

Annual Review 2001

The Wellcome Trust Annual Review 1 October 2000 – 30 September 2001

The Wellcome Trust

From the Director

One of the great strengths of the Wellcome Trust is its diversity. In any one day at the Trust, we can discuss issues as diverse as genome sequencing, clinical medicine, interactive science centres and an 18th-century Ottoman manuscript being acquired by the Wellcome Library. This breadth of interest gives us the chance to invest not only in stages in the scientific process – from 'blue skies' research through to the development of new therapeutics that can be taken forward to the market – but also in activities that explore the social and cultural implications of scientific research.

I use the word invest rather than funding, because I feel it reflects our activities more accurately. Through investment in infrastructure, we are putting in place the laboratories and equipment our scientists need. Through our personal support schemes, we are investing in researchers at all stages of their careers. And by investing in research itself, we are laying the foundations of knowledge that will underpin discoveries of the future.

Continued investment is essential to make use of discoveries and, in this day and age, such investment on a large scale is essential to drive research forward. In 2000/01, the Trust awarded grants worth nearly £400 million, backed a new five-year research programme at the Wellcome Trust Sanger Institute with £300 million, and launched a new £65 million programme in the Health Consequences of Population Change, to name just a few examples that you will find described in this year's *Annual Review*.

That such investment will bring improvements in healthcare I have no doubt. But to bring about such improvements the Trust must work in close partnership with other funding agencies and institutions.

Take, for example, the five new Wellcome Trust Clinical Research Facilities, the first of which opened in Edinburgh in June 2001. These new centres of patient-oriented research have come about through a close working relationship between the Trust, the Department of Health, the NHS and universities. In other areas, Trust research can best be taken forward by other funders. Take, for example, a new initiative to control malaria in Thailand. The Trust's South-East Asia unit has developed a new combination of drugs that can control malaria, and this new treatment is now being expanded to a large region with a US$4.7 million grant from the Bill and Melinda Gates Foundation.

A wider perspective

In his Nobel address in 1953, Dr Fritz Lipmann described scientists thus: "Their purpose often may be none but just to push back the limits of our comprehension. Their findings mostly have to be expressed in a scientific language that is understood only by a few. We feel nonetheless that the drive and urge to explore nature in all its facets is one of the most important functions of humanity."

Fifty years on from Fritz Lipmann's speech, scientists bring us ever more fascinating insights into the workings of nature. But more effort must be made to make such discoveries accessible and understandable. While major breakthroughs such as the human genome sequence received widespread media coverage and explanation, many other aspects of science remain couched in a jargonistic language peculiar to the scientific process. By opening up science to a wider audience – and publications such as our own *Wellcome News* and the interactive exhibitions at science centres across the country are just two of the ways in which the Trust works to do so – science can become part of society's consciousness.





For science should not be confined to ivory towers; it should be an essential part of the culture of the country, with everybody able to take an interest in new scientific and medical advances. Is such a dream achievable? I would argue that it has to be, and we have to strive to make it so. It is essential that people feel able to voice an opinion, debate the implications of new advances, and feel proud of the achievements of scientists who push back the limits of our comprehension.

Dr Mike Dexter
Director of the Wellcome Trust
May 2002

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Cover image '99 Genetic Maps of Love' by Liu Shih-Fen, an artwork created for the exhibition 'Working Drafts', held in the TwoTen Gallery.

Highlights of the year

KNOWLEDGE

Human genome papers
The scientific papers describing the human genome, one-third of which is being sequenced at the Wellcome Trust Sanger Institute, are published in *Nature* in February 2001.

New funding for the Sanger
The Wellcome Trust Sanger Institute announces a new five-year £300 million research programme.

Major award for diabetes research
The Wellcome Trust and the Juvenile Diabetes Research Foundation International award £20 million for the Diabetes and Inflammation Laboratory at the University of Cambridge.

New funding programme
A new £65 million, five-year Health Consequences of Population Change (HCPC) Programme is launched.

RESOURCES

Cell biology in Edinburgh
Full Centre status is awarded to the Wellcome Trust Centre for Cell Biology in Edinburgh.

Children of the 90s
ALSPAC, the Avon Longitudinal Study of Parents and Children, receives major grant from the Trust.

Darwin letters
The Darwin Correspondence Project at the University Library in Cambridge is awarded a further £700 000.

Radical thinking about careers
'Radical Thinking, Creative Solutions' conference looks at career issues in UK academic research.

TRANSLATION

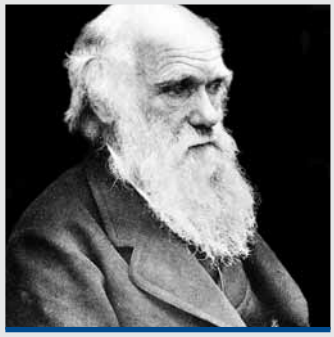
Clinical Research Facilities
Five new Wellcome Trust Clinical Research Facilities, sites for patient-oriented research, are completed.

Tak malaria initiative
Thai–UK collaboration receives US$4.7 million from the Gates Foundation to expand promising malaria treatment developed by Trust researchers in Thailand.

Catalyst
New business plan focuses on activities of strategic importance to Catalyst and the Trust.







Valuable lessons
Report finds little classroom discussion about the social and ethical impact of scientific developments.

Science centres
Centres in Birmingham and Glasgow open their doors.

UK's longest artwork
Jason Middlebrook's 'The Geology of Biology' unveiled.

The truest portrait
Marc Quinn produces a genetic portrait of Sir John Sulston for the National Portrait Gallery.

Science Centrestage
Schools drama initiative launched in September 2001.



Funding
The Wellcome Trust awards £388 million of grants, including £375 million for the support of biomedical science. The Trust's total expenditure for the year is £544 million.

Sir John Sulston
Knighthood for the former Director of the Wellcome Trust Sanger Institute.

New Governors
Professor Adrian Bird, Professor Jean Thomas, Professor Mark Walport, Edward Walker-Arnott and Alastair Ross Goobey become Governors of the Trust.

Planning for the future
New Constitution and Corporate Plan for the Trust.

Far left The Wellcome Trust Clinical Research Facility in Edinburgh, which opened in July 2001.

Middle Jason Middlebrook, creating 'The Geology of Biology'.

Left The Darwin Correspondence Project was awarded a further £700 000 by the Trust.

Left The new HCPC Programme is looking at the drivers of population change in the developing world.

The Wellcome Trust 2000–05

The Wellcome Trust's first Corporate Plan was published in October 2000. *Planning for the Future* sets out a philosophical and practical framework of mission, aims and values that will underpin all of the activities of the Trust for the next five years. Here, we present a brief overview of this framework and describe on the following pages how the Trust's activities in the past year are working towards the key aims and objectives of the Trust.

Mission

The Wellcome Trust's mission is to foster and promote research with the aim of improving human and animal health.

Aims

The four aims identify the priorities on which the Trust concentrates. Each aim is underpinned by a series of objectives which establish the practical measures being taken to achieve the aims and, ultimately, the mission of the Trust.

Knowledge

Supporting basic, applied and strategically important research in biomedical sciences.

Researching the societal impact of biomedical science – past, present and future.

Resources

Human resources: meeting training and career development needs of researchers.

Physical resources: building suitable conditions for research.

Translation

Promoting patient-oriented research and health services research.

Advancing the dissemination and exploitation of the results of Trust-funded research.

Values

In all that it does to achieve its mission, the Wellcome Trust is guided by a set of values, shared by the staff and Governors.

Independence

To retain our independence of decision making.

Leadership

To create and seize opportunities and help shape the agenda.

Evidence

To base funding priorities and policy making on the best available evidence.

Flexibility

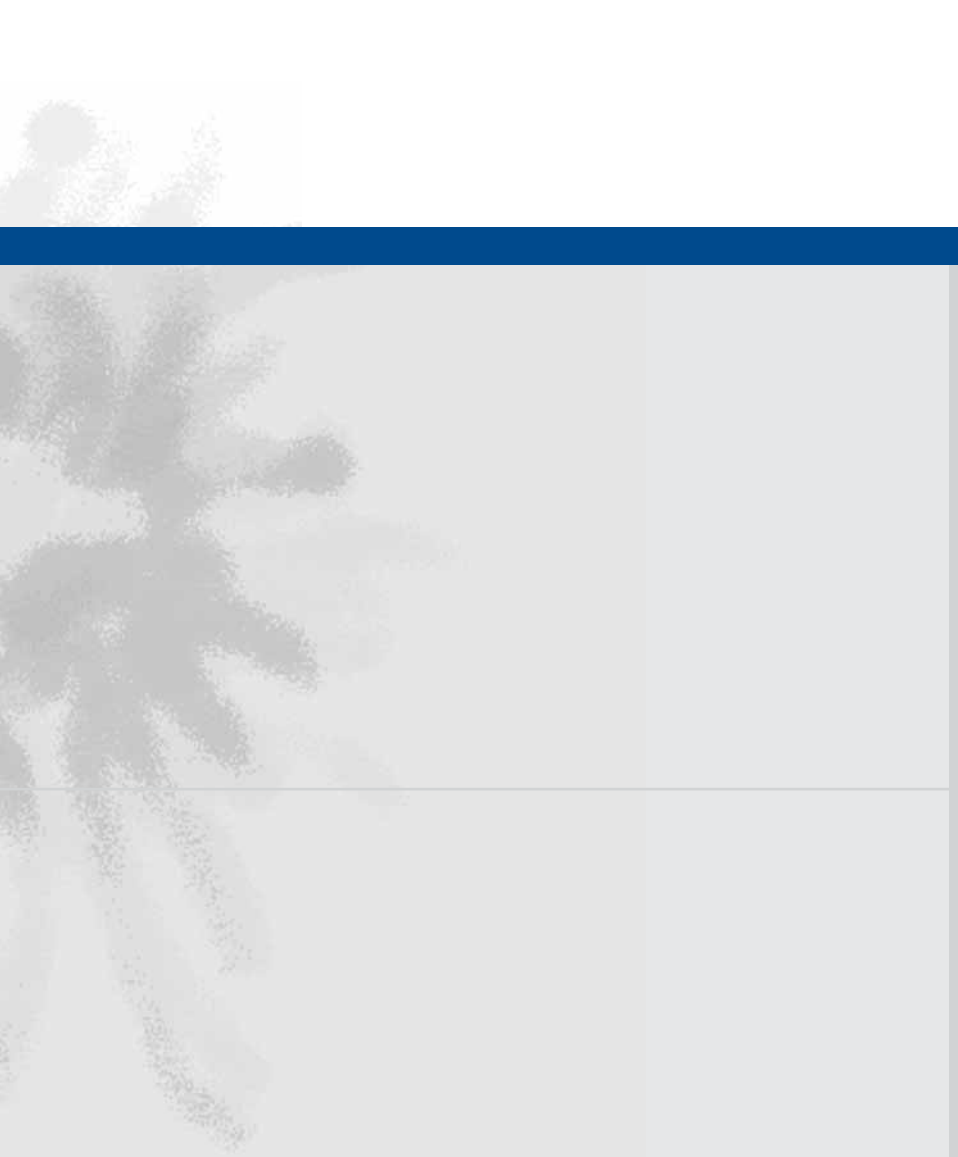
To support innovation and manage risk so that we can move rapidly into new and emerging areas in imaginative ways.

Excellence

To achieve excellence within our own work and in the work of those we support.

Integrity

To act responsibly and with integrity in our work and interactions with others.



Public engagement

Stimulating an informed dialogue to raise awareness and understanding of biomedical science, its achievements, applications and implications.

Responsiveness

To maintain close relationships with our communities and, through this, continue to respond flexibly to their needs.

Openness

To be open and transparent in our work.

Partnership

To work with others where this achieves the greatest benefits to achieve our mission.

Empowerment

To empower and develop our staff to enable them to fulfil their potential and the Trust to fulfil its mission.

Wellcome Trust organization

The structure of the Trust reflects the type of support provided to researchers. The activities of major funding divisions of the Trust over the last year are detailed on pages 48–59 of this *Annual Review*. This structure is currently being reviewed to ensure that the Trust's organization reflects and supports the Corporate Plan.

Science Funding
UK Panels
Career Schemes and Clinical Initiatives
Centres and Initiatives
International Programmes
Grants Administration

Medicine, Society and History
Medicine in Society
(Biomedical Ethics and Public Engagement with Science Programmes)
Consultation and Education
Exhibitions
History of Medicine Programme
Wellcome Library for the History and Understanding of Medicine
Tropical Medicine Resource

Research Partnerships and Ventures
Wellcome Trust Genome Campus
SNP Consortium
Synchrotron
Advanced Courses Programme

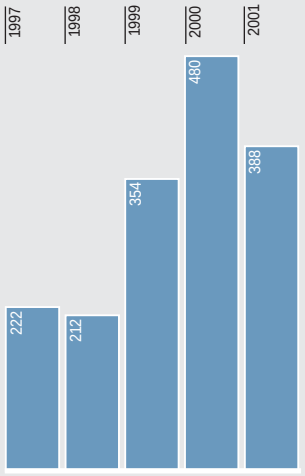
Catalyst BioMedica Ltd

Directorate
Director's Office
Communications
Legal
Policy Unit

Other divisions
Investments
Finance and Information Management
Personnel and Services

Financial summary

Figure 1
Grants awarded (£m)



Review of activities

The Trust awarded £388 million of grants in 2000/01: £375 million for the support of biomedical science and £13 million for the Medicine, Society and History programmes. Total funding was £443 million; this includes £55 million to subsidiaries such as Genome Research Limited (which is awarded the grants for the Wellcome Trust Sanger Institute) and Hinxton Hall Limited. Figure 1 shows this year's grants expenditure compared to previous years (the marked increase in 1999/2000 was due to the significant funding through the Joint Infrastructure Fund in that year) and Figure 2 shows the breakdown of funding.

The Trust received 3893 grant applications in 2000/01, and 2090 awards were made; Figure 3 shows the award rates. The level of outstanding commitments has increased to more than £1 billion, as shown in Figure 4. The graph shows that there is significant time lag between a grant award and the subsequent claims for funds by the institutions.

Expenditure on the direct activities of the Trust (which include the Wellcome Trust Genome Campus and the Wellcome Library) in 2000/01 was approximately £70 million, although expenditure at the Wellcome Trust Sanger Institute in the first half of the year was lower than anticipated as sequencing was interrupted for a month. During the year, the Governors agreed to provide £300 million of funding to the Wellcome Trust Sanger Institute over the next five years.

The total amount of resources expended during the year by the Trust was £544 million. The Trust's charitable and other expenditure is analysed in Figure 5 as a percentage of total resources expended.

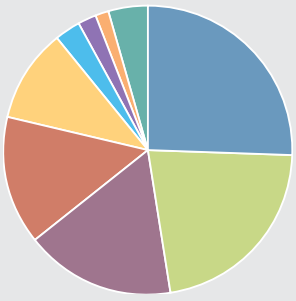
The Trust's investment portfolio

During the past 12 months, the business and financial environment has proved to be extremely challenging for the Trust's investment portfolio. The threat of world recession, and the terrible human tragedy surrounding the terrorist attacks in the USA have all served to heighten global business and economic uncertainty.

Nevertheless, the diversity of the Trust's asset base has served to mitigate the worst of the falls in markets, so that neither the day-to-day operation nor the long-term mission of the Trust has been adversely affected.

The value of the Trust's portfolio fell from £15 billion in September 2000 to just over £12 billion by September 2001. While it is disappointing to record this reduction, the performance of the Trust's portfolio continues to compare favourably against its own special benchmark and other investment peer groups. Despite this decline in market value, the investment portfolio has still supported increased payments of grants committed this year, as shown in Figure 4. The Trust's investment asset values for the past five years are shown in Figure 6, while Figure 7 shows the portfolio by investment classification.

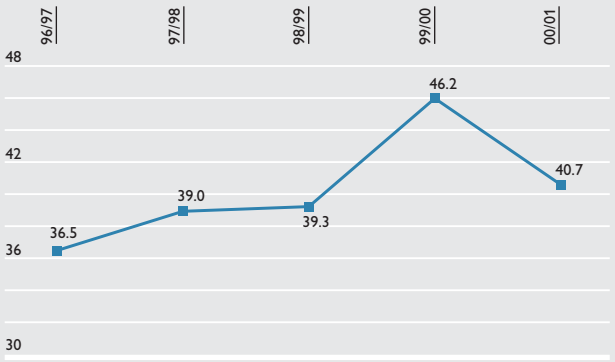
Figure 2
Breakdown of grants awarded 2000/01*



	£million
JIF and SRIF	113.2
UK Funding†	97.2
Genetics	74.5
Careers§	63.7
International	46.3
Medicine, Society and History	12.8
Buildings and equipment (other than JIF)	9.1
Other schemes	6.6
Salary supplements minus grants no longer required	19.6
Total: £443 million	

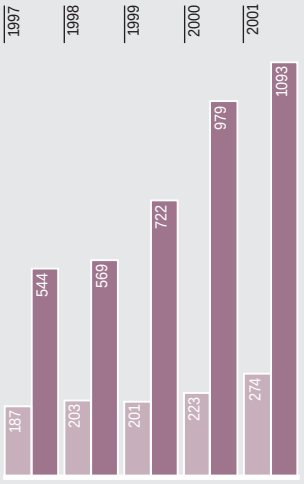
* Amounts include grants to subsidiaries
† UK Panels and Centres associated with Panels
§ Includes cardiovascular

Figure 3
Award rates for new grants*



* excluding Medicine, Society and History grants

Figure 4
Grants paid and outstanding (£m)



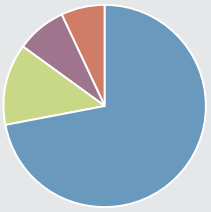
Grants paid
Outstanding grant commitments

Grants awarded, paid and outstanding

*Grants awarded in the year (**Figure 1**) represent the total funds committed to successful applications during the Trust's financial year. Most awards are made to researchers' host institutions, which then claim monies from the Trust. The light purple in **Figure 4** (grants paid) represents the amounts claimed by host institutions during the year for expenses incurred, while the dark purple (outstanding grants commitments) represents the total sums committed by the Trust to projects which had not been claimed by the end of the financial year. The gap between committed funds and cash paid is due to the long-term nature of many grants, and to the time lag between a grant award and the subsequent claim for funds from an institution. Claims from JIF grants, for example, will be received over several years.*

Additional financial information can be found in the Wellcome Trust's Annual Report 2001, available from the Trust's Marketing Department (address on inside back cover).

Figure 5
Resources expended %



Grants awarded	72
Direct activities	13
Support and administration costs	8
Investment costs	7

Total: £544 million

Figure 6
Investment assets (£b)

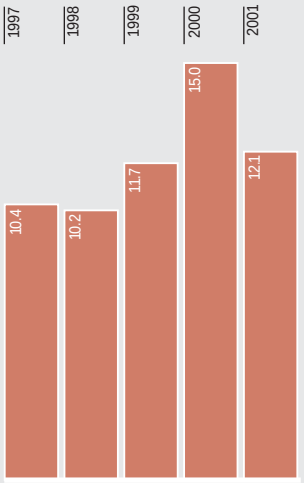
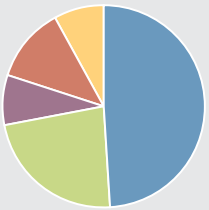


Figure 7
Investment assets %



UK equities	49
Overseas equities	23
Fixed interest securities	8
Unquoted investments	12
Investment property	8

Total: £12.1 billion (end September 2001)

The human genome unveiled

On 15 February 2001, the scientific papers describing the human genome were published in a special issue of the journal *Nature*. The Human Genome Project's landmark sequencing paper was published alongside a detailed human genome map and a number of other papers analysing or commenting on the sequencing data. Funded by the Wellcome Trust, scientists at the Wellcome Trust Sanger Institute contributed one-third of the total human sequence data.

The ten-year Human Genome Project is an international collaboration, involving 20 research groups from six countries. All genome sequence produced by the project is released immediately, with free and unrestricted access to researchers from academia and industry.

The scientific papers report the analysis of the 'draft sequence' of the human genome, a milestone reached and announced – to well-deserved fanfare – by the collaborators in June 2000. The draft sequence covers 90 per cent of the 3.2 gigabase human genome, at 99.9 per cent accuracy; the 'gold standard' final sequence, full coverage at 99.99 per cent accuracy, is scheduled for completion in 2003.

The human genome sequence threw up a number of surprising findings, including the relatively small number of genes it appears to contain – somewhere between 30 000 and 40 000. This compares with 6000 for a yeast cell, 13 000 for a fly, 18 000 for a worm and 26 000 for a plant. So it appears that humans do not gain their undoubted complexity over worms and plants by using many more genes; instead, humans appear to have sophisticated controls over how their genes are used.

The special issue of *Nature* also included a map of 1.42 million single nucleotide polymorphisms (SNPs or 'snips'). Individual humans differ from one another by about one base pair per thousand, and differences between human genomes underlie differences in susceptibility to, or protection from, a host of diseases. They can also provide information about our personal responses to medicines. In this way, the pharmaceutical industry will acquire new targets and tools to sharpen drug specificity. The SNP map was produced by the International SNP Map Working Group, a joint effort between the SNP Consortium, part-funded by the Trust, and the Human Genome Project.





New era for the Sanger Institute

The Wellcome Trust Sanger Institute announced its new five-year £300 million research programme in October 2001. The Sanger Institute, which is sequencing one-third of the human genome, enters a new era under the leadership of Director, Dr Allan Bradley.

The new postgenomic period builds on the Sanger Institute's ground-breaking work in sequencing the human genome. Teams of scientists at the Sanger Institute will now determine how genes build and control the human body. They will also study the roles that human and pathogen genomes play in health and disease.

Complementing and building on the Sanger Institute's considerable strengths in genome data generation, automation and bioinformatics, a raft of new initiatives will, as Dr Bradley describes it, 'bring biology to the genome'.

Wellcome News Supplement

Unveiling the Human Genome: The first draft 2001, *a commemorative* Wellcome News Supplement.
www.wellcome.ac.uk/genome

Top Dr Simon Gregory, who is leading the Sanger Institute's sequencing of human chromosome 1.

Above Staff at the Wellcome Trust Sanger Institute take a break from sequencing the human genome.

Comparing the genomes of pathogens

The Pathogen Sequencing Unit at the Wellcome Trust Sanger Institute has sequenced the genomes of some of the world's biggest killers, bringing insights into what makes microbes adaptable, infectious and dangerous.

While the Pathogen Sequencing Unit continues to sequence new species of pathogens, attention has also turned to different strains of the same species. Such comparative sequencing can help identify genes, and provide valuable information about genome organization and evolution, and why some strains are harmless and others deadly.

