

4th EMBO/EMBL Conference on Science and Society

# Genetics, Determinism and Human Freedom

14 – 15 November, 2003

at the

European Molecular Biology Laboratory  
Heidelberg, Germany

Organising Committee:

Frank Gannon (EMBO), Fotis C. Kafatos (EMBL),  
Andrew Moore (EMBO, Chair), Halldór Stefánsson (EMBL),  
Alessandra Bendiscioli (EMBO)

In February 2001, an international team of researchers published the first "complete" sequence of the human genome: 10 years after scientists had started the human genome project they were able, for the first time, to read what is sometimes referred to in a reductionist sense the "blue print" of a human being.

In the intervening years, human genetics had already made great strides in medicine. Scientists had discovered disease genes and developed new diagnostics. These advances allowed them to improve existing treatments, or develop new ones. But this process of scientific discovery and clinical application has consequences that reach far into the future, and which raise burning ethical and social questions.

With the sequencing of the complete human genome and the development of gene banks, scientists and medics have an unprecedented amount and quality of information at their disposal. By their very nature, some applications of this information lie at the delicate boundary between medicine and directed improvement of human beings. But it is not only in medicine that genetic information has found a use; in many areas of the information society, for example in law and justice, in security and insurance, it promises (or perhaps "threatens"?) to be of great utility.

As a society we must, therefore, ask ourselves important questions as to how genetic information is obtained, stored and used, such that the potentially enormous benefits can be reaped. This very powerful information must be used in a way that is acceptable to all members of society.

The most important parts of the equation are dialogue and understanding between the variety of stakeholders in the development of the modern day information society. The tradition of this conference is to promote closer relations between scientists and other members of society who are interested in discussing the social impact and relevance of the research and applications at the forefront of molecular biology.

The European Molecular Biology Organization (EMBO) and the European Molecular Biology Laboratory (EMBL) are delighted to host you for these two days of engaging discussion.

Frank Gannon  
Executive Director, EMBO

Fotis C. Kafatos  
Director General, EMBL



The European Molecular Biology Organization was founded in 1962 by European scientists at the forefront of the molecular study of biological entities. Its mission is to promote molecular biology in Europe and neighbouring countries.

Today EMBO has 1.200 members, mainly academic scientists, in all fields of molecular biology. The core EMBO activities consist of long term fellowships for postdoctoral scientists, short term training fellowships, and courses and workshops. These activities are funded through contributions from the member states (presently 25) of the EMBC (European Molecular Biology Conference). More recently EMBO has started programmes to support young investigators starting their own groups, researchers who take a break because of child care, and researchers moving within and to Europe. The programmes are completed by E-Biosci, a sophisticated hoster and search portal for scientific literature.

EMBO's science and society committee plays an important role in planning the events and activities in the coming year. These focus to an increasing degree on improving biology education at secondary school level (via teacher training workshops), promoting and rewarding the efforts of scientists who communicate with non-scientists and the media, and promoting the information flow between scientists and policy makers. More information is available at <http://www.embo.org/projects/scisoc/index.html>.

In November 2000 EMBL and EMBO jointly hosted their first Science & Society conference "Science and Society; developing a new dialogue", which brought together scientists (academic and industrial), social scientists, science communicators, policy makers and consumer associations in a highly stimulating debate. The conference has since become a respected cornerstone of collaborations between the two organisations, attracting prominent representatives of the sectors of society that produce, communicate, comment on and use the products of modern biology.



The European Molecular Biology Laboratory (EMBL) is a basic research institute funded by 16 member states, including most of the EU, Switzerland and Israel. Research at EMBL is conducted by approximately 80 independent groups covering the spectrum of molecular biology. The Laboratory has five units: the main Laboratory in Heidelberg, Outstations in Hinxton (the European Bioinformatics Institute), Grenoble (on the campus of ILL and ESRF), Hamburg (on the DESY site), and an external research programme in Monterotondo, Italy (sharing a campus with EMMA and the CNR.).

EMBL was founded with a four-fold mission: to conduct basic research in molecular biology, to provide essential services to scientists in its Member States, to provide high-level training to its staff, students and visitors, and to develop new instrumentation for biological research. Over its 25-year history, the Laboratory has had a deep impact on European science in all of these areas. EMBL has achieved so much because it is a truly international, European institution, because it has achieved a critical mass of services and facilities which are driven by cutting-edge biological research, and because it regards education – at all levels – as a way of life.

