, Yu LM, Finn A, Bona G, Esposito S, Principi N, Diez-Domingo J, Sokal E, Becker B, Kieninger D, Prymula R, Dull P, Ypma E, Toneatto D, Kimura A, Pollard AJ; European MenB Vaccine Study Group. Immunogenicity and tolerability of recombinant serogroup B meningococcal vaccine administered with or without routine infant vaccinations according to different immunization schedules: a randomized controlled trial. JAMA. 2012 Feb 8; 307(6):573-82.
2. Waddington CS, Darton TC, Jones C, Haworth K, Peters A, John T, Thompson BA, Kerridge SA, Kingsley RA, Zhou L, Holt KE, Yu LM, Lockhart S, Farrar JJ, Sztein MB, Dougan G, Angus B, Levine MM, Pollard AJ An outpatient, ambulant-design, controlled human infection model using escalating doses of Salmonella Typhi challenge delivered in sodium bicarbonate solution. Clin Infect Dis. 2014 May; 58(9):1230-40.
3. Kelly DF, Snape MD, Clutterbuck EC, Green S, Snowden C, Diggle L, Yu LM, Borkowski A , Moxon ER and Pollard AJ. CRM197-conjugated serogroup C meningococcal capsular polysaccharide, but not the native polysaccharide, induces persistent antigen-specific memory B cells. Blood 2006;108(8):2642-7.

ARTURO REYES-SANDOVAL
Plasmodium vivax malaria

I graduated in Microbiology in 1993 at the National Polytechnic Institute in Mexico, then undertook a M.Sc. programme in Cell Biology. In 1999, I began my PhD studies at the Wistar Institute in Philadelphia, USA. Our research led to the first report describing the use of a chimpanzee adenovirus as a vaccine vector, which used a rabies infection model. I am currently a Wellcome Trust Career Development Fellow working on the development of vaccines against neglected tropical diseases, such as *P. vivax* malaria, dengue and chagas.

Vaccines against *Plasmodium vivax* malaria

The fight against malaria is becoming of central importance to the global health agenda, following the initial commitment in 1969 by the World Health Organization to eradicate this disease. Such momentum has been driven by the growing appreciation of the humanitarian and economic issues in malaria-endemic populations, the development of novel tools to fight the disease and increased investment by funding organisations.

Of the two malaria parasites with the greatest prevalence, *Plasmodium vivax* is the most difficult to eliminate from endemic areas because of its ability to remain dormant as hypnozoites in the liver of an infected person for weeks, months or years, later reactivating and continuing with the transmission cycle. The presence of a parasite with the ability to hide for years constitutes a formidable challenge to its elimination from densely populated areas of Asia and Latin America, where it threatens nearly 40% of the worldwide human population and is responsible for an estimated 132-391 million cases of malaria each year.

There is currently no licensed vaccine for malaria, and vaccine development for *P. vivax* has been a particularly slow process, with only two candidates reaching clinical trials, that confer only modest protection against infection. Fortunately, modern technology should permit faster future progression towards the development of novel vaccine candidates.

P. falciparum malaria.

In recent years, I have contributed to the development of one of the leading vaccine candidates for *P. falciparum* malaria that targets the parasite in the liver, where it stops and multiplies before entering the blood (this is known as a pre-erythrocytic or liver-stage vaccine). This strategy uses novel recombinant viral vectors (ChAd63 and modified Vaccinia Ankara, MVA) expressing the recombinant antigen TRAP. By exploiting their extraordinary ability to stimulate both arms of the adaptive immune response, i.e. both antibodies and T cells, we can elicit immune responses able to provide outstanding protection in a sporozoite challenge model that mimics the infection process by which a mosquito innoculates parasites into a mammalian host. My research has contributed to the understanding of the mechanisms responsible for the extraordinary protective efficacy of recombinant viral vectors, forming the basis for their use as malaria vaccines, including the following examples:

- The first description of a single vaccination with a chimpanzee adenoviral vector malaria vaccine, and its ability to induce complete, sterile protection against a sporozoite challenge using the *P. berghei* malaria parasite;
- Demonstration that Ad-MVA prime-boost vaccination regimens elicit long-term protection against malaria and enhance the functionality of CD8+ T cells;
- Identification of correlates of protection for T cell-inducing vaccines in pre-erythrocytic malaria;
- Demonstration of the potential of viral-vectored vaccination for pre-erythrocytic malaria in non-human primates and humans;
- Various methods to enhance the immunogenicity and protective efficacy of viral vectors against malaria.

Key publications:

1. Reyes-Sandoval A, Bachmann MF. Plasmodium vivax malaria vaccines: Why are we where we are? Hum Vaccin Immunother. 2013. 1;9(12):2558-65.
2. 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. 2012 Aug;20(8):1633-47.
3. 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.

Ongoing research

My ongoing research focusses on the development of a novel malaria vaccine against *P. vivax*, using recombinant viral vectors expressing pre-erythrocytic antigens. Through the support of the Wellcome Trust, I aim to develop and investigate the following:

- A novel *P. vivax* vaccine using recombinant viral vectors expressing pre-erythrocytic antigens;
- Development of novel transgenic *P. berghei* parasites expressing *P. vivax* transgenes, which would permit the assessment of new vaccine candidates;
- The ability of viral-vectored vaccines to target the hypnozoites from *P. vivax*;
- Design, production and purification of proteins from *P. vivax* to be used for research and vaccine development.

An additional research interest focusses on the development of vaccines for Dengue Fever using recombinant viral vectors.

CHRISTINE ROLLIER (OXFORD VACCINE GROUP)
Serogroup B Meningococcus

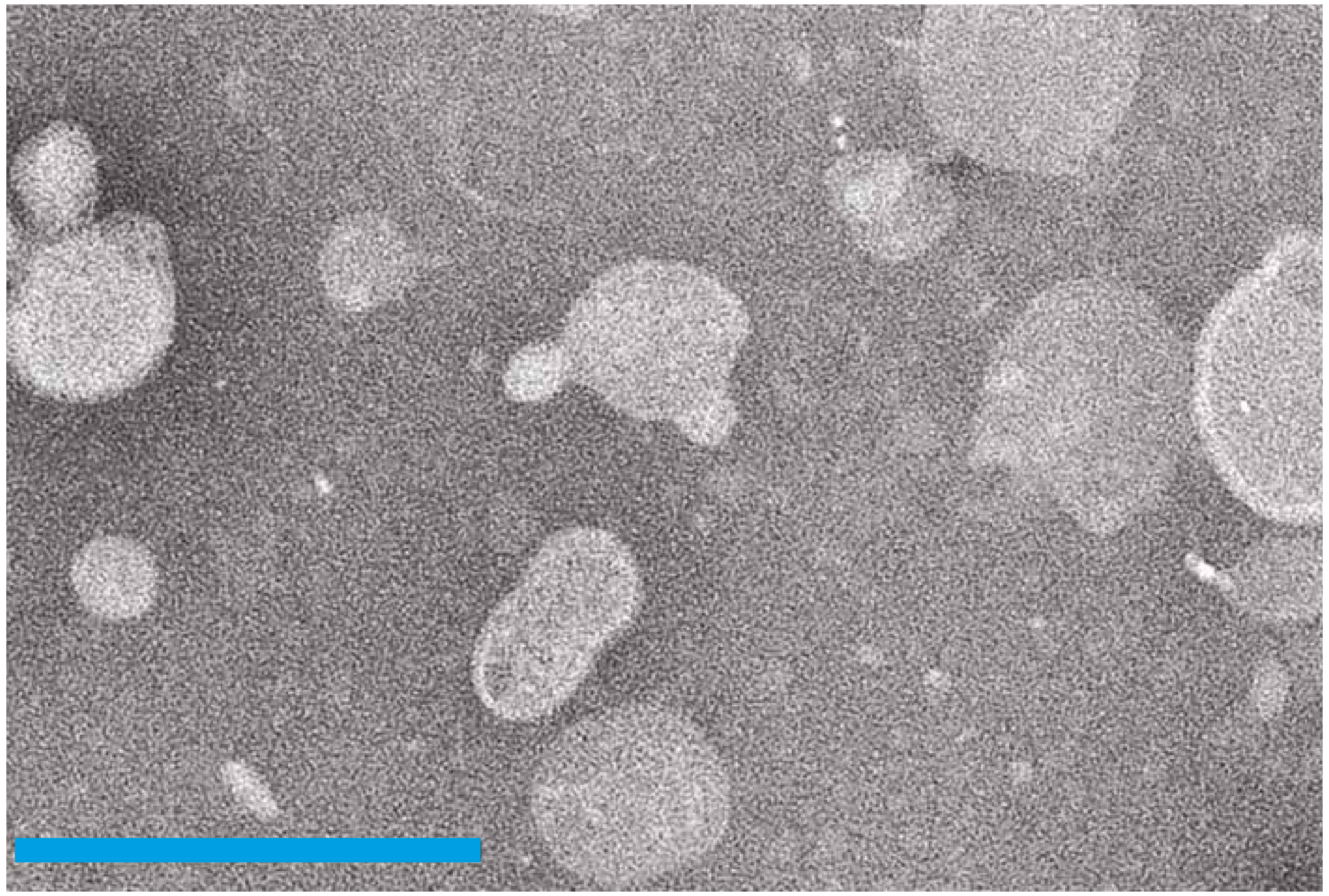
I trained in biochemistry at the University of Lyon I, France, and obtained a PhD in 2000, studying virology. I specialised in immunology and vaccine development at INSERM U271, Lyon, France, and proceeded to work on novel vaccine development against chronic infection by Hepatitis C Virus at the Biomedical Primate Research Center, The Netherlands. I joined the Jenner Institute at the University of Oxford in 2007, to work on improvements of vaccine vectors against malaria. I started my current position at the Oxford Vaccine Group in 2010. My research activities include pre-clinical and clinical investigation of new and improved vaccines against serogroup B meningococcus.

Neisseria meningitidis causes around 500,000 cases of meningitis and septicaemia every year, disproportionately affecting children under 2 years. The case-fatality rate is 10% in resource-rich settings, and has not decreased significantly since the 1950s. 30% of survivors suffer severe long-term disability including deafness, amputation and cognitive impairment. Vaccination is the optimal way to reduce the mortality and morbidity from this disease. Our objective is to develop a new vaccine against capsular group-B meningococcal disease (MenB), in order to address the need for an improved and more cost-effective vaccine which has lower manufacturing costs, higher immunogenicity, longer duration of protection and requires a single injection to protect infants, as compared to the currently available vaccines. Two vaccine candidates have recently been licensed, but they do not provide complete protection against MenB, especially in infants, who are at most risk of this devastating disease. Furthermore, these vaccines require multiple doses which increases the cost of vaccine implementation. Development of alternative vaccines is therefore required.

Improvement of Outer Membrane Vesicle vaccines

N. meningitidis produces non-infectious outer membrane vesicles (OMVs), which contain many subcapsular antigens during growth in liquid culture and *in vivo*. OMVs have been used successfully as vaccines during outbreaks of MenB and are also included in the multicomponent MenB vaccine Bexsero, which was licensed in Europe in 2013. However OMVs have considerable limitations: the immune responses are weak, strain-specific and short-lived. Therefore improving their immunogenicity may contribute to the design of more potent MenB vaccines or vaccine components. *N. meningitidis* has developed complex mechanisms to evade the immune system and especially the Complement cascade, in particular by binding human factor H (hFH), an inhibitor of the Alternative Complement Pathway (AP). By binding Complement inhibitors to turn off Complement activation, the bacteria or vaccine becomes less visible to the immune system. This is likely to have an impact on the immunogenicity of vaccine candidates such as OMVs containing such Complement-inhibitor binding proteins. Therefore the aim of this project is to create OMVs unable to bind hFH and thus able to activate the Complement AP, and test the hypothesis that these modified OMVs would raise a higher host immune response when compared to the wild-type counterpart. The objectives were to engineer a capsular group B *N. meningitidis* strain lacking the ability to bind hFH, to produce an OMV vaccine from this strain and to compare its immunogenicity to a wild-type counterpart in pre-clinical mouse models.

▼ Electron microscopy picture of outer membrane vesicles (bar scale 200 nm)



Development of novel MenB vaccines

We are investigating the potential of an alternative type of vaccine technology for the development of a new vaccine against MenB. The research group has developed proprietary vaccine candidates, through a method that is safe and effective at triggering an immune response. We have investigated this new approach for several antigens and have demonstrated that while all of the prototypes are able to induce strong antibody responses, these antibodies are not always able to kill the bacteria to a sufficient extent. Exploring the reasons behind these results allowed us to develop a novel and successful prototype vaccine, which is currently being optimised to progress to phase I clinical trial in 2016.

Key publications:

1. Rollier CS, Dold C, Marsay L, Sadarangani M and Pollard AJ. The Capsular group B Meningococcal Vaccine, 4CMenB: Clinical Experience and Potential Efficacy. Expert Opinion On Biological Therapy 2015 Jan;15(1):131-42.
2. Jerry C. Nagaputra, Christine S. Rollier, Manish Sadarangani, J. Claire Hoe, Ojas Mehta, Gunnstein Norheim, Muhammad Saleem, Hannah Chan, Jeremy P. Derrick, Ian Feavers, Andrew J. Pollard, and E. Richard Moxon. Neisseria meningitidis native outer membrane vesicles containing different LPS glycoforms adjuvant meningococcal and non-meningococcal antigens, Clin Vaccine Immunol. 2014 Feb;21(2):234-42.
3. Rollier CS, Reyes-Sandoval A, Cottingham MG, Ewer K, Hill AV. Viral vectors as vaccine platforms: deployment in sight. Curr Opin Immunol. 2011 23(3):377-82.

SARAH ROWLAND-JONES

Immunology of HIV infections in different geographical locations

I am an academic clinician who combines research into the immunology of HIV and other viral infections with clinical practice in adult infectious diseases. Between 2004 and 2008 I was Research Director of the MRC (Medical Research Council) Labs in the Gambia, and I am now Professor of Immunology in the Nuffield Department of Clinical Medicine. My research group studies the immunology of HIV infection in infected people with distinct clinical outcomes, particularly in cohorts in Africa and China. The fundamental aim is to understand the role of the cellular immune response in combating HIV infection, in order to contribute to new vaccine and therapeutic strategies.

In Zimbabwe, we are collaborating with epidemiologists and clinicians in Harare who have recently shown that a substantial proportion of older children and adolescents (up to 50% in hospital, 15-20% in primary care) are presenting with previously undiagnosed and hence untreated HIV infection, which they acquired in infancy. These young people have frequently developed life-threatening complications, including severe chronic lung disease and heart problems, predominantly cardiomyopathy. We are investigating the mechanisms underlying these unusual clinical complications and looking at protective immunity in the small proportion of long-term survivors with perinatal HIV infection who remain well and have evidence of viral control in the absence of anti-retroviral therapy (ART). Together with investigators from Zimbabwe, Malawi and South Africa, we will be taking part in a multi-centre clinical trial of Azithromycin in older HIV+ children with chronic lung disease, funded by the Research Council of Norway (Globvac programme).

Key publications:

1. 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
2. Blais, M-E., Zhang, Y, Brackenridge, S., Rostron, T., Griffin, H., Taylor, S., Xu, K.Y., Yan, H., James, I., McMichael, A.J., Dong, T., John, M. and Rowland-Jones, S.L Enhanced HLA-C-restricted CTL selective pressure associated with an AIDS-protective polymorphism Journal of Immunology (2012) 188: 4663-70
3. De Silva, T.I., Peng, Y., Leligdowicz, A., Zaidi, I., Li, L., Griffin, H., Blais, M-E., Vincent, T., Saraiwa, M., Yindom, L-M., van Tienen, C., Easterbrook, P., Jaye, A., Whittle, H., Dong T. and Rowland-Jones, S.L. Correlates of HIV-2 control: insights into natural containment of a human retroviral infection Blood (2013) 121: 4330–9

In China, we are working with clinical researchers providing care for villagers who acquired HIV during participation in an illegal plasma donor scheme. These subjects were infected with a very similar viral strain through the same route at approximately the same time, and had limited access to anti-retroviral therapy (ART) during the first decade of infection. We are investigating how different components of the immune response have shaped viral evolution from an almost identical starting point, which may provide evidence for the relative importance of these different immune components to viral control.

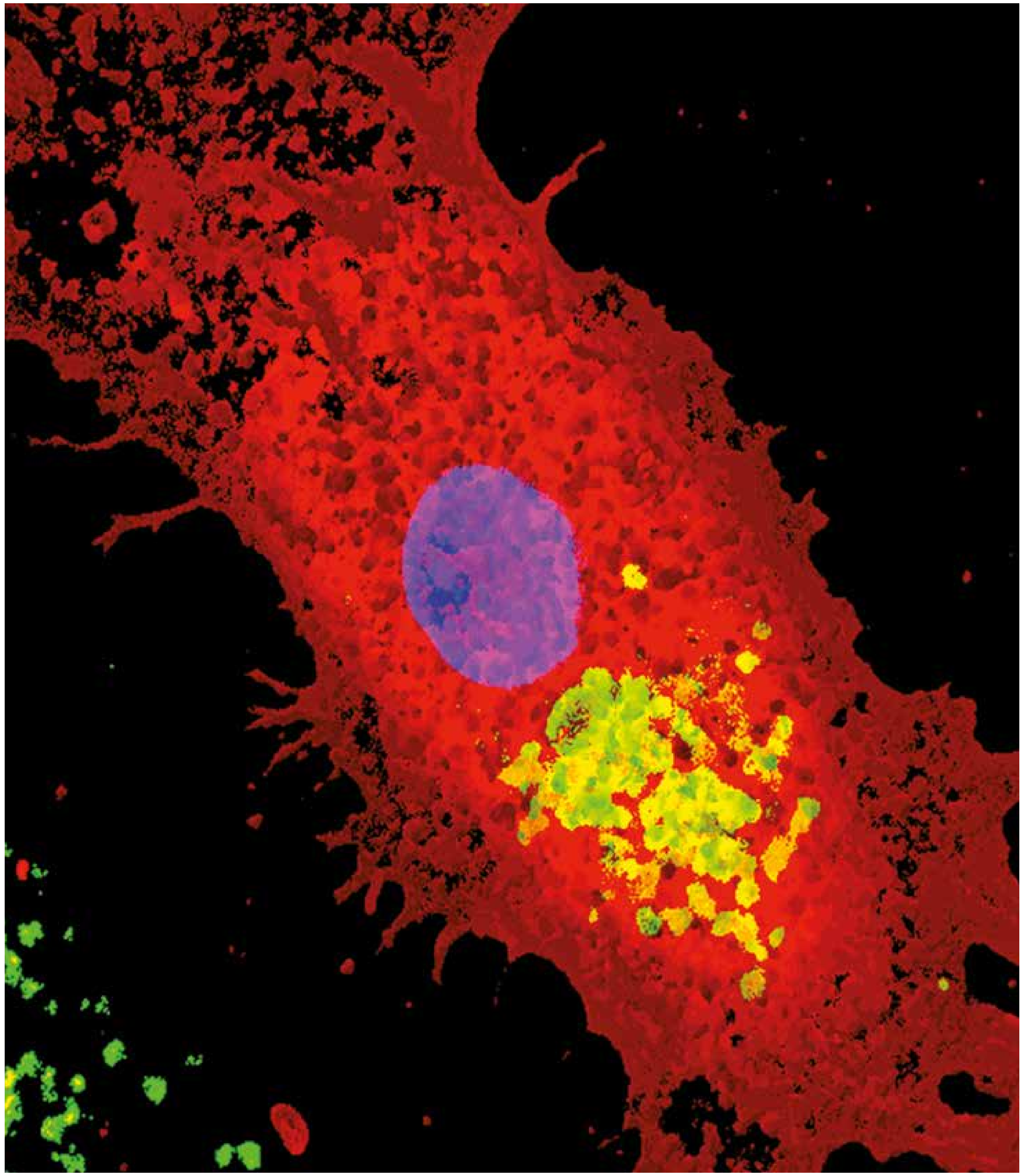
In Nairobi (Kenya), we are also studying viral evolution using samples collected 15-20 years ago, from infants who acquired HIV infection from their mothers. The course of infant HIV infection is very different from that in adults: whereas in adults the immune system rapidly brings down the blood viral load following acute infection, the viral load in infected babies is extremely high and falls very little in the first year of life. We are looking at how HIV changes over time using samples collected over the first 2 years of life, in order to estimate when the immune system firsts starts to exert selection pressure on the virus: these studies should provide insights into when the infant immune system is first able to respond effectively to HIV, important for deciding on the optimal timing for the deployment of candidate HIV vaccines in early childhood.

HIV-2: For over 20 years, our group has studied HIV-2, the second strain of HIV that has remained relatively limited to West Africa. Although some HIV-2-infected people progress to HIV disease and death in a manner very similar to AIDS caused by HIV-1, a substantial proportion (35-40% in the Caio community cohort in Guinea-Bissau) of HIV-2-infected patients spontaneously control the virus without anti-retroviral drugs for a decade or more, effectively experiencing what is now termed a "functional cure". We are working with researchers in Guinea-Bissau and London to investigate mechanisms of HIV control in such people.

In Kilifi (Kenya) and Malawi, we are also studying the immune response to vaccines and infections in uninfected infants exposed to HIV (HEU, HIV exposed uninfected) from their infected mothers. Although the roll-out of effective measures to prevent mother-to-child-transmission of HIV has provided huge benefits in terms of many fewer HIV+ children in countries with high HIV prevalence, HEU children often show immune system abnormalities and stunted growth: they are 2-3 times more likely to die than unexposed children, and are much more likely to develop severe infections in the first year of life. Working with investigators in Kilifi and Malawi, we are studying how HEU children respond to vaccines given in early life and looking at possible mechanisms that may underlie their increased susceptibility to infection.

◀ Children in the Gokwe North area of Zimbabwe. Given the current situation in the country they face a fairly bleak future. Both AIDS and malaria are problematic in the area in which they live.

▼ A dendritic cell (red) with nucleus (blue) containing internalised PEI-antigen complexes (green/yellow)



QUENTIN SATTENTAU

Antigens and adjuvants for antibody vaccines

I studied undergraduate microbiology at the University of Bristol (1980), and did my PhD at The Royal London Hospital, University of London (1985). My post-doctoral work was carried out in London and New York, after which I took up a tenured post in Marseille, France (1992-1998). I subsequently moved back to the UK as a Senior Lecturer at Imperial College London, before becoming a Lecturer in 2003, and a Professor in 2006 at the University of Oxford.

Stimulating antibody responses for HIV-1 vaccines

My recent work has focussed principally on developing antigens and adjuvants for use in antibody-based HIV-1 and other vaccines, which are designed to trigger neutralising antibody responses. HIV-1 is a difficult virus for vaccine development, largely because it has evolved multiple antibody evasion strategies. Of these, glycan coverage, antigen instability and amino acid variation are major challenges to be overcome. My laboratory has explored the modification of glycosylation, the stabilisation of antigen conformational flexibility and enhanced B cell targeting of highly conserved regions of the viral envelope glycoproteins (Env) as strategies to overcome these challenges. Recently, we demonstrated that cross-linking of soluble forms of HIV-1 Env enhances their stability, leading to increased titres and breadth of neutralising antibodies.

New vaccine adjuvants

Over the past 4 years, my laboratory has developed carbopol as a potent Th1-biased adjuvant that elicits robust antibody and T cell responses, and can be combined with oil-in-water adjuvants such as MF59 to elicit unusually strong antibody responses. A second adjuvant discovered by our laboratory is polyethyleneimine (PEI). PEI has strong mucosal and systemic adjuvant activity and drives a balanced Th1/Th2 biased T cell response. It may have particular utility in the protection of mucosal surfaces from viral infections. Future studies in these areas will involve pre-clinical and clinical assessment of PEI adjuvanticity, and preclinical analysis of cross-linked HIV-1 Env for potential use in man.

Additional research into anti-HIV immunity and allergy

Non-neutralising antibodies may also contribute to vaccine-elicited protection, and we have investigated Fc-mediated killing by innate immune cells of HIV-1-infected T cells (Fc mediated killing is triggered by binding of antibodies to ‘Fc receptors’ on the surface of various cytotoxic immune cells). We will continue to study this using vaccine and patient samples. Additional vaccine-related work in the laboratory relates to how HIV-1 uses cell-to-cell spread between contacting immune cells to evade neutralising antibodies. A final area of work concerns the contribution of oxidative modifications made to proteins in driving allergies and immune hypersensitivity. We are attempting to understand the molecular basis of this induction of aberrant immune responses.

Key publications:

1. Immune focusing and enhanced neutralization induced by HIV-1 gp140 chemical cross-linking. Schiffner T, Kong L, Duncan CJ, Back JW, Benschop JJ, Shen X, Huang PS, Stewart-Jones GB, DeStefano J, Seaman MS, Tomaras GD, Montefiori DC, Schief WR, Sattentau QJ. J Virol. 2013 87:10163-72.
2. Wegmann F, Gartlan K, Harandi AM, Brinckmann SA, Coccia M, Hillson W, Kok W-L, Cole S, Ho L-P, Lambe T, Puthia M, Svanborg C, Scherer EM, Krashias G, Williams A, Blattman JN, Greenberg PD, Flavell RA, Moghaddam AE, Sheppard NC and Sattentau QJ. (2012) Polyethyleneimine is a potent mucosal adjuvant for viral glycoprotein antigens. Nature Biotechnology 30: 883-888.
3. Kong L, Sheppard N, Stewart-Jones G, Robson CL, Chen H, Xu X, Krashias G, Bonomelli C, Scanlan CN, Kwong PD, Jeffs SA, Jones IM and Sattentau QJ (2010) Expression system-dependent modulation of HIV-1 envelope glycoprotein antigenicity and immunogenicity. J. Mol. Biol. 403: 131-147.

ADRIAN SMITH

Developing new vaccines and adjuvants for birds and mammals

My research group is based in the Department of Zoology, University of Oxford, where we explore a variety of topics including immunology and vaccine development against a variety of diseases of birds and mammals. I joined the Department in 2008 after spending 10 years at the Institute for Animal Health, Compton Laboratory, leading a group focussed on enteric immunology. Prior to this, I spent 4 years as a postdoctoral associate with Professor Adrian Hayday at Yale University in Connecticut, USA.

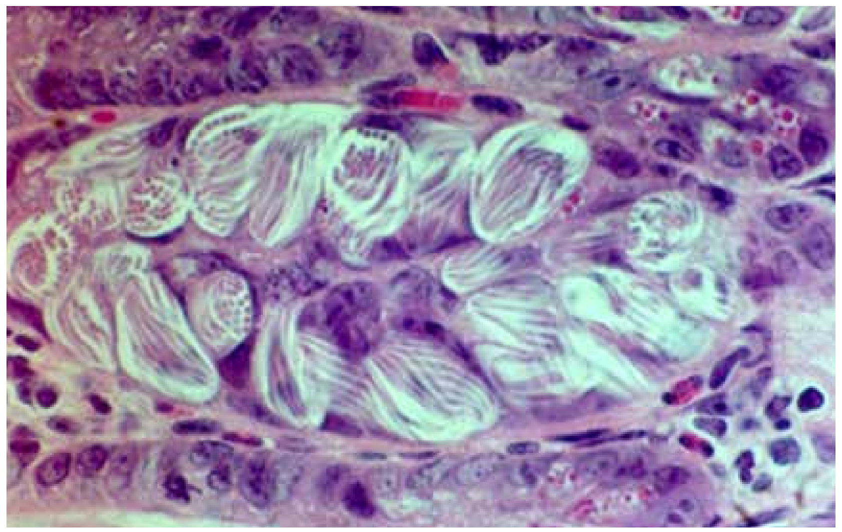
Improving immunity in young animals

Researchers in my group work on the immunology of birds and mammals, with a focus on developing vaccines and on improving the immune system of young animals. In the past few years, we have had notable success in developing strategies for determining which antigens are protective in antigenically complex pathogens (especially bacteria and parasites). We have employed two novel antigen discovery platforms to identify protective antigens, one based upon parasite genetics and the other based upon analysis of the T cell receptor repertoire (Protecta Technology). Both of these methods have the capacity to differentiate between responses that are generated against protective or irrelevant antigens, and both indicate that with complex pathogens most of the response is directed against antigens that are not protective. This point is important, since it is of little use to focus vaccine development on non-protective antigens, and the methods are currently being used to identify new protective antigens for inclusion into vaccines.

We have recently developed a range of tools to analyse the repertoire of the adaptive immune response in a range of different vertebrate species including rodents, humans and chickens. Our studies of T cell and B cell receptor repertoire are currently focussed on defining how different patterns of response or degrees of clonality arise during infection or vaccination, and how these influence the effectiveness of the response. By studying these processes in different vertebrate hosts, vaccination schedules and infection models, we aim to determine conserved and species distinct characteristics of the response. For example, how do the number of available variable gene segments affect the diversity of the responses seen in different animal species, and how relevant are these to developing vaccines?

Pattern recognition in the immune system

The other main thrust of our research programme is the comparative biology of pattern recognition, in particular the ways that different animals respond to molecules that might be included in vaccine adjuvants. In this area, we have recently published work on the nature of chicken Toll like Receptor 15 which is present in birds (and reptiles) but not mammals. This type of work may lead to species-specific adjuvants for use in livestock. Many of the projects have relevance to better understand the evolution of immunological processes and infectious disease.



◀ Photomicrograph of *Eimeria vermiformis* second generation schizonts

Key publications:

1. Blake, D.P., Billington K., Copestake S., Oakes R.D., Quail M.A., Wan, K-L,, Shirley M.W. and Smith A.L. (2011) Genetic mapping identifies novel highly protective antigens for an Apicomplexan parasite. Plos Pathogens, 7 (2) e1001279.
2. Mwangi, W. N., L. P. Smith, Baigent, S.J., Beal, R. K., Nair, V. and Smith, A. L. (2011). Clonal Structure of Rapid-Onset MDV-Driven CD4+ Lymphomas and Responding CD8+ T Cells. PLoS Pathog 7(5): e1001337.
3. Boyd, A.C., Peroval, M.Y., Hammond, J.A., Prickett, M.D., Young, J.R. and Smith A.L. (2012) Toll-like Receptor 15 is unique to avian and reptilian lineages and recognises a novel yeast-derived agonist. J Immunol: 189:4930-4938.

MATTHEW SNAPE (OXFORD VACCINE GROUP)

Meningococcal, pneumococcal and influenza vaccines

I am a Consultant in General Paediatrics and Vaccinology at the NIHR Oxford Biomedical Research Council and the Children's Hospital Oxford, Oxford University Hospitals NHS Trust. Having undertaken my training in paediatrics at the Royal Children's Hospital Melbourne and St Mary's Hospital London, I joined the Oxford Vaccine Group in 2003 and have been employed as a Consultant in General Paediatrics and Vaccinology since 2009. My principle areas of research relate to meningococcal, pneumococcal and influenza vaccines, and attitudes to immunisation in pregnancy.

Meningococcal disease

The European licensing of a vaccine against capsular group B meningococcal disease in 2013 represented a major breakthrough in the prevention of childhood meningitis. In the seven years prior to this the Oxford Vaccine Group (OVG) enrolled over 1000 children and adults in clinical trials of this vaccine, and published seven manuscripts reporting clinical trial data critical for this vaccine's licensure. Research continues post-licensure, with an on-going clinical trial studying the vaccine's immunogenicity in 'at-risk' children with complement deficiencies or splenic dysfunction, and another European Union funded study evaluating gene expression in infants following immunisation with this vaccine. In March 2015 it was announced that this vaccine will be administered to all UK infants at 2, 4 and 12 months of age from late 2015.

The OVG has also recruited over 780 infants and adults to clinical trials evaluating the immunogenicity of a recently licensed capsular group A, C, W and Y meningococcal vaccine (MenACWY). Over the last year there has been a dramatic increase in the incidence of serogroup W meningococcal disease in the UK, such that this serogroup now accounts for a quarter of all invasive meningococcal disease in England and Wales. In response to this increase, it was announced in 2015 that the MenACWY vaccine would be incorporated into the routine adolescent immunisation programme later in this year.

The OVG has also been extensively involved in studies informing vaccine protection against capsular group C meningococcal (MenC) disease, conducting the only clinical trials of a combination Hib-MenC vaccine used as a 12-month booster dose in the UK schedule. Further studies demonstrating waning of vaccine induced antibodies through school years and into adolescence directly informed the introduction of a routine adolescent booster dose of MenC vaccine in 2014, thus providing both direct protection against this devastating illness and maintaining herd immunity for younger children.

Pneumococcal Disease

The introduction of pneumococcal glyco-conjugate vaccines over the past decade has had a dramatic impact on this major cause of childhood meningitis and septicaemia. A 13-valent pneumococcal conjugate vaccine was introduced into the United Kingdom routine immunisation schedule in 2010, replacing the 7-valent vaccine. The Oxford Vaccine Group was the lead site for the clinical trials informing the use of this vaccine in the UK immunisation schedule, and also for a 'follow-on' study providing vital information on the persistence of the vaccine induced antibodies through pre-school years and response to a booster dose administered at that time.

Serogroup B Streptococcus

Serogroup B streptococcus is a major cause of neonatal meningitis, affecting approximately 1 in 2000 births in the United Kingdom. The peak incidence of this disease is in the first week of life, therefore prevention through infant immunisation is not feasible. An alternative strategy is immunisation of pregnant women to induce trans-placental transfer of antibodies to the unborn child, thereby providing them with 'passive immunity' in their first few months of life.

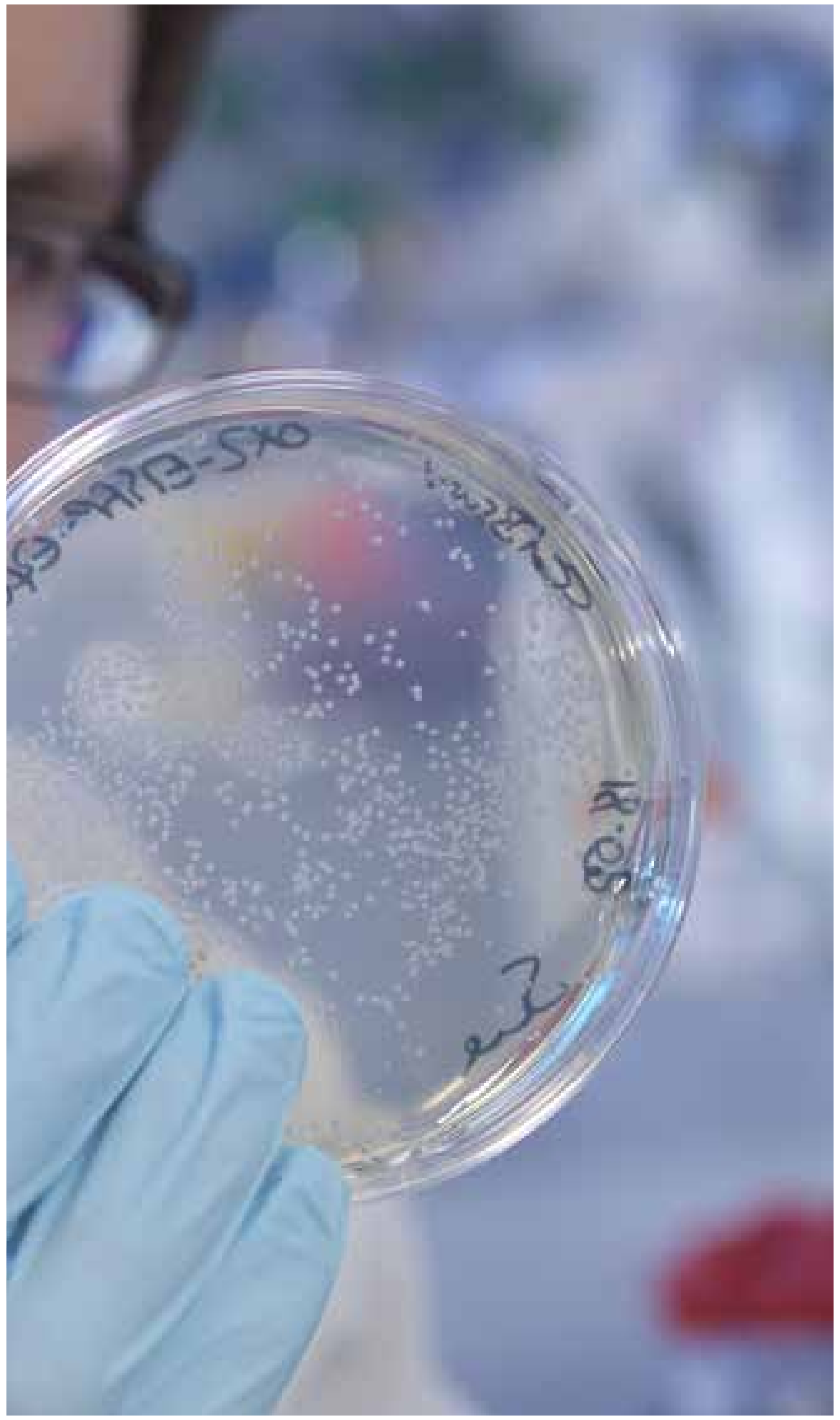
Vaccines for this purpose are currently in development, however the acceptability of such an intervention is uncertain. The Oxford Vaccine group therefore obtained funding from Meningitis Now to conduct a qualitative study of pregnant women and health care professionals involved in their care. Results from an on-line survey have already been published, while individual interviews and focus group discussions have informed a questionnaire survey currently being conducted across 7 sites in the United Kingdom.