The genomes of two strains of the same species of bacteria can vary by 10–15 per cent, and appear to be exchanging DNA continually, so by sequencing several strains the 'gene pool' of a species can be identified. The Wellcome Trust has therefore funded the Pathogen Sequencing Unit to perform comparative sequencing of *Escherichia coli* and *Shigella*, which cause gastrointestinal disease and are the leading causes of death in children in developing countries, and of salmonellas, which also cause food poisoning.

Joining these studies of bacteria is a new initiative to compare the genomes of six *Plasmodium* species to that of *Plasmodium falciparum* – almost completed by the Pathogen Sequencing Unit – which causes the severest form of malaria disease and many deaths, particularly in Africa and the Far East.

The comparative sequencing project will help the team identify where the genes are in the *P. falciparum* genome. While it is relatively easy to find genes in a bacterial genome, malaria genes have introns and exons, and it is often less clear which sequences are genes and which are not. But the genes and exons are conserved between species, so comparative genomics can be used to line the sequences up and find the coding sequences.



Above Dr Bart Barrell, Head of the Pathogen Sequencing Unit, compares two pathogen genomes.

Microbe genomes completed by the Pathogen Sequencing Unit or published in 2001

Mycobacterium leprae, *the causative agent of leprosy and a close relative of the agent of TB,* M. tuberculosis *[published in* Nature*].*

Yersinia pestis, *the bacterium which causes plague [published in* Nature*].*

Salmonella typhi, *the bacterium responsible for typhoid fever [published in* Nature*].*

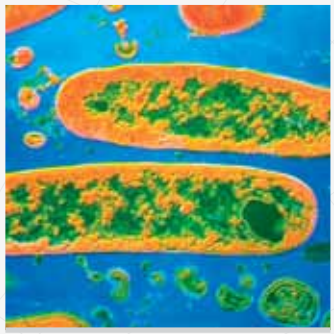
Bordetella pertussis, *the causative agent of whooping cough.*

Corynebacterium diphtheriae, *the causative agent of diphtheria.*

Staphylococcus aureus *(EMRSA-16), a recent clinical isolate of epidemic methicillin-resistant* S. aureus*, prevalent in hospitals.*

Streptomyces coelicolor, *a soil-dwelling organism which is used to produce pharmaceutically useful compounds including antitumour agents, immunosuppressants and more than two-thirds of all natural antibiotics currently available.*

Plague in Kazakhstan





Top *Yersinia pestis*, causative agent of plague.

Above The great gerbil, the main rodent host of plague in Kazakhstan.

Plague genome
The genome of Yersinia pestis, *the bacterium that causes plague, has been sequenced at the Wellcome Trust Sanger Institute.*

Collaborative grants
Collaborative Research Initiative Grants are aimed at established research workers based in developing countries or the restructuring countries of Central and Eastern Europe and the newly independent states of the former Soviet Union. The scheme enables them to undertake a research programme in their home laboratory, in conjunction with a collaborating institution in the UK.

Plague has had a huge impact on human history. In the 14th century, the 'Black Death' is believed to have killed 200 million people, wiping out one-third of the European population. Even today, up to 3000 cases are reported annually to the World Health Organization.

Caused by the bacterium *Yersinia pestis*, plague is a zoonosis, circulating naturally in populations of wild rodents, and transmitted between rodents and onto humans by fleas. Outbreaks of plague still occur in North America, Africa and South-East Asia, but some of the most active 'hot spots' of plague activity are found in Kazakhstan and other areas of Central Asia.

Financial difficulties in these latter areas have led to a decline in the surveillance of plague, making forecasts of infection cycles almost impossible, a problem now being addressed by a collaborative research project between Kazakh and UK scientists: Vladimir Ageyev, Senior Research Scientist at the Kazakh Anti-Plague Research Institute in Almaty, and Professor Michael Begon at the University of Liverpool.

The main rodent host of plague in Kazakhstan is the great gerbil. The study looks at the gerbil population in two areas, each 10 x 10 km, which contain 20–30 000 gerbil burrow systems (each burrow system is likely to contain three to ten gerbils and 300–1000 fleas). The Kazakh team has the expertise in trapping gerbils and testing them and their fleas for plague, while the UK team brings expertise in the analysis of data from the gerbil and flea populations. The joint project will therefore not only improve understanding of the dynamics of plague, and help devise systems to control plague in Central Asia, but will also transfer UK experience and expertise to the Kazakh scientists.



Talking ethics

The increasing sophistication of prenatal testing is enabling doctors to detect and diagnose many problems or abnormalities in a fetus. Yet many of these conditions are untreatable, while others can have very variable effects on individuals. This raises ethical dilemmas not only for the parents of an affected fetus, but also for the healthcare professionals with whom they interact.

To investigate how new genetic knowledge is affecting policy and practice in prenatal healthcare, Professor Priscilla Alderson and Dr Clare Williams of the Institute of Education, University of London, and Dr Bobbie Farsides at King's College, University of London, were awarded a Wellcome Trust Biomedical Ethics project grant in 1999 for a two-year project, 'Cross currents in genetics'.

The project brought together about 70 people in a series of discussion groups at a major teaching hospital and at a district general hospital. The groups involved professionals from all levels of seniority and from a range of disciplines and interests, including paediatricians, genetic counsellors, fetal medicine doctors, clergy, obstetricians, psychologists and midwives.

Often the first opportunity these professionals had had to discuss the ethical and legal issues raised by advances in genetic knowledge, the groups proved very popular. The discussions ranged over issues which included the difficulties of achieving nondirective counselling, informed choice and equity of provision in prenatal services; what the effects of increased screening and testing might be on pregnancy; and whether the status of the fetus is changing, and what the possible effects of that might be. They also highlighted the problem that the pressures of day-to-day work can impede practitioners' ability to anticipate problems that might arise in the future, whether in prenatal diagnosis and treatment, or in haematology, neonatal services or community paediatrics.

As well as helping to inform healthcare policy, the study suggests ways for hospitals to set up similar discussion groups in order to promote debate and to encourage practitioners to look ahead to the social and ethical issues of the future.





Above, left Guided by ultrasound, a sample of amniotic fluid is being removed for prenatal testing.

Above Professor John Todd's team are using highly automated systems in their search for the genes that underlie type 1 diabetes.

Further reading

Williams C, Alderson P, Farsides B (2002) Is nondirectiveness possible within the context of antenatal screening and testing? Social Science and Medicine *54: 17–25.*

Williams C, Alderson P, Farsides B (2002) 'Drawing the line' in prenatal screening and testing: health practitioners' discussions. Health, Risk and Society *4: 61–75.*

www.ioe.ac.uk/ssru/

Biomedical ethics

The Wellcome Trust's Biomedical Ethics Programme supports social, ethical, legal and public policy research with a focus on neuroscience, mental health and genetics. With the expansion of the Programme announced in 2001 (see page 56), international research ethics will be developed as a subject area and the Programme will develop ways of making the funded research more useful to policy makers and other users.

www.wellcome.ac.uk/biomedicalethics

Diabetes genes

In November 2000, the Wellcome Trust and the Juvenile Diabetes Research Foundation International awarded £20 million, over five years, to set up a new Diabetes and Inflammation Laboratory at the University of Cambridge. The new laboratory is led by Professor John Todd, one of the world's leading researchers on the genetic causes of type 1 diabetes (also known as 'juvenile' or 'insulin-dependent' diabetes).

The Diabetes and Inflammation Laboratory will bring a multidisciplinary approach to the genetics of type 1 diabetes, aiming to identify the genes that predispose to the disease and to study their function in mouse models. The group also aims to discover the genetic factors underlying susceptibility to the long-term complications of diabetes, such as kidney disease and heart disease.

One of the laboratory's most important projects will be a huge statistical analysis to identify genes involved in diabetes. Researchers will recruit some 10 000 patients who have diabetes (and similar numbers of healthy people) to collect DNA samples. This sample set will be used to identify the key chromosomal regions that house diabetes-related genes, to pinpoint these critical genes, to study how the genes contribute to or protect from diabetes, and to develop better forms of prevention and treatment. The second part of this project will involve study of patients over time in an attempt to identify genes involved in diabetes-associated kidney disease.

The data of life and death

In many parts of the developing world, there are no data on vital events in the community: when people are born, when they join or leave the community, when they die and what the causes of death are. Gathering such data – the data of life and death – is both expensive and time consuming, but is essential for the planning of national healthcare delivery.

Over the last year, the Wellcome Trust has funded three demographic surveillance projects – two in South Africa and one in Thailand. Each project is, in effect, a census, following tens of thousands of people at a household level. But by visiting every three months or every year, researchers can build up a picture of the structure and dynamics of the community and the population. Key data can be obtained on the impacts of disease and what people die of – as many people in these communities do not die in hospital – and on the impacts of migration as people join and leave communities.

In South Africa, communities in KwaZulu-Natal and in Agincourt are being surveyed by the Africa Centre for Health and Population Studies and by the University of Witwatersrand, respectively. In KwaZulu-Natal, the demographic mapping will cover a population of more than 80 000 living in 11 500 homesteads over 200 square miles in the Hlablisa District. This rural area of South Africa has been badly affected by HIV/AIDS and contains a highly mobile population. The information gathered will underpin a number of the Africa Centre's population-based studies. In Agincourt, approximately 60 000 people are being surveyed annually or biennially, building a dataset on the changing pattern of rural mortality, noncommunicable diseases and nutrition in a rural population.

Meanwhile, in Thailand, the Institute for Population and Social Research at Mahidol University is looking at the composition of communities on the Thai–Myanmar border and the effects of population migration and urbanization as Bangkok expands.

Health Consequences of Population Change

The Wellcome Trust has launched a £65 million, five-year Health Consequences of Population Change (HCPC) Programme, subsuming its Population Studies Programme and the Noncommunicable Diseases Initiative. The new Programme focuses on five key drivers of population change – growth, ageing, urbanization, migration and lifestyle changes – which impact on the size and composition of populations, producing new patterns of disease and ill health. The Programme aims to provide an evidence base to help governments, aid agencies and global health organizations plan for the best use of scarce healthcare resources.

Further details

www.wellcome.ac.uk/hcpc

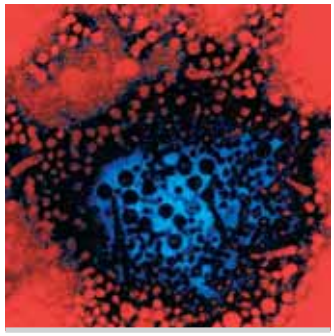
Wellcome News *28, Q3 2001*
All change for global health: The Health Consequences of Population Change Programme
www.wellcome.ac.uk/wellcomenews28

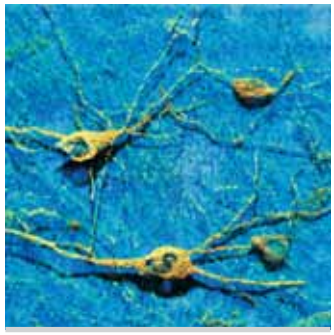
Mother-to-child transmission of HIV

Researchers at the Africa Centre for Health and Population Studies in KwaZulu-Natal, South Africa – which is supported through the Trust's HCPC Programme – were awarded £4 million for a three-year study aimed at reducing mother-to-child transmission of HIV. Studies elsewhere have shown that short-course antiretroviral drugs given to a mother in the last weeks of pregnancy and at the time of delivery can reduce transmission by up to 50 per cent, when combined with formula-feeding for the baby. This study will test whether exclusive breast-feeding in combination with the drug therapy will be as effective. If so, the reduction in transmission from mother to child can be achieved without the need to formula-feed the baby – which is itself often culturally unacceptable, and risky in areas where water is inaccessible and of poor quality. The study is led by Professor Jerry Coovadia, a paediatrician at the University of Natal and one of the world's leading AIDS experts, and Professor Michael Bennish, Director of the Africa Centre.



Beyond blood





Top Cells from the bone marrow could treat livers damaged by viruses such as hepatitis B, shown here.

Above Can cells from the bone marrow become neurons such as these? Dr Stefan Przyborski is investigating this controversial question.

Within the bone marrow are blood cell factories, constantly churning out the nine different types of blood cell. These factories – the blood stem cells – are the subject of intense research worldwide, not only because of their known clinical importance to major blood diseases such as thalassaemia and sickle cell anaemia, but also because they could possibly one day be used to repair body tissues damaged by age, trauma and disease. Two studies funded by the Wellcome Trust during the year aim to discover whether blood stem cells can produce very different cell types – liver cells and nerve cells – that make up the body, and which could therefore provide replacements for damaged tissues.

At Imperial College School of Medicine, London, Dr Malcolm Alison is investigating cell therapy for the treatment of liver diseases. The liver can be damaged by viruses, such as hepatitis B, drugs or toxins. He has shown that bone marrow contains cells that can produce liver cells, and is now going on to investigate how to graft the cells into the liver and help them differentiate into hepatocytes – strategies that could help support or repair a failing or damaged liver.

At the University of Durham, Dr Stefan Przyborski is investigating a controversial yet exciting possibility – that cells in the bone marrow might be able to differentiate into nerve cells. He aims to identify the growth conditions that could induce neural development, and then test whether these cells have the functional and electrophysiological characteristics of neurons. If successful, his study could help lead to the development of treatments for brain disorders such as Alzheimer's disease.

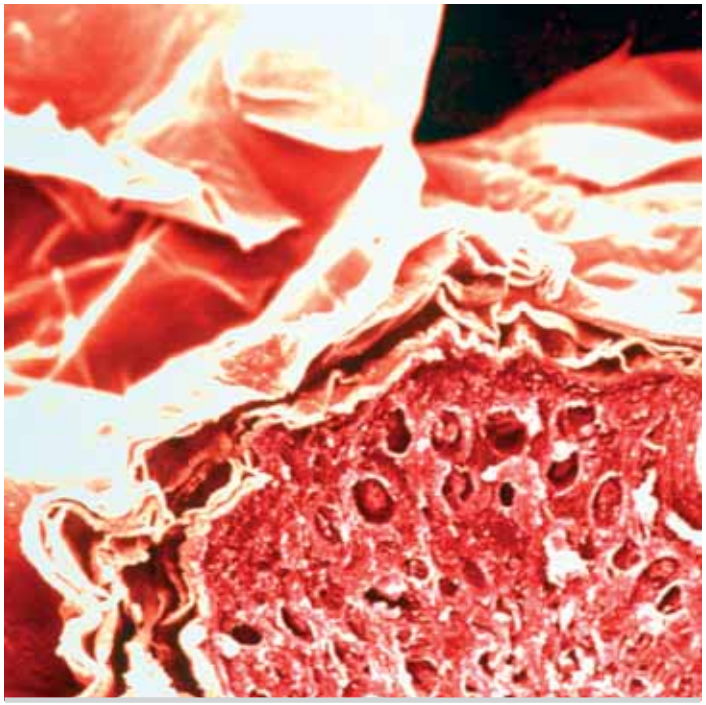


Responsive funding

The UK funding schemes are the primary route by which the Trust supports the UK biomedical research base, through its response-mode project and programme grant schemes and other awards. Applications are handled in topic areas and are considered by one of the Trust's four UK funding Panels – Infection and Immunity, Molecular and Cell, Neurosciences, and Physiology and Pharmacology.

See page 48.

On the surface



Further reading
Girardi M et al. *(2001) Regulation of cutaneous malignancy by γδ T cells.* Science *294: 605–609.*



Top A section through the surface of the skin.

Above UV radiation is used increasingly as a therapy for psoriasis, eczema (shown here) and vitiligo.

The largest organ in the body, skin is our most important barrier against infection and damage. Two Wellcome Trust projects are examining how skin keeps us safe.

An individual's risk from ultraviolet radiation (UVR) is largely determined by his or her genetically determined 'skin type' – whether they burn or tan in response to repeated exposure to UVR. With a Wellcome Trust project grant, Professor Jonathan Rees and colleagues at the University of Edinburgh are investigating the relationship between the melanocortin 1 receptor gene – often called the 'red hair gene' – and the pigment in skin and hair. They also aim to understand the tanning process – the increase in pigment that occurs with repeated exposure to UVR.

Understanding human pigmentation and the skin's response to UVR is of major clinical and biological interest. Ultraviolet radiation is used increasingly as a therapy for common skin diseases such as psoriasis, eczema and vitiligo, and Professor Rees's study will help improve this treatment. Yet dosing and treatment regimes remain empirical with little biological understanding of the large variation in sensitivity to UVR between people.

Although skin is remarkably resilient, constant exposure to chemicals and UVR from the outside world can lead to the development of cancers. That tumours are kept at bay most of the time is testament to skin-dwelling T cells, whose role as sentinels was uncovered by Professor Adrian Hayday and colleagues at Guy's, King's and St Thomas' Medical School, London.

The γδ T cells in the skin, close relatives of the αβ T cells that circulate in the blood and lymph ready to respond to infections, make a protein called NKG2d, which can focus in on a target called Rae-1. This protein is produced on the surface of skin cells that have begun the transformation into cancer cells but is not produced by normal skin. Once the T cells' NKG2d protein has engaged with Rae-1, the γδ T cell can kill the tumour cell.

Music and medicine



Throughout the ages, music has played an important role, as both an art and a science, in shaping and understanding human experience. Professor Penny Gouk at the Wellcome Unit for the History of Medicine at the University of Manchester is researching the impact of music between the 16th and 18th centuries on medical explanations of its effects on the human body and mind.

Classical scholars recognized the capacity of music to heal or harm through its control of the passions. They believed the passions of the mind were seated in the middle soul – between the appetites and reason – and bound together body and mind. Disharmony of the passions led to disease, while harmonization restored the patient to health.

In medieval times music continued to play a central role in medicine: musical literacy was essential to courtly life (Henry VIII composed his own pieces, for example) and was therefore an important requirement of physicians who depended on royal patrons. It was also a mark of scholarship. The study of music was a compulsory part of the university arts degree that was required before taking the higher medical degree.

In the 17th and 18th centuries, the scientific and mathematical qualities of music aided physicians' understanding of the mechanics of human biology. Doctors used musical notation to express the pulse and their knowledge of musical instruments to understand how human bodily systems worked. During the Enlightenment, music technologies helped scholars determine the universal laws supposedly governing physical and human nature.

During the five-year term of her University Award, Professor Gouk will explore the musical literacy of doctors in different European countries in 1500, 1600 and 1700. She will then compare the impact their musical knowledge had on their social position, their explanations of the effect of music on human nature, and their understanding of the workings of the human body and psyche.



History of Medicine Programme

To improve the understanding of the historical and cultural context of medicine, the Wellcome Trust runs a number of grant schemes that encourage academic study and a career in the history of medicine. Grants are awarded for research in the UK, the Republic of Ireland or The Netherlands, normally within an academic department of a university or at one of the Wellcome Units for the History of Medicine.

The Trust has a broad definition of the history of medicine, encompassing the historical study of all factors affecting the medical and health experience of people and animals in all countries at all periods.

See page 58.

Wellcome History

A free newsletter for all historians of medicine, Wellcome History *is published three times a year and features news of work in progress, research problems, conferences, letters and book reviews.*

www.wellcome.ac.uk/wellcomehistory

Top David playing the harp before Saul. An engraving by Lucas van Leyden (1494–1538).

Above A woodcut of a concert, published in Strasbourg, 1508.

Gene talking

First gene involved in speech and language identified

A research team from the Wellcome Trust Centre for Human Genetics in Oxford has identified the first gene whose function is thought to be involved in the development of speech and language in humans.

The research team, led by Professor Anthony Monaco (right), a Trust Principal Research Fellow, and colleagues at the Institute of Child Health in London, led by Professor Vargha-Khadem, found the gene by studying three generations of a family affected by a rare language impairment. Individuals suffering from the condition have difficulty understanding grammar and articulating speech.

Although scientists have suspected that there must be a genetic basis to speech and language because it is universal, complex and acquired almost instinctively by children at a young age, this is the first evidence of a particular gene that has been pinpointed as having a mutation leading to a language disorder.

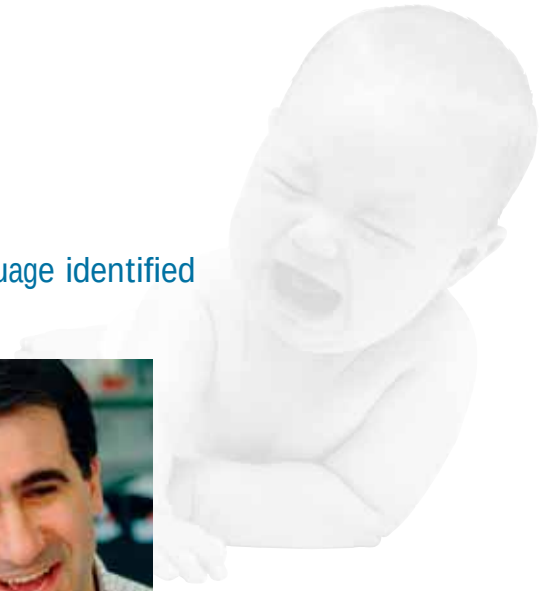
The mutation was found in a gene called *SPCH1* (also called *FOXP2*), which the researchers suspect is a transcription factor – whose role is to modulate the activity of other genes. Hence it is likely that *SPCH1* cooperates with other genes and proteins during the development of children's speech and language.

Speech and language disorders, which occur in autism and less well-known specific language impairment, are present in 4 per cent of the population. Professor Monaco is currently investigating whether *SPCH1* is altered in these other conditions.



Further reading

Lai C S L, Fisher S E, Hurst J A, Vargha-Khadem F, Monaco A P (2001) A forkhead-domain gene is mutated in a severe speech and language disorder. Nature *413: 519–23.*



Below The Wellcome Trust Centre for Human Genetics in Oxford.

Gene hunting

At the Wellcome Trust Centre for Human Genetics, Oxford, Dr Jonathan Flint, a Wellcome Trust Senior Research Fellow in Clinical Science, is investigating the genetic basis of psychiatric disorders using both mice and humans. Finding the genes influencing mouse behaviour is extremely difficult, as the genes that contribute to variation in a behavioural trait are likely to have only small individual effects.

The second area of work is to find genes that influence susceptibility to depression in people. Finding the susceptibility genes for psychiatric disorders is a demanding task because the intensive interviewing necessary for reliable diagnosis has made it very difficult to collect the large number of samples needed to detect relatively small genetic effects. Dr Flint and colleagues are using an alternative strategy: to map neuroticism – a personality trait that is a major genetic mediator of depression.

In 2001, Dr Flint, Professor William Cookson and Dr Richard Mott (also at the Wellcome Trust Centre for Human Genetics), and Professor Nick Rawlins (University of Oxford), were awarded a £2 million programme grant. The team will work together to look for genes that influence variation in anxiety, asthma, cognition, diabetes and obesity in mice.