In 1998, EMBL launched a Forum on Science and Society as an initiative among researchers and staff members to promote awareness of the impact that work within the life-sciences is having on society. The Forum offers events and activities dealing with subjects and themes relevant to the ways in which recent developments within the life sciences in general, and within molecular biology in particular, are having a profound impact on people, their societies as well as their cultures. More information can be found at the Science and Society website <http://www.EMBL-Heidelberg.DE/ExternallInfo/stefanss/>.

# table of contents

|   |    |
|---|----|
| Conference programme  | 1  |
| Session I: Technological revolutions in genetic information gathering<br>and application                        | 5  |
| Keynote lectures  | 8  |
| <i>Panel discussion</i>   | 13 |
| Session II: Genes and disease: the links and their consequences for<br>human freedom                            | 16 |
| Keynote lectures  | 19 |
| <i>Panel discussion</i>   | 24 |
| EMBO Award for Communication in the Life Sciences   | 27 |
| After dinner talk   | 28 |
| Session III: Use and abuse of genetic information in justice, security<br>and the information society           | 31 |
| Keynote lectures  | 34 |
| <i>Panel discussion</i>   | 38 |
| Session IV: Fast forward: human trait modulation, “Genomes’R’us”,<br>designer babies and genetic identity cards | 41 |
| Keynote lectures  | 44 |
| <i>Panel discussion</i>   | 48 |
| List of participants  | 51 |

# programme

**Friday, November 14, 2003**

08:15 - 08:45 *Registration*

08:45 - 09:00 Welcome address:

Andrew Moore, Chair, Conference Organising Committee, and  
Science and Society Programme Manager, EMBO

## Session I: Technological revolutions in genetic information gathering and application

---

**Chair** **Frank Gannon**, Executive Director, EMBO

### Keynote lectures

09:00 - 09:45 **Jean Weissenbach**, Director, Genoscope, France

09:45 - 10:30 **Hans Lehrach**, Director, Max Plank Institute for Molecular  
Genetics, Berlin, Germany

10:30 - 11:00 *Coffee break*

### Panel discussion joined by:

11:00 - 12:30 **Nick McCooke**, CEO, Solexa Ltd., United Kingdom

**Monica Konrad**, Institute of Commonwealth Studies, School  
of Advanced Study, University of London, United Kingdom

12:30 - 14:00 *Lunch*

12:45 - 14:00 Press conference, EMBO conference room

## Session II: Genes and disease; the links and their consequences for human freedom

---

**Chair** **Matthias Hentze**, Senior Scientist, and Dean of Graduate  
Studies, EMBL, Heidelberg, Germany

### Keynote lectures

14:00 - 14:45 **Michael Caldwell**, Director, Marshfield Clinic Research  
Foundation, Wisconsin, USA

14:45 - 15:30 **Jean-Louis Mandel**, Director, Institut de Génétique et de Biologie Moleculaire et Cellulaire, Illkirch, France

15:30 - 16:00 *Coffee break*

Panel discussion joined by:

16:00 - 17:45 **Klaus Lindpaintner**, Vice-President and Director, Roche Genetics, F. Hoffmann-La Roche, Switzerland

**Nigel Townsend**, Artistic Director, Y-Touring Theater Company, United Kingdom

**Jackie Leach Scully**, Center for Ethics in the Biosciences, University of Basel, Switzerland

17:45 - 18:00 *Brief intermission*

18:00 - 18:30 **Award ceremony: EMBO Award for Communication in the Life Sciences**

19:00 *Conference dinner*

After-dinner talk

20:30 - 21:15 **Jon Beckwith**, Department of Microbiology and Molecular Genetics, Harvard Medical School, Boston, USA

## Saturday, November 15, 2003

### Session III: Use and abuse of genetic information in justice, security and the information society

---

**Chair** **Salvör Nordal**, Director, Center for Ethical Studies, University of Iceland, Reykjavik, Iceland

#### Keynote lectures

09:00 - 09:45 **Ludger Honnefelder**, Director, Section of Biomedical Ethics, Institute of Science and Ethics, University of Bonn, Germany

09:45 - 10:30 **Alastair Kent**, Director, Genetic Interest Group, United Kingdom

10:30 - 11:00 *Coffee break*

Panel discussion joined by:

11:00 - 12:30 **Bob Bramley**, Chief Scientist, Forensic Science Service, United Kingdom

**Regine Kollek**, Research Center for Biotechnology, Society and the Environment, University of Hamburg, Germany

12:30 - 14:00 *Lunch*

Session IV: Fast forward: human trait modulation, “Genomes’R’us”, designer babies and genetic identity cards

---

Chair **Volker Stollorz**, Free Lance Science Journalist for the Frankfurter Allgemeine Sonntagszeitung, Germany

