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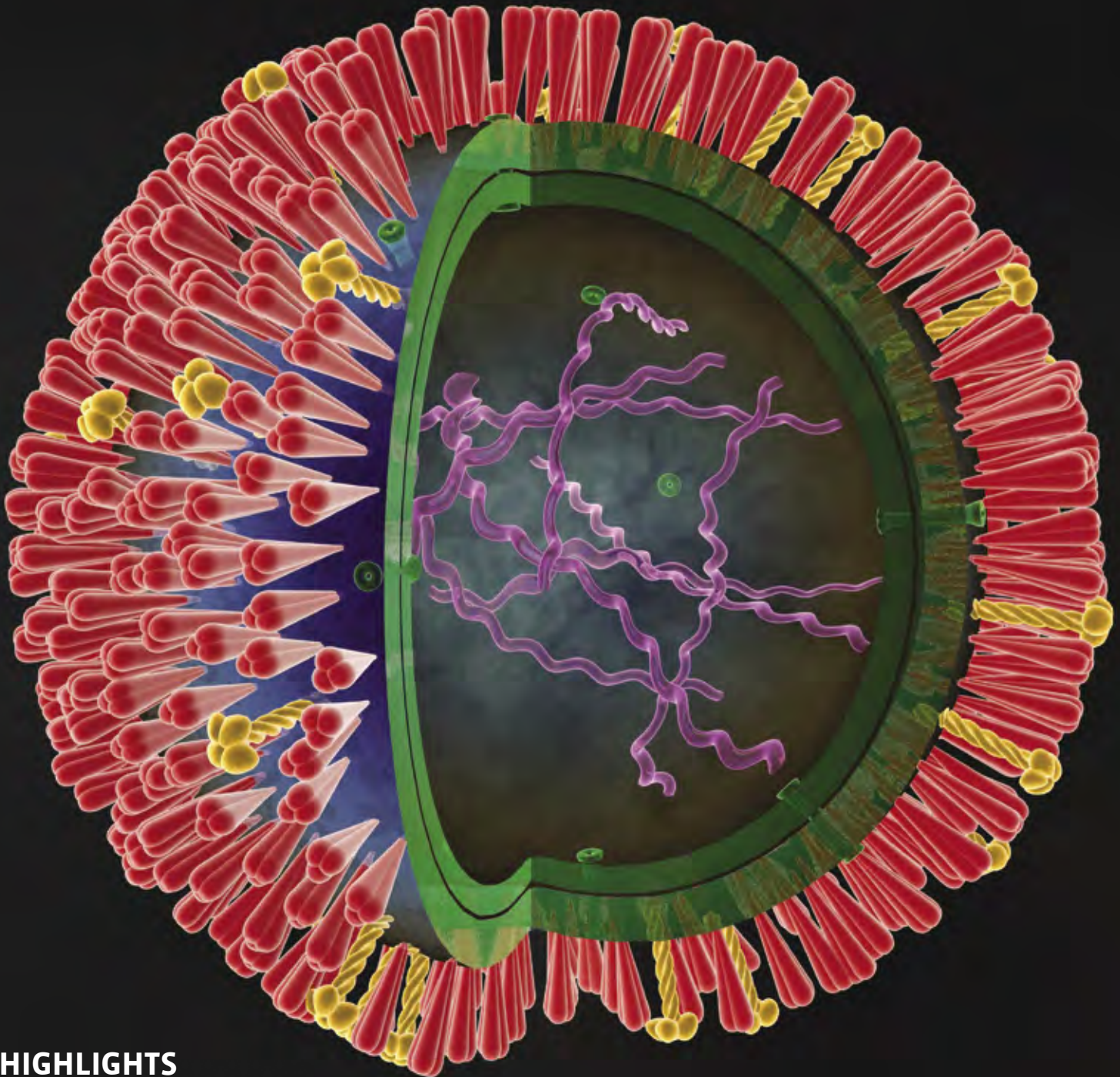
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OXFORD

Jenner Vaccine Foundation News

ISSUE 02 | MAY 2010

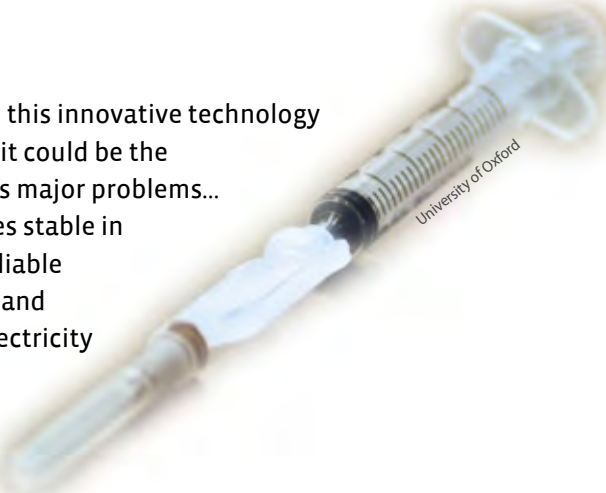


HIGHLIGHTS

H1N1 ...Lessons from a pandemic | FMD and essential global control
Livestock vaccines and the Millennium Development Goals
HIV-1 Achilles heel | Meningococcal Disease - vaccine development

Stable vaccines at tropical temperatures - a solution in sight

Simple and cheap is how this innovative technology has been described, and it could be the solution to one of Africa's major problems... how do you keep vaccines stable in environments with unreliable transport arrangements and without a guaranteed electricity supply for refrigeration purposes?



Researchers from the Grand Challenges in Global Health at the University of Oxford and Nova Bio-Pharma Technologies have developed a simple way of heat-stabilizing vaccines by mixing the vaccines with the sugars trehalose and sucrose. The mixture is then left to dry out slowly on a filter or a membrane. The water evaporates and the vaccine mixture turns into a syrup and then solidifies. The thin sugary film that forms can preserve the active part of the vaccine in a “suspended animation”...when the membrane is flushed with water the vaccine is rehydrated and applied to a patient using a normal plastic syringe.

The process is general and could be used for many types of vaccines and sensitive biological agents.

