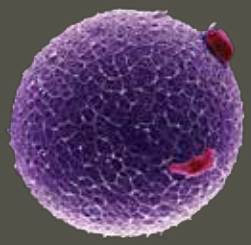
Volume 2: Research Profiles 2011/12



wellcome trust

Contents

Discoveries 2
A new antibiotic against *Clostridium difficile* 3
Neurodegenerative Disease Initiative 3
Artemisinin resistance 4
Making blood from stem cells 4
Role of the filaggrin gene in causing eczema 5

Applications of research 6
i-Snake® surgical robot 7
Gene therapy for blindness 7
Producing a more stable vaccine for foot-and-mouth disease 8
A new method of detecting neonatal seizures 8
Assessing the effectiveness of malaria control strategy 9
Developing a synthetic cell carrier membrane 9

Engagement 10
Science Gallery, Dublin 11
The Lion's Face: Addressing Alzheimer's through opera 11
I'm a Scientist, Get Me Out of Here! 12
Dirt season 12
In the Zone 13

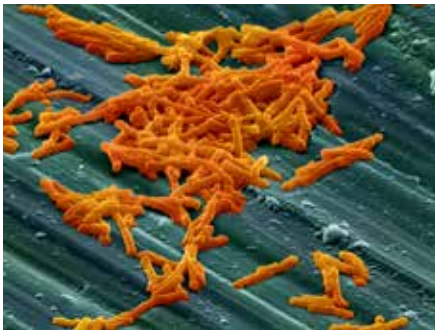
Research leaders 14
Nazneen Rahman 15
The Consortium of Health-Orientated Research in Transitioning Societies (COHORTS) 17
Andrew Hattersley 18
Sadaf Farooqi 19

Research environment 21
The Centre for the Study of Incentives in Health 22
Public Health Foundation of India 23
The KEMRI–Wellcome Trust Research Programme 24
UK Biobank 26

Cover: Human egg with coronal cells.
Yorgos Nikos/Wellcome Images

Discoveries

A new antibiotic against *Clostridium difficile*



Impact:

- Researchers have identified a new antibiotic specific to *Clostridium difficile*, a major cause of hospital-acquired infections.
- It is expected that phase I and phase II clinical trials of the antibiotic will be completed in 2015.

Wellcome Trust funding
Seeding Drug Discovery, 2009

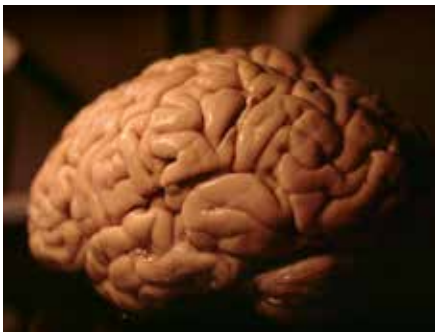
Annie Cavanagh/ Wellcome Images

The bacterium *Clostridium difficile* is a leading cause of hospital-acquired infectious diarrhoea and a particular danger for elderly or immunocompromised patients. The disease invariably occurs in patients given antibiotics for other illnesses, which destroy the normal protective gut bacteria, allowing *C. difficile* to colonise the large intestine. Very few antibiotics are available to treat *C. difficile*, and infection recurs in up to 30 per cent of cases. Each recurrence increases the severity of the disease and the risk of further recurrence. There were almost 24 000 cases of *C. difficile* recorded in England and Wales in 2010/11.

Summit plc, a drug discovery company spun out of the University of Oxford, received a Seeding Drug Discovery award in 2009 to develop and test a new antibiotic specific to *C. difficile*. The compound, SMT19969, has a different mode of action to other antibiotics – it leaves normal gut bacteria unaffected, allowing them to regrow and prevent reinfection by *C. difficile*.

Non-clinical studies showed that the drug is effective against all clinically important strains of *C. difficile*, has low toxicity and is retained within the gastrointestinal tract. Standard resistance development studies have shown no resistance development by *C. difficile*. In July 2012, Summit plc received a Translational Award to undertake a phase I clinical trial, assessing the safety and tolerability of the drug in healthy volunteers, and a phase IIa efficacy study in patients.

Neurodegenerative Disease Initiative



Impact:

- Researchers have identified how the protein α-synuclein aggregates – a change strongly associated with Parkinson's disease – allowing a possibility of therapeutic intervention for the disease.
- A mutation in the LRRK2 protein reduces ATP production, which may lead to selected neuronal death in Parkinson's disease.

Wellcome Trust funding
Strategic Awards, 2010

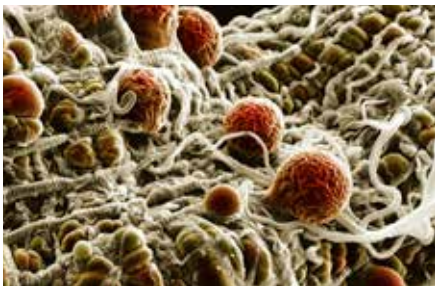
Heidi Cartwright/ Wellcome Images

Three major Strategic Awards were jointly funded by the Wellcome Trust and the MRC in 2009 as part of the Neurodegenerative Disease Initiative. The awards supported collaborations that brought together leading academic teams from across the UK to investigate the causes of Alzheimer's disease, Parkinson's disease and motor neurone disease.

The collaborations published several significant papers in 2012; for example, a collaboration between Professor David Klenerman and Chris Dobson (University of Cambridge) and Professor Nick Wood (UCL), published in *Cell*, showed how the protein α-synuclein aggregates – a change strongly associated with Parkinson's disease. Research led by Dr J Mark Cooper (UCL) in collaboration with Professors John Hardy, Michael Duchen and Anthony Schapira (UCL) has explained the effects of the most common genetic cause of Parkinson's, a mutation in the LRRK2 protein. It leads to decreased membrane potential in mitochondria, reducing ATP production, which may lead to selected neuronal death.

Other work, from Dr Lisa Saksida's laboratory (University of Cambridge), with Professor Bussey (University of Cambridge) and Professor Kwangwook Cho (University of Bristol), has increased our knowledge of the underlying causes of false recognition in Alzheimer's – patients suffer memory loss but also remember events that never happened. This work was published in *Brain*.

Artemisinin resistance



Impact:

- Researchers in Thailand have shown that, over time, malarial parasites have become increasingly resistant to the antimalarial drug artemisinin.
- Researchers have also identified a region within the *Plasmodium falciparum* genome that is associated with slow parasite clearance and therefore might be involved in artemisinin resistance.

Wellcome Trust funding

Wellcome Trust–Mahidol University–Oxford Tropical Medicine Research Programme core funding

Malaria parasites. *Hilary Hurd/Wellcome Images*

Artemisinin combination therapies are recommended by the World Health Organization as the first-line treatment for uncomplicated malaria, and artesunate (a derivative of artemisinin) is recommended for the treatment of severe malaria. However, a ten-year study on the border of Thailand and Myanmar has found evidence that *Plasmodium falciparum* – the most deadly species of the malaria parasite – is developing resistance to artemisinin-based drugs.

