sources of money are named in the acknowledgements,' Feußner concluded.

Not only researchers but also referees and editors may face conflicts of interest, in which case journals such as *Nature* ask the referees not to review a paper. These may not necessarily be financial interests; for example, a paper might be rejected by a competitor to safeguard her or his own interests. 'Unfortunately, the editors hear from cases like that often too late,'

Campbell said. 'In general, however, the peer-review system functions astonishingly well.' The *Nature* publishing group also has a policy for their editors and staff to avoid conflicts of interest.

Disclosure is an ethical decision to be taken by an individual, but if the scientific community resists this transparency, it could not only be harmful to research but may also reduce the already shaken trust the public has in science as a whole.

'Anything published that has an impact on what the public believes should have a mechanism in place that ensures it is obvious where the information and the funding for the study comes from,' JAMA's DeAngelis said.

Ellen Peerenboom

DOI: 10.1093/embo-reports/kvf018

From genomes to cures—a long way to go

More than a year after the publication of the first draft of the human genome, scientists took stock of its implications for science and society

The publication of the human genome caused quite a stir. US President of the time Bill Clinton and Prime Minister Tony Blair of Britain both lauded the deciphering of the 'book of life', and the media—as well as many scientists—never tired of stating that a new era in medicine had dawned.

Since the dust has now settled, a degree of sobriety has replaced the initial euphoria. This more realistic attitude was evident at the Science & Society Conference 'From genomes to cures' that was jointly organised by EMBO and EMBL last November in Heidelberg, and which took stock of the promises, expectations, fears and drawbacks of sequencing the human genome. 'The information provides a new tool for science and medicine,' Samuel Broder, Senior Vice President of Celera Genomics in Rockville, MD, said in the opening talk. And the implementation of

biomedical research in the future, Broder

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Samuel Broder: 'We have challenges of almost transcendental difficulty to overcome.'

developed countries, he commented, 'I think there has been progress but we need to do better in this world where cancer is our target.' Broder also showed a slide of a patient suffering from ataxia telangiectasia, a neurodegenerative disease caused by the modification of a single nucleotide, and said, 'there is no technology available today [...] that can promise to correct this single nucleotide exchange. [...] We have challenges of almost transcendental difficulty to overcome.'

And the challenges are not only scientific—the public are still wary of the biomedical revolution. Frank Burnet of the UK Biochemical Society presented surveys from European countries illustrating that public anxieties about cloning, cynicism about the ambiguous role of drug companies and distrust in regulators persist. On the other hand, 90% of those

The implementation of this new information, rather than its creation, will be the true revolutionary breakthrough

this tool, rather than its creation, will be the true revolutionary breakthrough. As the role of specific genes in any disease can now potentially be deciphered 'in ways that you wouldn't be thinking of in the realm of molecular biology,' the use of this information will form the basis of

said.

Indeed, the tasks ahead for medicine are numerous. Broder showed a collage of diseases caused by microbes, parasites and their vectors—most commonly occurring in the developing world—that was a clear reminder of the problems still unsolved. It is up to science to provide the tools to fight these 'agents of suffering and pain', as Broder called them. Turning to

Researchers have a responsibility not only to keep the promises about new cures, but also to be truthful about the real potential of their work

polled in the UK think that genetics should be used for better diagnosis and new cures to fight diseases. 'We are not talking about the public; we are talking

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Jonathan Knowles about the future of medicine: 'If you make medicine more personal, you will have less pain and suffering'.

about publics,' Burnet analysed these polls. 'Any sophisticated strategy for reaching the people is going to take that into account.' Indeed, scientists have come a long way in realising that it is important to engage society in their work to prevent future backlashes. But equally, they still have a long way to go. When Broder asked the scientists in the audience about the fears the public has about genetic research, most could not name any specific reservations. 'This is not a minor task,' Burnet reminded the gathered scientists. 'If you want to reap the benefits of molecular biology, you're going to have to invest very heavily into public perception in a very complicated way.'