Professor Adrian Hill, principal investigator and Director of the Jenner Institute in which the Grand Challenge in Global Health project is based, adds: “The World Health Organization’s immunization program vaccinates nearly 80% of the children

born today against six killer diseases: polio, diphtheria, tuberculosis, whooping cough, measles and tetanus. One of the biggest costs is maintaining what’s called the cold chain – making sure vaccines are refrigerated all the way from the manufacturer to the child, whether they are in the Western world or the remotest village in Africa. If most or all of the vaccines could be stabilized at high temperatures, it would not only remove cost, more children would be vaccinated.”

To watch the interview on this development, view the following URL
http://www.ox.ac.uk/media/news_stories/2010/100218_1.html.

This breakthrough technology has been published in Science Translational Medicine, Sci Transl Med 17 February 2010 2:19ra12.

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Matt Cottingham

BIOTECCanada Launches Vaccine Policy Paper Series

In Canada, as in the U.K., technology innovation continues to drive the discovery of leading-edge vaccines that will help transform the future of public health worldwide. Recently, the Vaccine Industry Committee of BIOTECCanada (the national non-profit association dedicated to building Canada’s bio-economy) has launched a 10-part series of policy papers that examines the current system for introducing vaccines in Canada – with a view towards promoting vaccine R&D and improving timely access to life-saving, cost-effective vaccine technologies to protect individuals and societies, both in Canada and abroad.

This comprehensive series, entitled, “*Building on the Legacy of Vaccines in Canada: Value, Opportunities, and Challenges*” (available at www.biotech.ca/vaccines), provides a unique, first-of-its-kind analysis of Canada’s vaccine environment, underscoring the tremendous medical, social and economic value of vaccines. It also presents an in-depth discussion of the opportunities and challenges across the entire vaccine development chain, from early-stage and clinical research, through to vaccine licensure, establishing national recommendations, identifying sustainable funding mechanisms, and creating an enabling infrastructure for vaccine manufacturing, education, surveillance, and immunization program implementation.

Each of the 10 policy papers provides recommendations for government officials and other key stakeholders, i.e. to help Canada maintain its leadership position in the context of global public health systems – and to encourage the adoption of international best practices for vaccine program development. The series also represents a broad-based educational resource for all immunization stakeholders, with the goal of fostering critical partnerships across vaccine researchers, manufacturers, investment/funding organizations, government agencies and national advisory bodies, public health officials, health professionals, public and private payers, and the general public.

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University of Oxford

Update on H1N1... lessons in responding to a pandemic

Andrew J Pollard,
Professor of Paediatric Infection & Immunity
Director of the Oxford Vaccine Group,
University of Oxford

While the H1N1 influenza pandemic of 2009 was very real with rapid spread around the world of this novel strain, and well documented and highly publicised serious disease and deaths in children, younger adults and pregnant women, the numbers of severe cases were far lower than seen in previous pandemics. Older adults, who suffer a high burden of influenza morbidity from seasonal flu, were relatively unaffected by this virus as a result of pre-existing immunity acquired from flu viruses that circulated in the 1950s. The active global influenza surveillance network and rapid access to genetic information identifying the H1N1 swine flu virus as novel, allowed the World Health Organisation to recognise its pandemic potential earlier than in any previous pandemic, and before there was extensive epidemiological data available.

In the future we may be able to fully predict the risk posed by novel influenza viruses from their genetic code but this is not the case yet, and decisions on the national and international responses to the threat must

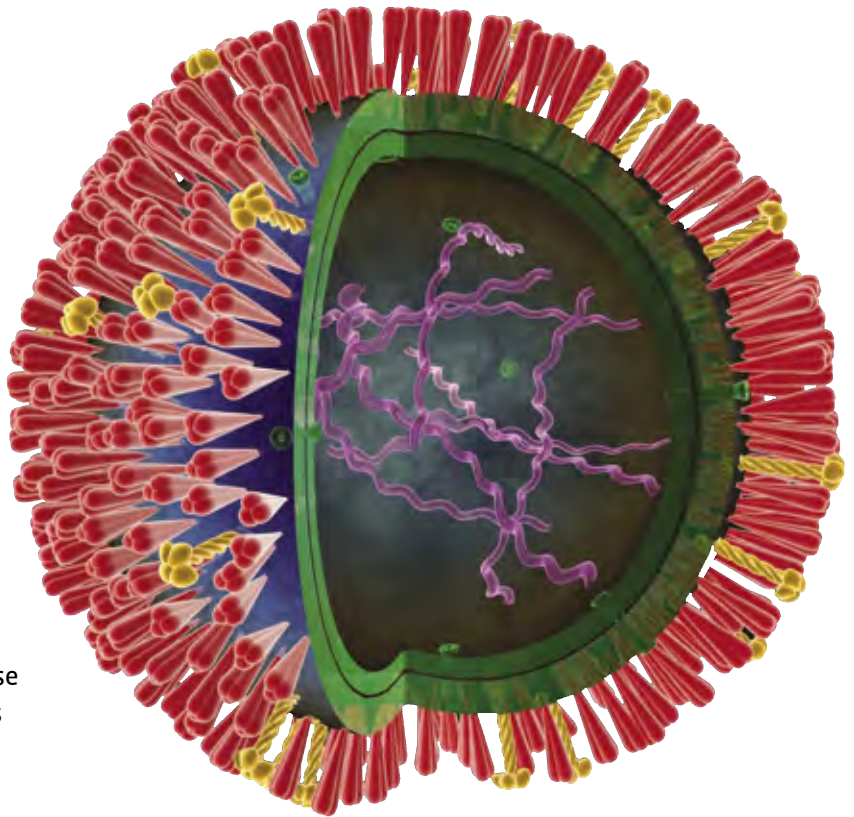
be made with this limited vision.

Because the pandemic claimed fewer lives than it might have, the policy makers have been heavily criticised for overuse of the drug oseltamivir to treat suspected cases and

wasting money on purchase of excessive numbers of doses of vaccines to prevent the disease that were not used.