Unpicking the immune system

A new collaboration between immunologists in Oxford and Australia was awarded a Wellcome Trust programme grant of £1.4 million to analyse the immune system of the laboratory mouse, using a systematic genetic approach.

The mouse genome closely resembles that of humans and is the subject of the Mouse Genome Sequencing Project (currently underway at the Wellcome Trust Sanger Institute and at two sequencing centres in the USA). At Canberra, Professor Chris Goodnow is screening mice to find ones that have defects in their immune systems. A group of immunologists and geneticists – led by Professor Goodnow and by Professor John Bell and Dr Richard Cornall at the University of Oxford – will then find the mutated genes and determine their effects on immunity.

Radical thinking about careers

The problems faced by the UK's academic research community have been well documented, and include insufficient rewards, lack of career structure and poor people management. The Wellcome Trust attaches considerable importance to the careers of the individuals it supports and has taken a number of steps to combat these problems by providing salaries which are above the normal university academic scales, and through membership of a number of forums that address key national issues relating to the challenges of an academic research career.

To help guide future policies and practices of funding bodies and higher education institutions, the Trust hosted a one-off conference in July 2001 to encourage people to discuss and develop innovative ways of changing the difficulties faced by UK academic researchers. 'Radical Thinking, Creative Solutions: Career issues in UK academic research', held at the Hinxton Hall Conference Centre, brought together a diverse group of individuals with an interest in academic careers, from young researchers to vice-chancellors, from journalists to senior administrators.

Following a series of discussions, workshops and personal accounts, delegates put together a number of 'calls to action' which, if implemented, could help tackle the problems encountered by researchers throughout their academic career:

- To develop and pilot a research institute-based model for university research, to allow greater flexibility and autonomy.
- Small research laboratories to be grouped within each university within a federal structure and be provided with core infrastructure support to provide long-term continuity.
- Research principal investigators in universities to be persuaded of their direct responsibility for management of research staff, and of the need for change and improved practices.
- A working party to be set up to address the problem faced by senior fellows at the end of their research tenure, for whom university-funded positions are unavailable or unattractive.
- University teaching to be returned to its previous position as a high-status, valued activity and rewarded in terms comparable to full-time, independently funded university researchers.
- A four-year PhD to be introduced as standard, with 'respectable exit points'.
- Postdoctoral research training and experience to be deemed a valued qualification for science teaching in schools, and an appropriate entry pathway to school teaching to be created.





Top and above
The 'Radical Thinking, Creative Solutions' conference brought together academics from all levels of seniority and other key stakeholders to discuss career issues.

Radical thinking report
The report is available at www.wellcome.ac.uk/radicalthinking

Ask the supervisors
The third in a trilogy of reports examining Wellcome Trust PhD research training has been published. The new study, 'The Supervisor's Perspective', investigated the opinions and experiences of the academic supervisors of Trust-funded PhD students, and follows on from 'The Student Perspective' and 'Career Paths of a 1988–1990 Prize Student Cohort', published in March 2000. Together, the three reports form a comprehensive review of just over a decade of provision of PhD student support by the Trust.

See page 50.

Children of the 90s

On 4 June 2001, at a meeting at the Royal Society in London, the Avon Longitudinal Study of Parents and Children (ALSPAC, also known as 'Children of the 90s') celebrated its tenth birthday and the award of new funding from the Wellcome Trust, the Medical Research Council and the University of Bristol.

ALSPAC began in 1991 with the enrolment of 14 000 mothers-to-be. Led by Professor Jean Golding from the University of Bristol, the study has followed the families over the last ten years with the aim of finding the pathways – both genetic and environmental – that lead over time to common disorders such as asthma, food and other allergies, autism, hyperactivity, and dyslexia. With this knowledge, preventative drug treatments, as well as diet and lifestyle changes, can be implemented to divert the pathways towards health rather than disease.

Researchers working with ALSPAC have found, for example, that breast-feeding and eating oily fish improve a child's eyesight, that babies are healthier when put to sleep on their backs, and that children brought up in very hygienic homes are more likely to develop asthma. Recent studies have found that eczema precedes peanut allergies in nine out of ten cases (with a possible link to skin creams containing peanut oils), and that pregnant women with high levels of the hormone testosterone have girls who show more tomboy-like behaviour.

The Wellcome Trust and the Medical Research Council are injecting core funding of more than £6 million, and the University of Bristol £5 million. The Trust is providing an additional £2 million to establish a collection of cells from children and their parents, which will allow DNA samples to be used as a long-term resource for future studies.



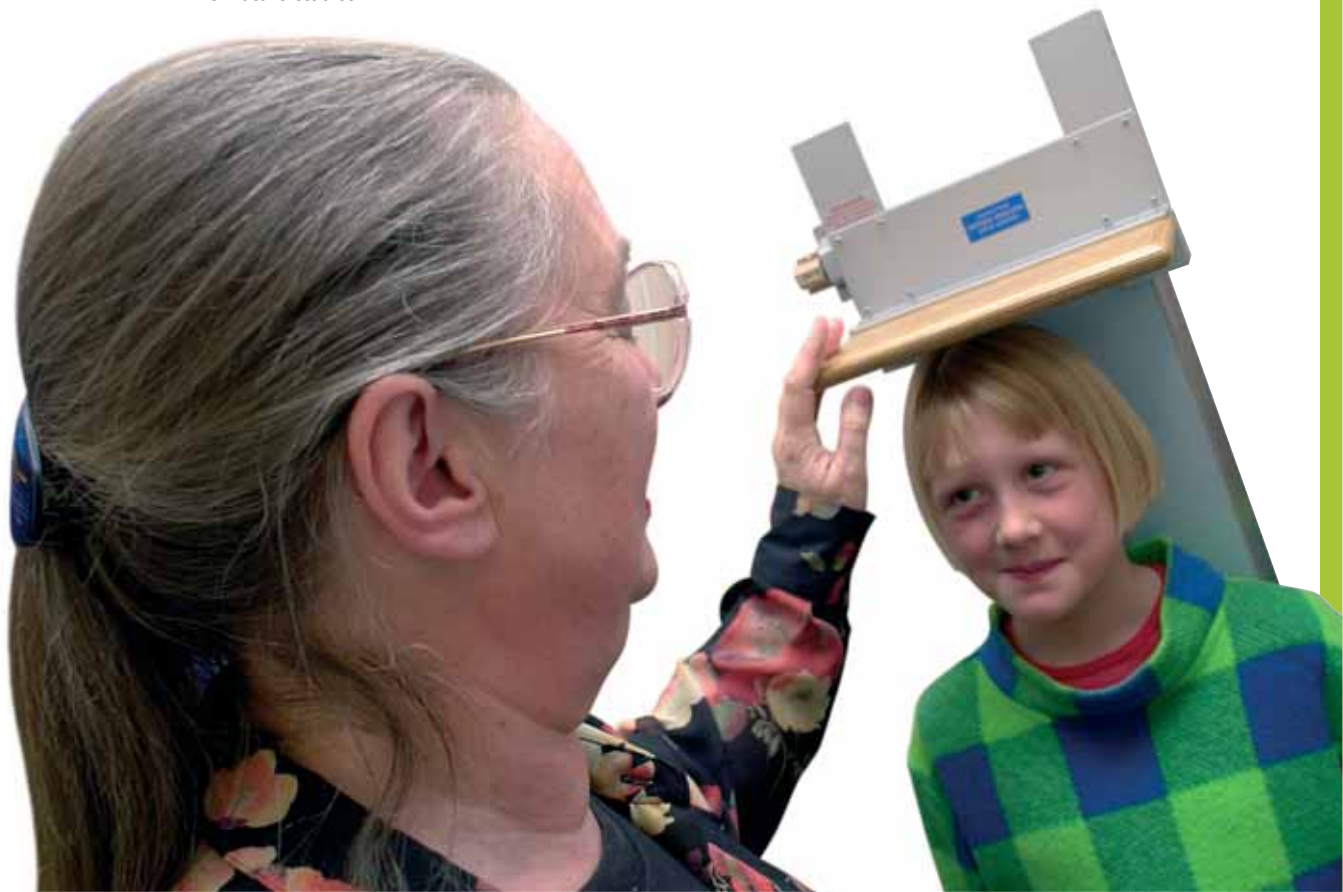


Top and above
The children involved in the ALSPAC project participate in a range of tests, including physical fitness.

Below Professor Jean Golding measures the height of a girl, just one of the thousands of measurements recorded by ALSPAC over the last decade.

ALSPAC and ethics

In their project 'Ethical protection in epidemiological genetic research', Professor Alastair Campbell and Dr Richard Ashcroft at the University of Bristol are investigating what 'genetics research' means to participants in ALSPAC, what issues they find ethically important, and what sort of ethical protection they want for themselves. The research is funded by a Wellcome Trust Biomedical Ethics project grant.



New labs for Bristol



Left The Henry Wellcome Laboratories for Integrated Cell Signalling at the University of Bristol were refurbished with funding from the Joint Infrastructure Fund.

The Henry Wellcome Laboratories for Integrated Cell Signalling at the University of Bristol opened in October 2001. The £9 million five-storey laboratory development is located at the core of the University's School of Medical Sciences.

The new laboratories will enable over 150 scientists in the University's anatomy, biochemistry, pharmacology and physiology departments to collaborate more effectively in research into the communication or 'signalling' within and between cells at the molecular level.

The development was made possible by a refurbishment grant from the Joint Infrastructure Fund. The University also put in over £1 million from its own resources.

The successor to the Joint Infrastructure Fund, the Science Research Investment Fund, has also made a major award to Bristol: part funding for an £18 million project to build state-of-the-art facilities for the University's Research Centre for Neuroendocrinology. Research in the new laboratories, led by Professor Stafford Lightman, will provide radical approaches to the treatment of stress-related disorders, hormonal and psychiatric disease, and Alzheimer's disease.

Through the Science Research Investment Fund, the Wellcome Trust awarded over £8 million for the project, and the University has committed a further £10 million from its own resources. The laboratories will be housed in purpose-built premises adjacent to the Bristol Royal Infirmary, called the Dorothy Hodgkin Building after the University's Nobel Prize-winning fifth Chancellor.

The University of Bristol already has an international reputation in the field of neuroendocrinology, but its scientists are working in cramped conditions and are scattered across a number of buildings that offer no scope for expansion. The new development will allow research teams to join forces on a single site with the space they need and shared facilities of a high standard. Work on the five-storey building is expected to be completed by March 2003.

Joint Infrastructure Fund
The £750 million Joint Infrastructure Fund (JIF), to which the Wellcome Trust contributed £300 million, completed its final rounds of funding in 2001. In all, 25 institutions received funding from the Wellcome Trust through JIF. The smallest award was for just under £1 million, the largest project £58 million (£30 million from JIF coffers). Wellcome Trust funds supported significant buildings – in excess of £18 million – in Birmingham, Cambridge and Sheffield.

Science Research Investment Fund
The £1.1 billion Science Research Investment Fund (SRIF), to which the Wellcome Trust has contributed £225 million, was established to provide further infrastructure funding; £150 million of the Trust's contribution was allocated to support highly ranked but unfunded applications to JIF, particularly those that aimed to improve otherwise poor working conditions.

International fellows

The Wellcome Trust's International Senior Research Fellowship (ISRF) scheme was set up in 1984 to encourage the return of high-quality scientists who are currently working abroad and to provide an incentive for leading scientists to remain committed to their home research base.

Launched in Australia and New Zealand, the scheme has brought back a cadre of excellent scientists to the region, and has helped to invigorate the biomedical research environment. The high calibre of these scientists is reflected in the fact that over 25 per cent of awards in the Howard Hughes Initiative in Infectious and Parasitic Disease went to Australia, and one-third of these were to Trust-funded scientists.

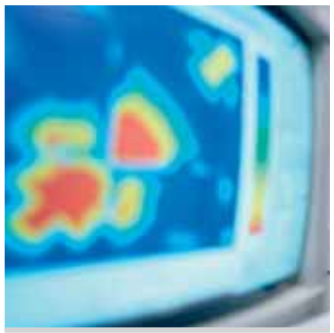
In the light of these developments, the Trust has decided that it is timely to evaluate and refocus the Trust's activities, and the ISRF scheme in Australia and New Zealand is being brought to a close at the end of the 2001/02 funding year. The Trust is now considering new forms of support in the region.

In 1992, the ISRF scheme was extended to South Africa and in 1998 to India. There are currently eight Senior Research Fellows in South Africa and 20 in India, studying a diverse range of topics that include infectious diseases, porphyria, protein structure and neuroscience.

Senior Fellows in Europe
In 2001 the Trust extended the International Senior Research Fellowship scheme to Hungary, Poland, the Czech Republic and Estonia. Despite profound changes in the political and social climate, the region continues to produce many outstanding scientists – a number of whom have already been funded by the Trust through its collaborative grant schemes.

Marking the genome





Top Dr Lon Cardon is using statistical genetics and bioinformatics to build a map of DNA variations across the human genome.

Career Development

The Wellcome Trust's Career Development Programmes provide opportunities, through fellowships and scholarships, for promising scientists to develop into highly skilled and independent research workers who make important contributions to the advance of biomedical knowledge.

The portfolio of personal award schemes provides salary as well as research support for individuals at key stages of their research career from the early (PhD) through to senior (professorial) academic level. Separate portfolios of schemes exist for basic scientists, and for medical and dental graduates. Veterinary graduates are accommodated in either portfolio, depending on the nature of their research and clinical activity.

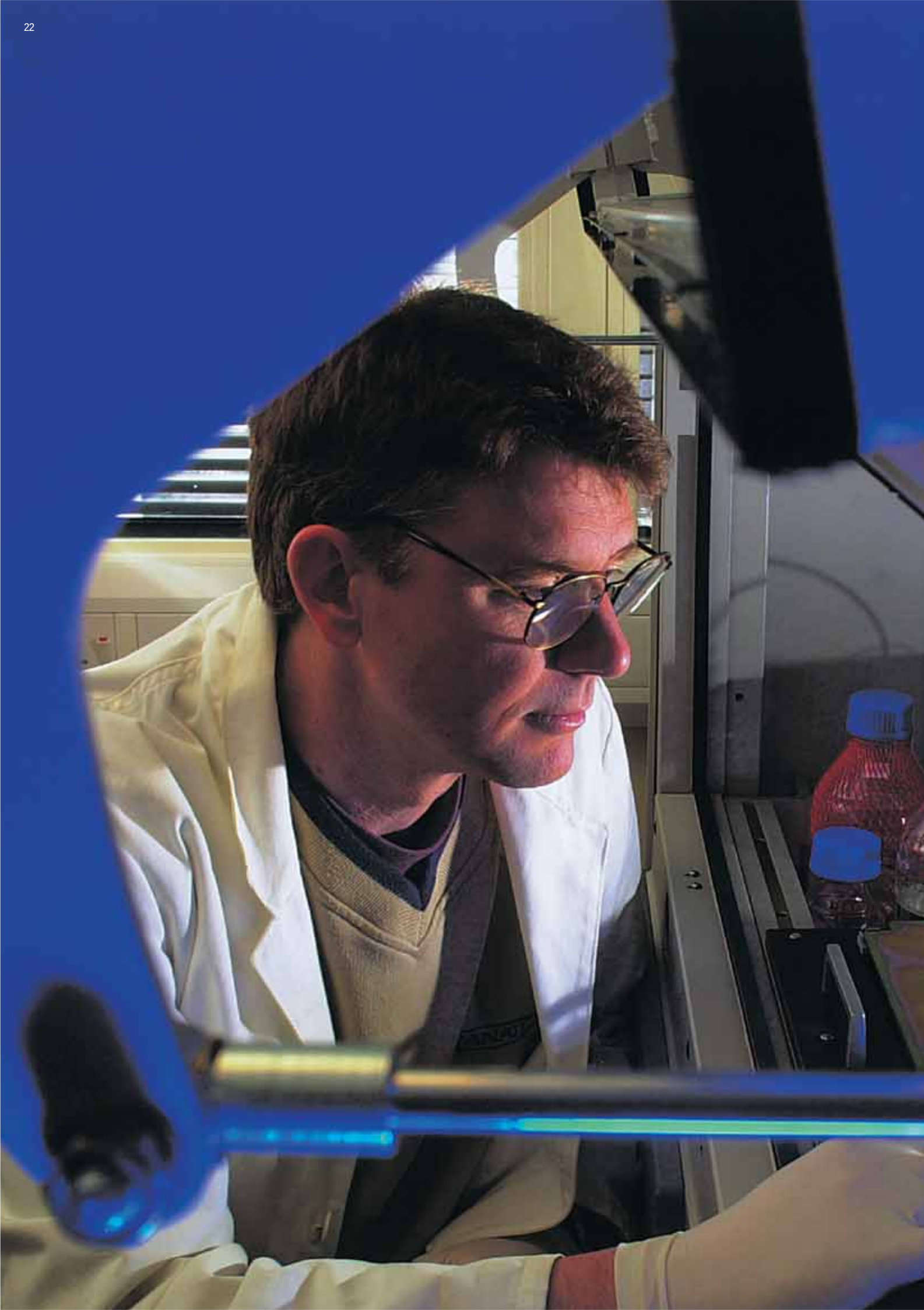
See page 50.

Common diseases such as asthma, diabetes and obesity are thought to be caused by a number of genetic and environmental factors. Many such factors are likely to have only small, subtle effects, however, so it is extremely difficult to identify specific genes that might confer susceptibility to a disorder.

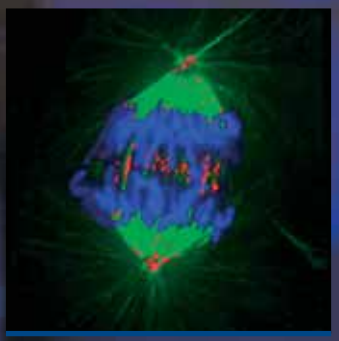
At the Wellcome Trust Centre for Human Genetics in Oxford, which marries high-throughput technology with basic genetics research, Dr Lon Cardon has been awarded one of the Trust's prestigious Principal Research Fellowships to investigate this problem. With £2.2 million funding from the Trust, Dr Cardon aims to build a map of long-range associations between DNA variants in the human genome. Using statistical genetics and bioinformatics to analyse the data, Dr Cardon will build a map of 300 000 DNA variations spaced closely together across entire chromosomes. The resulting map of haplotypes – sets of closely linked genetic markers present on one chromosome which are inherited together – will help researchers to distinguish between variations that occur by chance as a result of common human ancestry and those that have a genuine association with a disorder.

Development of genome-wide haplotype maps follows directly from the human genome sequencing project, and is the focus of an international initiative to catalogue the correlations between variant DNA sites in different populations. Dr Cardon's focused, chromosome-specific research will help guide the design and analysis of the various genome-wide haplotype maps.

Not only will such analysis help accelerate Dr Cardon's own work on genetic influences in late-onset diabetes, Huntington's disease, reading disabilities and endometriosis (a disorder of the female reproductive system), but its unrestricted availability on the Internet, linked to the sequence of the human genome, will also make it an essential database for studies aimed at discovering how genes influence disease onset and progression.



Cell biology in Edinburgh



Above Research into cell division is bringing insights into the biology of the cell and is of direct relevance to the processes of cancer.

Main picture
Professor David Tollervey, a Principal Research Fellow at the Wellcome Trust Centre for Cell Biology, which was awarded full Centre status during the year.

In October 2001, full Centre status was awarded to the Wellcome Trust Centre for Cell Biology in Edinburgh. Since 1996, the Centre has been housed in the Swann Building, a purpose-built facility funded by the Wellcome Trust, the Darwin Trust, the Wolfson Foundation and the University of Edinburgh.

The 17 research groups at the Centre – the leaders of which include two Wellcome Trust Principal Research Fellows, seven Wellcome Trust Senior Research Fellows and two Wellcome Trust Research Career Development Fellows – already receive approximately £3 million funding from the Trust to support their studies. From October 2001, the Centre will receive core funding of £3.4 million for five years to help underpin its work.

The scientists at the Centre study cell biology in many different ways. Research spans the fundamental characteristics of cells, such as growth, movement, self-replication and development, as well as how their malfunction can contribute to disease.

The programmes of research therefore fall within several interrelated areas of cell biology: the cell cycle and chromosome structure and biology, structure and function of the cytoskeleton, control of gene expression, and RNA processing, localization and stability. These are studied in a variety of experimental organisms including *Xenopus*, *Drosophila* and yeast.

Wellcome Trust Research Centres

Wellcome Trust Research Centres are UK-based centres of excellence. Centre status is awarded when the Trust perceives that the work of outstanding senior Trust-funded researchers, individually and collectively, is of major international significance within a designated field of study, and where the total impact of the group is felt to be greater than the sum of its parts.

Each Wellcome Trust Centre has a core award which provides long-term support. These awards aim to create, in partnership with the host university, an intellectually stimulating environment that is well resourced, will encourage collaboration and productivity, and will attract the most able scientists from the UK and abroad.

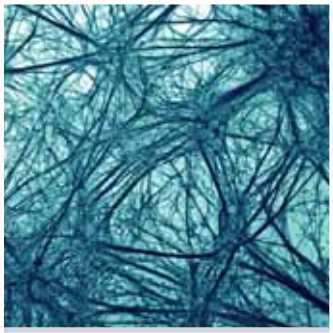
Wellcome Trust Centres:

- *Wellcome Trust/Cancer Research UK Institute of Cancer and Developmental Biology, University of Cambridge*
- *Wellcome Trust Centre for Cell Biology, University of Edinburgh*
- *Wellcome Centre for Molecular Parasitology, University of Glasgow*
- *Wellcome Trust Centre for the History of Medicine at University College London*
- *Wellcome Trust Centre for Cell-Matrix Research, University of Manchester*
- *Wellcome Trust Centre for Human Genetics, University of Oxford*

New acquisitions in the Wellcome Library

The Wellcome Library preserves the record of medicine past and present to foster understanding of medicine, its history, and its impact on society. The collections, which cover the history of medicine, current biomedical topics and visual resources, include books, journals, manuscripts, images and films, to name just a few.

Throughout the year the collections continued to be developed with a range of new acquisitions, just a few of which are showcased here.



A network of neurons
The Medical Photographic Library includes images on the history of medicine, modern biomedical science and clinical medicine. These neurons in culture, photographed by Q-L Ying and A Smith, have differentiated from embryonic stem cells. They show typical features of nervous tissue with axons and dendrites making multiple connections with each other. Cells derived in this way could form the basis of future treatments for brain diseases such as Parkinson's.