But the public also consists of those who suffer from disease. Ysbrand Poortman, Chairman of the European Platform Patients' Organisation, told the scientists about those patients who are waiting in hope for the cures and therapies promised by the deciphering of the human genome. 'We want to fight to increase research because our lives are at stake,' Poortman simply stated.

Researchers, therefore, have a responsibility not only to keep these promises, but also to be truthful about the real potential of their work. 'Hype can lead to unrealistic expectations,' Barbara Jasny, Senior Editor of *Science*, warned. She agreed with Broder that although the human genome offers a wondrous tool for discovery,

the applications will take time. 'Does it mean that now that we have the human genome we will develop all kinds of cures for all kinds of diseases?' she asked. Not necessarily, she states. 'We have very powerful tools [...] but it is up to us to use these tools and it is up to us to put it in balance with other society issues.'

Personalised medicine is one such application, and Jonathan Knowles, Head of Global Pharmaceutical Research at Hoffmann-La Roche, explained in his keynote speech why he thinks that this approach is inevitable. 'If you make medicine more personal, you will have less pain and suffering,' he said. Knowles described it as 'Now you can ask questions about 5000, 10 000, 30 000, all human genes. That is the power. It is the parallelism.' And combining all the data from SNPs, gene chips and proteomics will eventually revolutionise the way medicine is done in the future, he expects.

But first, scientists need to understand the role of genes and the influence of environmental factors in pathogenesis. Knowles compared this to a jigsaw puzzle: 'The more you put the pieces together, the bigger and clearer the picture gets.' Actually, this is simplified by the fact that humans, relatively speaking, have only a few more genes than do mice or flies, the realisation of which Broder described as 'buying a Rolls Royce, opening the hood and discovering that you have a series of 2CV engines.' Although humans undoubtedly have complex regulation at the protein level, this genetic knowledge is already a powerful tool. 'Genetics gives you the answer if you do the experiment right,' Knowles explained the strategy. 'If you are able to do the experiment, you will be able to understand the underlying causes of disease

Alain Fischer about gene therapy: 'There could be bad surprises. It would be extremely unwise to proceed before there is better knowledge about the risks'.

society at large. However, some scientists do not see a sound basis for this, but rather the opposite, as it will eventually become clear that each of us carries thousands of potentially detrimental mutations. 'So that should eliminate some of the fears of stigmatisation that people feel,' Leena Peltonen, UCLA, said. And the benefits are just too large to be ignored. 'I passionately believe that this can make a huge difference in terms of alleviating suffering,' Knowles said. 'It's going slower than we wish but it's going faster than we predicted.'

One field that is developing more slowly than many wish is gene therapy. The prospect of curing inherited diseases and many forms of cancer has drawn significant attention and expectation from the public. 'There is obviously a large potential to gene therapy,' Alain Fischer,

As gene therapy is still in its infancy, inclusion into clinical trials is limited, leaving scientists to explain to desperate parents that their child will not be treated with an unproven therapy

rather than the symptoms.' In addition, increased predisposition screening for disease alleles and more preventive medicine in the form of lifestyle changes or preventive medication will eventually supplement today's strategy of disease diagnosis and treatment.

But the spectre of predisposition screening also raises many fears of discrimination by employers, insurers or

Director of the Hôpital Necker-Enfants Malades in Paris, France, said, 'but gene therapy is in its infancy.'

In fact, the theory of replacing faulty genes is striking in its elegance, but 'the problem is that you want to introduce the new gene for a long time, ideally lifelong,' as Fischer described it. Although many technologies and strategies are theoretically available, the success rate is rather

Andrew Blake: 'If we stop animal research, then who becomes the guinea pig?'

low, mainly due to cancerous growth of transgenic cells or inflammatory responses of the host immune system.

Nevertheless, there have been some successes. In his keynote speech to the session, Fischer outlined his own work to treat a certain form of SCID, an immune system failure due to a defective receptor gene in immune precursor cells. Of the six children Fischer's group initially treated by gene therapy, five have so far survived and show normal immune functions. His team has also made advances in treating haemophilia in an animal model by inserting transgenic cells that release a coagulation factor into the bloodstream.