While some of the policy decisions made as the pandemic evolved can be criticised (oseltamivir policy being a good example), I see no conspiracy here. The authorities predictions turned out to be wrong, but we only really know that with hindsight and it might have been so different. If the death rate had been higher and our hospitals over-flowing with critically ill patients, the extensive preparations and cost would have been fully justified (and likely the authorities would have been criticised for not going further!). However, because we escaped devastation this time, the greatest risk to our safety with the next pandemic threat may well be the hesitation of bruised governments and international authorities who fear calling it too soon.

This pandemic has driven new knowledge in the influenza field and our experiences with new vaccines could lead to improvements in influenza prevention in the future, both for pandemic and seasonal flu. Influenza is a serious disease which claims vulnerable lives across the age range and burdens our health care systems every year, even in the absence of a pandemic, so it is right to continue to take this virus seriously.



Anna Tanczos/Wellcome Images



Connecting the dots; clearing a pathway from livestock vaccines to Millennium Development Goals

Brian Perry,
Visiting Professor of Tropical Veterinary Medicine
Nuffield Department of Clinical Medicine, University of Oxford, UK
and Honorary Professor, College of Medicine and Veterinary Medicine,
University of Edinburgh, UK and Honorary Professor,
Department of Veterinary Tropical Diseases, University of Pretoria, South Africa

As an epidemiologist in the development arena I am regularly asked to substantiate the connection between technological innovations, such as vaccines, and measurable outcomes of benefit to global society, such as the Millennium Development Goals (MDGs). Metrics of potential impact are increasingly demanded by many research investors, who need evidence of demonstrable returns. MDG 1 aims to halve the proportion of people whose income is less than US\$ 1 per day, and the proportion of people who suffer from hunger, by 2015.

In considering returns to livestock vaccines, our baseline is that three quarters of the world's poor live in rural areas, in Africa 65% of rural income

comes from farming, and livestock contribute some 30% of agricultural GDP in developing countries. Livestock are an expression of poverty for most, a bank account for some, and an opportunity to escape from poverty for a few; how will vaccines bring change, and which ones should we focus on?

I led a conceptualisation of livestock's contributions to processes of poverty reduction, developed to illustrate how different animal diseases and their control affect the poor; it presented a troika of livestock-mediated "pathways to poverty reduction". These are: reducing vulnerability, improving productivity performance, and improving market access. Different diseases affect these pathways in different ways. Epidemic and zoonotic diseases (Newcastle disease, rinderpest, Rift Valley fever) destroy fundamental assets and increase vulnerability; vector-borne and parasitic diseases disturb performance; and transboundary (foot-and-mouth disease and African swine fever) and zoonotic (cysticercosis) diseases disrupt or prevent market access. The conceptualisation also produced a ranking of

disease importance, based on expert opinion of the impacts of the diseases on the poor, overlaid with the calculated density of poor people. A crude approach, perhaps, but a first cut. What this did not do was to calculate the returns to reducing the incidence of these diseases through vaccines and other interventions, and use the differential benefits as the basis for priority setting; given the inadequacies of data, this gap remains largely unfilled.

Perhaps the best model of vaccine's contribution to the MDGs is that of rinderpest; we are shortly to hear that this ancient disease has been eradicated. An effective vaccine (pioneered by the late Walter Plowright, a former department head at IAH) combined with a well-funded, coordinated global programme have yielded extraordinary results. The disappearance of rinderpest has undoubtedly removed a significant threat to the vulnerability of poor livestock keepers, particularly in the pastoralist systems of Africa. The irony is that we have still not been able to measure effectively the impacts of rinderpest eradication, nor synthesise objectively the reasons for this formidable success. The decision in 1960 to embark on a pan-African eradication programme was made without an *ex ante* economic impact assessment, before most African countries had gained independence, and long before the mindset of poverty reduction and MDGs had hit the disease control investment world. While vaccines are almost universally recognised as the most effective tools to prevent infectious diseases, the justification for livestock vaccine research, and certainly for embarking on disease eradication, now demands a more quantitative and comparative understanding of the future benefits to be reaped by different stakeholders engaged in livestock enterprises and value chains, if it is to attract the sort of investment and political commitment required to achieve the ultimate prize of eradication.



The Ethiopian, British and French team engaged in rinderpest vaccination on the southern border with Kenya in 1972



Brian Perry flying rinderpest vaccine in to his teams in 1972



Cattle threshing the teff harvest in Ethiopia

Attacking the Achilles heel of HIV-1

Dealing with HIV-1 diversity

Lucy Dorrell and Tomáš Hanke, Jenner Investigators,
Weatherall Institute of Molecular Medicine,
University of Oxford

Development of an effective, accessible vaccine is the best hope for halting the HIV-1 epidemic. As discussed in the previous newsletter, most researchers believe that a vaccine should induce effective B cell responses and T cell responses at the same time. Nature does not provide an example of a protective immune response since no-one has ever been confirmed to have successfully cleared HIV-1 infection. Therefore, both of these goals present substantial challenges which need to be overcome separately before combining two successful solutions into a single vaccine strategy.

We have focused on developing vaccines which aim to promote T cell responses. Because of the extensive genetic variation in circulating HIV-1 strains, T cell responses must be effective against diverse viral variants circulating in the target population and against viral escape mutants arising in individuals who fail to prevent the infection. We hypothesized that HIV-1 variation would be best tackled by targeting functionally

conserved regions of the virus. Thus, we assembled from the 14 most invariable segments of the HIV-1 proteome into a single chimeric protein called HIVconsv. Each segment is 27-128 amino acids in length and is derived from the four major HIV-1 clades A, B, C and D alternating to ensure that they are equally represented. Clade consensus (or average) sequences are used to ensure coverage of the variability within individual clades. We predict that the functional conservation of these regions limits the chance of mutations allowing HIV-1 to escape the vaccine-elicited T cell responses and that any mutations which would arise will result in a significantly reduced viral fitness (capacity to replicate). The HIVconsv immunogen is expressed from DNA plasmid and two attenuated, non-replicating viral vectors: MVA used in the past as a smallpox vaccine and ChAdV-63, a highly immunogenic adenovirus of chimpanzee origin, which does not have a pre-existing immunity in humans that dampens its efficacy as observed in the STEP trial for its human cousin HAdV-5. A triple heterologous



vector regimen delivering HIVconsv elicits stronger T cell responses than simpler regimens, which have not been hugely successful in human efficacy trials so far.

