WellcomeNews

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FUNDING

Funding boost for Sanger Institute

Major new funding has been agreed for the Wellcome Trust Sanger Institute at Hinxton, near Cambridge. The Sanger Institute will receive some £340 million over five years to support its work on genomes and their role in health and disease.

A world leader in DNA sequencing and analysis, the Sanger Institute plays a major role in important national and international partnerships, such as the International HapMap Project on human variation and the Wellcome Trust Case Control Consortium, defining the genetic factors underpinning a range of common diseases.

The new funding will also help the Sanger Institute's successful Cancer Genome Project focus on breast, lung and kidney cancer to try to identify the majority of mutations involved in disease development. Outline studies will be carried out on 1000 other cancer samples.

Infectious disease is a massive health problem for developing countries. New programmes at the Sanger Institute will combine research on disease-causing organisms with studies of host resistance. Proposals include work on typhoid fever and malaria, in projects that exemplify integration of research between disciplines, a key aspect of the new plan.

Meanwhile, in collaboration with researchers from the UK and around the world, the Sanger Institute will examine the genetic foundation of diabetes and obesity.

Using its unique combination of expertise in computer analysis, DNA sequencing, DNA variation and antibody production, and gene activity in cells and model organisms, the Sanger Institute aims to release the fruits of all research rapidly to the research community.

Sanger breaks a billion

On Tuesday 17 January 2006 the Sanger Institute's World Trace Archive database of DNA sequences hit one billion entries. The Trace Archive (**http://trace.ensembl.org**) is a store of all the sequence data published worldwide. Each 'trace' is the output of a single sequencing experiment, on average 864 characters long. At 22 terabytes, the archive is in the global 'top ten' of UNIX databases, and may well be the world's largest single scientific database.

Spore formation in the fungus *Aspergillus*. The spores form on a special structure known as a conidiophore, which ends in this characteristic 'mop head'. The genomes of several species of *Aspergillus* have been sequenced recently, including that of the human pathogen *A. fumigatus*, sequenced by a team at the Wellcome Trust Sanger Institute. See page 13.
M I Walker

IN THIS ISSUE...

wellcome trust

Flexible funding

How can research funders ensure that they are facilitating significant advances in the generation of new knowledge? At the Wellcome Trust we believe that we can achieve this by supporting a balance of the best ideas and the best people. We believe that it is extremely important that we preserve a large fraction of the funding we provide for investigator-led advancement of science. We recognise that it is this that underpins future discovery and the application of knowledge.

Our strategy has been to create a framework that can guide, but not constrain, those that look to us for funding. Flexible funding mechanisms are key; we must not inhibit or provide perverse drivers to our research communities through the shape of our internal processes or mechanisms.

To increase the flexibility within our portfolio of funding schemes, last year we launched Strategic Awards. These important new grants will enable us to fund strategic initiatives of many kinds in a timely manner. They will provide research groups with considerable freedom to enhance their current research in ways they think most appropriate, but that cannot be supported by our existing grant-making mechanisms.

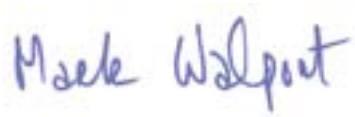
A broad range of components could be included within a Strategic Award, from training and capacity building to the advancement of specific strategic areas or the translation of basic research into policy and practice.

The scope of Strategic Awards is really only limited by the imagination of the research community. However, we cannot completely ignore the issue of unmet need. Through our Strategy Committees a number of areas have been highlighted where there are gaps in expertise; these include '*in vivo*' physiology, public health research and mathematical biology (see page 14).

Advancing our knowledge of the causes of health and disease increasingly requires interdisciplinary working. Research of this nature has not always been well served by the funding mechanisms research funders provide. Large projects may fall outside the scope of traditional funding mechanisms or, because of their breadth, face the double jeopardy of being reviewed by multiple funding committees. I hope that Strategic Awards will provide a more suitable vehicle for interdisciplinary research and training.

Lastly, I believe Strategic Awards will help strengthen our partnerships with the institutions in which our research communities work, ensuring these large and important grants are fully embedded and securely supported through their lifetime.

I have been delighted by the interest of the research community in these awards and look forward to the first grant awards later this year.



Mark Walport
Director of the Wellcome Trust

FUNDING

Healthier porridge?

Rex Features

Can changes to diet affect the behaviour of those detained at Her Majesty's pleasure?

In a pilot study, Professor John Stein and colleagues at the University of Oxford discovered that a healthy diet reduced prisoners' reoffending by more than a quarter. A new programme grant will enable the group to test this association with a larger group of inmates.

The links between diet and behaviour are not well understood, but there is growing evidence that what we eat affects the way we behave. In the pilot study, prisoners' diets were supplemented with vitamins, minerals and essential fatty acids for nine months. As a result, the reoffence rate was 26 per cent lower than in a control group.

With the new funding, Professor Stein's team will recruit 1200 male prisoners aged 16 to 21 years. If diet does appear to be having an impact, the group also plans to examine the vitamin, mineral and essential fatty acid status of prisoners to explore the physiological mechanisms by which these supplements modify behaviour.

If the initial findings are confirmed, the implications would be significant for both our understanding of dietary influences on behaviour and the dietary regimes used at secure institutions.

FUNDING

Sciart support

Applications are now invited for grants to support imaginative and experimental arts projects drawing on themes in biomedical science.

Sciart projects should explore new modes of enquiry and stimulate interest, learning and debate in areas surrounding contemporary biomedical science.

Applications are encouraged from all contemporary arts practitioners and organisations, including visual artists, photographers, poets, film-makers, animators and performance groups, as well as from science communicators and researchers.

There are two types of award: Research and Development Awards of up to £15 000, and Production Awards of up to £120 000.

The deadline for applications is 28 April 2006.
www.wellcome.ac.uk/sciart

FUNDING

Wound healing

S Wilson

Professor Paul Martin and colleagues at the University of Bristol have received programme grant funding to investigate the role of inflammation in wound healing.

Inflammation is triggered when body tissues need to be repaired. It enables the body's white blood cells and other defences to protect us from infection or foreign substances, but it can become a clinical problem itself.

The Bristol team will study the cell biology and genes involved in the wound-triggered inflammatory response in mouse and zebrafish (above) models. They aim to use a translucent model – the tail fin of zebrafish larvae – to image white blood cells migrating from the bloodstream to a wound. They will also test how the recruitment and activation of these cells is modulated in fish in which specific genes have been knocked out.

The team will also explore genetic control of inflammatory responses in the mouse. The ultimate aim is pave the way for the design of new medicines to control inflammation and improve human wound healing.

FUNDING

Monkey malaria

Researchers in Malaysia are aiming to discover whether malarial parasites are being transmitted from monkeys to humans.

Transmission of animal pathogens to humans can lead to potentially catastrophic emerging diseases. Malaria is already a huge human health problem, and a new project will explore whether malaria parasites infecting monkeys are being transmitted to people.

Human malaria is usually caused by one of four *Plasmodium* species (*falciparum*, *vivax*, *malariae* and *ovale*), but another has also been found to cause the disease: *P. knowlesi,* normally restricted to monkeys, is particularly common in Sarawak, Malaysian Borneo.

Professor Balbir Singh of the University of Malaysia Sarawak, and colleagues in the UK, aim to find out whether humans contract malaria just from other humans or from monkeys as well.

The team will also analyse two newly discovered monkey malaria parasites, and see whether they too are being transmitted to humans. Such information will be valuable input into malaria control strategies.

FUNDING

Burn or tan

Researchers led by Dr Anna Nicolaou at the University of Bradford are examining the biological mechanisms underlying sunburn, and why it particularly affects people who tan poorly.

Tanning involves the production of melanin by particular cells in the skin, melanocytes. With new project grant funding, the Bradford researchers are testing the novel idea that melanocytes that are not actively producing melanin secrete inflammatory mediators, including nitric oxide and a pro-inflammatory hormone, prostaglandin E2, which cause the symptoms of sunburn.