As well as the technical difficulties, there is also the ethical minefield of gene therapy to be navigated. As the approach is still in its infancy, inclusion into clinical trials is limited, leaving scientists to explain to desperate parents that their child will not be treated with an unproven therapy, even if it is their only potential hope. On the other hand, the death of Jesse Gelsinger during a gene therapy trial 2 years ago has shown the scientific community the potential risks that still exist. Fischer thinks that it is better to proceed cautiously. 'There could be bad surprises. It would be extremely unwise to proceed before there is better knowledge about the risks,' Fischer said. 'I think it is the way to go, step by step.'

If the translation of genomes to cures is to become a reality, there is a price to be paid. Although the use of animals in biomedical research has decreased substantially during the last two decades, the recent explosion in sequence information

has reversed this trend due to the increasing use of transgenic mice. Bert van Zutphen, Head of the Department of Animal Laboratory Science at the University of Utrecht, estimated that worldwide, 75–100 million vertebrates are used each year in every discipline of biomedical science, but mainly in drug and vaccine development. And since there are currently very few alternatives, he said, 'We cannot afford as a society to stop using animals.' Indeed, this was starkly portrayed by the presence of Andrew Blake, the Director of the society 'Seriously Ill for Medical Research', who has been confined to a wheelchair since being diagnosed with Friedrich's ataxia in childhood. He campaigns constantly for the continuation of animal research since animal models provide the only means to study his and other incurable and debili-

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Nadia Rosenthal, speaking about transgenic mice: 'The knowledge that we've gained and the results we've obtained outweigh the criticisms we've heard'.

tating diseases at the molecular level. 'Those who wish to abolish the use of animals in research call themselves "Animal Rights Activists", but I'd call them "Disney World Evangelists" [...] They live in a fantasy world where people do not suffer from disease,' Blake told the conference.

The intrinsic value of using animals for medical research therefore needs to be recognised while at the same time the problem of preventing undue suffering and improving their well-being need to be considered. The European Science Foundation, through its High Level Expert Group, of which van Zutphen is a member, released a policy paper last year encouraging the observance of the three Rs: replacement, reduction and refinement. Roman Kolar of the German Animal Welfare Association would only be truly satisfied with replacement, although even he

admitted that this 'will not happen overnight.' In the meantime, the most fundamental question that should always be asked is: does the benefit of the experiment outweigh the suffering of the animal? Kolar, pointed out that 'The real weighing of cost and benefit is only taking place in a small number of cases.' This is exacerbated by the fact that, despite legislation in most countries, the upper limit of the cost to the animal and the minimum standard for the benefit to society has not actually been set. 'We need some reflection on the use of animals on a broader scale,' Kolar concluded. 'It is in the interests of scientists to develop more responsibility for animals and therefore work towards a more responsible, humane and better science.' But Nadia Rosenthal, the Co-ordinator of the EMBL Mouse Biology Programme in Monterotondo and a self-confessed 'animal lover' insisted that 'The knowledge that we've gained and the results we've obtained outweigh the criticisms we've heard [...]. There are several cases where the animals have improved our understanding of a disease and where they haven't necessarily suffered.' In fact, her research on muscular dystrophy is strongly dependent on transgenic mouse models and human gene therapy trials based on this work are currently under way. One measure to reduce the potential suffering of animals would be to collate experimental results. Kolar pointed out, 'Records of suffering are often kept in the laboratory, but there should be a database. There is a need for an initiative to publish this information broadly.' Rosenthal agreed and confirmed that there has been an attempt to coalesce a phenotypic database for mouse research-

It is a significant responsibility for 'society' to make judgements without first knowing all of the facts

ers worldwide, but that the major problem is one of standardisation, particularly for more subjective observations such as behaviour. Overall, the general consensus of opinion was that society needs to set the borderline of what is ethical in animal experimentation and that the impetus for any change will need to come from the public as opposed to the professional sphere. But as Blake said, 'If we stop

Izchak Parnas: 'The knowledge exists with us, the universities, the research institutions and we have to bring this knowledge to the teachers'.

knowledge exists with us, the universities, the research institutions and we have to bring this knowledge to the teachers,' he stressed. Belmonte trains teachers in performing advanced experiments and provides free access to their laboratories to around 160 pupils per day. 'It's a great opportunity to expose students to the spirit of science,' Parnas enthused.