Influenza

In 2009/2010 the Oxford Vaccine Group was the lead site for an expedited multi-centre study providing a 'head to head' comparison of the two influenza A H1N1 'swine flu' vaccines available to respond to the influenza pandemic. Over 940 children were recruited in 5 weeks, 270 of whom were recruited by Oxford. The early provision of reactogenicity data to the Department of Health directly informed the decision to offer these vaccines to all children under 5 years of age in the winter of 2009/2010, while a 'follow-on' study conducted in 2010/11 provided novel data demonstrating a clear difference in persistence of protective antibody response between the two vaccines studied.

Subsequent work has compared the gene expression profile of 1 to 2 year olds immunised with either an adjuvanted or un-adjuvanted vaccine in 2012/2013, and supported development of 'quadrivalent' influenza vaccines (containing four rather than the traditional three influenza vaccine strains).

Over the last two influenza vaccine seasons the OVG has participated in clinical trials of the intra-nasal influenza vaccine in egg allergic children. This live attenuated vaccine is routinely recommended for all children aged 2 to 4 years, however it contains small amounts of egg albumin. Accordingly, the vaccine was initially contra-indicated for children with egg allergy, who comprise approximately 3% of the paediatric population in the United Kingdom. The safety data accrued through conduct of these national, multi-centre studies has now provided reassurance that this vaccine can be given in a primary care setting to children suffering non-anaphylactic egg allergy, thus removing this potential obstacle to immunisation.



Key publications:

1. Snape MD, Saroey P, John TM, Robinson H, Kelly S, Gossger N, Yu LM, Wang H, Toneatto D, Dull PM, Pollard AJ . Persistence of bactericidal antibodies following early infant immunisation with serogroup B meningococcal vaccines and pre-school booster dose immunogenicity. Can Med Assoc J. 2013; 185; E715–24
2. Snape MD, Klinger CL, Daniels ED, John TM, Layton H, Rollinson L Pestridge S, Dymond S, Galiza E Tansey S, Scott DA, Baker SA, Jones TR, Yu LM, Gruber WC, Emini EA, Faust SN, Finn A, Heath PT, Pollard AJ. Immunogenicity and reactogenicity of a 13-valent pneumococcal conjugate vaccine administered at 2, 4 and 12 months of age: a double-blind randomized active-controlled trial. Pediatr Infect Dis J. 2010; 29: e80–90
3. Snape MD, Perrett KP, Ford KJ, John TM, Pace D, Yu LM, Langley JM, McNeil S, Dull PM, Ceddia F, Anemona A, Halperin SA, Dobson S, Pollard AJ. Immunogenicity of a tetravalent meningococcal glycoconjugate vaccine in infants: a randomized trial. JAMA. 2008; 299: 173–84

GERALDINE TAYLOR

Vaccines for bovine respiratory syncytial virus and peste des petits ruminants virus

I am Head of the Vaccinology group at The Pirbright Institute. My research interests are directed at developing new and improved vaccines against respiratory syncytial virus, and vaccines against African swine fever virus (ASFV), in collaboration with Linda Dixon's group at Pirbright, and against PPR in collaboration with Michael Baron's group at Pirbright.

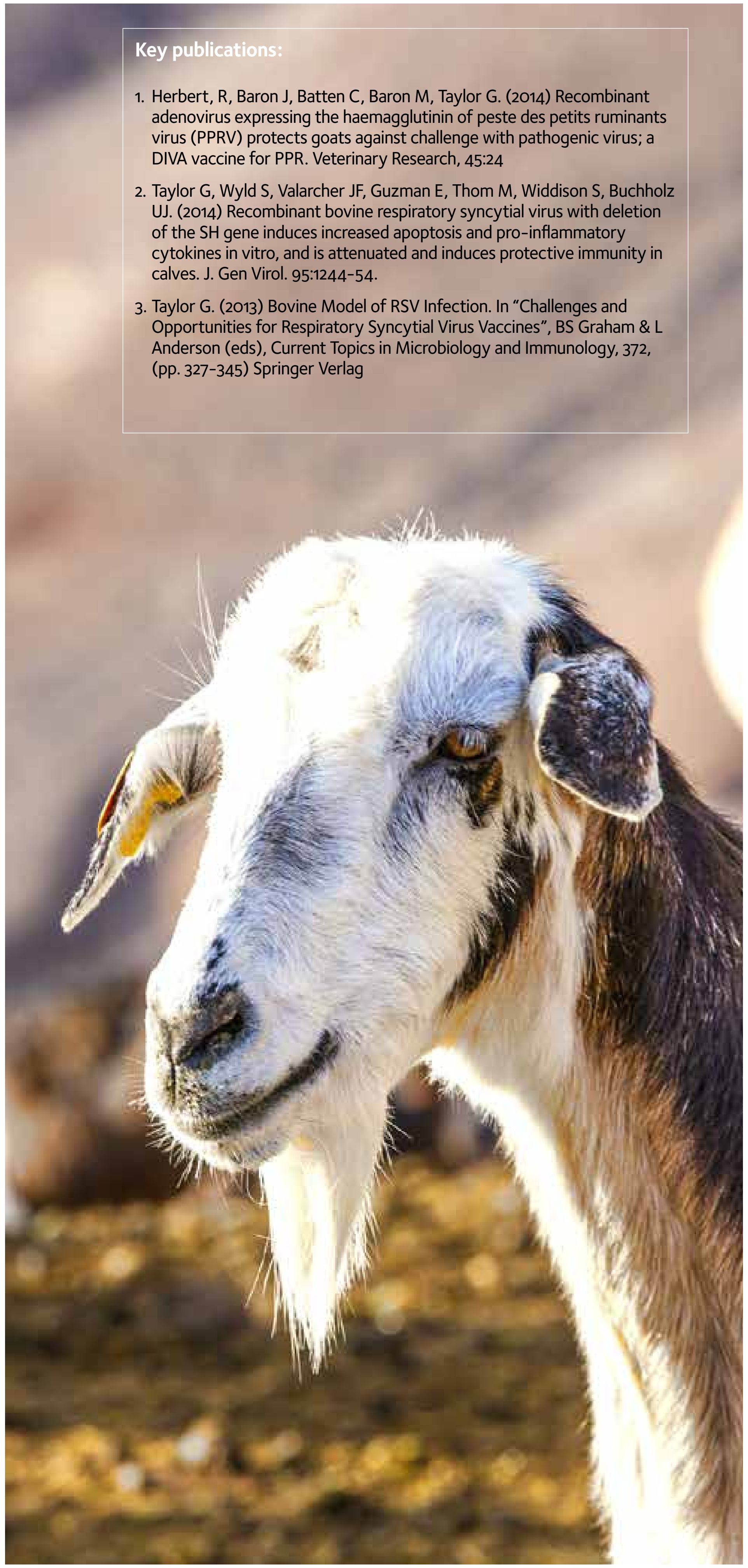
Peste des petits ruminants virus

Peste des petits ruminants virus (PPRV) causes a devastating disease in sheep and goats, with mortality rates reaching up to 70%. Disease is characterised by a fever, ocular and nasal discharges, diarrhoea, pneumonia, and lesions on mucous membranes, particularly in the mouth. Globally, over 1 billion small ruminants, which are of great socio-economic importance amongst poorer livestock keepers in many developing countries, are at risk from PPR. Economic losses due to PPRV are estimated to be $2972.5 million/year, and despite the availability of effective live attenuated PPR vaccines, the distribution of disease has increased in recent years. The eradication of the closely related rinderpest virus has provided a road map for the elimination of PPRV; vaccination and surveillance are central to such an eradication programme. However, animals that have been vaccinated with live PPR vaccines produce the same spectrum of antibodies as those that have been infected with virulent virus, so it is not possible to distinguish infected and vaccinated animals.

My group, and that of Michael Baron at the Pirbright Institute, have shown that a single vaccination with a replication-defective human adenovirus expressing the PPRV surface glycoprotein H, is safe and immunogenic in goats, and induces complete protection against challenge with virulent PPRV 4 months after vaccination. The vaccinated goats develop antibodies only to the H protein, whereas animals infected with virulent virus or given live vaccine have antibodies to other PPRV proteins. The novel glycoprotein H vaccine therefore allows the differentiation of vaccinated from infected animals, and will facilitate PPRV sero-surveillance programmes and speed up the steps leading to disease eradication. Future studies funded by Bill and Melinda Gates, Grand Challenges Explorations, will evaluate the vaccine's efficacy in native goats in Kenya.

Bovine respiratory syncytial virus

Bovine respiratory syncytial virus (BRSV) is a major cause of respiratory disease in young calves. As well as being an important cause of economic loss to farmers, BRSV infections impact on animal welfare. Although commercial BRSV vaccines are available, there is a need for greater efficacy especially in young calves with maternally-derived antibodies (MDA), which are the main target for vaccination. The ability to manipulate the genome of RS viruses has provided opportunities for the development of stable, live attenuated virus vaccines. However, a problem with this approach has been that attenuation is usually based on decreased virus replication, which is associated with reduced immunogenicity. My group has analysed the effects of deleting the SH protein, a small membrane-anchored protein that is non-essential for virus replication *in vitro*, on the pathogenesis of BRSV in young calves. Although replication of recombinant (r)BRSV lacking SH (ΔSH) and wild type (WT) rBRSV were similar *in vitro*, replication of rBRSVΔSH was moderately reduced in the lower, but not the upper, respiratory tract of experimentally infected calves. Furthermore, in contrast to calves infected with WT virus, calves infected with rBRSVΔSH did not develop pneumonic lesions. Despite having reduced ability to replicate in the lungs of calves, virus lacking SH appeared to be immunogenic and effective in inducing resistance to virulent virus challenge 6 months later. Furthermore, a single intranasal vaccination induced protection even when given to calves with MDA. These findings suggest that BRSVΔSH may be an ideal live attenuated virus vaccine candidate for calves, combining safety with a high level of immunogenicity.



Key publications:

1. Herbert, R, Baron J, Batten C, Baron M, Taylor G. (2014) Recombinant adenovirus expressing the haemagglutinin of peste des petits ruminants virus (PPRV) protects goats against challenge with pathogenic virus; a DIVA vaccine for PPR. Veterinary Research, 45:24
2. Taylor G, Wyld S, Valarcher JF, Guzman E, Thom M, Widdison S, Buchholz UJ. (2014) Recombinant bovine respiratory syncytial virus with deletion of the SH gene induces increased apoptosis and pro-inflammatory cytokines in vitro, and is attenuated and induces protective immunity in calves. J. Gen Virol. 95:1244-54.
3. Taylor G. (2013) Bovine Model of RSV Infection. In "Challenges and Opportunities for Respiratory Syncytial Virus Vaccines", BS Graham & L Anderson (eds), Current Topics in Microbiology and Immunology, 372, (pp. 327-345) Springer Verlag

Human respiratory syncytial virus

BRSV is closely related to human (H)RSV, which 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. Annual epidemics of RSV infection occur during the winter and early spring, causing most severe disease in infants less than 6 months of age. Nearly all children have been infected with HRSV by 2 years of age and the virus readily re-infects throughout life, even with closely related virus strains. 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 no effective HRSV vaccine, and progress in vaccine development has been hampered by a vaccine programme in the 1960s involving an inactivated viral vaccine that enhanced disease following RSV infection, rather than preventing it, in children not previously exposed to the virus. 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 the circulation of RSV in the community. My group, in collaboration with ReiThera (previously Okairos), has used a new approach to induce protective immunity. A replication-defective chimpanzee adenovirus (ChAd) vector, to which there is limited pre-existing immunity in man, and an attenuated poxvirus vector, MVA, expressing a string of conserved RSV proteins, were evaluated for their ability to protect calves against bovine (B) RSV. Studies in calves showed that intranasal vaccination with ChAd/RSV, followed by intramuscular boosting with MVA/RSV, induced antibodies able to neutralise RSV as well as T cells that help to clear the virus. This novel vaccine was safe and induced complete protection against BRSV infection in calves. The vaccine is now in Phase I clinical trials 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.

MARTIN VORDERMEIER
Human and bovine tuberculosis

I am a cellular immunologist with more than 24 years' experience of working on tuberculosis (TB), both human and bovine. At present, I lead a work group at the Animal Heath and Veterinary Laboratories Agency (AHVLA) engaged in vaccine development for cattle TB vaccines, immunodiagnostic development and biomarker studies looking at correlates of protection and disease development.

Mycobacterial infections in cattle

I am interested in host responses to mycobacterial infections, in particular *Mycobacterium bovis*, in cattle. Most of my work is geared towards developing better vaccines or vaccine strategies that improve on BCG, and the development of associated vaccine-strategy compatible immune-diagnostic reagents not compromised in their specificity by vaccination (so-called DIVA reagents). Underpinning both of these applications are studies to understand the mechanisms of protective immunity, and in particular why vaccination fails in a proportion of vaccinated individuals. These biomarker studies are therefore aimed at generating robust stage gating parameters, whose application would accelerate vaccine development by reducing the reliance on expensive and resource-intensive large animal CL3 accommodation. Our approaches are closely linked and harmonised as much as possible with the effort to produce better human vaccines, in particular with Prof. McShane's group at the Jenner Institute.

Vaccines against bovine TB, *Mycobacterium bovis*

Over the last few years we have concentrated on vaccination strategies that combine BCG priming with heterologous boosting, using recombinant viral vectors such as MVA and human adenovirus type 5. We have demonstrated that a strategy of combining BCG with Ad5 expressing the protective antigen Ag85A can significantly improve vaccine efficacy measured in an experimental challenge model, compared to BCG vaccination alone. Using samples generated from these experiments, we have also undertaken biomarker discovery studies applying both hypothesis and data-driven approaches. For example, we have shown that memory T cells measured by cultured ELISPOT correlated with protection and the duration of immunity when measured after vaccination but before infection, using the outcome of infection measured at post-mortem as a relevant clinical endpoint.

Data-driven approaches have concentrated on a host (cattle) RNASeq methodology, which identified a number of immune markers that predicted the outcome of vaccination, such as IL17A and IL22. The validation of these markers in a larger sample set is a priority for the future. We will also expand our biomarker repertoire by conducting, for example, more in-depth RNASeq studies, and including parameters such as micro-RNA expression to study gene regulation. We are in the process of characterising the cells that are being measured in the cultured ELISPOT, and those that are producing IL-22, with a view to gaining more insights into the biology of these populations and to design simpler biomarker assays more amenable to routine testing.

Key publications:

1. Bhuju, S., Aranday-Cortes, E., Villarreal-Ramos, B., Xing, Z., Singh, M. & Vordermeier, H. M. 2012. Global gene transcriptome analysis in vaccinated cattle revealed a dominant role of IL-22 for protection against bovine tuberculosis. *PLoS Pathog*, 8, e1003077.
2. Dean, G., Whelan, A., Clifford, D., Salguero, F. J., Xing, Z., Gilbert, S., McShane, H., Hewinson, R. G., Vordermeier, M. & Villarreal-Ramos, B. 2013. Comparison of the immunogenicity and protection against bovine tuberculosis following immunization by BCG-priming and boosting with adenovirus or protein based vaccines. *Vaccine*, 32, 1304-10.
3. Jones, G. J., Steinbach, S., Clifford, D., Baldwin, S. L., Ireton, G. C., Coler, R. N., Reed, S. G. & Vordermeier, H. M. 2013. Immunisation with ID83 fusion protein induces antigen-specific cell mediated and humoral immune responses in cattle. *Vaccine*, 31, 5250-5.

Animal transmission model for bovine TB

We have established a transmission model in Ethiopia that allows us to test vaccine (BCG) efficacy in a natural transmission setting. We are also interested in antigen discovery, and have recently begun to look at antigens recognised by non-conventional immune cell populations such as natural killer T cells, by mining antigens based on lipids and glycolipids. This will form a main area of our future research, in particular to determine whether such antigens contribute to immunity and whether they can be used as additional subunit vaccines against bovine TB.

RESEARCH PROGRAMMES AND CORE FACILITIES

CLINICAL TRIAL COLLABORATIONS IN AFRICA

Malaria, HIV-1 and TB

▲ The Kenya Medical Research Institute (KEMRI) at Kilifi

Over the last few years, the Jenner Institute's activities in Africa have been guided by its strategy of translational research, specifically in progressing candidate vaccines for the prevention of malaria, TB and HIV-1 from initial Phase I/IIa clinical trials in Europe to Phase I/IIb clinical trials in target populations in Africa. Transitioning these vaccines into African clinical trials requires satisfactory safety, immunogenicity and in some cases efficacy data from the Oxford vaccine trials. This has resulted in several collaborations with old and new partners, either directly or as part of an international consortium of partners (Table 1). Major clinical trial consortia involving Jenner Institute staff/scientists include the Malaria Vectored Vaccines Consortium (MVVC/MVVC2) for malaria, PedVacc 001 and PedVacc 002, and HIV-CORE004 for HIV, as well as several collaborations enabling the assessment of the TB vaccine MVA85A in different populations (Table 1). These collaborations have ensured the performance of clinical trials to international standards at African trial sites and provided invaluable clinical trial data for these vaccine fields.

Malaria vaccine trials

Within the period 2011-2013, four malaria vaccine trials were initiated in Africa. These vaccine trials tested the prime-boost combination of viral vectors expressing the antigen ME-TRAP (ChAd63 ME-TRAP and MVA ME-TRAP), which targets the liver-stage life cycle of *P. falciparum* malaria. VAC042 (2011-2013) was a safety and immunogenicity clinical trial in infants aged either 10 weeks or 5-12 months. VAC046 and VAC047 (2012-2013) were efficacy, safety and immunogenicity clinical trials in adults in Kenya and Senegal, respectively. Both of these clinical trials involved an intensive study design that required the administration of the study vaccines, clearance of malaria parasites using anti-malaria drug combination therapy, and follow up for the detection of malaria parasitaemia by PCR over a two-month period. VAC050 (2012-2014) is a safety, immunogenicity and efficacy clinical trial in children aged 5-17 months in Burkina Faso. Intertwined with clinical trial performance, staff at the Jenner Institute have been involved with capacity building and infrastructure/laboratory upgrades at African clinical trial institutions. Aside from assistance with the purchasing of state-of-the-art laboratory equipment and training on the conduct of immunoassays and Polymerase Chain Reaction (PCR) molecular biology techniques, Jenner staff have ensured that the quality assurance processes at these African laboratories meet the required international standards for on-going and future studies. This was mainly achieved by on-the-job training, combined with laboratory and clinical trial staff exchange visits with the specific clinical trial sites. These staff training and exchange visits have resulted in better quality data from assays conducted in laboratories in Africa.

Table 1: African Clinical Trial collaborators

S/no	Lead Collaborator(s)	Institution	Disease Area	Project
1.	Phillip Bejon	KEMRI-Kilifi, Kenya	Malaria	MVVC/MVVC2
2.	Kalifa Bojang/Muhammed Afolabi	MRC Unit, The Gambia	Malaria	MVVC/MVVC2
3.	Sodiomon Sirima/Alfred Tiono	CNRFP, Burkina Faso	Malaria	MVVC/MVVC2
4.	Badara Cisse	UCAD, Senegal	Malaria	MVVC/MVVC2
5.	Seth Owusu Ageyi	KHRC, Ghana	Malaria	MVVC2
6.	Michelle Tameris/ Hassan Mahomed/ Greg Hussey/ Mark Hatherill/ Willem Hanekom	SATVI, South Africa	TB	TB020
7.	Michelle Tameris	SATVI, South Africa	TB	TB027
8.	Mark Hatherill	SATVI, South Africa	TB	TB029
9.	Anneke Hesseling	Stellenbosch University, S Africa	TB	TB029
10.	Souleymane Mboup	CHU Le Dantec, Senegal	TB	TB021
11.	Robert Wilkinson	UCT, South Africa	TB	TB021
12.	Martin Ota	MRC Unit, The Gambia	TB	TB021
13.	Alison Elliott/ Pontiano Kaleebu	MRC/UVRI, Uganda	TB	TB036
14.	Sarah Rowland-Jones/Katie Flanagan	MRC Unit, The Gambia	HIV	PedVacc 001
15.	Walter Jaoko	University of Nairobi, KAVI-ICR	HIV	HIV-CORE 004, PedVacc 002

▲ The Consortium for the MVA85A efficacy trial in HIV-infected adults, with members from UCT, CHU Le Dantec, MRC The Gambia, Aeras and Oxford

HIV-1 vaccine trials

Three HIV-1 vaccine trials have been carried out since 2011. The EDCTP (European and Developing Countries Clinical Trials Partnership) funded project entitled *"Building capacity of Infant HIV-1 Vaccine Clinical Trial Centres in Nairobi, Kenya and Fajara, The Gambia"*, with the acronym "PedVacc", ran from 2008 to 2012. As part of the study, facilities were substantially refurbished and redesigned, significantly increasing capacity and efficiency. Staff were trained in many activities (laboratory, GCP, data management, project management) and six Masters and PhD students were supported. Another EDCTP and International AIDS Vaccine Initiative funded study, HIV-CORE 004, is currently underway in Nairobi and is designed to evaluate the safety and immunogenicity of different delivery regimens using three novel HIV-1 vaccines: a) pSG2.HIVconsv DNA with and without electroporation; b) adenovirus Ad35-GRIN; and c) poxvirus MVA.HIVconsv administered in heterologous prime-boost regimens.

TB vaccine trials

For the TB group, this period saw the first efficacy trial of a new TB vaccine in infants in 40 years, with the TB020 phase IIb double-blind, placebo controlled efficacy trial of MVA85A at SATVI, South Africa. 2797 BCG vaccinated infants were enrolled at 4-6 months of age, and followed up every 3 months for up to 37 months. MVA85A has also been in trial in HIV-infected adults in Cape Town (UCT) and Dakar (CHU Le Dantec). During both these trials, significant capacity building has been achieved at the clinical sites in terms of clinical and laboratory facilities, as well as staff training, substantially improving these sites' future clinical trial capabilities. Additionally, during this period MVA85A has been in trial TB029, a phase II randomised controlled trial to evaluate the safety and immunogenicity of MVA85A prime and delayed BCG boost vaccination in HIV-exposed infants in South Africa. More recently, in 2014, an exciting new collaboration with UVRI Uganda was initiated using MVA85A to investigate the effect of *Schistosoma mansoni* infection on immune responses to vaccination in Ugandan adolescents. This is the first IMP trial for this Ugandan team, and the sharing of clinical trial expertise from the Oxford team has provided invaluable capacity building. All these collaborations with our African partners have been crucial in moving the TB vaccine field forwards.

Training and technology development

An important reality in conducting research in Africa is the difficulty African scientists face in attending training at institutions outside their regions of origin. Recognising this, the Jenner Institute initiated the five day Masters level "Vaccinology in Africa" course in September 2013. More detail is given in the Education section (p81). Finally, in addition to new vaccines that will enter the Jenner Institute vaccine portfolio in the near future, we recognise the urgent need for transfer of technology enabling the development of pre-clinical vaccinology and vaccine design to institutions in Africa. This includes the ability to set up vaccine manufacturing capacity in African countries. This is a huge task, but funds permitting we hope that we will be able to initiate the process in incremental steps over the next few years.

PROSTATE CANCER PROGRAMME

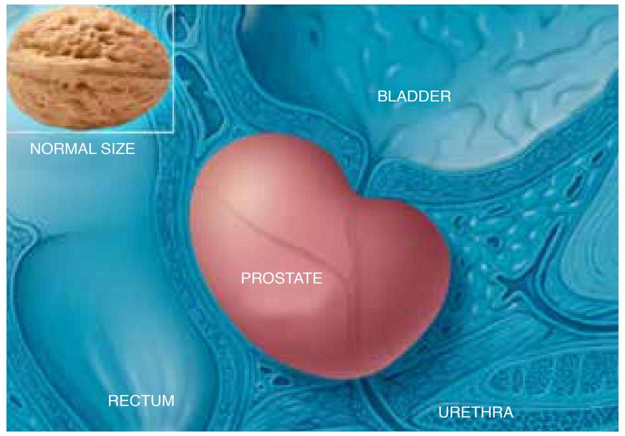
The prostate cancer vaccine programme was launched in 2012, building on the success of heterologous viral-vectored vaccination employing adenovirus and MVA vectors in various infectious disease settings. The programme is led by Dr. Irina Redchenko.

Prostate cancer is the most prevalent non-cutaneous malignancy, and the second most common cause of cancer-related death among men in developed countries. The treatment options for advanced prostate cancer are limited, with immunotherapy one of the few options. The only licensed vaccine for the therapeutic treatment of prostate cancer, Sipuleucel-T, is an individualised treatment that costs over $90,000 per patient and provides a modest survival benefit of 4.5 months. A more efficacious and affordable vaccine is clearly needed.

A therapeutic vaccine for prostate cancer

The development of a vaccine against cancer is a challenge because tumours originate from normal tissues that are invisible to the immune system. Our work has started by selecting several prostate tissue associated antigens (PAP, PSCA, STEAP and PSMA) and expressing them from simian adenovirus (ChAdOx1) and MVA virus vectors in a mouse model, in order to break immunological tolerance to these self-antigens. Following on from the immunogenicity studies, we have demonstrated that a T cell immune response induced against some of these antigens is modestly protective in a mouse tumour challenge model. The on-going preclinical studies are focussed on improving the vaccine's tumour-protective efficacy, by counteracting the suppressive tumour microenvironment with monoclonal antibodies against immune checkpoint inhibitors (PD-1 and PDL-1 mAbs).

In parallel, with support from a recently awarded European Commission grant, we are currently progressing a heterologous viral vector-based vaccination strategy into clinical trials in prostate cancer. A Phase I clinical trial in early stage prostate cancer patients deploying ChAdOx1 and MVA vectors targeting a "pan-tumour" antigen, 5T4, (previously evaluated in the clinic in a homologous MVA vaccination setting) should initiate in the first quarter of 2015, followed by a Phase II efficacy study one year later.



Location of the prostate gland

VACCINE DELIVERY PROGRAMME

Sugar-membrane stabilisation of vaccines

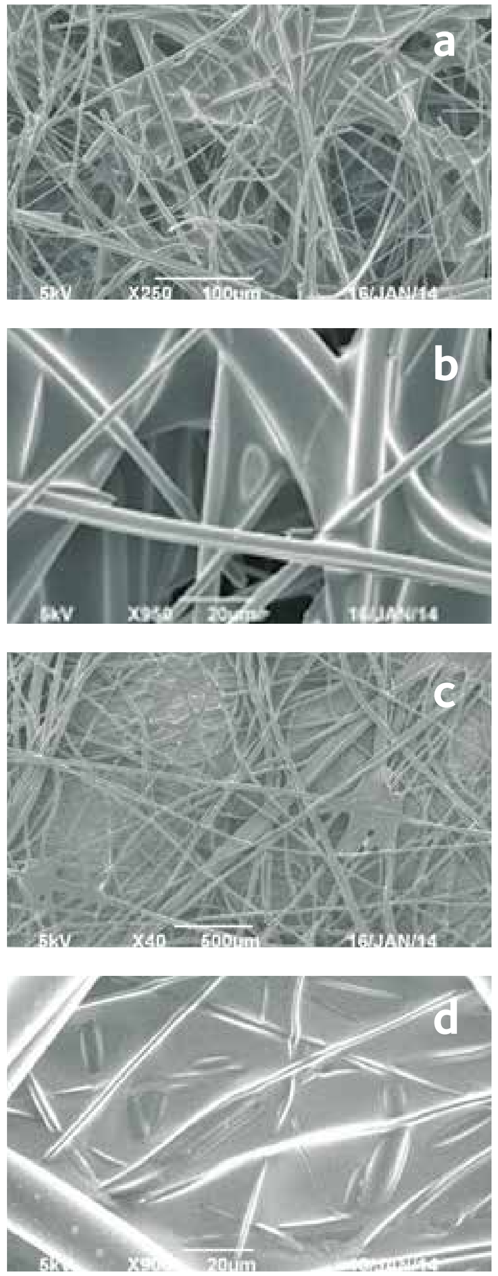
In both developed countries and the developing world there is an urgent need for vaccines that are thermostable. The impact of vaccination is compromised significantly by the need to maintain a cold chain for vaccine distribution and administration. Huge numbers of vaccine doses are consequently lost, thereby vaccination is more expensive, fewer individuals are effectively immunised and lives are lost. Introducing thermostable vaccines into vaccination programmes for developing countries would reduce, and could eventually eliminate, the need for the cold chain. The advantages of such a breakthrough are well known and documented: maintaining the cold chain has been estimated by the World Health Organization to cost up to $200m each year, and to increase the cost of immunisation by 14%. Vaccine damage as a result of cold chain breakages costs several million dollars annually.

How the technology works

As with other approaches to stable vaccine formulation, sugar-membrane stabilisation technology adheres to the basic principle that macromolecules require water to perform physiological activities and to retain their structural integrity. The simple principle of removing water from a molecule's environment can inhibit its intrinsic activity, keep it immobile and thus enhance its shelf life. We have exploited the ability of disaccharides, in particular trehalose and sucrose, to form inert glasses on specific membranes after dehydration to less than 5% water content. A sugar glass is an infinitely viscous anhydrous liquid in which molecules, including proteins and viral particles, can be immobilised and remain stable for long periods of time. A crucial component of the technology is the use of membranes composed of thin fibres, to provide a large surface area that can be thinly coated or intercalated with sugar glass containing vaccine. Impregnated membranes can potentially be stored at ambient temperatures for long periods of time, and the vaccines rapidly reconstituted in a liquid buffer phase with very little loss of active material. The sugar-membrane technology was originally developed as a collaboration with Cambridge Biostability from 2005-2009, as part of the Gates Grand Challenges in Global Health programme.

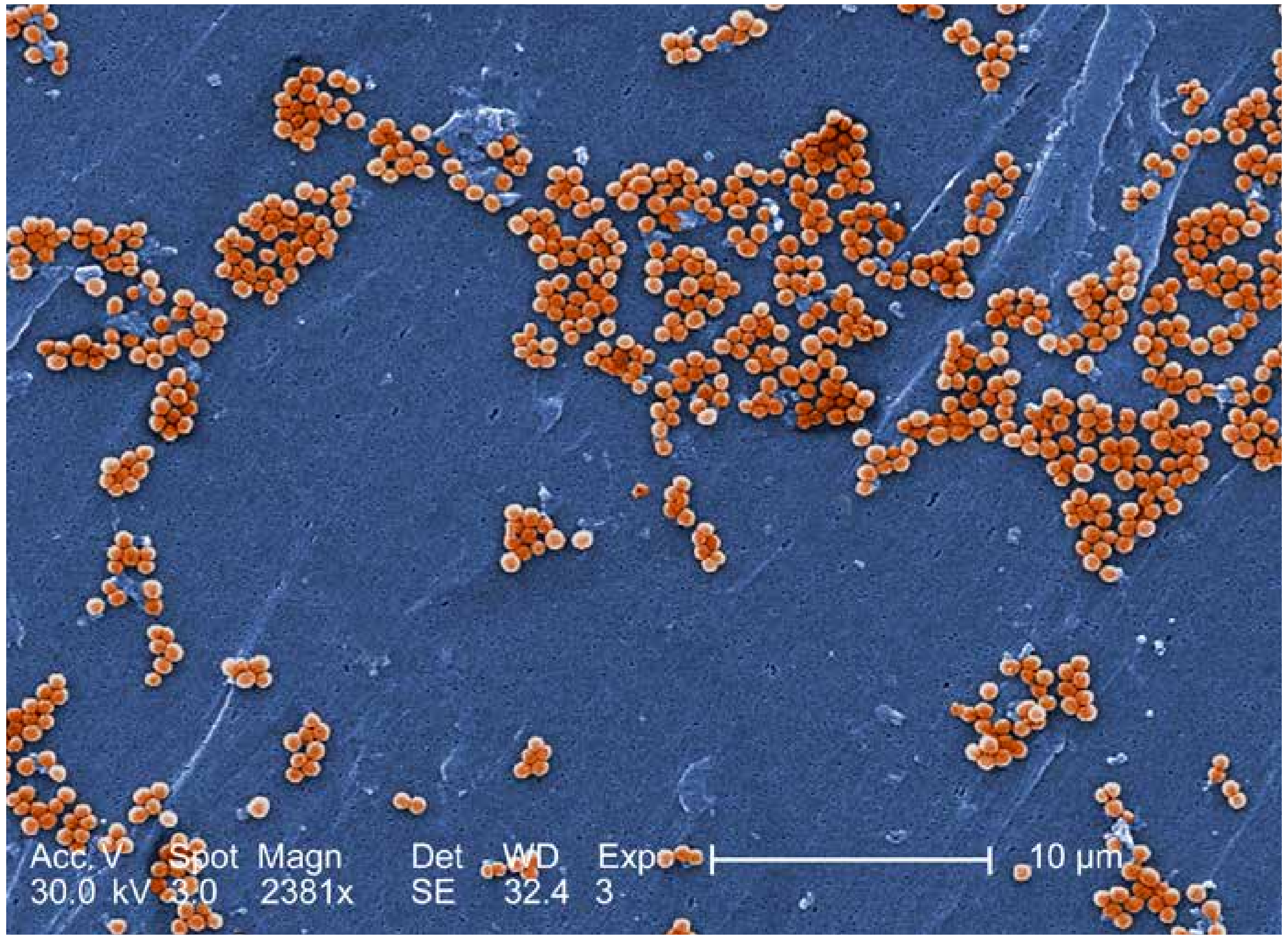
Successful vaccine stabilisation

We have stabilised a range of different vaccines at temperatures of 25-55°C over weeks, and in some cases many months, including: a) live attenuated viral vectors (Adenovirus and modified vaccinia virus Ankara, MVA) that are in Phase II clinical development for diseases such as malaria and HIV; b) a live attenuated virus vaccine (measles); and c) recombinant protein particles (hepatitis B and human papilloma virus) formulated with and without different adjuvants. We have worked in collaboration with a biopharmaceutical company to stabilise one of their vaccine products.



Electron micrograph images showing thin layers of sugar-glass containing vaccine formed on different membranes

▼ Photomicrograph of *Eimeria vermiformis* second generation schizonts



MRSA AND *STAPHYLOCOCCUS AUREUS*

The *S. aureus* programme is led by Dr David Wyllie, a clinical microbiologist involved in infectious disease surveillance and control. David has a PhD in innate immune recognition of bacteria and has worked to improve the immunogenicity of viral vectors. Since 2010, David has led a *S. aureus* vaccine development project, which aims to take a candidate into Phase I clinical trials.

Staphylococcus aureus is one of the most important human pathogens, of which MRSA (meticillin-resistant *Staphylococcus aureus*) species are resistant variants. Common disease manifestations include skin abscesses (boils), with less common but more serious disease including wound infections (sometimes after surgery), bone infections, joint infections (septic arthritis) and heart infection (endocarditis). Disease is caused both in the community, and in hospitals, where it is estimated that about half of all infections are due to *Staphylococcus aureus*. The organism is also found in farm animals, including cows and pigs.

S. aureus vaccine development is complicated by an incomplete understanding of both the mechanisms of disease pathogenesis, and the mechanisms by which the host protects itself from *S. aureus*. This was illustrated by a recent Phase III efficacy trial (the V710 trial) in which a vaccine against a cell-surface protein appeared to be immunogenic in man, but increased the severity of disease and did not offer significant protection.

Viral vectors developed in the Jenner Institute allow us to generate potent immune responses against a wide range of antigens, including those from *S. aureus*. We have identified a cell-surface lipoprotein that appears to have some efficacy as a vaccine; the protective responses appear associated with high levels of T cells against this antigen. This is in keeping with data published by other groups suggesting that T cell action, as well as the induction of antibodies, may be very important in *S. aureus* protection. Because of this data, we are currently working as part of an EU-funded programme (www.bellerophon-project.eu/about-bellerophon) to generate *S. aureus* vaccines eliciting both T and B cell responses, using vectored vaccines. A multi-antigen vaccine is being evaluated, with a view to possible phase I assessment later in the programme. We are also working on an antigen-discovery programme, which is supported by a bacterial RNA profiling project.