Keynote lectures

14:00 - 14:45 **Antoine Danchin**, Director of Research and Head of the Unit “Genetics of Bacterial Genomes”, Institut Pasteur, Paris, France

14:45 - 15:30 **Steven Rose**, UCL Visiting Professor, and Director of Brain and Behaviour Research Group, Dept. of Biological Sciences, The Open University, United Kingdom

15:30 - 16:00 *Coffee break*

Panel discussion joined by:

16:00 - 17:45 **Ruth Chadwick**, Professor of Bioethics and Director, ESRC Centre for Economic & Social Aspects of Genomics, Lancaster University, United Kingdom

**John Durant**, Chief Executive, At-Bristol, United Kingdom

**Peter McGuffin**, Director, Social, genetic and Developmental Psychiatry Research Center, Institute of Psychiatry, King’s College London, United Kingdom

17:45 Closing remarks:

Halldór Steffánsson, Conference Organising Committee, and Head of the Science and Society Office, EMBL

18:00 *Conference ends*



OH BRAD, THEY SAY THERE'S  
DNA IN MY BODY!

WHO CARES, DARLING,  
... WHO CARES ...

## Session I:

# Technological revolutions in genetic information gathering and application

In this opening session of the meeting the focus is on the technologies available today, and those that can be imagined for the near future, that allow genetic information to be obtained more rapidly. The two keynote speakers are experts in the domain, and will present and give updates on current sequencing and array methodologies.

The human genome project has provided clear evidence of the power of DNA sequencing methodology, and the consequences of this major experiment in biology are still being examined. DNA array methodology and future approaches based on proteins open completely new possibilities. Samples from individuals can be analysed, and the most probable course of development of a tumour, for instance, can be projected. The likely usefulness of chemotherapy or other therapeutics in treating an individual's specific cancer can also be deduced from a DNA array analysis.

These powerful techniques lead us into the core of this meeting, namely how rapidly advancing technology can move from laboratory experimentation to direct medical or social consequences. Questions that will be addressed in this session could include:

- What else can be expected from the technologies?
- Will an individual's DNA sequences contribute to a medical diagnosis?
- Should society welcome or fear such new developments?
- Is the emphasis on the predictive power of DNA arrays ultimately going to be beneficial to society as a whole, or will it act as an excluding force (either by the personal nature of genetic information or by the costs associated with the use of this approach)?
- What are the responsibilities of those who are developing the methodologies to society in general, and how are these responsibilities being integrated into their research programmes?

- The involvement of companies in this is inevitable, but is it desirable, and can it then cause distortions or limited choices that will be regretted?
- With the increasing threat of terrorism, does the right to national security outweigh the loss of anonymity that can come from genetics based methodologies?

These questions lead inevitably to others, which will be dealt in other sessions of the meeting, but in the first session it is hoped that the technical possibilities will be outlined and the immediate consequences of these for society will be discussed.

Frank Gannon, session chair



# Frank Gannon

Executive Director, EMBO, and Secretary General, EMBC

Frank Gannon has been the Executive Director of the European Molecular Biology Organisation (EMBO) in Heidelberg, Germany, since 1994. He is also Secretary General of the European Molecular Biology Conference (EMBC), and Senior Scientist at the European Molecular Biology Laboratory (EMBL) in Heidelberg.

He graduated in Biochemistry from University College, Galway, Ireland in 1966 and obtained his PhD in Enzymology from the University of Leicester, UK. Between 1973 and 1977 he was a postdoctoral fellow, first at the University of Wisconsin, USA, and then at the University of Strasbourg, France. In 1990 he became Associate Professor at the Department of Microbiology, University College, Galway, and from 1987 to 1994, he was Director of The National Diagnostics Centre, BioResearch Ireland, University College, Galway.

He is Associate Editor of the EMBO Journal and Senior Editor of the EMBO Reports, and he has published over 100 research articles in International Journals.

At present he is member of the following boards: the International Advisory Board of the International Institute for Molecular and Cell Biology, Warsaw, the Board of the Institute for Molecular Bioscience Board, University of Queensland, Brisbane, Australia, the Scientific Advisory Board of the Millennium Institute, Santiago, Chile, and of an EU External Advisory Group.

In the past he was Member of the Irish Science Technology and Innovation Advisory Council (1994), Irish representative on EC research committees for Biomedicine and Biotechnology (1988-1994), reviewer for EC, of the China European Community Biotechnology Centre (CEBC) (1993), Member of the Board of the European Doctorate in Biotechnology (1995-1999), Member of the Scientific Advisory Committee of the SARS International Center, Bergen (1996-2000), Member of the European Science and Technology Assembly (ESTA) (1997-1998), Member of the Scientific Council of the Stazione Zoologica, 'Anton Dohrn', Naples, (1998-2000), Coordinator of EBNIC (European Biotechnology Node for Interaction with China) (1998-2001), and Member of the board of the Science Foundation Ireland.