They will also test the idea that melanocortins – hormones secreted by the anterior pituitary gland and that control the degree of pigmentation in melanocytes – play a key role in tanning and sunburn by stimulating melanin production and inhibiting prostaglandin production. This could explain why people who readily tan tend to avoid sunburn, unlike pale-skinned people.

The group will compare the effects of artificial sunlight on volunteers who are prone to sunburn or who tan poorly.

The work could also confirm the melanocyte as a potential target in the treatment of sunburn and other inflammatory skin disorders.

Above:
Why do some of us tan well and others burn?
A Sieveking

FUNDING

African urbanisation

Left:
Urbanisation causes significant public health problems in developing countries.
© J and P Hubley/ Courtesy of the International Health Image Collection

A new project aims to assess the health impact of rapid urbanisation in sub-Saharan developing countries.

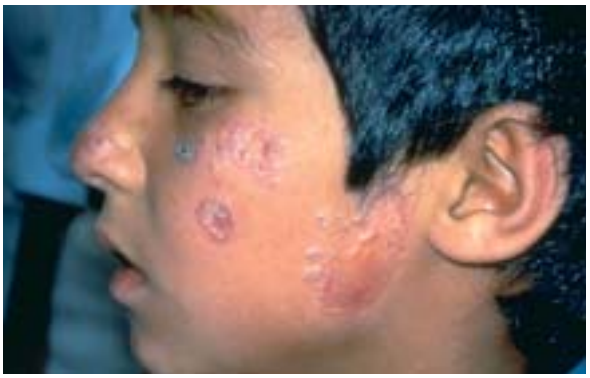
Many African cities are growing rapidly, while their countries' economies remain in a poor state. As a result, many migrants from rural areas end up poor and living in city slums.

Dr Eliya Zulu of the African Population and Health Research Center in Nairobi, Kenya, has, with colleagues in Kenya and the UK, been awarded a programme grant to investigate the reciprocal links between poverty and ill health, to help health officials plan the most effective strategies to improve the health of people living in slums.

The research will build on an existing demographic study of nearly 60 000 people in two Nairobi slums.

FUNDING

Leishmania resistance



Right:
Cutaneous leishmaniasis in a young boy.
© R Killick-Kendrick/ Courtesy of the International Health Image Collection

In parts of Syria, antimonial drugs are losing their potency against the *Leishmania* parasite. A new project will test the theory that the parasite is gaining resistance to the drugs.

Leishmania is a single-celled parasite affecting a swathe of tropical countries. It causes a variety of conditions, including a disfiguring skin form, cutaneous leishmaniasis, where non-healing ulcers form and gradually eat away surface tissue.

Cutaneous leishmaniasis can be treated with antimonial drugs, which have been in use for many decades. In Aleppo, Syria, there are reports that people are not responding well to the drugs, which suggests that the parasite may be developing resistance to them – a possibility that will be tested by Dr Clive Davies and Dr Vanessa Yardley from the London School of Hygiene and Tropical Medicine.

As few other drugs are available to treat this 'neglected disease', development of drug resistance in cutaneous leishmaniasis would be very worrying.

FUNDING

Those left behind

Many developing countries are experiencing extensive population migrations. The health of migrants receives considerable attention, but what about those 'left behind'?

With new project grant support, Professor Martin Prince of the Institute of Psychiatry, and colleagues at Mahidol University in Thailand, will be studying the impact of 'out-migration' in an area of western Thailand.

Generally, those left behind will be older adults, who are less mobile than their younger compatriots. This may have a negative impact, undermining their social roles or removing valuable support networks, but very little is currently known about how older adults are affected.

The project will build on an existing demographic study in Kanchanaburi province, established in 2000 by Dr Bencha Yoddumnern-Attig and colleagues with Wellcome Trust support.

FUNDING

New clinical fellowships

New Academic Clinical Fellowships, providing fresh training opportunities for doctors and dentists with an interest in research and teaching, have been announced by the UK Clinical Research Collaboration and the NHS-based Modernising Medical Careers team.

Universities, local NHS Trusts and Postgraduate Deaneries across England and Wales will host 104 programmes for the new Academic Clinical Fellowships. Over the next five years nearly 600 new Fellowships will be created.

These Fellowships are a key part of new flexible and integrated academic training schemes set out in the report 'Medically and Dentally Qualified Academic Staff: Recommendations for training the researchers and educators of the future' (**www.ukcrc.org/Default.aspx?page=320**).

The Academic Clinical Fellowships will support doctors and dentists in the early years of specialist training and help them to compete for a training fellowship for a higher degree. The Fellowships will part-fund the basic salary (25 per cent) and allow trainees to set aside time to develop academic skills. Funding is for a maximum of three years (four years for GPs).

Full details can be found on the Research Capacity Development Programme website (www.nccrcd.nhs.uk/intetacatrain/successfullist).

FUNDING

Deadly dengue

Research on the immune response to the dengue virus may reveal why some people show mild symptoms while others suffer the potentially deadly dengue haemorrhagic fever.

Around 2.5 billion people are at risk from dengue in tropical and subtropical countries, with 50 million infections occurring each year.

Infection with the dengue virus is not normally life-threatening, but in a minority of cases the potentially deadly dengue haemorrhagic fever ensues. It seems to develop when people have had previous dengue infections, suggesting that pre-existing immunity is actually harmful rather than protective.

Professor Gavin Screaton from Imperial College London and colleagues in Thailand will study the T-cell response to different strains of dengue, to identify the immunological mechanisms underlying severe disease. The work is particularly important for vaccine strategies, as any vaccine providing less than 100 per cent protection could actually predispose people to serious disease.

UPDATE

Intellectual property

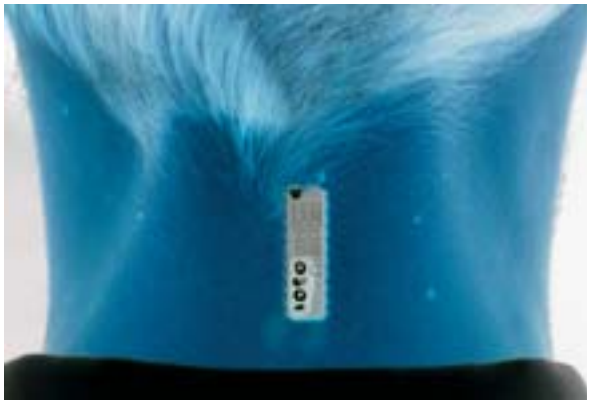
With Wellcome Trust support, the Centre for the Management of Intellectual Property in Health Research and Development (MIHR) organised two training workshops to help develop Kenyan capacity in the management of intellectual property and technology transfer.

The first workshop, in January 2006, was aimed at senior research scientists new to intellectual property and technology transfer, while the second, in February 2006, was geared towards the needs of research institute managers.

MIHR (**www.mihr.org**) is an independent not-for-profit centre based in Oxford. The workshops received Technology Transfer funding from the Wellcome Trust and were run in collaboration with the Medical Research Council of South Africa, the Kenya Medical Research Institute and the Kenya Industrial Property Institute.

UPDATE

Better by design



Worden Sports College

An event co-organised by the Wellcome Trust and the independent think-tank Demos generated debate on the potential and perils of human enhancement.

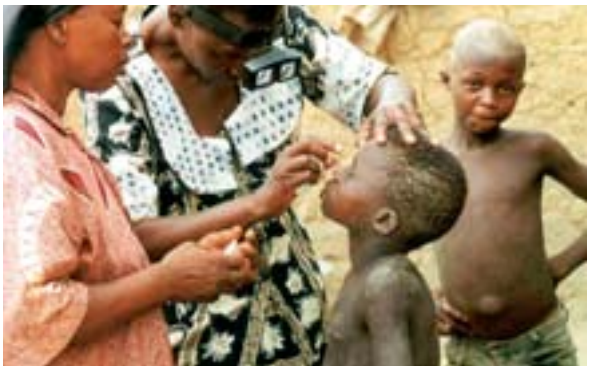
Medical advances aim to help those whose health is impaired, but increasingly they may be adopted by the healthy in search of improvement. Drugs to aid cognitive function in people with Alzheimer's disease, for example, could also be used to improve normal memory. And many people are excited about the prospect of significantly extended lifespans.