Key publications:

1. Decline of meticillin-resistant Staphylococcus aureus in Oxfordshire hospitals is strain-specific and preceded infection-control intensification. Wyllie DH, Walker AS, Miller R, Moore C, Williamson SR, Schlackow I, Finney JM, O'Connor L, Peto TE, Crook DW. BMJ Open. 2011 Aug 27;1(1):e000160.
2. Irradiated wild-type and Spa mutant Staphylococcus aureus induce anti-S. aureus immune responses in mice which do not protect against subsequent intravenous challenge. van Diemen PM, Yamaguchi Y, Paterson GK, Rollier CS, Hill AV,Wyllie DH. Pathog Dis. 2013 Jun;68(1):20-6.
3. Surveillance of infection severity: a registry study of laboratory diagnosed Clostridium difficile. Schlackow I, Walker AS, Dingle K, Griffiths D, Oakley S, Finney J, Vaughan A, Gill MJ, Crook DW, Peto TE, Wyllie DH. PLoS Med. 2012;9(7):e1001279.

THE CLINICAL BIOMANUFACTURING FACILITY (CBF)

The CBF is headed by Dr Sarah Moyle. Prior to joining CBF in 2008, Sarah had over 30 years' experience including research within both academic and industrial sectors, initially involving research and development management of people and projects, and later in Quality Assurance in formally regulated translational environments.

Since 1995, the Clinical BioManufacturing Facility (www.cbf.ox.ac.uk) has had an unrivalled track record in bringing novel products to the clinic for both medical researchers and some commercial collaborators. The CBF enables academic-led translational research in Oxford to progress effectively, both in terms of numbers of products it has succeeded in manufacturing, and also the speed of progress from the research lab to the manufacture of novel first-in-class products for phase I first-in-man clinical trials.

In 2004, the CBF became the first (and for a while the only) university facility to hold a Medicines and Healthcare products Regulatory Agency (MHRA) Manufacturing Authorisation, permitting it to manufacture Investigational Medicinal Products (IMPs) for phase I /II and III clinical trials. This authorisation permits it to manufacture a broad range of cutting edge biotechnology products for clinical application, including more complex Advanced Therapy Medicinal Products (ATMPs). Products include: viral vaccines, adjuvants, gene therapy products, cellular therapies, viral therapies, proteins, and monoclonal antibodies. Over the last 19 years, the facility has proved itself as a key asset for the translational research programmes of the University of Oxford, facilitating cost effective and rapid translation of basic research to clinical trials in research areas for which there is no or limited GMP (good manufacturing practice)-compatible manufacturing methodology or history, because they are ground breaking, highly novel in nature or possibly even a 'disruptive technology'. The CBF opened in 1995 as the Therapeutic Antibody Centre (TAC), and for 11 years manufactured monoclonal antibodies and other related biologicals that have been used worldwide in clinical trials involving more than 5,000 patients. With the maturing of monoclonal antibody manufacturing technologies, the facility moved from the Sir William Dunn School of Pathology to the Jenner Institute in the Nuffield Department of Medicine, and started manufacturing viral vectors for use as novel vaccines and gene-based therapeutics. In October 2007, the first clinical trial volunteer was immunised with a novel malaria vaccine manufactured by the CBF (AdCh63 ME-TRAP). Since then, over 1000 volunteers have been immunised with this vaccine in more than 15 clinical trials. In total, over 1400 volunteers have received eleven different CBF-manufactured vaccine vectors since 2007.

Manufacturing at the CBF

Manufacturing IMPs (investigational medicinal products) to GMP standards for clinical trials on the Churchill Hospital site is a major enabling factor for translational research in the Jenner Institute, and also helps strengthen the Biomedical Research Centre partnership between the Oxford University Hospitals Trust and the broader University of Oxford. It also enables close interaction between the research workers (located in the ORCRB) and the clinical team (located at the CCVTM), and thus considerably speeds up the translation pathway from fundamental scientific advances into clinical research with the ultimate aim of benefiting patients by providing new and better treatments.

▶ The CBF team

Manufacturing and Process Development

Adenovirus vaccines or starting materials made and released by CBF 2011-2013

Name of Project	Product	Starting material	Process development	Tox. and stability batches	GMP manufacturing/ release toclinical trial (year)	"Company" involvement
AdCh63 ME-TRAP (large batch)	Malaria Vaccine	CBF	CBF	N/A	CBF (2011)	
AdNRGM	Cancer Therapy	CBF	CBF	CBF	CBF (2011)	University of Birmingham
ChAd63CS	Malaria Vaccine	CBF	CBF	CBF	CBF (2012)	
ChAdOx1 NP + M1	Flu Vaccine	CBF	CBF	CBF	CBF (2012)	
ColoAd1	Cancer Therapy	CBF (2012)	CBF	Ark	Ark Finland	Hybrid Systems/PsiOxus
ChAd63 PvDBP	Malaria Vaccine	CBF	CBF	CBF	CBF (2013)	
ChAdOx1 85A	TB Vaccine	CBF	CBF	CBF	CBF (2013)	(Company has looked to licence early)
ChAd63 RH5	Malaria Vaccine	CBF (2013)	Okairos/GSK	Okairos	Advent Italy	GSK

Clinical Trial Labelling and Certification

Before a product can be used in a clinical trial, it has to be certified by a Qualified Person (QP) and labelled according to the European Clinical Trials Directive (2004). The CBF not only releases its own products to trial, but also assists clinical researchers with the importation, QP certification and labelling of IMPs from within and outside the European Union (EU). Between 2011 and mid-2014, 11 new batches of CBF products and 29 batches of external IMPs (imported from the US and EU countries) were certified for 27 different vaccine trials, two of which took place in endemic areas. As part of the importation process, several manufacturing sites in the US, Italy, Sweden, Norway and the Netherlands were audited by our QPs to ensure that the investigational medicinal products (IMPs) were manufactured to EU GMP.

Disease Area	Number of certified/labelled CBF batches	Number of certified/labelled non-CBF batches	Number of clinical trials
Malaria	3	15	10
Influenza	1	2	5
Tuberculosis	1	5	5
HIV	1	2	3
other (HCV, choroideremia, prostate cancer)	5	5	4
Total	**11**	**29**	**27**

TRANSCRIPTOMICS CORE FACILITY (TCF)

Dr Adaikalavan Ramasamy is Head of the Transcriptomics Facility and Senior Leadership Fellow in Bioinformatics. Adai joined the Jenner Institute in December 2013.

Transcriptomics is the measurement of the expression of thousands of genes simultaneously by quantifying RNA levels, to create a global picture of cellular function and examine differences between samples, for example blood lymphocytes isolated from vaccinated or diseased individuals compared to controls. The Transcriptomics Core Facility (TCF) was established in late 2013, with the support of a Wellcome Trust Strategic Award, and consists of two bioinformaticians and a wet lab scientist. The purpose of this facility is to support Jenner Investigators in identifying correlates of immunogenicity and efficacy for a broad range of human and veterinary vaccines, and to evaluate new immunomodulatory molecules suggested by transcriptomics data.

The Jenner Institute has pioneered the development of many novel vaccine candidates. Clinical trial data from some of these candidates are encouraging, although there are often variations in immunogenicity and efficacy between individuals in a given trial. We can also use transcriptomics to understand why some vaccinees are not protected when challenged with infectious agents, while others are protected. Understanding these differences can lead to new ideas for developing improved vaccines.

Services offered by the facility

The TCF provides: (1) funding for consumables; (2) wet lab services; and (3) bioinformatics analysis. The TCF can fund a maximum of 50% of the study lab consumables costs for Jenner Investigators. The standard wet lab services include the following RNA processing steps: extraction, globin clearing, amplification, hybridisation onto microarray chips and quality assessment after each step. As of July 2014, the TCF has provided partial funding amounting to £72,175, and wet lab services to generate transcriptomics data using Illumina HT12-v4 microarray chips for 2,513 samples from 10 different vaccine trials (including malaria, TB, influenza, RSV001, meningococcal disease, and Hepatitis B and C).

Bioinformatics, statistical and other analytical services are available at no cost to Jenner investigators. These include design, data management, quality control and analyses as well as re-using publicly available datasets for replication or meta-analyses with their own datasets. We also have experience of analysing RNA-sequencing, ChIP-Seq and eQTL datasets.

To date, we have conducted a preliminary analysis of transcriptomics data from two malaria vaccine trials that have been generated in-house. In addition, we have also analysed existing data from a Kenyan malaria challenge trial and from the IDEA consortium, a large European Commission 7th Framework Programme (FP7), to look at genes related to malaria and TB in the presence and absence of worm infection.

▶ Left to right:
Dr Julius Muller,
Dr Eneida Parizotto,
Dr Amanda Stranks,
Dr Adaikalavan Ramasamy.

VIRAL VECTOR CORE FACILITY

The Viral Vector Core Facility (VVCF) produces all recombinant viral vector vaccines required by Jenner Investigators, and also supplies external academic and industrial collaborators. Previously, a major bottleneck in vector production and development was the small number of scientists, particularly immunologists, with experience in the generation of recombinant viral vectors. The purpose of the facility is to generate a wide range of high quality recombinant vectors and provide these at adequate yield, with appropriate quality control, for all Jenner Institute scientists and external requesters. The facility is led by Dr Alison Turner.

The majority of new vaccine candidates developed by Jenner Investigators have been viral vectors, which have the capacity to induce strong protective T cell responses against pathogens. For example, the Institute's Malaria Vaccine Programme has taken MVA, fowlpox (FP9) and simian adenoviral vectors to clinical trials using a prime-boost approach (adenovirus or FP9 priming and MVA boosting). Using adenovirus vectors as the priming immunisation results in strong antibodies as well as T cell responses, extending the range of applications for this technology.

Services provided by the facility

Once a candidate antigen has been identified, DNA is synthesised and cloned into a suitable shuttle vector by an Institute scientist. VVCF production commences with the introduction of this shuttle vector into a suitable cell culture system to generate recombinant viral vectors. These vectors are amplified and purified using standardised protocols to produce individual batches of vector, which are subjected to Quality control (QC) tests that assay infectivity and sterility, and also confirm that the inserted DNA sequence is in place.

Until recently, all vectors made by VVCF were Adenovirus, MVA or fowlpox vectors modified at a single site in the vector backbone. The VVCF has now begun production of Adenoviral and MVA vectors expressing proteins at two different sites, and these dual expressing constructs allow the delivery of multiple antigens within a single batch of viral vector.

The majority of viral constructs produced are used in preclinical studies to identify the most promising vaccine candidates. Where a successful vaccine candidate has been identified, the VVCF can produce a preclinical batch of virus, using methods approved by the MHRA, which can be used as an input for clinical manufacture (the VVCF itself is not a GMP production facility).

The VVCF produces approximately 200 batches of viral vector each year. Since starting in 2008, the majority of viral vectors produced have targeted the Jenner priority research areas of malaria, influenza, FMDV, HIV and tuberculosis. In recent years, the range of disease areas has expanded to include:

HUMAN
Breast Cancer
Chagas
C. trachomatis
HepC
HPV
Melioidosis
Meningitis
Polio
Prostate cancer
Rabies
Rift Valley Fever
S. aureus

VETERINARY
African Horse Sickness
African Swine Fever
Bluetongue
BRSV
Classical Swine Fever
Marek's Disease
Paratuberculosis
PPRV
Schmallenberg Virus
T. parva

Whilst the majority of these vectors were developed for use by Jenner Investigators based in Oxford and Pirbright, the VVCF has also provided vectors to external collaborators including:

Dr Tim Bull (St George's University of London)
Dr Alejandro Brun (INIA, Madrid)
Dr Timothy Connelley (Roslin Institute, Edinburgh)
Dr Elizabeth Fry (STRUBI, Oxford)
Dr John T Harty (University of Iowa)
Prof Peter Holst (University of Copenhagen)
Dr Laura Madrigal-Estebas (Trinity College, Dublin)
Dr Anne Moore (University College Cork)
Dr Roger Pelle (ILRI, Kenya)
Prof Robin Shattock (Imperial College London)
Dr David B Wallace (ARC-Onderstepoort Veterinary Institute, S Africa)
Dr Qibo Zhang (University of Liverpool)

JENNER ADJUVANT BANK

The Jenner Adjuvant Bank was established in 2009 through a Wellcome Trust Strategic Award, with the key objective of obtaining a large range of promising adjuvants and building an in-house capacity for adjuvant application, optimisation and evaluation in the development of novel human and livestock vaccines. The Bank has collected a variety of adjuvants from different sources, ranging from academic collaborations to novel proprietary compounds developed by small or large pharmaceutical companies, in addition to more widely used commercially available generic adjuvants.

An adjuvant (from the Latin *adiuvare*, meaning "to help") can be any compound or vaccine additive used to enhance the immune response to a vaccine antigen. Simple adjuvants, such as aluminium salts, have been employed to enhance vaccine efficacy for nearly a century. More recently, advances in our understanding of the innate immune system have given rise to new vaccine adjuvants, able to induce a stronger as well as more targeted immune response to the vaccine antigen, opening up possibilities for developing vaccines against more complex infectious diseases such as malaria or HIV. The Jenner Adjuvant Bank currently holds over 50 different adjuvants with immunostimulatory and/or antigen delivery properties, from oil and water emulsions, liposomes, TLR agonists and polymers, to more complex multicomponent adjuvants such as saponin and lipid-based Immunostimulating Complexes (ISCOMs). In terms of novel adjuvants, particular focus has been placed on proprietary pilot research compounds obtained through material transfer agreements. For selected preclinical applications, we have been successful in negotiating access to adjuvants with proven safety and efficacy, licensed for human use. More recently, the Bank has been granted access to adjuvants through the TRANSVAC infrastructure funded by the European Commission FP7 programme, and coordinated by the European Vaccine Initiative (EVI). This involves access to biosimilars of established potent adjuvants, formulated and tested by the Vaccine Formulation Laboratory (VFL), a WHO Collaborating Centre in Lausanne.

Preclinical and clinical testing of adjuvants

Experimental assessment of adjuvants from the Bank has been carried out with vaccines against malaria (liver, blood and transmission stage), influenza, tuberculosis (TB), *Staphylococcus aureus*, Meningitis B and prostate cancer. Good protective efficacy with our leading liver-stage malaria vaccine, tested with a range of adjuvants in preclinical challenge models, led to a Phase I clinical trial of the vaccine combined with Matrix M, an ISCOM adjuvant, which showed a good safety profile. Veterinary applications to date include Rift Valley Fever Virus in preclinical (mice) and clinical (sheep) settings, as well as the evaluation of adjuvants in combination with a Foot-and-Mouth Disease Virus (FMDV) vaccine in cattle, and *E. coli* infection in turkeys. Two manuscripts resulting from the preclinical work above have been published, and three more are currently in preparation. An internal Adjuvant Workshop was held in January 2013 on past and current use of adjuvants within the Institute. Our work on adjuvants has led to a patent application on "Viral Vector Immunogenic Compositions", filed by Isis Innovation Ltd. in September 2011.

We welcome opportunities for collaboration or business partnership; enquiries can be directed to Dr. Anita Milicic: anita.milicic@ndm.ox.ac.uk

THE JENNER INSECTARY

The Jenner Institute Insectary is used for the rearing of mosquitoes. Researchers then use these mosquitoes to test vaccines against malaria, a disease caused by *Plasmodium* parasites that are transmitted from one person to another by female *Anopheles* mosquitoes. Our colony of *Anopheles stephensi* mosquitoes are reared in state-of-the-art temperature and humidity-controlled incubators. The female mosquito lays her eggs in water, where they hatch after a few days. These aquatic larvae feed and develop through four stages, or instars, before pupation and emergence into adulthood. It takes two weeks after hatching for the mosquitoes to become adults.

The mosquitoes are used to produce sporozoites, which grow inside the mosquito salivary gland and are infective to the vertebrate host. We use sporozoites to test vaccines targeting the liver and blood stages of malaria infection.

The facility is also used to test transmission-blocking malaria vaccines that aim to halt the sexual development of the malaria parasite in the mosquito. The mosquitoes are kept in highly secure cabinets for the time required for the parasites to develop within the midgut and then dissected. Effective vaccines block the appearance of sporozoite-producing oocysts in the midgut.

▼ Scientists working in the advanced animal health laboratories of ILRI, in Nairobi, Kenya (photo credit ILRIDavid White)

▼ ILRI campus (Nairobi) courtyard (photo credit ILRI)

EDUCATION PROVIDED BY THE JENNER INSTITUTE

The Jenner Institute encourages students to apply for DPhil (PhD) and Masters degrees, and also welcomes undergraduate students carrying out short research projects. Students are enrolled either at the Jenner Institute in Oxford (University of Oxford) or at the Pirbright Institute. During 2011–2013, 15 students working at the Jenner in the Old Road Campus Research Building were awarded DPhil degrees; approximately 50% of the students were British in nationality, with other students coming from a wide range of countries including China, India, Nigeria and Thailand. The Jenner Institute also regularly participates in public engagement events to keep members of the public informed about our activities, and ways in which they can become involved, for example through volunteering to participate in a clinical trial.

The Pirbright Institute has a vigorous postgraduate student programme. This has a three-fold purpose: to produce excellent research scientists in animal health; to make the unique facilities in the Institute available more widely; and to strengthen the links between the Institute and the Universities. The Pirbright Institute has recently formed partnerships with a number of academic and commercial bodies to offer studentships in viral diseases of livestock. These include: the Universities of Oxford, Cambridge, Warwick and Oxford Brookes; Oxford Expression Technologies; and Pfizer Animal Health Europe.

Vaccinology in Africa Course

The Jenner Institute initiated the five-day Masters level "Vaccinology in Africa" Course in September 2013. This course, jointly organised by the Jenner Institute, Fondation Mérieux and the African host institution, is aimed at students, researchers and professionals who are resident in Africa. The course covers the main aspects of vaccinology, the vaccine development process, biomanufacturing, regulatory and ethical issues. It is unique in that it is held in Africa, has an exceptional faculty of academic and industrial speakers, and resonates with the 'One Health' agenda by highlighting human and veterinary links and synergies from scientific, technological and regulatory perspectives. The 1st Vaccinology in Africa Course was held at the Noguchi Memorial Institute for Medical Research (NMIMR) in Accra, Ghana in September 2013, with excellent reviews from students and speakers at the course. The 2nd course will be held in Nairobi, Kenya in October 2014. It is envisaged that the course will be held annually and will rotate between different regions of Africa.

Oxford Vaccinology Courses

Two further courses on vaccinology organised by the Jenner Institute are held annually at the Department of Continuing Education in Oxford; the speakers are world-leading experts, some of whom are Jenner Investigators. The courses are aimed at students, anyone working in the vaccinology field or scientists planning to work in the field. The five-day "Human and Veterinary Vaccinology" course is designed to be stand-alone, and address all aspects of vaccinology including economic and ethical considerations. "Clinical Vaccine Development and Biomanufacturing" is a four-day course, covering vaccine manufacturing and clinical development.

Vaccine Knowledge Project

Oxford Vaccine Group (OVG)'s Vaccine Knowledge Project website (www.vaccine-knowledge.info) provides detailed, reliable and independent information about infectious diseases, vaccines and vaccine safety designed for a general audience, especially parents. A key aspect of the website is its series of short films showing the impact of infectious diseases on individuals and their families. The website receives around 10,000 page views a month. See www.ovg.ox.ac.uk/vaccine-knowledge-home

Professional education and vaccine advice

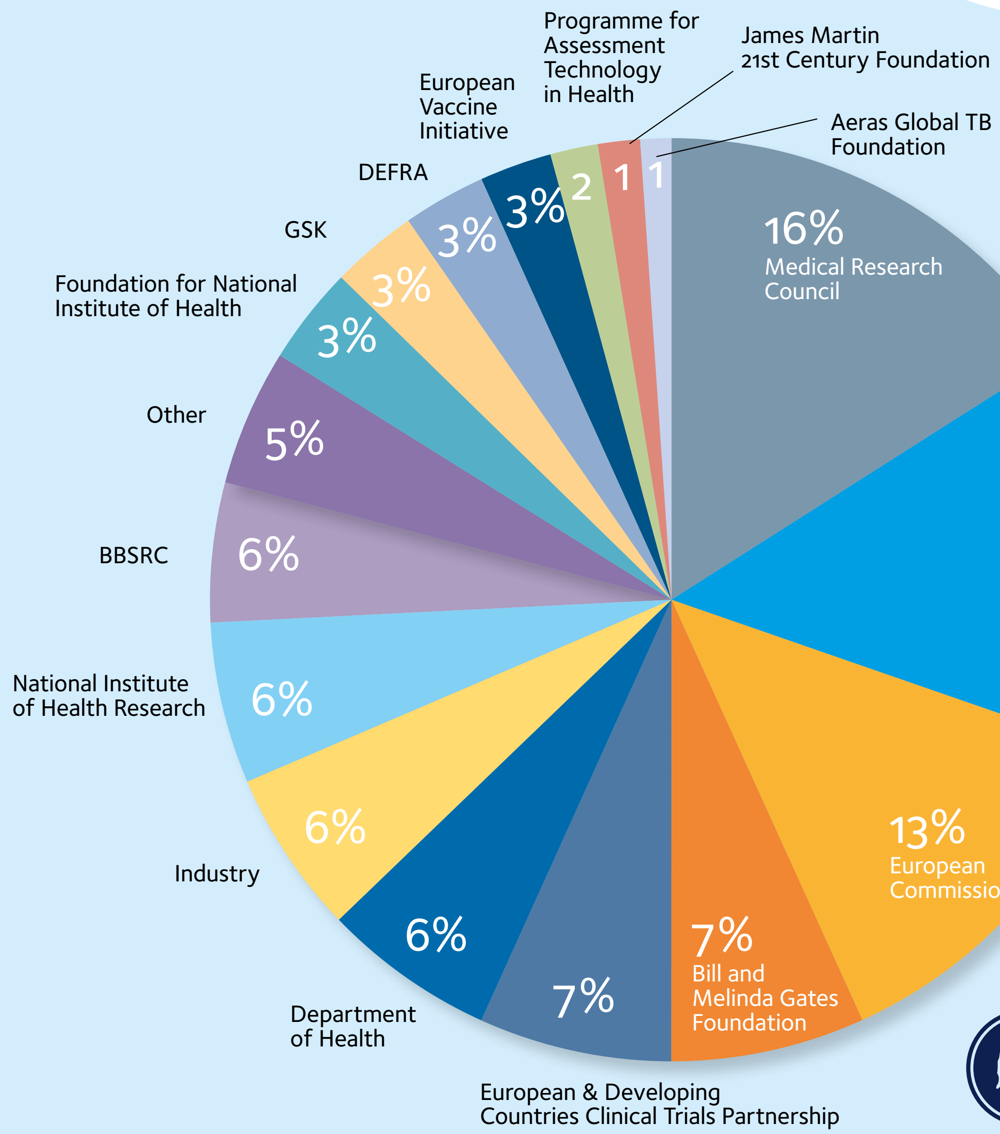
OVG provides education for health care professionals working with immunisation/infectious diseases, both locally and internationally. Of note is the perennially popular annual immunisation seminar, which is led and organised by the research and immunisation nurses and the Infection and Immunity in Children (IIC) conference, attended by over 200 trainees in Paediatric Infectious Disease every Summer.

Reactive and proactive expert clinical vaccine advice is provided to immunisers across the Thames Valley, along with education and tools to support practice through the Vaccine Advice for Clinicians Service (VACCSline). This specialist immunisation service is a collaboration between OVG and the Thames Valley Public Health England Centre. VACCSline responds to around 1,500 enquiries each year. See www.ovg.ox.ac.uk/vaccsline

FINANCE

Jenner Laboratories at the Churchill Hospital site receive funding from a variety of sources.

The breakdown of more than 30 million pounds of funding for the 2011-2013 period is shown below.



THE JENNER INSTITUTE
DEVELOPING INNOVATIVE VACCINES

PUBLICATIONS

Publications

Martin Bachmann

Low et al. Safety and immunogenicity of a virus-like particle pandemic influenza A (H1N1) 2009 vaccine: results from a double-blinded, randomized Phase I clinical trial in healthy Asian volunteers. Vaccine 2014; 32: 5041-48.

Klimek et al. Immunotherapy of type-1 allergies with virus-like particles and CpG-motifs. Expert Rev Clin Immunol. 2014; 10: 1059-67.

Zabel et al. Viral particles drive rapid differentiation of memory B cells into secondary plasma cells producing increased levels of antibodies. J Immunol. 2014; 192: 5499-508.

Fettelschoss et al. Vaccination against Alzheimer disease: an update on future strategies. Human Vaccin Immunother. 2014; 10: 847-51.

Kündig et al. Intralymphatic immunotherapy: time interval between injections is essential. J Allergy Clin Immunol. 2014; 133: 930-1.

Uermösi C et al. IgG-mediated down-regulation of IgE bound to mast cells: a potential novel mechanism of allergen-specific desensitization. Allergy 2014; 69: 338-47.

Tissot et al. A VLP-based vaccine against interleukin-1α protects mice from atherosclerosis. Eur J Immunol. 2013; 43: 716-22.

Beeh et al. The novel TLR-9 agonist QbG10 shows clinical efficacy in persistent allergic asthma. J Allergy Clin Immunol. 2013; 131: 866-74.

Skibinski et al. Enhanced neutralizing antibody titers and Th1 polarization from a novel Escherichia coli derived pandemic influenza vaccine. PLoS One. 2013; 8: e76571.

Tars et al. Different binding modes of free and carrier-protein-coupled nicotine in a human monoclonal antibody. J Mol Biol. 2012; 415: 118-27.

Braun al. Virus-like particles induce robust human T-helper cell responses. Eur J Immunol. 2012; 42: 330-40.

Link et al. Innate Immunity Mediates Follicular Transport of Particulate but not Soluble Protein Antigen. J Immunol. 2012; 188: 3724-33.

Schmitz et al. Universal vaccine against influenza virus: linking toll-like receptor signaling to anti-viral protection. Eur J Immunol. 2012; 42: 863-69.

Goldinger et al. Nano-particle vaccination combined with TLR-7 and -9 ligands triggers memory and effector $CD8^+$ T-cell responses in melanoma patients. Eur J Immunol. 2012; 42: 3049-3061.

Bessa et al. Low-affinity B cells transport viral particles from the lung to the spleen to initiate antibody responses. Proc Natl Acad Sci U S A 2012; 109: 20566-20571

Klimek et al. Assessment of clinical efficacy of CYT003-QbG10 in patients with allergic rhinoconjunctivitis: a phase IIb study. Clin Exp Allergy 2011; 41: 1305-1312

Rohn et al. A virus-like particle-based anti-nerve growth factor vaccine reduces inflammatory hyperalgesia: potential long-term therapy for chronic pain. J Immunol. 2011; 186: 1769-1780.

Tissot et al. Versatile virus-like particle carrier for epitope based vaccines. PloS one 2011; 5: e9809.

Guler et al. Blocking IL-1alpha but not IL-1beta increases susceptibility to chronic Mycobacterium tuberculosis infection in mice. Vaccine 2011; 29: 1339-1346.

Hou et al. Selective utilization of Toll-like receptor and MyD88 signaling in B cells for enhancement of the antiviral germinal center response. Immunity 2011; 34: 375-384.

Uermosi et al. Mechanisms of allergen-specific desensitization. J Allergy Clin Immunol. 2011; 126: 375-383.

Wiesel et al. Th cells act via two synergistic pathways to promote antiviral CD8+ T cell responses. J Immunol. 2011; 185: 5188-5197.

Wiessner et al. The Second-Generation Active A{beta} Immunotherapy CAD106 Reduces Amyloid Accumulation in APP Transgenic Mice While Minimizing Potential Side Effects. J Neurosci. 2011; 31: 9323-9331.

Fettelschoss et al. Inflammasome activation and IL-1β target IL-1α for secretion as opposed to surface expression. Proc Natl Acad Sci U S A. 2011; 108: 18055-60.

Ellie Barnes

Smit and Barnes. The emerging mysteries of IgG4-related disease. Clin Med. 2014; 14 Suppl 6: s56-60.

Swadling et al. A human vaccine strategy based on chimpanzee adenoviral and MVA vectors that primes, boosts, and sustains functional HCV-specific T cell memory. Sci Transl Med. 2014; 6: 261ra153.

Halliday et al. Hepatitis E virus infection, Papua New Guinea, Fiji, and Kiribati, 2003-2005. Emerg Infect Dis. 2014; 20:1057-8.

Abdel-Hady et al. Treatment of chronic viral hepatitis C in children and adolescents: UK experience. Arch Dis Child. 2014; 99: 505-10.

Huggett et al. Type 1 autoimmune pancreatitis and IgG4-related sclerosing cholangitis is associated with extrapancreatic organ failure, malignancy, and mortality in a prospective UK cohort. Am J Gastroenterol. 2014; 109: 1675-83.

Boonstra et al. Serum immunoglobulin G4 and immunoglobulin G1 for distinguishing immunoglobulin G4-associated cholangitis from primary sclerosing cholangitis. Hepatology 2014; 59: 1954-63.

Lighaam et al. Phenotypic differences between IgG4+ and IgG1+ B cells point to distinct regulation of the IgG4 response. J Allergy Clin Immunol. 2014; 133: 267-70.

Banerjee et al. Multiparametric magnetic resonance for the non-invasive diagnosis of liver disease. J Hepatol. 2014; 60: 69-77

Taylor et al. Effect of interferon-α on cortical glutamate in patients with hepatitis C: a proton magnetic resonance spectroscopy study. Psychol Med. 2014; 44: 789-95

Clutton et al. Emergence of a distinct HIV-specific IL-10-producing CD8+ T-cell subset with immunomodulatory functions during chronic HIV-1 infection. Eur J Immunol. 2013; 43: 2875-85.

Rowland et al. Determining the validity of hospital laboratory reference intervals for healthy young adults participating in early clinical trials of candidate vaccines. Hum Vaccin Immunother. 2013; 9: 1741-51.

Swadling et al. Ever closer to a prophylactic vaccine for HCV. Expert Opin Biol Ther. 2013; 13: 1109-24.

Orlicka et al. Prevention of infection caused by immunosuppressive drugs in gastroenterology. Ther Adv Chronic Dis. 2013; 4, 167-85.

Bucci et al. 'Favourable' IL28B polymorphisms are associated with a marked increase in baseline viral load in hepatitis C virus subtype 3a infection and do not predict a sustained virological response after 24 weeks of therapy. J Gen Virol. 2013; 94(Pt 6): 1259-65.

Harrison et al. Infection frequency of hepatitis C virus and IL28B haplotypes in Papua New Guinea, Fiji, and Kiribati. PLoS One 2013; 8: e66749.

Walker et al. CD8αα Expression Marks Terminally Differentiated Human CD8+ T Cells Expanded in Chronic Viral Infection. Front Immunol. 2013; 4: 223.

Batty et al. A modified RNA-Seq approach for whole genome sequencing of RNA viruses from faecal and blood samples. PLoS One 2013; 8: e66129.

Wang et al. Eight novel hepatitis C virus genomes reveal the changing taxonomic structure of genotype 6. J Gen Virol. 2013: 94(Pt1): 76-80.

Humphreys et al. HCV genotype-3a T cell immunity: specificity, function and impact of therapy. Gut. 2012; 61: 1589-99.

Culver et al. A rare cause of an ileocaecal mass and lymphadenopathy. Gut. 2012; 61: 819-20, 917.

Walker et al. Human MAIT and CD8αα cells develop from a pool of type-17 precommitted CD8+ T cells. Blood. 2012; 119: 422-33.

Colloca et al. Vaccine vectors derived from a large collection of simian adenoviruses induce potent cellular immunity across multiple species. Sci Transl Med. 2012; 4: 115ra2.

Barnes et al. Novel adenovirus-based vaccines induce broad and sustained T cell responses to HCV in man. Sci Transl Med. 2012; 4: 115ra1.

Kang et al. CD161(+)CD4(+) T cells are enriched in the liver during chronic hepatitis and associated with co-secretion of IL-22 and IFN-γ. Front Immunol. 2012; 3: 346.

Gangadharan et al. Discovery of novel biomarker candidates for liver fibrosis in hepatitis C patients: a preliminary study. PLoS One 2012; 7:e39603.

Kelly et al. Interferon lambdas: the next cytokine storm. Gut 2011; 60: 1284-93.

Gangadharan et al. New approaches for biomarker discovery: the search for liver fibrosis markers in hepatitis C patients. J Proteome Res. 2011; 10: 2643-50.

Halliday et al. Vaccination for hepatitis C virus: closing in on an evasive target. Expert Rev Vaccines 2011; 10: 659-72.

di Iulio et al; Swiss HIV Cohort Study. Estimating the net contribution of interleukin-28B variation to spontaneous hepatitis C virus clearance. Hepatology 2011; 53: 1446-54.

Persephone Borrow

Armitage et al. Distinct patterns of hepcidin and iron regulation during HIV-1, HBV, and HCV infections. PNAS 2014; 111: 12187-92

Tandon et al. Galectin-9 is rapidly released during acute HIV-1 infection and remains sustained at high levels despite viral suppression even in elite controllers. AIDS Res Hum Retroviruses. 2014; 30: 654-64.

Fenton-May et al. Relative resistance of HIV-1 founder viruses to control by interferon-alpha. Retrovirology 2013; 10: 146.

Clutton et al. Emergence of a distinct HIV-specific IL-10-producing CD8+ T-cell subset with immunomodulatory functions during chronic HIV-1 infection. Eur. J. Immunol. 2013; 43: 2875-85.

Clark et al. Activation of CCR2+ human proinflammatory monocytes by human herpesvirus-6B chemokine N-terminal peptide. J. Gen. Virol. 2013; 94: 1624-35.

Parrish et al. Phenotypic characteristics of transmitted HIV-1. Proc. Natl. Acad. Sci, USA 2013; 110: 6626-33.

Yates et al. HIV-1 gp41 envelope IgA is frequently elicited after transmission but has an initial short response half-life. Mucosal Immunol. 2013; 6: 692-703.

Murphy et al. Viral escape from neutralizing antibodies in early subtype A HIV-1 infection drives an increase in autologous neutralization breadth. PLoS Pathog. 2013; 9: e1003173.

Liu et al. Vertical T cell immunodominance and epitope entropy determine HIV-1 escape. J. Clin. Invest. 2013; 123: 380-93.

Frleta et al. HIV-1 infection-induced apoptotic microparticles inhibit human DCs via CD44. J. Clin. Invest. 2012; 122: 4685-97.

Brown et al. Hepatitis C virus envelope glycoprotein fitness defines virus population composition following transmission to a new host. J. Virol. 2012; 86:11956-66.

Borrow and Nash. Chapter 13. Immunity to Viruses. In Immunology, 8th edition D. Male, J. Brostoff, D. Roth and I Roitt, eds., Elsevier Ltd. p211-222, 2012;

Ribeiro dos Santos et al. Chronic HIV infection affects the expression of the two transcription factors required for CD8 T cell differentiation into cytolytic effectors. Blood 2012. 119: 4928-38.

Riou et al. Asynchronous kinetics of Gag-specific CD4+ and CD8+ T-cell responses during acute HIV-1 infection. J. Immunol. 2012; 188: 2198-206.

Pelak et al. on behalf of NIAID Center for HIV/AIDS Vaccine Immunology (CHAVI). Copy number variation of KIR genes influences HIV-1 control. PLoS Biology 2011; 9: e1001208.

Mahlokozera et al. The magnitude and kinetics of the mucosal HIV-specific CD8+ T lymphocyte response and virus RNA load in breast milk. PLoS One 2011; 6: e23735.

Ganusov et al. Fitness costs and diversity of CTL response determine the rate of CTL escape during the acute and chronic phases of HIV infection. J. Virol. 2011; 85: 10518-28.

Borrow, P. Innate immunity in acute HIV-1 infection. Curr. Opin. HIV AIDS 2011; 6: 353-363.

Breen et al. Multi-site comparison of high-sensitivity multiplex cytokine assays. Clin. and Vaccine Immunol. 2011; 18: 1229-1242.

Turnbull et al. Escape is a more common mechanism than avidity reduction for evasion of CD8+ T cell responses in primary human immunodeficiency virus type 1 infection. Retrovirology 2011; 8: 41.

Haddow et al. Circulating inflammatory biomarkers can predict and characterize tuberculosis-associated immune reconstitution inflammatory syndrome. AIDS 2011; 25: 1163-1174.

Gay et al. Cross-sectional detection of acute HIV infection: timing of transmission, inflammation and antiretroviral therapy. PLoS One 2011; 6: e19617.

Ferrari et al. Evolution of polyfunctional HIV-1-specific $CD8^+$ T cell responses and their impact on the selection of escape mutants during acute HIV-1 infection. PLoS Pathog. 2011. 7: e1001273.

Corrah et al. A reappraisal of the relationship between the HIV-1 protective single nucleotide polymorphism 35KB upstream of the HLA-C gene and surface HLA-C expression. J. Virol. 2011. 85: 3367-3374.