We aim to use the HIVconsv vaccines both for treatment and prevention. For vaccine inducing T cell responses this means to provide a long-term drug-free control of HIV-1 in patients who already have the infection and in healthy, HIV-1-uninfected individuals who are likely to be exposed to HIV-1 in the future. For therapeutic immunisation, we envisage using ChAdV-63 and MVA-vectored HIVconsv vaccines in combination with a course of antiretroviral drug treatment started in early infection. For prevention, all three HIVconsv vaccines will be combined in a heterologous regimen using the plasmid DNA as a prime. In future, when an effective B cell vaccine is developed, our T cell-eliciting regimen could be combined with the B cell approach into a single formulation/regimen for maximum benefit to vaccinees.

We began first-in-human testing of MVA.HIVconsv as a therapeutic vaccine in Oxford in January 2010. Twenty patients with HIV-1 infection will receive MVA.HIVconsv vaccinations in addition to antiretroviral therapy. Later in 2010, we will begin phase I testing of the triple vaccine combination in 32 healthy, HIV-1-seronegative low-risk volunteers.



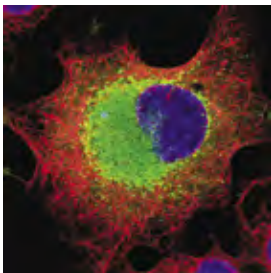


FMD - not without its challenges, but its global control is essential for international development

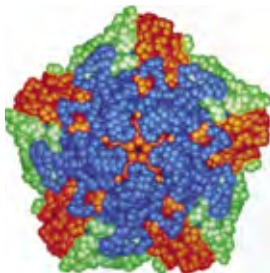
David Paton, Head, Foot-and-Mouth Disease Programme, Institute for Animal Health

Foot-and-mouth disease is considered one of the biggest threats to livestock and the losses that it causes are most severe amongst modern and highly productive breeds of animal. It is caused by a small but highly contagious virus that affects multiple domestic species including cattle, sheep, pigs and buffalo as well as a range of wildlife. Its worldwide distribution closely mirrors economic prosperity; most developed countries have eradicated FMD and most developing countries lack the resources to do so. This imbalance impacts international trade because FMD-free countries restrict imports of animals and their products if they originate from infected countries. This has a knock-on effect in reducing investment in and development of livestock industries in countries where such improvements are most needed. Meanwhile, periodic incursions of the disease into previously FMD-free countries can cost billions of pounds, such as occurred in the UK in 2001.

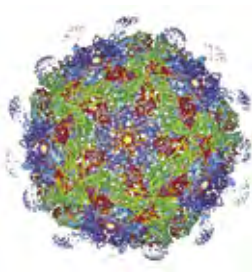
Better control of FMD in endemically affected countries will also benefit countries that are disease-free but current vaccines are less than ideal for achieving this goal. Their most significant failings are that they have to be given repeatedly to sustain immune protection and that they are very unstable in warm climates making it difficult to get them to their point of use without a well organised and resourced system of refrigeration. In addition, current vaccines are produced from growing up and then inactivating large quantities of live virulent FMD virus, a procedure that is not without risk of virus escape. One approach to overcome these difficulties is to use genetic engineering to produce viral shells that retain the immunogenic components, lack the infectious viral genome, but have been altered to enhance their thermal stability. This would be a safe way to produce a vaccine that would not require a cold chain. Meanwhile, the enhanced stability might also lead directly to a more long lasting immune response, as well as providing options for new delivery systems that could also prolong immune memory.



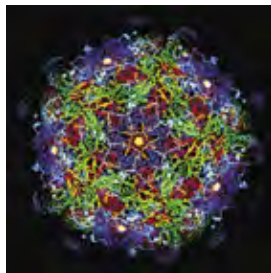
Cell (red) supporting the replication of FMDV (green) adjacent to the nucleus (blue)



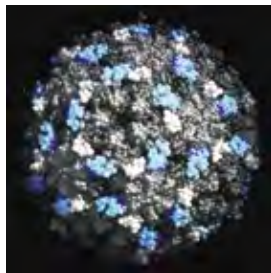
3D structure of FMDV 1



3D structure of FMDV 2



3D structure of FMDV 3



3D structure of FMDV 4

All images: Institute for Animal Health

One Health Initiative

One Health is a world-wide initiative that supports improvement in the lives of both species - human and animal - through the increased and enhanced integration of human and animal medicine. The Jenner Vaccine Foundation newsletter is now featured in the Publications section of the One Health Initiative website

<http://www.onehealthinitiative.com/index.php>.

The Foundation looks forward to working closer with the One Health Initiative and bringing news and developments to the attention of our readership.

The two Jenner Fellow appointments advertised in the previous Newsletter have

been appointed, one working with the Bovine TB group at Compton lead by Jayne Hope and the Oxford human TB vaccine programme lead by Helen McShane, and the other linking the activities of the human influenza vaccine programme (Sarah Gilbert, Oxford) and avian flu vaccine development (Colin Butter, Compton).



IAH



IAH



Development of a Protein (PorA/FetA) vaccine to prevent meningococcal disease - Group B meningitis.

Andrew J Pollard,
Professor of Paediatric Infection & Immunity
Director of the Oxford Vaccine Group,
University of Oxford

Meningitis B (the group B meningococcus) is the leading cause of bacterial meningitis and septicaemia in the UK causing up to 1500 cases each year and is the leading cause of death in childhood by infectious agents.