The evening event heard from a range of speakers, including Aubrey de Grey (a provocative supporter of extended-lifespan research), neuroscientist Daniel Glaser and sociologist Sarah Franklin, who spoke on prenatal diagnosis and the 'designer baby' debate. After short presentations, the audience had a chance to comment and raise issues with the panellists.

The event also saw the launch of a collection of essays on human enhancement, *Better Humans? The politics of enhancement and life extension*, published by Demos. It is available for download free at **www.demos.co.uk/catalogue/betterhumanscollection**.

FUNDING

Trachoma diagnosis



Left:
Trachoma is a painful condition that eventually leads to blindness.
© The Carter Center/ Courtesy of the International Health Image Collection

A trial in Ghana and Tanzania will test whether a cheap 'dipstick' diagnostic test for *Chlamydia trachomatis* can aid campaigns to eliminate blinding trachoma.

Trachoma, caused by infection with the *C. trachomatis* bacterium, is the world's commonest infectious cause of blindness. It can, however, be eliminated with a single round of the antibiotic azithromycin, which protects treated populations for two years.

A global campaign has been established by the World Health Organization to eliminate trachoma, and the manufacturer of azithromycin has agreed to donate the drug to control programmes. The programmes would be more effective, however, if the disease could be reliably diagnosed – visual inspection of eyes is not foolproof.

To this end, tropical health specialist Professor David Mabey of the London School of Hygiene and Tropical Medicine, and Dr Helen Lee at the University of Cambridge, who has developed a low-cost 'dipstick' diagnostic technology, have joined forces to trial a new diagnostic test for *C. trachomatis*. If this performs well in the field, reliable diagnosis could easily and cheaply be integrated into elimination programmes.

UPDATE

New Governor

Professor Sir Leszek Borysiewicz has joined the Wellcome Trust's Board of Governors. Professor Borysiewicz is Deputy Rector of Imperial College London, where he is responsible for overall academic and scientific direction, particularly the development of interdisciplinary research between engineering, physical sciences and biomedicine.

Above:
Professor Sir Leszek Borysiewicz.

UPDATE

New head for Africa Centre

Marie-Louise Newell, Professor of Paediatric Epidemiology at the Institute of Child Health in London, has been appointed the new Head of the Africa Centre for Health and Population Studies in KwaZulu-Natal, South Africa. Professor Newell specialises in the epidemiology of paediatric HIV infection.

Above:
Marie-Louise Newell, new Head of the Africa Centre.

RESEARCH

Stimulating growth-stunted children

Panos

Giving poorly nourished, growth-stunted children mental and social stimulation early in life has lasting cognitive benefits.

In developing countries, poor nutrition early in life causes stunting in a third of all children under the age of five (above). This early growth retardation is associated with cognitive deficits and poor performance at school in late adolescence.

Researchers led by Professor Susan Walker at the University of the West Indies in Jamaica have been following a cohort of growth-retarded children since 1987. In previous work, these children had received nutritional supplements and/or psychosocial stimulation – home visits for mothers and children by community health workers trained to demonstrate stimulation activities and encourage mother–child interaction. The interventions lasted two years, starting between ages nine and 24 months. Both interventions benefited development in early childhood.

In this follow-up, the team discovered that children who had received psychosocial stimulation scored significantly higher, aged 17–18, on cognitive tests than stunted non-stimulated adolescents (though still lower than their non-stunted peers). Nutritional supplementation alone provided no cognitive benefits at this age.

Walker SP et al. Effects of early childhood psychosocial stimulation and nutritional supplementation on cognition and education in growth-stunted Jamaican children: prospective cohort study. Lancet 2005;366(9499):1804–7.

UPDATE

Wellcome Witness

Volume 25 in the Wellcome Witnesses to Twentieth Century Medicine series, Prenatal Corticosteroids for Reducing Morbidity and Mortality after Preterm Birth, has been published by the Wellcome Trust Centre for the History of Medicine at UCL. The volume covers the important work on prenatal steroids carried out in New Zealand by Mont Liggins and Ross Howie in the 1960s, and its eventual impact on clinical practice (see Wellcome News issue 41, pages 8–9). The publication can be downloaded free of charge at **www.ucl.ac.uk/histmed**, following the links to 'Publications' and then 'Wellcome Witnesses'.

UPDATE

Queen's Prizes

Wellcome Trust-funded researchers at Birkbeck College London, Exeter and Dundee received their 2005 Queen's Anniversary Prizes for Higher and Further Education in February 2006.

Professor Martin Eimer and colleagues at Birkbeck Centre for Brain Function and Development investigate the neural basis of human mental abilities, such as the perception of faces and objects, attention, memory, and language. In 2006, the Centre will move to a new purpose-built research building, the Woburn Link Building, part-funded by the Wellcome Trust.

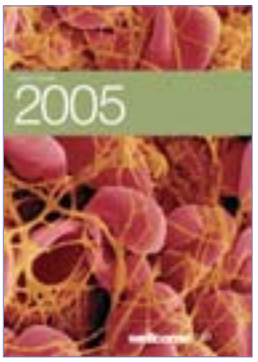
Professor Andrew Hattersley and colleagues in Exeter received a prize for their pioneering work unravelling the genetic causes of diabetes (see *Wellcome Science* issue 1, pages 26–29).

And Sir Philip Cohen, Director of the Wellcome Trust Biocentre at the University of Dundee, and colleagues in the School of Life Sciences and Medical Research Council Protein Phosphorylation Unit, were recognised for their creation of a consortium of six leading pharmaceutical companies to develop new drugs for major diseases including cancer and diabetes. A Dundee team led by Professor Mike Ferguson was recently awarded £8.1 million by the Trust to progress potential new therapies for neglected diseases such as leishmaniasis and Chagas' disease.

Wellcome Science

The second issue of the Wellcome Trust's new publication, *Wellcome Science,* is about to be published. The issue includes in-depth features on germ-cell development, social cognition, and the effects of HIV on human evolution, as well as an analysis of clinical use of stem cells. *Wellcome Science* is available free – see **www.wellcome.ac.uk/wellcomescience**.

Annual Review



The Wellcome Trust has published its *Annual Review 2005*, covering the year October 2004 to September 2005. The *Annual Review* features brief summaries of some of the most important discoveries emerging from Wellcome Trust-funded projects, as well as an overview of funding awarded through the year. See **www.wellcome.ac.uk/annualreview**.

UPDATE

Beastly Beasties

Scottish textile designers Timorous Beasties have created the latest instalment for the windows of the Trust's headquarters on Euston Road, London (above). The designs, inspired by the Trust's work on the human genome and malaria, include 48 lampshades featuring tsetse flies, paisley patterns made from infectious agents, argyle checks derived from syringes, and other motifs on a biological theme.

RESEARCH

Getting attached

A protein receptor called beta-1 integrin is vital for the development of glandular tissue.

Integrins are cell surface proteins involved in adhesion to the extracellular matrices that surround cells. This process is vital for the creation and maturation of many tissues. But little is known about the role of integrins in glandular epithelium, so Professor Charles Streuli and colleagues from the Wellcome Trust Centre For Cell-Matrix Research at the University of Manchester deleted the gene for beta-1 integrin and examined the effects on the development of mouse mammary glands and on mammary epithelial cells grown in culture.

The team found that the lack of beta-1 integrin affected the development of both acini (multicellular epithelial structures within the breast involved in milk production) and milk production (lactation). Lactation was defective even if the cells were allowed to differentiate before the gene was deleted. The epithelial cells did not adhere normally, and morphogenesis of the acini was defective.

It is well known that endocrine signals such as prolactin control the development and differentiation of the mammary gland in a temporal fashion, but this new study demonstrates the importance of adhesion mediated by beta-1 integrin in both the development of glandular epithelium and its biological function, lactation. Moreover, the study suggests ways in which integrins integrate with other cell-signalling molecules, thereby controlling the expression of tissue-specific genes.