In 1999 he was awarded Doctor Honoris Causa by the Josef Attila University in Szeged, Hungary.

# What can we predict from the human genome sequence?



## Jean Weissenbach

Chief Executive, Genoscope, and University of Evry, France

The announcement of an almost complete sequence of the human genome in April this year marked a milestone in the history of biology and medicine. Although such announcements need to be taken cautiously, the present version of the human genome sequence represents a major improvement for the daily users in human genetics, compared with the initial draft of June 2000. In this presentation I will briefly review the present state of the sequence with regard to quality and completeness, what the human genome has taught us in the recent past and what improvements could still provide a better utilization of what should be considered as the infrastructure on which molecular medicine will be established.

With about one error event for 100,000 base pairs, the accuracy substantially exceeds the threshold fixed at one error for 10,000 base pairs. About 300 gaps in the assembly corresponding essentially to DNA fragments missing from the existing collections of large DNA fragments remain to be filled. They correspond mainly to regions difficult to isolate or to map, such as segmental duplications. An impressive number of DNA sequence variants (single nucleotide polymorphisms or SNPs) have been identified. These SNPs may be distributed in a very limited number of combinations that are conserved over large segments of a few thousand to hundred thousand bases (haplotype blocks). The blocks are largely shared by the major human populations. A map of haplotype blocks consisting of 600,000 SNPs (one every 5000 bases on average) in three human

populations (West African, Caucasian and East-Asian) is in progress. It should be available by the end of 2004 and will give us a much deeper insight on haplotype structure and occurrence in human populations. Such a tool is needed to dissect the complexity of multifactorial traits (those due to more than one gene).

The identification of genes on the DNA sequence remains a complex task and is not yet complete. It is largely based on automated annotation procedures that have their limitations. Surprisingly we still observe a decrease in the present estimates of the number of protein-encoding genes, which will probably remain below 30,000. The recent availability of additional vertebrate genome sequences (mouse, rat, etc.) should be of great help in this issue. Comparative studies also highlight the conservation of non-coding sequence elements. The potential role(s) of such elements as well as of non-conserved non-coding transcripts remains a matter of speculation and discussion.

**B**orn in Strasbourg in 1946, Jean Weissenbach has pursued his career in the CNRS (French National Research Council), concentrating on molecular biology. He received his Ph.D. from the University of Strasbourg in 1977 for sequencing and studies of the coding properties of transfer RNAs. From 1977 to 1981 he focused on cDNA cloning of human interferons, work which led him to his next field of interest: human molecular genetics (since 1982). He was at the Pasteur Institute from 1979 to 1992, and from 1990 to 1997 at Généthon.

His work in human genetics include:

- Studies on the human sex chromosomes and sex determination (1982-1989). He paved the way for mapping the male sex determining factor and showed that the human X and Y chromosomes normally exchanged genetic material at each meiosis (cell division that produces eggs and sperm).
- Linkage mapping which led to the construction of the first extensive genetic map of the human genome (1990-1995). This map has had a major impact in mapping of human disease genes and has greatly accelerated research in this field.
- Disease gene mapping and cloning both directly by his active pursuit of disease genes and indirectly by an extensive series of collaborations that have greatly benefitted from unpublished data from the genetic linkage map.

In 1997 Jean Weissenbach was appointed Director of the French National Sequencing Centre, Genoscope. This centre is actively contributing to the sequencing of the human genome (chromosome 14) and to other international large-scale projects on genomes of higher organisms (Arabidopsis, Drosophila, Anopheles, rice, Tetraodon pufferfish, etc.) and of micro-organisms. Using DNA sequence comparisons between the genomes of pufferfish and humans, Genoscope was the first to propose a drastic reduction in the estimate of the number of human genes to only about 30,000.

# Systems biology, the logical consequence of the human genome project



## Hans Lehrach

Max Plank Institute for Molecular Genetics,  
Berlin, Germany

**E**ach organism is essentially the result of a computation: the computation of the phenotype from the genome, given a specific environment. This ‘computation’ is, however, carried out by a complex molecular and cellular machinery, ultimately involving all genes and gene products of each organism.