Public health in Russia
During the year, the Wellcome Library acquired a number of Russian public health posters dating from the 1920s to the 1990s. The posters range in subject from typhus, cholera, smallpox and dysentery in the early Soviet period, to alcoholism, heroin dependency and AIDS in the post-Soviet years. In this watercolour design for a poster, probably from the 1950s, a sick man thinks he is being helped to walk by a cigarette and a vodka bottle, whereas they are really false friends who are hindering him.







Heavenly bodies

In the 16th and 17th centuries, almanacs were the most popular form of publication apart from the Bible, but as most were thrown away at the end of the year, they are now quite rare. In 2001, the Wellcome Library acquired an almost complete almanac for the year 1581, printed in Breslau (now Wroclaw in Poland). The compiler was Petrus Slovacius, astrologer to the University of Cracow. At the foot of the almanac is the traditional 'zodiac man' (shown top left), illustrating the influence of the signs of the zodiac on the parts of the body. There are symbols to indicate suitable days for bloodletting, bathing, haircutting, taking medicine, castrating animals and other activities.

Other interesting acquisitions were:

- The tresuri of helth, *London, 1558.*
- *Jean Cousin,* La vraye science de la pourctraicture, *1672 (for teaching anatomy to artists).*
- *Single-sheet veterinary chart on the care of horses, 17th century.*
- *Robert Hooke's copy of J Becher,* Novum organum philologicum, *1674.*
- *Medical recipe book of Theodosia Henshaw, 17th century.*
- *Letters on the health of the Duchess of York, 1820, by Henry Halford and Matthew Baillie.*
- *Papers of Thomas Buzzard, doctor in the Crimean War.*
- *Painting of the yellow fever epidemic in Buenos Aires, by Juan Manual Blanes, 1871.*
- *Mid-17th-century painting of a surgeon removing a plaster from a patient, by Adrien Rombouts.*
- *Watercolour of* The operating theatre *by J H Ramberg, early 19th century.*
- *Papers of Elsie Widdowson and Robert McCance.*
- *Photographic archive of G H F Nuttall, Professor of Pathology at Cambridge University.*
- *An early copy of a 14th-century Arabic work on the interpretation of dreams, written in Cairo.*
- *A copy of George Lowrey's* The evil of intoxicating liquor and the remedy, *translated into Cherokee, 1844.*
- *Thirteen boxes of papers by Dr Roger Altounyan (1922–87), received from his widow Mrs Hella Altounyan. A chronic asthma sufferer, Dr Altounyan was the first to develop an efficient dry powder inhaler, the Spinhaler, for the administration of inhaled drugs in the 1950s.*

Opening up the archives



Research Resources in Medical History

Launched in January 2001, Research Resources in Medical History is providing £1 million over two years (2001–02) to support projects that open up access to important documentary resources in medical history, or to help conserve them. The scheme aims to ensure the preservation of fragile historical material and to safeguard these unique sources for future generations of researchers. By utilizing current developments in electronic delivery of archival information, including provision of digital images, many of the projects will offer the widest possible access to researchers who are increasingly using the Internet as a core part of their historical studies.

The scheme is funded by the Wellcome Trust and administered by the British Library.

Further details at www.bl.uk/concord

In July 2001, the Wellcome Trust and the British Library awarded just over £300 000 to archival projects under the Research Resources in Medical History scheme.

Grants will go to a number of institutions, including: London Metropolitan Archives, to complete the cataloguing of a range of hospital archives; the Borthwick Institute in York, to preserve the York NHS Trust archives; Dundee University, to catalogue and conserve a range of important sets of papers relating to medicine; and Exeter University, to catalogue the papers of the Royal Western Counties Institution at Starcross, a psychiatric hospital.

The various projects will open up access to documents as diverse as the records of the Court of Arches, relating to the prosecution of a midwife for practising without a licence in 1665, and Emma Durham's diary of 1879 as a nurse in the Zulu war.



Left Staff from the Royal Western Counties Institution, a psychiatric hospital in Starcross, Devon, *c.* 1880.

From the pen of Charles Darwin



One of the most ambitious cataloguing projects ever undertaken, the Darwin Correspondence Project at the University Library in Cambridge, was awarded a further £700 000 by the Wellcome Trust. The latest award will support staff working on the project in Cambridge for the next five years, during which time the project will establish an endowment enabling it to become self-financing and achieve its objective of completing its Herculean task by 2025.

Darwin, whose ideas revolutionized biology, was an enthusiastic letter writer. This was in part due to his ill health and the consequent reclusive life he led at Down House, Kent, his home from 1842 until his death in 1882. It also reflected the nature of his work, which required communication with scientists in every part of the world. He collected data from every field of natural history and from any corner of the globe that might provide information relevant to his theory. To date, the project has located more than 15 000 letters exchanged by Darwin and hundreds of correspondents. New letters continue to be discovered at the rate of about 60 a year.

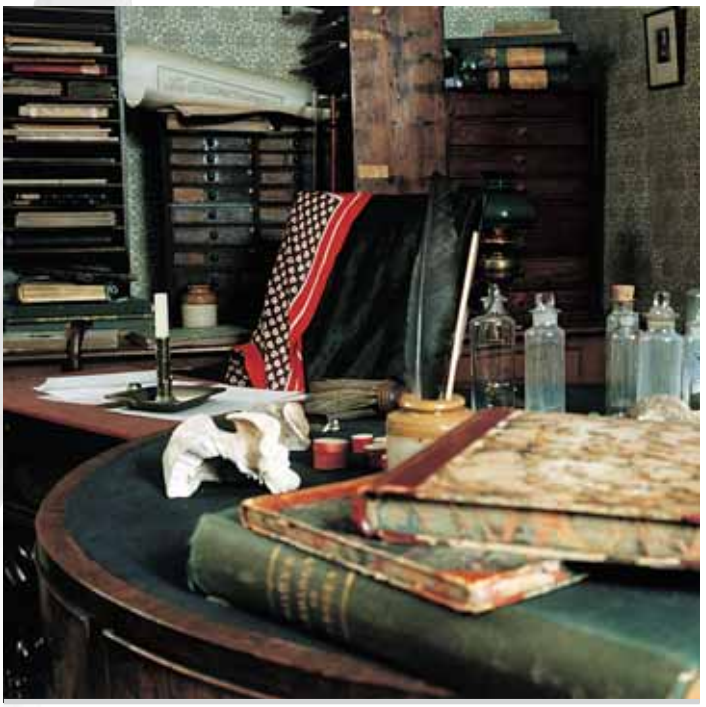
When complete, *The Correspondence of Charles Darwin* will comprise approximately 32 volumes. It provides, for the first time, the full, authoritative texts of Darwin's letters. Work on the correspondence is based in the University Library in Cambridge and in the USA, and the project has a wide range of sponsors.

Further details
www.lib.cam.ac.uk/departments/darwin/index.html

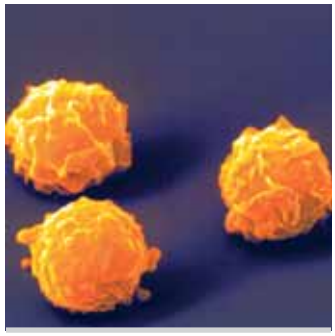


Left Charles Darwin, a colour lithograph, 1871, by R Burgess.

Right Down House, Charles Darwin's home from 1842 to 1882. In 1996, the Wellcome Trust gave £700 000 to English Heritage for the purchase of the Down House freehold.



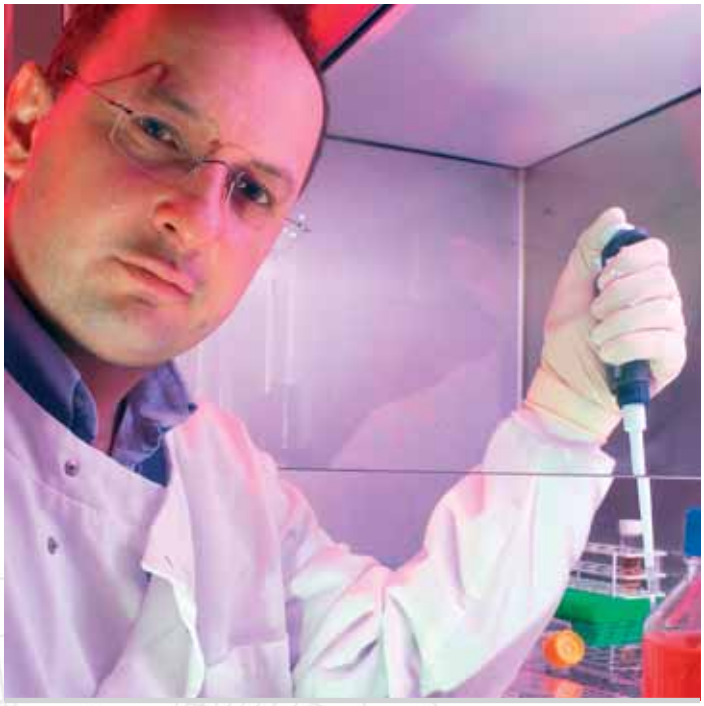
Gene therapy for faulty immunity



The immune system is remarkably complex and sophisticated – as it needs to be to defend us against the myriad pathogens in the environment. A flaw in one part of the system can leave the body exposed to infection; in severe cases, such as in primary immunodeficiency disorders, children are susceptible to frequent and unusual infections, have to be isolated in 'bubbles', and often die at a young age.

At the Institute of Child Health, Dr Adrian Thrasher, a Wellcome Trust Senior Research Fellow in Clinical Science, is investigating a primary immunodeficiency disorder called Wiskott–Aldrich syndrome. Mutations in the protein involved in this disorder, WASP, disrupt the internal scaffolding of immune cells; the cells appear to be unable to move around the body – an essential part of the immunity process.

To complement his research on the causes of Wiskott–Aldrich syndrome, Dr Thrasher is developing a gene therapy treatment that can reprogramme the faulty immune system of children with the disorder. The treatment, already used successfully at the Institute of Child Health to treat children with other primary immunodeficiencies, involves removing bone marrow from the child and isolating the stem cells that make the blood. A genetically modified virus similar to the cold virus is used to insert a normal copy of the relevant gene into the bone marrow stem cells; the cells are then transferred back into the child and, once in the body, produce functioning immune cells.



Above Scanning electron micrograph of bone marrow stem cells.

Left Dr Adrian Thrasher, part of a team making significant progress in gene therapy for immunological diseases.



New home for cognitive therapy research

The Henry Wellcome Building for Psychology at the Institute of Psychiatry (above) was formally opened by HRH The Princess Royal on 4 April 2001. The new building, which was largely funded by a Joint Infrastructure Fund award from the Wellcome Trust, houses a specialized area for research into the causes and treatments of severe anxiety or trauma. The research group, led by Professor David Clark, Professor Anke Ehlers (both of whom are Wellcome Trust Principal Research Fellows) and Professor Paul Salkovskis (a Wellcome Trust Senior Research Fellow), is internationally renowned for its pioneering work in the field of cognitive behaviour therapy – 'talking treatment' for severe psychiatric disorders.

Moods and food

The sight of the emaciated Jane Horrocks secretly bingeing on chocolates in her bedroom, only to vomit them up again later, in Mike Leigh's film *Life is Sweet*, is all too illustrative of the physical and mental trauma caused by eating disorders. As well as dominating sufferers' thoughts and often devastating their relationships, eating disorders have profound health consequences. The heart muscle of the starving anorexic wastes away leading to the possibility of organ failure, while a patient with bulimia nervosa runs the risk of potentially life-threatening electrolyte disturbance.

Such disorders are also notoriously difficult to treat. A team headed by Wellcome Trust Principal Research Fellow Professor Christopher Fairburn at the University of Oxford is investigating the psychological processes that contribute to their persistence, and is developing cognitive-based treatments to counteract them.

Professor Fairburn's earlier work using cognitive behaviour therapy to treat bulimia nervosa focused on the behavioural and psychological traits specific to the eating disorder: a pronounced tendency to evaluate self-worth in terms of eating, shape or weight, leading to extreme methods of weight control, such as excessive dieting, bingeing and purging, and laxative abuse. The resulting treatment has been shown to be the most effective therapy for bulimia nervosa in numerous trials worldwide, but still only half of patients make a full recovery.

His new cognitive treatment programme has broadened its focus to encompass three more general psychological disturbances, which, although not specific to eating disorders, appear to play an important role in maintaining them in subgroups of patients.

Patients with eating disorders have a tendency to judge themselves extremely negatively, and their sense of low self-worth is exacerbated by the mood changes induced by starvation or the self-disgust following binge-eating and/or purging. Marked perfectionism is a key feature in anorexia nervosa, leading to over-determined attempts to control eating. Difficulty tolerating adverse mood states is an important aspect of bulimia nervosa: the bingeing and purging which characterize this disorder bring about a temporary but much-craved respite from these moods.

These three disturbances are not all active in every case, accounting for the fluidity and interchangeability of these disorders (an anorexic patient may become bulimic and vice versa, for example). The new treatment aims to find out to what degree each disturbance – low self-worth, perfectionism or adverse mood intolerance – is operating in an individual patient, so that a tailor-made treatment programme can be constructed accordingly.

Pilots of this new, broader therapy have been successful: around three-quarters of a group of treatment-resistant patients made lasting improvements, a considerably higher proportion than the 30 to 40 per cent predicted. A formal evaluation of the treatment and the hypotheses underlying it, including a programme of experimental studies and a clinical trial, is now underway. The results should also help shed light on an important question regarding cognitive behaviour therapy in general: whether therapy should focus only on psychological mechanisms specific to a particular disorder, or should also address more general areas of disturbance.



Clinical research in Edinburgh

The Wellcome Trust Clinical Research Facility at the Western General Hospital in Edinburgh was opened by Her Majesty The Queen on 6 July 2001. The facility is housed in a new three-storey building and is jointly funded by the Wellcome Trust (with an initial £4.7 million grant for construction and equipment costs), the Chief Scientist Office (Scottish Executive), the University of Edinburgh, Lothian University Hospital NHS Trust and the Lothian Primary Care NHS Trust.

Under the leadership of its Director, Professor Peter Hayes, the facility will act as a central site for patient-oriented research within the Edinburgh area, and offer a supportive environment for investigators developing their research or undertaking training in clinical research.

The Edinburgh facility has five scientifically themed core areas – for epidemiology and statistics, genetics, image analysis, integrative physiology and mass spectrometry – as well as consulting and in-patient rooms, an intensive studies room, and a research ward. Research projects include studies of the causes of bowel cancer; complications following liver transplantation; diabetes and insulin sensitivity in obesity; the genetics and psychology of major mental illness; vascular malfunction; whether aspirin can reduce the risk of future heart disease, and cognitive decline.





Wellcome Trust Clinical Research Facilities

In an £18 million venture, the Wellcome Trust has funded the capital costs of five new Clinical Research Facilities, partnerships between the Trust, the NHS and university researchers. These new centres will provide major sites for patient-oriented research, helping to ensure that advances in biomedical research feed through into improvements in healthcare.

The Clinical Research Facilities are linked to local hospitals and biomedical research departments in universities, and have been kitted out with modern, state-of-the-art equipment. Patients will be studied in newly built or refurbished wards, consultation rooms, day clinics and laboratory facilities which are dedicated to clinical research.

The Clinical Research Facilities have been set up in Birmingham, Cambridge, Edinburgh, Manchester and Southampton.

Further reading

Wellcome News *Q3 2001*
From bench to bedside revisited: Clinical Research Facilities open their doors
www.wellcome.ac.uk/wellcomenews28

Clear water



Left A dehydrated six-year-old girl drinking oral rehydration solution.

Below Indian mothers listen to instructions from a health worker on the preparation of oral rehydration solution fluids.

Diarrhoea is a major cause of mortality in developing countries. The main treatment is oral rehydration therapy, the administration of a controlled glucose-based solution. This simple but effective treatment has saved many lives, and been hailed as one of the great medical advances of the 20th century. However, while oral rehydration solution corrects dehydration, it does not reduce the diarrhoea itself. It has therefore been assumed in some communities to be ineffective, which militates against its widespread use.

Between 1957 and 1990, the Trust funded an overseas unit based at the Christian Medical College and Hospital in Vellore, India. One of its staff, Professor Siddartha Ramakrishna, is now principal applicant on a trilateral programme, funded through the Wellcome Trust–Burroughs Wellcome Fund Infectious Diseases Initiative, to improve oral rehydration therapy for diarrhoea.

Professor Ramakrishna, Professor Henry Binder of Yale University School of Medicine and Professor Michael Farthing of the University of Glasgow Faculty of Medicine are taking advantage of recent scientific advances in the physiology of the intestine to try and overcome the perceived limitations of oral rehydration therapy.

Professors Binder and Ramakrishna have discovered that short chain fatty acids stimulate fluid absorption from parts of the colon, and that resistant starch, a substrate for short chain fatty acids, reduces diarrhoea and shortens illness in cholera. In addition, Professor Farthing has shown that very dilute oral rehydration solutions are particularly effective in noncholera diarrhoea in children.

The researchers will combine these two advances to create a new oral rehydration solution that both rehydrates and reduces diarrhoea. They hope that the enhanced antidiarrhoea action of the new solution will produce a more directly tangible effect for patients and their carers, and thus provide both a more effective – and a more acceptable – version of this life-saving treatment.



Trilateral partnerships

Six awards, totalling £5.6 million, were made in the final competition for the Wellcome Trust–Burroughs Wellcome Fund Infectious Diseases Initiative. These awards will support research in countries throughout Africa, South America and Asia, and cover some of the major public health problems in the developing world, including tuberculosis, malnutrition and diarrhoea.

Launched in 1998, the Initiative was set up to support trilateral international collaborations between centres in the developing countries, the UK and the USA or Canada, with the 'centre of gravity' of research in the developing world.

Gastroenteritis research

The Christian Medical College in Vellore, India, successfully competed for a second WT–BWF award in the 2000 competition. Dr Gagandeep Kang in Vellore, Professor Mary Estes, Baylor College, and Dr Jeremy Wheeler, Cambridge, were funded to investigate what factors are important in the protection of children against rotaviral gastroenteritis.

Taking on malaria in Thailand

The Wellcome Trust's South-East Asia unit, led by Professor Nick White, has pioneered a new strategy for controlling falciparum malaria – the most serious form of the disease – based on careful, long-term research carried out in Thailand.

The key to this achievement has been the use of a combination of drugs containing a derivative of artemisinin or 'qinghaosu', an antimalarial derived from a Chinese plant. These combinations have proved highly effective in controlling malaria in camps for displaced persons located along Thailand's border with Myanmar, and have slowed the development of drug resistance. The approach has recently been endorsed by the World Health Organization as part of its Roll Back Malaria initiative.

With the backing of a US$4.7 million grant from the Bill and Melinda Gates Foundation, the Communicable Disease Control Department of the Thai Ministry of Public Health and Mahidol University will now extend this new control strategy throughout Tak province in north-western Thailand. The most malaria-affected province in the country, Tak also harbours the greatest number of drug-resistant falciparum malaria parasites in the world.

Building on the established network of village health volunteers, the programme will use recently developed simple methods of rapid malaria diagnosis and will provide the new combination treatments to those who are diagnosed with malaria. The Trust's research team will evaluate the outcomes of this initiative and if it proves successful in controlling falciparum malaria in Tak province, it could then become a model for malaria control throughout the region.





Top A Karen girl from northern Thailand.

Above The prevalence of malaria in north-western Thailand puts newborn babies and their mothers at particular risk.

New spins on tropical medicine

The Wellcome Trust's Tropical Medicine Resource has continued to improve its 'Topics in International Health' series of educational CD-ROMs. In collaboration with Trust-funded researchers, including Professor Nick White at the Trust's South-East Asia unit in Thailand and Dr Bob Snow at the Kenyan unit, the content of *Malaria* was revised and updated, and new tutorials and an enhanced interface added. The second edition was released in December 2000.

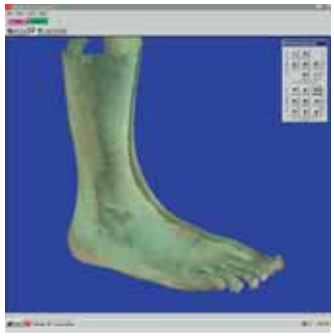
In partnership with Netherlands Leprosy Relief, TMR's *Leprosy* CD-ROM was translated into Indonesian and Portuguese, and distributed to Indonesia in September 2000 and Brazil in May 2001.

By the end of September 2001, TMR had sold 8500 disks in 102 countries. With each CD-ROM often used by five or six people, it is estimated there are now 35–50 000 users worldwide, with the biggest overseas markets being Brazil, Kenya, Nigeria, South Africa, India, Indonesia and the Philippines.



Right TMR's *Leprosy* CD-ROM includes a database of images that cover clinical leprosy, and the diagnosis, pathology and treatment of leprosy.

Precision knitwear





Top Body scanners are used to capture the dimensions of the patient's leg.

Above and below Data are then fed into the computer controlling the knitting machine to produce a stocking with the precise pressure characteristics required for optimal wound healing.

Textiles and medicine are not an obvious association, but the latest knitting technology could help people with deep venous or diabetic ulcers in their legs.

Ulcers of this type are difficult to treat and can persist for many months without healing. At present, one approach to treatment is to use a special bandage – the four-layer bandage – to compress the wound. Applying the bandage is not as simple as it sounds however: if the bandage is too tight, it can impair the patient's circulation; if it is too loose, there is not enough compression and the wound will fail to heal. It therefore can only be applied by a specialist nurse who visits the patient's home, a solution that is both labour-intensive, inconvenient for the patient and costly for the health service.

The problem could be solved by new technology developed by a team at the University of Manchester Institute of Science and Technology (UMIST) Department of Textiles led by Dr Tilak Dias and Dr Bill Cooke. This group has developed an innovative adaptation of industrial knitting machines, whereby elastometric fibre can be woven into knitted fabric at precisely controlled tensions.

In November 2000, Catalyst's Development Fund awarded the team £500 000 to use this technology to develop a new type of compression stocking that will fit each individual patient's leg at a precise pressure. Working in collaboration with the Leg Ulcer Clinic at the University of Manchester Department of Surgery, the team is using imaging software to ascertain the dimensions of the patient's leg. These data are then fed into the computer controlling the knitting machine, to produce a stocking with the precise pressure characteristics required for optimal wound healing. A small clinical trial of the bandages, led by Professor Charles McCollum, will be conducted at Wythenshawe Hospital in Manchester during 2002/03.

As well as aiming to improve wound healing, these new bandages will improve the quality of life for patients, who will be able to go about their daily lives more easily without having to wait for the arrival of a nurse.