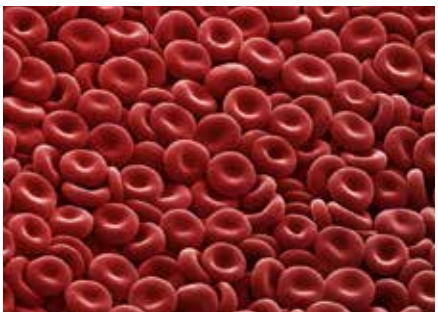
The study, led by researchers from the Shoklo Malaria Research Facility (part of the Wellcome Trust-funded Mahidol Oxford Tropical Medicine Research Programme), examined parasites in blood samples taken from patients who visited malaria clinics between 2001 and 2010. The results showed that, over the ten years, it was taking increasingly longer for the antimalarial drugs to clear parasites from the blood, indicating that the drugs were becoming less effective. This work, published in the *Lancet*, raises concerns that resistance could spread to Africa and India. The Shoklo researchers also featured in a separate study, published in *Science*, which identified a DNA region on chromosome 13 of the *P. falciparum* genome that is associated with slow parasite clearance. This region contains several candidate genes that may be involved with artemisinin resistance, although the exact mechanisms involved have yet to be identified.

These studies were jointly funded by the Wellcome Trust and the US National Institutes for Health.

Phyo AP et al. Emergence of artemisinin-resistant malaria on the western border of Thailand: a longitudinal study. Lancet 2012;379(9830):1960-6.

Cheeseman IH et al. A major genome region underlying artemisinin resistance in malaria. Science 2012;336(6077):79-82.

Making blood from stem cells



Impact:

- Researchers are developing techniques to produce infection-free blood from embryonic stem cells, removing the need for blood donation.
- After a successful proof-of-concept, researchers will work towards scalable manufacture.

Wellcome Trust funding

Strategic Translational Award, 2009

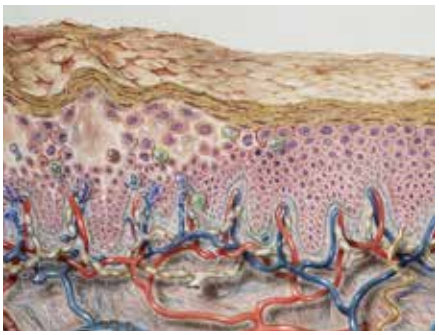
EM Unit, UCL Medical School, Royal Free Campus/Wellcome Images

Although the NHS receives around 2 million blood donations a year, stocks in the UK are only just sufficient. The situation worldwide is even more precarious, as the availability of blood in some low-income countries struggles to reach a tenth of that in wealthier ones. In addition to this, the risk of infection from transfusions, which are poorly screened in some countries, remains high.

Professor Marc Turner from the Scottish National Blood Transfusion Services and team – including researchers at the Centre for Regenerative Medicine in Edinburgh, University of Glasgow and NHS Blood Transfusion services – are developing techniques to produce large quantities of infection-free blood. This is achieved using human embryonic stem cells produced as a by-product of routine IVF. The stem cells are encouraged to develop into red blood cells by the careful use of growth factors, proteins capable of stimulating proliferation and differentiation.

The researchers, assisted by a Wellcome Trust Strategic Translation Award, will produce small volumes of blood demonstrating proof-of-concept. If future clinical trials are successful, the technology could prove significant for countries struggling with blood supplies.

Role of the filaggrin gene in causing eczema



Impact:

- Professor Irwin McLean has identified common mutations that increase the risk of eczema, asthma and allergy.
- Further research is underway to identify other genes and mutations associated with skin conditions to pave the way for new therapies.

Wellcome Trust funding
Programme grant, 2010

Medical Art Service, Munich/Wellcome Images

More than 25 per cent of the UK population have a significant skin disease, and approximately 14 per cent require treatment at any one time. Dermatological prescriptions are outnumbered only by painkillers.

Irwin McLean, Professor of Human Genetics at the University of Dundee, has made important advances in our understanding of the genetic factors underlying skin disease. His group has identified the genes involved in more than 20 'single-gene keratinizing disorders' – disorders that cause blistering, overgrowth, scaling or flaking of the epidermis. He has also shown that mutations in the filaggrin gene are a major predisposing factor in eczema, asthma and allergies. The discovery of these mutations changed the way researchers viewed eczema. Previously, it was thought that a person's overactive immune system caused the disease. Professor McLean's work showed that mutations in the filaggrin gene weaken the skin, allowing allergens to enter the body, and the resulting immune response leads to inflammation of the skin. Professor McLean's group have won numerous research prizes as a result of this work.

In 2012, he received a Wellcome Trust Strategic Award of more than £6 million to identify further mutations that cause skin diseases and to translate findings from genetic studies into therapies.

Applications of research

i-Snake® surgical robot

Impact:

- Collaboration between surgeons and engineers has generated a novel surgical snake-like robot.
- i-Snake® can carry sophisticated instruments and an image sensor into the body during minimally invasive surgery.

Wellcome Trust funding
Strategic Translation Award, 2008

Wellcome Trust

The development of minimally invasive surgical techniques has already brought widespread benefits to patients. By performing 'keyhole' surgery through small incisions, operations can be completed with reduced trauma and scarring and improved outcomes. Next-generation minimally invasive surgery will be assisted by increasingly small, dexterous robotic devices.

The i-Snake® resulted from collaboration between engineers, surgeons and computer scientists at Imperial College. They aim to provide clinicians with better ways to observe and articulate inside the body during surgery, necessitating advances in imaging, sensing and automatic navigation.

The snake-like robot is 0.5 inches in diameter. Its design allows the articulated segments to move freely while retaining a hollow core in which instruments, such as cameras and sensors, can be placed. The sophisticated control system allows the surgeon to control i-Snake's progress through the body, preventing damage to the surrounding tissue.

Several iterations of the device have already proved successful in pigs. The team is now looking to plan for the next stage of clinical trials in human subjects. If successful, the device will offer new capabilities to surgeons carrying out gastrointestinal, gynaecological and, potentially, cardiothoracic procedures.

Gene therapy for blindness

Impact:

- In clinical trials, six patients have received gene therapy for choroideraemia, a progressive form of genetic blindness.
- If the trial is successful, the therapy could stop the disease developing with a single treatment.

Wellcome Trust funding
Health Innovation Challenge Fund, 2010

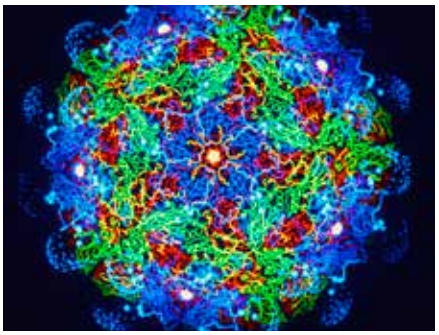
Kate Whitley/ Wellcome Images

Choroideraemia is an incurable disease that leads to the progressive degeneration of the retina and choroidal blood vessels. The disease, which is caused by a defect in the *CHM* gene on the X chromosome, leads to blindness and affects approximately one in 50 000 people in the UK. Symptoms begin in affected patients in late childhood, and their vision continues to deteriorate until around the age of 40, when they become legally blind.

A new UK multicentre trial, led by Professor Robert MacLaren (University of Oxford), has used a specially designed viral vector to halt the advance of the disease. An engineered virus containing the *CHM* gene was injected beneath the retina of one eye in six patients with choroideraemia, introducing a working copy of the gene into the light-sensing cells. This initial trial is assessing the safety of the procedure, and it is hoped it will lead to long-term expression of *CHM* in the patients' eyes. The patients will be observed for two years; since the trial began in October 2011, none of the six patients treated have had any adverse side-effects. The second phase of the study began in late 2012, treating a further six patients at a higher dose.

The trial is jointly funded by the Wellcome Trust and the Department of Health, through the Health Innovation Challenge Fund. Professor MacLaren has also visited ophthalmologists around the world to explore further trials using the viral vector.

Producing a more stable vaccine for foot-and-mouth disease



Impact:

- An international consortium of researchers has developed a more stable vaccine for foot-and-mouth disease, which is better suited to use in low- and middle-income countries.
- The team has also developed a method for adapting foot-and-mouth virus to tissue culture, increasing the efficiency and cost-effectiveness of production.