Targeting students so that tomorrow's public is capable of making informed choices was a recurring theme and similar initiatives were presented by Eva-Maria Neher, Director of the 'X-lab' in Göttingen, Germany, and Wilbert Garvin, founder

science. Gauging people's attitudes before and after their visit, she said, 'We actually found an incredible shift from a one-dimensional way of thinking to realising science is something much more complex.'

And, of course, scientists as part of society have their role to play. '91% of scientists thought they had a responsibility to communicate the social and ethical implications of their research to a non-specialist audience. But less than 20% had held any talk or discussion in the last year,' Matterson said. So there appears to be confusion on both sides: the scientists

animal research, then who becomes the guinea pig?'

Indeed, it is a significant responsibility for 'society' to make judgements such as these without first knowing all of the facts. And the prevailing fears of what the publication of the human genome actually holds for the future can only be addressed through informed discussions. In this regard, Israel is forging ahead and Izchak Parnas, Director of the Belmonte Science Centre for Youth at the Hebrew University of Jerusalem, described the success of his scheme to address the fear and lack of knowledge in the population. 'The best way is to start in schools. That way you are not being selective; it exposes science to the whole population.' He criticised the education system for the general lack of time and facilities in schools and for not keeping pace with science. 'The

The scientists generally do not understand the public's fears and misconceptions, while the public generally do not understand what scientists are doing

member of the European Initiative for Biotechnology Education. Clare Matterson, Director of Medicine Science and History at the UK's Wellcome Trust, also described the many aspects of their 'Medicine in Society' programme to raise awareness and understanding of biomedical science. This is not a simple undertaking as they had found that 'The more people understood, the more questions, the more concerns they had.' Among their more creative ongoing initiatives are the establishment of many interactive centres around the UK to encourage people to think more about science, together with 'Theatre in Education' and 'Sci-Art' to reach the typical high-earner sceptics of

generally do not understand the public's fears and misconceptions, while the public generally do not understand what scientists are doing. There needs to be greater awareness and it is only through bringing the different factions together that the potential of the human genome will be realised. 'Society is not yet prepared for dealing with the new genetics, and therefore a new public dialogue must be established,' Poortman said.

Susan R. Owens & Holger Breithaupt

DOI: 10.1093/embo-reports/kvf019

Fast tracking drugs to patients

Drug approval agencies are frequently criticised for either being too slow or too fast

Regulatory approval of drugs can be an obstacle course and is a process that frequently comes under fire for being too rapid or too lax. Critics often complain that pharmaceuticals are approved too slowly by a process that is too costly and byzantine, which has fatal effects for patients when life-saving anti-cancer and anti-HIV drugs are involved. The US Food and Drug Administration (FDA), the agency responsible for approving new

drugs, has reacted to long standing criticism by streamlining some of its guidelines and procedures, but the bioterrorism crisis in the USA has prompted further scrutiny of the whole drug approval system. The FDA's European counterpart, however, the European Agency for the Evaluation of Medicinal Products (EMA) in London, so far has largely resisted expediting its approval process. But it is unclear whether a faster and slimmed-

down approval process is indeed better for public health. Critics of more rapid approval point to 12 drugs in the past 4 years that were withdrawn from the US market due to serious side-effects and that were, they believe, approved too hastily.

The recent bioterrorism attacks with anthrax spores have again pushed this topic onto the front pages. With frightened Americans hoarding Cipro, the only anti-biotic approved by the FDA to treat