Salazar-Gonzalez et al. Origin and evolution of HIV-1 in breast milk determined by single genome amplification and sequencing. J. Virol. 2011; 85: 2751-2763.

Enzo Cerundolo

Galluzzi et al. Classification of current anticancer immunotherapies. Oncotarget. 2014; 5: 12472-508.

Salio et al. Essential role for autophagy during invariant NKT cell development. Proc Natl Acad Sci U S A. 2014; 111: E5678-87.

Puleston et al. Autophagy is a critical regulator of memory CD8(+) T cell formation. Elife. 2014; 3. doi: 10.7554/eLife.03706.

Dawoodji et al. High frequency of cytolytic 21-hydroxylase-specific CD8+ T cells in autoimmune Addison's disease patients. J Immunol. 2014; 193: 2118-26.

Salio et al. Biology of CD1- and MR1-restricted T cells. Annu Rev Immunol. 2014; 32: 323-66.

Shenderov et al. Cutting edge: Endoplasmic reticulum stress licenses macrophages to produce mature IL-1β in response to TLR4 stimulation through a caspase-8- and TRIF-dependent pathway. J Immunol. 2014; 192: 2029-33.

Pan et al. Combinatorial HLA-peptide bead libraries for high throughput identification of $CD8^+$ T cell specificity. J Immunol Methods. 2014; 403: 72-8.

Salio et al. Saposins modulate human iNKT cells self-reactivity and facilitate lipid exchange with CD1d molecules during antigen presentation. Proc Natl Acad Sci USA. 2013; 110:E4753-61

Scher et al. Expansion of intestinal Prevotella copri correlates with enhanced susceptibility to arthritis. Elife. 2013; 2:e01202.

Hipp et al. Processing of human TLR7 by furin-like proprotein convertases is required for its accumulation and activity in endosomes. Immunity 2013; 39: 711-21.

Crawford G et al. DOCK8 is critical for the survival and function of NKT cells. Blood 2013; 122: 2052-61.

Duman et al. Nanomapping of CD1d-glycolipid complexes on THP1 cells by using simultaneous topography and recognition imaging. J Mol Recognit. 2013; 26: 408-14.

Mussai et al. Acute myeloid leukaemia creates an arginase-dependent immunosuppressive microenvironment. Blood 2013; 122: 749-58.

Shenderov et al. Cord Factor and Peptidoglycan Recapitulate the Th17-Promoting Adjuvant Activity of Mycobacteria through Mincle/CARD9 Signaling and the Inflammasome. J Immunol. 2013; 190: 5722-30.

Jervis et al. Design, Synthesis, and Functional Activity of Labeled CD1d Glycolipid Agonists. Bioconjug Chem. 2013; 24: 586-94.

Stock et al. Intestinal DC in migrational imprinting of immune cells. Immunol Cell Biol. 2013; 91: 240-9.

Davis et al. NAADP activates Two-Pore Channels on T Cell Cytolytic Granules to Stimulate Exocytosis and Killing. Curr Biol. 2012; 22: 2331-7.

Srivastava et al. An open invitation to the cancer immunology community. Cancer Immun. 2012; 12:1.

Silk et al. Cross-presentation of tumour antigens by human induced pluripotent stem cell-derived CD141(+)XCR1(+) dendritic cells. Gene Ther. 2012; 19: 1035-40.

Porubsky et al. Gröne HJ. Globosides but not Isoglobosides Can Impact the Development of Invariant NKT Cells and Their Interaction with Dendritic Cells. J Immunol. 2012; 189: 3007-17.

Jervis et al. Towards multivalent CD1d ligands: synthesis and biological activity of homodimeric α-galactosyl ceramide analogues. Carbohydr Res. 2012; 356: 152-62.

Mussai et al. Interaction between invariant NKT cells and myeloid-derived suppressor cells in cancer patients: evidence and therapeutic opportunities. J Immunother.2012; 35: 449-59.

Speak et al. Invariant natural killer T cells are not affected by lysosomal storage in patients with Niemann-Pick disease type C. Eur J Immunol. 2012; 42: 1886-92.

Wojno et al. Amide Analogues of CD1d Agonists Modulate iNKT-Cell-Mediated Cytokine Production. ACS Chem Biol. 2012; 7: 847-55.

Barral et al. The location of splenic NKT cells favours their rapid activation by blood-borne antigen. The EMBO Journal 2012; 31: 2378-90.

Robert et al. Kinetics and mechanics of two-dimensional interactions between T cell receptors and different activating ligands. Biophys J. 2012; 102: 248-57.

Chang et al. Identification of Bcl-6-dependent follicular helper NKT cells that provide cognate help for B cell responses. Nat Immunol. 2011; 13: 35-43.

Huang et al. Discovery of deoxyceramides and diaglycerols as CD1b scaffold lipids among diverse groove-blocking lipids of the human CD1 system. Proc Natl Acad Sci U S A. 2011; 108: 19335-40.

Silk et al. IDO induces expression of a novel tryptophan transporter in mouse and human tumor cells. J Immunol. 2011; 187: 1617-1625.

Kaur et al. Preparation, characterisation and entrapment of a non-glycosidic threitol ceramide into liposomes for presentation to invariant natural killer T cells. J Pharm Sci. 2011; 100: 2724-2733.

Stinchcombe et al. Centriole polarisation to the immunological synapse directs secretion from cytolytic cells of both the innate and adaptive immune systems. BMC Biol. 2011; 9: 45.

Dushek et al. Antigen potency and maximal efficacy reveal a mechanism of efficient T cell activation. Sci Signal. 2011; 4: ra39.

Bozna et al. Binding Strength and Dynamics of Invariant Natural Killer Cell T Cell Receptor/CD1d-Glycosphingolipid Interaction on Living Cells by Single Molecule Force Spectroscopy. J Biol Chem. 2011; 286:15973-9.

Stock et al. Prostaglandin E2 suppresses the differentiation of retinoic acid-producing dendritic cells in mice and humans. J Exp Med. 2011; 208: 761-773.

Hutchinson et al. A dominant role for the immunoproteasome in CD8+ T cell responses to murine cytomegalovirus PLoS One 2011; 6: e14646.

Pei et al. Diverse endogenous antigens for mouse NKT cells: self-antigens that are not glycosphingolipids. J Immunol. 2011; 186: 1348-1360.

Veerapen et al. Synthesis of truncated analogues of the iNKT cell agonist, alpha-galactosyl ceramide (KRN7000), and their biological evaluation. Bioorg Med Chem. 2011; 19: 221-228.

Bryan Charleston

Habiela et al. Laboratory animal models to study foot-and-mouth disease: a review with emphasis on natural and vaccine-induced immunity. J Gen Virol. 2014; 95: 2329-45.

Reid and Charleston. Type I and III interferon production in response to RNA viruses. J Interferon Cytokine Res. 2014; 34: 649-58.

Guzman et al. Bovine γδ T cells are a major regulatory T cell subset. J Immunol. 2014; 193: 208-22.

Opperman et al. Determining the epitope dominance on the capsid of a serotype SAT2 foot-and-mouth disease virus by mutational analyses. J Virol. 2014; 88: 8307-18.

Chase-Topping et al. Understanding foot-and-mouth disease virus transmission biology: identification of the indicators of infectiousness. Vet Res. 2013; 44: 46.

Charleston B. Eradicating bovine viral diarrhoea virus. Vet Rec. 2013; 172: 659-60.

Mullarkey et al. Improved adjuvanting of seasonal influenza vaccines: preclinical studies of MVA-NP+M1 coadministration with inactivated influenza vaccine. Eur J Immunol. 2013; 43: 1940-52.

Seago et al. An infectious recombinant foot-and-mouth disease virus expressing a fluorescent marker protein. J Gen Virol. 2013; 94: 1517-27.

Porta et al. Rational engineering of recombinant picornavirus capsids to produce safe, protective vaccine antigen. Plos Pathogens 2013; 9: e1003255.

Porta et al. Efficient production of foot-and-mouth disease virus empty capsids in insect cells following down regulation of 3C protease activity. J Virol Methods 2013; 187: 406-12.

Grant et al. Assessment of T-dependent and T-independent immune responses in cattle using a B cell ELISPOT assay. Vet Res. 2012; 43: 68.

Juleff et al. Accumulation of Nucleotide Substitutions Occurring During Experimental Transmission of Foot-and-Mouth Disease Virus. J Gen Virol. 2013; 94: 108-19.

Carr et al. CD4+ T-Cell Responses to Foot-and-Mouth Disease Virus in Vaccinated Cattle. J Gen Virol. 2013; 94: 97-107.

Williamson et al. Descriptive clinical and epidemiological characteristics of influenza A H1N1 2009 virus infections in pigs in England. Vet Rec. 2012; 171: 271.

Seago et al. Characterization of epitope-tagged foot-and-mouth disease virus. J Gen Virol. 2012; 93: 2371-81.

Howey et al. Modelling the within-host dynamics of the foot-and-mouth disease virus in cattle. Epidemics. 2012; 4: 93-103.

Lefevre et al. Immune Responses in Pigs Vaccinated With Adjuvanted and Non-Adjuvanted A(H1N1)pdm/09 Influenza Vaccines Used in Human Immunization Programmes. PLoS One 2012; 7: e32400.

Guzman et al. MVA-based vaccine vectors induce apoptosis in DC draining the skin via both the extrinsic and intrinsic caspase pathways preventing efficient antigen presentation. J Virol. 2012; 86: 5452-66.

Schley et al. Modelling the Influence of Foot-and-Mouth Disease Vaccine Antigen Stability and Dose on the Bovine Immune Response. PLoS One 2012; 7: e30435.

Hope et al. Migratory sub-populations of afferent lymphatic dendritic cells differ in their interactions with Mycobacterium bovis Bacille Calmette Guerin. Vaccine 2012; 30: 2357-67.

Windsor et al. Cattle remain immunocompetent during the acute phase of foot-and-mouth disease virus infection. Vet Res. 2011; 42: 108.

Cubillos-Zapata et al. Differential effects of viral vectors on migratory afferent lymph dendritic cells in vitro predict enhanced immunogenicity *in vivo*. J Virol. 2011; 85: 9385-94.

Juleff et al. The importance of FMDV localisation in lymphoid tissue. Vet Immunol Immunopathol. 2012; 148: 145-8.

Charleston et al. Relationship between clinical symptoms and transmission of an infectious disease and the implications for control. Science 2011; 332: 726-9.

Reid E et al. Bovine plasmacytoid dendritic cells are the major source of type I interferon in response to foot-and-mouth disease virus *in vitro* and *in vivo*. J Virol. 2011; 85: 4297-308.

Robinson et al. Foot-and-mouth disease virus exhibits an altered tropism in the presence of specific immunoglobulins, enabling productive infection and killing of dendritic cells. J Virol. 2011; 85: 2212-23.

McLaughlin et al. Hsp110-mediated enhancement of CD4+ T cell responses to the envelope glycoprotein of members of the family Flaviviridae *in vitro* does not occur *in vivo*. Clin Vaccine Immunol. 2011; 18: 311-7.

Linda Dixon

Guinat et al. Dynamics of African swine fever virus shedding and excretion in domestic pigs infected by intramuscular inoculation and contact transmission. Vet Res. 2014; 45: 93.

Lithgow et al. Correlation of cell surface marker expression with African swine fever virus infection. Vet Microbiol. 2014; 168: 413-9.

Fishbourne et al. Modulation of chemokine and chemokine receptor expression following infection of porcine macrophages with African swine fever virus. Vet. Microbiol. 2013; 162: 937-943.

Abrams et al. Deletion of virulence associated genes from attenuated African swine fever virus isolate OUR T88/3 decreases its ability to protect against challenge with virulent virus. Virology 2013; 443: 99-105.

Fishbourne et al. Increase in chemokines CXCL10 and CCL2 in blood from pigs infected with high compared to low virulence African swine fever virus isolates. Vet. Res. 2013; 44: Article no 87.

Radford et al. Application of next-generation sequencing technologies in virology. J Gen Virol. 2012; 93: 1853-68.

Diaz et al. African swine fever virus strain Georgia 2007/1 in *Ornithodoros erraticus* ticks [letter]. Emerg Infect Dis [serial on the Internet]. 2012 http://dx.doi.org/10.3201/eid1806.111728

Dixon et al. Family *Asfarviridae* IXth Report InternationalCommittee on Taxonomy of Viruses. ed King AMQ, Adams MJ, Carstens EB, Lefkowitz EJ, 2012; Elsevier, ISBN: 978-0-12-384684-6: p153-167.

Fishbourne et al. Modulation of chemokine and chemokine receptor expression following infection of porcine macrophages with African swine fever virus. Vet Microbiol. 2013;162: 937-43.

Dixon et al. African swine fever virus replication and genomics. Virus Res. 2013; 173: 3-14.

Abrams and Dixon. Sequential deletion of genes from the African swine fever virus genome using the cre/loxP recombination system. Virology 2012; 433: 142-148.

Dixon and Takamatsu. African Swine Fever Virus: Current Situation and Prospects for Control. The Pig Journal 2012; Vol 67.

King et al. Protection of European domestic pigs from virulent African isolates of African swine fever virus by experimental immunisation. Vaccine 2011; 29: 4593-4600.

Chapman et al. Genomic Analysis of Highly Virulent Georgia 2007/1 Isolate of African Swine Fever Virus. Emerging Infectious Diseases 2011; 17: 599-605.

Goatley and Dixon. Processing and localisation of the African swine fever virus CD2v transmembrane protein. J. Virol. 2011; 85: 3294-3305.

Fernando et al.The Persistence of African Swine Fever Virus in Field-Infected *Ornithodoros erraticus* during the ASF Endemic Period in Portugal. PLoS ONE 2011; 6: e20383.

Brun et al. Current strategies for subunit and genetic viral veterinary vaccine development. Virus Research 2011; 157: 1-12.

Dixon et al. Family *Asfarviridae*. IXth Report International Committee on Taxonomy of Viruses, ed King AMQ, Adams MJ, Carstens EB, Lefkowitz EJ, Elsevier 2011; ISBN: 978-0-12-384684-6: p153-167.

Dixon et al. Asfivirus, Asfarviridae. 2nd Edition Springer Index of Viruses, ed Tidona C, Darai G, 2011.

Lucy Dorrell

Rider et al. HIV is an independent predictor of aortic stiffness. J Cardiovasc Magn Reson. 2014; 16: 57.

Hayton et al. Safety and tolerability of conserved region vaccines vectored by plasmid DNA, simian adenovirus and modified vaccinia virus ankara administered to human immunodeficiency virus type 1-uninfected adults in a randomized, single-blind phase I trial. PLoS One. 2014; 9: e101591.

Vince et al. HLA class I and KIR genes do not protect against HIV type 1 infection in highly exposed uninfected individuals with hemophilia A. J Infect Dis. 2014; 210: 1047-51.

McMichael and Dorrell. Comment on clinical development of candidate HIV vaccines: different problems for different vaccines. AIDS Res Hum Retroviruses. 2014; 30: 331-2.

Borthwick et al. Vaccine-elicited human T cells recognizing conserved protein regions inhibit HIV-1. Mol Ther. 2014; 22: 464-75.

Huang et al. Linking genotype to phenotype on beads: high throughput selection of peptides with biological function. Sci Rep. 2013; 3: 3030.

Clutton et al. Emergence of a distinct HIV-specific IL-10-producing CD8+ T-cell subset with immunomodulatory functions during chronic HIV-1 infection. Eur J Immunol. 2013; 43: 2875-85.

Wainwright et al. Hypophosphataemia with non-tenofovir-containing antiretroviral therapy. Int J STD AIDS 2013; 24: 579-81.

Schiffner et al. Development of prophylactic vaccines against HIV-1. Retrovirology 2013; 10: 72.

Holloway et al. Comprehensive cardiac magnetic resonance imaging and spectroscopy reveals a high burden of myocardial disease in HIV infection. Circulation 2013; 128: 814-22.

Yang et al. Improved quantification of HIV-1-infected CD4+ T cells using an optimised method of intracellular HIV-1 gag p24 antigen detection. J Immunol Methods 2013; 391: 174-8.

Lane et al. A genome-wide association study of resistance to HIV infection in highly exposed uninfected individuals with hemophilia A. Hum Mol Genet 2013; 22: 1903-10.

Descours et al.; DECAMUNE and ORVACS Study Groups. Direct quantification of cell-associated HIV DNA in isolated rectal and blood memory CD4 T cells revealed their similar and low infection levels in long-term treated HIV-infected patients. J Acquir Immune Defic Syndr. 2013; 62: 255-9.

Yang et al. The antiviral inhibitory capacity of CD8+ T cells predicts the rate of CD4+ cell decline in HIV-1 infection. J Infect Dis 2012; 206: 552-61.

Papagno et al.; ORVACS Study Group. Comprehensive analysis of virus-specific T-cells provides clues for the failure of therapeutic immunization with ALVAC-HIV vaccine. AIDS 2011; 25: 27-36.

Simon Draper

Hodgson et al. Evaluating controlled human malaria infection in Kenyan adults with varying degrees of prior exposure to Plasmodium falciparum using sporozoites administered by intramuscular injection. Front Microbiol 2014; 5: 686.

Biswas et al. Assessment of Humoral Immune Responses to Blood-Stage Malaria Antigens following ChAd63-MVA Immunization, Controlled Human Malaria Infection and Natural Exposure. PLoS One 2014; 9: e107903.

Hodgson et al. Combining Viral Vectored and Protein-in-adjuvant Vaccines Against the Blood-stage Malaria Antigen AMA1: Report on a Phase 1a Clinical Trial. Mol Ther. 2014; 22: 2142-2154.

Carey et al. Microneedle-mediated immunization of an adenovirus-based malaria vaccine enhances antigen-specific antibody immunity and reduces anti-vector responses compared to the intradermal route. Sci Rep. 2014; 4: 6154.

Wright et al. Structure of malaria invasion protein RH5 with erythrocyte basigin and blocking antibodies. Nature 2014; 515: 427-430.

Elias et al. Analysis of human B-cell responses following ChAd63-MVA MSP1 and AMA1 immunization and controlled malaria infection. Immunology 2014; 141: 628-644.

Douglas et al. Neutralization of Plasmodium falciparum Merozoites by Antibodies against PfRH5. J Immunol. 2014; 192: 245-258.

Llewellyn et al. Assessment of antibody-dependent respiratory burst activity from mouse neutrophils on Plasmodium yoelii malaria challenge outcome. J Leukoc Biol. 2014; 95: 369-382.

Elias et al. Assessment of immune interference, antagonism, and diversion following human immunization with biallelic blood-stage malaria viral-vectored vaccines and controlled malaria infection. J Immunol 2013; 190: 1135-1147.

Ewer et al. Protective CD8(+) T-cell immunity to human malaria induced by chimpanzee adenovirus-MVA immunisation. Nat Commun. 2013; 4: 2836.

Publications

Williams et al. Immunisation against a serine protease inhibitor reduces intensity of Plasmodium berghei infection in mosquitoes. Int J Parasitol. 2013; 43: 869–874.

Sheehy et al. Challenges of assessing the clinical efficacy of asexual blood-stage Plasmodium falciparum malaria vaccines. Hum Vaccin Immunother 2013; 9: 1831–40.

Goodman et al. The utility of Plasmodium berghei as a rodent model for anti-merozoite malaria vaccine assessment. Sci Rep. 2013; 3: 1706.

Draper et al. Utilizing poxviral vectored vaccines for antibody induction-Progress and prospects. Vaccine 2013; 31: 4223–4230.

Douglas et al. Comparison of Modeling Methods to Determine Liver-to-blood Inocula and Parasite Multiplication Rates During Controlled Human Malaria Infection. J Infect Dis. 2013; 208: 340–345.

de Cassan and Draper. Recent advances in antibody-inducing poxviral and adenoviral vectored vaccine delivery platforms for difficult disease targets. Expert Rev Vaccines 2013; 12: 365–378.

Williams et al. Enhancing Blockade of Plasmodium falciparum Erythrocyte Invasion: Assessing Combinations of Antibodies against PfRH5 and Other Merozoite Antigens. PLoS Pathog. 2012; 8: e1002991.

Vrdoljak et al. Coated microneedle arrays for transcutaneous delivery of live virus vaccines. J Control Release 2012; 159: 34–42.

Spencer et al. Fusion of the Mycobacterium tuberculosis Antigen 85A to an Oligomerization Domain Enhances Its Immunogenicity in Both Mice and Non-Human Primates. PLoS One 2012; 7: e33555.

Sheehy et al. ChAd63-MVA-vectored Blood-stage Malaria Vaccines Targeting MSP1 and AMA1: Assessment of Efficacy Against Mosquito Bite Challenge in Humans. Mol Ther. 2012; 20: 2355–2368.

Sheehy et al. Phase Ia Clinical Evaluation of the Safety and Immunogenicity of the Plasmodium falciparum Blood-Stage Antigen AMA1 in ChAd63 and MVA Vaccine Vectors. PLoS One 2012. 7: e31208.

Forbes et al. T cell responses induced by adenoviral vectored vaccines can be adjuvanted by fusion of antigen to the oligomerization domain of c4b-binding protein. PLoS One 2012 7: e44943.

Duncan and Draper. Controlled human blood stage malaria infection: current status and potential applications. Am J Trop Med Hyg. 2012; 86: 561–565.

Biswas et al. Recombinant Viral-Vectored Vaccines Expressing Plasmodium chabaudi AS Apical Membrane Antigen 1: Mechanisms of Vaccine-Induced Blood-Stage Protection. J Immunol. 2012; 188: 5041–5053.

Shi et al. The generation and evaluation of recombinant human IgA specific for Plasmodium falciparum merozoite surface protein 1-19 (PfMSP119). BMC Biotechnol. 2011; 11: 77.

Sheehy et al. Phase Ia Clinical Evaluation of the Plasmodium falciparum Blood-stage Antigen MSP1 in ChAd63 and MVA Vaccine Vectors. Mol Ther. 2011; 19: 2269–2276.

Goodman et al. A Viral Vectored Prime-Boost Immunization Regime Targeting the Malaria Pfs25 Antigen Induces Transmission-Blocking Activity. PLoS ONE 2011; 6: e29428.

Forbes et al. Liver- and Blood-Stage Malaria Viral-Vectored Vaccines: Investigating Mechanisms of CD8+ T Cell Interference. J Immunol. 2011; 187: 3738–3750.

Duncan et al. Impact on Malaria Parasite Multiplication Rates in Infected Volunteers of the Protein-in-Adjuvant Vaccine AMA1-C1/Alhydrogel+CPG 7909. PLoS One 2011; 6: e22271.

Douglas et al. The blood-stage malaria antigen PfRH5 is susceptible to vaccine-inducible cross-strain neutralizing antibody. Nat Commun. 2011; 2: 601.

Douglas et al. Substantially Reduced Pre-patent Parasite Multiplication Rates Are Associated With Naturally Acquired Immunity to Plasmodium falciparum. J Infect Dis. 2011; 203: 1337–1340.

de Cassan et al. The requirement for potent adjuvants to enhance the immunogenicity and protective efficacy of protein vaccines can be overcome by prior immunization with a recombinant adenovirus. J Immunol. 2011; 187: 2602–2616.

Bregu et al. Accelerating vaccine development and deployment: report of a Royal Society satellite meeting. Philos Trans R Soc Lond B Biol Sci. 2011; 366: 2841–2849.

Biswas et al. Transgene Optimization, Immunogenicity and In Vitro Efficacy of Viral Vectored Vaccines Expressing Two Alleles of Plasmodium falciparum AMA1. PLoS One 2011; 6: e20977.

Sarah Gilbert

Pavot et al. Poly(lactic acid) and poly(lactic-co-glycolic acid) particles as versatile carrier platforms for vaccine delivery. Nanomedicine (Lond). 2014; 9: 2703–18.

Barra et al. A phase Ia study to assess the safety and immunogenicity of new malaria vaccine candidates ChAd63 CS administered alone and with MVA CS. PLoS One. 2014; 9: e115161.

Bull et al. Immunity, safety and protection of an Adenovirus 5 prime--Modified Vaccinia virus Ankara boost subunit vaccine against Mycobacterium avium subspecies paratuberculosis infection in calves. Vet Res. 2014; 45: 112.

Spencer et al. 4-1BBL enhances CD8+ T cell responses induced by vectored vaccines in mice but fails to improve immunogenicity in rhesus macaques. PLoS One. 2014; 9: e105520.

Busquets et al. Efficacy assessment of an MVA vectored Rift Valley Fever vaccine in lambs. Antiviral Res. 2014; 108: 165–72.

Kimani et al. Translating the immunogenicity of prime-boost immunization with ChAd63 and MVA ME-TRAP from malaria naive to malaria-endemic populations. Mol Ther. 2014; 22: 1992–2003.

Murphy et al. External quality assurance of malaria nucleic acid testing for clinical trials and eradication surveillance. PLoS One. 2014 May 16; 9:e97398.

Dean et al. Effect of dose and route of immunisation on the immune response induced in cattle by heterologous Bacille Calmette-Guerin priming and recombinant adenoviral vector boosting. Vet Immunol Immunopathol. 2014;158: 208–13.

Antrobus et al. Clinical assessment of a novel recombinant simian adenovirus ChAdOx1 as a vectored vaccine expressing conserved Influenza A antigens. Mol Ther. 2014; 22: 668–74.

Dean et al. Comparison of the immunogenicity and protection against bovine tuberculosis following immunization by BCG-priming and boosting with adenovirus or protein based vaccines. Vaccine. 2014; 32: 1304–10.

Antrobus et al. Coadministration of seasonal influenza vaccine and MVA-NP+M1 simultaneously achieves potent humoral and cell-mediated responses. Mol Ther. 2014; 22: 233–8.

Boyd et al. Towards a universal vaccine for avian influenza: protective efficacy of modified Vaccinia virus Ankara and Adenovirus vaccines expressing conserved influenza antigens in chickens challenged with low pathogenic avian influenza virus. Vaccine 2013; 31: 670–5.

Douglas et al. Comparison of modeling methods to determine liver-to-blood inocula and parasite multiplication rates during controlled human malaria infection. J Infect Dis. 2013; 208: 340–5.

Draper et al. Utilizing poxviral vectored vaccines for antibody induction-progress and prospects. Vaccine 2013; 31: 4223–30.

Ewer et al. Protective CD8+ T-cell immunity to human malaria induced by chimpanzee adenovirus-MVA immunisation. Nature Commun. 2013; 4: 2836.

Gilbert, SC, Clinical development of Modified Vaccinia virus Ankara vaccines. Vaccine 2013; 31: 4241–6.

Gilbert, SC, No easy route to a pandemic influenza vaccine. Lancet Infect Dis. 2013; 13: 188–9.

Gilbert, SC, Advances in the development of universal influenza vaccines. Influenza Other Respir Viruses 2013; 7: 750–8.

Goodman et al. The utility of Plasmodium berghei as a rodent model for anti-merozoite malaria vaccine assessment. Scientific reports 2013; 3: 1706.

Kreijtz et al. Poxvirus vectors. Vaccine 2013; 31: 4217–9.

Lambe et al. Immunity against heterosubtypic influenza virus induced by adenovirus and MVA expressing nucleoprotein and matrix protein-1. Scientific reports 2013; 3: 1443.

Lopez-Gil et al. A single immunization with MVA expressing GnGc glycoproteins promotes epitope-specific CD8+-T cell activation and protects immune-competent mice against a lethal RVFV infection. PLoS negl trop dis. 2013; 7: e2309.

Mullarkey et al. Improved adjuvanting of seasonal influenza vaccines: preclinical studies of MVA-NP+M1 coadministration with inactivated influenza vaccine. Eur J Immunol. 2013; 43: 1940–52.

Ogwang et al. Safety and immunogenicity of heterologous prime-boost immunisation with Plasmodium falciparum malaria candidate vaccines, ChAd63 ME-TRAP and MVA ME-TRAP, in healthy Gambian and Kenyan adults. PLoS One 2013; 8: e57726.

Pearson et al. Dry-coated live viral vector vaccines delivered by nanopatch microprojections retain long-term thermostability and induce transgene-specific T cell responses in mice. PLoS One 2013; 8: e67888.

Perez de Val et al. A multi-antigenic adenoviral-vectored vaccine improves BCG-induced protection of goats against pulmonary tuberculosis infection and prevents disease progression. PLoS One 2013; 8: e81317.

Powell et al. Examination of influenza specific T cell responses after influenza virus challenge in individuals vaccinated with MVA-NP+M1 vaccine. PLoS One 2013; 8: e62778.

Rowland et al. Determining the validity of hospital laboratory reference intervals for healthy young adults participating in early clinical trials of candidate vaccines. Human vaccines & immunotherapeutics, 2013; 9: 1741–51.

Rowland et al. Safety and immunogenicity of an FP9-vectored candidate tuberculosis vaccine (FP85A), alone and with candidate vaccine MVA85A in BCG-vaccinated healthy adults: a phase I clinical trial. Human vaccines & immunotherapeutics 2013; 9: 50–62.

Warimwe et al. Immunogenicity and efficacy of a chimpanzee adenovirus-vectored Rift Valley fever vaccine in mice. Virol J. 2013; 10: 349.

Antrobus et al. A T cell-inducing influenza vaccine for the elderly: safety and immunogenicity of MVA-NP+M1 in adults aged over 50 years. PLoS One 2012; 7: e48322.

Biswas et al. Recombinant viral-vectored vaccines expressing Plasmodium chabaudi AS apical membrane antigen 1: mechanisms of vaccine-induced blood-stage protection. J Immunol. 2012; 188: 5041–53.

Cottingham et al. Preventing spontaneous genetic rearrangements in the transgene cassettes of adenovirus vectors. Biotechnol Bioeng. 2012; 109: 719–28.

Dicks et al. A novel chimpanzee adenovirus vector with low human seroprevalence: improved systems for vector derivation and comparative immunogenicity. PLoS One 2012; 7: e40385.

Duncan et al. Incidental diagnosis in healthy clinical trial subjects. Clin and transl science 2012; 5: 348–50.

Gilbert, SC, Influenza vaccines and immunopathology. Expert Rev Vaccines, 2012; 11: 873–5.

Gilbert, SC, T-cell-inducing vaccines - what's the future. Immunology 2012; 135: 19–26.

Guzman et al. MVA-based vaccine vectors induce apoptosis in DC draining the skin via both the extrinsic and intrinsic caspase pathways preventing efficient antigen presentation. J virol. 2012; 86: 5452–66

Guzman et al. Modified vaccinia virus Ankara-based vaccine vectors induce apoptosis in dendritic cells draining from the skin via both the extrinsic and intrinsic caspase pathways, preventing efficient antigen presentation. J Virol. 2012; 86: 5452–66.

Hope et al. Migratory sub-populations of afferent lymphatic dendritic cells differ in their interactions with Mycobacterium bovis Bacille Calmette Guerin. Vaccine 2012; 30: 2357–67.

Lambe et al. T-Cell Responses in Children to Internal Influenza Antigens, 1 Year after Immunization with Pandemic H1N1 Influenza Vaccine, and Response to Revaccination with Seasonal Trivalent Inactivated Influenza Vaccine. The Pediatric Infect Dis J. 2012; 31: e86–91

Lillie et al. Preliminary assessment of the efficacy of a T-cell-based influenza vaccine, MVA-NP+M1, in humans. Clin Infect Dis. 2012; 55: 19–25.

Lillie et al. Distinguishing malaria and influenza: early clinical features in controlled human experimental infection studies. Travel Med Infect Dis. 2012; 10: 192–6.

O'Haraet al. Clinical assessment of a recombinant simian adenovirus ChAd63: a potent new vaccine vector. J Infect Dis. 2012; 205: 772–81.

Orubu et al. Expression and cellular immunogenicity of a transgenic antigen driven by endogenous poxviral early promoters at their authentic loci in MVA. PLoS One. 2012; 7: e40167.

Sheehyet al. Phase Ia clinical evaluation of the safety and immunogenicity of the Plasmodium falciparum blood-stage antigen AMA1 in ChAd63 and MVA vaccine vectors. PLoS One 2012; 7: e31208.

Sheehy et al. ChAd63-MVA-vectored blood-stage malaria vaccines targeting MSP1 and AMA1: assessment of efficacy against mosquito bite challenge in humans. Mol Ther. 2012; 20: 2355–68.

Spencer et al. Fusion of the Mycobacterium tuberculosis antigen 85A to an oligomerization domain enhances its immunogenicity in both mice and non-human primates. PLoS One. 2012; 7: e33555.

Berthoud et al. Potent CD8+ T-cell immunogenicity in humans of a novel heterosubtypic influenza A vaccine, MVA-NP+M1. Clin Infect Dis. 2011; 52: 1–7.

Biswas et al. Transgene Optimization, Immunogenicity and In Vitro Efficacy of Viral Vectored Vaccines Expressing Two Alleles of Plasmodium falciparum AMA1. PLoS ONE 2011; 6: e20977.

Cubillos-Zapata et al. Differential effects of viral vectors on migratory afferent lymph dendritic cells in vitro predict enhanced immunogenicity in vivo. J Virol. 2011; 85: 9385–94.

de Cassan et al. The requirement for potent adjuvants to enhance the immunogenicity and protective efficacy of protein vaccines can be overcome by prior immunization with a recombinant adenovirus. J Immunol. 2011; 187: 2602–16.

Douglas et al. Substantially reduced pre-patent parasite multiplication rates are associated with naturally acquired immunity to Plasmodium falciparum. Journal of infect.dis. 2011; 203: 1337–40.

Duncan et al. Impact on Malaria Parasite Multiplication Rates in Infected Volunteers of the Protein-in-Adjuvant Vaccine AMA1-C1/Alhydrogel+CPG 7909. PLoS ONE 2011 6: e22271.

Forbes et al. Combining Liver- and Blood-Stage Malaria Viral-Vectored Vaccines: Investigating Mechanisms of CD8+ T Cell Interference. J Immunol. 2011; 187: 3738–50.

Gharbi et al. Prime-boost immunisation against tropical theileriosis with two parasite surface antigens: evidence for protection and antigen synergy. Vaccine 2011; 29: 6620–8.

Hopkins et al. Dual neonate vaccine platform against HIV-1 and M. tuberculosis. PLoS ONE 2011; 6: e20067.

Porter et al. A human Phase I/IIa malaria challenge trial of a polyprotein malaria vaccine. Vaccine 2011; 29: 7514–22.

Sheehy et al. Phase Ia clinical evaluation of the Plasmodium falciparum blood-stage antigen MSP1 in ChAd63 and MVA vaccine vectors. Molecular therapy 2011; 19: 2269–76.

Tomáš Hanke

Bowles et al. Comparison of neutralizing antibody responses elicited from highly diverse polyvalent heterotrimeric HIV-1 gp140 cocktail immunogens versus a monovalent counterpart in rhesus macaques. PLoS One. 2014; 9: e114709.

Ondondo et al. Characterization of T-cell responses to conserved regions of the HIV-1 proteome in BALB/c mice. Clin Vaccine Immunol. 2014; 21: 1565–72.

Clutton et al. Optimizing parallel induction of HIV type 1-specific antibody and T-cell responses by multicomponent subunit vaccines. AIDS. 2014; 28: 2495–504.

Njuguna et al. PedVacc 002: a phase I/II randomized clinical trial of MVA.HIVA vaccine administered to infants born to human immunodeficiency virus type 1-positive mothers in Nairobi. Vaccine. 2014; 32: 5801–8.

Hayton et al. Safety and tolerability of conserved region vaccines vectored by plasmid DNA, simian adenovirus and modified vaccinia virus ankara administered to human immunodeficiency virus type 1-uninfected adults in a randomized, single-blind phase I trial. PLoS One. 2014; 9: e101591.

Chen L et al. Critical role of endoplasmic reticulum aminopeptidase 1 in determining the length and sequence of peptides bound and presented by HLA-B27. Arthritis Rheumatol. 2014; 66: 284–94.

Hanke T. Conserved immunogens in prime-boost strategies for the next-generation HIV-1 vaccines. Expert Opin Biol Ther. 2014; 14: 601–16.

Naarding et al. Development of a luciferase based viral inhibition assay to evaluate vaccine induced CD8 T-cell responses. J Immunol Methods. 2014; 409: 161–73.

Borthwick et al. Vaccine-elicited human T cells recognizing conserved protein regions inhibit HIV-1. Mol Ther. 2014; 22: 464–75.

Afolabi et al. Phase I randomized clinical trial of candidate human immunodeficiency virus type 1 vaccine MVA.HIVA administered to Gambian infants. PLoS ONE 2013; 8: e78289.

Ondondo et al. Absence of systemic toxicological changes following intramuscular administration of novel pSG2.HIVconsv DNA, ChAdV63.HIVconsv and MVA.HIVconsv vaccines to BALB/c mice. Vaccine 2013 31: 5594–5601.

Koopman et al. DNA/long peptide vaccination against conserved regions of SIV induces protection against high dose intrarectal SIVmac251 challenge. AIDS 2013; 27: 2841–51.