Meningitis is a disease affecting the protective membrane covering the brain and spinal fluid. The membrane becomes inflamed following infection by bacteria, of which the most common in the UK are group B and group C meningococci. Vaccine development is a public health priority and the development and introduction of a vaccine in 1999 for Group C meningococcus has already successfully reduced the incidence in the targeted age groups by over 90%.¹

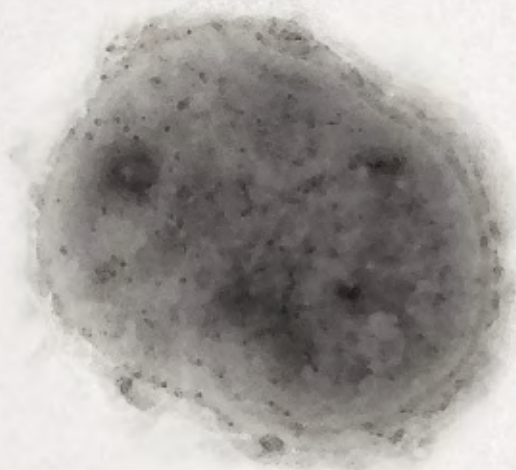
However, the development of a vaccine for Group B is a far bigger challenge. The successful meningitis vaccines developed to date have been based on the sugar coat of the bacteria, but, with meningococcus B, the

surface of the organism is cloaked in sugars which are identical to polysaccharides found on some human cells and therefore are not recognised by our immune system. Development of a vaccine has been hampered even further by the variability of many of the surface proteins beneath the sugar coat.

Professor Andrew Pollard and Professor Martin Maiden, both at the Jenner Institute, with Professor Jeremy Derrick (Manchester University) and Professor Ian Feavers (National Institute for Biological Standards and Control) have been awarded a Wellcome Trust Strategic Translation Award, building on a previous Wellcome Trust vaccine development grant, to develop a promising meningococcal B vaccine candidate that could prevent thousands of cases.

The unique potential of the vaccine has arisen from important observations showing that a limited repertoire of the variable surface proteins are associated with the bacteria that cause the disease in humans. The vaccine is therefore composed of a combination of these proteins known

as PorA (porin), and FetA (iron-regulated surface protein). The prototype vaccine is currently being manufactured for testing in humans in 2011.



Immunogold electron micrograph of a meningococcus, showing binding of antibodies in murine sera following immunisation of mice with recombinant Opa protein (black dots). These antibodies resulted in bacterial killing, providing proof in principle that Opa proteins could be a novel serogroup B meningococcal vaccine candidate.

¹ <http://www.meningitis.org/disease-info/vaccines>



Attendees from Oxford, Senegal, South Africa and The Gambia at the MVA85A Grant Start-up Meeting in Dakar, Senegal, February 2010

New TB Vaccine in Multiple Phase IIb Trials In Africa

The new TB vaccine, MVA85A, was developed by Dr Helen McShane (a Jenner Investigator) and has already undergone successful testing in Phase I and IIa trials in the UK and Africa. MVA85A is designed to enhance the immune response to the currently used TB vaccine, BCG, which although protective in infants, does not work well in adults or against lung disease.

As reported in the previous Jenner newsletter, MVA85A is now being evaluated in a Phase IIb efficacy trial in South African infants. Of the total 2800 infants in this study, over 800 have so far been enrolled with recruitment proceeding well.

Now, a second Phase IIb efficacy trial with MVA85A is about to commence

in HIV-infected adults. The trial, which is planned to start later this year, will recruit ~1400 HIV-infected subjects from two different sites – one in Cape Town, South Africa and one in Dakar, Senegal. Previous Phase IIa trials have shown that the vaccine is safe in this population and stimulates a good immune response, but this is the first time that MVA85A will be tested to see if it

prevents TB disease in this population. The trial will run over about four years and, like the infant trial, half the subjects will receive MVA85A and half will receive a placebo.

Funding for the trial comes, predominantly, from the European and Developing Countries Clinical Trials Partnership (EDCTP). This trial will be run in conjunction with the University of Cape Town, Le Dantec University in Dakar, the MRC unit in The Gambia, the Institute for Public Health in Brussels, the Oxford-Emergent Tuberculosis Consortium (OETC) and the Aeras Global TB Vaccine Foundation, who are also the trial sponsor and are providing additional funding.

License agreement news ...

Biopharmaceutical company Imaxio has announced that it has entered a reciprocal license agreement with Isis Innovation, the technology transfer arm of Oxford University, to exploit know-how arising out of joint research at one of the world's premier research institutions, the Jenner Institute, for the development of new vaccines. The agreement will allow Imaxio to use its proprietary aXent adjuvant technology with viral vectors such as Modified Vaccinia Ankara (MVA) and adenoviruses. The University of Oxford is internationally recognised for its expertise in the creation and development of virally vectored vaccines.

"The technology Isis has licensed to us further validates the ability of Imaxio's aXent™ technology to enhance immune responses to current and future vaccines, and particularly those using viral vectors," said Francois Miceli, Chief Executive Officer of IMAXIO. "Oxford and the Jenner Institute have been excellent sources of innovation in the vaccine field."

Oxford also benefits, as it secures the right to use the Imaxio adjuvant in developing its own vaccine candidates, which would then be made available for partnering and further development through Isis. The current agreement is the result of a collaboration which

started in 2004 and has already led to joint patent filings. This collaboration is financed in part by the Grand Challenges in Global Health consortium, a programme supported by the Gates Foundation to promote innovation in global health.



Profiling: Jenner Investigators

Lucy Dorrell



I received my Bachelor of Medicine degree from the University of Southampton in 1988 and began my research career in 1993 as a Clinical Research Fellow in Communicable Diseases and Genitourinary Medicine at Imperial College. Initially, I was involved in clinical trials of new antiretroviral drugs; there was no effective treatment for HIV infection at this time. My interest in immunology began with research into antigen-presenting cell function in HIV infection, leading to an DM degree (1998). I moved to Oxford University in 1997 to study immunity to HIV-1/HIV-2 in exposed-infected individuals with Professors Sarah Rowland-Jones and Hilton Whittle,

spending two years at MRC Laboratories, The Gambia. After completing specialist clinical training (Genitourinary / HIV Medicine), I returned to the lab as a Clinician Scientist Fellow and began investigating the potential to augment protective CD8+ T cell responses against HIV-1 by therapeutic vaccination using novel DNA and viral-vectored HIV-1 vaccines developed by Dr Tomáš Hanke and Professor Andrew McMichael (MRC Human Immunology Unit, Weatherall Institute of Molecular Medicine). I became a Senior Clinical Lecturer in 2007 and continue to work on immunomodulation in HIV-1 infection within the Immunity theme of the Oxford NIHR Biomedical Research Centre. Currently, we are testing a new approach to tackling HIV-1 variability and immune escape using heterologous prime-boost vaccinations with a novel immunogen based on highly conserved regions of the HIV-1 genome. Another obstacle to the development of an effective HIV-1 vaccine candidate is the lack of a correlate of protective immunity. We are investigating novel immune correlates, including the antiviral inhibitory capacity of HIV-specific CD8+ T cells, which may provide a better measure of a protective immune response than widely used cytokine-based assays, and thus could be used to predict vaccine efficacy in early trials.