Since biological processes are highly interlinked, involving many of the genes and gene products of the organism, we have to be able to identify all the components in these networks, and to understand their function and interactions, using the same types of approaches, that we are currently applying to try to understand the function of single ‘interesting’ genes. Since all genes are ultimately ‘interesting’ (otherwise they would not have been conserved in evolution), these data must however be generated systematically on all genes and gene products in highly automated high throughput data production pipelines (functional genomics).

To be able to analyse these massive amounts of data, and to ‘understand’ the complex networks of biological processes, we will ultimately have to establish computer models of these processes, representing all information we have on the genes, gene products, interactions and regulatory networks. This is the goal of systems biology, the essential next step in the understanding of biology, and our best hope for a real understanding of many complex biological phenomena. In principle, computer models are the best way to make use of the enormous amounts

of information and are also able to generate quantitative predictions and thus duplicate and simulate the complexity of biology. In addition to helping us to 'understand' biology, such models will, however, also have enormous practical implications. It seems, for example, quite feasible to establish, within the next decade, quantitative models able to predict the response of a specific tumour in a specific patient to specific courses of treatment. This would help enormously in the optimisation of cancer therapy.

Genome research and systems biology are therefore in our view by far the best hope we have to better understand, diagnose and cure many diseases. These new forms of carrying out biological research do, however, require some changes in the way support for biological research is structured, since genome projects are, in a sense, more similar to projects in high energy physics or space research in their planning requirements, and the need to establish and support for longer periods interdisciplinary centres. In view of the potential importance of these developments for society, they also still seem vastly underfunded.

The central project in medical genomics in Germany is the NGFN, which is German citizens' best chance for understanding and curing many diseases. With luck it may be funded to the tune of 60 cents per citizen. Each cow in Europe is subsidised at a level of two Euros per day.

**H**ans Lehrach is currently Director of the Max-Planck Institute for Molecular Genetics in Berlin.

After 4 years at Harvard University, he returned to Europe and became head of a research group at the EMBL in Heidelberg. He then moved to the UK, where he was Head of Department Genome Analysis at the ICRF in London for 7 years. Prof. Lehrach is member of several national and international organisations:

- EMBO
- Austrian Biochemical Society
- Human Genome Organisation Council
- Steering Committee Biotechnology Berlin-Brandenburg
- Project Committee of the National Genome Research Network
- Scientific Advisory Board of the Austrian Genome Research Projekt (GEN-AU)

Prof. Lehrach sits on the Editorial Boards of various international scientific journals, such as Human Genetics, Physiological Genomics, Genome Biology, and Journal of Molecular Medicine.

His is also the co-founder of private biotech companies, such as Sequana (Axis), La Jolla, USA, Genome Pharmaceutical Corporation Biotech AG, Munich, Scienion AG, Berlin, Prot@gen AG, Dortmund, and PSF Biotech AG, Berlin.

# Panel discussion

- Participants:
- Frank Gannon (chair)
  - Jean Weissenbach
  - Hans Lehrach
  - Nick McCooke
  - Monica Konrad



## Nick McCooke

CEO, Solexa Ltd., United Kingdom

**N**ick McCooke (Chief Executive Officer, Solexa Ltd) was previously President of the Seattle-based genomics company Rapigene, now part of Qiagen N.V., which was one of the pioneers of high throughput genotyping. From 1991 to 1998, he held a number of general management positions in Innovex (which merged with the contract pharmaceutical organisation Quintiles Transnational Corp in 1996), including responsibility, as President of Innovex Japan, for setting up a successful business based in Tokyo. Formerly, he worked for the UK biotech company Celltech, in a number of commercial and general management roles.

Solexa is a spin out from the University of Cambridge, UK, developing a revolutionary DNA sequencing technology. It has raised \$22 million to date from leading international life science investors. By the end of 2003 the Company aims to complete the prototype of a system that will allow rapid, base-by-base, comparison of whole genome DNA sequences, thereby determining individual sequence variations.



# Monica Konrad

Institute of Commonwealth Studies, School of Advanced Study, University of London, United Kingdom

**M**onica Konrad (University of Cambridge) is a social anthropologist and active researcher in the life sciences. Since gaining her PhD from the London School of Economics & Political Science, she has held posts at the Universities of Sussex, London and the School of Advanced Study, and has written several papers on the cultural and kinship implications of the new reproductive and genetic technologies for British publics. She is author of a forthcoming book on the relevance of anthropological approaches for contemporary debates on public health and predictive genetic information. Other research interests in international bioethics led to her involvement with the European Group on Ethics in Science and New Technologies and the Report of Roundtable Proceedings on Ethics Aspects of Biomedical Research in Developing Countries (2002). She serves as a Member on the Review Committee of the Rights and Responsibilities of Science and Society for the International Council for Science.