Saubi et al. Pre-clinical development of BCG.HIVA^{CAT}, an antibiotic-free selection strain, for HIV-TB pediatric vaccine vectored by lysine auxotroph of BCG. PLoS ONE 2012; 7: e42559.

Roshorm et al. T cells induced by recombinant chimpanzee adenovirus alone and in prime-boost regimens protect against chimeric HIV-1 challenge. Eur J Immunol. 2012; 42: 1–13.

Knudsen et al. Superior induction of T cell responses to conserved HIV-1 regions by electroporated alphavirus replicon DNA compared to conventional plasmid DNA vaccine. J Virol. 2012; 86: 4082–4090.

Kelschenbach et al. Mice chronically infected with chimeric HIV resist peripheral and brain superinfection: a model of protective immunity to HIV-1. J Neuroimmune Pharmacol. 2012; 7: 380–387.

Rosario et al. Prime-boost regimens with adjuvanted synthetic long peptides elicit T cells and antibodies to conserved regions of HIV in macaques. AIDS 2012; 26: 275–284.

Hopkins et al. Optimizing HIV-1-specific CD8$^+$ T cell induction by recombinant BCG in prime-boost regimens with heterologous viral vectors. Eur J Immunol. 2011; 41: 3542–3552.

Hanke and McMichael. HIV-1: from escapism to conservatism. Eur J Immunol. 2011; 41: 3390–3393.

Joseph et al. Newborn mice vaccination with rBCG.HIVA^{222} + MVA.HIVA enhances HIV-1- specific immune responses. Influence of age and immunization routes. Clin Develop Immunol 2011: Article ID 516219.

Hopkins et al. Dual neonate vaccine platform against HIV-1 and M. tuberculosis. PLoS ONE 2011; 6: e20067.

Im et al. Protective efficacy of serially up-ranked subdominant CD8+ T cell epitopes against virus challenge. PLoS Pathog. 2011; 7: e1002041.

Glyn Hewinson

Villarreal-Ramos et al. Development of a BCG challenge model for the testing of vaccine candidates against tuberculosis in cattle. Vaccine. 2014; 32: 5645–9.

Chambers et al. Vaccination against tuberculosis in badgers and cattle: an overview of the challenges, developments and current research priorities in Great Britain. Vet Rec. 2014; 175: 90–6.

Vordermeier et al. Vaccination of domestic animals against tuberculosis: review of progress and contributions to the field of the TBSTEP project. Res Vet Sci. 2014; 97 Suppl: S53–60.

Dean et al. Effect of dose and route of immunisation on the immune response induced in cattle by heterologous Bacille Calmette-Guerin priming and recombinant adenoviral vector boosting. Vet Immunol Immunopathol. 2014; 158: 208–13.

Dean et al. Comparison of the immunogenicity and protection against bovine tuberculosis following immunization by BCG-priming and boosting with adenovirus or protein based vaccines. Vaccine. 2014; 32: 1304–10.

Golby et al. Genome-level analyses of Mycobacterium bovis lineages reveal the role of SNPs and antisense transcription in differential gene expression. BMC Genomics 2013; 14: 710.

Ameni et al. Transmission of Mycobacterium tuberculosis between farmers and cattle in central Ethiopia. PLoS One 2013; 8: e76891.

Rodriguez-Campos et al. Splitting of a prevalent Mycobacterium bovis spoligotype by variable-number tandem-repeat typing reveals high heterogeneity in an evolving clonal group. J Clin Microbiol. 2013; 51: 3658–65.

Allen et al. The phylogeny and population structure of Mycobacterium bovis in the British Isles. Infect Genet Evol. 2013; 20: 8–15.

Buddle et al. Subcutaneous administration of a 10-fold-lower dose of a commercial human tuberculosis vaccine, Mycobacterium bovis bacillus Calmette-Guerin Danish, induced levels of protection against bovine tuberculosis and responses in the tuberculin intradermal test similar to those induced by a standard cattle dose. Clin Vaccine Immunol. 2013; 20: 1559–62.

Firdessa et al. Mycobacterial lineages causing pulmonary and extrapulmonary tuberculosis, Ethiopia. Emerg Infect Dis. 2013; 19: 460–3.

Firdessa et al. High prevalence of bovine tuberculosis in dairy cattle in central ethiopia: implications for the dairy industry and public health. PLoS One 2012; 7: e52851.

Carter et al. BCG vaccination reduces risk of tuberculosis infection in vaccinated badgers and unvaccinated badger cubs. PLoS One 2012; 7: e49833.

Khatri et al. A natural-transmission model of bovine tuberculosis provides novel disease insights. Vet Rec. 2012; 171: 448.

Karolemeas et al. Estimation of the relative sensitivity of the comparative tuberculin skin test in tuberculous cattle herds subjected to depopulation. PLoS One 2012; 7: e43217.

Vordermeier et al. Conserved immune recognition hierarchy of mycobacterial PE/PPE proteins during infection in natural hosts. PLoS One 2012; 7: e40890.

Thom et al. Duration of immunity against Mycobacterium bovis following neonatal vaccination with bacillus Calmette-Guérin Danish: significant protection against infection at 12, but not 24, months. Clin Vaccine Immunol. 2012; 19: 1254–60.

Casal et al. Evaluation of two cocktails containing ESAT-6, CFP-10 and Rv-3615c in the intradermal test and the interferon-γ assay for diagnosis of bovine tuberculosis. Prev Vet Med. 2012; 105: 149–54.

Vordermeier et al. The influence of cattle breed on susceptibility to bovine tuberculosis in Ethiopia. Comp Immunol Microbiol Infect Dis. 2012; 35: 227–32.

Wedlock et al. Protection against bovine tuberculosis induced by oral vaccination of cattle with Mycobacterium bovis BCG is not enhanced by co-administration of mycobacterial protein vaccines. Vet Immunol Immunopathol. 2011; 144: 220–7.

Rodriguez-Campos et al. European 2--a clonal complex of Mycobacterium bovis dominant in the Iberian Peninsula. Infect Genet Evol. 2012; 12: 866–72.

Buddle et al. Low oral BCG doses fail to protect cattle against an experimental challenge with Mycobacterium bovis. Tuberculosis (Edinb). 2011; 91: 400–5.

Kaveh et al. Systemic BCG immunization induces persistent lung mucosal multifunctional CD4 T(EM) cells which expand following virulent mycobacterial challenge. PLoS One 2011; 6: e21566.

Jones et al. Immune responses to the enduring hypoxic response antigen Rv0188 are preferentially detected in Mycobacterium bovis infected cattle with low pathology. PLoS One 2011; 6: e21371.

Whelan et al. Lack of correlation between BCG-induced tuberculin skin test sensitisation and protective immunity in cattle. Vaccine 2011; 29: 5453–8.

Smith et al. European 1: a globally important clonal complex of Mycobacterium bovis. Infect Genet Evol. 2011; 11: 1340–51.

Bezos et al. Assessment of in vivo and in vitro tuberculosis diagnostic tests in Mycobacterium caprae naturally infected caprine flocks. Prev Vet Med. 2011; 100: 187–92.

Jones et al. The use of binding-prediction models to identify M. bovis-specific antigenic peptides for screening assays in bovine tuberculosis. Vet Immunol Immunopathol. 2011; 141: 239–45.

Lesellier et al. Protection of Eurasian badgers (Meles meles) from tuberculosis after intra-muscular vaccination with different doses of BCG. Vaccine 2011; 29: 3782–90.

Buddle et al. Update on vaccination of cattle and wildlife populations against tuberculosis. Vet Microbiol. 2011; 151: 14–22.

Cadmus et al. Exploring the use of molecular epidemiology to track bovine tuberculosis in Nigeria: an overview from 2002 to 2004. Vet Microbiol. 2011; 151: 133–8.

Vordermeier et al. Mycobacterium bovis antigens for the differential diagnosis of vaccinated and infected cattle.Vet Microbiol. 2011; 151: 8-13.

Hope et al. Identification of surrogates and correlates of protection in protective immunity against Mycobacterium bovis infection induced in neonatal calves by vaccination with M. bovis BCG Pasteur and M. bovis BCG Danish. Clin Vaccine Immunol. 2011; 18: 373–9.

Adrian Hill

Hodgson et al. Evaluating controlled human malaria infection in Kenyan adults with varying degrees of prior exposure to Plasmodium falciparum using sporozoites administered by intramuscular injection. Front Microbiol. 2014; 5: 686.

de Barra et al. A phase Ia study to assess the safety and immunogenicity of new malaria vaccine candidates ChAd63 CS administered alone and with MVA CS. PLoS One. 2014; 9: e115161.

Swadling et al. A human vaccine strategy based on chimpanzee adenoviral and MVA vectors that primes, boosts, and sustains functional HCV-specific T cell memory. Sci Transl Med. 2014; 6: 261ra153.

Hodgson et al. Evaluation of the efficacy of ChAd63-MVA vectored vaccines expressing circumsporozoite protein and ME-TRAP against controlled human malaria infection in malaria-naive individuals. J Infect Dis. 2015; 211: 1076–86.

Biswas et al. Assessment of humoral immune responses to blood-stage malaria antigens following ChAd63-MVA immunization, controlled human malaria infection and natural exposure. PLoS One. 2014; 9: e107903.

Naranbhai et al.; HPTN 046 Protocol Team. The association between the ratio of monocytes: lymphocytes and risk of tuberculosis among HIV-infected postpartum women. J Acquir Immune Defic Syndr. 2014; 67: 573–5.

Hodgson et al. Combining viral vectored and protein-in-adjuvant vaccines against the blood-stage malaria antigen AMA1: report on a phase 1a clinical trial. Mol Ther. 2014; 22: 2142–54.

Carey et al. Microneedle-mediated immunization of an adenovirus-based malaria vaccine enhances antigen-specific antibody immunity and reduces anti-vector responses compared to the intradermal route. Sci Rep. 2014; 4: 6154.

Spencer et al. 4-1BBL enhances CD8+ T cell responses induced by vectored vaccines in mice but fails to improve immunogenicity in rhesus macaques. PLoS One. 2014; 9: e105520.

Naranbhai et al. The association between the ratio of monocytes:lymphocytes at age 3 months and risk of tuberculosis (TB) in the first two years of life. BMC Med. 2014; 12: 120.

Spencer et al. Enhanced vaccine-induced CD8+ T cell responses to malaria antigen ME-TRAP by fusion to MHC class ii invariant chain. PLoS One. 2014; 9: e100538.

Kimani et al. Translating the immunogenicity of prime-boost immunization with ChAd63 and MVA ME-TRAP from malaria naive to malaria-endemic populations. Mol Ther. 2014; 22: 1992–2003.

Murphy et al. External quality assurance of malaria nucleic acid testing for clinical trials and eradication surveillance. PLoS One. 2014; 9: e97398.

Colak et al. RNA and imidazoquinolines are sensed by distinct TLR7/8 ectodomain sites resulting in functionally disparate signaling events. J Immunol. 2014; 192: 5963–73.

O'Connor et al. Exonic single nucleotide polymorphisms within TLR3 associated with infant responses to serogroup C meningococcal conjugate vaccine. Vaccine. 2014; 32: 3424–30.

Nébié et al. Assessment of chimpanzee adenovirus serotype 63 neutralizing antibodies prior to evaluation of a candidate malaria vaccine regimen based on viral vectors. Clin Vaccine Immunol. 2014; 21: 901–3.

Bauza et al. Efficacy of a Plasmodium vivax malaria vaccine using ChAd63 and modified vaccinia Ankara expressing thrombospondin-related anonymous protein as assessed with transgenic Plasmodium berghei parasites. Infect Immun. 2014; 82: 1277–86.

Antrobus et al. Clinical assessment of a novel recombinant simian adenovirus ChAdOx1 as a vectored vaccine expressing conserved Influenza A antigens. Mol Ther. 2014; 22: 668–74.

Elias et al. Analysis of human B-cell responses following ChAd63-MVA MSP1 and AMA1 immunization and controlled malaria infection. Immunology. 2014; 141: 628–44.

Borthwick et al. Vaccine-elicited human T cells recognizing conserved protein regions inhibit HIV-1. Mol Ther. 2014; 22: 464–75.

Naranbhai et al. Ratio of monocytes to lymphocytes in peripheral blood identifies adults at risk of incident tuberculosis among HIV-infected adults initiating antiretroviral therapy. J Infect Dis. 2014; 209: 500–9.

Mills et al. IFITM3 and susceptibility to respiratory viral infections in the community. J Infect Dis. 2014; 209: 1028–31.

Antrobus et al. Coadministration of seasonal influenza vaccine and MVA-NP+M1 simultaneously achieves potent humoral and cell-mediated responses. Mol Ther. 2014; 22: 233–8.

Warimwe et al. Immunogenicity and efficacy of a chimpanzee adenovirus-vectored Rift Valley fever vaccine in mice. Virol J. 2013; 10: 349.

Ewer et al. Protective CD8+ T-cell immunity to human malaria induced by chimpanzee adenovirus-MVA immunisation. Nat Commun. 2013; 4: 2836.

Shields et al. Five-year follow-up for women with subclinical hypothyroidism in pregnancy. J Clin Endocrinol Metab. 2013; 98:E1941–5.

Warimwe et al. Peripheral blood monocyte-to-lymphocyte ratio at study enrollment predicts efficacy of the RTS,S malaria vaccine: analysis of pooled phase II clinical trial data. BMC Med. 2013; 11: 184.

Pearson et al. Dry-coated live viral vector vaccines delivered by nanopatch microprojections retain long-term thermostability and induce transgene-specific T cell responses in mice. PLoS One 2013; 8: e67888.

Williams et al. Immunisation against a serine protease inhibitor reduces intensity of Plasmodium berghei infection in mosquitoes. Int J Parasitol. 2013; 43:869–74.

Sheehy et al Optimising Controlled Human Malaria Infection Studies Using Cryopreserved P. falciparumParasites Administered by Needle and Syringe. PLoS One 2013; 8: e65960.

Rowland et al. Determining the validity of hospital laboratory reference intervals for healthy young adults participating in early clinical trials of candidate vaccines. Hum Vaccin Immunother. 2013; 9: 1741–51.

Hafalla et al. Identification of targets of CD8$^+$ T cell responses to malaria liver stages by genome-wide epitope profiling. PLoS Pathog. 2013; 9: e1003303.

Powell et al. Examination of influenza specific T cell responses after influenza virus challenge in individuals vaccinated with MVA-NP+M1 vaccine. PLoS One 2013; 8: e62778.

van Diemen et al. Irradiated wild-type and Spa mutant Staphylococcus aureus induce anti-S. aureus immune responses in mice which do not protect against subsequent intravenous challenge. Pathog Dis. 2013 68: 20–6.

Bowdish et al. Genetic variants of MARCO are associated with susceptibility to pulmonary tuberculosis in a Gambian population. BMC Med Genet. 2013; 14: 47.

Goodman et al. The utility of Plasmodium berghei as a rodent model for antimerozoite malaria vaccine assessment. Sci Rep. 2013; 3: 1706.

Douglas et al. Comparison of modeling methods to determine liver-to-blood inocula and parasite multiplication rates during controlled human malaria infection. J Infect Dis. 2013; 208: 340–5.

Ogwang et al. Safety and immunogenicity of heterologous prime-boost immunisation with Plasmodium falciparum malaria candidate vaccines, ChAd63 ME-TRAP and MVA ME-TRAP, in healthy Gambian and Kenyan adults. PLoS One 2013; 8: e57726.

Warimwe et al. The ratio of monocytes to lymphocytes in peripheral blood correlates with increased susceptibility to clinical malaria in Kenyan children. PLoS One 2013; 8: e57320.

Publications

Grossman et al. Identifying recent adaptations in large-scale genomic data. Cell 2013; 152: 703-13.

McDermid et al. Host iron redistribution as a risk factor for incident tuberculosis in HIV infection: an 11-year retrospective cohort study. BMC Infect Dis. 2013; 13:48.

Elias et al. Assessment of immune interference, antagonism, and diversion following human immunization with biallelic blood-stage malaria viral-vectored vaccines and controlled malaria infection. J Immunol. 2013; 190: 1135-47.

Boyd et al. Towards a universal vaccine for avian influenza: protective efficacy of modified Vaccinia virus Ankara and Adenovirus vaccines expressing conserved influenza antigens in chickens challenged with low pathogenic avian influenza virus. Vaccine 2013; 31: 670-5.

Pollard et al. Human microbial challenge: the ultimate animal model. Lancet Infect Dis. 2012; 12: 903-5.

Rowland et al. Safety and immunogenicity of an FP9-vectored candidate tuberculosis vaccine (FP85A), alone and with candidate vaccine MVA85A in BCG-vaccinated healthy adults: a phase I clinical trial. Hum Vaccin Immunother. 2013; 9: 50-62.

Antrobus et al. A T cell-inducing influenza vaccine for the elderly: safety and immunogenicity of MVA-NP+M1 in adults aged over 50 years. PLoS One 2012; 7: e48322.

Wellcome Trust Case Control Consortium, Maller et al. Bayesian refinement of association signals for 14 loci in 3 common diseases. Nat Genet. 2012; 44: 1294-301.

Sheehy et al. ChAd63-MVA-vectored blood-stage malaria vaccines targeting MSP1 and AMA1: assessment of efficacy against mosquito bite challenge in humans. Mol Ther. 2012; 20: 2355-68.

Forbes et al. T cell responses induced by adenoviral vectored vaccines can be adjuvanted by fusion of antigen to the oligomerization domain of C4bbinding protein. PLoS One 2012; 7: e44943.

Duncan et al. Incidental diagnosis in healthy clinical trial subjects. Clin Transl Sci. 2012; 5: 348-50.

Wyllie et al. Identification of 34 novel proinflammatory proteins in a genome-wide macrophage functional screen. PLoS One 2012; 7: e42388.

Dicks et al. A novel chimpanzee adenovirus vector with low human seroprevalence: improved systems for vector derivation and comparative immunogenicity. PLoS One 2012; 7: e40385.

Pathan et al. Effect of vaccine dose on the safety and immunogenicity of a candidate TB vaccine, MVA85A, in BCG vaccinated UK adults. Vaccine 2012; 30: 5616-24.

Parks et al. The perpetual challenge of infectious diseases. N Engl J Med. 2012; 367: 90.

Roestenberg et al. Comparison of clinical and parasitological data from controlled human malaria infection trials. PLoS One 2012; 7: e38434.

Laurens et al. A consultation on the optimization of controlled human malaria infection by mosquito bite for evaluation of candidate malaria vaccines. Vaccine 2012; 30: 5302-4.

Lillie et al. Distinguishing malaria and influenza: early clinical features in controlled human experimental infection studies. Travel Med Infect Dis. 2012; 10: 192-6.

Duncan et al. Can growth inhibition assays (GIA) predict blood-stage malaria vaccine efficacy? Hum Vaccin Immunother. 2012; 8: 706-14.

Biswas et al. Recombinant viral-vectored vaccines expressing Plasmodium chabaudi AS apical membrane antigen 1: mechanisms of vaccine-induced bloodstage protection. J Immunol. 2012; 188: 5041-53.

Milicic et al. Small cationic DDA:TDB liposomes as protein vaccine adjuvants obviate the need for TLR agonists in inducing cellular and humoral responses. PLoS One 2012; 7: e34255.

Spencer et al. Fusion of the Mycobacterium tuberculosis antigen 85A to an oligomerization domain enhances its immunogenicity in both mice and nonhuman primates. PLoS One 2012; 7: e33555.

Lambe et al. T-cell responses in children to internal influenza antigens, 1 year after immunization with pandemic H1N1 influenza vaccine, and response to revaccination with seasonal trivalent-inactivated influenza vaccine. Pediatr Infect Dis J. 2012; 31: e86-91.

Lillie et al. Preliminary assessment of the efficacy of a T-cell-based influenza vaccine, MVA-NP+M1, in humans. Clin Infect Dis. 2012; 55:19-25.

Minassian et al. A human challenge model for Mycobacterium tuberculosis using Mycobacterium bovis bacille Calmette-Guerin. J Infect Dis. 2012; 205: 1035-42.

Sheehy et al. Phase Ia clinical evaluation of the safety and immunogenicity of the Plasmodium falciparum blood-stage antigen AMA1 in ChAd63 and MVA vaccine vectors. PLoS One 2012; 7: e31208.

Hill. RTS,S/AS01 malaria vaccine in African children. N Engl J Med. 2012; 366: 764; author reply 765-6.

Reyes-Sandoval et al. Mixed vector immunization with recombinant adenovirus and MVA can improve vaccine efficacy while decreasing antivector immunity. Mol Ther. 2012; 20: 1633-47.

Hill. Evolution, revolution and heresy in the genetics of infectious disease susceptibility. Philos Trans R Soc Lond B Biol Sci. 2012; 367: 840-9.

Chapman and Hill. Human genetic susceptibility to infectious disease. Nat Rev Genet. 2012; 13: 175-88.

Thye et al. Common variants at 11p13 are associated with susceptibility to tuberculosis. Nat Genet. 2012; 44: 257-9.

Scriba et al. A phase IIa trial of the new tuberculosis vaccine, MVA85A, in HIVand/ or Mycobacterium tuberculosis-infected adults. Am J Respir Crit Care Med. 2012; 185: 769-78.

O'Hara et al. Clinical assessment of a recombinant simian adenovirus ChAd63: a potent new vaccine vector. J Infect Dis. 2012; 205: 772-81.

Cottingham et al. Preventing spontaneous genetic rearrangements in the transgene cassettes of adenovirus vectors. Biotechnol Bioeng. 2012; 109: 719-28.

Vrdoljak et al. Coated microneedle arrays for transcutaneous delivery of live virus vaccines. J Control Release 2012; 159: 34-42.

Colloca et al. Vaccine vectors derived from a large collection of simian adenoviruses induce potent cellular immunity across multiple species. Sci Transl Med. 2012; 4: 115ra2.

Goodman et al. A viral vectored prime-boost immunization regime targeting the malaria Pfs25 antigen induces transmission-blocking activity. PLoS One 2011; 6: e29428.

Moore et al. Single nucleotide polymorphisms in the Toll-like receptor 3 and CD44 genes are associated with persistence of vaccine-induced immunity to the serogroup C meningococcal conjugate vaccine. Clin Vaccine Immunol. 2012; 19: 295-303.

Douglas et al. The blood-stage malaria antigen PfRH5 is susceptible to vaccine inducible cross-strain neutralizing antibody. Nat Commun. 2011; 2: 601. Erratum in: Nat Commun. 2013; 4.

Duncan and Hill.What is the efficacy of the RTS,S malaria vaccine? BMJ. 2011; 343: d7728.

Nussenzweig et al. Mixed results for a malaria vaccine. Nat Med. 2011; 17: 1560-1.

Checkley et al. Identification of antigens specific to non-tuberculous mycobacteria: the Mce family of proteins as a target of T cell immune responses. PLoS One 2011; 6: e26434.

Bregu et al. Accelerating vaccine development and deployment: report of a Royal Society satellite meeting. Philos Trans R Soc Lond B Biol Sci. 2011; 366: 2841-9.

Hill. Vaccines against malaria. Philos Trans R Soc Lond B Biol Sci. 2011; 366: 2806-14.

Greenwood et al. Vaccines and global health. Philos Trans R Soc Lond B Biol Sci. 2011; 366: 2733-42.

Griffiths et al. Th1/Th17 cell induction and corresponding reduction in ATP consumption following vaccination with the novel Mycobacterium tuberculosis vaccine MVA85A. PLoS One 2011; 6: e23463.

Thøgersen et al. Comparative decline in funding of European Commission malaria vaccine projects: what next for the European scientists working in this field? Malar J. 2011; 10: 255.

Forbes et al. Combining liver- and blood-stage malaria viral-vectored vaccines: investigating mechanisms of CD8+ T cell interference. J Immunol. 2011; 187: 3738-50.

Sheehy et al. Phase Ia clinical evaluation of the Plasmodium falciparum bloodstage antigen MSP1 in ChAd63 and MVA vaccine vectors. Mol Ther. 2011; 19: 2269-76.

de Cassan et al.The requirement for potent adjuvants to enhance the immunogenicity and protective efficacy of protein vaccines can be overcome by prior immunization with a recombinant adenovirus. J Immunol. 2011; 187: 2602-16.

Carey et al. Microneedle array design determines the induction of protective memory CD8+ T cell responses induced by a recombinant live malaria vaccine in mice. PLoS One 2011; 6: e22442.

Duncan et al. Impact on malaria parasite multiplication rates in infected volunteers of the protein-in-adjuvant vaccine AMA1-C1/Alhydrogel+CPG 7909. PLoS One 2011; 6: e22271.

Pollard and Hill. Antibody repertoire: embracing diversity. Sci Transl Med. 2011; 3: 93ps32.

Reyes-Sandoval et al. CD8+ T effector memory cells protect against liver-stage malaria. J Immunol. 2011; 187: 1347-57.

Biswas et al. Transgene optimization, immunogenicity and in vitro efficacy of viral vectored vaccines expressing two alleles of Plasmodium falciparum AMA1. PLoS One 2011; 6: e20977.

Ota et al. Immunogenicity of the tuberculosis vaccine MVA85A is reduced by coadministration with EPI vaccines in a randomized controlled trial in Gambian infants. Sci Transl Med. 2011; 3: 88ra56.

Minassian et al. Preclinical development of an in vivo BCG challenge model for testing candidate TB vaccine efficacy. PLoS One 2011; 6: e19840.

Scriba et al. Dose-finding study of the novel tuberculosis vaccine, MVA85A, in healthy BCG-vaccinated infants. J Infect Dis. 2011; 203: 1832-43

Rollier et al. Viral vectors as vaccine platforms: deployment in sight. Curr Opin Immunol. 2011; 23: 377-82.

Porter et al. A human Phase I/IIa malaria challenge trial of a polyprotein malariavaccine. Vaccine 2011: 29: 7514-22.

Douglas et al. Substantially reduced pre-patent parasite multiplication rates are associated with naturally acquired immunity to Plasmodium falciparum. J Infect Dis. 2011; 203: 1337-40.

Vannberg et al. Human genetic susceptibility to intracellular pathogens. Immunol Rev. 2011; 240: 105-16.

Cavenaugh et al. Partially randomized, non-blinded trial of DNA and MVA therapeutic vaccines based on hepatitis B virus surface protein for chronic HBV infection. PLoS One. 2011; 6: e14626.

Fairfax et al. A common haplotype of the TNF receptor 2 gene modulates endotoxin tolerance. J Immunol. 2011; 186: 3058-65.

Berthoud et al. Potent CD8+ T-cell immunogenicity in humans of a novel heterosubtypic influenza A vaccine, MVA-NP+M1. Clin Infect Dis. 2011; 52: 1-7.

Paul Klenerman

Sims et al. CD73 is dispensable for the regulation of inflationary CD8+ T-cells after murine cytomegalovirus infection and adenovirus immunisation. PLoS One. 2014; 9: e114323.

Fergusson et al. CD161 defines a transcriptional and functional phenotype across distinct human T cell lineages. Cell Rep. 2014; 9: 1075-88.

Puleston et al. Autophagy is a critical regulator of memory CD8(+) T cell formation. Elife. 2014; 3.

Swadling et al. A human vaccine strategy based on chimpanzee adenoviral and MVA vectors that primes, boosts, and sustains functional HCV-specific T cell memory. Sci Transl Med. 2014; 6: 261ra153.

Ussher et al. Mucosal-associated invariant T-cells: new players in anti-bacterial immunity. Front Immunol. 2014; 5: 450.

Rajoriya et al. Gamma Delta T-lymphocytes in Hepatitis C and Chronic Liver Disease. Front Immunol. 2014; 5: 400.

Walker et al. The rise and fall of MAIT cells with age. Scand J Immunol. 2014; 80: 462-3.

Iles et al. Phylogeography and epidemic history of hepatitis C virus genotype 4 in Africa. Virology. 2014; 464-465: 233-43.

Lopez-Granados et al. A mutation in X-linked inhibitor of apoptosis (G466X) leads to memory inflation of Epstein-Barr virus-specific T cells. Clin Exp Immunol. 2014; 178: 470-82.

Beverley et al. A novel murine cytomegalovirus vaccine vector protects against Mycobacterium tuberculosis. J Immunol. 2014; 193: 2306-16.

Matthews et al. Epidemiology and impact of HIV coinfection with hepatitis B and hepatitis C viruses in Sub-Saharan Africa. J Clin Virol. 2014; 61: 20-33.

Jo et al. Toll-like receptor 8 agonist and bacteria trigger potent activation of innate immune cells in human liver. PLoS Pathog. 2014;10:e1004210.

Kløverpris et al. Programmed death-1 expression on HIV-1-specific CD8+ T cells is shaped by epitope specificity, T-cell receptor clonotype usage and antigen load. AIDS. 2014; 28: 2007-21.

Halliday et al. Hepatitis E virus infection, Papua New Guinea, Fiji, and Kiribati, 2003-2005. Emerg Infect Dis. 2014; 20: 1057-8.

Matthews et al. PARV4: an emerging tetraparvovirus. PLoS Pathog. 2014; 10: e1004036.

Stacey et al. Neutrophils recruited by IL-22 in peripheral tissues function as TRAIL-dependent antiviral effectors against MCMV. Cell Host Microbe. 2014; 15: 471-83.

Williams et al. Quantification of hepatic FOXP3+ T-lymphocytes in HIV/hepatitis C coinfection. J Viral Hepat. 2014; 21: 251-9.

Xue L et al. Prostaglandin D2 activates group 2 innate lymphoid cells through chemoattractant receptor-homologous molecule expressed on TH2 cells. J Allergy Clin Immunol. 2014; 133: 1184-94.

Ussher et al. CD161++ CD8+ T cells, including the MAIT cell subset, are specifically activated by IL-12+IL-18 in a TCR-independent manner. Eur J Immunol. 2014; 44: 195-203.

Taylor et al. Effect of interferon-α on cortical glutamate in patients with hepatitis C: a proton magnetic resonance spectroscopy study. Psychol Med. 2014; 44: 789-95.

Wong et al. Low levels of peripheral CD161++CD8+ mucosal associated invariant T (MAIT) cells are found in HIV and HIV/TB co-infection. PLoS One 2013; 8: e83474. Erratum in: PLoS One 2014; 9: e95115.

Newey et al. Mutant prolactin receptor and familial hyperprolactinemia. N Engl J Med. 2013; 369: 2012-20.

Harrison et al. Infection frequency of hepatitis C virus and IL28B haplotypes in Papua New Guinea, Fiji, and Kiribati. PLoS One 2013; 8: e66749.

Walker et al. CD8αα Expression Marks Terminally Differentiated Human CD8+ T Cells Expanded in Chronic Viral Infection. Front Immunol. 2013; 4: 223.

Batty et al. A modified RNA-Seq approach for whole genome sequencing of RNA viruses from faecal and blood samples. PLoS One 2013; 8: e66129.

Rowland et al. Determining the validity of hospital laboratory reference intervals for healthy young adults participating in early clinical trials of candidate vaccines. Hum Vaccin Immunother. 2013; 9: 1741-51.

Swadling et al. Ever closer to a prophylactic vaccine for HCV.Expert Opin Biol Ther. 2013; 13: 1109-24.

Griffiths et al. Age -associated increase of low-avidity cytomegalovirus-specific CD8+ T cells that re-express CD45RA. J Immunol. 2013; 190: 5363-72.

Bolinger et al. A new model for CD8+ T cell memory inflation based upon a recombinant adenoviral vector. J Immunol. 2013; 190: 4162-74.

Bucci et al. 'Favourable' IL28B polymorphisms are associated with a marked increase in baseline viral load in hepatitis C virus subtype 3a infection and do not predict a sustained virological response after 24 weeks of therapy. J Gen Virol. 2013; 94: 1259-65.

Iles et al. Hepatitis C virus infections in the Democratic Republic of Congo exhibit a cohort effect. Infect Genet Evol. 2013; 19: 386-94.

Simmons et al. Evolution of CD8+ T cell responses after acute PARV4 infection. J Virol. 2013; 87: 3087-96.

Cosgrove et al. Early and nonreversible decrease of CD161++ /MAIT cells in HIV infection. Blood 2013; 121: 951-61.

Schmidt et al. Rapid antigen processing and presentation of a protective and immunodominant HLA-B*27-restricted hepatitis C virus-specific CD8+ T-cell epitope. PLoS Pathog. 2012; 8: e1003042.

Kang et al. CD161(+)CD4(+) T cells are enriched in the liver during chronic hepatitis and associated with co-secretion of IL-22 and IFN-γ. Front Immunol. 2012; 3: 346.

Wang et al. Eight novel hepatitis C virus genomes reveal the changing taxonomic structure of genotype 6. J Gen Virol. 2013; 94: 76-80.

Prendergast et al. The impact of differential antiviral immunity in children and adults. Nat Rev Immunol. 2012; 12: 636-48.

Farci et al. Profibrogenic chemokines and viral evolution predict rapid progression of hepatitis C to cirrhosis. Proc Natl Acad Sci U S A 2012; 109: 14562-7.

Klapa et al. Increased frequency of IL-7 and IL-15 receptor alpha chain (CD127, CD215) co-expressing CD4(+) T cells in granulomatosis with polyangiitis (Wegener's). Clin Exp Rheumatol. 2012; 30: S171.

Oo et al. CXCR3-dependent recruitment and CCR6-mediated positioning of Th-17 cells in the inflamed liver. J Hepatol. 2012; 57: 1044-51.

Gangadharan et al. Discovery of novel biomarker candidates for liver fibrosis in hepatitis C patients: a preliminary study. PLoS One 2012; 7: e39603.

Campbell et al. Transient CD8-memory contraction: a potential contributor to latent cytomegalovirus reactivation. J Leukoc Biol. 2012; 92: 933-7.

Mitchell et al. Prospective monitoring reveals dynamic levels of T cell immunity to Mycobacterium tuberculosis in HIV infected individuals. PLoS One 2012; 7: e37920.

Gray et al. A new evolutionary model for hepatitis C virus chronic infection. PLoS Pathog. 2012; 8: e1002656.

Simmons et al. Parvovirus 4 infection and clinical outcome in high-risk populations. J Infect Dis. 2012; 205: 1816-20.

Kasprowicz et al. MIGRAs: are they the new IGRAs? Development of monokine-amplified IFN-γ release assays. Biomark Med. 2012; 6: 177-86.

Humphreys et al. HCV genotype-3a T cell immunity: specificity, function and impact of therapy. Gut. 2012; 61: 1589-99.

Phadwal et al. A novel method for autophagy detection in primary cells: impaired levels of macroautophagy in immunosenescent T cells. Autophagy 2012; 8: 677-89.

O'Hara et al. Memory T cell inflation: understanding cause and effect. Trends Immunol. 2012; 33: 84-90.

Colloca et al. Vaccine vectors derived from a large collection of simian adenoviruses induce potent cellular immunity across multiple species. Sci Transl Med. 2012; 4: 115ra2.

Barnes et al. Novel adenovirus-based vaccines induce broad and sustained T cell responses to HCV in man. Sci Transl Med. 2012; 4: 115ra1.

Xue et al. Leukotriene E4 activates human Th2 cells for exaggerated proinflammatory cytokine production in response to prostaglandin D2. J Immunol. 2012; 188: 694-702.

Klenerman and Gupta Hepatitis C virus: current concepts and future challenges. QJM. 2012; 105: 29-32.

Klenerman. Viral infection and immunity: balancing protection and pathology. QJM. 2012; 105: 103-4.

Walker et al. Human MAIT and CD8αα cells develop from a pool of type-17 precommitted CD8+ T cells. Blood. 2012; 119: 422-33.

Li et al. Impact of host responses on control of hepatitis C virus infection in Chinese blood donors. Biochem Biophys Res Commun. 2011; 415: 503-8.

Wills et al. Report from the second cytomegalovirus and immunosenescence workshop. Immun Ageing 2011; 8: 10.

Klenerman and Thimme. T cell responses in hepatitis C: the good, the bad and the unconventional. Gut 2012; 61: 1226-34.

Kasprowicz et al. A molecular assay for sensitive detection of pathogen-specific T-cells. PLoS One 2011; 6: e20606.

Thomson et al. The natural history of early hepatitis C virus evolution; lessons from a global outbreak in human immunodeficiency virus-1-infected individuals. J Gen Virol. 2011; 92: 2227-36.

Halliday et al. Vaccination for hepatitis C virus: closing in on an evasive target. Expert Rev Vaccines. 2011; 10: 659-72.

Fitzmaurice et al. Molecular footprints reveal the impact of the protective HLA-A*03 allele in hepatitis C virus infection. Gut 2011; 60: 1563-71.

Huang et al. Progression to AIDS in South Africa is associated with both reverting and compensatory viral mutations. PLoS One 2011; 6: e19018.