Key Publications

Yang H, Guimarães-Walker A, Hibbs S, Dong T, Stacey A, Borrow P, Hanke T, Davenport MP, McMichael A, Dorrell L. Interleukin-10 responses to therapeutic vaccination during highly active antiretroviral therapy and after analytical therapy interruption. *AIDS*. 2009 Oct 23;23(16):2226-30.

Murphy RL, Autran B, Katlama C, Brucker G, Debre P, Calvez V, Clotet B, Clumeck N, Costagliola D, Deeks SG, Dorrell L, Gatell J, Haase A, Klein M, Lazzarin A, McMichael AJ, Papagno L, Schacker TW, Wain-Hobson S, Walker BD, Youle M. A step ahead on the HIV collaboratory. *Science*. 2009; 324(5932):1264-5.

Yang H, Dong T, Turnbull E, Ranasinghe S, Ondondo B, Goonetilleke N, Winstone N, di Gleria K, Conlon C, Borrow P, Hanke T, McMichael A & Dorrell L. Broad TCR usage in functional HIV-1-specific CD8+ T cell expansions driven by vaccination during highly active antiretroviral therapy. *J Immunol*. 2007;179:597-606.

Ondondo B, Yang H, Dong T, de Gleria K, Goonetilleke N, Winstone N, Conlon C, Rowland-Jones S, Hanke T, McMichael A & Dorrell L. Immunisation with recombinant modified vaccinia virus Ankara expressing HIV-1 gag in HIV-1-infected subjects stimulates broad functional CD4+ T cell responses. *Eur J Immunol*. 2006 ;36:2585-94.

Dorrell L, Yang H, Ondondo B, Dong T, di Gleria K, Suttill A, Conlon C, Brown D, Williams P, Bowness P, Goonetilleke N, Rostron T, Rowland-Jones S, Hanke T & McMichael A. Expansion and diversification of virus-specific T cells following immunisation of HIV-1-infected individuals with a recombinant modified vaccinia virus Ankara / HIV-1 gag vaccine. *J Virol* 2006; 80: 4705-4716.

David Paton



I obtained my BA (Hons) Natural Sciences and VetMB degrees from the University of Cambridge, UK in 1981 and 1984 respectively, and a PhD degree, from the University of Surrey, UK, in 1992. After three

years working in veterinary practice in UK and Australia, I have spent the last 23 years as a veterinary virologist specialising in the epidemiology, diagnosis and control of various viral livestock diseases. I joined the Virology Department of the Central Veterinary Laboratory (later Veterinary Laboratories Agency, VLA). I was for six years secretary of the European Society for Veterinary Virology and became head of the Virology department at VLA in 1998. In 2001, I left VLA to join the Institute for Animal Health (IAH) as head of the department for vesicular disease control that includes the FAO foot-and-mouth disease (FMD) world reference laboratory. In 2007, I became head of the FMD Programme at IAH with 45 scientists plus students. The work of the Programme includes a wide range of strategic and applied research on FMD control including the evaluation of vaccination strategies as well as the development of improved vaccines and vaccine selection methods.

Key Publications

Parida S, Fleming L, Oh Y, Mahapatra M, Hamblin P, Gloster J, Paton DJ. (2008). Emergency vaccination of sheep against foot-and-mouth disease: significance and detection of subsequent sub-clinical infection. *Vaccine* 26(27-28): 3469-79.

Cottam EM, Wadsworth J, Shaw AE, Rowlands RJ, Goatley L, Maan S, Maan NS, Mertens PPC, Ebert K, Li Y, Ryan ED, Juleff N, Ferris NP, Wilesmith JW, Haydon DT, King DP, Paton DJ, Knowles NJ. (2008). Transmission pathways of foot-and-mouth disease virus in the United Kingdom in 2007. *PLoS Pathogens* 4, 1-8.

Arnold ME, Paton DJ, Ryan E, Cox SJ, Wilesmith JW. (2008). Modelling studies to estimate the prevalence of foot-and-mouth disease carriers after reactive vaccination. *Proc Biol Sci*.275(1630):107-15.

Paton DJ, Sumption KJ, Charleston B. (2009). Options for control of foot-and-mouth disease: knowledge, capability and policy. *Phil Trans R Soc B* 364, 2657-2667.

Valarcher J-F, Knowles NJ, Zakharov V, Sherbakov A, Zhang Z, Shang Y-J, Liu Z-X, Liu X-T, Sanyal A, Hemadri D, Tosh C, Rasool TJ, Pattnaik B, Schumann K, Beckham TR, Linchongsombokoch W, Ferris NP, Roeder PL, Paton DJ. (2009). Multiple origins of a foot-and-mouth disease virus serotype Asia 1 epidemic. *Emerging Infectious Diseases*, 15(7):1046-51.

Fowler VL, Knowles NJ, Paton DJ, Barnett PV. (2010). Marker vaccine potential of a foot-and-mouth disease virus with a partial VP1 G-H loop deletion. *Vaccine* 28, 3428-3434.