Naylor MJ et al. Ablation of beta1 integrin in mammary epithelium reveals a key role for integrin in glandular morphogenesis and differentiation. J Cell Biol 2005;171(4):717–28.

UPDATE

Web archiving workshop

The Digital Curation Centre and the Wellcome Trust jointly hosted a two-day workshop on future-proofing institutional websites on 19–20 January 2006 at the Wellcome Library. Delivered over three sessions – international web archiving activity, practical tools and techniques, and examples of real-life experiences – the workshop aimed to help institutions ensure the long-term survival, value and usability of their websites by protecting them against future risks such as institutional change and technological obsolescence.

UPDATE

HTA sets dates

The newly established Human Tissue Authority (HTA) has announced key dates in the establishment of its regulatory regime. On 7 April 2006 the HTA will implement the EU Tissues and Cells Directive, which covers the licensing of tissue banks that store tissue and cells for human application. Also in April, the HTA will publish its revised statutory codes of practice guidelines, as well as a detailed timetable and arrangements for the licensing and regulation of other activities, including research. Licences for these activities will be granted from 1 September 2006. See **www.hta.gov.uk** for more details.

UPDATE

Speed-dating for scientists

A 'matchmaking' event was held in February 2006 to catalyse long-term relationships between 25 Wellcome Trust-funded scientists and TV producers. A 'speed-dating' format gave the scientists five minutes to tell their stories to 12 science producers, editors and commissioning editors from the broadcast media. The event was held at the Hiscox Art Café in London, and was compered by BBC radio and TV presenter Barbara Myers.

UPDATE

Glasgow triumph

Students on the Wellcome Trust four-year PhD programme at the University of Glasgow swept all before them in the 2005 Biotechnology Young Entrepreneurs Scheme (YES) competition. A team of three Wellcome students and one Biotechnology and Biological Sciences Research Council PhD student won the tenth anniversary final of the scheme, which is held annually to raise awareness of commercialisation opportunities among young researchers. As well as winning a cash prize of £1000, the Glasgow scientists are being flown to Texas to present their business case at a biotech forum at Rice University.

Above (from left): Jana Vavrova, Colm Nester and Adrienne Edkins, YES winners.

RESEARCH

Schizophrenia: cAMP interactions

The identification of a candidate susceptibility gene for schizophrenia provides insight into molecular mechanisms that may underlie the disease.

The new susceptibility gene, *phosphodiesterase 4B* (*PDE4B*) was identified by Professor David Porteous (University of Edinburgh) and colleagues through studies of a chromosome abnormality found in an individual with schizophrenia. The gene is particularly interesting as PDE4B inactivates cyclic AMP (cAMP) – a messenger molecule involved in learning, memory and mood.

Even more intriguingly, the researchers showed that PDE4B interacts with the protein produced by the *disrupted in schizophrenia 1* (*DISC1*) gene, one of the most promising candidate genes for schizophrenia. This interaction is influenced by levels of cAMP: increased levels in the cell lead to the phosphorylation and activation of PDE4B (by protein kinase A), which then dissociates from DISC1, ready to inactivate cAMP.

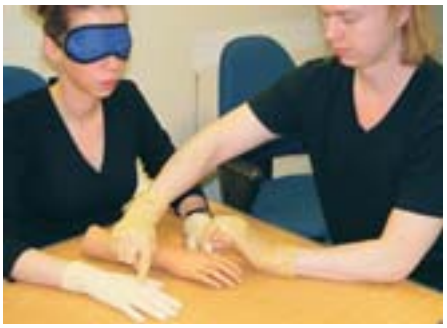
Schizophrenia and bipolar affective disorder are increasingly thought to be closely related. This new research suggests a mechanistic link, particularly given that mice lacking an equivalent gene behave as if they are taking antidepressants, and the antidepressant Rolipram is a selective inhibitor of PDE4.

If cAMP signalling is a unifying link between schizophrenia and bipolar affective disorder, as the researchers suggest, drugs that tweak the balance of the PDE4B–DISC1 interaction could become important new therapies for these disorders.

Millar JK et al. DISC1 and PDE4B are interacting genetic factors in schizophrenia that regulate cAMP signaling. Science 2005;310(5751):1187–91.

RESEARCH

All in hand



The feeling of body ownership is associated with many different sensory signals, not just vision.

In the 'rubber hand illusion', someone can be made to believe that a fake hand being rubbed in front of them is their own, if their own (hidden) hand is rubbed at the same time. The trick is associated with activity in several areas in the brain, particularly the ventral premotor cortex. The significance of this activity is unclear, however – the phenomenon could mainly be due to the powerful effects of the visual system.

Now Dr Henrik Ehrsson and colleagues at the Wellcome Department of Imaging Neuroscience at UCL have eliminated the visual input, by blindfolding subjects. The team used the subject's own left hand to stroke the rubber hand, while simultaneously stroking the subject's right hand (above). After about ten seconds, subjects perceive that they are stroking their own hand.

Functional magnetic resonance imaging showed that specific, separate parts of the brain, including the ventral premotor cortex, were involved in the illusion, and the stronger the sensation, the greater the activity. This suggests that the sensation of body ownership is due to a range of sensory signals from the body, not just vision.

Ehrsson HH et al. Touching a rubber hand: feeling of body ownership associated with activity in multisensory brain areas. J Neurosci 2005;25(45):10564–73.

Above:
As alcohol consumption rises, so do liver cirrhosis mortality rates.

RESEARCH

British livers

The incidence of death from liver cirrhosis is rising alarmingly in the UK.

Fifty years ago, England and Wales had the lowest cirrhosis mortality rates in western Europe; now, recent research reveals, deaths from liver cirrhosis are rising faster in the UK than anywhere else in western Europe.

Professor David A Leon at the London School of Hygiene and Tropical Medicine and Dr Jim McCambridge, holder of a Wellcome Trust Health Services Research Fellowship at the Institute of Psychiatry, compared cirrhosis mortality rates during 1955–2002 in the UK and in 12 western European countries.

The analysis shows that cirrhosis mortality rates in the UK increased steadily until the end of the 1970s, with accelerations in the 1980s and again from 1990–94 onwards. Rates among men in England and Wales rose by over two-thirds and in women by over a third. In Scotland, rates in men more than doubled and among women increased by almost two-thirds. Scottish cirrhosis mortality rates are now among the highest in western Europe.

In contrast, mortality rates in most other European countries have been falling since the late 1970s, particularly in southern Europe and France.

The most obvious cause of the increase in Britain is rising overall alcohol consumption: there was a doubling between 1960 and 2002.

Leon DA, McCambridge J. Liver cirrhosis mortality rates in Britain from 1950 to 2002: an analysis of routine data. Lancet 2006;367(9504):52–6.

In brief

Nicotine patches

Nicotine replacement therapy is not associated with any increase in the risk of myocardial infarction, stroke or death. A study of more than 33 000 people found that the incidence of illness rose progressively in the 56 days before the start of replacement therapy but declined in the 56 days after.

Hubbard R et al. Use of nicotine replacement therapy and the risk of acute myocardial infarction, stroke, and death. Tob Control 2005;14(6):416–21.

Mathematical malaria

A mathematical analysis of data from 90 communities affected by malaria suggests that the impact of the disease is not spread evenly across a population – 20 per cent of people account for 80 per cent of infections. The analysis will provide important input into malaria control programmes.

Smith DL et al. The entomological inoculation rate and Plasmodium falciparum infection in African children. Nature 2005;438(7067):492–5.

Healing powers

Lack of the hormone dehydroepiandrosterone (DHEA), a precursor to sex hormones such as oestrogen, slows wound healing in the elderly. Levels of DHEA strongly correlated with protection against chronic venous ulceration in humans, while loss of DHEA inhibited healing in a susceptible mouse strain. DHEA also accelerated wound healing in ageing mice. DHEA may therefore be valuable in the treatment of injuries in elderly people.

Mills SJ et al. The sex steroid precursor DHEA accelerates cutaneous wound healing via the estrogen receptors. J Invest Dermatol 2005;125(5):1053–62.