NO BRAD, I'M NOT GOING TO HAVE MY DNA SCREENED!  
THESE DOTS ARE NORMAL!



## *Session II:*

# Genes and disease; the links and their consequences for human freedom

Over the past couple of decades, medicine has undergone a revolution. Medicine used to be an empirical discipline that evolved largely on the basis of clinical experience and correlative analyses. Now the molecular life sciences have taken over as the major driving force, affecting not only how healthcare is administered, but having a profound impact on society at large.

Following an initial phase in which “disease genes” of common or rare “single gene” defects were identified and studied (e.g. sickle cell anemia, cystic fibrosis, Huntington’s disease), much research now focuses on defining the genetic basis of common, complex “multifactorial” and/or polygenetic disorders including diabetes, allergies, asthma, cancer, obesity and mental disorders, just to name a few. Both areas have changed medical practice with regard to diagnostics and the ability to make a prognosis. Huntington’s disease and different forms of cancer (including leukemias) are excellent examples of this. There has also been significant progress in understanding the underlying causes of disease. In spite of important and life-saving contributions to therapy (e.g. recombinant proteins), some expectations for rapid cures have met with difficulties and led to disappointment (e.g. gene therapy). The benefits of molecular diagnosis and prognosis will be less obvious for patients who suffer from diseases that currently cannot be effectively treated. In fact, knowledge of the diagnosis of a serious disease associated with a poor prognosis can negatively affect the “quality of life” of the individual concerned, irrespective of the fact that an accurate diagnosis can provide a more informed basis for important life decisions (e.g. whether or not to have children; possibilities for prenatal diagnosis; choice of profession). In this context, the “right not to know” should be respected if individuals prefer.

Public debate has accompanied this medical revolution. While the current “stem cell debate” is not strictly connected to the question of “genes and disease”, the question of “genetic predisposition” to diseases clearly is. Individuals and society have to decide how to handle statistical information that identifies a 5-fold increased or a 3-fold decreased risk of being affected by a serious, common disorder. This problem is not new to the age of “molecular medicine”, but the frequency of its occurrence has changed, and is likely to increase much more. The outcome of this discussion will have a profound impact on human freedom.

Matthias Hentze, session chair



# Matthias Hentze

European Molecular Biology Laboratory,  
Heidelberg, Germany

**M**atthias W. Hentze graduated at the Faculty of Medicine at Münster University and received his M.D. at the Physiological-Chemical Institute of the same University in 1984. He is currently Dean of Graduate Studies, Group Leader, Senior Scientist and Coordinator of the Programme "Training, Partnership & Endowment" at the European Molecular Biology Laboratory (EMBL), in Heidelberg, Germany. He also holds a number of positions in educational committees, being a member of the Board of the European Association for Higher Education in Biotechnology and the Chair of the Curriculum Committee, European Association for Higher Education in Biotechnology.

His membership of scientific societies notably includes: the European Molecular Biology Organisation, the Deutsche Gesellschaft für Biologische Chemie, The Nitric Oxide Society and the RNA Society. He has published over 100 articles in international peer reviewed journals, and is a member of the editorial board of several international scientific journals, including the EMBO Journal, EMBO reports, Trends in Biochemical Sciences and RNA. He has also published 5 books on clinical and molecular medicine.

His primary scientific interests are RNA-protein interactions, post-transcriptional gene regulation, Molecular Medicine, particularly iron metabolism, oxidative stress, NO, genetic disease and nonsense-mediated decay.

He has received several distinctions, notably the Leibniz Prize in 2000. In the course of his research into the molecular biology of cellular iron metabolism, Matthias Hentze has discovered important regulatory processes that control the formation of the receptors that regulate the uptake and storage of iron. He was amongst the first to conduct a systematic study of gene regulation via control of translation, the process in which the genetic code in RNA is translated into a protein sequence. These pioneering studies are of great significance for understanding metabolic disorders, cell differentiation and development.

# Personalized medicine in the post-genomic era



## Michael D. Caldwell

Director, Marshfield Clinic Research Foundation, Wisconsin, USA

Although new genetic information is being generated at a rapid rate, genetics research is faced with the daunting task of linking this information in a meaningful way to health and disease. The concept of personalized medicine has evolved from these pursuits but can only be realized through vigorous scientific discovery supported by appropriate, carefully designed research methodology and resources.