Andrew Pollard



I am Professor of Paediatric Infection and Immunity at the University of Oxford, Director of the Oxford Vaccine Group in the University Department of Paediatrics, Fellow of St Cross College and Honorary Consultant Paediatrician at the Children's Hospital, Oxford, UK. I chair the UK's NICE meningitis guidelines development committee. I obtained my

medical degree at St Bartholomew's Hospital Medical School, University of London in 1989 and trained in Paediatrics at Birmingham Children's Hospital, UK, specialising in Paediatric Infectious Diseases at St Mary's Hospital, London, UK and at British Columbia Children's Hospital, Vancouver, Canada. I obtained my PhD at St Mary's Hospital, London, UK in 1999 studying immunity to *Neisseria meningitidis* in children and proceeded to work on anti-bacterial innate immune responses in children in Canada before returning to my current position at the University of Oxford, UK in 2001. Current research activities include clinical trials of new and improved vaccines for children, invasive bacterial diseases in children in Nepal, studies of cellular and humoral immune responses to glycoconjugate vaccines, research on the genetic control of the human immune response and investigations on meningococcal host-pathogen interactions and development of a serogroup B meningococcal vaccine. My publications include over 200 manuscripts and books on various topics in paediatrics, and infectious diseases.

Key Publications

Snape MD, Perrett KP, Ford KJ, John TM, Pace D, Yu L, Langley JM, McNeil S, Dull P, Ceddia F, Anemona A, Halperin SA, Dobson S, Pollard AJ. A randomized controlled trial of a novel tetravalent meningococcal glycoconjugate vaccine in infants. *JAMA* 2008 Jan 9;299(2):173-84.

Lee YC, Kelly DF, Yu LM, Slack MP, Booy R, Heath PT, Siegrist C-A, Moxon ER, Pollard AJ. Haemophilus influenzae type b vaccine failure in children is associated with inadequate production of high quality antibody. *Clinical Infectious Disease*, 2008 Jan 15;46(2):186-92.

Snape MD, Kelly DF, Lewis S, Banner C, Kibwana L, Moore C, Diggle L, John T, Yu LM, Borrow R, Borkowski A, Nau C, Pollard AJ. Sero-protection against serogroup C meningococcal disease in adolescents in the United Kingdom: an observational study. *BMJ* 2008 Jun 28;336(7659):1487-91. Epub 2008 Jun 5.

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.

Pollard AJ, Perrett KP, Beverley PC. Maintaining protection against invasive bacteria in childhood with protein-polysaccharide conjugate vaccines. *Nature Reviews of Immunology* 2009 Mar;9(3):213-20.

Tomáš Hanke



I started my undergraduate studies at Charles University in Prague, Czechoslovakia reading Chemistry and completed my B.Sc. Honours degree in Biochemistry at McMaster University in Hamilton, Canada, where I also received an M.Sc. for my studies on Herpes simplex virus immunology. I then moved to St. Andrews University in Scotland for my Ph.D. degree developing antiviral-vaccines as solid matrix-antibody-antigen complexes. In 1994, I arrived as a post-doctoral scientist in Professor McMichael's laboratory in the Weatherall Institute of Molecular Medicine in Oxford, where I started working on the development of HIV vaccines, my current interest. With the establishment of the MRC Human Immunology Unit in 1998, I started my own group and 5 years later, I obtained my MRC tenure position. Since 2007 and 2008, I have been a Jenner Investigator and Reader in Immunology, respectively.

Key Publications

Rosario M, Hopkins R, Borthwick N, Fulkerson J, Quigley MF, Hill BJ, Joseph J, Douek DC, Price DA, Both GW, Sadoff JC and Hanke T. Novel recombinant BCG, ovine atadenovirus and modified vaccinia virus Ankara vaccines combine to induce robust polyfunctional human immunodeficiency virus-specific CD4 and CD8 T cell responses in rhesus macaques. *J Virol* In press (2010).

Bridgeman A, Roshorn Y, Lockett LJ, Xu Z-Z, Hopkins R, Shaw J, Both GW and Hanke T. Ovine *Atadenovirus*, a novel highly immunogenic vector for candidate HIV-1 vaccines. *Vaccine* 28:474-483 (2009).

Roshorn Y, Hong JP, Kobayashi N, McMichael AJ, Volsky AJ, Potash MJ, Takiguchi M and Hanke T. Protection of mice against chimeric human immunodeficiency virus type 1 challenge by clade B vaccine designed for HLA-B*5101+ patients. *Eur J Immunol* 39:1831-1840 (2009).

Létourneau S, Im E-J, Mashishi T, Brereton C, Bridgeman A, Yang H, Dorrell L, Dong T, Korber B, McMichael AJ and Hanke T. Design and pre-clinical evaluation of a universal HIV-1 vaccine. *PLoS ONE* 2:e984 (2007).

Im E-J, Saubi N, Virgili G, Sander C, Teoh D, McShane H, Joseph J and Hanke T. Vaccine platform for prevention of tuberculosis and mother-to-child transmission of HIV-1 through breastfeeding. *J Virol* 81:9408-9418 (2007).

Hanke T, and McMichael AJ. Design and construction of an experimental HIV-1 vaccine for a year-2000 clinical trial in Kenya. *Nat Med* 6, 951-955 (2000).

Brian Perry



I graduated as a vet from the University of Edinburgh in 1969, and after a brief spell in mixed animal practice took the Diploma in Tropical Veterinary Medicine, also in Edinburgh. This set me up to join the rinderpest eradication programme, working for the Imperial Ethiopian government and supported by the UK Overseas Development Administration (now DFID). I then returned to the UK to take a MSc in tropical veterinary science (again in Edinburgh), before moving to Colombia to run an investigation laboratory specialising in sheep diseases. Three years later I was next taken on by the Food and Agriculture Organisation of the United Nations (FAO) as epidemiologist in Zambia, studying

the dynamics and impacts of livestock diseases affecting the smallholder farming sector. The next leap was to Virginia, USA, where I was recruited as the epidemiologist in the newly established Virginia-Maryland Regional College of Veterinary Medicine, where as an Associate Professor I obtained tenure, and a Doctorate (yet again from Edinburgh!). After almost two decades of nomadic behaviour I returned to Africa in 1987 to lead the newly created Epidemiology and Socioeconomics Programme at the International Laboratory for Research on Animal Diseases (ILRAD) in Nairobi, Kenya. In 1995 ILRAD became ILRI (the International Livestock Research Institute), and broadened its geographical mandate to regions outside Africa. I left ILRI three years ago in 2007, but still live in Kenya, now in the Rift Valley. Under the auspices of the Jenner, I have led the development of two large strategic research award proposals on the understanding of endemic foot-and-mouth disease (FMD), and have recently led the independent team evaluating FAO's global programmes on avian influenza.