Modelling space

Cresset Biomolecular Discovery Ltd

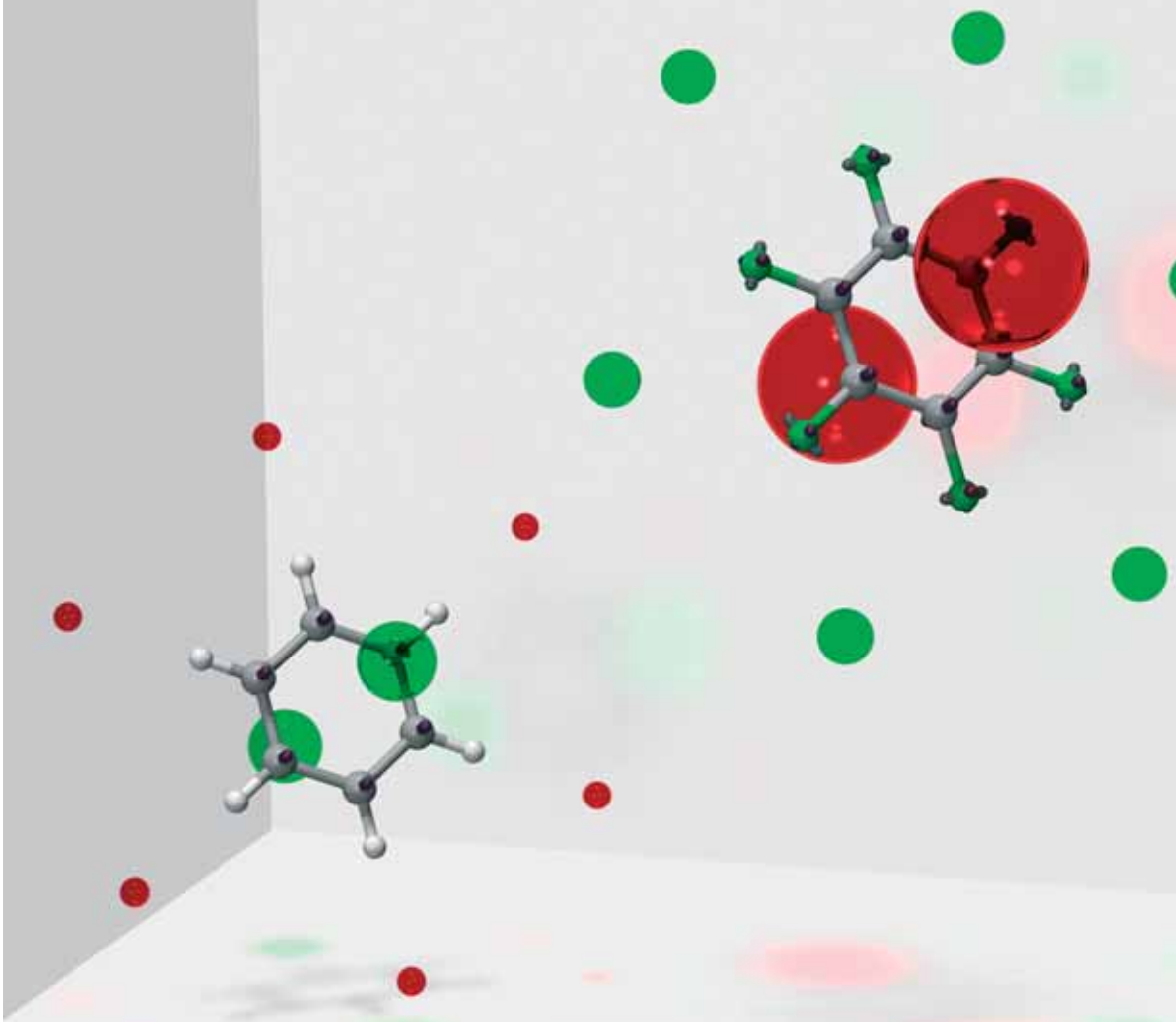
For the past ten years Andy Vinter has been running a one-man consultancy in computer drug design from home.

Formerly a chemist working for SmithKline Beecham and Wellcome plc in Beckenham, he made a name for himself in the UK molecular design community for his unique approach to analysing molecules. Conventional computational models of molecules analyse the skeleton structures of compounds, assuming for convenience sake that the electrons are within the nucleus. Dr Vinter's algorithms, by contrast, focus on the actual positions of the electrons – whose distorted fields are wrapped around the skeleton like a skin – in the hope of producing more accurate models.

In late 2001 Catalyst made its biggest Development Fund award so far, investing £780 000 directly into a start-up company, Cresset Biomolecular Discovery Ltd – a move that reflects a general UK and European growth in entrepreneurialism. The award will expand and enhance Dr Vinter's software package, turning it into a more automated, informative technology that pharmaceutical companies can use for high-throughput, *de novo* drug design.

Cresset aims to build a large database containing millions of three-dimensional models of electron-field distributions of small molecules and their component structures. Pharmaceutical scientists will then be able to search the database to find small molecules that will bind to and inhibit or activate the proteins being modelled.

This could lead the way to the discovery of new, non-obvious chemical solutions for an industry in need of novel approaches to drug design.



Cresset's software produces more accurate models of compounds by adding electron field points to the skeleton structures. In this example, the field points explain why benzene (left) and hexafluorobenzene (above) interact with other molecules very differently. The field points above and below the plane of the fluorinated benzene ring are positive (red spheres), but are negative (green spheres) above and below the benzene ring. The field points in the plane of the rings are also of opposite sign.

Teaching science in schools



Teenagers are missing out on essential classroom discussion about the social and ethical impact of scientific developments such as the sequencing of the human genome and stem-cell research, according to a report published by the Wellcome Trust.

The report, *Valuable Lessons: Engaging with the social context of science in schools*, shows that the traditional 'test-tube and textbook' approach to science in secondary and post-16 education should be enhanced by more debate and exploration of the social dimension of science. Unless school children are encouraged to argue the rights and wrongs of new discoveries, the 'genome generation' of adult citizens may be ill equipped to deal with the new life choices presented by the genetic revolution.

The way forward, the report argues, is curriculum reform, professional development and cultural change to develop a holistic, cross-curricular approach to teaching science and related issues, which should involve both science and humanities staff.

The Wellcome Trust commissioned the Institute of Education to carry out the research with more than 300 schools and colleges across England and Wales. The study found that science in school is too often perceived as 'value free' and humanities as 'value laden'. Science teachers are still tied to teaching 'the facts' of science without involving children in debate or providing opportunities for children to think about how science will impact on their lives. Though humanities staff deal with controversy well, they are often unfamiliar with the science. The teachers taking part in the research were also ready for change: six in ten agreed that there is too little classroom time devoted to issues linked to biomedical science.

The report recommends that greater cross-curricular collaboration is needed to bridge the gap between teaching facts and developing opinions, and urges a rethink of the school curriculum. The curriculum agencies such as the Qualification and Curriculum Authority in England should identify where 'socioscientific issues' should be covered in lessons. The science curriculum in particular needs to be flexible enough for teachers to explore the power and limitations of science within an ethical framework.

The research also examined which biomedical issues were being addressed in schools. The most popular subjects were AIDS, genetic engineering and eating disorders, with more than half of science teachers covering them in lessons. However, other important areas – animal-to-human transplants, for example (29 per cent of teachers covered this) – fared less well. Despite being a topical issue at the time of the research, only a quarter of teachers, mainly science staff, had covered the Human Genome Project in the classroom.

More details at www.wellcome.ac.uk/education

Wellcome News *Q4 2000*
The facts of life: Contemporary science issues in the classroom
www.wellcome.ac.uk/wellcomenews25



Right 'Traditional' science is well catered for in schools. But how should controversial socioscientific issues be addressed?

Science communication

Asking the public and the scientists

Most people are 'amazed' by the achievements of science, but many are also concerned about its regulation and control. These were the key findings from the first of two major consultations published by the Wellcome Trust during the year.

As well as asking people for their opinions of science, engineering and technology, the research looked at science communication and found that such activities tend to be skewed towards activities that provide facts about science rather than activities that highlight the ethical and policy issues raised by science. The report, *Science and the Public: A review of science communication and public attitudes to science in Britain*, is published jointly by the Trust and by the Office of Science and Technology.

The second report asked scientists for their opinions of science communication, and whether they consider themselves to be the people most responsible for and best equipped to communicate scientific research and its implications to the public.

The research found that more than half of scientists had participated in some form of communication of research to nonspecialist audiences in the previous year, but fewer than one in five have had training to deal and communicate with the media or the public and more than a third of scientists feel ill-equipped to discuss the social and ethical implications of their research. Public lack of education about and interest in science and the perceived distorting effect of the media were considered to be the main barriers to an improved public understanding of science.



Further details of the reports: www.wellcome.ac.uk/consultations

Wellcome News *Q1 2001*
Time to talk: Scientists' perception of science communication
www.wellcome.ac.uk/wellcomenews26

New methods of public consultation

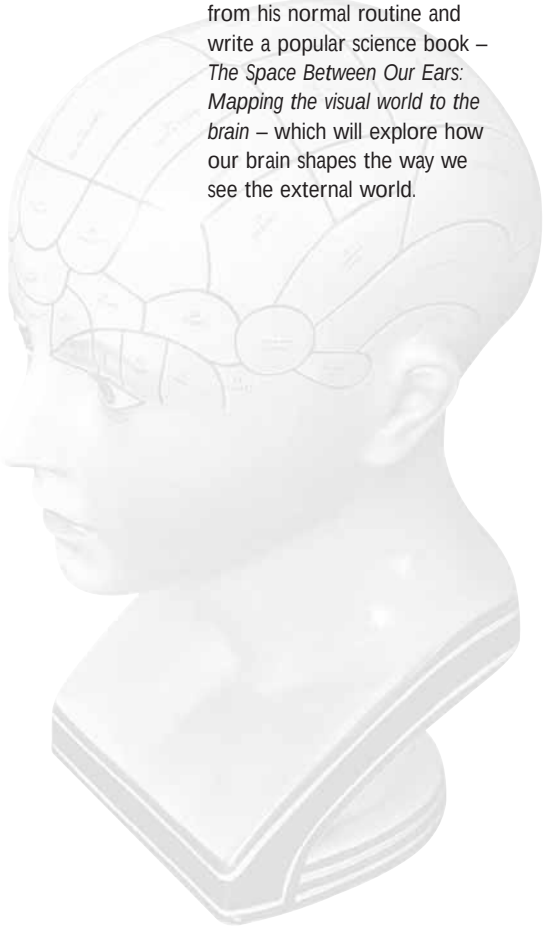
With medical science increasingly throwing up issues that are technically complex and occupy ethical grey areas, finding out what the wider nonscientific public thinks about these issues is correspondingly difficult. Following a call in 2000 for proposals in public consultation methods, the Trust has funded five projects that are exploring innovative ways to engage in two-way communication with the wider public. The studies include a combined newspaper and Internet-based consultation, 'deliberative mapping', to combine expert and lay assessments, and the use of videotaped interviews to structure debate.

Further information on these projects and the Public Engagement with Science grants programme can be found at www.wellcome.ac.uk/mis.

Wellcome News *Q4 2001*
A matter of opinion: New methods of public consultation
www.wellcome.ac.uk/wellcomenews29

Book Prize winner

Michael Morgan, Professor of Visual Psychophysics at City University in London, is the winner of the 2001 Wellcome Trust Book Prize. The £25 000 award will enable Dr Morgan to take a break from his normal routine and write a popular science book – *The Space Between Our Ears: Mapping the visual world to the brain* – which will explore how our brain shapes the way we see the external world.



New science centres in Birmingham and Glasgow

Two major science centres in Glasgow and Birmingham opened in 2001, part of a network of science centres supported by the Wellcome Trust and other funders. The science centres are not only bringing science to the people, but are also contributing to the economic regeneration of areas in these cities.

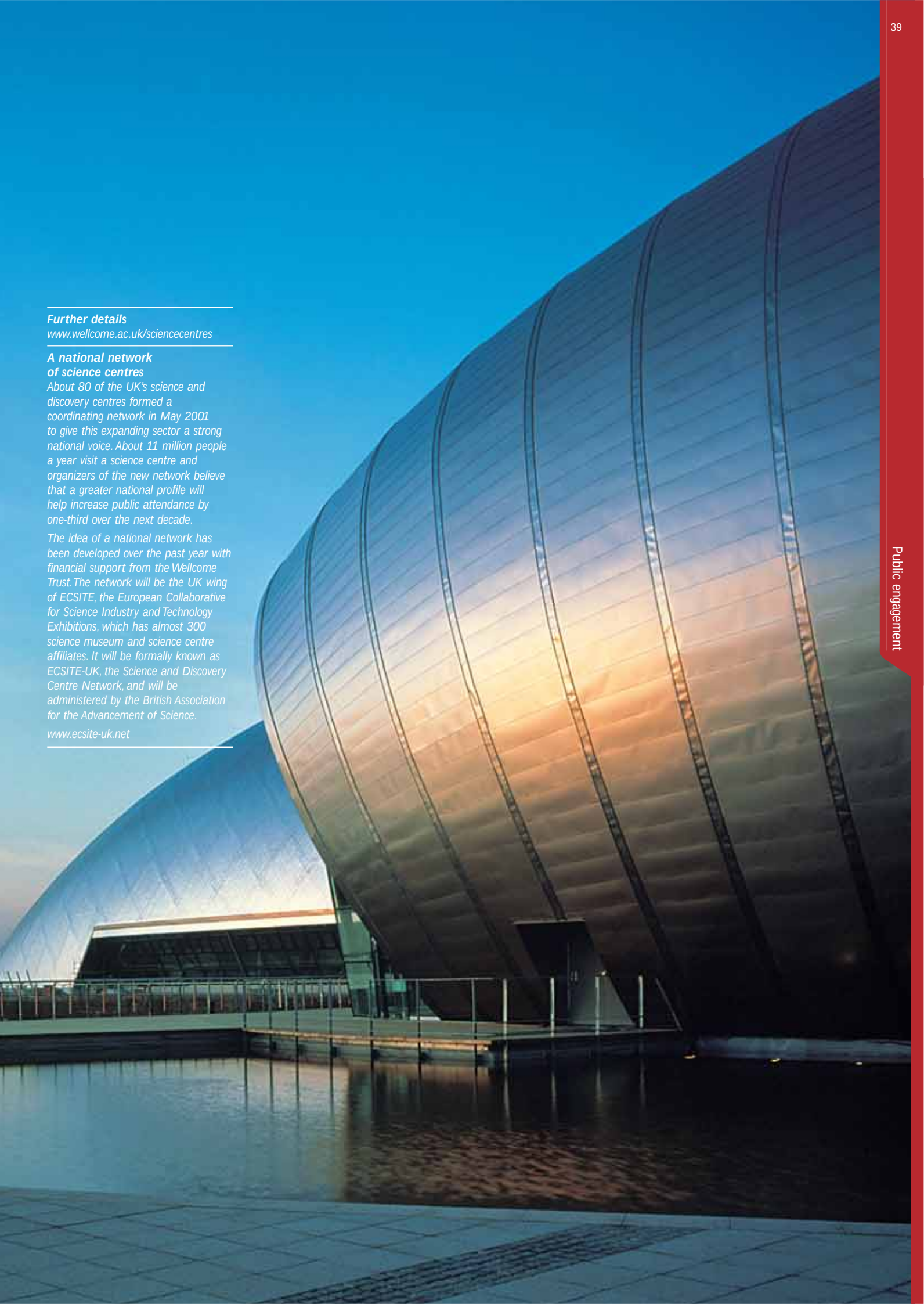
The Glasgow Science Centre was officially opened by HM The Queen on 5 July 2001. Built on reclaimed dockland at Pacific Quay in the heart of Glasgow, an area largely derelict since the 1960s, the site consists of three main buildings: the IMAX Theatre, the Science Mall, and the Glasgow Tower. All three are unique: the first two are the first buildings in the UK and only the second in Europe to be clad in titanium, while the Tower is the only such structure in the world capable of revolving 360 degrees from the ground up. Four floors house hundreds of interactive exhibits on science and technology, aimed at entertaining and informing the whole family. Themes covered include 'exploration and technology', 'creativity and innovation', and 'issues and impacts'.

The Thinktank in Birmingham opened on 29 September 2001. A combination of museum, science centre and visitor attraction, Thinktank has ten themed galleries set on four floors of purpose-built space. Exhibitions include 'Things About Me', which gives children the chance to find out more about how the human body works, and 'Medicine Matters', which explores the science behind modern medicine and some of the ethical challenges it brings. The centre is part of Millennium Point, England's largest Millennium project outside London.



Above Thinktank in Birmingham features interactive exhibits that explore the science behind modern medicine.

Main picture
Glasgow Science Centre.



Further details
www.wellcome.ac.uk/sciencecentres

A national network of science centres

About 80 of the UK's science and discovery centres formed a coordinating network in May 2001 to give this expanding sector a strong national voice. About 11 million people a year visit a science centre and organizers of the new network believe that a greater national profile will help increase public attendance by one-third over the next decade.

The idea of a national network has been developed over the past year with financial support from the Wellcome Trust. The network will be the UK wing of ECSITE, the European Collaborative for Science Industry and Technology Exhibitions, which has almost 300 science museum and science centre affiliates. It will be formally known as ECSITE-UK, the Science and Discovery Centre Network, and will be administered by the British Association for the Advancement of Science.

www.ecsite-uk.net

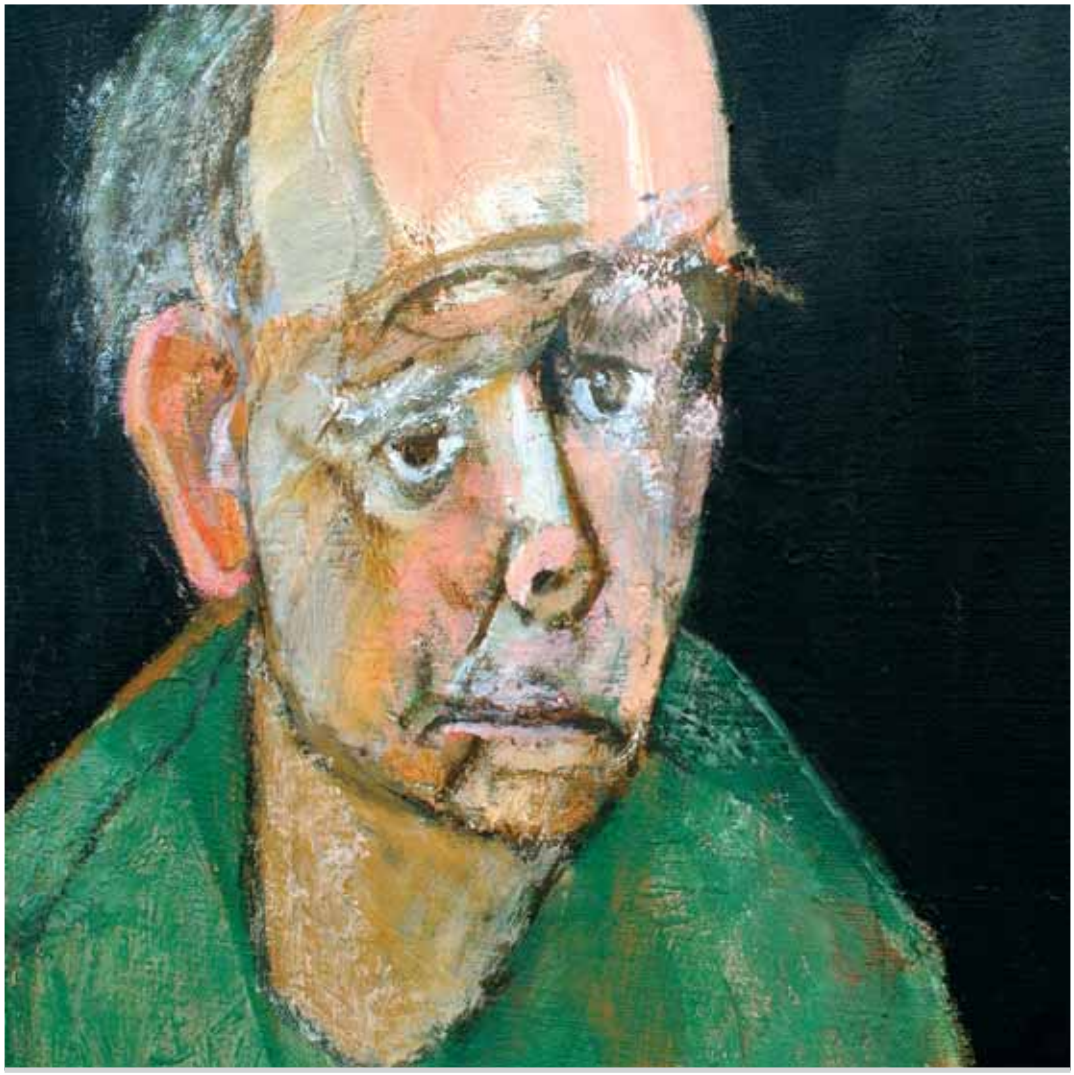
Alzheimer's and art



A series of paintings by William Utermohlen was displayed in the Wellcome Trust's TwoTen Gallery in August 2001, as part of its series of exhibitions on science and art.

The exhibition 'Art and the Brain: Portraits by William Utermohlen' included paintings and drawings from the last ten years, with three large-scale paintings from the artist's 'conversation' series. But it is the self-portraits – most of which were painted after the artist was diagnosed with Alzheimer's disease in 1996 – which provide a revealing and moving glimpse into his changing mental state as the disease has progressed.

The exhibition was co-sponsored by the Alzheimer's Society.



TwoTen Gallery

The TwoTen Gallery, at 210 Euston Road, hosts a series of innovative exhibitions on aspects of the relationship between medical science and art. Other exhibitions this year were:

Working Drafts: *Envisioning the human genome. Seven artists created artworks inspired by the 'working draft' sequence of the human genome.*

Growth and Form: *Winners of the Biomedical Image Awards 2001 – from the Wellcome Trust Medical Photographic Library – were exhibited alongside artworks inspired by biomedical science from nine contemporary artists and designers.*

Shelf Life: *What does the content of your medicine cabinet reveal about you? Are you a hypochondriac? Do you hoard out-of-date prescription drugs? 'Shelf Life' looked at home healthcare through a series of medicine cabinets, both real and artistic.*

These exhibitions can be found online at www.wellcome.ac.uk/exhibitions

Above and top left
Self-portraits by
William Utermohlen.

Science Centrestage

A dramatic opportunity for schools

Secondary school students are being offered the exciting opportunity to write, produce and perform a short play exploring some of the social and ethical issues raised by scientific progress. The most successful works will even find themselves on a national stage.