Marashi et al. Inflammation in common variable immunodeficiency is associated with a distinct CD8(+) response to cytomegalovirus. J Allergy Clin Immunol. 2011; 127: 1385-93.e4.

Simmons et al. High frequency, sustained T cell responses to PARV4 suggest viral persistence in vivo. J Infect Dis. 2011; 203: 1378-87.

Gangadharan et al. New approaches for biomarker discovery: the search for liver fibrosis markers in hepatitis C patients. J Proteome Res. 2011; 10: 2643-50.

di Iulio et al. and the Swiss HIV Cohort Study. Estimating the net contribution of interleukin-28B variation to spontaneous hepatitis C virus clearance. Hepatology 2011; 53: 1446-54.

Arens et al. Differential B7-CD28 costimulatory requirements for stable and inflationary mouse cytomegalovirus-specific memory CD8 T cell populations. J Immunol. 2011; 186: 3874-81.

Pfafferott et al. Constrained pattern of viral evolution in acute and early HCV infection limits viral plasticity. PLoS One 2011; 6: e16797.

Hutchinson et al. A dominant role for the immunoproteasome in CD8+ T cell responses to murine cytomegalovirus. PLoS One 2011; 6: e14646.

Kelly et al. Interferon lambdas: the next cytokine storm. Gut 2011; 60: 1284-93.

Merani et al. Effect of immune pressure on hepatitis C virus evolution: insights from a single-source outbreak. Hepatology 2011; 53: 396-405.

Fergusson et al. CD161-expressing human T cells. Front Immunol. 2011; 2: 36.

Martin Maiden

Bratcher et al. A gene-by-gene population genomics platform: de novo assembly, annotation and genealogical analysis of 108 representative Neisseria meningitidis genomes. BMC Genomics. 2014; 15: 1138.

Bull et al. The domestication of the probiotic bacterium Lactobacillus acidophilus. Sci Rep. 2014; 4: 7202.

Read et al. Effect of a quadrivalent meningococcal ACWY glycoconjugate or a serogroup B meningococcal vaccine on meningococcal carriage: an observer-blind, phase 3 randomised clinical trial. Lancet. 2014; 384: 2123-31.

van Tonder et al. Defining the estimated core genome of bacterial populations using a Bayesian decision model. PLoS Comput Biol. 2014; 10: e1003788.

Maiden and MacLennan. Editorial commentary: fifteen years of protection by meningococcal C conjugate vaccines: lessons from disease surveillance. Clin Infect Dis. 2014; 59:1222-4.

Jolley and Maiden. Using multilocus sequence typing to study bacterial variation: prospects in the genomic era. Future Microbiol. 2014; 9: 623-30.

Bambini et al. Neisseria adhesin A variation and revised nomenclature scheme. Clin Vaccine Immunol. 2014; 21:966-71.

Brehony et al. Implications of differential age distribution of disease-associated meningococcal lineages for vaccine development. Clin Vaccine Immunol. 2014; 21: 847-53.

Wörmann et al. Sequence, distribution and chromosomal context of class I and class II pilin genes of Neisseria meningitidis identified in whole genome sequences. BMC Genomics. 2014;15: 253.

Sheppard et al. Cryptic ecology among host generalist Campylobacter jejuni in domestic animals. Mol Ecol. 2014; 23: 2442-51.

Méric et al. A reference pan-genome approach to comparative bacterial genomics: identification of novel epidemiological markers in pathogenic Campylobacter. PLoS One. 2014; 9: e92798.

Bennett et al. Identifying Neisseria species by use of the 50S ribosomal protein L6 (rplF) gene. J Clin Microbiol. 2014; 52: 1375-81.

Daugla et al. Effect of a serogroup A meningococcal conjugate vaccine (PsA-TT) on serogroup A meningococcal meningitis and carriage in Chad: a community study [corrected]. Lancet. 2014; 383: 40-7.

Wimalarathna et al. Widespread acquisition of antimicrobial resistance among Campylobacter isolates from UK retail poultry and evidence for clonal expansion of resistant lineages. BMC Microbiol. 2013; 13: 160.

Suarez et al. Ribosomal proteins as biomarkers for bacterial identification by mass spectrometry in the clinical microbiology laboratory. J microbiol methods 2013; 94: 390-396.

Strachan et al. Identifying the seasonal origins of human campylobacteriosis. Epidemiol Infect. 2013; 141; 1267-1275.

Strachan et al. Operationalising factors that explain the emergence of infectious diseases: a case study of the human campylobacteriosis epidemic. PLoS One 2013; 8: e79331.

Sheppard et al. Genome-wide association study identifies vitamin B5 biosynthesis as a host specificity factor in Campylobacter. Proc Natl Acad Sci U S A 2013; 110: 11923-11927.

Sheppard et al. Progressive genome-wide introgression in agricultural Campylobacter coli. Mol Ecol. 2013; 22; 1051-1064.

Saleem, M et al. Use of a molecular decoy to segregate transport from antigenicity in the FrpB iron transporter from Neisseria meningitidis. PLoS One 2013; 8: e56746.

Roux et al. Elucidating the Aetiology of Human Campylobacter coli Infections. PLoS One 2013; 8: e64504.

Read et al. Evidence for phenotypic plasticity among multihost Campylobacter jejuni and C. coli lineages, obtained using ribosomal multilocus sequence typing and Raman spectroscopy. Appl Environ Microbiol. 2013; 79: 965-973.

Mason et al. Campylobacter infection in children in Malawi is common and is frequently associated with enteric virus co-infections. PLoS One 2013; 8: e59663.

Maiden et al. MLST revisited: the gene-by-gene approach to bacterial genomics. Nat reviews Microbiol. 2013; 11: 728-736.

Maiden. The impact of protein-conjugate polysaccharide vaccines: an endgame for meningitis? Philos Trans R Soc Lond B Biol Sci 2013; 368: 20120147.

Maiden. The endgame for serogroup a meningococcal disease in Africa? Clin Infect Dis. 2013; 56: 364-366.

Lucidarme et al. Genetic distribution of noncapsular meningococcal group B vaccine antigens in Neisseria lactamica. Clin Vaccine Immunol. 2013; 20: 1360-1369.

Jolley et al. Automated extraction of typing information for bacterial pathogens from whole genome sequence data: Neisseria meningitidis as an exemplar. Euro Surveill. 2013; 18: 20379.

Henry et al. Horizontally Transmitted Symbionts and Host Colonization of Ecological Niches. Current biology 2013; 9: 1713-1717.

Harrison et al. Description and Nomenclature of Neisseria meningitidis Capsule Locus. Emerg Infect Dis. 2013; 19: 566-573.

Harrison et al. Distribution and diversity of the haemoglobin-haptoglobin iron-acquisition systems in pathogenic and non-pathogenic Neisseria. Microbiology 2013; 159; 1920-1930.

Griekspoor et al. Marked host specificity and lack of phylogeographic population structure of Campylobacter jejuni in wild birds. Mol Ecol. 2013; 22: 1463-1472.

Daugla et al. Effect of a serogroup A meningococcal conjugate vaccine (PsA-TT) on serogroup A meningococcal meningitis and carriage in Chad: a community trial. Lancet 2013; 383: 40-47.

Cody et al. Real-time genomic epidemiology of human Campylobacter isolates using whole genome multilocus sequence typing. J Clin Microbiol. 2013; 51: 2526-2534.

Bennett et al. Genome sequence analyses show that Neisseria oralis is the same species as 'Neisseria mucosa var. heidelbergensis'. Int J Syst Evol Microbiol. 2013; 63: 3920-3926.

Basta et al. Methods for identifying Neisseria meningitidis carriers: a multi-center study in the African meningitis belt. PLoS One 2013; 8: e78336.

Altmann et al. Priorities for research on meningococcal disease and the impact of serogroup A vaccination in the African meningitis belt. Vaccine 2013; 31: 1453-1457.

Ali et al. Meningococcal carriage in the African meningitis belt. Trop Med Int Health 2013; 18: 968-978.

Abid et al. Duck Liver-associated Outbreak of Campylobacteriosis among Humans, United Kingdom, 2011. Emerg Infect Dis. 2013; 19: 1310-1313.

Yu et al. Estimating the Relative Roles of Recombination and Point Mutation in the Generation of Single Locus Variants in Campylobacter jejuni and Campylobacter coli. J Mol Evol. 2012; 74: 273-280.

Watkins & Maiden. Persistence of Hyperinvasive Meningococcal Strain Types during Global Spread as Recorded in the PubMLST Database. PLoS ONE 2012; 7: e45349.

Sheppard et al. Whole Genome MLST of Campylobacter: a Gene-by-gene approach. Genes 2012; 3: 261-277.

Sanders et al. The effect of iron availability on transcription of the Neisseria meningitidis fHbp gene varies among clonal complexes. Microbiology 2012; 158; 869-876.

McCarthy et al. Molecular epidemiology of human Campylobacter jejuni shows association between seasonal and international patterns of disease. Epidemiol Infect. 2012; 140: 2247-55.

Maiden and Frosch. Can we, should we, eradicate the meningococcus? Vaccine 2012; 30: 52-56.

Jounio et al. Genotypic and phenotypic characterization of carriage and invasive disease isolates of Neisseria meningitidis in Finland. J Clin Microbiol. 2012; 50: 264-273.

Jolley et al. Resolution of a meningococcal disease outbreak from whole genome sequence data with rapid web-based analysis methods. J Clin Microbiol. 2012; 50; 3046-3053.

Jolley et al. Ribosomal Multi-Locus Sequence Typing: universal characterisation of bacteria from domain to strain. Microbiology 2012; 158: 1005-1015.

Colles and Maiden Campylobacter sequence typing: applications and future prospects. Microbiology 2012; 158: 695-709.

Cody et al. A longitudinal six-year study of the molecular epidemiology of clinical Campylobacter isolates in Oxfordshire, UK. J Clin Microbiol. 2012; 50; 3193-3201.

Bratcher et al. Evolutionary and genomic insights into meningococcal biology. Future Microbiol 2012; 7: 873-885.

Bennett et al. A genomic approach to bacterial taxonomy: an examination and proposed reclassification of species within the genus Neisseria. Microbiology 2012; 158: 1570-1580.

Zollinger et al. Meningococcal serogroup B vaccines: will they live up to expectations? Expert Review of Vaccines 2011; 10; 559-561.

Tauseef et al. Influence of the combination and phase variation status of the haemoglobin receptors HmbR and HpuAB on meningococcal virulence. Microbiology 2011; 157: 1446-1456.

Sheppard et al. Introgression in the genus Campylobacter: generation and spread of mosaic alleles. Microbiology 2011; 157: 1066-1074.

Sheppard et al. Niche segregation and genetic structure of Campylobacter jejuni populations from wild and agricultural host species. Mol Ecol. 2011; 20: 3484-3490.

Omer et al. Genotypic and Phenotypic Modifications of Neisseria meningitidis after an Accidental Human Passage. Plos One 2011: 6: e17145.

Maiden. The Impact of Horizontal Genetic Exchange on Bacterial Population Structure: Insights from the Genera Neisseria and Campylobacter. In Population Genetics of Bacteria: A Tribute to Thomas S. Whittam, pp. 15-30. 2011; Edited by S. T. Walk & P. C. H. Feng. Washington: ASM Press.

Laukkanen-Ninios et al. Population structure of the Yersinia pseudotuberculosis complex according to multilocus sequence typing. Environ Microbiol. 2011; 13: 3114-3127.

Ibarz-Pavon et al. Changes in Serogroup and Genotype Prevalence Among Carried Meningococci in the United Kingdom During Vaccine Implementation. J Infect Dis. 2011; 204: 1046-1053.

Hastings et al. Campylobacter genotypes from poultry transportation crates indicate a source of contamination and transmission. J of Appl Microbiol. 2011; 110: 266-276.

Harrison et al. Molecular typing methods for outbreak detection and surveillance of invasive disease caused by Neisseria meningitidis, Haemophilus influenzae and Streptococcus pneumoniae, a review. Microbiology 2011; 157; 2181-2195.

Publications

Colles et al. The prevalence of Campylobacter amongst a free-range broiler breeder flock was primarily affected by flock age. PLoS One 2011; 6: e22825.

Colles et al. Campylobacter populations in wild and domesticated Mallard ducks (Anas platyrhynchos). Environ Microbiol Reports 2011; 3: 574–580.

Callaghan et al. Potential of Recombinant Opa Proteins as Vaccine Candidates against Hyperinvasive Meningococci. Infect Immun. 2011; 79: 2810–2818.

Andrew McMichael

Bowles et al. Comparison of neutralizing antibody responses elicited from highly diverse polyvalent heterotrimeric HIV-1 gp140 cocktail immunogens versus a monovalent counterpart in rhesus macaques. PLoS One. 2014; 9: e114709.

Liu et al. Preexisting compensatory amino acids compromise fitness costs of a HIV-1 T cell escape mutation. Retrovirology. 2014; 11: 101.

Ritchie et al. Recombination-mediated escape from primary CD8+ T cells in acute HIV-1 infection. Retrovirology. 2014; 11: 69.

Song et al. Reversion and T cell escape mutations compensate the fitness loss of a CD8+ T cell escape mutant in their cognate transmitted/founder virus. PLoS One. 2014: 9: e102734.

Campion et al. Proteome-wide analysis of HIV-specific naive and memory CD4(+) T cells in unexposed blood donors. J Exp Med. 2014; 211: 1273–80.

Crawshaw et al. Abnormalities in iNKT cells are associated with impaired ability of monocytes to produce IL-10 and suppress T-cell proliferation in sarcoidosis. Eur J Immunol. 2014; 44: 2165–74.

Haywardet al.; Flu Watch Group. Comparative community burden and severity of seasonal and pandemic influenza: results of the Flu Watch cohort study. Lancet Respir Med. 2014 ; 2: 445–54.

McMichael and Koff. Vaccines that stimulate T cell immunity to HIV-1: the next step. Nat Immunol. 2014; 15: 319–22.

Cole et al. Involvement of the 4-1BB/4-1BBL pathway in control of monocyte numbers by invariant NKT cells. J Immunol. 2014; 192: 3898–907.

McMichael and Dorrell. Comment on clinical development of candidate HIV vaccines: different problems for different vaccines. AIDS Res Hum Retroviruses. 2014; 30: 331–2.

Unanue and McMichael. Ita Askonas and her influence in the field of antigen presentation. Curr Opin Immunol. 2014; 26: 111–4.

Huang et al. Virus-specific antibody secreting cell, memory B-cell, and sero-antibody responses in the human influenza challenge model. J Infect Dis. 2014; 209: 1354–61.

Borthwick et al. Vaccine-elicited human T cells recognizing conserved protein regions inhibit HIV-1. Mol Ther. 2014; 22: 464–75.

Clutton et al. Emergence of a distinct HIV-specific IL-10-producing CD8+ T-cell subset with immunomodulatory functions during chronic HIV-1 infection. Eur J Immunol. 2013; 43: 2875–2885.

Goonetilleke and McMichael Immunology. Antigen processing takes a new direction. Science 2013; 340: 937–938.

Goonetilleke and McMichael HIV-1 vaccines: let's get physical. Immunity 2013; 38: 410–413.

Lane et al. and N.C.f.H.A.V. Immunology. A genome-wide association study of resistance to HIV infection in highly exposed uninfected individuals with hemophilia A. Hum Mol Genet. 2013; 22: 1903–1910.

Liu et al. Vertical T cell immunodominance and epitope entropy determine HIV-1 escape. J Clin invest. 2013; 123: 380–393.

McMichael et al. Another HIV vaccine failure: where to next? Nature Med. 2013; 19: 1576–1577.

McMichael. In pursuit of an HIV vaccine: an interview with Andrew McMichael. BMC Biol. 2013; 11: 60.

McMichael & Haynes. Influenza vaccines: mTOR inhibition surprisingly leads to protection. Nature Immunol. 2013; 14: 1205–1207.

Pala et al. Quantitative and qualitative differences in the T cell response to HIV in uninfected Ugandans exposed or unexposed to HIV-infected partners. J Virol. 2013; 87: 9053–9063.

Powell et al. Examination of influenza specific T cell responses after influenza virus challenge in individuals vaccinated with MVA-NP+M1 vaccine. PloS One 2013; 8: e62778.

Rai et al. HLA correlates in a cohort of slow progressors from China: effects on HIV-1 disease progression. Aids 2013; 27: 2822–2824.

Zhang et al. Interferon-induced transmembrane protein-3 genetic variant rs12252-C is associated with severe influenza in Chinese individuals. Nature Commun. 2013; 4: 1418.

Armitage et al. APOBEC3G-induced hypermutation of human immunodeficiency virus type-1 is typically a discrete "all or nothing" phenomenon. PLoS Genetics 2012; 8: e1002550.

Denney et al. Activation of invariant NKT cells in early phase of experimental autoimmune encephalomyelitis results in differentiation of Ly6Chi inflammatory monocyte to M2 macrophages and improved outcome. J Immunol. 2012; 189: 551–557.

Freel et al. Initial HIV-1 antigen-specific CD8+ T cells in acute HIV-1 infection inhibit transmitted/founder virus replication. J Virol. 2012; 86: 6835–6846.

Kok et al. Pivotal Advance: Invariant NKT cells reduce accumulation of inflammatory monocytes in the lungs and decrease immune-pathology during severe influenza A virus infection. J leukocyte biol. 2012; 91: 357–368.

McMichael and Chantler. Awards: Beit fellowships forge a Nobel link. Nature 2012; 490: 487.

McMichael and Haynes. Lessons learned from HIV-1 vaccine trials: new priorities and directions. Nature Immunol. 2012; 13: 423–427.

Phadwal et al. A novel method for autophagy detection in primary cells: impaired levels of macroautophagy in immunosenescent T cells. Autophagy 2012; 8: 677–689.

Powell et al. Identification of H5N1-specific T-cell responses in a high-risk cohort in vietnam indicates the existence of potential asymptomatic infections. The J Infect Dis. 2012; 205: 20–27.

Rajapaksa et al. HLA-B may be more protective against HIV-1 than HLA-A because it resists negative regulatory factor (Nef) mediated down-regulation. Proc Nat Acad Sci USA 2012; 109: 13353–13358.

Riou et al. Distinct kinetics of Gag-specific CD4+ and CD8+ T cell responses during acute HIV-1 infection. J Immunol. 2012; 188: 2198–2206.

Ritchie et al. Comparison of sexual behavior and HIV risk between two HIV-1 serodiscordant couple cohorts: the CHAVI 002 study. PloS One 2012; 7: e37727.

Rosario et al. Prime-boost regimens with adjuvanted synthetic long peptides elicit T cells and antibodies to conserved regions of HIV-1 in macaques. Aids 2012; 26: 275–284.

Sant and McMichael. Revealing the role of CD4(+) T cells in viral immunity. J Exp Med. 2012; 209: 1391–1395.

Schmidt et al. Background morbidity in HIV vaccine trial participants from various geographic regions as assessed by unsolicited adverse events. Hum Vaccines & Immunotherapeutics 2012; 8: 630–638.

Sharma et al. Workshop summary: Novel biomarkers for HIV incidence assay development. AIDS Res and Hum Retroviruses 2012; 28: 532–539.

Song et al. Impact of immune escape mutations on HIV-1 fitness in the context of the cognate transmitted/founder genome. Retrovirol. 2012; 9: 89.

Stewart-Jones et al. Structural features underlying T-cell receptor sensitivity to concealed MHC class I micropolymorphisms. Proc Nat Acad Sci USA 2012; 109: E3483–3492.

Walker and McMichael. The T-cell response to HIV. Cold Spring Harbor Perspectives in Medicine 2012; 2 pii: a007054.

Wilkinson et al: Preexisting influenza-specific CD4+ T cells correlate with disease protection against influenza challenge in humans. Nat Medicine 2012: 18: 274–280.

Yang et al. Antiviral inhibitory capacity of CD8+ T cells predicts the rate of CD4+ T-cell decline in HIV-1 infection. J Infect Dis. 2012; 206: 552–561.

Zhao et al. High levels of virus-specific CD4+ T cells predict severe pandemic influenza A virus infection. Am J Resp Crit Care Med. 2012; 186: 1292–1297.

Altman et al. Phenotypic analysis of antigen-specific T lymphocytes. Science. 1996. 274: 94–96. J Immunol. 2011; 187: 7–9.

Benam et al. Alternative spliced CD1d transcripts in human bronchial epithelial cells. PloS One 2011; 6: e22726.

Bowness et al. Th17 cells expressing KIR3DL2+ and responsive to HLA-B27 homodimers are increased in ankylosing spondylitis. J immunol. 2011; 186: 2672–2680.

Brackenridge et al. An early HIV mutation within an HLA-B*57-restricted T cell epitope abrogates binding to the killer inhibitory receptor 3DL1. J Virol. 2011; 85: 5415–5422.

Campion et al. Improved detection of latent Mycobacterium tuberculosis infection in HIV-1 seropositive individuals using cultured cellular assays. Eur J immunol. 2011; 41: 255–257.

Cohen et al. High clade C HIV-1 viremia: how did we get here and where are we going? Aids 2011; 25: 1543–1545.

Cohen et al. Acute HIV-1 Infection. New Engl J Med. 2011; 364: 1943–1954.

Corrah et al. Reappraisal of the relationship between the HIV-1-protective single-nucleotide polymorphism 35 kilobases upstream of the HLA-C gene and surface HLA-C expression. J Virol. 2011; 85: 3367–3374.

Dong et al. Extensive HLA-driven viral diversity following a narrow-source HIV-1 outbreak in rural China. Blood 2011; 118: 98–106.

Ferrari et al; Relationship between functional profile of HIV-1 specific CD8 T cells and epitope variability with the selection of escape mutants in acute HIV-1 infection. PLoS Path. 2011; 7: e1001273.

Ganusov et al. Fitness costs and diversity of the cytotoxic T lymphocyte (CTL) response determine the rate of CTL escape during acute and chronic phases of HIV infection. J Virol. 2011; 85: 10518–10528.

Haig et al. Identification of self-lipids presented by CD1c and CD1d proteins. J Biol Chem. 2011; 286: 37692–37701.

Hanke and McMichael. HIV-1: from escapism to conservatism. Eur J Immunol. 2011; 41: 3390–3393.

Im et al. Protective efficacy of serially up-ranked subdominant CD8+ T cell epitopes against virus challenges. PLoS Path. 2011; 7 :e1002041.

Kok et al. Pivotal Advance: Invariant NKT cells reduce accumulation of inflammatory monocytes in the lungs and decrease immune-pathology during severe influenza A virus infection. J Leukocyte Biol. 2011; 91: 357–368.

Petrovski et al. Common human genetic variants and HIV-1 susceptibility: a genome-wide survey in a homogeneous African population. Aids 2011; 25: 513–518.

Powell et al. Identification of H5N1-specific T-cell responses in a high-risk cohort in vietnam indicates the existence of potential asymptomatic infections. J Infect Dis. 2011; 205: 20–27.

Ranasinghe et al. The antiviral efficacy of HIV-specific CD8(+) T-cells to a conserved epitope is heavily dependent on the infecting HIV-1 isolate. PLoS Path. 2011; 7: e1001341.

Ritchie et al. Differences in HIV-specific T cell responses between HIV-exposed and -unexposed HIV-seronegative individuals. J Virol. 2011; 85: 3507–3516.

Wu et al. Optimal vaccination strategies for 2009 pandemic H1N1 and seasonal influenza vaccines in humans. Vaccine 2011; 29: 1009–1016.

Zhang et al. Multilayered defense in HLA-B51-associated HIV viral control. J Immunol. 2011; 187: 684–691.

Helen McShane

Tanner et al. Serum indoleamine 2,3-dioxygenase activity is associated with reduced immunogenicity following vaccination with MVA85A. BMC Infect Dis. 2014; 14: 660.

Naranbhai et al.; HPTN 046 Protocol Team. The association between the ratio of monocytes: lymphocytes and risk of tuberculosis among HIV-infected postpartum women. J Acquir Immune Defic Syndr. 2014; 67: 573–5.

Satti et al. Safety and immunogenicity of a candidate tuberculosis vaccine MVA85A delivered by aerosol in BCG-vaccinated healthy adults: a phase 1, double-blind, randomised controlled trial. Lancet Infect Dis. 2014; 14: 939–46.

Villarreal-Ramos et al. Development of a BCG challenge model for the testing of vaccine candidates against tuberculosis in cattle. Vaccine. 2014; 32: 5645–9.

Naranbhai et al. The association between the ratio of monocytes:lymphocytes at age 3 months and risk of tuberculosis (TB) in the first two years of life. BMC Med. 2014; 12: 120.

Iqbal et al. Human CD68 promoter GFP transgenic mice allow analysis of monocyte to macrophage differentiation in vivo. Blood. 2014; 124: e33–44.

Matsumiya et al. Inflammatory and myeloid-associated gene expression before and one day after infant vaccination with MVA85A correlates with induction of a T cell response. BMC Infect Dis. 2014; 14: 314.

Harris et al. Process of assay selection and optimization for the study of case and control samples from a phase IIb efficacy trial of a candidate tuberculosis vaccine, MVA85A. Clin Vaccine Immunol. 2014; 21: 1005–11.

O'Shea et al. Tuberculin skin testing and treatment modulates interferon-gamma release assay results for latent tuberculosis in migrants. PLoS One. 2014; 9: e97366.

Dean et al. Effect of dose and route of immunisation on the immune response induced in cattle by heterologous Bacille Calmette-Guerin priming and recombinant adenoviral vector boosting. Vet Immunol Immunopathol. 2014; 158: 208–13.

Poyntz et al. Non-tuberculous mycobacteria have diverse effects on BCG efficacy against Mycobacterium tuberculosis. Tuberculosis (Edinb). 2014; 94: 226–37.

Tameris et al. The candidate TB vaccine, MVA85A, induces highly durable Th1 responses. PLoS One. 2014; 9: e87340.

McShane and Williams. A review of preclinical animal models utilised for TB vaccine evaluation in the context of recent human efficacy data. Tuberculosis (Edinb). 2014; 94: 105–10.

McShane H. Understanding BCG is the key to improving it. Clin Infect Dis. 2014; 58: 481–2.

Harris et al. Evaluation of a human BCG challenge model to assess antimycobacterial immunity induced by BCG and a candidate tuberculosis vaccine, MVA85A, alone and in combination. J Infect Dis. 2014; 209: 1259–68.

Dean et al. Comparison of the immunogenicity and protection against bovine tuberculosis following immunization by BCG-priming and boosting with adenovirus or protein based vaccines. Vaccine. 2014; 32: 1304–10.

Naranbhai et al. Ratio of monocytes to lymphocytes in peripheral blood identifies adults at risk of incident tuberculosis among HIV-infected adults initiating antiretroviral therapy. J Infect Dis. 2014; 209: 500–9.

Pérez de Val et al. A Multi-Antigenic Adenoviral-Vectored Vaccine Improves BCG-Induced Protection of Goats against Pulmonary Tuberculosis Infection and Prevents Disease Progression. PLoS One 2013; 8: e81317.

Griffiths et al. Cholera Toxin Enhances Vaccine-Induced Protection against Mycobacterium Tuberculosis Challenge in Mice. PLoS One 2013; 8: e78312.

Fletcher et al. Inhibition of mycobacterial growth in vitro following primary but not secondary vaccination with Mycobacterium bovis BCG. Clin Vaccine Immunol. 2013; 20: 1683–9.

Matsumiya et al. Roles for Treg expansion and HMGB1 signaling through the TLR1-2-6 axis in determining the magnitude of the antigen-specific immune response to MVA85A. PLoS One 2013; 8: e67922.

Dieye et al. Two doses of candidate TB vaccine MVA85A in antiretroviral therapy (ART) naïve subjects gives comparable immunogenicity to one dose in ART+ subjects. PLoS One 2013; 8: e67177.

Dintwe et al. Heterologous vaccination against human tuberculosis modulates antigen-specific CD4+ T-cell function. Eur J Immunol. 2013; 43: 2409–20.

Tameris et al. Tuberculosis Vaccine Trials – Authors' reply. Lancet. 2013; 381: 2254.

Rowland et al. Determining the validity of hospital laboratory reference intervals for healthy young adults participating in early clinical trials of candidate vaccines. Hum Vaccin Immunother. 2013; 9: 1741–51.

Marsay et al. Mycobacterial growth inhibition in murine splenocytes as a surrogate for protection against Mycobacterium tuberculosis (M. tb). Tuberculosis (Edinb). 2013; 93: 551–7.

Meyer and McShane. The next 10 years for tuberculosis vaccines: do we have the right plans in place? Expert Rev Vaccines 2013; 12: 443–51.

White et al. Evaluation of the safety and immunogenicity of a candidate tuberculosis vaccine, MVA85A, delivered by aerosol to the lungs of macaques. Clin Vaccine Immunol. 2013; 20: 663–72.

Tameris et al. Lessons learnt from the first efficacy trial of a new infant tuberculosis vaccine since BCG. Tuberculosis (Edinb). 2013; 93: 143–9.

Tameris et al. MVA85A 020 Trial Study Team. Safety and efficacy of MVA85A, a new tuberculosis vaccine, in infants previously vaccinated with BCG: a randomised, placebo-controlled phase 2b trial. Lancet 2013; 381: 1021–8.

Betts et al. Optimising immunogenicity with viral vectors: mixing MVA and HAdV-5 expressing the mycobacterial antigen Ag85A in a single injection. PLoS One 2012; 7: e50447.

Meyer et al. Comparing the safety and immunogenicity of a candidate TB vaccine MVA85A administered by intramuscular and intradermal delivery. Vaccine 2013; 31: 1026–33.

Rustomjee et al. Designing an adaptive phase II/III trial to evaluate efficacy, safety and immune correlates of new TB vaccines in young adults and adolescents. Tuberculosis (Edinb). 2013; 93: 136–42.

Pitt et al. Vaccination against tuberculosis: how can we better BCG? Microb Pathog. 2013; 58: 2–16.

Rowland et al. Safety and immunogenicity of an FP9- vectored candidate tuberculosis vaccine (FP85A), alone and with candidate vaccine MVA85A in BCG-vaccinated healthy adults: a phase I clinical trial. Hum Vaccin Immunother. 2013; 9: 50–62.

Pathan et al. Effect of vaccine dose on the safety and immunogenicity of a candidate TB vaccine, MVA85A, in BCG vaccinated UK adults. Vaccine 2012; 30: 5616–24.

Minassian et al. A human challenge model for Mycobacterium tuberculosis using Mycobacterium bovis bacille Calmette-Guerin. J Infect Dis. 2012; 205: 1035–42.

McShane et al. BCG: myths, realities, and the need for alternative vaccine strategies. Tuberculosis (Edinb). 2012; 92: 283–8.

Duncan et al. Incidental Diagnosis in Healthy Clinical Trial Subjects. Clin Transl Sci. 2012; : 348–50.

Scriba et al. A phase IIa trial of the new TB vaccine, MVA85A, in HIV and/or M. tuberculosis infected adults. Am J Respir Crit Care Med. 2012; 185: 769–78.

Hatherill et al.; Taskforce on Clinical Research Issues, Stop TB Partnership Working Group on TB Vaccines. Consensus statement on diagnostic end points for infant tuberculosis vaccine trials. Clin Infect Dis. 2012; 54: 493–501.

Minassian et al. A Phase I study evaluating the safety and immunogenicity of MVA85A, a candidate TB vaccine, in HIV-infected adults. BMJ Open 2011; 1: e000223.

Checkley et al. Identification of Antigens Specific to Non-Tuberculous Mycobacteria: The Mce Family of Proteins as a Target of T Cell Immune Responses. PLoS One 2011; 6: e26434.

McShane. TB Vaccines: Beyond BCG. Philos Trans R Soc Lond B Biol Sci. 2011; 366: 2782–9.

McShane and Williams. Tuberculosis vaccine promises sterilizing immunity. Nature Med. 2011; 17: 1185–6.

Checkley and McShane. TB Vaccines: progress and challenges. Trends Pharmacol Sci. 2011; 32: 601–6.

Ota et al. Immunogenicity of the Tuberculosis Vaccine MVA85A Is Reduced by Coadministration with EPI Vaccines in a Randomized Controlled Trial in Gambian Infants. Sci Transl Med 2011; 3: 88ra56.

Scriba et al. A dose-finding study of the novel tuberculosis vaccine, MVA85A, in healthy BCG vaccinated infants. JID 2011; 203:1832–43.

Hopkins et al. Dual neonate vaccine platform against HIV-1 and M. tuberculosis. PLoS One 2011; 6: e20067.

Minassian et al. Preclinical development of an in vivo BCG challenge model for testing candidate TB vaccine efficacy. PLoS One 2011; 6: e19840.

Rowland & McShane. Tuberculosis vaccines in clinical trials. Expert Rev Vaccines 2011; 10: 645–58.

Peter Mertens

Belaganahalli et al. Full genome characterization of the culicoides-borne marsupial orbiviruses: Wallal virus, Mudjinbarry virus and Warrego viruses. PLoS One. 2014; 9:e108379.

Caporale et al. Virus and host factors affecting the clinical outcome of bluetongue virus infection. J Virol. 2014; 88: 10399–411.

Tuppurainen et al. Characterization of sheep pox virus vaccine for cattle against lumpy skin disease virus. Antiviral Res. 2014; 109: 1–6.

Mohd Jaafar et al. Immunisation with bacterial expressed VP2 and VP5 of bluetongue virus (BTV) protect α/β interferon-receptor knock-out (IFNAR(-/-)) mice from homologous lethal challenge. Vaccine 2014; 32: 4059–67.

Alberca et al. Vaccination of horses with a recombinant modified vaccinia Ankara virus (MVA) expressing African horse sickness (AHS) virus major capsid protein VP2 provides complete clinical protection against challenge. Vaccine. 2014; 32: 3670–4.

Bachanek-Bankowska et al. Real time RT-PCR assays for detection and typing of African horse sickness virus. PLoS One. 2014; 9: e93758.

Mohd Jaafar et al. Full-genome characterisation of Orungo, Lebombo and Changuinola viruses provides evidence for co-evolution of orbiviruses with their arthropod vectors. PLoS One. 2014; 9: e86392.

Calvo-Pinilla et al. Vaccination of mice with a modified Vaccinia Ankara (MVA) virus expressing the African horse sickness virus (AHSV) capsid protein VP2 induces virus neutralising antibodies that confer protection against AHSV upon passive immunisation. Virus Res. 2014; 180: 23–30.

Aklilu et al. African horse sickness outbreaks caused by multiple virus types in Ethiopia. Transbound Emerg Dis. 2014; 61: 185–92.

Belaganahalli et al. Full Genome Sequencing of Corriparta Virus, Identifies California Mosquito Pool Virus as a Member of the Corriparta Virus Species. PLoS One 2013; 8: e70779.

Veronesi et al. Measurement of the infection and dissemination of bluetongue virus in culicoides biting midges using a semi-quantitative rt-PCR assay and isolation of infectious virus. PLoS One 2013; 8: e70800.

Shaw et al. Bluetongue virus infection induces aberrant mitosis in mammalian cells. Virol J. 2013; 10: 319.

Mertens et al. Full genome sequence of a western reference strain of bluetongue virus serotype 16 from Nigeria. Genome Announc. 2013; 5: e00684-13.

Belaganahalli et al. Full genome sequencing of Corriparta virus, identifies California mosquito pool virus as a member of the Corriparta virus species. PLoS One 2013; 8: e70779.

Jabbar et al. Protection of IFNAR (2/2) Mice against Bluetongue Virus Serotype 8, by Heterologous (DNA/rMVA) and Homologous (rMVA/rMVA) Vaccination, Expressing Outer-Capsid Protein VP2. PLOS One 2013; Volume 8: e60574.

Veronesi et al. Implicating Culicoides Biting Midges as Vectors of Schmallenberg Virus Using Semi-Quantitative RT-PCR. PLOS One 2013; Volume 8: e57747.

Shaw et al. Reassortment between Two Serologically Unrelated Bluetongue Virus Strains Is Flexible and Can Involve any Genome Segment. J Virol. 2013; 87: 543–57.

Maan et al. The genome sequence of a reassortant bluetongue virus serotype 3 from India. J.Virol. 2012; 86: 6375–6.

Maan et al. Trans-national phylodynamics of Bluetongue Virus, with particular reference to the Indian subcontinent. J Virol. 86: 8342–3.

Shaw et al. Drosophila melanogaster as a model organism for bluetongue virus replication and tropism. J Virol. 2012; 86: 9015–24.

Mayo et al. The combination of abundance and infection rates of Culicoides sonorensis estimates risk of subsequent bluetongue virus infection of sentinel cattle on California dairy farms. Vet Parasitol. 2012; 187: 295–301.

Maan et al. Genome sequence of a reassortant strain of bluetongue virus serotype 23 from Western India. J Virol. 2012; 86: 7011–2.

Maan et al. The genome sequence of bluetongue virus type 10 from India: evidence for circulation of a western topotype vaccine strain. J Virol. 2012; 86: 5971–2.