My specialisation has been in developing country livestock systems and in veterinary epidemiology, and I have applied the expanding inventory of epi and impact assessment tools in researching several different diseases such as gastro-intestinal parasitism, rabies, theileriosis, heartwater and FMD, mostly associated with the improved use of vaccines in their control. Frustrated at the slowness of change in disease control in much of the developing world, I have specialised in advocating the use of the products of epidemiology and economics studies to influence the development of sound evidence-based policies and strategies.

Key Publications

Brian has published more than 250 scientific articles in refereed journals, books and proceedings. Below is a brief selection.

Perry, B.D. and Grace, D. (2009). The impacts of livestock diseases and their control on growth and development processes that are pro-poor. *Philosophical Transactions of the Royal Society, B*, 364, 2643 – 2655.

Perry, B.D. and Sones, K.R. (Editors) (2007). Global Roadmap for Improving the Tools to Control Foot-and-Mouth Disease in Endemic Settings. Report of a workshop held at Agra, India, 29 November – 1 December 2006, and subsequent Roadmap outputs. ILRI (International Livestock Research Institute), Nairobi, Kenya, 88 pp. and CD-ROM.

Perry, B.D. and Rich, K. (2007). The poverty impacts of foot-and-mouth disease and the poverty reduction implications of its control. *Veterinary Record*, 160, 238–241.

Perry, B.D., McDermott, J.J. and Randolph, T.F. (2001). Can epidemiology and economics make a meaningful contribution to national animal disease control? *Preventive Veterinary Medicine*, 48, 231–260.

Coleman, P. G., Perry, B.D. & Woolhouse, M.E.G. (2001). Endemic stability: a veterinary idea applied to human public health. *The Lancet*. 357, 1284–1286.

Perry, B.D., McDermott, J.J. and Randolph, T.F. (2004). Control of infectious diseases: making appropriate decisions in different epidemiological and socio-economic conditions In: *Infectious Diseases of Livestock*, Volume 1, Editors J.A.W. Coetzer and R.C. Tustin, Oxford University Press, Cape Town, 178–224.

Perry, B.D., Randolph, T.F., McDermott, J.J., Sones, K.R. and Thornton, P.K. (2002). Investing in Animal Health Research to Alleviate Poverty. International Livestock Research Institute (ILRI), Nairobi, Kenya, 140 pp plus CD-ROM.

O'Callaghan, C.J., Medley, G.F., Peter, T.F. and Perry, B.D. (1998). Analysis of the epidemiology of heartwater (*Cowdria ruminantium* infection) in a transmission dynamics model. *Parasitology*. 117, 49–61.

James Martin 21st Century School \$50m Challenge to benefit innovative vaccine design, 1 of the 19 projects that were successful in the matched funding scheme

The innovative vaccine design programme seeks to design and develop promising new vaccines against infectious diseases of global health importance such as pandemic influenza, malaria and meningitis, using a broad multi-disciplinary set of approaches ranging from structural biology, genomics and mathematical modeling to immunology, clinical trials and health economics.

Lead Researcher(s): Professor Adrian Hill, Director of the Jenner Institute, and Professor Susan Lea, Professor of Chemical Biology, University of Oxford, meet with philanthropist James Martin following the announcement of their successful application



Take note....

A Discussion Meeting on "New Vaccines for Global Health" is to be held at the Royal Society, London, on 15- 16 November 2010. Many new vaccine technologies are becoming available to address global health priorities. This 2-day meeting will review vaccine design, development and deployment, in the search for vaccines against major killers such as malaria, HIV/AIDS and tuberculosis.

Organised by Professor Adrian Hill and Professor Brian Greenwood, CBE FRS, the meeting is intended for researchers in relevant fields and is free to attend, but pre-registration online is essential. For full details, visit <http://www2.royalsociety.org/events/forms/1010.htm>

Next Vaccinology Course at Oxford

This programme provides state-of-the-art teaching in both veterinary and human vaccinology, drawing on the experience of Oxford University, through the Jenner Institute based in Oxford, the Institute for Animal Health (IAH) and our partners in industry to provide training in areas related to vaccine design and construction, including: immunology and molecular biology, manufacturing, clinical trial design, immunomonitoring, regulatory strategy, post-marketing surveillance, vaccine financing and the ethics of vaccination.

There are three courses currently in the Vaccinology Programme:

Human and Veterinary Vaccinology

29 November - 3 December 2010
(five-day course)

Clinical Vaccine Development

(two-day course)

Vaccine Biomanufacturing

(two-day course)

For more information visit
<http://cpd.conted.ox.ac.uk/vaccinology>

Wellcome Grant Award

The Wellcome Trust has awarded £1.3M to the IAH and collaborators to investigate the translation of fundamental research into novel ways of producing better foot-and-mouth disease virus (FMDV) vaccines at a commercial level. The collaboration partnership will be led by Dr Bryan Charleston of IAH, and will involve the Department of Structural Biology (University of Oxford), Intervet-Schering Plough Animal Health (Intervet-SPA, Netherlands), ARC-Onderstepoort Veterinary Institute (South Africa), the Agricultural Research Service (USA), and the USDA - Foreign Animal Disease Research Unit at Plum Island (USA)



Bryan Charleston, Kruger National Park 2009

Decade of Vaccines - \$10billion pledged by the Bill and Melinda Gates Foundation

In Davos, Switzerland, at the World Economic Forum in January this year, the Bill and Melinda Gates Foundation announced the unprecedented donation of \$10billion to fund a Decade of Vaccines. Urging the world's donor agencies, business concerns, governments and non-profits to assist in this effort that will

dramatically reduce child mortality in the world's poorest countries, Bill Gates estimated that 8 million lives could be saved by 2020.

For more on this topic
<http://www.gatesfoundation.org/vaccines/Pages/decade-of-vaccines.aspx>

See next issue: "News of the efficacy flu trials answering key questions"



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