Launched in September 2001 as part of Science Year, the Wellcome Trust's Science Centrestage initiative aims to inspire students aged between 11 and 16 years to take an interest in science and communicate some of the related issues. Students taking part in Science Centrestage are encouraged to think about advances in biomedicine, debate the wider implications and devise a short 20-minute dramatic piece that will convey their views and ideas to a live audience.

The teachers and pupils are being supported by experts in science and drama – including professional actors, playwrights, representatives from local theatre companies and Wellcome Trust-funded PhD students and research scientists – to help them write and rehearse a 20-minute play to high standards of artistic excellence and scientific accuracy. The process will enable students to develop both creative and analytical skills, and to discuss issues that may affect their lives.

In March 2002, the productions were performed to audiences at ten regional festivals in theatrical venues or science centres. In the Wellcome Trust's National Festival of Drama, six pieces from selected schools will also be performed at the Royal Opera House in London to an invited audience of the national media, and representatives from science education and national drama.

Further details at www.wellcome.ac.uk/sciencecentrestage





Above and right
The Science Centrestage workshops, held in October 2001, brought students and drama teachers together with creative drama specialists and scientists.

The art of pain

Many people live with chronic pain, such as back pain, for months or years. Not only does such pain reduce the physical quality of life, but many patients also feel isolated because they find it difficult to tell others about their problem. As a consultant in pain relief at Guy's and St Thomas' Hospitals, London, Dr Charles Pither heads an interdisciplinary team that uses cognitive behavioural treatment to help patients manage their pain by accepting it and living around it. But he is also involved in two science–art projects that are exploring new ways to understand life with pain.

In the sciart project 'A Visual Language for Chronic Pain', a sciart research winner in 2001, Dr Pither and artist Deborah Padfield are exploring the use of visual images



to help sufferers communicate their experience and improve treatment outcome. Ten patients with chronic pain receiving residential treatment at St Thomas' Hospital worked with Deborah during their stay to produce photographs that express and communicate their individual experience of pain. The photographs will help the discussion between doctor, therapists and patient to enable greater mutual understanding and improve treatment outcome.

For the project 'Feeling Hurt', a Wellcome Trust Science on Stage and Screen award winner in 2001, doctors and artists have come together to investigate pain. The team of seven – two playwrights (Diane Samuels and Sarah Woods), a visual artist (Alexa Wright), a performer (Catherine Long) and three medical specialists (Drs Pither, Anita Holdcroft, and Mick Serpell) – aims to use a variety of media to produce a new theatrical production that can present the many facets of pain and pain experiences.





sciart

The sciart initiative invites scientists and artists to collaborate and develop new artwork inspired by all areas of science. Following the success of the Wellcome Trust's sciart awards in 1997 and 1998, a consortium comprising the Arts Council of England, the British Council, the Calouste Gulbenkian Foundation, the National Endowment for Science, Technology and the Arts (NESTA), the Scottish Arts Council and the Wellcome Trust was formed in 1999 to continue and extend the remit of the sciart initiative.

www.sciart.org

Science on Stage and Screen

Launched in 1998, the Science on Stage and Screen production award scheme encourages the development of creative projects that engage the public's interest in biomedical science or human health, through the use of performance, film/ video and television, and multimedia.

www.wellcome.ac.uk/soss

Top and above
An arm with ants, and a distant doorway, are just two of the images produced by Deborah Padfield in collaboration with sufferers of chronic pain.

Left The Science on Stage and Screen project 'Feeling Hurt' presents the many facets of pain.

The truest portrait



Sir John Sulston and prominent young British artist Marc Quinn unveiled a new portrait at the National Portrait Gallery in September 2001.

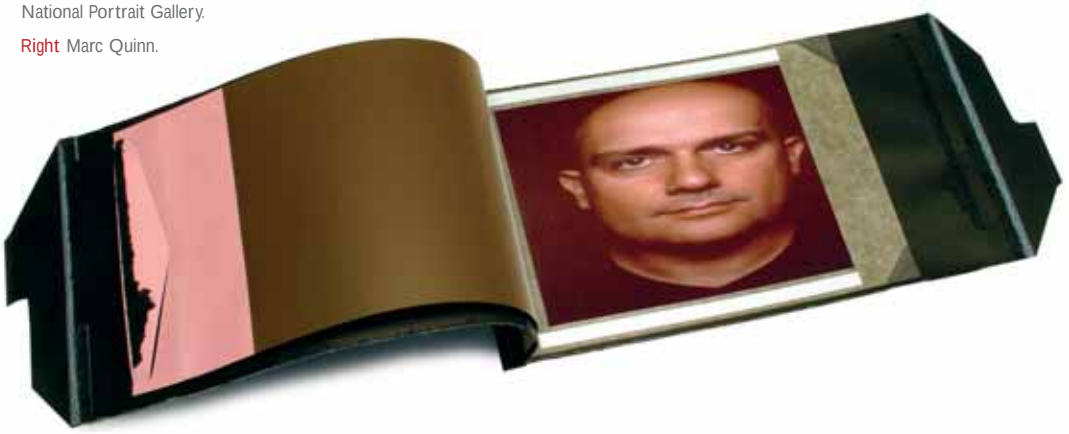
'A Genomic Portrait: Sir John Sulston' by Marc Quinn is the result of a collaboration between the artist and the sitter in which John Sulston contributed a sample of his DNA to be used by Marc Quinn in the work. The work is the first entirely conceptual portrait to be acquired by the gallery and was commissioned with the support of the Trust.

While abstract in the aesthetic sense, the portrait provides an exact representation of the sitter, and precisely captures what is unique about him, in that it presents a detail of Sulston's genome.

Marc Quinn first came to prominence in 1991 when he exhibited 'Self', a cryogenic sculpture, in which his head was cast in his own frozen blood.

Above right 'A Genomic Portrait: Sir John Sulston' by Marc Quinn was the first conceptual portrait to be acquired by the National Portrait Gallery.

Right Marc Quinn.



Man and machine

Launched at a special event on 23 March 2001, 'Sci-art: Bio-robotic choreography' brought together artists, scientists and technicians for an intriguing exploration of the relationships between humans and machines.

With funding from the Trust, the Performance Arts Digital Research Unit at Nottingham Trent University joined forces with the School of Cognitive and Computer Sciences at the University of Sussex to develop an insect-like robot large enough to support a human.

The robot works in partnership with a human body – performance artist Stelarc – to experiment with alternative kinds of choreography. Over the last 30 years, Stelarc has gained acclaim for his examination of the body's capabilities and experiences through augmentation and extension using prosthetics, robotics, virtual reality systems and the Internet.

The 13-month project concluded with a series of performances held at Nottingham, Brighton and London in November and December 2001.

More details at
www.stelarc.va.com.au/exoskeleton
art.ntu.ac.uk/dru/sci-art.htm

Geology of Biology

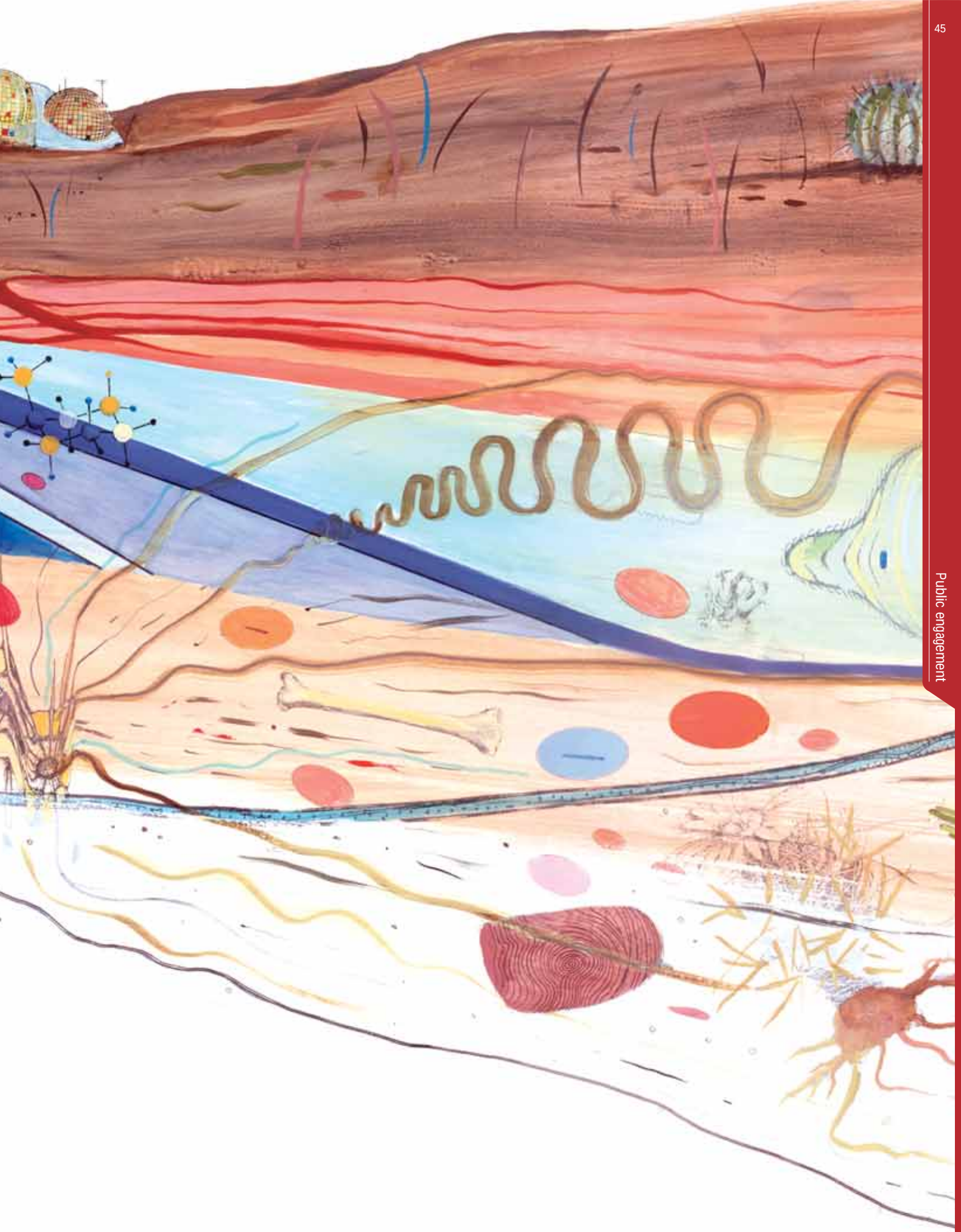


The Wellcome Trust unveiled the UK's longest public artwork in October 2001. New York artist Jason Middlebrook was commissioned to create a visually stimulating artwork for the hoarding obscuring the construction site for the new Wellcome Trust headquarters at 215 Euston Road. The artwork fills a three-metre high space running 90 metres along Euston Road and a further 30 metres down Gower Street.

Jason Middlebrook's work, 'The Geology of Biology', was inspired by the work of the international Human Genome Project. Jason worked closely with his immunologist brother, Aaron, who took leave of absence from his research to brief him on the science.

The hoarding is reflected in a sculpture Middlebrook created for the windows of the TwoTen Gallery, on the other side of Euston Road, which complemented the exhibition 'Working Drafts: Envisioning the human genome'.

The 'Geology of Biology' can be explored online at www.wellcome.ac.uk/geologyofbiology.



A year at the Trust





Far left The *Wellcome News Supplement* 'Unveiling the Human Genome', commemorated the publication of the scientific papers describing the human genome. www.wellcome.ac.uk/genome

Left An artist's impression of the Wellcome Trust's new headquarters at 215 Euston Road, due to be completed in 2004.

Below Chris Coyer.



New Governors

Four new Governors joined the Trust in October 2000.

Professor Adrian Bird has held the Buchanan Chair of Genetics at the University of Edinburgh since 1999, and he is Director of the Wellcome Trust Centre for Cell Biology at the University of Edinburgh.

Professor Jean Thomas has been in Cambridge since 1967. She became Professor of Macromolecular Biochemistry in 1991 and Director of the Cambridge Centre for Molecular Recognition in 1993.

Professor Mark Walport has been head of the Rheumatology Section in the Royal Postgraduate Medical School at Hammersmith Hospital since 1985, and became head of the Division of Medicine at Imperial College of Science, Technology and Medicine, London, in 1997.

Edward Walker-Arnott has extensive experience as a commercial lawyer, including banking, insurance, employment, venture capital and intellectual property rights.

Alastair Ross Goobey became a Governor in January 2002. An experienced investment manager, he retired as Chief Executive of Hermes Pensions Management Ltd in December 2001.

New heads of Science Funding and MSH

Rick Fuller, formerly a Vice-President at GlaxoSmithKline, was appointed the new Director of Science Funding at the Wellcome Trust. Clare Matterson, formerly Head of the Policy Unit at the Trust, was appointed Director of the Medicine, Society and History (MSH) Division.

Chris Coyer (1955–2001)

Chris Coyer, Head of the Wellcome Trust's Tropical Medicine Resource, died suddenly in November 2001.

Chris joined the Tropical Medicine Resource in 1997, spearheading its production of 'Topics in International Health' CD-ROMs – interactive teaching aids for tropical diseases. Under his guidance the Tropical Medicine Resource flourished, producing a stream of well-received disks and achieving impressive sales figures. Chris's dedication to the Tropical Medicine Resource was undoubted, yet those who knew him will most remember his good nature, his sense of humour, his down-to-earth attitude, and perhaps most of all his ability to enjoy life to the full. He will be sadly missed.

Cornerstone project

Work on the Wellcome Trust's new headquarters at 215 Euston Road – the 'Cornerstone project' – continued apace over the year. The new building, designed by architects Michael Hopkins and Partners, will bring together the Trust's 600 or so staff, who are currently dispersed over five buildings. The building will be completed in early 2004.

Sir John Sulston knighted

Sir John Sulston, former Director of the Wellcome Trust Sanger Institute, received his knighthood from HM The Queen on 5 June 2001. Sir John also appeared on BBC Radio's *Desert Island Discs*. As well as revealing an eclectic taste in music – from Mozart to Kirsty MacColl – the ever democratic Sir John also persuaded the studio team to take a vote on his record selection.



New constitution

In collaboration with the Charity Commission, the Wellcome Trust has produced a new constitution to replace Sir Henry Wellcome's will and 60 years of court orders interpreting the will. The new constitution, which came into effect in February 2001, is the Trust's governing document, establishing exactly what the Trust is able to do. The Wellcome Trust's Memorandum and Articles of Association – which specify some of the mechanics of how the constitution will operate in practice – have also been updated.

Trust website

The Wellcome Trust's website continues to be expanded and improved. A major revamp of the 'About the Wellcome Trust' section was launched during the year, and the microsite on the human genome, produced to coincide with the publication of the human genome papers and the commemorative *Wellcome News* supplement (*see page 8*) received tens of thousands of visitors.

www.wellcome.ac.uk/awt
www.wellcome.ac.uk/genome

Hanging

Aya Ben Ron, the Trust's second Artist-in-residence, produced the remarkable 25-metre fiberglass banner, 'Hanging', on display in the stairwell of the Wellcome Building.



Stem cells

The Trust, along with other medical research charities, briefed members of the House of Commons and the House of Lords on the potential that stem-cell research offers for the development of new treatments for a wide range of debilitating or life-threatening diseases. Both Houses approved changes in the Act covering the use of human embryos in research. More recently, the Director of the Trust appeared before a House of Lords Select Committee to give further evidence and answer questions on this topic



Far left John Sulston was awarded a knighthood for services to genome research.

Left 'Hanging' by Aya Ben Ron.

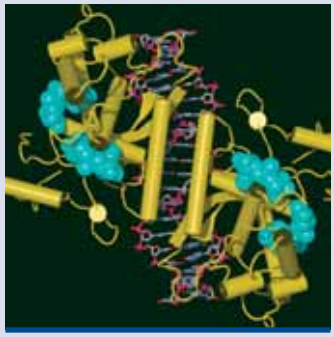
Above The Trust's new constitution replaces Sir Henry Wellcome's will, and 60 years of court orders interpreting the will, as its governing document.

Encouraging good practice

The Wellcome Trust has produced draft guidelines on good practice in biomedical research, including the handling of allegations of scientific misconduct. Central to the proposed guidelines is the need for institutions in the UK and Republic of Ireland that apply for Trust funding to have in place published standards of good research practice, including a formal written procedure for the investigation of allegations of scientific misconduct. The guidelines, when finalized, will be incorporated into the Wellcome Trust's formal Grant Conditions from October 2002.

UK Funding

The Wellcome Trust makes an important contribution to UK research through its ongoing support of innovative, investigator-led proposals in all areas of biomedical science. During 2000/01, more than £95 million was allocated through the four main UK Panels, supporting project grants and 30 new five-year programme grants in academic institutions across the UK. Nine University Awards were also made, helping to create permanent academic posts in universities.



Neurosciences

The Neurosciences Panel awarded £26.6 million of project and programme grants, including seven new programme grants, and five University Awards.

A cluster of Neurosciences grants awarded focused on the cognitive processes involved in various neuropsychiatric conditions. At the University of Oxford, Professor Chris Fairburn was awarded a programme grant in association with his Principal Research Fellowship to look at cognitive behaviour therapy for eating disorders (*see page 29*); Dr Kate Davidson received a project grant to study cognitive behaviour therapy and borderline personality disorder at the University of Glasgow; Professor David Clark at King's College, London, was awarded a programme grant to look at cognitive processes in treating post-traumatic stress; and Professor Philippa Garety at St Thomas' Hospital, London, received a programme grant to examine cognitive processes in treating psychosis.

Infection and Immunity

The Infection and Immunity Panel spent £26.5 million, including six new programme grants and one University Award.

The Panel took over the management of grant applications to sequence the genomes of pathogens, previously handled by the Beowulf Genomics Initiative. A number of pathogen-sequencing projects funded during the year focused on comparative sequencing of pathogen strains, including the genomes of six *Plasmodium* (malaria) species, *Escherichia coli* and *Shigella* (gastrointestinal diseases) and *Salmonella* (food poisoning).

A meeting on *Salmonella* genome projects was held at Hinxton Hall Conference Centre in November 2000, as part of a series of Trust-funded pathogen genome meetings, which provide a forum for the debate and dissemination of research data and information related to pathogen genome sequencing.

Physiology and Pharmacology

The Physiology and Pharmacology Panel funded £15.6 million of project and programme grants, including seven new programme grants and one University Award.

Grants awarded included three related to studies of the heart: Professor Charles McCollum at the University of Manchester received a project grant to investigate the causes of cardiovascular death in young people; Dr Douglas Corfield at Imperial College, London, received a project grant to examine the interactions between respiratory and cerebrovascular regulation during sleep; and Professor Michael Marber at St Thomas' Hospital, London, received a project grant to identify genes that protect the heart from ischaemia (damage caused by lack of oxygen).

Molecular and Cell

The Molecular and Cell Panel awarded £23.4 million of project and programme grants, including ten new programme grants.

Four grants relating to the structural analysis of DNA and the interaction of proteins with DNA were awarded: Professor Simon Phillips at the University of Leeds received a programme grant to study the structure and function of proteins that recognize unusual branched DNA structures; at the University of Bristol, Professor Stephen Halford was awarded a programme grant to study the role of proteins in DNA looping; Professor Ernest Laue at the University of Cambridge received a programme grant to carry out structural studies of proteins involved in the control of chromatin structure; and Professor Robert Lloyd at the University of Nottingham was awarded a project grant to investigate genome dynamics and the interplay between DNA replication, transcription and repair.

Showcase

A review of the Showcase scheme indicated it had been successful in supporting innovative, high-risk projects, the majority of which would not otherwise have received funding, and therefore occupied a neglected niche in UK biomedical science funding. An important feature of the scheme was that it enabled young postdoctoral researchers to be principal grant holders. However, the use of peer review slowed the decision-making process, and the 18-month funding period for initial Showcase projects was often insufficient to investigate novel concepts adequately.

The scheme was relaunched for a further five years in October 2001, with a few significant changes: external peer review has been removed so that applicants should now receive a decision within three months; and awards will be made for two years, providing support of up to £125 000.

Bioarchaeology

In 2000/01, one postdoctoral Bioarchaeology Fellowship, one Advanced Training Fellowship, and two University Awards were funded.





Advisory committee	Infection and Immunity Panel	Molecular and Cell Panel	Neurosciences Panel	Physiology and Pharmacology Panel
Remit	Funds fundamental and applied research relating to infectious diseases and immunology. This ranges from epidemiology and the pathology of infections through to genetic and molecular studies relevant to infectious disease.	Considers grants applications that fall into the general area of molecular and cell biology, including biochemistry, developmental biology and genetics; proposals may involve basic, clinical or veterinary research.	Considers applications investigating the function of the nervous system in health and disease. It considers proposals in both cellular and cognitive neuroscience as well as clinically oriented proposals investigating common neurological, ophthalmological and psychiatric conditions.	Supports physiology and pharmacology in its broadest context, ranging from basic cellular and molecular studies in model systems to whole-organ and animal studies and clinical investigation, including studies of integrative physiology. Epidemiological and mathematical studies are also covered.
Total spend	£26.5 million	£23.4 million	£26.6 million	£15.6 million
Applications (new grants)	366 applications 115 awards	361 applications 119 awards	307 applications 121 awards	266 applications 88 awards
Award rate	31%	33%	39%	33%

Top, left Professor Simon Phillips is studying protein–DNA interactions.

Top, middle Dr Kate Davidson at the University of Glasgow is studying cognitive behaviour therapy and borderline personality disorder.

Top, right A meeting on *Salmonella* genome projects was held at Hinxton Hall in November 2000.

Career Schemes and Clinical Initiatives

The Wellcome Trust's programme of personal support schemes aims to provide flexible career opportunities for UK-based basic and clinical researchers, at key stages from starting out through to the pinnacle of a research career. Specific clinical initiatives help ensure that patients continue to reap improved healthcare benefits from Trust-funded research. In 2000/01, £64.8 million was spent providing personal support for outstanding scientists at all levels and supporting specific clinical initiatives.



Personal awards

In 2000/01, the Trust awarded two new Principal Research Fellowships to Dr Lon Cardon at the Wellcome Trust Centre for Human Genetics, University of Oxford (*see page 21*), and to Dr Robin Allshire at the Wellcome Trust Centre for Cell Biology at the University of Edinburgh. There are currently 38 Principal Research Fellows.

Two Principal Research Fellows, Professor Christopher Frith at the Institute of Neurology, London, and Professor Patricia Simpson at the University of Cambridge, were elected Fellows of the Royal Society, while two others, Professor Alan Fairlamb and Professor Jeffrey Williams at the University of Dundee, were elected Fellows of the Royal Society of Edinburgh.