Maan et al. Full genome sequence of bluetongue virus serotype 1 from India. J Virol. 2012; 86: 4717–8.

Maan et al. Complete genome sequence of an isolate of bluetongue virus serotype 2, demonstrating circulation of a Western topotype in southern India. J Virol. 2012; 86: 5404–5

Maan et al. The genome sequence of bluetongue virus type 2 from India: evidence for reassortment between eastern and western topotype field strains. J Virol. 2012; 86: 5967–8.

Belaganahalli et al. Full Genome Sequencing and Genetic Characterization of Eubenangee Viruses Identify Pata Virus as a Distinct Species within the Genus Orbivirus. PLoS One 2012; 7: e31911.

Maan et al. Identification and differentiation of the twenty six Bluetongue virus serotypes by RT–PCR amplification of the serotype-specific genome segment 2. PLoS One 2012; 7: e32601.

Darpel et al. Involvement of the skin during bluetongue virus infection and replication in the ruminant host. Vet Res. 2012; 43: 40.

Ruscanu et al. Bluetongue virus, a double-stranded RNA virus, induces type I IFN in primary lasmacytoid dendritic cells via a MyD88 dependent TLR7/8 independent signalling pathway. J Virol. 2012; 86: 5817–28.

Lv et al. Isolates of Liao ning virus from wild-caught mosquitoes in the Xinjiang province of China in 2005. PLoS One 2012; 7: e37732.

Attoui et al. The family Reoviridae. In Virus Taxonomy, ninth report of the International Committee for the Taxonomy of Viruses. 2011; Elsevier Academic Press.

Belhouchet et al. Detection of a fourth orbivirus non-structural protein. PLoS One 2011; 6: e25697.

Aharonson-Raz et al. Isolation and phylogenetic grouping of equine encephalosis virus in Israel. Emerg Infect Dis. 2011; 17: 1883–6.

Maan et al. Complete genome characterisation of a novel 26th bluetongue virus serotype from Kuwait. PLoS One 2011; 6: e26147.

Maan et al. Serotype specific primers and gel-based RT-PCR assays for 'typing' African horse sickness virus: identification of strains from Africa. PLoS One 2011; 6: e25686.

Anthony et al. RNA segment 9 exists as a duplex concatemer in an Australian strain of epizootic haemorrhagic disease virus (EHDV): Genetic analysis and evidence for the presence of concatemers as a normal feature of orbivirus replication. Virology 2011; 420: 164–71.

Moulin et al. Clinical disease in sheep caused by bluetongue virus serotype 8, and prevention by an inactivated vaccine. Vaccine 2012; 30: 2228–35.

Caporale et al. Determinants of bluetongue virus virulence in murine models of disease J Virol. 2011; 85: 11479–89.

Matthijnssens et al. Uniformity of Rotavirus Strain Nomenclature Proposed by the Rotavirus 1 Classification Working Group (RCWG) 2. Archives of Virol. 156: 1397–1413.

Belaganahalli et al. Umatilla Virus Genome Sequencing and Phylogenetic Analysis: Identification of Stretch Lagoon Orbivirus as a New Member of the Umatilla virus Species. PLoS One 2011; 6: e23605.

Oura et al. African horse sickness in The Gambia: circulation of a live-attenuated vaccine-derived strain. Epidemiol Infect. 2012; 140: 462–5.

Oura et al. Equine encephalosis virus: evidence for circulation beyond southern Africa. Epidemiol Infect. 2012; 140:1982–6.

Crafford et al. A competitive ELISA for the detection of group-specific antibody to equine encephalosis virus. J Virol Methods 2011; 174: 60–4.

Darpel et al. Saliva proteins of vector Culicoides modify structure and infectivity of bluetongue virus particles. PLoS One 2011; 6: e17545.

Franceschi et al. Immunization of knock-out α/β interferon receptor mice against lethal bluetongue infection with a BoHV-4-based vector expressing BTV-8 VP2 antigen. Vaccine 2011; 29: 3074–82.

Maan et al. Novel bluetongue virus serotype from Kuwait. Emerg Infect Dis. 2011; 17: 886–9.

Castillo-Olivares et al. A Modified Vaccinia Ankara Virus (MVA) Vaccine Expressing African Horse Sickness Virus (AHSV) VP2 Protects Against AHSV Challenge in an IFNAR - / - Mouse Model. Plos One 2011; 6: e16503.

Cêtre-Sossah et al. Molecular epidemiology of bluetongue virus serotype 1 isolated in 2006 from Algeria. Res Vet Sci. 2011; 91: 486–97.

Venugopal Nair

Tahiri-Alaoui et al. Poly(A) binding protein 1 enhances cap-independent translation initiation of neurovirulence factor from avian herpesvirus. PLoS One. 2014; 9: e114466.

Ciccone et al. A B-cell targeting virus disrupts potentially protective genomic methylation patterns in lymphoid tissue by increasing global 5-hydroxymethylcytosine levels. Vet Res. 2014; 45: 108.

Sacco and Nair. Prototype endogenous avian retroviruses of the genus Gallus. J Gen Virol. 2014; 95: 2060–70.

Yao and Nair. Role of virus-encoded microRNAs in Avian viral diseases. Viruses 2014; 6: 1379–94.

Yao et al. An avian retrovirus uses canonical expression and processing mechanisms to generate viral microRNA. J Virol. 2014; 88: 2–9.

Yao et al. MicroRNA expression profiles in avian haemopoietic cells. Frontiers in Genetics 2013 4: 153.

Tahiri-Alaoui et al. Identification of a neurovirulence factor from Marek's disease virus. Avian Dis. 2013; 57 Suppl: 387–394.

Baigent et al. Relationship between levels of very virulent MDV in poultry dust and in feather tips from vaccinated chickens. Avian Dis. 2013; 57 Suppl.: 440–447.

V Nair. Latency & Tumorigenesis in Marek's disease. Avian Dis. 2013; 57 Suppl. 360–365.

Mwangi et al. Induction of lymphomas by inoculation of Marek's disease virus-derived lymphoblastoid cell lines: Prevention by CVI988 vaccination. Avian Pathol. 2012; 41: 589–98.

Yao et al. Novel microRNA encoded by duck enteritis virus. J General Virol. 2012; 93: 1530–36.

Biggs and Nair. The long view: 40 years of Marek's disease research and Avian Pathology. Avian Pathol. 2012; 41: 3–9.

Payne and Nair. The long view: 40 years of avian leukosis research. Avian Pathol. 2012; 41: 11–19.

Brown et al. Epigenetic regulation of the latency-associated region of Marek's disease virus (MDV) in tumour-derived T-cell lines and primary lymphoma. J Virol. 2012; 86: 1683–95.

Smith et al. Systems analysis of immune responses in Marek's disease virus infected chickens identifies a gene involved in susceptibility and highlights a possible novel pathogenicity mechanism. J. Virol 2011; 85: 11146–58.

Mwangi et al. Clonal structure of rapid-onset MDV-driven CD4+ lymphomas and responding CD8+ T cells. PLoS Pathogens 2011; 7: e1001337.

Spatz et al. Genotypic characterization of two BAC clones derived from a single DNA source of the very virulent gallid herpesvirus-2 strain C12/130. J Gen Virol. 2011; 92: 1500–1507.

Smith et al. Pathogenicity of a very virulent strain of Marek's disease herpesvirus cloned as infectious bacterial artificial chromosomes. J Biomedicine Biotechnol. 2011; 2011: 412829

Baigent et al. Differential quantification of cloned CVI988 vaccine 1 strain and virulent RB-1B strain of Marek's disease viruses in chicken tissues, using real-time PCR. Res Vet Sci. 2011; 91: 167–74.

Satya Parida

Sen et al. Detection of subclinical peste des petits ruminants virus infection in experimental cattle. VirusDisease 2014;25: 408–11.

Muthuchelvan et al. Molecular characterization of peste-des-petits ruminants virus (PPRV) isolated from an outbreak in the Indo-Bangladesh border of Tripura state of North-East India. Vet Microbiol. 2014; 174: 591–5.

Publications

Banyard et al. Peste des petits ruminants virus, eastern Asia. Emerg Infect Dis. 2014; 20: 2176-8.

Muniraju et al. Molecular evolution of peste des petits ruminants virus. Emerg Infect Dis. 2014; 20: 2023-33.

Muniraju et al. Emergence of Lineage IV Peste des Petits Ruminants Virus in Ethiopia: Complete Genome Sequence of an Ethiopian Isolate 2010. Transbound Emerg Dis. 2014; doi: 10.1111/tbed.12287

Dhanasekaran et al. Toll-like receptor responses to Peste des petits ruminants virus in goats and water buffalo. PLoS One. 2014; 9: e111609.

Muniraju et al. Complete Genome Sequences of Lineage III Peste des Petits Ruminants Viruses from the Middle East and East Africa. Genome Announc. 2014; 2: e01023-14.

Kumar et al. Molecular characterisation of lineage IV peste des petits ruminants virus using multi gene sequence data. Vet Microbiol. 2014; 174: 39-49.

Bari et al. Genetic and antigenic characterisation of serotype A FMD viruses from East Africa to select new vaccine strains. Vaccine. 2014; 32: 5794-800.

Madhanmohan et al. Transmission of foot-and-mouth disease virus from experimentally infected Indian buffalo (Bubalus bubalis) to in-contact naïve and vaccinated Indian buffalo and cattle. Vaccine 2014; 32: 5125-30.

Buczkowski et al. Morbillivirus vaccines: recent successes and future hopes. Vaccine 2014; 32: 3155-61.

Fowler et al. Characteristics of a foot-and-mouth disease virus with a partial VP1 G-H loop deletion in experimentally infected cattle. Vet Microbiol. 2014; 169: 58-66.

Lembo et al. Peste des petits ruminants infection among cattle and wildlife in northern Tanzania. Emerg Infect Dis. 2013; 19: 2037-40.

Pope et al. Early Events following Experimental Infection with Peste-Des-Petits Ruminants Virus Suggest Immune Cell Targeting. PLoS ONE 2013; 8: e55830.

Muniraju et al. Complete genome sequence of peste des petits ruminants virus recovered from an Alpine goat during a 2008 Moroccan outbreak. Genome Announc. 2013; 1: e00096-13.

Oh et al. Interferon-γ Induced by *In Vitro* Re-Stimulation of CD4+ T-Cells Correlates with *In Vivo* FMD Vaccine Induced Protection of Cattle against Disease and Persistent Infection. PLoS ONE 2012; 7: e44365.

Bao et al. Complete Genome Sequence of a Peste des Petits Ruminants Virus Recovered from Wild Bharal in Tibet, China. J. Virol. 2012; 86: 10885-10886

El Harrak et al. A reliable and reproducible experimental challenge model for Peste-des-petits ruminants. J. Clin. Microbiol. 2012; 50: 3738-40

Buczkowski et al. A novel approach to generating morbillivirus vaccines: Negatively marking the rinderpest vaccine. Vaccine 2012; 30: 1927-35.

Madhanmohan et al. Development and evaluation of a real-time reverse transcription-loop-mediated isothermal amplification assay for rapid serotyping of foot-and-mouth disease virus. J Virol Methods. 2013; 187: 195-202.

Ko et al. Field application of a recombinant protein-based ELISA during the 2010 outbreak of foot-and-mouth disease type A in South Korea. J Virol Methods. 2012; 179: 265-8.

Fowler et al. A DNA vaccination regime including protein boost and electroporation protects cattle against foot-and-mouth disease. Antiviral Res. 2012; 94: 25-34

Baron et al. Peste des petits ruminants: a suitable candidate for eradication? Vet Rec. 2011; 169: 16-21.

Nagendrakumar et al. Evaluation of cross-protection between O(1) Manisa and O(1) Campos in cattle vaccinated with foot-and-mouth disease virus vaccine incorporating different payloads of inactivated O(1) Manisa antigen. Vaccine 2011; 29: 1906-12.

Waheed et al. Molecular Characterisation of Foot-and-Mouth Disease Viruses from Pakistan, 2005-2008. Trans and Emerg Dis. 2011; 58:166-172.

Brian Perry

Perry. Good Friday Slaughter. EcoHealth 2014; 11, 284-285.

Perry. Seeking sustainability in livestock production. Vet Rec. 2014; 175: 501.

Perry and Grace. How increasing complexity of consumer choices and deep drivers of consumption behaviour affect demand for livestock-derived products; what can be done to better understand and measure this? Proc Ann Vet Congress 2013, Swedish Vet Assoc. pp176 - 184.

Perry and Roeder. Goodbye rinderpest, hullo Peste des Petits Ruminants (PPR) control: is this an opportunity to bring the neglected small ruminant systems into the 21st Century? Proc Ann Vet Congress 2013; Swedish Vet Assoc. pp 63-68.

Perry et al. Meeting the demands for livestock vaccines: but for whom? A developing country perspective. Proc Ann Vet Congress 2013; Swedish Vet Assoc. pp 18-22.

Perry et al. Independent Evaluation of the Agricultural and Fisheries Development Fund (AFDF) in the Sultanate of Oman. FAO Office of Evaluation, FAO, Rome, 116 pp.

Perry. The structure and dynamics of cut flower export markets from Kenya and Ethiopia, with particular reference to trade with Norway. Norwegian Institute of International Affairs, Oslo, 2012; 26 pp.

Perry et al. Evaluación independiente del Proyecto Regional Integrado para el Control Progresivo de la Fiebre Aftosa en Bolivia, Colombia, Ecuador, Perú y Venezuela. FAO Office of Evaluation, FAO, Rome, 2012; 55 pp. + anexos.

Perry et al. Independent evaluation of "Supporting Food Security and Reducing Poverty in Kenya and the United Republic of Tanzania through Dynamic Conservation of Globally Important Agricultural Heritage System (GIAHS)- GCP/GLO/198/GER". FAO Office of Evaluation, FAO, Rome, 2012; 76 pp.

Henning et al. Incidence of highly pathogenic avian influenza H5N1 in Nigeria, 2005-2008. Transbound Emerg Dis. 2013; 60: 222-30.

Melchior et al. Norsk handel med de fattigste – mellom profitt og utviklingspolitikk (Norway's trade with the least developed - between profit and development politics). Norwegian Institute for Int Affairs, 2012; ISBN 978-82-7002-318-9, Oslo, 138 pp.

Perry et al. Current drivers and future directions of global livestock disease dynamics. Proc Natl Acad Sci U S A. 2013; 110: 20871-7.

Perry and Lora. Independent Evaluation of Project Development Assistance to Farmers in Remote Areas of Kosovo and Montenegro. 2011; GCP/RER/019/LUX, FAO Office of Evaluation, Rome.

Perry et al. Swaziland Agricultural Development Programme; mid-term evaluation of the US$ 20 million investment by the European Union in the resuscitation of Swaziland's agriculture. Report, 2011.

Perry et al. Independent Impact Assessment of the World Bank-funded Nigeria Avian Influenza Control and Human Pandemic Preparedness and Response Project (NAICP), Government of Nigeria. 258 pp.

Perry et al. Independent Evaluation of the Programmes and Cooperation of the Food and Agriculture Organisation of the United Nations in Ethiopia. FAO Rome, 2011; 89 pp.

Rich and Perry. The economic and poverty impacts of animal diseases in developing countries: new roles, new demands for economics and epidemiology. Prevent Vet Med. 2011; 101: 133-147.

Rich and Perry. Whither commodity-based trade? Development Policy Review 2011; 29: 331-357.

Andrew Pollard, Christine Rollier, Matthew Snape and the Oxford Vaccine Group

Jones et al. Why the development of effective typhoid control measures requires the use of human challenge studies. Front Microbiol. 2014; 5: 707.

Mehta et al. Adjuvant effects elicited by novel oligosaccharide variants of detoxified meningococcal lipopolysaccharides on Neisseria meningitidis recombinant PorA protein: a comparison in mice. PLoS One. 2014; 9: e115713.

Trück et al. Effect of cryopreservation of peripheral blood mononuclear cells (PBMCs) on the variability of an antigen-specific memory B cell ELISpot. Hum Vaccin Immunother. 2014; 10: 2490-6.

Curtis et al. Hot topics in infection and immunity in children. J Infect. 2014; 69 Suppl 1: S1.

Stoesser et al. Genome sequencing of an extended series of NDM-producing Klebsiella pneumoniae isolates from neonatal infections in a Nepali hospital characterizes the extent of community- versus hospital-associated transmission in an endemic setting. Antimicrob Agents Chemother. 2014; 58: 7347-57.

Burton et al. Tonsillectomy for periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis syndrome (PFAPA). Cochrane Database Syst Rev. 2014; 9: CD008669.

Read et al. Effect of a quadrivalent meningococcal ACWY glycoconjugate or a serogroup B meningococcal vaccine on meningococcal carriage: an observer-blind, phase 3 randomised clinical trial. Lancet. 2014; 384: 2123-31.

Waddington et al. Reply to Farmakiotis et al. Clin Infect Dis. 2014; 59: 1198-9.

Khatami et al. Evaluation of the induction of immune memory following infant immunisation with serogroup C Neisseria meningitidis conjugate vaccines – exploratory analyses within a randomised controlled trial. PLoS One. 2014; 9: e101672.

Pollard. Meningococcal disease prevention in India. Indian Pediatr. 2014; 51: 445-6.

Ramasamy et al. Randomized clinical trial to evaluate the immunogenicity of quadrivalent meningococcal conjugate and polysaccharide vaccines in adults in the United Kingdom. Clin Vaccine Immunol. 2014; 21: 1164-8.

Hanieh et al. Streptococcus pneumoniae carriage prevalence in Nepal: evaluation of a method for delayed transport of samples from remote regions and implications for vaccine implementation. PLoS One. 2014; 9: e98739.

Reynolds et al. The serodominant secreted effector protein of Salmonella, SseB, is a strong CD4 antigen containing an immunodominant epitope presented by diverse HLA class II alleles. Immunology. 2014; 143: 438-46.

Lang et al. Immunisation errors reported to a vaccine advice service: intelligence to improve practice. Qual Prim Care. 2014; 22: 139-46.

Galson et al. Studying the antibody repertoire after vaccination: practical applications. Trends Immunol. 2014; 35: 319-31.

Pollard et al. No conspiracy regarding recommendation for a group B meningococcus vaccine. BMJ. 2014; 348: g2859.

O'Connor et al. Exonic single nucleotide polymorphisms within TLR3 associated with infant responses to serogroup C meningococcal conjugate vaccine. Vaccine 2014; 32: 3424-30.

McQuaid et al. Persistence of bactericidal antibodies to 5 years of age after immunization with serogroup B meningococcal vaccines at 6, 8, 12 and 40 months of age. Pediatr Infect Dis J. 2014; 33: 760-6.

Andrews and Pollard. A vaccine against serogroup B Neisseria meningitidis: dealing with uncertainty. Lancet Infect Dis. 2014; 14: 426-34.

Pollard et al. Group B meningococcal vaccine: recommendations for UK use. Lancet. 2014; 383: 1103-4.

Mitchell et al. Polysaccharide-specific B cell responses to vaccination in humans. Hum Vaccin Immunother. 2014; 10: 1661-8.

Martin et al. Hospital admission rates for meningitis and septicaemia caused by Haemophilus influenzae, Neisseria meningitidis, and Streptococcus pneumoniae in children in England over five decades: a population-based observational study. Lancet Infect Dis. 2014; 14: 397-405.

Trück et al. Pneumococcal serotype-specific antibodies persist through early childhood after infant immunization: follow-up from a randomized controlled trial. PLoS One. 2014; 9: e91413.

Waddington et al. An outpatient, ambulant-design, controlled human infection model using escalating doses of Salmonella Typhi challenge delivered in sodium bicarbonate solution. Clin Infect Dis. 2014; 58: 1230-40.

Norheim et al. Association between population prevalence of smoking and incidence of meningococcal disease in Norway, Sweden, Denmark and the Netherlands between 1975 and 2009: a population-based time series analysis. BMJ Open. 2014; 4: e003312.

Waddington et al. Advancing the management and control of typhoid fever: a review of the historical role of human challenge studies.

J Infect. 2014; 68: 405-18. Marshall et al. The seroepidemiology of Haemophilus influenzae type b prior to introduction of an immunization programme in Kathmandu, Nepal. PLoS One. 2014; 9: e85055.

Perrett et al. Long-term persistence of immunity and B-cell memory following Haemophilus influenzae type B conjugate vaccination in early childhood and response to booster. Clin Infect Dis. 2014; 58: 949-59.

Nagaputra et al. Neisseria meningitidis native outer membrane vesicles containing different lipopolysaccharide glycoforms as adjuvants for meningococcal and nonmeningococcal antigens. Clin Vaccine Immunol. 2014; 21: 234-42.

Darton et al. Typhoid epidemiology, diagnostics and the human challenge model. Curr Opin Gastroenterol. 2014; 30: 7-17.

O'Connor et al. The effect of chronic cytomegalovirus infection on pneumococcal vaccine responses. J Infect Dis. 2014; 209: 1635-41.

Hoschler et al. Administration of AS03B-adjuvanted A(H1N1)pdm09 vaccine in children aged <3 years enhances antibody response to H3 and B viruses following a single dose of trivalent vaccine one year later. Clin Infect Dis. 2014; 58: 181-7.

Waddington et al. The challenge of enteric fever. J Infect. 2014; 68 Suppl 1: S38-50.

Curtis et al. Hot topics in infection and immunity in children--Papers from the 10th annual IIC meeting, Oxford, UK, 2012. Preface. J Infect. 2014; 68 Suppl 1: S1.

Trück et al. The zwitterionic type I Streptococcus pneumoniae polysaccharide does not induce memory B cell formation in humans. Immunobiol. 2013; 218: 368-72.

de Whalley and Pollard. Pandemic influenza A (H1N1) 2009 vaccination in children: A UK perspective. J Paediatr Child Health. 2013; 49: E183-8.

Khatami et al. Phase II Study of a Three-Dose Primary Vaccination Course of DTPa-IPV/Hib-MenC-TT Followed by a 12-Month Hib-MenC-TT Booster in Healthy Infants. Pediatr Infect Dis J. 2013; 32: 675-81.

Snape & Pollard. The beginning of the end for serogroup B meningococcus? Lancet. 2013; 381: 785-7.

Prando et al. Inherited IL-12p40 Deficiency: Genetic, Immunologic, and Clinical Features of 49 Patients From 30 Kindreds. Medicine (Baltimore). 2013; 92: 109-122.

Yates et al. UK vaccination schedule: persistence of immunity to hepatitis B in children vaccinated after perinatal exposure. Arch Dis Child. 2013; 98: 429-33.

Pollard et al. Adolescents need a booster of serogroup C meningococcal vaccine to protect them and maintain population control of the disease. Arch Dis Child. 2013; 98: 248-51.

Rohner et al. Seroprevalence and Placental Transmission of Maternal Antibodies Specific for Neisseria meningitidis Serogroups A, C, Y and W135 and Influence of Maternal Antibodies on the Immune Response to a Primary Course of MenACWY-CRM Vaccine in the United Kingdom. Pediatr Infect Dis J. 2013; 32: 768-76.

Blanchard-Rohner et al. The B-cell response to a primary and booster course of MenACWY-CRM197 vaccine administered at 2, 4 and 12 months of age. Vaccine 2013; 31: 2441-8.

Bolze et al. Ribosomal Protein SA Haploinsufficiency in Humans with Isolated Congenital Asplenia. Science 2013; 340: 976-8.

McGregor et al. Prospects for prevention of Salmonella infection in children through vaccination. Curr Opin Infect Dis. 2013; 26: 254-62.

Moxon and Snape. The price of prevention: what now for immunisation against meningococcus B? Lancet 2013; 382: 369-370.

Martin and Snape. A multicomponent serogroup B meningococcal vaccine is available for use in Europe: what do we know, and what are we yet to learn? Expert Rev Vaccines 2013; 12: 837-58.

Pulickal et al. Prevalence and Genetic Analysis of Phenotypically Vi-Negative Salmonella Typhi Isolates in Children from Kathmandu, Nepal. J Trop Pediatr. 2013; 59: 317-20.

Trück et al. Genetic material should be routinely collected in clinical vaccine trials - High consent rates can be achieved across all age groups. Vaccine 2013; 31: 2744-8.

Xie et al. Emergence of serogroup X meningococcal disease in Africa: Need for a vaccine. Vaccine 2013; 31: 2852-61.

De Whalley et al. Long-term seroprotection after an adolescent booster meningococcal serogroup C vaccination. Arch Dis Child. 2013; 98: 686-91.

Weissmueller et al. Intradermal powder immunization with protein-containing vaccines. Expert Rev Vaccines 2013; 12: 687-702.

O'Connor and Pollard. Characterizing Vaccine Responses Using Host Genomic and Transcriptomic Analysis. Clin Infect Dis. 2013; 57: 860-9.

Rodgers et al. Immune response to 13-valent pneumococcal conjugate vaccine with a reduced dosing schedule. Vaccine 2013; 31: 4765-74.

Snape et al. Bactericidal Antibody Persistence Two Years Following Immunization with Two Investigational Serogroup B Meningococcal Vaccines at 6, 8 And 12 Months and Immunogenicity of Pre-School Booster Doses: A Follow-On Study to a Randomized Clinical Trial. Pediatr Infect Dis J. 2013; 32: 1116-21.

Bambery et al. The case for mandatory flu vaccination of children. Am J Bioeth. 2013; 13: 38-40.

Mitchell et al. Use of the 13-valent pneumococcal conjugate vaccine in children and adolescents aged 6 – 17 years. Expert Opin Biol Ther. 2013; 13: 1451-65.

Snape et al. Persistence of bactericidal antibodies following early infant vaccination with a serogroup B meningococcal vaccine and immunogenicity of a preschool booster dose. CMAJ. 2013; 185: E715-24.

McCann et al. Self-reported adverse events in adolescents aged 13-18 years after mass vaccination with pertussis-containing vaccine, following a school outbreak. Public Health 2013; 127: 1133-6.

Khatami et al. Persistence of Antibody Response Following a Booster Dose of Hib-MenC-TT Glycoconjugate Vaccine to Five Years: A Follow-Up Study. Pediatr Infect Dis J. 2012; 31:1069-73.

Moore et al. SNPs in the TLR3 and CD44 genes are associated with persistence of vaccine-induced immunity to serogroup C meningococcal conjugate vaccine. Clin Vaccine Immunol. 2012; 19: 295-303.

Sadarangani et al. Construction of Opa-Positive and Opa-Negative Strains of Neisseria meningitidis to Evaluate a Novel Meningococcal Vaccine. PLoS One. 2012; 7: e51045.

Pollard et al. Human microbial challenge: the ultimate animal model. Lancet Infect Dis. 2012; 12: 903-5.

Pradhan et al. Bloodstream Infection among Children Presenting to a General Hospital Outpatient Clinic in Urban Nepal. PLoS One. 2012; 7: e47531.

Grant et al. Assessment of T-dependent and T-independent immune responses in cattle using a B cell ELISPOT assay. Vet Res. 2012; 43: 68.

Sibley et al. Assent is not consent. J Med Ethics. 2012; 38: 3.

Walker et al. H1N1 Antibody Persistence 1 Year After Immunization With an Adjuvanted or Whole-Virion Pandemic Vaccine and Immunogenicity and Reactogenicity of Subsequent Seasonal Influenza Vaccine: A Multicenter Follow-on Study. Clin Infect Dis. 2012; 54: 661-9.

Gossger et al. and European MenB Vaccine Study Group. Immunogenicity and tolerability of recombinant serogroup B meningococcal vaccine administered with or without routine infant vaccinations according to different immunization schedules: a randomized controlled trial. JAMA. 2012; 307: 573-82.

Snape et al. The challenge of post-implementation surveillance for novel meningococcal vaccines. Vaccine 2012; 30 Suppl 2: B67-72.

Khatami et al. Persistence of the immune response at 5 years of age following infant immunisation with investigational quadrivalent MenACWY conjugate vaccine formulations. Vaccine 2012; 30: 2831-8.

de Whalley et al. A 1-year follow-on study from a randomised, head-to-head, multicentre, open-label study of two pandemic influenza vaccines in children. Health Technol Assess. 2011; 15: v-vi, xi-xiii, 1-128.

Metz et al. Evaluation of Haemophilus influenzae Type b Vaccine for Routine Immunization in Nepali Infants. Pediatr Infect Dis J. 2012; 31: e66-72.

Scott et al. Management of lymphadenitis due to non-tuberculous mycobacterial infection in children. Pediatr Surg Int. 2012; 28: 461-6.

Clutterbuck et al. Pneumococcal conjugate and plain polysaccharide vaccines have divergent effects on antigen-specific B cells. J Infect Dis. 2012; 205: 1408-16.

Lambe et al. T-Cell Responses in Children to Internal Influenza Antigens, 1 Year after Immunization with Pandemic H1N1 Influenza Vaccine, and Response to Revaccination with Seasonal Trivalent Inactivated Influenza Vaccine. Pediatr Infect Dis J. 2012; 31: e86-91.

Pace and Pollard. Meningococcal disease: Clinical presentation and sequelae. Vaccine. 2012; 30 Suppl 2:B3-9.

Blanchard-Rohner et al. Baseline polysaccharide-specific antibodies may not consistently inhibit booster antibody responses in infants to a serogroup C meningococcal protein-polysaccharide conjugate vaccine. Vaccine 2012; 30: 4153-9.

Trück et al. Pneumococcal polysaccharide vaccine efficacy and routine use of conjugate vaccines in infants: there is no need for a vaccine programme in older adults at present. Clin Infect Dis. 2012; 55: 1577-9.

Perrett et al. B cell memory to a serogroup C meningococcal conjugate vaccine in childhood and response to booster: little association with serum IgG antibody. J Immunol. 2012; 189: 2673-81.

Zhou and Pollard. A novel method of selective removal of human DNA improves PCR sensitivity for detection of Salmonella Typhi in blood samples. BMC Infect Dis. 2012; 12: 164.

Xie et al. Characterization of size, structure and purity of serogroup X Neisseria meningitidis polysaccharide, and development of an assay for quantification of human antibodies. Vaccine 2012; 30: 5812-23.

Pollard. Non-specific effects of vaccines: RCTs, not observational studies, are needed. Arch Dis Child. 2012; 97: 677-8.

Kelly et al. The burden of vaccine-preventable invasive bacterial infections and pneumonia in children admitted to hospital in urban Nepal. Int J Infect Dis. 2011; 15:e17-23.

Williams et al. Haemophilus influenzae type b carriage and novel bacterial population structure among children in urban Kathmandu, Nepal. J Clin Microbiol. 2011; 49: 1323-30.

Su and Snape. A combination recombinant protein and outer membrane vesicle vaccine against serogroup B meningococcal disease. Expert Rev Vaccines. 2011; 10: 575-88.

Snape and Kelly. Fine with five? Shorter antibiotic courses for childhood meningitis. Lancet 2011; 377: 1809-10.

Lazarus et al. A randomized study comparing combined pneumococcal conjugate and polysaccharide vaccination schedules in adults. Clin Infect Dis. 2011; 52: 736-42.

Chhetri et al. Clinical profile of invasive pnemococcal diseases in patan hospital, Nepal. Kathmandu Univ Med J (KUMJ). 2011; 9: 45-9.

Harrison et al. The Global Meningococcal Initiative: Recommendations for reducing the global burden of meningococcal disease. Vaccine 2011; 29: 3363-71.

Callaghan et al. The potential of recombinant Opa proteins as vaccine candidates against hyperinvasive meningococci. Infect Immun. 2011; 79:2810-8.

Barnes and Pollard. Vaccines in clinical trials: infectious disease. Expert Rev Vaccines.2011; 10: 555-7.

Blanchard-Rohner and Pollard. Long-term protection after immunization with protein-polysaccharide conjugate vaccines in infancy. Expert Rev Vaccines. 2011; 10: 673-84.

de Whalley et al. Persistence of Serum Bactericidal Antibody One Year After a Booster Dose of Either a Glycoconjugate or a Plain Polysaccharide Vaccine Against Serogroup C Neisseria meningitidis Given to Adolescents Previously Immunized With a Glycoconjugate Vaccine. Pediatr Infect Dis J. 2011; 30: e203-8.

Thompson et al. Typhoid burden greater than previously recognised in Nepal. Global Immunization News 2011; 29.07: p2.

Pollard and Hill. Antibody repertoire: embracing diversity. Sci Transl Med. 2011; 3: 93ps32.

Andrews et al. Predictors of immune response and reactogenicity to AS03B-adjuvanted split virion and non-adjuvanted whole virion H1N1 (2009) pandemic influenza vaccines. Vaccine 2011; 29: 7913-9.

Pollard. Infectious disease: Childhood meningitis may be preventable if we can afford it. Nat Rev Neurol. 2011; 7: 539-40.

PENPACT-1 (PENTA 9/PACTG 390) Study Team. First-line antiretroviral therapy with a protease inhibitor versus non-nucleoside reverse transcriptase inhibitor and switch at higher versus low viral load in HIV-infected children: an open-label, randomised phase 2/3 trial. Lancet Infect Dis. 2011; 11: 273-83.

Khatami et al. Maintenance of Immune Response Throughout Childhood Following Serogroup C Meningococcal Conjugate Vaccination in Early Childhood. Clin Vaccine Immunol. 2011; 18: 2038-42.

Pollard and Constable. Expert Review of Vaccines 10-year anniversary issue. Expert Rev Vaccines. 2011; 10: 1489-91.

Arturo Reyes-Sandoval

Bauza et al. Efficacy of a Plasmodium vivax malaria vaccine using ChAd63 and modified vaccinia Ankara expressing thrombospondin-related anonymous protein as assessed with transgenic Plasmodium berghei parasites. Infect Immun. 2014; 82: 1277-86.

Warimwe et al. Immunogenicity and efficacy of a chimpanzee adenovirus-vectored Rift Valley fever vaccine in mice. Virol J. 2013; 10: 349.

Ewer et al. Protective CD8+ T-cell immunity to human malaria induced by chimpanzee adenovirus-MVA immunisation. Nat Commun. 2013; 4: 2836.

Reyes-Sandoval and Bachmann. Plasmodium vivax malaria vaccines: Why are we where we are? Hum Vaccin Immunother. 2013; 9: 2558-65.

White et al. Evaluation of the safety and immunogenicity of a candidate tuberculosis vaccine, MVA85A, delivered by aerosol to the lungs of macaques. Clin Vaccine Immunol. 2013; 20: 663-72.

Betts et al. Optimising Immunogenicity with Viral Vectors: Mixing MVA and HAdV-5 Expressing the Mycobacterial Antigen Ag85A in a Single Injection. PLoS One 2012; 7: e50447.

Milicic et al. Small Cationic DDA:TDB Liposomes as Protein Vaccine Adjuvants Obviate the Need for TLR Agonists in Inducing Cellular and Humoral Responses. PLoS One 2012; 7: e34255.

Reyes-Sandoval et al. Mixed Vector Immunization With Recombinant Adenovirus and MVA Can Improve Vaccine Efficacy While Decreasing Antivector Immunity. Mol. Ther. 2012; 20: 1633-47.

Knudsen et al. Superior induction of T cell responses to conserved HIV-1 regions by electroporated alphavirus replicon DNA compared to conventional plasmid DNA vaccine. J. Virol. 2012; 86: 4082-4090.

O'Hara et al. Clinical assessment of a recombinant simian adenovirus ChAd63: a potent new vaccine vector. J. Infect. Dis. 2012; 205: 772-781.

Reyes-Sandoval et al. CD8+ T Effector Memory Cells protect against Liver-Stage Malaria. J Immunol. 2011; 187: 1347-57.

Rollier et al. Viral vectors as vaccine platforms: deployment in sight. Curr. Opin. Immunol. 2011; 23: 377-82.

Sarah Rowland-Jones

Rafferty et al. How can we design better vaccines to prevent HIV infection in women? Front Microbiol. 2014; 5: 572.

Yindom et al. Complete genomic sequence of KIR3DL1*0150102. Tissue Antigens. 2014; 84: 595-6.

Yindom et al. Isolation of full-length genomic sequences of the KIR3DL1*0040103 allele from African donors using sequence-based techniques. Tissue Antigens. 2014; 84: 594-5.

Yindom et al. Description of a novel KIR3DL1*0150211 allele isolated using molecular techniques. Tissue Antigens. 2014; 84: 596-7.

Yindom et al. Genomic full length sequence of a novel killer-cell immunoglobulin-like receptor, KIR3DL1*0010103 identified by sequencing. Tissue Antigens. 2014; 84: 520-1.

Yindom et al. A new variant of killer-cell immunoglobulin-like receptor KIR3DL1*03101 isolated using sequence-based techniques. Tissue Antigens. 2014; 84: 521-2.

Yindom et al. Full-length KIR3DL1*022 detected in an African donor. Tissue Antigens. 2014; 84: 427-9.