Common disease processes are thought to involve multiple genes and interactions with environmental factors. Complex patterns of inheritance have proved challenging in establishing the genetic basis of disease. Susceptibility loci have been studied by different strategies including familial segregation analysis, linkage analysis, candidate gene approaches, positional cloning and association studies in homogeneous populations. Association studies are recommended for the study of genetic basis of common diseases. Limitations of association studies have also emerged including inability to replicate or corroborate a previous observation. There have been three recent reviews of the repeatability of results from genetic association studies. The authors of all three papers note that the first paper published to suggest a genetic association generally has the highest LOD score and that population stratification and other biases have led to results that cannot be repeated in other populations. Multivariate analyses to predict success in genetic studies identified two factors: 1) increased sample size, and 2) a sample drawn from only one ethnic group as needed for reproducibility. The Marshfield Clinic Personalized Medicine Research Project is designed to address

these two crucial factors for successful studies seeking to understand the genetic basis of disease.

The concept underlying the Marshfield Clinic Personalized Medicine Research Project is that availability of population-based cohorts, which can be phenotypically characterized and whose subjects will repeatedly undergo high density genetic mapping will give rise to informative genetic patterns which can be effectively evaluated for their relationship to disease.

This project is recruiting patients from an epidemiological study area whose longitudinal health care information has been captured by a sophisticated electronic medical record. To date almost 14,000 of these patients have given permission to use their health care information, serum, plasma and DNA to investigate the genetic basis of disease, the response of patients to medications and other forms of treatment and to better understand the structure of population genetics.

The overall goal of the Marshfield Clinic Personalized Medicine Research Project is to create a population based cohort and a comprehensive research database capable of integrating phenotypic, genotypic, familial and environmental data that can be interrogated to further define the genetic basis of disease and disease resistance and serve as a national resource. Only a few population based genetic repositories are currently available throughout the world as a resource for genetic association studies. The ability to create and store phenotypic profiles from comprehensive medical, familial and environmental data in a secure database and link these data with genetic information while maintaining patient confidentiality, allows for the creation of unique, powerful and unprecedented research tool to further scientific discovery and the understanding of clinical genetics as it relates to disease origin, prevention, diagnosis and treatment.

In his recent text, *Playing God?*, Ted Peters delineates the nature of humanness as the interaction of three things – genetics, environment and free will. It can be reasoned that this holds true for the nature of human disease. By its formation and structure the Marshfield Clinic Personalized Medicine Research Project purports to investigate these elements of human disease and using the power of a retrospective glance wade into the controversy of genetic determinism as it relates to disease etiology and therapeutic response.

The early investigations will involve the realm of pharmacogenetics where 50 years of investigation have suggested an appreciable role for a reductionistic approach. Examples of these investigations will be presented. The broader area of genetic epidemiology will evaluate the role of environment, genetic predisposition and free will on the ultimate

development of human disease, predictably a much more complex and lengthy investigation.

The overarching element in the delineation of genetic determinism in human disease, its effects on human freedom and the ability to use the power of medical genomics at the nexus of patients and illness rests in the still open question of the predictability of the consequences of human genetic variation.

**M**ichael Caldwell is the Director of the Marshfield Clinic Research Foundation (a Division of the Marshfield Clinic) and Director of the Marshfield Clinic's Personalized Medicine Program. The Marshfield Clinic is a large, multidisciplinary, private clinic that provides highly integrated health care for approximately 400,000 patients annually. The Marshfield Clinic Research Foundation is the largest private research foundation in Wisconsin and one of the largest in the USA.

Prior to joining the Marshfield Clinic, Dr. Caldwell held positions as Professor of Surgery and Biochemistry at the University of Minnesota and Associate Professor and Professor of Surgery at Brown University. He has over 20 years of research experience in the field of wound healing, with grant funding from various agencies, including the National Institutes of Health. His bibliography contains more than 110 published articles, books, and book chapters, and over 80 abstracts. He has spoken at more than 250 national and international events on wound healing research and treatments.

Michael Caldwell received his MD from the Medical University of South Carolina and his PhD in Physiology from Vanderbilt University. Surgical residencies were performed at the Medical University of South Carolina and the Hospital of the University of Pennsylvania.

# Genetic diseases affecting cognitive functions and behaviour



## Jean-Louis Mandel

Director, Institut de Génétique et de Biologie Moléculaire et Cellulaire, Illkirch, France

**M**uch progress has recently been accomplished in the understanding of the molecular basis of genetic diseases (monogenic or chromosome microdeletion syndromes) that result in mental retardation or more subtle cognitive deficiencies, sometimes accompanied by rather specific behavioral troubles. I will present some examples (such as the fragile X, 22q11 deletion and Williams syndromes). Mutation detection allows reliable diagnosis of these conditions, and also the provision of genetic counselling in affected families (information on recurrence risk, prenatal diagnosis). I will discuss the ethical problems that may be linked to such diagnostic possibilities, and notably the difficulties caused by the variable severity of mental handicap in patients with the same genetic anomaly. One has to consider the effect of diagnosis on the patient, on the family, and also the issue of possible population screening for some of the most common diseases, such as fragile X. On the other hand, while many genes responsible for rarer monogenic forms of non syndromic mental retardation have recently been identified, there is currently no available strategy to use this knowledge for diagnosis in sporadic cases of mental retardation.