T-cell control

Regulatory T cells have been found to limit the risk of autoimmune disease provoked by weak antigens. T cells recognising foreign antigens can cross-react with the body's own structures, potentially causing autoimmune disease. Work in a mouse model of multiple sclerosis suggests that these T cells, when exposed to weakly cross-reactive foreign antigens, are prevented from becoming autoaggressive by the action of regulatory T cells. This highlights the importance of regulatory T cells in maintaining a diverse T-cell repertoire without increasing the risk of autoimmune disease.

Stephens LA et al. CD4+CD25+ regulatory T cells limit the risk of autoimmune disease arising from T cell receptor crossreactivity. Proc Natl Acad Sci USA 2005;102(48):17418–23

Baby face

Babies seem to be able to detect the presence of faces, even as newborns. This could reflect in-built biases in the brain that direct the babies' attention towards face-like patterns. Studies of newborns' responses to different stimuli suggest that the contrast that corresponds to that within the human eye, or to natural illumination of faces, plays a crucial role in directing babies' attention.

Farroni T et al. Newborns' preference for face-relevant stimuli: effects of contrast polarity. Proc Natl Acad Sci USA 2005;102(47):17245–50.

RESEARCH

Guiding the optic nerve

A key molecule guiding the growth of nerve cells that link the eye and the brain has been identified.

In the development of the amphibian visual system, the transcription factor Engrailed-2 is known to set up a gradient of ephrinA ligands that guide the growth of nerves linking the retina and the brain. But Professor Christine Holt (University of Cambridge) and colleagues have now found that it forms a chemical gradient in its own right, attracting axons from one side of the developing eye and repelling axons from the other side.

The optic nerve of each eye is made up of thousands of axons, which, in amphibians and birds, connect to a region of the brain called the optic tectum. (The optic nerve from the right eye makes connections with the left optic tectum, and vice versa.) During the development of the eye, retinal neurons extend axons that grow towards the brain, guided into the correct position by gradients of chemical signals.

The researchers found that retinal growth cones – the growing tips of axons – from one side of the eye (nasal, nearer the nose) were attracted by Engrailed-2, while growth cones from the other side (temporal) were repelled. This corresponds with the arrangement of retinal axons in the optic tectum, where Engrailed-2 is expressed in a gradient from posterior to anterior.

They also found that Engrailed-2 enters the growing axon tips and, by activating translation initiation pathways, stimulates the production of new proteins. Transcription factors classically act inside the cells that produce them in animals, so this is the first evidence that a transcription factor protein can influence cell behaviour from the outside.

Brunet I et al. The transcription factor Engrailed-2 guides retinal axons. Nature 2005;438(7064):94–8.

Above:
Tip of a growing retinal axon, with internalised Engrailed-2 labelled green.
I Brunet

Senior fellowships

Application timetable

Senior Research Fellowships in Basic Biomedical Science 2006/07
(International – Czech Republic/Estonia/Hungary/Poland/India/South Africa – and UK/Republic of Ireland)

- Preliminary application forms available from: 24 April 2006.
- Preliminary applications by: 9 June 2006.
- Invited full applications by: 1 September 2006.

For more information:
International Senior Research Fellowships: **www.wellcome.ac.uk/intsrf**

UK/Republic of Ireland Senior Research Fellowships: **www.wellcome.ac.uk/uksrf**

RESEARCH

RNase structure

Right:
RNase E may act as a molecular 'mousetrap'.
MJ Marcaida and B Luisi

The structure of a bacterial RNA-processing enzyme provides clues to its mechanisms of action.

RNA has many vital roles in the cell. Messenger RNA (mRNA), for example, is a key intermediary between DNA and protein. Not surprisingly, then, production of RNA is finely regulated – as is its destruction.

In the bacterium *E. coli,* the enzyme RNase E plays a key role in mRNA stability, destroying unwanted RNA molecules and trimming others in carefully controlled ways. The structure of this enzyme, produced by Wellcome Trust Senior Research Fellow Dr Ben Luisi and colleagues at the University of Cambridge, suggests ways in which it operates.

The active protein is built from four interwoven subunits, and its active site is surprisingly similar to a DNA-processing enzyme, suggesting they may have a common evolutionary origin. Interestingly, the part of the enzyme recognising the mRNA (at one of its ends) is some way away from the active site, suggesting that the enzyme may act as a hinged molecular 'mousetrap' when an RNA target molecule has been snared.

Callaghan AJ et al. Structure of Escherichia coli RNase E catalytic domain and implications for RNA turnover. Nature 2005;437(7062):1187–91.

Stop press

Visit our website (www.wellcome.ac.uk/news) for latest news on:

- The official opening of the National Science Learning Centre by the Prime Minister, Tony Blair.
- Launch of the recruitment phase of the UK Biobank project.

RESEARCH

Reassessing BCG

The BCG vaccine is thought to protect against the development of tuberculous disease but not infection with *Mycobacterium tuberculosis.* New research in Istanbul, however, raises doubts about this assumption.

TB is one of the world's commonest infectious diseases. The BCG vaccine has been used in many parts of the world for decades, but its exact value has been hard to judge, as standard diagnostic tests cannot easily distinguish between an *M. tuberculosis* infection and prior BCG vaccination.

Wellcome Trust Senior Clinical Fellow Dr Ajit Lalvani and colleagues in Oxford have developed a new, more sophisticated test for TB (see *Wellcome News* issue 35, pages 20–21), which is not influenced by BCG. Using this test, his team studied the factors affecting TB infection of children in Istanbul, Turkey.

Surprisingly, BCG-vaccinated children were significantly less likely to be infected with *M. tuberculosis*. This suggests that BCG is helping to prevent new infections – a finding that could have significant implications for TB control and public health programmes.

Soysal A et al. Effect of BCG vaccination on risk of Mycobacterium tuberculosis infection in children with household tuberculosis contact: a prospective community-based study. Lancet 2005;366(9495):1443–51.

RESEARCH

Opening the gate

Structural studies have identified how a neurotransmitter-gated ion channel operates.

Many neurotransmitter receptors are ion channels whose opening is controlled by binding of the appropriate neurotransmitter. A number of receptor variants exist, with slightly different properties but sharing a similar overall structure.

Dr Sarah Lummis and colleagues at the University of Cambridge and the California Institute of Technology have examined the structure of the 5-HT3 receptor, one of a family of receptors whose mechanisms of action have been unclear.

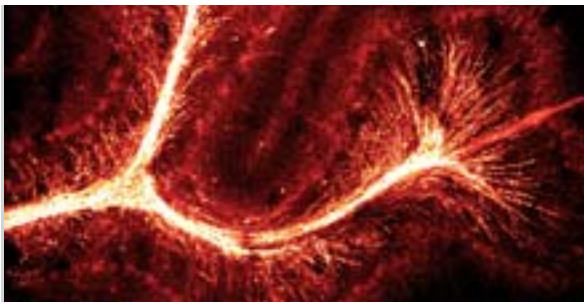
They focused on a specific proline residue occupying a critical position within a potential hinge region of the receptor. Proline can exist in two alternative chemical forms, *cis*- and *trans*-isomers. By replacing the proline with a series of analogues favouring one or the other isomer, the team showed that receptors with *trans*-isomer proline were non-functional.

Furthermore, nuclear magnetic resonance analysis suggested that the proline exists in two forms – presumably *cis*- and *trans*-arrangements. Thus, they conclude, ion channel opening is governed by ligand-induced *cis–trans* isomerisation of this key proline residue.

Lummis SC et al. Cis-trans isomerization at a proline opens the pore of a neurotransmitter-gated ion channel. Nature 2005;438(7065):248–52.

RESEARCH

Rethinking NMDA



R Káradóttir and D Attwell, UCL

The neurotransmitter NMDA may have a larger role in neurodegeneration than previously suspected.

Damage to oligodendrocytes – support cells that, among other things, make the myelin sheaths insulating neurons (above) – has been implicated in several conditions, including cerebral palsy, multiple sclerosis and stroke. The main culprit has been thought to be the neurotransmitter glutamate acting through AMPA receptors.