Other fellowships for experienced researchers in basic science included eight new Senior Research Fellowships (of which six progressed from Research Career Development Fellowships) and 16 new Research Career Development Fellowships.

Awards made for research training in basic science included five Advanced Training Fellowships, seven Prize Fellowships, 73 Prize Studentships and 308 Vacation Studentships. Five awards were also made for Research Training Fellowships in Mathematical Biology. Ongoing support was provided for 12 Four-year PhD Programmes in the UK.

For UK-based clinically qualified researchers, the Trust continued to provide a range of awards, including four Senior Research Fellowships in Clinical Science, three Research Leave Awards for Clinical Academics and 15 intermediate-level fellowships. For those beginning a research career, 46 awards were made (27 Research Training Fellowships and 19 Entry Level Training Fellowships).

The Trust also provided five fellowships for research training in Clinical Epidemiology and one Health Services Research fellowship.

Hinxton meeting on careers

In July 2001, delegates from academia, funding agencies, the Government and industry attended the 'Radical Thinking, Creative Solutions: Career issues in UK academic research' conference at Hinxton Hall. This one-off Trust-hosted conference aimed to stimulate innovative thinking on some of the difficulties faced by UK academic researchers. *See page 18* and www.wellcome.ac.uk/radicalthinking.

'Review of Wellcome Trust PhD Research Training: The supervisor perspective'

July 2001 saw the publication of the third and final report in a series of studies examining Wellcome Trust PhD research training. 'Review of Wellcome Trust PhD Research Training: The supervisor perspective' follows on from previously published reports, 'The Student Perspective', and 'Career Paths of a 1988–1990 Prize Student Cohort'.

Taken together, the three reports constitute a comprehensive review of just over a decade of PhD student support by the Trust. This final report explores the opinions and experiences the views of 172 UK academic supervisors of current Wellcome Trust-funded PhD students. Among other important highlights, the report showed that:

- The majority of supervisors thought that it was unrealistic to train a student solely for a career in academic research, and that the purpose of PhD training was to train students for a career in scientific research in general; moreover, a fifth of supervisors thought that such training should foster a wide range of careers, not only for scientific research.
- Almost half of the supervisors felt that it is now more difficult to recruit PhD students than it was five years ago, citing poor financial rewards and long-term career prospects as reasons.
- Supervisors' suggestions for improving the quality of UK PhD student recruitment centred on improving academic salaries and career structure.

Cardiovascular Research Initiative

The Cardiovascular Research Initiative, based in Edinburgh and Oxford, continues to build research capacity in the molecular and cellular aspects of cardiovascular disease by supporting the training and career development of clinical and basic scientists in the field. Each centre provides a portfolio of personal award schemes at all levels of research experience.

Clinical Research Facilities

In a £18 million venture, five Clinical Research Facilities (CRFs) – major new facilities dedicated to patient-oriented research – have been built across the UK. The CRFs, which will be run collaboratively by universities and hospital trusts, will enable diseases to be studied in greater detail and potential new therapies to be tested on patients in a hospital setting.

The Edinburgh Clinical Research Facility was opened by Her Majesty The Queen on 6 July 2001. The Southampton CRF opened in November 2001, the Cambridge CRF and the Birmingham CRF in January 2002, and the Manchester CRF is due to open in July 2002.

Primary Care Sciences Research Centre in Keele

At the University of Keele, Professor Peter Croft was awarded a grant of nearly £740 000 to fit out the research space for the Primary Care Sciences Research Centre. The Centre works with 18 general practices in the North Staffordshire area on a mutual programme of research aimed at determining the most effective way to treat back, neck and joint pain in primary care. To date it has been





Advisory committee	Basic Science Interest Group	Clinical Interest Group	Veterinary Medicine Interest Group
Remit	This group is responsible for several schemes including: the Prize (PhD) Studentships, Four-year PhD Training Programmes, Research Career Development Fellowships in Basic Biomedical Science. A separate subcommittee is responsible for Research Training Fellowships in Mathematical Biology.	The schemes that support the clinical and research training needs of medical and dental graduates are the responsibility of this group. A separate subcommittee advises on Training Fellowships in Clinical Epidemiology and Health Services Research (CEHSR). The CEHSR portfolio includes a scheme for project grant support.	The Group advises the Trust on any matters relating to veterinary research in a national context and on the training needs of the profession. It considers applications for intercalated BSc awards to veterinary undergraduates and for other veterinary research training grants.*
Total spend	£39.1 million	£16 million	£0.2 million
Awards include:			
Senior-level fellowships	£17.3 million	£5.3 million	
Intermediate-level fellowships	£7.4 million	£5.0 million	
Training fellowships and studentships	£14.4 million	£5.7 million	£0.2 million
Subcommittees	Mathematical Biology committee: £0.7 million	CEHSR committee: £2.2 million	

dispersed across several sites on the university campus, at local hospitals and a number of general practices and health centres. The award will enable the academics, support staff and a coordinating centre for the clinical network to be housed in a single building on a green-field site on the campus complex. Construction began in the summer of 2001, and the building is due to open in late 2002.

* Applications for project and programme grant support for veterinary research are considered by the Trust Panel most relevant to the subject of the proposed research. Applications from veterinary graduates for personal support (fellowships and studentships) are taken through the schemes run by either the Basic Science Interest Group or the Clinical Interest Group, depending on which is most appropriate for the research training and career needs of the individual.

Top Patient-oriented research at the Wellcome Trust Clinical Research Facilities in Southampton (left) and Birmingham (middle) aims to ensure that advances in biomedical science feed through into improvements in healthcare.

Top, right The Primary Care Sciences Research Centre in Keele is investigating the most effective way to treat back, neck and joint pain.

International Programmes

Although the greater part of its annual spend goes to foster and promote UK research, the Trust also funds research outside the UK, spending £60 million in 2000/01. The Trust's three International Programmes aim to support research and associated activities aimed at improving human and animal health in developing countries, fostering a research environment in which such countries are able to address their own health needs through research, and facilitating the application of research results into policy, practice and product development.

INTERNATIONAL BIOMEDICAL

International Senior Research Fellowships (ISRFs)

Of the 12 five-year ISRFs awarded to outstanding scientists in New Zealand, Australia, South Africa and India this year – enabling them to advance their research careers in their home countries – five went to researchers in India. These were Drs Amit Sharma, Sahid Jameel, Rajesh Gokhale and Neeraj Jain in New Delhi and Dr Sikha Laloraya in Bangalore.

A new ISRF scheme was launched in central Europe, inviting applications for five-year ISRFs in biomedical science in the Czech Republic, Estonia, Hungary and Poland to build capacity in these countries by encouraging indigenous scientists to establish laboratories in their home countries. Interviews are due to take place in June 2002.

Having achieved most of its aims, the highly successful ISRF scheme in Australia and New Zealand will be brought to a close at the end of the 2001/02 funding year. *See page 20.*

Collaborative Research Initiative Grants

The Wellcome Trust awarded three CRIGs to neuroscience research at the Bogomoletz Institute in Kiev, Ukraine during 2000/01, all for work on signalling mechanisms in excitable cells. Dr Sergey Marchenko is collaborating with the University of Cambridge; Dr Alexander Zholos with St George's Hospital Medical School, London; and Professor Vladimir Skok with University College London. Three earlier CRIGs awarded to the Bogomoletz Institute also remained active during the year, and Dr Oleksander Tarasenko received an International Research Development Award in collaboration with University College London.

Three CRIGs remained active at the Camponar Institute in Argentina during 2000/01. These were held by Dr Gonzalo de Prat Gay, Dr Pablo Wappner and Dr Pitossi Fernando, in collaboration with the Universities of Cambridge, Oxford and Southampton, respectively.

TROPICAL MEDICINE

Overseas Fellowships

Eight awards were made to scientists in developing regions to study diseases of particular local relevance, including human herpes virus, Buruli ulcer, trypanosomiasis, leishmaniasis and cysticercosis. Research Development Awards in Tropical Medicine were made to: Dr F Kasolo in Zambia, Dr J E Chisi in Malawi, Dr A Y Mensah in Ghana, Dr R Rodriguez-Canul and Dr E A Rebollar-Tellez in Mexico, and Dr J E Salcedo Sora in Colombia. Training Fellowships were awarded to Dr R Phillips in Ghana and Dr R Nwuba in Nigeria.

Nine personal awards were made in association with the five UK Centres for Research in Clinical Tropical Medicine: five Training Fellowships, three Career Development Fellowships and a Career Post in Clinical Tropical Medicine. These awards enabled European researchers to work in Peru, Kenya, Vietnam, Malawi, The Gambia, Zimbabwe and Uganda. In addition, two fellowships were awarded to nonclinical scientists, Dr P Holding and Dr C Molyneux, to work on malaria at the Kenyan unit in Kilifi, and one award to a veterinary scientist, Dr C Oura.

Wellcome Trust–Burroughs Wellcome Fund

Six awards, totalling £5.6 million, were recommended in the second and final competition of the Wellcome Trust–Burroughs Wellcome Fund Infectious Diseases (WT–BWF) Initiative. The awards support research throughout Africa, South America and Asia, covering some of the major public health problems in the developing world, including tuberculosis, malnutrition and diarrhoea.

Clusters

Clusters of Trust awards are starting to form in Uganda, Peru and India. Considerable added value can be gained in collaborations, leading to the growth and flourishing of local centres of excellence in tropical medicine research through shared expertise, facilities and other resources.

Trust-funded research teams in Uganda are focusing on important local infectious diseases. For example, Dr Alison Elliott, who holds a Career Post in Clinical Tropical Medicine, is a collaborator on a WT–BWF programme grant to work on multidrug-resistant tuberculosis, and is supervising Dr Mike Brown, a Training Fellow working on the effect of HIV on helminth infections.

There are now two WT–BWF awards based in Peru. Both involve teams from Imperial College, London working with partners in the USA and Peru studying cysticercosis and intervention strategies for the prevention of sexually transmitted infections.

Two scientists from the Trust's former Tropical Medicine unit at the Christian Medical College in Vellore, India, successfully competed for WT–BWF awards. *See page 32.*

Tropical units

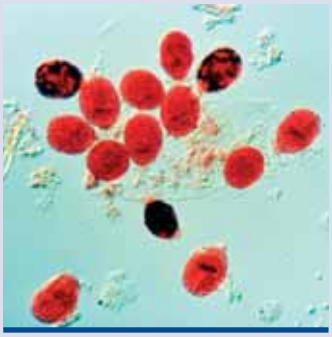
The Bill and Melinda Gates Foundation awarded a grant to build upon an innovative malaria treatment developed by Professor Nick White, Dr François Nosten and colleagues through research at the Wellcome Trust's South-East Asia unit in Thailand. *See page 33.*

HCPC

Launch of new programme

The Wellcome Trust's Population Studies Programme and the Noncommunicable Diseases Initiative were combined and relaunched in 2001 as the Health Consequences of Population Change (HCPC) Programme. *See page 12.*
www.wellcome.ac.uk/hcpc







Advisory committee	International Interest Group	Population Studies Panel*	Tropical Medicine Interest Group
Remit	Develops international research strengths, through fellowship exchange and collaboration. Senior fellowship schemes are run in several overseas countries.	Supports research in population studies and reproductive health targeted at areas of most need – developing and restructuring countries.	Promotes research in tropical medicine (infectious and noninfectious diseases) in developing countries through major programmes, training and career opportunities.
Total spend	£22.2 million	£9.3 million	£12.7 million§
On longer-term support†	£5 million	£6.7 million	£8.9 million§
Applications			
Number considered	539 applications 288 awards	76 applications 36 awards	99 applications 52 awards
Success rate			
All new grants	53%	47%	53% (excluding WT–BWF awards)
Major awards	12 International Senior Fellowships (New awards total: £5.3 million)	£670 000 to the American University in Beirut	6 WT–BWF awards recommended (2 awards finalized in 2000/01)
	21 Major equipment awards	£1 million to the Asian Metacentre	1 Senior Fellowship
		£4 million to the Africa Centre	1 Programme grant

Beirut Centre

Dr Huda Zurayk and her team at the American University of Beirut were awarded £670 000 for a wide-ranging study of the health consequences of population change across the Middle East. The award will enable Dr Zurayk and her colleagues to forge links with other centres in the Middle East, such as the American University of Cairo in Egypt, and will contribute to the regeneration of the academic science base in Lebanon.

Asian Meta-centre

Professor Brenda Yeoh at the National University of Singapore and her colleagues at Chulalongkorn University, Thailand, successfully applied for a renewal of the Asian Meta-centre award.

The Meta-centre – a 'virtual' centre electronically linking six centres of population research in Asia with technical support from Vienna – will receive over £1 million for a further three years.

Africa Centre

Researchers at the Africa Centre for Health and Population Studies in KwaZulu-Natal, South Africa – which is supported through the Trust's HCPC Programme – were awarded £4 million for a three-year study aimed at reducing mother-to-child transmission of HIV. *See page 12.*

The work of the Africa Centre is underpinned by a £5 million demographic study to understand the structure and dynamics of the population. *See page 12.*

* Replaced by the HCPC Programme in October 2001.

† Includes overseas research units and grants over three years' duration.

§ Includes £2 million for WT–BWF Initiative.

Top, left Kevin Marsh, Director of the Kenya unit at Kilifi.

Top, middle Cysticercosis – a tapeworm infection – affects millions of people worldwide, and is the subject of a WT–BWF award in Peru and a Research Development Award in Tropical Medicine in Mexico.

Top, right A new £4 million study at the Africa Centre aims to reduce mother-to-child transmission of HIV.

Centres and Initiatives

The Wellcome Trust supports a number of important enterprises in academic institutions through major awards, including infrastructure awards, core funding for centres of excellence, and large-scale initiatives in strategic areas such genome sequencing and functional genomics.



Wellcome Trust Sanger Institute

On 15 October 2001, the Wellcome Trust Sanger Institute announced a new five-year £300 million programme to take it into the postgenomic era. Research teams at the Sanger Institute will begin to determine the roles genes play in building and maintaining a healthy body, and in the development of disease. Under the leadership of its new Director, Dr Allan Bradley, the Sanger Institute will build on its strengths: large-scale genome analysis of human, pathogen and model organism systems; new high-throughput technologies; and bioinformatics.

Integrative Physiology

The Integrative Animal and Human Physiology initiative – promoting research exploring the relationship between genomic data and physiological mechanisms in humans and animals – received 31 preliminary applications by October 2000. Of these, ten full applications were invited, from which the Trust expects to support three to five proposals from a total budget of £15 million over five years.

Functional Genomics

The Functional Genomics Development Initiative's thematic programmes scheme – which aims to build multidisciplinary collaborations in functional genomics technologies focusing on a single biological question – was launched with a budget of £45 million. From the 37 preliminary applications considered in May 2001, 11 full applications were invited for consideration in January 2002. It is expected that awards will be in the region of £5 million each.

In June 2001, the Wellcome Trust announced core funding for the Avon Longitudinal Study of Parents and Children (ALSPAC). *See page 19.*

In 2000/01 the Functional Genomics Development Initiative committed £12.6 million on grants, including funding for seven bioinformatics grants and ten biological collections grants.

Centres

In the light of the new Wellcome Trust Corporate Plan, published in December 2000, the Centres programme is being reviewed and no new applications are being accepted at this time. To date, Centre status has been awarded to six research groupings:

- Wellcome Centre for Molecular Parasitology at the University of Glasgow;
- Wellcome Trust Centre for Cell Biology at the University of Edinburgh;
- Wellcome Trust Centre for Cell-Matrix Research at the University of Manchester;
- Wellcome Trust–Cancer Research UK Institute of Cancer and Developmental Biology at the University of Cambridge;
- Wellcome Trust Centre for Human Genetics at the University of Oxford; and
- Wellcome Trust Centre for the History of Medicine at University College London.

The Wellcome Trust Centre for Cell Biology in Edinburgh was awarded full Centre status in October 2001, receiving core funding of £3.4 million for five years. Three members of staff – Professors Jean Beggs, David Tollervey and Adrian Bird – were also coapplicants on a successful JIF bid for the Edinburgh Protein Interaction Centre, to be based in the Chemistry Department (the principal applicant was Professor Peter Sadler).

Special initiatives

In November 2000, the Wellcome Trust and the Juvenile Diabetes Research Foundation International (JDRF) provided a joint major award of £20 million, over five years, to set up a new Diabetes and Inflammation Laboratory at the University of Cambridge. Led by Professor John Todd, one of the world's leading researchers on the genetic causes of type 1 diabetes, the new laboratory is situated in the new Wellcome Trust–MRC Building, which was opened by HRH The Princess Royal on 30 October 2000.

The former Wellcome Trust Centre for Molecular Mechanisms in Disease at the University of Cambridge became a 'Strategic Initiative in Clinical Sciences' and gained funding for a further five years.

JIF/SRIF

The fourth and fifth rounds of the £750 million Joint Infrastructure Fund (JIF) were completed, bringing the initiative to a close. The Wellcome Trust contributed £300 million to the initiative, providing funding to 25 institutions.

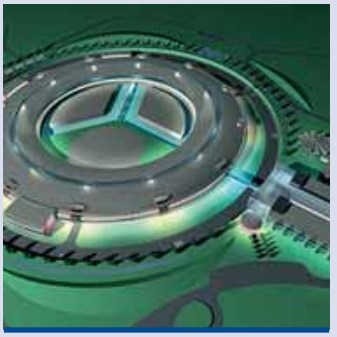
The final Joint Executive Committee at which the remainder of the funds were allocated was held in March 2001.

Eight JIF construction projects were completed during the year in London, Bristol, Strathclyde, Dundee, Edinburgh, Newcastle and Liverpool. A further 17 were in progress.

The first four awards under the £150 million Science Research Investment Fund were made by the Trust. These awards, worth £25 million, were made to the Institute of Cancer Research, the University of Bristol, the University of Aberdeen, and the Imperial College of Science, Technology and Medicine in London.

Research Partnerships and Ventures

The Wellcome Trust is involved in a number of collaborations with academic centres, other funding agencies, governments and industry to speed up biomedical discovery, avoid duplication of effort, and disseminate knowledge so that healthcare advances can be achieved more swiftly.





SNP Consortium

The SNP Consortium is a £30 million collaboration between the Trust, 13 pharmaceutical and technological companies and leading academic centres, in which the Wellcome Trust invested £9 million. It vastly exceeded its original goal to identify 300 000 single nucleotide polymorphisms (SNPs) in the human genome. By September 2001, the Consortium had identified 1 255 326 SNPs, all of which had been mapped onto the working draft of the human genome.

The information gathered by the SNP Consortium is publicly available to researchers on the Internet, and should help in the development of treatments specifically tailored to individuals.

The Consortium is currently considering its future role and the potential for future funding of other scientific projects.

Mouse Consortium

In October 2000, the US National Institutes of Health, the Wellcome Trust and three private companies announced that they had formed a US$58 million (£40 million) public–private consortium to sequence the mouse genome.

On 8 May 2001, the Mouse Sequencing Consortium announced that it had completed the first phase of reading the mouse genome (covering an estimated 94 per cent of the genome), reaching its goal on time and within budget.

Synchrotron

On 31 October 2000, the interim Board of Directors for the Diamond Project agreed unanimously on the design for 'Diamond' (the name of the new synchrotron). Their decision was in line with advice received from the Scientific Advisory Committee and the Technical Advisory Committee, which met during September and October 2000, and consultations held with the wider user community over the past two years. The decision represented a major milestone in the project.

Also on 31 October 2000, the Board initiated the process of recruiting a number of key senior appointments for the project.

On 25 July 2001, Professor Gerhard Materlik, from the DESY Laboratory in Hamburg, Germany, was appointed the new Chief Executive Officer for the Diamond Synchrotron Project.

Structural Genomics

The business plan for the Structural Genomics Consortium – a potential public–private initiative aiming to produce three-dimensional structures for all human proteins – was completed and four companies committed in principle to the Consortium.

Advanced Courses

The 28th, 29th, 30th and 31st Wellcome Trust Advanced Courses were held at the Genome Campus in Hinxton, Cambridge in 2000/01. These advanced, residential, laboratory-based courses aim to provide scientists with 'hands-on' training in advanced, state-of-the-art, research techniques directly applicable to their current research interests. 'Molecular Cytogenetics and Microarrays' took place in March 2001 followed by 'Functional Genomics' in June 2001. 'Human Genome Analysis: Genetic analysis of multifactorial diseases' was held in July 2001 and 'Genetic, Molecular and Informatic Methods for *C. elegans*' rounded off the academic year in September 2001.

Genome Annotation Conference with Cold Spring Harbor

In August 2001, 'Genome Informatics', the first of a new series of conferences jointly funded by the Wellcome Trust and Cold Spring Harbor Laboratory, was held at the Hinxton Hall Conference Centre. Some 271 delegates attended to disseminate new genomics-related knowledge and network with other scientists. The next 'Genome Informatics' conference will be held in September 2002.

Genome Campus: Hinxton retreat meetings

Hinxton Hall Conference Centre is the venue for a series of Wellcome Trust-funded 'invitation-only' meetings, which address areas of current scientific interest in an informal but intensive way.
Four meetings were held during the year: 'Intellectual Property Rights' in December 2000, 'Behavioural Genetics' in March 2001, 'Infectious Disease' in June 2001, and 'Genome Informatics' in August 2001.

Above, left Plans for the new synchrotron.

Above The Hinxton Hall Conference Centre.

Opposite page Construction of JIF-funded buildings, such as this centre for research in clinical vaccinology and tropical medicine in Oxford, continued apace in 2001.

Medicine, Society and History

Through its Medicine, Society and History division, the Wellcome Trust aims to deepen understanding of the impact of science on society in the past, present and future, to foster public trust and confidence in science and ultimately to create an environment conducive to scientific exploration informed and guided by sound ethical principles.



BIOMEDICAL ETHICS

Programme renewal

Following an internal review of the Biomedical Ethics Programme, in June 2001 the Programme was renewed and expanded with a threefold increase in funding – £15 million over the next six years – to continue its support of research into the ethical, legal and social implications of biomedical research. There are two changes to the Programme:

- as research funded by the Programme starts to come to fruition, there will be an increased emphasis on disseminating research outputs to policy makers;
- a third theme, international biomedical ethics, will be added to the existing themes of genetics and neuroscience.

Outputs

Following a workshop organized by the UK Forum on Healthcare Ethics, Dr Priscilla Alderson's two reports: 'On Doing Qualitative Research Linked to Ethical Healthcare' and 'Qualitative Research: A vital resource for ethical healthcare' were published by the Trust.

Professor Hilary Rose followed her original report on Iceland's DNA database project with a new report, 'The Commodification of Bioinformation: The Icelandic Health Sector Database', published in March 2001.