Yindom et al. Full length KIR3DS1*0130110 allele isolated by SBT. Tissue Antigens. 2014; 84: 423-4.

Yindom et al. KIR3DS1*0130108 isolated using full length sequence-based typing. Tissue Antigens. 2014; 84: 251-2.

Abidi et al. HIV-1 subtype A gag variability and epitope evolution PLoS One. 2014; 9: e93415.

Yindom et al. Report of a novel activating killer-cell immunoglobulin-like receptor allele 3DS1*078 identified using sequence-based typing. Tissue Antigens. 2014; 84: 252-4.

Yindom et al. A novel KIR3DS1*0130107 allele identified by sequencing from an Asian donor. Int J Immunogenet. 2014; 41: 267-8.

Kanki and Rowland-Jones. The protective effect of HIV-2 infection: implications for understanding HIV-1 immunity. AIDS. 2014; 28: 1065-7.

Yindom et al. A novel KIR3DL1*0200102 allele isolated from a West African donor by sequence-based typing. Tissue Antigens. 2014; 83: 305-6.

Wang et al. Identification of KIR3DL1*0150208 using long-range sequence-based techniques. Tissue Antigens. 2014; 83: 372-3.

Wang et al. A novel full-length KIR3DS1*0130106 allele identified by sequencing. Tissue Antigens. 2014; 83: 371-2.

Wang et al. Detection of a novel killer-cell immunoglobulin-like receptor allele - KIR3DL1*0150207 - in Asian individuals. Tissue Antigens. 2014; 83: 304-5.

Yindom et al. The KIR3DS1*0130105 allele identified using high-resolution sequence-based typing. Tissue Antigens. 2014; 83: 302-3.

Yindom et al. Identification of KIR3DL1*0200101 by long-range sequence-based techniques. Tissue Antigens. 2014; 83: 127-8.

Yindom et al. A novel KIR3DL1*0200102 allele isolated from a West African donor by sequence-based typing. Tissue Antigens. 2014; 83: 124-5.

Wang et al. Identification of the KIR3DL1*0050105 allele by sequence-based techniques. Tissue Antigens. 2014; 83: 301-2.

Yindom et al. Killer-cell immunoglobulin-like receptor gene 3DL1*077 isolated using long-range sequence-based techniques. Tissue Antigens. 2014; 83: 206-7.

Yindom et al. A novel KIR3DL1*0070104 allele found in individuals from Asia. Tissue Antigens. 2014; 83: 204-6.

Afran et al. HIV-exposed uninfected children: a growing population with a vulnerable immune system? Clin Exp Immunol. 2014; 176: 11-22.

Yindom et al. Report of a novel KIR3DS1*0130104 allele discovered using advanced molecular techniques. Tissue Antigens. 2014; 83: 121-2.

Yindom et al. Full-length genomic sequence of a new KIR3DL1*0150203 allele. Tissue Antigens. 2014; 83: 122-3.

Yindom et al. Full-length sequence of KIR3DL1*01501 allele found in Sub-Saharan Africa by long-range sequencing. Tissue Antigens. 2014; 83: 126-7.

Yindom et al. Long-range sequencing revealed a new KIR3DL1*0150204 allele in 20 individuals of Asian descent. Tissue Antigens. 2014; 83: 123-4.

Yindom et al. Two novel KIR3DL1 alleles, 3DL1*0150205 and 3DL1*0150206, identified by full-length DNA sequencing. Tissue Antigens. 2014; 83: 128-9.

Abidi et al. HIV-1 progression links with viral genetic variability and subtype, and patient's HLA type: analysis of a Nairobi-Kenyan cohort. Med Microbiol Immunol. 2014; 203: 57-63. -

De Silva et al. Population dynamics of HIV-2 in rural Guinea-Bissau: comparison with HIV-1 and ongoing transmission at the heart of the epidemic. AIDS 2013; 27: 125-134.

Abidi et al. Population-specific evolution of HIV gag epitopes in genetically diverged patients. Infect Genet Evol. 2013; 16: 78-86.

De Silva et al. Correlates of HIV-2 control: insights into natural containment of a human retroviral infection. Blood 2013; 121: 4330-9.

Powell et al. Examination of Influenza Specific T Cell Responses after Influenza Virus Challenge in Individuals Vaccinated with MVA-NP+M1 Vaccine. PLoS One 2013; 8: e62778.

Rai et al. HLA correlates in a cohort of slow progressors from China: effects on HIV-1 disease progression. AIDS 2013; 27: 2822-4.

Afolabi et al. A Phase I Randomized Clinical Trial of Candidate Human Immunodeficiency Virus type 1 Vaccine MVA.HIVA Administered to Gambian Infants. PLoS One 2013; 8: e78289.

Publications

Yindom et al. Identification of KIR3DL1*0050103 by sequence--based techniques. Tissue Antigens 2013; 82: 444-5.

Yindom et al. A novel full-length KIR3DL1*0070103 identified by molecular typing. Tissue Antigens 2013; 82: 445-6.

Nyamweya et al. Comparing HIV-1 and HIV-2 infection: lessons for viral immunopathogenesis. Rev. Med. Virol. 2013; 23: 221-240.

De Silva et al. Potent autologous and heterologous neutralising antibody responses in HIV-2 infection: further insight into disparities with HIV-1 pathogenesis. J. Virol. 2012; 86: 930-946.

Powell et al. Identification of H5N1 specific T-cell responses in a high-risk cohort in Viet Nam indicate the existence of potential asymptomatic infections. J Infect Diseases 2012; 205: 20-7.

Culshaw et al. A two amino acid shift in position leads to a substantial difference in the pattern of processing of two HIV-1 epitopes. J AIDS 2012; 59: 335-339.

Sabbah et al. T cell immunity to Kaposi's sarcoma-associated herpesvirus: targeting primary effusion lymphoma with LANA-specific CD4+ T cells. Blood 2012; 119: 2083-92.

Khalid et al. Efficient nef-mediated down-modulation of TCR-CD3 and CD28 is associated with high CD4+ T-cell counts in viremic HIV-2 infection. J Virol. 2012; 86: 4906-20.

Njie-Jobe et al. Immunological impact of an additional early measles vaccine in Gambian children: responses to a boost at 3 years. Vaccine 2012; 30: 2543-50.

Gourlay et al. Clinical predictors cannot replace biological predictors in HIV-2 infection in a community setting in West Africa. Int J Infect Diseases 2012; 16: e337-43.

Walther et al. High HO-1 levels in response to P. Falciparum malaria are associated with severe disease and death. PLOS Pathogens 2012; 8: e1002579.

Jayasooriya et al. Revisiting the effect of acute P. falciparum malaria on EBV: host balance in the setting of reduced malaria endemicity. PLoS One 2012; 7: e31142.

Blais et al. Enhanced HLA-C-restricted CTL selective pressure associated with an AIDS-protective polymorphism. J Immunol. 2012; 188: 4663-70.

Zaidi et al. Immune reconstitution inflammatory syndrome and the influence of T regulatory cells: a cohort study in the Gambia. PLoS One 2012; 7: e39213.

Simpson et al. Functional differences exist between TNFalpha promoters encoding the common -237G SNP and the rarer HLA-B*5701-linked A variant. PLoS One 2012; 7: e40100.

Nyamweya et al. Are serum biomarkers of immune activation predictive of HIV progression? A longitudinal comparison and analysis in HIV-1 and HIV-2 infections. PLoS One 2012; 7: e44411.

Slyker et al. Acute CMV infection is associated with increased frequencies of activated and apoptotic-vulnerable T-cells in HIV-1-infected infants. J Virol. 2012; 86: 11373-9.

Kong et al. Epitope mapping of broadly neutralizing human HIV-2 monoclonal antibodies. J Virol. 2012; 86: 12115-28.

Lohman-Payne et al. Breastmilk cellular HIV-1-specific interferon gamma responses are associated with protection from early breastmilk transmission. AIDS 2012; 26: 2007-2016.

De Silva et al. Effect of HIV-2 infection on HIV-1 disease progression (letter). N. Engl. J. Med. 2012; 367: 1961-2.

Stewart-Jones et al. Structural features underlying T-cell receptor recognition of a bulged HLA-B*57-restricted HIV-1 epitope and sensitivity to MHC class I polymorphisms. PNAS 2012; 109: E3483-92.

Slyker et al. The impact of HIV-1 infection and exposure on NK cell phenotype in Kenyan infants during the first year of life. Frontiers in Immunology 2012; 3: 399.

Peterson and Rowland-Jones. Novel agents for the treatment of HIV-2 infection (commentary). Antiviral ther. 2012; 17:435-8.

Lohman-Payne et al. Immune approaches for the prevention of breast-milk transmission of HIV-1. Adv. Exp. Med. Biol. 2012; 743: 185-195.

Quentin Sattentau

Bowles et al. Comparison of neutralizing antibody responses elicited from highly diverse polyvalent heterotrimeric HIV-1 gp140 cocktail immunogens versus a monovalent counterpart in rhesus macaques. PLoS One. 2014; 9: e114709.

Baxter et al. Macrophage infection via selective capture of HIV-1-infected CD4+ T cells. Cell Host Microbe. 2014; 16: 711-21.

Moghaddam et al. Dry roasting enhances peanut-induced allergic sensitization across mucosal and cutaneous routes in mice. J Allergy Clin Immunol. 2014; 134: 1453-6.

Sheppard et al. Polyethyleneimine is a potent systemic adjuvant for glycoprotein antigens. Int Immunol. 2014; 26: 531-8.

Sattentau QJ. Immunogen design to focus the B-cell repertoire. Curr Opin HIV AIDS. 2014; 9: 217-23.

Noti et al. Exposure to food allergens through inflamed skin promotes intestinal food allergy through the thymic stromal lymphopoietin-basophil axis. J Allergy Clin Immunol. 2014; 133: 1390-9

Duncan et al. High-multiplicity HIV-1 infection and neutralizing antibody evasion mediated by the macrophage-T cell virological synapse. J Virol. 2014; 88: 2025-34.

Smalls-Mantey et al. Comparative efficiency of HIV-1-infected T cell killing by NK cells, monocytes and neutrophils. Plos One 2013; e74858.

Duncan et al. High multiplicity HIV-1 cell-to-cell transmission from macrophages to CD4+ T cells limits antiretroviral efficacy. AIDS 2013; 27: 2201-2206.

Schiffner et al. Cell-to-cell spread of HIV-1 and evasion of neutralizing antibodies. Vaccine 2013; 31: 5789-5797.

Jolly and Sattentau. Attachment factors. Adv. Exp. Med. Biol. 2013; 790: 1-23.

Schiffner et al. Development of prophylactic vaccines against HIV-1. Retrovirology 2013; 10: 72.

Tan and Sattentau The HIV-1-containing macrophage compartment: a perfect cellular niche? Trends Microbiol. 2013; 21: 405-12.

Noti et al. Thymic stromal lymphopoietin-elicited basophil responses promote eosinophilic esophagitis. Nat Medicine 2013; 19: 1005-13.

Schiffner et al. Immune focussing and enhanced neutralization induced by HIV-1 gp140 chemical cross-linking. J. Virol. 2013; 87: 10163-10172.

Watkins et al.; CAVD Project Group. Anti-IgA isotypes: differential virion capture and inhibition of trancytosis are linked to prevention of mucosal R5 SHIV transmission. AIDS 2013; 27: F13-20.

Russell et al. Multiple proviral integration events after virological synapse-mediated HIV-1 spread. Virology 2013; 443: 143-149.

Wegmann et al. Polyethyleneimine is a potent mucosal adjuvant for viral glycoprotein antigens. Nat Biotech. 30: 883-888.

Heyndrickx et al. International network for comparison of HIV neutralization assays: the NeutNet report II. PLoS One 2012; 7:e36438.

Lai et al. Mixed adjuvant formulations reveal a new combination that elicits antibody responses comparable to Freund's adjuvants. PLoS One 2012; 7: e35083.83.

Kong and Sattentau. Antigenicity and immunogenicity in HIV-1 antibody-based vaccine design. J AIDS Clin Res.2012; S8: 3.

Sattentau. The direct passage of animal viruses between cells. Curr Opinion. Virol. 2011; 1: 396-402.

Sattentau. A sweet cleft in HIVs armour. Nature 2011; 480: 324-325.

Duncan and Sattentau. Viral determinants of HIV-1 macrophage tropism. Viruses 2011; 3: 2255-2279.

Sattentau and McMichael. New templates for HIV-1 antibody-based vaccine design. F1000 reports 2011; 2: 60.

Wegmann et al. A novel strategy for inducing enhanced mucosal HIV-1 antibody responses in an anti-inflammatory environment. Plos One 2011; 6: e15861.

Arias et al. Carnauba wax nanoparticles enhance strong systemic and mucosal cellular and humoral immune responses to HIV-gp140 antigen. Vaccine 2011; 29: 1258-1269.

Welsch et al. Architecture and regulation of the HIV-1 assembly and holding compartment in macrophages. J. Virol. 2011; 85: 7922-7927.

Moghaddam et al. Reactive carbonyls are a major Th2-inducing damage –associated molecular pattern generated by oxidative stress. J Immunol. 2011; 187: 1626-1633.

Pruzina et al. Human monoclonal antibodies to HIV-1 gp140 from mice bearing YAC-based human immunoglobulin transloci. Protein Eng. Des. Sel. 2011; 24: 791-799.

Jolly et al. The regulated secretory pathway in CD4 T cells contributes to human immunodeficiency virus type 1cell-to-cell spread at the virological synapse. Plos Pathogens 2011; 7:e1002226.

Adrian Smith

Salomonsen et al. Sequence of a complete chicken BG haplotype shows dynamic expansion and contraction of two gene lineages with particular expression patterns. PLoS Genet. 2014; 10: e1004417.

Guzman et al. Bovine γδ T cells are a major regulatory T cell subset. J Immunol. 2014; 193: 208-22.

Peroval et al. A critical role for MAPK signalling pathways in the transcriptional regulation of Toll like receptors. Plos One 2013; 8: e51243.

Mideo et al. The Cinderella Syndrome: Why do malaria-infected cells burst at midnight? Trends Parasitol. 2012; 29: 10-12.

Boyd et al. Toll-like Receptor 15 is unique to avian and reptilian lineages and recognises a novel yeast-derived agonist. J Immunol. 2012; 189: 4930-4938.

Barrow et al. The long view: Salmonella – the last forty years. Avian Pathology 2012; 41: 413-420.

Blake et al. EmaxDB: A first draft genome sequence for the apicomplexan Eimeria maxima and its use in the identification of genes of relevance to parasite motility and invasion. Mol. Biochem. Parasitol. 2012; 184: 48-51.

Blake et al. A genetic linkage map for the apicomplexan protozoan parasite Eimeria maxima and comparison with Eimeria tenella. Int J Parasitol. 2011; 41: 263-270.

Inagaki-Ohara et al. Gamma-delta T cells play a protective role during infection with Nippostrongylus brasiliensis by promoting goblet cell function in the small intestine. Immunology, 2011; 134: 448-458.

Blake et al. Genetic mapping identifies novel highly protective antigens for an Apicomplexan parasite. Plos Pathogens, 2011: 7: e1001279.

Mwangi et al. Clonal Structure of Rapid-Onset MDV-Driven CD4+ Lymphomas and Responding CD8+ T Cells. PLoS Pathog. 2011; 7: e1001337.

Geraldine Taylor

Blodörn et al. Vaccine safety and efficacy evaluation of a recombinant bovine respiratory syncytial virus (BRSV) with deletion of the SH gene and subunit vaccines based on recombinant human RSV proteins: N-nanorings, P and M2-1, in calves with maternal antibodies. PLoS One. 2014; 9: e100392.

Guzman et al. Bovine γδ T cells are a major regulatory T cell subset. J Immunol. 2014; 193: 208-22.

Hägglund et al. Characterization of an experimental vaccine for bovine respiratory syncytial virus. Clin Vaccine Immunol. 2014; 21: 997-1004.

Taylor et al. Recombinant bovine respiratory syncytial virus with deletion of the SH gene induces increased apoptosis and pro-inflammatory cytokines in vitro, and is attenuated and induces protective immunity in calves. J Gen Virol. 2014; 95: 1244-54.

Herbert et al. Recombinant adenovirus expressing the haemagglutinin of Peste des petits ruminants virus (PPRV) protects goats against challenge with pathogenic virus; a DIVA vaccine for PPR. Vet Res. 2014; 45: 24.

Baron et al. Early changes in cytokine expression in peste des petits ruminants disease. Vet Res. 2014; 45: 22.

Dixon et al. Prospects for development of African Swine Fever virus vaccines. Dev Biol (Basel). 2013; 135: 147-57.

Taylor. Bovine Model of RSV Infection. In "Challenges and Opportunities for Respiratory Syncytial Virus Vaccines", BS Graham & L Anderson (eds), Current Topics in Microbiol and Immunol. 2013; 372.

King et al. Protection of European domestic pigs from virulent African isolates of African swine fever virus by experimental immunisation. Vaccine 2011; 29: 4593-600.

Hogg et al. Characterization of age-related changes in bovine CD8+ T-cell. Vet Immunol Immunopathol. 2011; 140: 47-54.

Paton and Taylor. Developing vaccines against foot-and-mouth disease and some other exotic viral diseases of livestock. Phil. Trans. R. Soc. B 2011; 366: 2774-2781.

Hägglund et al. Bovine respiratory syncytial virus ISCOMs – Immunity, protection and safety in young conventional calves. Vaccine 2011; 29: 8719-30.

Martin Vordermeier

Villarreal-Ramos et al. Development of a BCG challenge model for the testing of vaccine candidates against tuberculosis in cattle. Vaccine 2014; 32: 5645-9.

Golby et al. MicroRNA expression profiling of PPD-B stimulated PBMC from M. bovis-challenged unvaccinated and BCG vaccinated cattle. Vaccine 2014; 32: 5839-44.

Chambers et al. Vaccination against tuberculosis in badgers and cattle: an overview of the challenges, developments and current research priorities in Great Britain. Vet Rec. 2014; 175: 90-6.

Dean et al. Comparison of the immunogenicity and protection against bovine tuberculosis following immunization by BCG-priming and boosting with adenovirus or protein based vaccines. Vaccine 2014; 32: 1304-10.

Coad et al. The consequences of vaccination with the Johne's disease vaccine Gudair on diagnosis of bovine tuberculosis. Vet Rec. 2013; 172: 266.

Buddle et al. Subcutaneous administration of a 10-fold lower dose of a commercial human tuberculosis vaccine, bacille Calmette-Guerin Danish, induced similar levels of protection against bovine tuberculosis and responses in the tuberculin intradermal test compared to a standard cattle dose. Clin Vaccine Immunol. 2013; 20: 1559-62.

Vrieling et al. Hsp70 vaccination-induced primary immune responses in efferent lymph of the draining lymph node. Vaccine 2013; 31: 4720-7.

Jones et al. Immunisation with ID83 fusion protein induces antigen-specific cell mediated and humoral immune responses in cattle. Vaccine 2013; 31: 5250-5.

Jones et al. Development of an Unbiased Antigen Mining Approach to Identify Novel Vaccine Antigens and Diagnostic Reagents for Bovine Tuberculosis. Clin Vaccine Immunol. 2013; 20: 1675-82.

Aranday Cortes et al. Transcriptional profiling of disease-induced host responses in bovine tuberculosis and the identification of potential diagnostic biomarkers. PLoS One 2012; 7: e30626.

Vordermeier and Whelan. ELISPOT assays to enumerate bovine IFN-gamma secreting cells for the development of novel vaccines against bovine tuberuclosis. Methods Mol Biol. 2012; 792: 219-27.

Vordermeier et al. The influence of cattle breed on susceptibility to bovine tuberculosis in Ethiopia. Compar Immunol Microbiol Infect Diseases. 2012; 35: 227-32.

Casal et al. Evaluation of two cocktails containing ESAT-6, CFP-10 and Rv-3615c in the intradermal test and the interferon-γ assay for diagnosis of bovine tuberculosis. Prev Vet Med. 2012; 105: 149-54.

Flores-Villalva et al. Tuberculin skin test specificity is modified by the use of a protein cocktail containing ESAT-6 and CFP-10 in Mycobacterium bovis naturally infected cattle. Clin Vaccine Immunol. 2012; 19: 797-803.

Jones et al. Improved Skin Test for the Differential Diagnosis of Bovine Tuberculosis by the Addition of Rv3020c-Derived Peptides. Clin Vaccine Immunol. 2012; 19: 620-22.

Waters et al. Evaluation of Gamma Interferon (IFN-γ)-Induced Protein 10 Responses for Detection of Cattle Infected with Mycobacterium bovis: Comparisons to IFN-γ Responses. Clin Vaccine Immunol. 2012; 19: 346-51.

Hogan et al. Characterisation of bovine leukocyte Ig-like receptors. PLoS One 2012; 7: e34291.

Ameni et al. T-Cell and Antibody Responses to Mycobacterial Antigens in Tuberculin Skin-Test-Positive Bos indicus and Bos taurus Cattle in Ethiopia. Vet Med Int. 2012; ID 457872.

Waters et al. Bovine tuberculosis vaccine research: historical perspectives and recent advances. Vaccine. 2012; 30: 2611-22.

Thom et al. Duration of immunity against Mycobacterium bovis following neonatal vaccination with BCG Danish: significant protection against infection at 12, but not 24 months. Clin Vaccine Immunol. 2012; 19: 1254-60.

Pirson et al. Differential effects of Mycobacterium bovis - derived polar and apolar lipid fractions on bovine innate immune cells. Vet Res 2012; 43: 54.

Pérez de Val et al. Goats primed with BCG and boosted with a recombinant adenovirus expressing Ag85A show enhanced protection agaist tuberculosis. Clin Vaccine Immunol. 2012; 19: 1339-47.

Vordermeier et al. Conserved Immune Recognition Hierarchy of Mycobacterial PE/PPE Proteins during Infection in Natural Hosts. PLoS One 2012; 7: e40890.

Whelan et al. Immunogenicity comparison of the intradermal or endobronchial boosting of BCG vaccinates with Ad5-85A. Vaccine 2012; 30: 6294-300.

Aranday-Cortes et al. Upregulation of IL-17A, CXCL9 and CXCL10 in Early-Stage Granulomas Induced by Mycobacterium bovis in Cattle. Transbound Emerg Dis. 2013; 60: 525-37.

Rhodes et al. Evaluation of IFNγ and Antibody TB Tests in Alpacas. Clin Vaccine Immunol. 2012; 19: 1677-83.

Khatri et al. A natural-transmission model of bovine tuberculosis provides novel disease insights. Vet Rec. 2012; 171: 448

Nguyen et al. The bovine CD1D gene has an unusual gene structure and is expressed but cannot present alpha-galactosylceramide with a C26 fatty acid. Int Immunol. 2013; 25: 91-98.

de Val et al. Effects of vaccination against paratuberculosis on tuberculosis in goats: diagnostic interferences and cross-protection. BMC Vet Res. 2012; 16: 191.

Bhuju et al. Global gene transcriptome analysis in vaccinated cattle revealed a dominant role of IL-22 for protection against bovine tuberculosis. PLoS Pathogens 2012; 8: 31003077.

Gideon et al. Bioinformatic and empirical analysis of novel hypoxia-inducible targets of the human antituberculosis T cell response. J Immunol. 2012; 189: 5867-76.

Firdessa et al. High prevalence of bovine tuberculosis in dairy cattle in central ethiopia: implications for the dairy industry and public health. PLoS One 2012; 7: e52851.

Ameni et al. Mycobacterium tuberculosis infection in grazing cattle in central Ethiopia. Vet J. 2011; 188: 359-61.

Bezos et al. Assessment of in vivo and in vitro tuberculosis diagnostic tests in Mycobacterium caprae naturally infected caprine flocks. Prev Vet Med. 2011; 100: 187-92.

Buddle et al. Low oral BCG doses fail to protect cattle against an experimental challenge with Mycobacterium bovis. Tuberculosis (Edinb). 2011; 91: 400-5.

Buddle et al. Update on vaccination of cattle and wildlife populations against tuberculosis. Vet Microbiol. 2011; 151: 14-22.

de Val Perez et al. Experimental model of tuberculosis in the domestic goat after endobronchial infection with Mycobacterium caprae. Clin Vaccine Immunol. 2011; 18: 1872-81.

Hope et al. Identification of surrogates and correlates of protection in protective immunity against Mycobacterium bovis infection induced in neonatal calves by vaccination with M. bovis BCG Pasteur and M. bovis BCG Danish. Clin Vaccine Immunol. 2011; 18: 373-9.

Jones et al. The use of binding-prediction models to identify M. bovis-specific antigenic peptides for screening assays in bovine tuberculosis. Vet Immunol Immunopathol. 2011; 141: 239-45.

Jones et al. Immune responses to the enduring hypoxic response antigen Rv0188 are preferentially detected in Mycobacterium bovis infected cattle with low pathology. PLoS One. 2011; 6: e21371.

Lyashchenko et al. Diagnostic value of animal-side antibody assays for rapid detection of Mycobacterium bovis or Mycobacterium microti infection in South American camelids. Clin Vaccine Immunol. 2011; 18: 2143-7.

Pirson et al. Vaccines designed to protect against Mycobacterium tuberculosis infection may aid the identification of novel vaccine constructs and diagnostic antigens for bovine tuberculosis. Vet Microbiol. 2011; 148: 232-7.

Schiller et al. Bovine tuberculosis in Europe from the perspective of an officially tuberculosis free country: trade, surveillance and diagnostics. Vet Microbiol. 2011; 151: 153-9.

Tchilian et al. Simultaneous immunization against tuberculosis. PLoS One. 2011; 6: e27477.

Twomey et al. Controlling tuberculosis in a llama (Lama glama) herd using clinical signs, tuberculin skin testing and serology. Vet J. 2011; 192: 246-8.

Vordermeier et al. Cytokine responses of Holstein and Sahiwal zebu derived monocytes after mycobacterial infection. Trop Anim Health Prod. 2011; 44: 651-5.

Vordermeier et al. Mycobacterium bovis antigens for the differential diagnosis of vaccinated and infected cattle. Vet Microbiol. 2011; 151: 8-13.

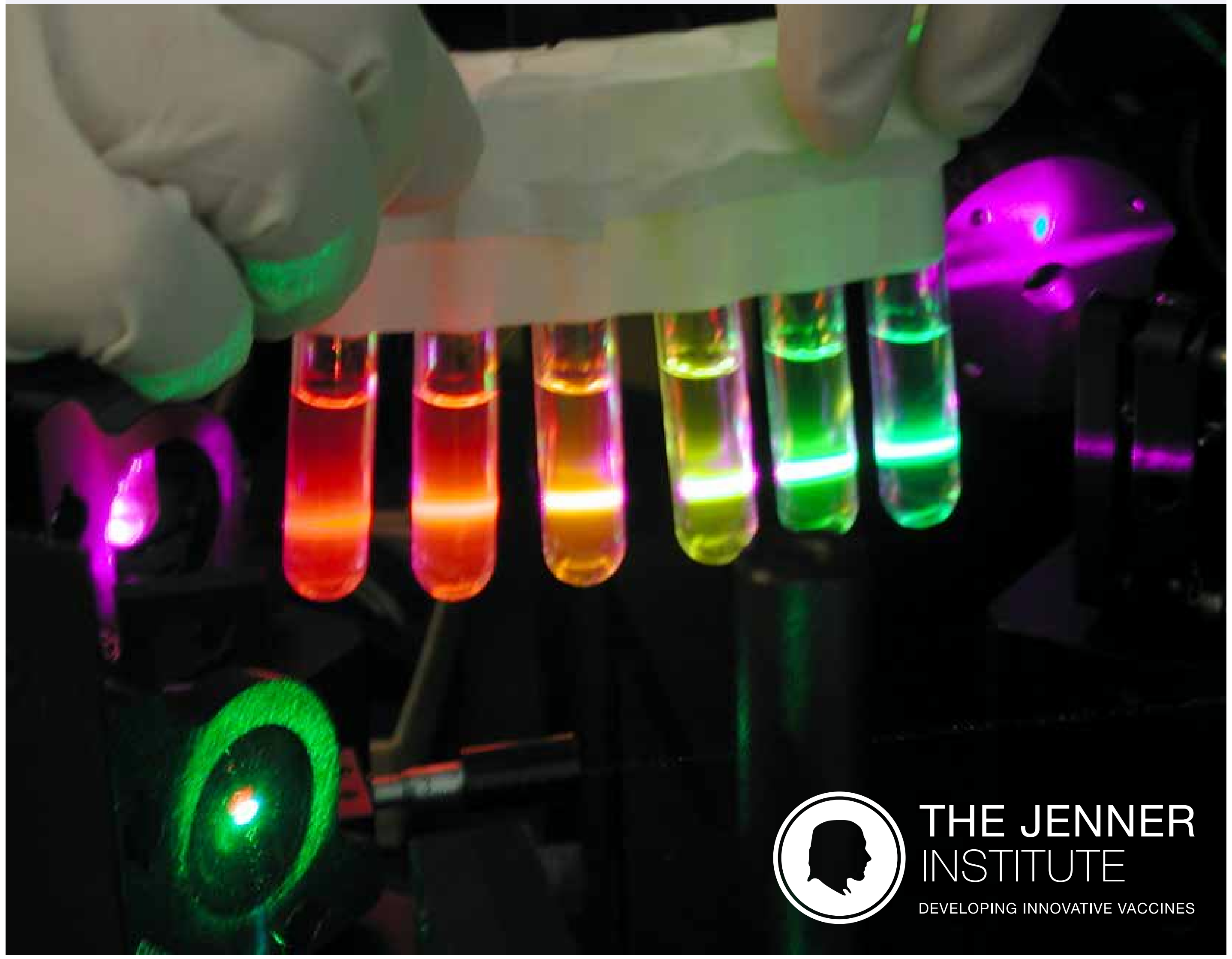
Vordermeier et al. DIVA reagents for bovine tuberculosis vaccines in cattle. Expert Rev Vaccines. 2011; 10: 1083-91.

Waters et al. Development and evaluation of an enzyme-linked immunosorbent assay for use in the detection of bovine tuberculosis in cattle. Clin Vaccine Immunol. 2011; 18: 1882-8.

Wedlock et al. Protection against bovine tuberculosis induced by oral vaccination of cattle with Mycobacterium bovis BCG is not enhanced by co-administration of mycobacterial protein vaccines. Vet Immunol Immunopathol. 2011; 144: 220-7.

Whelan et al. Lack of correlation between BCG-induced tuberculin skin test sensitisation and protective immunity in cattle. Vaccine 2011; 29: 5453-8.

Whelan et al. Development of an Antibody to Bovine IL-2 Reveals Multifunctional CD4 T(EM) Cells in Cattle Naturally Infected with Bovine Tuberculosis. PLoS One 2011; 6: e29194.



THE JENNER VACCINE FOUNDATION

The Foundation seeks to enhance philanthropic support of vaccinology and is currently evaluating options for enhanced fundraising activities. The Foundation currently supports vaccine research and development through the Jenner Institute. The Foundation Board appoints the Director of the Institute, elects Jenner Investigators and has funded space and facilities for vaccine research and development.

The Foundation actively supports enhanced collaborative interactions between researchers at The Pirbright Institute working on veterinary vaccines and those at the University of Oxford developing new vaccines for human use. The Foundation has also provided support for scientists from the former Edward Jenner Institute for Vaccine Research to continue their work as part of the Jenner Institute. The Foundation draws Trustees from both the University of Oxford and the Pirbright Institute, and has an external chair and three further independent trustees.

Trustees

Prof David Salisbury CB (Chairman)
Director of Immunisation,
UK Department of Health
(until end 2013)

Dr Norman Begg
VP and Chief Medical Officer, GSK Biologicals

Prof John Fazakerley
Director, The Pirbright Institute

Prof Paul Fine
Professor of Communicable Disease Epidemiology, London School of Hygiene and Tropical Medicine

Prof Sir Andrew McMichael FRS
Professor of Molecular Medicine
and Group Head

Dr Bryan Charleston
Head of Livestock Viral Diseases Programme, The Pirbright Institute

Prof Andrew Pollard
Director of the Oxford Vaccine Group, University of Oxford

Dr Ian Tarpey
Head Global Poultry / Discovery and Technology, MSD Animal Health, Netherlands

Company Secretary

Mr Gary Strickland
Business Manager, Nuffield Department of Medicine

Scientific Advisory Board

The aim of the Scientific Advisory Board is to advise The Jenner Institute on both specific vaccine programmes and the overall strategy and organisational structure of the Institute's activities.

Board Members

Prof Jonathan Heeney (Chair)
University of Cambridge

Prof Ivan Morrison (Vice-Chair)
University of Edinburgh

Dr Rene Aerts
Independent Consultant, Veterinary Vaccines

Dr Jeffrey Almond
Visiting Professor, University of Oxford

Dr Steve Chatfield
Independent Consultant, Human Vaccines

Dr Tim Doel
Independent Consultant, Veterinary Vaccines

Prof Bruno M Goddeeris
University of Louvain

Prof Margaret Liu
Karolinska Institute, Stockholm

Dr Bonnie Mathieson
NIAID, Bethesda

Dr James Merson
Pfizer, San Diego

Dr Alfredo Nicosia
ReiThera, Rome

Prof Albert Osterhaus
Erasmus University, Rotterdam

Dr Allan Saul
Novartis Global Health Vaccines Institute, Siena

EBOLA

PostScript and Update

The declaration of the West African Ebola outbreak in August 2014 as a public health emergency of international concern by the World Health Organization (WHO), set in train an ambitious and unprecedented attempt to develop a new vaccine and test it for efficacy in clinical trials during the course of the outbreak. The Jenner Institute was invited to test the first vaccine destined for use in West Africa. This was a chimpanzee adenovirus, ChAd3, encoding the surface glycoprotein of the strain of Ebola causing the outbreak. The vaccine candidate had been developed and tested by Okairos, a biotechnology company and the Institute's longstanding collaborator on adenovirus vectors, and the National Institutes of Health (NIH) which has undertaken promising non-human primate studies. Following a request from the WHO in August 2014, it proved possible to start a phase I first-in-human trial of this vaccine in 60 subjects with full approvals by mid-September. This allowed a phase I trial to start in early October in Mali, and by the end of the year sufficient safety and immunogenicity data was available to proceed to start a phase III efficacy trial in Liberia in January 2015.

Oxford played the key role in accelerating the initiation and conduct of the phase I trials, with support from the Wellcome Trust, Department for International Development and the Medical Research Council. The same grant award funded both the manufacture of tens of thousands of vaccine doses, and also a booster trial of an MVA vector, to determine whether better immunogenicity could be achieved, similar to that found to be protective in non-human primates. This goal too was achieved by mid-December, providing a vaccination regime that appears highly promising. In addition, Oxford led an initiative to manufacture tens of thousands of doses of a new MVA vector using an immortalised cell line, allowing future manufacture of much larger batches of MVA than conventional processes. The whole programme entailed close collaboration with GlaxoSmithKlein, who had acquired Okairos, the WHO, the NIH and several other clinical trial sites.

By December 2014, Johnston and Johnston had developed a related prime-boost regime using an Ad26 adenoviral vector, again with MVA. They too chose Oxford for their first-in-human trial. This time, Matthew Snape led a study conducted by the Oxford Vaccine Group that rapidly enrolled the required 87 subjects and this vaccine is progressing to further larger scale trials at the Oxford Vaccine Group, in France and in West Africa.

The accelerated delivery of phase I Ebola vaccine trials in the UK has been dependent upon the prioritisation of regulatory and ethical review, aided by frequent and open dialogue between investigators, manufacturers, trial sponsors and senior staff in the reviewing agencies. Regulatory approval for ChAd3-EBOZ was granted in four working days by the Medicines and Healthcare Regulatory Agency (MHRA) and within a week by the Research Ethics Committee. Jenner researchers here benefitted from critical support across the relevant Government departments, and from extensive experience with phase I trials of live viral vectors as investigational vaccines for many disease indications.

The pace of development of these Ebola vaccine candidates is remarkably fast, with some in phase III testing even as phase II trials begin, contrasting sharply with the more standard timelines of a decade or more for vaccine design and development. A mechanism is now needed to ensure that we are ready for the next epidemic, with vaccines available for roll-out against key pathogens, as well as adaptable antigen delivery platforms and regulatory processes in place to rapidly develop vaccines when an unexpected or novel pathogen emerges. The list of known outbreak pathogens against which no vaccines are available is long: at least fifteen have caused outbreaks in the last two decades. There are clearly challenges in trying to achieve this important goal, not least the weak business case for investment in many such vaccines, but the lesson of the 2014 Ebola outbreak is that vaccine development can no longer afford to ignore these important threats.

THE JENNER INSTITUTE

DEVELOPING INNOVATIVE VACCINES

The Jenner Institute Laboratories
University of Oxford
Old Road Campus Research Building
Roosevelt Drive
Oxford OX3 7DQ