But there have been hints that activation of NMDA receptors may also be significant. Professor David Attwell and colleagues therefore re-examined NMDA responses in oligodendrocytes, finding NMDA-triggered currents in these cells in the cerebellum and corpus callosum in response to oxygen starvation.

These results suggest that NMDA neurotransmission may be important in various forms of nerve damage, and highlight oligodendrocyte NMDA receptors as a potential new therapeutic target.

Káradóttir R et al. NMDA receptors are expressed in oligodendrocytes and activated in ischaemia. Nature 2005;438(7071):1162–6.

RESEARCH

Resistance to Tamiflu

The avian influenza H5N1 strain can develop resistance to oseltamivir (Tamiflu) during treatment of human infections.

The Wellcome Trust-funded Oxford University Clinical Research Unit and the Hospital for Tropical Diseases in Ho Chi Minh City, Vietnam, have been at the forefront of clinical research and treatment of H5N1 avian flu. One of the few useful treatment options is the antiviral drug oseltamivir (Tamiflu). In two recent cases, however, the drug was rendered ineffective by the development of resistance during treatment.

Of eight patients with H5N1 virus who were followed during oseltamivir treatment, four experienced a rapid decline of viral load and survived. In another four, however, the virus was still detectable at the end of treatment; these patients all died and oseltamivir-resistant virus was detected in two of them.

Strategies to prevent or delay resistance developing, such as higher dosing of oseltamivir or combination therapy with other antivirals, deserve exploration.

de Jong MD et al. Oseltamivir resistance during treatment of influenza A (H5N1) infection. N Engl J Med 2005;353(25):2667–72.

RESEARCH

Shotgun haplotyping

Researchers at the Sanger Institute have developed a new method of identifying different forms of genetic variation.

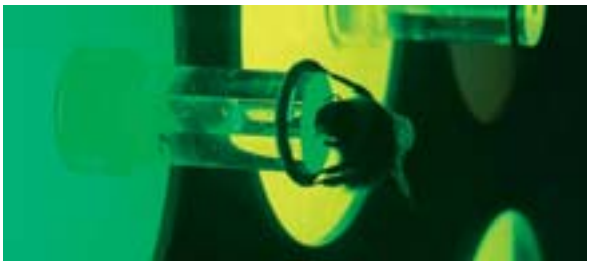
In shotgun haplotyping, a region of DNA is amplified from both chromosomes of an individual, then sheared randomly; the fragments are cloned and the clones sequenced from both ends. The DNA sequences are then reassembled against a reference sequence, and a new computational algorithm highlights positions that vary between the chromosomes, and then identifies on which chromosome each variant lies.

Although shotgun haplotyping requires a lot of sequencing reactions in order to be effective, it can identify all the variation in a particular region, including single nucleotide polymorphisms and small insertions or deletions, and by producing sequences of individual chromosomes this method generates the most informative form of data on genetic variation.

Lindsay SJ et al. Shotgun haplotyping: a novel method for surveying allelic sequence variation. Nucleic Acids Res 2005;33(18):e152.

RESEARCH

Bee seen



Bees' colour vision is more sophisticated than previously thought.

Like humans, bees are sensitive to light at three different wavelengths (trichromatic). Also like humans, they can recognise the colour of objects such as flowers even when their illumination changes (so-called colour constancy).

Experimentally, this has been observed by training bees to recognise a particular coloured flower on a uniformly coloured background under different lighting conditions. But real life is very different – how does a bee cope with a more complex scene, such as the dappled lighting of a woodland glade?

Dr Beau Lotto and Dr Martina Wicklein at the Institute of Ophthalmology have shown that bees can identify a particular flower among a grid of 64 flowers, each on a black background, even when they are illuminated in different ways (above). Thus bees' colour constancy abilities seem to hold even in more complex situations.

As well as shedding light on how bees cope with changing illumination, the research could also impact on the development of robotic visual systems.

Lotto RB, Wicklein M. Bees encode behaviorally significant spectral relationships in complex scenes to resolve stimulus ambiguity. Proc Natl Acad Sci USA 2005;102(46):16870–4.

RESEARCH

Sizing things up

Corbis

Our brains perceive body size by combining signals from different body areas.

Unlike touch and pain, there are no specialised areas for body size in the brain. Instead it is thought that body size is calculated relative to other objects in the environment, through sensory input from different parts of the body.

Dr Henrik Ehrsson and colleagues from the Wellcome Department of Imaging Neuroscience at UCL and other centres set out to unravel how the brain perceives changes in the size and shape of our bodies.

Since bodies do not normally change in size very quickly, the researchers took advantage of a perceptual illusion known as the 'Pinocchio illusion', which made subjects feel that their waists were shrinking. The team then used functional magnetic resonance imaging to see what was happening in their brains.

The illusion triggered activity in a part of the brain called the parietal cortex, which may be processing signals from different body parts to produce a sense of body size.

Ehrsson HH et al. Neural substrate of body size: illusory feeling of shrinking of the waist. PLoS Biol 2005;3(12):e412.

RESEARCH

Facing the fear

The brain registers frightened faces unconsciously, even if conflicting facial expressions are present.

Although we are normally conscious of other people's facial expressions, we can sometimes register this information without being consciously aware of it.

But what happens when the brain is confronted with conscious and non-conscious stimuli? To answer this question, a team including Professor Ray Dolan from the Wellcome Department of Imaging Neuroscience at UCL, and colleagues in The Netherlands, performed a series of experiments on an individual with normal sight in one half of visual space, and blindness – but residual subconscious vision – in the other half.

To examine conscious and non-conscious recognition, they presented a range of pictures to the seeing and 'blind' visual fields respectively.

Greater activity was seen in parts of the brain associated with emotional processing when frightened faces were shown to either visual field, indicating that facial expressions can be registered even in the absence of conscious awareness. A frightened face in the blind field enhanced the response to a frightened face in the intact field. Strikingly, even if the seeing visual field was presented with a happy face, a frightened face presented in the blind field still triggered an emotional response – conscious awareness fails to swamp the unconscious negative response.

This influence appeared to be restricted to faces – other images with negative emotional connotations (such a pit bull terriers and snakes) did not show similar effects.

de Gelder B et al. Unconscious fear influences emotional awareness of faces and voices. Proc Natl Acad Sci USA 2005;102(51):18682–7.

RESEARCH

Craniofacial development genes

Deletion of the transcription factor gene *GTF2IRD1* has been identified as a cause of some of the craniofacial defects seen in Williams–Beuren syndrome, a rare congenital craniofacial and neurological disorder.

The syndrome is characterised by a distinctive facial appearance, short stature, heart and blood vessel problems, an overly friendly personality, and numerical and spatial difficulties. Severe cases are caused by a deletion in one copy of chromosome 7 that removes 28 genes, but some people have smaller deletions and only some of the disorder's features. Dr May Tassabehji (a Wellcome Trust Senior Research Fellow at the University of Manchester) and colleagues have been studying the latter individuals to pinpoint which deleted genes are associated with which features of the disorder.

One key individual they identified with a smaller deletion had milder mental retardation and cognitive deficits, and less severe facial changes (measured using 3D face-imaging technology). Dr Tassabehji found that the transcription factor gene *GTF2IRD1* was disrupted, and went on to show that mice with deletions of both copies of the equivalent *Gtf2ird1* gene had defects reminiscent of the human condition: they were small and had craniofacial abnormalities including short snouts and fullness around the eyes, and some had twisted snouts with misaligned jaws.

People with severe Williams–Beuren syndrome have larger deletions and have lost additional genes – in particular the gene encoding GTF2I, a transcription factor related to GTF2IRD1. The researchers suggest that losing GTF2IRD1 has mild effects, but losing both GTF2IRD1 and GTF2I leads to most of the pathologies associated with the full syndrome.

Tassabehji M et al. GTF2IRD1 in craniofacial development of humans and mice. Science 2005;310(5751):1184–7

RESEARCH

Sensing oxygen

An ion channel's sensitivity to oxygen deprivation depends on processing of its RNA.