Summer school

A residential summer school, 'Genetics and Society', took place on 3–6 September 2001. The aims of the summer school are to generate interest in the field, foster understanding across the physical and social sciences and the humanities, and to stimulate new thinking and research collaborations.

CONSULTATION AND EDUCATION

Research grants

The first Public Engagement with Science Postdoctoral Fellowship was awarded to Dr Kerry Kidd at the University of Nottingham, to study the representation of mental illness in contemporary television programmes for a three-year period.

The call for proposals for Novel Public Consultation Methods was launched in early 2000 with the aim of developing more effective methods for divining public opinion. Five proposals were funded, covering a spectrum of methods, including the combining of expert and lay opinions of risk; use of local newspaper questionnaires and video recordings.

Public Engagement Impact Awards

The Science and Plants in Schools (SAPS) Biotechnology Project was awarded funding for three week-long residential summer schools at Edinburgh University in 2001, 2002 and 2003. The aim is to update teachers and lecturers about recent developments in molecular biology.

The Trust awarded a grant to set up a permanent network of 20 Cafés Scientifiques in major cities throughout the UK over the next three years. These bars or cafés will provide a forum for people to come and listen to expert speakers and discuss the latest ideas of science and technology.

'Ego', a Trust-funded series of four evening talks, was held at the Old Operating Theatre at South Bank University, London. Controversial and leading practitioners from the worlds of science and art shared and discussed fundamental ideas behind their work.

In July 2001, two performances of 'Yerma's Eggs' were held at the University of North London. This theatre and multimedia project, supported by the Wellcome Trust, explores infertility and biomedical ethical issues surrounding assisted reproduction technologies.

Major awards

The Glasgow Science Centre was opened in June 2001 and Thinktank at Millennium Point in Birmingham opened in September 2001. *See page 38.*

The Wellcome Trust awarded £3 million to create a new centre for public engagement with science: the Dana Centre. Co-funded by the Wolfson Foundation, the Dana Foundation and the Garfield Weston Foundation, the centre will be housed in the Wellcome–Wolfson building, due to be completed in 2003, which is located next to the Wellcome Wing of the Science Museum. Public engagement activities will be run as a partnership between the Science Museum and the British Association for the Advancement of Science.

Commissioned research

The Wellcome Trust commissioned research to find out how teachers tackled socioscientific issues in the classroom. A summary – *Valuable Lessons: Engaging with the social context of science in schools* – was published in July 2001. *See page 36.*

Research sponsored by the Wellcome Trust and the Office of Science and Technology looked into public attitudes to science in the UK. *See page 37.*

The Trust commissioned a large-scale survey of scientists' attitudes to communicating science. *See page 37.*

Other direct activities

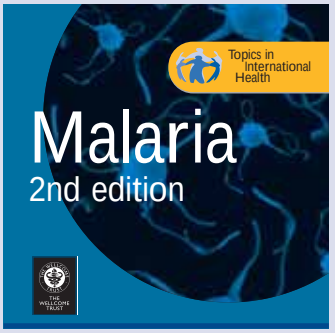
In November 2000, 'Genescope', a behavioural simulation designed to explore the relationships between different sectors of society affected by advances in genetics, was held.

The management of the Researchers-in-Residence Biosciences scheme – a joint initiative by the Wellcome Trust and three of the Research Councils – was taken over by the Centre for Science Education at Sheffield Hallam University. The scheme organizes four-day placements of PhD researchers in secondary schools.

Continued on page 58







Advisory committee	Medicine in Society Panel – Public Engagement with Science		Medicine in Society Panel – Biomedical Ethics	History of Medicine Grants Panel
Remit	To make recommendations on grant applications in the areas of public understanding of science. Awards may be for research or activities (Impact Awards).		To make recommendations on grant applications in the field of biomedical ethics.	A broad definition of the history of medicine embraces the study of all factors affecting the health experience of people and animals in all countries at all periods.
Total spend	Research awards £0.6 million	Impact Awards £0.6 million	£2.2 million	£4.4 million
Applications Number considered	37	21	36	182
Award rate	16%	48%	39%	44%*
Other initiatives				£200 000 for Research Resources in Medical History scheme.

* Of applications going to Panel.

Far left 'Yerma's Eggs', a theatre and multimedia project, explored infertility and ethical issues surrounding assisted reproduction technologies.

Above, left 'Screen' by Amirthi Perera was created for the exhibition 'Working Drafts' held in the TwoTen Gallery.

Above, middle A 'theatre' of medicine and surgery, portrayed in gouache by Johann Heinrich Ramberg (*c.* 1800) – just one of the Wellcome Library's acquisitions in the year. *See page 24.*

Above, right The second edition of the *Malaria* CD-ROM, produced by the Trust's Tropical Medicine Resource, features new tutorials and an enhanced interface.

Professor Michael Morgan from City University in London won the 2001 Wellcome Trust Book Prize, scooping £25 000 to write a popular science book. *The Space Between Our Ears: Mapping the visual world to the brain*.

The Trust's Science Centrestage initiative was launched in September 2001. *See page 41.*

EXHIBITIONS AND ART

Artists Andrea Roe and Aya Ben Ron each won a six-month residency at the Trust to research and develop artistic ideas related to biomedical science. Andrea Roe's work was inspired by the 18th-century tale of Mary Tofts who tricked the English medical establishment into believing she had given birth to rabbits. Aya Ben Ron created a 25-metre banner, 'Hanging', influenced by historical and contemporary images which scientifically depict illnesses or situations of physical crisis. *See page 49.*

New York artist Jason Middlebrook created 'The Geology of Biology'. *See page 44.*

Nine winners of the 2001 Science on Stage and Screen awards were announced in September 2001. There were two categories of awards – Live Theatre, and Broadcast and Communication Technologies – and winners received up to £40 000 to work on their projects.

Exhibitions at the TwoTen Gallery in 2000/01 included 'Shelf Life', an artistic exploration of domestic medicine cabinets; 'Growth & Form', art inspired by biomedical science displayed alongside winners of the Biomedical Image Awards 2001; 'Art and the Brain', paintings by William Utermohlen (*see page 40*); and 'Working Drafts: Envisioning the human genome', an exploration of the social and scientific implications of the Human Genome Project as depicted by seven international artists.

The first conceptual portrait to be acquired by the National Portrait Gallery – a genomic portrait of Sir John Sulston by Marc Quinn – was unveiled on 18 September 2001. *See page 43.*

HISTORY OF MEDICINE

Priority areas

The History of Medicine Programme identified seven areas that it is particularly keen to support:

- global networks of health and medicine;
- medical markets and healthcare systems;
- health, medicine and environment;
- comparative medical history;
- 20th- and 21st-century biomedical science and genetics;
- medical technologies;
- ethics and law.

New public engagement outreach activities

The Governors agreed a budget of £250 000 to bring the history of medicine to wider audiences through television, radio, exhibitions, theatre, websites, educational resources, lectures and debates. Projects which look at the past to shed light on, and stimulate informed debate around, current issues such as animal experimentation, genetics, cloning, abortion and stem-cell research are particularly encouraged.

Darwin letters

The Darwin Correspondence Project was awarded a further £700 000 by the Wellcome Trust. *See page 27.*

Foot-and-mouth debate

A Wellcome Trust PhD student's account of the history of foot-and-mouth disease in the UK contributed significantly to the press debate. Abigail Woods – a veterinary-qualified history of medicine PhD student at the Wellcome Unit for the History of Medicine at the University of Manchester – produced a detailed background to the controversial policy of slaughter adopted to control the 2001 outbreak.

THE WELLCOME LIBRARY FOR THE HISTORY AND UNDERSTANDING OF MEDICINE

Opening up access

New technology has continued to widen access to the Wellcome Library's rich collections. An automated system for archives and manuscripts was installed during the year and it will soon be possible to search for material which hitherto has only been catalogued in printed or word-processed lists. An online version of the Medical Archives and Manuscripts Survey for London went live via the Wellcome Library website. The psci-com Internet gateway – which offers guided access to websites dealing with public engagement with science – was also redeveloped and relaunched.

Collaborating with others

The Wellcome Library's Mapping Medicine project began, working with a group of other major medical libraries in central London to look at possibilities for effective collaboration in collecting and retaining medical literature, and avoiding duplication of effort.

Research Resources in Medical History

In January 2001, the Trust allocated £1 million to the two-year Research Resources in Medical History funding scheme. *See page 26.*

Acquisitions in 2000/01

The Wellcome Library's collections continued to be developed throughout the year. *See page 24.*

TROPICAL MEDICINE RESOURCE

New funding

Following an evaluation of the Tropical Medicine Resource (TMR) in June 2001, TMR was awarded five years' further funding, primarily to produce interactive training materials for healthcare professionals in resource-poor countries.

The highly successful 'Topics in International Health' series presents aspects of international and tropical health on a range of CD-ROMs, each focusing on a disease (or group of diseases) of global significance.

Updating titles

The content of the *Malaria* CD-ROM was revised and updated. The *Leprosy* CD-ROM was translated into Portuguese and Indonesian. *See page 33.*

The Open University is about to order 9000 updated *HIV/AIDS*, *Malaria* and *Tuberculosis* disks to include in a new course, 'Infectious Diseases', due to start in February 2003.

At the end of September 2001, TMR had sold 8500 disks in 102 countries. *See page 33.*

New projects

In February 2001, the Bill and Melinda Gates Foundation announced an award of US$20 million over five years to the Lymphatic Filariasis Elimination Programme – a worldwide collaboration to eliminate the disease. Professor David Molyneux at the Liverpool School of Tropical Medicine received a portion of the award, in part to develop a lymphatic filariasis CD-ROM in collaboration with TMR for distribution in Africa, India and South America. (www.filariasis.org.uk)

TMR is undertaking a two-year collaborative project with Dr Janet Browne and colleagues at the Wellcome Trust Centre for the History of Medicine at University College London to produce *Medicine in Literature*. This CD-ROM, aimed at introducing second-year medical students to the history of medicine, looks at the representation of medicine and disease in fiction, drama and poetry ranging from Homer to contemporary science fiction.

Catalyst BioMedica Ltd

Catalyst BioMedica Ltd, the business subsidiary of the Wellcome Trust, was set up to take forward promising research that is at too early a stage or too high risk to attract venture capital or be taken up by industry. Ultimately, the aim is to make research available to the commercial sector, which has the skills and resources necessary to develop it into new therapies that will benefit patients.



Above Human chromosomes in a living breast cancer cell that is about to divide.

Revised strategy

A new Business Plan refocusing Catalyst's activities in line with the Corporate Plan, was approved by Catalyst's Board of Directors and the Trust's Board of Governors in June 2001. The Plan has two main aims:

- To increase the flow of science into healthcare innovations, emphasizing the translation of innovative but high-risk science for which the venture and industry sectors have limited interest or capacity.
- To ensure a fair economic return for all parties involved (institutions, academics, local technology transfer groups, Catalyst and the Wellcome Trust).

Priority areas

The revised Plan focuses on programmes of strategic significance for Catalyst and the Trust, including the Development Fund, the Wellcome Trust Sanger Institute and other prioritized Centres and Initiatives. During the year, activity at key centres led for example to conclusion of significant collaboration and licence deals at the Diabetes and Inflammation Laboratory in Cambridge, and the generation of a plan for the structuring and financing of a start-up company to develop the outputs of the Cancer Genome Project.

The Development Fund

A major focus of Catalyst's activities is the Development Fund, which aims to support focused, milestone-driven research to drive forward the translation process.

During the course of the year, some 60 outline Development Fund proposals were considered, of which 12 were worked up and evaluated in full and nine were approved for funding by the Development Fund Appraisal Board. This brought the total number of approved awards as of 30 September 2001 to 21 (total committed funds £7.1 million; the average award was £360 000).

The new Business Plan provides for Development Fund awards to drive forward translational research within the framework of start-up companies, as well as within academic institutions as previously. During the course of the year, approval was given for three awards directly into start-up companies: International Interstitial in Manchester, Proxara Biotechnology in Bristol and Cresset Biomolecular Discovery in Hertfordshire (*see page 35*), in line with the new business model.

During the year, the outputs of two Development Fund projects were transferred into the start-up sector – to Paradigm Therapeutics in Cambridge, and Oxxon Pharmaccines in Oxford – for further development, in addition to the three direct start-up awards outlined above. A total of £1.7 million worth of equity in start-up companies was received during the year.

Other partnerships and negotiations

Some 23 agreements were concluded during the year. As well as shareholdings in start-up companies worth about £1.7 million, about £170 000 of revenues were generated from licensing and enabling technology deals, milestones and royalties.

£20 million venture funds were leveraged to advance translational research and development during 2000/01.

Catalyst also led discussions with commercial companies that enabled Wellcome Trust researchers to use technology developed by industry to further their research.

Board of Governors

The Board of Governors of The Wellcome Trust Limited, the corporate trustees of the Wellcome Trust, carries out the charitable objects of the Wellcome Trust as laid out in the Trust's constitution.

May 2002

Governors

Sir Dominic Cadbury
Chairman

Professor Sir Michael Rutter
Deputy Chairman

Professor Adrian Bird
Governor

Professor Martin Bobrow
Governor

Professor Christopher Edwards
Governor

Professor Julian Jack
Governor

Mr Alastair Ross Goobey
Governor

Professor Jean Thomas
Governor

Mr Edward Walker-Arnott
Governor

Professor Mark Walport
Governor

Executive Board

Dr Mike Dexter
Director (Chief Executive) of the Wellcome Trust

Linda Arter
Director of Finance and Information Management

John Cooper
Director of Personnel and Services

Dr Rick Fuller
Director of Science Funding

Clare Matterson
Director of Medicine, Society and History

Dr Michael Morgan
Director of Research Partnerships and Ventures, and Chief Executive of the Wellcome Trust Genome Campus

Gary Steinberg
Chief Investment Officer

Other senior staff

Dr Ted Bianco
Head of Centres and Initiatives

Dr Graham Fagg
Managing Director, Catalyst BioMedica Ltd

Dr Pat Goodwin
Head of UK Panels

Dr Richard Lane
Head of International Programmes

Jill Saunders
Head of Grants Administration

John Stewart
Head of Legal Services and Company Secretary

Dr Sally Woodward
Head of Career Schemes and Clinical Initiatives

Advisory committees

The Wellcome Trust is committed to the principles of peer review. It is indebted to the many researchers who give up their time to sit on the Trust's advisory committees, and to the many thousands of scientific referees, in the UK and overseas, who provide comments on grant applications. The following pages list the membership of the Trust's advisory committees during 2000/01.

UK FUNDING PROGRAMME

Bioarchaeology Panel

Professor M K Jones
(Chair) University of Cambridge

Dr D J Ortner
(Vice Chair) Smithsonian Institute, USA

Professor J O Thomas
Governor, The Wellcome Trust

Professor L C Aiello
University College London

Dr D G Bradley
University of Dublin Republic of Ireland

Professor J E Buikstra
University of New Mexico, USA

Professor P Halstead
University of Sheffield

Professor M Stoneking
Max Planck Institute for Evolutionary Anthropology, Germany

Biodiversity Interviewing Committee

Dr D Rollinson
(Chair) Natural History Museum, London

Professor M Akam
(from December 2000) University of Cambridge

Dr W Gibson
(from December 2000) University of Bristol

Professor A F Read
University of Edinburgh

Professor B G Spratt
Imperial College School of Medicine, London

Professor H Townson
University of Liverpool

Infection and Immunity Panel

Professor W I Morrison
(Chair) BBSRC Institute for Animal Health, Compton

Professor N A R Gow
(Vice Chair) University of Aberdeen

Professor A P Bird
Governor, The Wellcome Trust

Professor P W Andrew
University of Leicester

Professor J D Barry
University of Glasgow

Professor P C L Beverley
The Edward Jenner Institute for Vaccine Research, Compton

Dr J P Derrick
University of Manchester Institute of Science and Technology

Dr D W Dunne
University of Cambridge

Dr A A Holder
MRC National Institute for Medical Research, London

Dr M C J Maiden
University of Oxford

Professor P J M Openshaw
Imperial College School of Medicine at St Mary's, London

Professor A F Read
University of Edinburgh

Professor T F Schulz
Medizinische Hochschule Hannover, Germany

Professor S Siddell
University of Würzburg, Germany

Dr B Stockinger
MRC National Institute of Medical Research, London

Dr J M Woof
University of Dundee

Professor D C Wraith
University of Bristol

Medical Microbiology Interviewing Committee

Professor K A V Cartwright
(Chair) Public Health Laboratory Service, London

Professor J S Kroll
(Vice Chair) Imperial College of Science, Technology and Medicine, London

Professor D H Crawford
(from December 2000) University of Edinburgh

Dr F A Drobniewski
King's College School of Medicine and Dentistry, London

Professor T Mitchell
(from December 2000) University of Glasgow

Professor I S Roberts
(from December 2000) University of Manchester

Professor T F Schulz
Medizinische Hochschule Hannover, Germany

Molecular and Cell Panel

Professor D R Critchley
(Chair) University of Leicester

Professor M J P Arthur
(Vice Chair) University of Southampton

Professor J J B Jack
Governor, The Wellcome Trust

Dr G Banting
University of Bristol

Professor S Busby
University of Birmingham

Professor I D Campbell
University of Oxford

Professor B Caterson
University of Cardiff

Professor A Hall
University College London

Dr T Hunt
Imperial Cancer Research Fund Laboratories (Clare Hall)

Professor P W Ingham
University of Sheffield

Professor A F Markham
St James's University Hospital, Leeds

Professor C G P Mathew
Guy's, King's and St Thomas' School of Medicine, London

Dr M J Owen
Imperial Cancer Research Fund Laboratories (Lincoln's Inn Fields)

Professor L Pearl
Institute of Cancer Research, London

Dr S Rastan
Ceros Ltd, Cambridge

Dr A Sharrocks
University of Manchester

Dr A Smith
University of Edinburgh

Neurosciences Panel

Professor D Attwell
(Chair) University College London

Professor D A S Compston
(Vice Chair) Addenbrooke's Hospital, Cambridge

Professor M Bobrow
Governor, The Wellcome Trust

Professor Sir Michael Rutter
Governor, The Wellcome Trust

Professor N J Abbott
King's College, London

Professor M L J Ashford
University of Dundee

Dr H Bading
(until August 2001) University of Cambridge

Advisory committees

Neurosciences Panel cont.
Professor G Bates
King's College, London

Professor D J Brooks
Imperial College School of Medicine, London

Professor N J Buckley
University of Leeds

Professor M G Castro
University of Manchester

Professor S Dunnett
Cardiff University

Dr M Gill
Trinity College Dublin

Dr G G R Green
University of Newcastle upon Tyne

Professor I Grierson
University of Liverpool

Professor J Henley
University of Bristol

Professor E Kuipers
Institute of Psychiatry, London

Professor R Lemon
The National Hospital for Neurology and Neurosurgery, London

Professor S Lewis
University of Manchester

Professor P A McNaughton
University of Cambridge

Professor R A North
University of Sheffield

Dr D Price
University of Edinburgh

Professor A Stein
Warneford Hospital

Professor A W Young
University of York

Professor M P Young
University of Newcastle upon Tyne

Physiology and Pharmacology Panel
Professor M J Whitaker
(Chair) University of Newcastle upon Tyne

Professor S J Hill
(Vice Chair) University of Nottingham

Professor J O Thomas
Governor, The Wellcome Trust

Professor F M Ashcroft
University of Oxford

Dr J E Compston
University of Cambridge

Professor J R E Davis
University of Manchester

Professor G J Dockray
University of Liverpool

Professor C J Garland
University of Bath

Professor M A Hanson
University of Southampton

Professor D O Haskard
Imperial College School of Medicine, London

Professor J J Mullins
University of Edinburgh Medical School

Professor C P Page
Guy's, King's and St Thomas' School of Biomedical Sciences, London

Professor D P Strachan
St George's Hospital Medical School, London

Professor P Vallance
University College London

Professor J S Yudkin
University College London Medical School

Showcase Panel
Professor G Dougan
(Chair) Imperial College, London

Professor M Bobrow
Governor, The Wellcome Trust

Professor J J B Jack
Governor, The Wellcome Trust

Professor S Homans
University of Leeds

Professor M Horton
University College London

Professor Sir Alec Jeffreys
University of Leicester

Professor R Maizels
University of Edinburgh

Professor N J Rothwell
University of Manchester

Professor R Wolf
University of Dundee

Integrative Animal and Human Physiology Panel
Dr R Hill
(Chair) Neuroscience Research Centre, Merck UK

Professor J J B Jack
Governor, The Wellcome Trust

Professor L Avery
University of Texas, USA

Professor T V P Bliss
MRC National Institute for Medical Research, London

Professor K R Chien
University of California, USA

Professor A W Cowley
Medical College of Wisconsin, USA

Professor K Eichmann
Max Planck Institute, Germany

Professor M C Fishman
Massachusetts General Hospital, USA

Dr J Hunter
SmithKlineBeecham, UK

Professor B B Lowell
Beth Israel Deaconess Medical Center, USA

Dr J A Shadduck
Shadduck Consulting LCC, USA

Professor T Tully
Cold Spring Harbor Laboratory, USA

CAREER SCHEMES AND CLINICAL INITIATIVES PROGRAMME

Basic Science Interest Group
Professor C R M Bangham
(Chair) Imperial College School of Medicine at St Mary's, London

Professor M J Humphries
(Vice Chair) University of Manchester

Professor A P Bird
Governor, The Wellcome Trust

Professor J O Thomas
Governor, The Wellcome Trust

Professor D A Brown
University College London

Professor J C Buckingham
Imperial College School of Medicine at Charing Cross, London

Professor W C Earnshaw
University of Edinburgh

Professor E B Lane
University of Dundee

Dr J Langhorne
(from May 2001) MRC National Institute of Medical Research, London

Professor G Murphy
University of East Anglia, Norwich

Professor J N P Rawlins
University of Oxford

Professor A P Read
University of Manchester

Professor J C Smith
University of Cambridge

Professor J M Thornton
University College London

Professor M K B Whyte
(Clinical Interest Group representative) University of Sheffield

Cardiovascular Research Working Party
Professor P Poole-Wilson
(Chair) Imperial College School of Medicine at St Mary's, London

Professor J E Tooke
(Vice Chair) University of Exeter

Professor M J Walport
Governor, The Wellcome Trust

Dr G FitzGerald
University of Pennsylvania, USA

Professor A W Segal
University College London Medical School

Professor M Spyer
University College London

Professor P Weissberg
University of Cambridge

Clinical Interest Group
Professor S O'Rahilly
(Chair) University of Cambridge

Professor C M Black
(Vice Chair) Royal Free Hospital School of Medicine, London

Professor M Bobrow
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