Wellcome Trust funding
Translation Award, 2010

Structure of foot-and-mouth disease virus. *David Stuart, Uni of Oxford/Wellcome Images*

Foot-and-mouth disease affects cloven-hooved animals, such as cows and pigs, causing them considerable suffering. It also has serious economic consequences. Inactivated whole-virus vaccines against the disease exist but are affected by the instability of the foot-and-mouth disease virus (FMDV). The instability reduces yield during vaccine production, increasing costs, and limits the vaccine's efficacy, so frequent booster vaccinations are required. In addition, the low temperature needed to store the vaccine is difficult to maintain, particularly in low- and middle-income countries.

Dr Bryan Charleston (Institute of Animal Health) and colleagues have increased the stability of the two most prevalent forms of the virus – O and SAT2. The team included researchers at Oxford University and the Diamond synchrotron who predicted mutations in the virus shell to improve its stability. These more stable viruses have been produced through a commercial partnership with MSD Animal Health and are now being tested for stability during cold storage and for their ability to provoke a long-term immune response.

The group is also adapting FMDV to tissue culture. FMDV can be hard to grow in a lab setting, which delays the production of sufficient amounts of vaccine when a new strain develops. Preliminary work – altering the coat proteins of viral strains to be more amenable to tissue culture – has been completed, increasing production efficiency.

A new method of detecting neonatal seizures

Impact:

- Engineers and clinicians have developed a computer algorithm that can detect seizures in babies being treated in neonatal intensive care units.
- This algorithm is compatible with existing EEG units and will help clinicians identify the frequency and severity of seizures, enabling appropriate treatment steps to be taken.

Wellcome Trust funding
Translation Award, 2008

Wellcome Photo Library/ Wellcome Images

Seizures in newborn babies often indicate underlying neurological problems. If the seizures are not identified and the causes go untreated, long-term brain damage can result. However, neonatal seizures are difficult to diagnose – often, they are 'clinically silent' and only detectable via EEG. Many hospitals lack the expertise required to interpret the complex brain patterns.

An automated system that can be used in neonatal intensive care units to detect seizures has been developed by a team of engineers and clinicians. Led by Dr Liam Marnane and Professor Geraldine Boylan (University College Cork), the team has created an algorithm that can monitor EEG outputs in real time, telling doctors when seizures happen and how long they last. The new algorithm is compatible with existing infant EEGs.

An initial Translation Award in 2008 allowed the group to evaluate the algorithm against large amounts of real world data, in collaboration with Dr Janet Rennie, Consultant Neonatologist at University College Hospital. A Strategic Translational Award, made in 2012, will fund a multicentre validation of the algorithm, comparing its seizure detection with that of international experts. The Award will also fund a trial testing the algorithm in a clinical setting in hospitals across Europe.

Assessing the effectiveness of malaria control strategy

Impact:

- Dr Badara Cissé's work on seasonal malaria prevention has influenced WHO policy on treatment in the Sahel and sub-Sahel regions of Africa.
- He is involved in several research projects in Senegal assessing the efficacy and effectiveness of different malaria control methods.

Wellcome Trust funding

Global Health Trials award, 2012

Hugh Sturrock/ Wellcome Images

In the Sahel, a sub-Saharan region of Africa, most childhood malaria cases occur during the rainy season between July and September. In 2012, the WHO recommended seasonal malaria chemoprevention (SMC) to control malaria in the region: courses of cheap antimalarial combination drugs are given to children under five years of age during the disease transmission season. This approach has been shown to markedly reduce the incidence of both severe and uncomplicated malaria cases.

Badara Cissé carried out much of the early research into SMC as part of his PhD at the London School of Hygiene and Tropical Medicine, funded by the Gates Malaria Partnership. During his studies, he developed the concept of SMC and ran a double-blind, randomised controlled trial in a rural area of Senegal. The trial resulted in an 86 per cent reduction in malaria episodes, and further trials in other African countries showed similar reductions. Dr Cissé and collaborators then demonstrated that SMC can be delivered on a large scale by providing 791 000 courses to young Senegalese children. He has been involved in the development of WHO implementation guidelines and has met with members of the Senegalese Health Ministry to organise the SMC programme, which began in September 2012.

At present, he is working on a research project funded by the Trust, the MRC and the UK Department for International Development, evaluating the effectiveness of a targeted malaria control strategy in Senegal. He is also working as part of the Malaria Vectored Vaccine Consortium to test a new malaria vaccine.

Developing a synthetic cell carrier membrane

Impact:

- Researchers in Sheffield have developed a new synthetic membrane to support the growth of cells to replace damaged corneal tissue in the eye.
- Work is underway in India to adapt the membrane for use in resource-poor settings and trial in people with blindness caused by corneal damage.

Wellcome Trust funding

R&D for Affordable Healthcare in India, 2010

Stacks of cell culture flasks. *Wellcome Library, London/Wellcome Images*

A small proportion of India's millions of blind or partially sighted people suffer visual impairment because the front of their eyes (the cornea) is scarred. The limbal epithelial stem cells, which cover the cornea, are easily damaged by common industrial accidents such as acid splashes.

To repair the damage, stem cells taken from the patient's other eye are cultured in the lab and transplanted. The cells are grown on a membrane, which breaks down once it is in place, leaving the cells in position. Until recently, the membrane had to be sourced from human amniotic sac, only obtainable after pregnancy.

Now, Professor Sheila MacNeil at the University of Sheffield has developed a synthetic membrane to carry the cells. The biodegradable membranes are made from spun biopolymers, which are imprinted to provide a suitable surface. This new scaffold can support cultured cells and cell outgrowth from small pieces of corneal tissue.

Aided by funding from an R&D for Affordable Healthcare in India award, MacNeil's partner, Dr Virender Sangwan at LV Prasad Eye Institute, is obtaining permission to test the membrane on patients in Hyderabad. If successful, thousands of people could have their sight restored.

Engagement

Science Gallery, Dublin

Impact:

- This year saw the Science Gallery at Trinity College Dublin receive its one millionth visitor, with its *Biorhythm* exhibition touring to Science Centre Singapore.
- The Gallery's engagement model saw it awarded a €1 million gift from Google in 2011 to develop further galleries in cities around the world.

Wellcome Trust funding
MSH Capital Award, 2008

Science Gallery

Science Gallery at Trinity College Dublin opened in 2008 to explore the interface between science and culture. A five-year Capital Award from the Wellcome Trust funded the development of the Gallery and several exhibitions. Major exhibitions at the Gallery have included *Infectious*, which looked at contagious diseases, and the Society Award-funded *Human+*, on the future of human evolution. The exhibitions typically last for three months and attract more than 50 000 visitors. In 2011, the *Biorhythm* exhibition toured to New York as part of the World Science Festival, and it was hosted this year by Science Centre Singapore.

The Gallery is attached to Trinity College Dublin and uses this link to bring together scientists and the public to discuss research and ethics. It also hosts month-long 'Lab in the Gallery' programmes, where Irish research groups do experiments involving the public in the Gallery's main space. In 2011, *Memory Lab* featured experiments on functional memory, and 2012's *Happy?* investigated the roots of emotion. These programmes have produced extensive research data, and several papers have been published as a result.

The Gallery's engagement model has attracted international interest. In 2011, the Gallery received a €1 million gift from Google to support the creation of Science Gallery International, which will set up eight science galleries (attached to universities) in cities around the world by 2020.