Mammalian cells depend on oxygen for their survival and must respond quickly if levels drop (hypoxia). This response is mediated, in part, by particular potassium channels known as BK channels (short for large-conductance voltage- and calcium-activated potassium channels). Why some of these channels are exquisitely sensitive to hypoxia, while others are almost insensitive, has now been uncovered by a team led by Dr Iain Rowe and Dr Mike Shipston at the University of Edinburgh, with collaborators at the University of Strathclyde.

The channel's pore is built from four subunits coded for by *KCNMA1*, a gene that undergoes extensive pre-mRNA splicing. The new research found that the channels were only sensitive to hypoxia when a particular splice variant, containing the stress-regulated exon (STREX), was expressed.

This exon encodes a chracteristic sequence that is highly conserved throughout evolution; when this sequence is mutated, sensitivity to hypoxia is abolished. As the expression of the STREX variant is tissue-specific, and can be regulated dynamically, it may be that alternative splicing of BK channels allows for differing sensitivity of tissues to hypoxia to be established, and to be altered according to the body's needs.

McCartney CE et al. A cysteine-rich motif confers hypoxia sensitivity to mammalian large conductance voltage- and Ca-activated K (BK) channel alpha-subunits. Proc Natl Acad Sci USA 2005;102(49):17870–6.

RESEARCH

Future scanning

Offering people suffering from regular headaches a brain scan may yield medical and financial benefits.

Chronic daily headache is a debilitating and difficult-to-treat condition. Dr Louise Howard at the Institute of Psychiatry and King's College Hospital and colleagues have been investigating whether people suffering from chronic daily headache and anxiety are reassured by having a brain scan – or whether this increases anxiety.

In a randomised controlled trial, individuals who were offered a scan were, after three months, less worried about a serious cause of their headaches (though this effect did not persist a year later).

However, although anxiety was only alleviated in the short term, cost savings for people with high levels of psychiatric morbidity were significant, because they used fewer medical resources after the scan. This suggests that scanning anxious individuals who suffer from daily headaches could help to reduce costs, as well as temporarily easing symptoms.

Howard L et al. Are investigations anxiolytic or anxiogenic? A randomised controlled trial of neuroimaging to provide reassurance in chronic daily headache. J Neurol Neurosurg Psychiatry 2005;76(11):1558–64.

RESEARCH

Fungus sequenced

The genome of *Aspergillus fumigatus* – a common airborne fungus that is a leading cause of death in vulnerable individuals – has been sequenced by an international collaboration including the Wellcome Trust Sanger Institute.

One of the most widely spread airborne fungi, *A. fumigatus*, is found in cellars, household plant pots, composting facilities, ground pepper and spices – and computers. It is likely that we all inhale several hundred *A. fumigatus* spores every day.

The vast majority of us are unaffected, but when we are weakened or exposed to particularly high levels of the fungus, it invades our lungs and other tissues. It is a leading cause of death in bone marrow transplant patients, people with HIV/AIDS, and others whose immune systems are compromised.

The genome was sequenced by an international consortium led by the Sanger Institute, The Institute for Genomic Research in Rockville, USA, and the University of Manchester.

The team identified 10 000 genes on the eight chromosomes of *A. fumigatus* – including a set of genes that are likely to be important for its disease-causing properties and will be the first targets in the search for new treatments.

Nierman W et al. Genomic sequence of the pathogenic and allergenic filamentous fungus Aspergillus fumigatus. Nature 2005;438(7071):1151–6.

RESEARCH

Intergenic interference

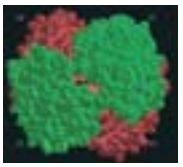
RNA-mediated silencing may be taking place in the human beta-globin gene cluster.

It is becoming increasingly clear that protein-coding genes are not the only important components of the genome. In particular, many RNA transcripts are copied from DNA outside genes and have biological roles controlling the activity of genes.

Professor Nick Proudfoot and Dr Dirk Haussecker at the University of Oxford have detected such intergenic transcripts in a cluster of genes coding for globin proteins, but have found no clear links with globin gene activity.

However, after eliminating the messenger RNA encoding the DICER protein, and thereby blocking RNA interference, they discovered that intergenic transcript levels increased across the globin cluster. This suggests that RNA interference is normally acting to silence genes, a phenomenon previously seen only at specialised areas of the chromosome, called centromeres.

Haussecker D, Proudfoot NJ. Dicer-dependent turnover of intergenic transcripts from the human beta-globin gene cluster. Mol Cell Biol 2005;25(21):9724–33.



Above: Structure of haemoglobin, composed of four globin monomers. *T Blundell and N Campillo*

Strategic Awards 2006

New priority areas have been announced for Strategic Awards.

Launched in 2005, the Wellcome Trust's Strategic Awards are intended to provide a flexible funding mechanism enabling researchers to add value to their existing work.

The Awards are open to internationally competitive groups seeking to develop their research in innovative ways. "The doors are open to good ideas in any subject area," emphasises Sohaila Rastan, Director of Science Funding at the Wellcome Trust. As long as the proposals are within the Trust's remit and applicants are eligible to apply for Trust support, any well-established group can apply for funding to take research to another level.

In addition, says Dr Rastan, the initiative is "an exciting and flexible vehicle allowing us to take forward the strategic priorities identified by Strategy Committees".

Strategy Committees came into operation in October 2004, as part of the new 'streams' model of research funding (see **www.wellcome.ac.uk/funding**). Since then they have been meeting regularly to consider the needs and opportunities within their respective areas of science. They have begun to make recommendations to the Trust's Board of Governors about possible future priority areas (see box).

"This is currently a menu of five things that would be particularly welcome," emphasises Dr Rastan, "but we will look outside these too. The menu is a movable feast and might change after each Strategy Meeting, if approved by the Board of Governors."

Of course, what is valuable in one area may not be appropriate for another, so the Strategic Awards scheme has been deliberately designed to be flexible, allowing researchers to put together proposals best suited to individual situations.

A number of major applications are currently being considered, and the first Awards are likely to be made later in 2006. The applications so far, suggests Dr Rastan, have picked up on some of the key features of the initiative. "We're very keen to see more interdisciplinary working," she says. "Advances in biomedical science are increasingly going to depend on input from chemists, physical scientists and mathematicians. We need to get these people working together on a common biological or medical problem, so they can bring their different expertise together around a common purpose."

She also sees the potential for Strategic Awards to catalyse the growth of research programmes abroad. "Our Major Overseas Programmes in South-east Asia and Africa have been phenomenally successful. They're tackling globally important medical problems and are having an internationally significant impact. If a research programme already has a foothold in an overseas location, then Strategic Awards would be one mechanism by which research could be developed further." Such a mechanism could also provide a significant input into local capacity building.

"We firmly believe in supporting the best researchers with the best ideas," stresses Dr Rastan, setting out a challenge to the UK's research communities. "We've tried to be imaginative in terms of the ways in which we can provide support for people. Now we want them to come up with the big ideas that we can fund."

For more information about Strategic Awards, see **www.wellcome.ac.uk/funding**.

Priority Areas

Mathematical biology/statistical methods – training and capacity building

All the Strategy Committees have highlighted the urgent need to address the lack of expertise in statistics, study design, data analysis (e.g. from cohort or demographic surveillance studies) and mathematical biology.

Public health research – training and capacity building

The Populations and Public Health Strategy Committee has identified a need to address training of and interactions between clinicians, basic scientists and practitioners in public health research.

'*In vivo*' physiology – training and capacity building

The Physiological Sciences Strategy Committee has expressed concern about the lack of exposure that young scientists have to *in vivo* research, and the imminent loss of skills in this area as the current experts retire.

Neuroimaging – interdisciplinary networks/programmes

To take full advantage of the UK's strengths in neuroimaging, the Neurosciences Strategy Committee has identified a need for increased networking between major imaging centres and interdisciplinary programmes involving mathematicians, physicists and engineers.

Emerging diseases – interdisciplinary networks/programmes

Research that enables the rapid, accurate diagnosis and response to emerging diseases has been seen as crucial by the Immunology and Infectious Disease Strategy Committee. Applications for networks that bring together epidemiologists, molecular biologists, clinicians and veterinarians, and that link surveillance data with research, are therefore particularly encouraged.

FUNDING

Human and avian flu

The Wellcome Trust is actively seeking high-quality research proposals that aim to further the understanding of avian and human flu via the project grant and programme grant schemes.

Research proposals addressing questions that are particularly urgent and timely will be fast-tracked through our assessment procedures. All applications will be assessed on the basis of the excellence of the science presented.

Research proposals would be particularly welcome in the following areas:

- epidemiology
- molecular basis of virulence
- molecular architecture and evolution of influenza viruses
- interspecies transmission
- genetic susceptibility to infection
- diagnostics
- approaches to prevention and treatment.

For full details see
www.wellcome.ac.uk/funding

Interested in public engagement with science?

Our website includes a summary of the funding opportunities open to researchers and others keen to engage with the public.

This includes details of funding schemes as well as other options, such as the Researchers in Residence and BA Media Fellowship schemes, which receive support from the Wellcome Trust.

For full details see
www.wellcome.ac.uk/node2570.html

Calendar 2006

April

26 Scientists, Sea-trials and International Espionage: Who really invented the balance-spring watch?
Roy Porter Lecture, London
www.ucl.ac.uk/histmed

May

8–10 Working with the Human Genome Open Door Workshop **GC**

14–20 Molecular Basis of Infection: Basic and applied research approaches
Advanced Course **GC**

31 Utilising the Human Genome
HGM2006 Satellite Workshop
Helsinki, Finland
http://hgm2006.hgu.mrc.ac.uk

June

5–9 Signalling to Chromatin – Epigenetics
European Science Foundation–Wellcome Trust Conference **GC**
www.wellcome.ac.uk/conferences

5–15 First Pasteur Institute–Wellcome Trust Course on Genomics in South America
Pasteur Institute, Montevideo, Uruguay

21–30 Functional Genomics
Advanced Course **GC**

July

3–8 Wellcome Library closed week
http://library.wellcome.ac.uk

5–9 Animal Models in Drug Discovery
Wellcome Trust Conference **GC**
www.wellcome.ac.uk/conferences

15–19 Euroscience Open Forum 2006
Deutches Museum, Munich
www.esof2006.org

19–25 Human Genome Analysis: Genetic analysis of multifactorial diseases
Advanced Course **GC**

20–26 Molecular Neurology and Neuropathology
Advanced Course **GC**

31 Working with the HapMap (until 2 Aug.)
Advanced Course **GC**

August

30 Interactome Networks (until 3 Sep.)
Wellcome Trust–Cold Spring Harbor Laboratory Conference **GC**
www.wellcome.ac.uk/conferences

September

3–6 Animal Biotechnology
European Science Foundation–Wellcome Trust Conference **GC**
www.wellcome.ac.uk/conferences

7–10 Genomic Perspectives to Host–Pathogen Interactions
Wellcome Trust–Cold Spring Harbor Laboratory Conference **GC**
www.wellcome.ac.uk/conferences

13–17 Genome Informatics
Wellcome Trust–Cold Spring Harbor Laboratory Conference **GC**
www.wellcome.ac.uk/conferences

28 Integrated Approaches to Brain Complexity (until 1 Oct.)
Wellcome Trust–Cold Spring Harbor Laboratory Conference **GC**
www.wellcome.ac.uk/conferences

October

4–7 Design and Analysis of Genetic-based Association Studies
Advanced Course **GC**

November

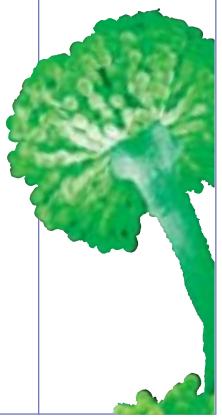
8–12 Integrated Biology of Crop Plants
www.wellcome.ac.uk/conferences

December

6–10 Humanising Model Organisms to Understand the Pathogenesis of Human Disease
European Science Foundation–Wellcome Trust Conference **GC**
www.wellcome.ac.uk/conferences

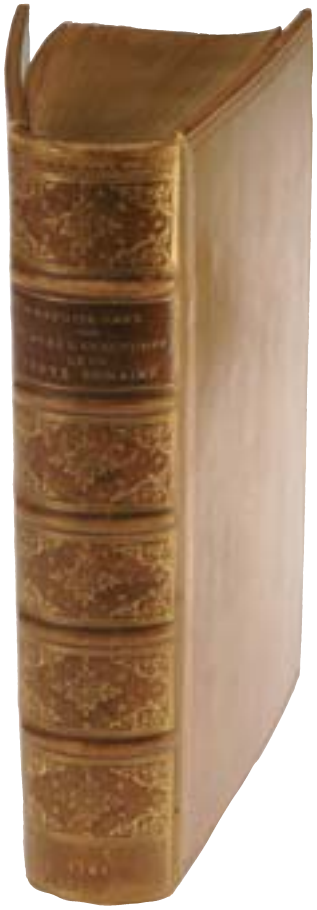
GC: Event takes place at the Wellcome Trust Genome Campus, Hinxton, Cambs.

For further information on Advanced Courses and Open Door Workshops see **www.wellcome.ac.uk/advancedcourses**.



Right:
Spores of *Aspergillus.*
D Gregory and D Marshall

A cut above



A beautifully illustrated book acquired by the Wellcome Library provides a hair-raising insight into 16th-century surgery.

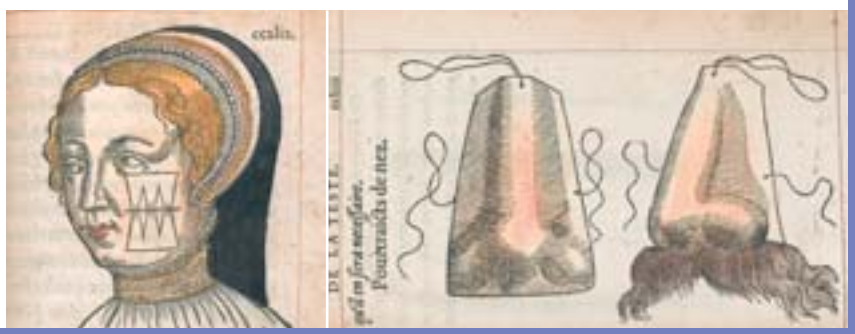
Ambroise Paré's *La méthode curative des playes et fractures de la teste humaine* was published in Paris by Jean le Royer in 1561.

Paré, an important figure in the development of surgery in the 16th century, was royal surgeon to four French kings. This work was begun after the death in 1559 of Henri II, who had been struck in the eye by the tip of a jousting lance. He survived, in great pain, for 11 days and was treated by Paré and Vesalius, who were sent from Brussels by the Emperor Charles V. The following year Paré treated François II for an abscess on the brain caused by an ear infection, but was again unsuccessful.

Illustrations show a technique for suturing wounds and a false nose, complete with fetching moustache.

Details of other major acquisitions appear in the *Wellcome Library Annual Review*, out in April 2006.

http://library.wellcome.ac.uk



The Wellcome Trust is an independent biomedical research-funding charity, established under the will of Sir Henry Wellcome in 1936. It is funded from a private endowment, which is managed with long-term stability and growth in mind.

The Wellcome Trust's mission is to foster and promote research with the aim of improving human and animal health. During 2005–2010, our aims are:

Advancing knowledge: To support research to increase understanding of health and disease, and its societal context

Using knowledge: To support the development and use of knowledge to create health benefit

Engaging society: To engage with society to foster an informed climate within which biomedical research can flourish

Developing people: To foster a research community and individual researchers who can contribute to the advancement and use of knowledge

Facilitating research: To promote the best conditions for research and the use of knowledge

Developing our organisation: To use our resources efficiently and effectively.

Wellcome News is published four times a year. Comments and suggestions are positively encouraged, and should be sent to:

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