The Lion's Face: Addressing Alzheimer's through opera

Impact:

- The Opera Group's piece *The Lion's Face*, its first collaboration with a scientific institution, reached 4000 people through a tour featuring performance, debates and workshops.
- *The Lion's Face* also received national media coverage, both in print and on television, helping it to reach numerous secondary audiences.

Wellcome Trust funding
Large Arts Award, 2009

The Opera Group

Dementia is a widespread affliction in which memory and communication abilities break down. The musical memory is often the last part of the brain to decline – late-stage patients frequently sing tunes from their childhood. This inspired The Opera Group, funded by a Large Arts Award, to create an opera exploring the experience of living with Alzheimer's disease and its wider impact.

This was The Opera Group's first collaboration with a scientific institution. In the research period, the creative team worked closely with Professor Lovestone and colleagues at the King's College London Institute of Psychiatry and the National Institute for Health Research biomedical research centre. They shadowed research scientists and met with patients, relatives, clinicians and carers.

The resulting opera – *The Lion's Face* – premiered at the international Brighton Festival for the Arts, where it was awarded an Argus Angel award for artistic excellence. The group then completed a tour to seven venues, including the Royal Opera House, and was featured in The Identity Project, the Wellcome Trust's UK-wide initiative. An extensive public engagement programme was included at each venue for context; this included an interdisciplinary in-school initiative exploring memory with young people.

In total, The Opera Group reached approximately 4000 people directly. Media coverage (which was very positive, with several national reviews and a feature on *Channel 4 News*) helped the project reach numerous secondary audiences.

I'm a Scientist, Get Me Out of Here!

Impact:

- *I'm a Scientist, Get Me Out of Here*! has engaged more than 30 000 students and 540 scientists across the UK. The project has expanded internationally, with four events run in Australia and one in Ireland.
- The project develops the students' critical thinking and the researchers' outreach skills.

Wellcome Trust funding
Society Award, 2010

I'm a Scientist, Get Me Out of Here!

I'm a Scientist, Get Me Out of Here! is an online project that gives students aged between seven and 19 the opportunity to question and interact with researchers from a wide variety of disciplines. It began in 2008 with support from a Wellcome Trust People Award and received a Society Award in 2010.

In the event, the scientists are split between 'zones', each with a research theme such as genes, materials or general science. Teachers decide which zone their classes will join, and the students can ask the researchers questions in live or asynchronous chat. The latter allows the students to ask longer questions that the scientists can answer in greater depth. The students can also vote on their favourite researcher, and the winners receive £500 to spend on engagement projects. The event runs three times a year and has seen more than 23 000 students and 400 scientists from across the UK take part. Because it is based online, the project can reach rural schools away from large research institutes and enable scientists who are undertaking field work to take part. By giving students free rein to question researchers, *I'm a Scientist* helps to develop their critical thinking. It also benefits the scientists, helping them to articulate their work and hone their outreach skills.

I'm a Scientist has run two events in Australia and will expand to Ireland in November 2012. In future, the project is looking to open up to international and independent schools.

Dirt season

Impact:

- Wellcome Collection's Dirt season engaged new audiences through high-profile collaborations with the BBC, Glastonbury Festival and the Eden Project.
- The season also featured the *Dirt* exhibition at Wellcome Collection, which had the highest six-month visitor numbers to date.

Wellcome Collection

Building on the success of the Identity Project, the Dirt season aimed to engage the public with the filthy reality of everyday life. The season hoped to engage new audiences outside of Wellcome Collection's audience, work with the partners and grantholders likely to have the biggest impact and raise the Trust's profile by showcasing high-quality research and public engagement.

The season's major exhibition, *Dirt*, ran from March to August 2011 and had 132 365 visitors over six months. At the time, this was the highest six-month total for an exhibition, and *Dirt* also garnered excellent reviews.

A programme of events and commissions across the UK also tackled the subject of dirt. Guerrilla Science and Shangri-La at Glastonbury brought the theme of contamination to the UK's largest music festival in the form of an installation in which visitors could have direct one-on-one interaction with microbiologists and psychiatrists. The installation, which received excellent press coverage, had more than 900 visitors in 24 hours.

The season also included the art commission *Laid to Rest*, the iPhone and iPad app Filth Fair, and historical tours of former slum areas in Glasgow. It also commissioned the Eden Project family interactive exhibits, 'Freaky Nature with Poo'. Evaluation of the exhibits revealed that 38 per cent of visitors knew of the funding link between the exhibits and the Wellcome Trust.

In the Zone

Impact:

- In the Zone has helped teachers from schools across the UK deliver physiology classes to young people aged 4–19, by providing 31 000 experiment kits to UK schools and further education colleges.
- The event also had a touring exhibition, which was visited by almost 55 000 people, in locations throughout the UK.

In the Zone – the Wellcome Trust's major initiative inspired by the London 2012 Olympic and Paralympic Games – developed school kits and a touring exhibition on the theme of using science to explore the mind and body in motion.

The kits contained scientific equipment, teaching resources and experiments to help teachers deliver practical science lessons exploring human physiology. Nearly 30 000 kits were sent to primary and secondary schools, and more than 1300 kits were sent to special schools. The British Council is adapting the kits for use as an English Teaching Resource overseas.

The touring exhibition, which included five interactive exhibits and a live stage show, was designed and delivered by the At-Bristol Science Centre. It toured the UK between March and September and visited 16 locations, including BT London Live, throughout the Olympic Games period. Nearly 55 000 people of all ages visited the exhibition, and another 36 000 people viewed the busking and live shows. The exhibition is still available to tour.

In the Zone 'lite' – a pop-up interactive sport science experience – has been part of the BBC's Bang Goes the Theory and Blue Peter's Big Olympics Tour roadshows and has appeared at 21 community events across the UK. By mid-August, 79 000 people of all ages had discussed the science and activities with the staff. Most recently, In the Zone 'lite' has been delivered at the Bangkok Science Festival, in partnership with the British Council.

In the Zone was awarded an Inspire Mark from the London Organising Committee and was part of the national *Get Set+* initiative. The project is championed by Sir Steve Redgrave CBE.

Wellcome Library, London/Wellcome Images

Research leaders

Professor Nazneen Rahman

Impact:

- Professor Nazneen Rahman has identified many genetic mutations that can cause cancers in women and children, and she has used these discoveries to develop genetic tests to provide better screening options and treatments for people at increased risk of cancer.
- She is currently producing a universal test for cancer patients that can detect genetic changes important for the causation and treatment of cancer, and she is working to make genetic testing accessible to patients on the NHS.

Nazneen Rahman is Professor of Human Genetics at the Institute of Cancer Research, where she Heads the Division of Genetics and Epidemiology, and a Consultant Clinical Geneticist at the Royal Marsden Hospital, where she heads the Cancer Genetics Unit. In her research role, Professor Rahman leads research to identify genes that cause cancer.

Professor Rahman's work focuses particularly on identifying genes that cause cancers in women and children by researching families with multiple cases of cancer. Her team leads national studies that have recruited more than 15 000 families with breast and/or ovarian cancer and more than 6000 children with cancer.

Professor Rahman has identified four breast cancer predisposition genes (*CHEK2*, *BRIP1*, *ATM* and *PALB2*), an ovarian cancer predisposition gene (*RAD51D*), three childhood cancer predisposition genes (*BUB1B*, *PALB2* and *CEP57*) and two genes that cause childhood overgrowth, a condition that can be associated with cancer (*RNF135* and *EZH2*). She has also identified common genetic variants that increase the risk of breast cancer and a childhood kidney cancer known as Wilms tumour.

In a 2012 *Nature* paper, Professor Rahman and colleagues identified mutations in the *PPM1D* gene that are associated with increased risks of both breast and ovarian cancer. This discovery has important implications for our understanding of cancer risk because the mutations, known as 'mosaic', are only present in some cells, are not inherited and are not present in the cancers with which they are associated. This work was part funded by the Wellcome Trust Case Control Consortium.

Professor Rahman was awarded a Wellcome Trust Strategic Award in 2012 to develop a Cancer Predisposition panel, intended to provide a cost-effective, universal test of genetic variants relevant for cancer patients. The test would provide information about why a cancer has occurred and how it can best be treated. Initially, the work will focus on specific cancers (such as ovarian cancer), but the programme aims, ultimately, to enable all cancer patients to benefit from genetic testing.

Funding

2002
Cancer Research UK Programme Grant (Co-investigator)
2005
Wellcome Trust Case Control Consortium Grant (Co-investigator)
2005
US Army Medical Research Acquisition Activity Era of Hope Scholar Award
2005
MRC Career Establishment Grant
2007
Cancer Research Programme Grant
2007
Cancer Research Programme Grant
2008
Wellcome Trust Genome Wide Association Study Grant
2008
Cancer Research UK Programme Grant
2009
Wellcome Trust Genome Wide Association Study Grant
2011
Royal Marsden Charity Fund Award
2012
Wellcome Trust Strategic Award

Achievements

1991
Awarded medical degree, University of Oxford
1999
Awarded PhD, University of London
2002
Nature Genetics paper: 'Low penetrance susceptibility to breast cancer due to CHEK2(*)1100delC in non-carriers of BRCA1 or BRCA2 mutations'
2004
Nature Genetics paper: 'Constitutional aneuploidy and cancer predisposition caused by biallelic mutations in BUB1B'
2005
Elected Fellow of the Royal College of Physicians
2006
Nature Genetics paper: 'Truncating mutations in the Fanconi anemia J gene BRIP1 are low penetrance breast cancer susceptibility alleles'
2006
Nature Genetics paper: 'ATM mutations that cause ataxia-telangiectasia are breast cancer susceptibility alleles'
2007
Divisional Head of Genetics and Epidemiology, Institute of Cancer Research
2007
Nature Genetics paper: 'Mutations in RNF135, a gene within the NF1 microdeletion region, cause phenotypic abnormalities including overgrowth'
2007
Nature Genetics paper: 'PALB2, which encodes a BRCA2-interacting protein, is a breast cancer susceptibility gene'
2007
Nature Genetics paper: 'Biallelic mutations in PALB2 cause Fanconi anemia subtype FA-N and predispose to childhood cancer'
2008
Nature Genetics paper: 'Constitutional 11p15 abnormalities, including heritable imprinting center mutations, cause non-syndromic Wilms tumor'
2008
Head of Clinical Unit, Royal Marsden Hospital
2009
Elected as a Fellow of the Academy of Medical Sciences
2010
Nature Genetics paper: 'Genome-wide association study identifies five new breast cancer susceptibility loci'
2011
Nature Genetics paper: 'Germline mutations in RAD51D confer susceptibility to ovarian cancer'

Research leaders: Histories

2011
Nature paper: 'Integrative genomics identifies LMO1 as a neuroblastoma oncogene'

2011
Nature Genetics paper: 'Mutations in CEP57 cause mosaic variegated aneuploidy syndrome'

2012
Nature Genetics paper: 'A genome-wide association study identifies susceptibility loci for Wilms Tumor'

2012
Nature paper: 'Mosaic truncating mutations in PPM1D are associated with predisposition to breast and ovarian cancer'

2012
Nature Genetics paper: 'Germline RAD51C mutations confer susceptibility to ovarian cancer'

The Consortium of Health-Orientated Research in Transitioning Societies (COHORTS)

Impact:

- A longstanding collaboration between five large cohort studies in low- or middle-income countries has shown how nutrition in early life affects the health and economic productivity of adults.
- The Wellcome Trust has supported this collaboration from its inception.

In 2005, the *Lancet* commissioned a series of research papers investigating the impact of maternal and infant nutrition on human health. The second of the papers was by Cesar Victora, Professor of Epidemiology at the Federal University of Pelotas, Brazil, who received funding from the Wellcome Trust to pool the data from five long-term cohort studies in low- or middle-income countries, collaborating with their principal investigators.

The five studies in Professor Victora's review were the 1982 Pelotas Birth Cohort Study (Brazil), the Institute of Central America and Panama Nutrition Trial (Guatemala), the New Delhi Birth Cohort (India), the Cebu Longitudinal Health and Nutrition Survey (the Philippines) and the Birth to Twenty study (South Africa). In total, more than 10 000 people were involved in the studies, all of whom had been enrolled at or before birth and were being followed for at least 15 years. (The Trust also provides funding for the Brazilian and South African studies.) The analysis showed, across all five studies, that maternal and child undernutrition are strongly associated with less schooling, shorter adult height, lower offspring birth weight and reduced economic productivity.

Further Trust funding helped strengthen the collaborative network between the studies that became known as the Consortium of Health-Orientated Research in Transitioning Societies (COHORTS). This second project, which began in 2007, showed that infants who began eating solid foods in their first six months of life were more likely to become overweight adults. Having a high birth weight or gaining weight rapidly during the first two years of life was associated with increased height and school performance. Rapid weight gain after two years was not associated with increased performance but was strongly associated with an increased risk of several non-communicable diseases. The third phase of the COHORTS project began in 2009 with a Trust project grant awarded to Professor Linda Richter, from the Human Sciences Research Council, South Africa. This series of analyses looked at how environmental and socioeconomic factors in early life affect growth and adult health.

Funding

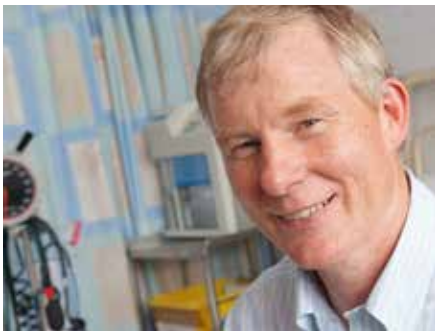
1982
Wellcome Trust funding for the Pelotas study
1998
The Wellcome Trust begins to fund the Birth to Twenty study
2007
Wellcome Trust Project Grant
2008
Wellcome Trust Project Grant
2009
Wellcome Trust Programme Grant

Achievements

1969
Institute of Central America and Panama Nutrition Trial begins in Guatemala
1969
New Delhi Birth Cohort begins in India
1982
Pelotas Birth Cohort Study begins
1983
Cebu Longitudinal Health and Nutrition Survey begins
1990
The Birth to Twenty study begins in South Africa
2007
The Consortium of Health-Orientated Research in Transitioning Societies (COHORTS) is founded
2008
Lancet paper: 'Maternal and child undernutrition: consequences for adult health and human capital'
2009
American Journal of Clinical Nutrition paper: 'Size at birth, weight gain in infancy and childhood, and adult blood pressure in 5 low- and middle-income-country cohorts: when does weight gain matter?'
2010
Journal of Nutrition paper: 'Weight gain in the first two years of life is an important predictor of schooling outcomes in pooled analyses from five birth cohorts from low- and middle-income countries'

John and Penny Hubley/ Wellcome Images

Professor Andrew Hattersley



Impact:

- Professor Andrew Hattersley and colleagues have identified mutations in eight genes that cause monogenic diabetes and provide diagnostic genetic testing for patients around the world.
- His studies have shown that patients with the commonest cause of both neonatal diabetes and maturity-onset diabetes of the young can replace their insulin injections with sulphonylurea tablets.

Monogenic diabetes is a disease usually caused by a mutation in one of the genes involved in insulin production. It is often misdiagnosed as the more common type 1 or type 2 diabetes, but it can be identified correctly by clinical criteria, biomarkers and genetic testing. Monogenic diabetes affects between 40 000 and 60 000 people in the UK. There are two main types: maturity-onset diabetes of the young (MODY) and neonatal diabetes. MODY is diagnosed before 25 years of age and is often passed down from a family member. Neonatal diabetes is diagnosed before six months of age and is rare.

Andrew Hattersley, Professor of Molecular Medicine at Peninsula Medical School, Exeter, has played a key part in defining the genetics of monogenic diabetes. He began working in Exeter as an NHS Diabetes Consultant working one day a week on research, and set up a genetics laboratory in the Royal Devon and Exeter Hospital with Professor Sian Ellard that combines research with an NHS diagnostic laboratory.

Professor Hattersley and colleagues have identified eight genes involved with neonatal diabetes. The most common, *KCNJ11*, encodes a protein that, when mutated, results in no insulin secretion. His work identified that 90 per cent of patients with mutations in this gene could replace their insulin injections with sulphonylurea tablets to greatly improve the control of their diabetes. As a result of his work, new international guidelines for neonatal diabetes have been produced, emphasising the need for urgent genetic testing.

In 2000, Professor Hattersley's work showed that patients with the most common subtype of MODY were four times more sensitive to the glucose-lowering effects of sulphonylureas than those with type 2 diabetes. As a result, thousands of patients worldwide can be treated with tablets and are no longer reliant on daily insulin injections. He leads a research team that provides genetic testing and advice on diagnosis and management for patients throughout the world. Currently, the team have analysed samples from more than 80 countries.

In 2012, Professor Hattersley was awarded a joint Senior Investigator Award with Professor Ellard to look at the development and function of human pancreatic beta cells by genetic, physiological and clinical studies of patients with neonatal diabetes.

Funding

1996
Diabetes UK Project grants
1998
Diabetes UK Project grants
1999
NHS Executive South and West Research & Development Programme Grant
2003
Research Leave Award, Wellcome Trust
2005
Diabetes UK Project Grant
2005
Wellcome Trust Strategic Grant
2005
MRC Project Grant
2006
Department of Health Grant
2007
Wellcome Trust Project Grant
2007
Department of Health Grant
2007
MRC Project Grant
2008
Diabetes UK Grant
2008
European Union FP7 Grant
2008
Wellcome Trust Project Grant
2009
Wellcome Trust Genome Wide Association Study
2010
Wellcome Trust Health Innovation Challenge Fund
2011
Wellcome Wolfson Capital Bid
2012
Joint Wellcome Trust Senior Investigator Award

Achievements

1984
Completes medical training, University of Oxford
1990
MRC Research Fellow, University of Oxford
1995
Consultant Physician Royal Devon an Exeter Hospital and part time Senior Lecturer at University of Exeter
1998
Reader at University of Exeter
1998
Nature Genetics paper: 'Mutations in the glucokinase gene of the fetus result in reduced birth weight'
1999
Professor of Molecular Medicine, University of Exeter
1999
Made Fellow of Royal College of Physicians
1999
Lancet paper: 'The fetal insulin hypothesis: an alternative explanation of the association of low birthweight with diabetes and vascular disease'
2000
Established with Professor Ellard diagnostic testing for MODY for the NHS
2003
The Joseph Hoet Research Award: of the International Diabetes and Pregnancy Study Group
2003
Lancet paper: 'Genetic cause of hyperglycaemia and response to treatment in diabetes
2003
Novartis Award for best young clinical investigato
2004
New England Journal of Medicine paper: 'Activating mutations in the gene encoding the ATP-sensitive potassium-channel subunit Kir6.2 and permanent neonatal diabetes'

2004
Made Fellow of Academy of Medical Sciences
2004
Established with Professor Ellard International Centre for Molecular Diagnosis in Neonatal Diabetes
2005
Academic Team of the Year to the Diabetes Molecular Genetic team
2006
New England Journal of Medicine paper: 'Switching from insulin to oral sulfonylureas in patients with diabetes due to Kir6.2 mutations'
2006
The Queen's Anniversary Prize for Higher and Further Education awarded to an entry from the Diabetes genetics team
2007
Science paper: 'A common variant in the FTO gene is associated with body mass index and predisposes to childhood and adult obesity'
2007
Science paper: 'Replication of genome-wide association signals in UK samples reveals risk loci for type 2 diabetes'
2007
Dorothy Hodgkin Prize Lecture, Diabetes UK
2007
William Osler Prize Lecture, Association of Physicians, UK
2008
Royal College of Physicians of Edinburgh, Sir Stanley Davidson lecture
2009
Society for Endocrinology Gold Medal
2010
Elected Fellow of the Royal Society
2011
Moxon Trust Medal awarded from the Royal College of Physicians
2011
Nature Genetics paper: 'GATA6 haploinsufficiency causes pancreatic agenesis in humans'

Professor Sadaf Farooqi

Impact:

- Professor Sadaf Farooqi has identified several genetic mutations associated with obesity.
- Her work is informing basic physiology and is helping to define the links between metabolism and behaviour.

Professor Sadaf Farooqi is a Wellcome Trust Senior Clinical Fellow at the Institute of Metabolic Science, University of Cambridge. She is investigating the genetic roots of obesity by studying an international cohort of more than 4500 severely obese patients who form part of the Genetics of Obesity Study. Her work is based both in the laboratory, where her team identifies the genetic mutations associated with obesity, and in the Trust-funded Cambridge Clinical Research Facility, identifying the effects of these mutations in patients.

In 2009, Professor Farooqi and colleagues found that obese patients with a mutation in the *MC4R* gene had significantly lower blood pressures than equally obese patients lacking the mutation. This work has informed basic physiology and helped to explain the link between weight gain and increased blood pressure. This work was a collaboration with the pharmaceutical company Eli Lilly. New compounds, developed as a result of the research, are currently undergoing phase I clinical trials for obesity and are being considered for phase II studies in patients with *MC4R* deficiency, the most common genetic form of obesity.

In 2010, Professor Farooqi and collaborators at the Wellcome Trust Sanger Institute found that deletion of the gene *SH2B1* can lead to severe childhood obesity and can be inherited within families. She is now working with the Trust-funded UK10K consortium and comparing the DNA of 1000 patients with severe obesity to more than 4000 healthy volunteers, in great detail, to identify additional genetic variants.

In another collaboration, Professor Farooqi is working with Professor Paul Fletcher, a Wellcome Trust Senior Clinical Fellow from the Department of Psychiatry at the University of Cambridge, to investigate the links between metabolism and behavioural neuroscience in obesity.

Funding
1997
Wellcome Trust Training Fellowship
2002
Wellcome Trust Clinician Scientist Fellowship
2006
Co-applicant Medical Research Council Experimental Medicine Research Grant
2007
Co-applicant National Institute for Health Research grant
2007
Wellcome Trust Senior Research Fellowship in Clinical Science
2008
Wellcome Trust Project Grant
2009
Co-applicant MRC Programme grant
2010
Co-applicant EU 7th Framework grant
2010
Co-applicant Wellcome Trust Strategic Award
2012
European Research Council Starter/Consolidator grant
2012
Wellcome Trust Senior Research Fellowship in Clinical Science (renewed)

Achievements
1993
Awarded medical degree from the University of Birmingham
1997
Nature paper: 'Congenital leptin deficiency is associated with severe early-onset obesity in humans'
1998
Nature Genetics paper: 'A frameshift mutation in MC4R associated with dominantly inherited human obesity'
1999
New England Journal of Medicine paper: 'Effects of recombinant leptin therapy in a child with congenital leptin deficiency'
2000
Journal of Clinical Investigation paper: 'Dominant and recessive inheritance of morbid obesity associated with melanocortin 4 receptor deficiency'
2001
Nature paper: 'Partial leptin deficiency and human adiposity'

Wellcome Library, London/Wellcome Images

Research leaders: Histories

2001
Awarded PhD from the University of Cambridge
2002
Journal of Clinical Investigation paper: 'Beneficial effects of leptin on obesity, T cell hyporesponsiveness and neuroendocrine/metabolic dysfunction of human congenital leptin deficiency'
2003
New England Journal of Medicine paper: 'Clinical spectrum of obesity and mutations in the melanocortin 4 receptor gene'
2004
Nature Neuroscience paper: 'A *de novo* mutation affecting human TrkB associated with severe obesity and developmental delay'
2006
Honorary Consultant, Addenbrooke's Hospital, Cambridge
2007
Science paper: 'Leptin regulates striatal regions and human eating behavior'
2007
New England Journal of Medicine paper: 'Clinical and molecular genetic spectrum of congenital deficiency of the leptin receptor'
2008
Nature Genetics paper: 'Common variants near MC4R are associated with fat mass, weight and risk of obesity'
2009
New England Journal of Medicine paper: 'Modulation of blood pressure by central melanocortinergic pathways'
2009
Nature Genetics paper: 'Six new loci associated with body mass index highlight a neuronal influence on body weight regulation
2010
Nature Genetics paper: 'Association analyses of 249,796 individuals reveal 18 new loci associated with body mass index'
2010
Nature paper: 'Large, rare chromosomal deletions associated with severe early-onset obesity'
2011
Professor of Metabolism and Medicine
2012
New England Journal of Medicine paper: 'A mutation in the thyroid hormone receptor alpha gene'
2013
Nature paper: 'Genome-wide SNP and CNV analysis identifies common and low-frequency variants associated with severe early-onset obesity'

Research environment

The Centre for the Study of Incentives in Health

Impact:

- New research on the use of financial incentives to encourage healthy choices and lifestyles is receiving high-profile media interest in the UK.
- The research suggests that financial incentives can be an effective tool to encourage pregnant women to seek help to stop smoking.

Wellcome Trust funding
Biomedical Ethics Strategic Award, 2009

Libby Welch/ Wellcome Images

When is it right to use financial incentives to improve health? This is the question that the Centre for the Study of Incentives in Health, funded by a Strategic Award in Biomedical Ethics, aims to answer. Although incentives can encourage people to act in beneficial ways, they have been criticised for discouraging personal accountability and being too forceful.

The team – led by Professor Theresa Marteau from Kings College London, Professor Richard Ashcroft from Queen Mary, University of London, and Professor Paul Dolan from the London School of Economics – has published the results of several important studies assessing the use of financial incentives to change behaviour. These include smoking cessation in pregnant women, an analysis of media coverage of incentive schemes, and observational and experimental studies of UK and US public attitudes towards using incentives to change behaviour.

The highest-profile research to date, which was published in April 2012, described the results of a pilot study of the financial incentives for smoking cessation in pregnancy. The study found that women who were incentivised to stop smoking reported using more services than women who were not incentivised. The research was featured on BBC Radio 4's *Medical Matters*.

Members of the team have participated in several national radio and regional TV programmes discussing this work and have produced articles in several publications, including the *British Medical Journal*. Professor Marteau also gave evidence at an Ethics and Behaviour Change seminar at the House of Lords in December 2010.

Public Health Foundation of India

Impact:

- The PHFI was established to address the shortage of highly qualified public health professionals in India.
- Wellcome Trust funding is supporting initiatives to improve public health capacity in India.

Wellcome Trust funding
Strategic Awards, 2008

John and Penny Hubley/ Wellcome Images

With approximately 30 per cent of its population of 1.2 billion people still living below the poverty line, India faces substantial public health challenges. To help address these issues, the Prime Minister of India, Dr Manmohan Singh, founded the Public Health Foundation of India (PHFI) in 2006. The PHFI aims to improve health outcomes in Indians by training a new generation of public health workers.

The PHFI is a public–private partnership of government agencies, academic institutions and charitable foundations, including the Wellcome Trust. Led by Professor K Srinath Reddy, the Foundation has established four Indian Institutes of Public Health, each with teaching and research programmes. A PHFI Centre of Excellence in chronic diseases has also been established, along with three other centres focusing on cardiometabolic risk reduction, disability-inclusive development and social determinants of health.

In 2008, the Trust awarded a £5 million Strategic Award to the PHFI to fund Master's degrees, PhD studentships and research grants. This grant was split between India and the UK, and the London School of Hygiene and Tropical Medicine (LSHTM) is managing the UK consortium. Students undertaking these courses split their time between India and one of 16 UK institutions; their fieldwork takes place in India. After completing their courses, students are expected to stay in India, working in one of the Indian Institutes of Public Health. At present, 19 PhD studentships are being undertaken and 15 Master's projects have been completed or are in progress.

Since 2008, more than 5000 people have completed short courses run by the PHFI on public health issues such as health communication and quantitative analysis. Many government employees have taken the courses, and some states make them mandatory for their staff. Although government-run public health institutes exist in India, they generally do not operate to a standardised qualification level. The PHFI is working to establish an independent accreditation body for degrees in public health.

Research is also central to the work of the PHFI. The Trust funding supports India- and UK-based research fellowships, as well as grants for Indian research staff to undertake collaborative projects with UK partner institutions. Currently, 11 fellowships are being undertaken and 11 research grants have been awarded.

A Wellcome Trust Strategic Award made to Professor Shah Ebrahim from the LSHTM has led to the establishment of the South Asia Network for Chronic Diseases. This collaboration between the PHFI and the Wellcome Trust Bloomsbury Centre for Clinical Tropical Medicine aims to strengthen capacity in chronic disease research. In other work, a translational award has been made to PHFI researchers to investigate the effectiveness of 'mWELLCARE' – mobile phone software for community health centres that will be used to assess a patient's health profile and help inform health workers of best treatment practices. In 2012, a $38 million grant from USAID was awarded to the PHFI to help strengthen the national HIV/AIDS control programme. This is the first time that a consortium led by an Indian NGO has been selected for such a grant.

In February 2012, the Indian Prime Minister announced that India should look to increase its healthcare spending from 1.4 per cent to 2.5 per cent of GDP, at a cost of over $40 billion at today's prices. The Trust is working closely with the India–UK CEO Forum, founded by the Indian and UK Prime Ministers, to investigate how India might develop healthcare provision.

The KEMRI–Wellcome Trust Research Programme

Impact:

- Work from researchers at the KEMRI–Wellcome Trust Research Programme has led to evidence-based policies and practice that are being used to improve public health in Kenya.
- The resulting improvements in clinical practice and epidemiology are applicable to many other African countries.

Wellcome Trust funding

Senior Research Fellowships, 2005, 2008; Principal Research Fellowship, 2006

Wellcome Library, London/Wellcome Images

The KEMRI–Wellcome Trust Research Programme is known internationally for its work on malaria and other diseases such as bacterial and viral childhood infections. The Programme was formally established in 1989 in partnership with the Kenya Medical Research Institute (KEMRI). It carries out basic and clinical research, and its results feed into local and international health policy. Its aim is to expand Kenya's capacity to conduct multidisciplinary research that is strong, sustainable and internationally competitive.

Professor Mike English

Professor Mike English is a Wellcome Trust Senior Research Fellow who is working to improve the care of severely ill children in Kenya. He began working for the Programme in the Kilifi District of Kenya in 1992 before moving to Nairobi in 2004, where he now leads the Child and Newborn Health Group.

In 2011, Professor English and colleagues showed that a comprehensive approach to care is required to improve survival rates for Kenyan children in rural government hospitals. During this three-year project, eight Kenyan hospitals were assigned to either 'full' or 'control' intervention groups. Those in the full intervention group received clinical guidelines and training in their use, along with other training aids and external supervision. Those in the control group received the same guidelines, but less training and no feedback. The research showed that hospitals in the full intervention group completed more admission assessment tasks and incorporated more good clinical practices into their treatments, and a lower proportion of children in these hospitals received inappropriate doses of drugs.

In 2005 and 2010, work from the Child and Newborn Health Group was used in the development of national treatment guidelines for Kenya, based on locally conducted systematic reviews. These guidelines and the training they are linked to are now widely disseminated in Kenya and have been adopted in Uganda and Rwanda. Professor English continues to work closely with the Kenyan Ministries of Health, the University of Nairobi and the WHO, where he acts as a technical advisor. In 2012, Professor English won the Sir Rickard Christophers Medal, awarded by the Royal Society of Tropical Medicine and Hygiene, for his contribution to tropical medicine.

Professor Bob Snow

Professor Bob Snow is a Wellcome Trust Principal Research Fellow and head of the Malaria Public Health and Epidemiology Group at the KEMRI-Wellcome Trust Research Programme. He was one of the top five authors of highly cited malaria research papers worldwide between 1989 and 2008, and has written more than 300 papers on malaria. He is also an advisor to the Kenyan Government and other international panels.

Professor Snow's work mapping malaria transmission and its impact on health evolved into a global initiative known as the Malaria Atlas Project, which began in 2005. The project has assembled a spatial database of medical information and satellite-derived climate data on *Plasmodium falciparum* and *Plasmodium vivax*. This work, provided free to researchers and public health officers, is the first evidence-based map of malaria prevalence and risk, which has already begun to provide international agencies with a framework to prioritise investment.

Professor Snow's group has used a combination of operational research and detailed statistical models to guide the Kenyan Government's malaria strategies on delivering insecticide-treated bednets and where to target donor-

assisted malaria funding. The team is also working with neighbouring countries to provide research evidence to support the best use of limited financial resources in the treatment, control and elimination of malaria in Somalia, Djibouti, Sudan, Uganda, Malawi and Namibia.

In 2011, Professor Snow was jointly awarded the George Macdonald Medal for his contribution to tropical hygiene research.

Professor Anthony Scott
Professor Anthony Scott is a Wellcome Trust Senior Research Fellow and Head of the Invasive Bacterial Diseases Group at the KEMRI–Wellcome Trust Research Programme. His work focuses on the evaluation of vaccines in children, particularly those that protect against bacterial pneumococcal disease – a leading cause of infant death in Africa. He also studies the epidemiology of the disease, investigating how its prevalence is linked with that of malaria.

In 2011, Professor Scott and colleagues showed that immunising babies against pneumococcus within the first three days of life is both safe and effective. The vaccine given at birth, ten weeks and 14 weeks was shown to be as safe as when given at six, ten and 14 weeks, one of the schedules recommended by WHO. Many deaths occur before babies receive their first dose of vaccine, so early immunisation could have a considerable impact on the health of African children. Professor Scott's work on the epidemiology of pneumococcal disease in Kenya was instrumental in developing a successful application to the Global Alliance for Vaccines and Immunization; this meant Kenya became the first African country to provide pneumococcal conjugate vaccine as part of its routine immunisation programme.

His research on *Haemophilus influenzae* type b (Hib) has led to a direct policy change in Kenya. Infection by Hib can cause pneumonia or meningitis, but is difficult to diagnose and expensive to treat. Despite these difficulties, the Ministry of Health in Kenya introduced Hib vaccine into the routine childhood immunisation programme in 2001. Professor Scott's work showed that this reduced the incidence of Hib by 88 per cent among children under five. As a result, the Kenyan government has decided to sustain the vaccination programme, originally funded by the Global Alliance for Vaccines and Immunization.

UK Biobank

Impact:

- UK Biobank has collected samples and health data from 500 000 participants to help understand the causes of diseases that occur in mid- and later life.
- The resource is now available for researchers to access and contains one of the most detailed collections of cross-sectional health data in the world.

UK Biobank was launched in 2002 by the Wellcome Trust, the Medical Research Council (MRC), the Department of Health and the Scottish Government. The goal was to create a resource for researchers investigating how lifestyle, the environment and genetic factors influence the risk of a wide range of diseases that affect people in mid- to later life.

Between 2006 and 2010, 500 000 men and women aged between 40 and 69 were recruited to the study across the UK. Volunteers completed detailed health and lifestyle questionnaires, had physical measurements, and provided samples of blood and urine. Further funds were provided by the Trust, the MRC, the Department of Health and British Heart Foundation to enable a more detailed study of a subset of participants, including eye measurements from more than 117 000 people in the UK. When recruitment was completed, around one in 50 of the eligible UK population had participated.

Large cohort studies such as UK Biobank often collect either a large amount of data on a small number of people or a small amount of data on a large number of people. As UK Biobank has collected both, it is one of the world's most detailed large-scale collections of health data. In 2010, the Wellcome Trust and the MRC awarded £25 million of funding to maintain the resource, repeat measurements in some of the volunteers and to establish links to participants' medical and other health-related records.

After a public consultation in 2011, the procedures that researchers must follow to access UK Biobank were finalised. The resource was launched in March 2012, and its data and samples are now available to approved academic and commercial scientists internationally for health research in the public interest. Information provided to researchers will not identify participants, whose data are anonymised. The independent UK Biobank Ethics and Governance Council monitors UK Biobank's adherence to an ethics and governance framework, which describes the ethical, legal and sociological standards that the resource must adhere to.

Funding

2002
Funding from the Wellcome Trust, MRC, the Department of Health and the Scottish Government
2009
Further funding from the Wellcome Trust, MRC, the Department of Health and the British Heart Foundation to allow UK Biobank to collect more information on the last 100 000 participants
2010
Welsh Assembly Government provides funding for a mobile assessment centre
2010
Renewal of core funding from the Wellcome Trust and the MRC, to include repeat assessments and linkage to health records
2012
UK Biobank receives funding from WT, MRC, BHF and Diabetes UK for assays of biomarkers from blood samples of all 500 000 participants

Achievements

2002
UK Biobank launched
2006
Pilot recruitment project undertaken in Altrincham
2007
Recruitment of participants begins
2008
The Automation Partnership is runner up in the Royal Academy of Engineering MacRobert Award for designing 'Polar' – UK Biobank's robotic storage system
2009
UK Biobank recruits its 250 000th participant. Its archive facility, a giant freezer to store blood and urine, is officially opened by HRH The Princess Royal
2010
Recruitment of participants is completed
2011
Expert groups established to advise on follow-up of participants' health, enhancements to the resource, imaging, outcomes and to consider how researchers might use the resource to their best advantage
2011
Public Consultation on UK Biobank access procedures
2012
UK Biobank opens to the research community and first research applications from investigators wishing to access Biobank samples are approved.
2012
Repeat assessments on 20 000 participants are started to address variability in baseline measures
2012
Activity monitor pilot study gets underway

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Wellcome Trust

We are a global charitable foundation dedicated to achieving extraordinary improvements in human and animal health. We support the brightest minds in biomedical research and the medical humanities. Our breadth of support includes public engagement, education and the application of research to improve health. We are independent of both political and commercial interests.

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