Jean-Louis Mandel (MD, PhD), born in 1946 in Strasbourg, is Professor of Genetics at the Faculty of Medicine of Strasbourg and directs the Human Molecular Genetic group at IGBMC (Institut de Génétique et de Biologie Moléculaire et Cellulaire). He has been director of the IGBMC since September 2002.

His team has identified the genes that are mutated in 9 hereditary diseases, and has notably played an important role in the discovery and analysis of triplet repeat expansions causing several neurological diseases, including the fragile X syndrome, spinocerebellar ataxias and Friedreich ataxia. His research is now concentrating on the functional analysis of the genes implicated in some of these diseases, and in analysis of the pathogenic mechanisms. He has won international awards, including the Louis Jeantet prize in 1999, and the Zülch prize for research in neurology in 2001.

Jean-Louis Mandel is also director of the DNA diagnostic laboratory for genetic diseases at the University Hospital in Strasbourg, which carries out tests for about 30 diseases.

# Panel discussion

- Participants:
- Matthias Hentze (chair)
  - Michael Caldwell
  - Jean-Louis Mandel
  - Klaus Lindpaintner
  - Nigel Townsend
  - Jackie Leach Scully



## Klaus Lindpaintner

Vice-President and Director, Roche Genetics,  
F. Hoffmann-La Roche, Switzerland

A native of Innsbruck, Austria, Klaus Lindpaintner graduated from the University of Innsbruck Medical School with a degree in Medicine, and from Harvard University with a degree in Public Health. He pursued postgraduate training and specialization in Internal Medicine, Cardiology, and Genetics in the United States and Germany, and holds board certifications in these specialties. He practiced cardiology and pursued research in the area of cardiovascular disease genetics and genetic epidemiology, most recently as an Associate Professor of Medicine at Harvard Medical School in Boston, Massachusetts. In 1997, he joined Roche Basel as Head of Preclinical Research in Cardiovascular Diseases. Since 1998, he has been VP of Research and Director of Roche Genetics, coordinating the company's efforts and activities in genomics, genetics, and proteomics. He has co-authored more than 100 original scientific papers, holds adjunct and honorary professorships at Harvard University in Boston and University of London, and serves on the editorial board of several scientific journals. Klaus Lindpaintner lives near Basel, Switzerland; he is married to an internist, and has two daughters.



# Nigel Townsend

Artistic Director, Y-Touring Theater Company,  
United Kingdom

Between 1973 and 1989 Nigel Townsend was actor, playwright and director. The companies he worked for include: Coventry Belgrade TIE, HumberSide Theatre, Cockpit, Greenwich YPT, Young Vic, Battersea Arts, The Unicorn, BBC. In 1989 he founded Y-Touring theatre company, the Central YMCA's award-winning young people's touring theatre company, dedicated to exploring contemporary issues through theatre and drama ([www.ytouring.org.uk](http://www.ytouring.org.uk)), of which he is currently Artistic Director. Y-Touring (in partnership with organisations including the Wellcome Trust, the DfEE, the Nuffield Council, the BBC, Guys Kings and St Thomas', and the National Theatre) has produced over 33 national and international tours of plays with workshops and online resources for over half a million young people, teachers, youth leaders, health and science professionals and members of the general public, exploring HIV/AIDS, teenage pregnancy, parenting, relationships, first sex, sexuality and ethics.

Between 1995 and 2001 Y-Touring Theatre Company commissioned, developed and produced UK wide schools and theatre tours of 5 THEATRE OF DEBATE productions – original specially commissioned plays with debates and online resources about the ethical issues arising from advances in biotechnology: The Gift (Genetic selection) Cracked (Biological basis of mental illness), Sweet as you are (GM foods), Learning to Love the Grey (stem cell therapy), and Pig in the Middle (xenotransplantation). In 2003 Nigel is responsible for the launch of an innovative new website, Genetic Futures ([www.geneticfutures.com](http://www.geneticfutures.com)), the development of a new Theatre of Debate production on the ethics of brain research, and a pilot training course for science teachers.



# Jackie Leach Scully

Center for Ethics in the Biosciences,  
University of Basel, Switzerland

Jackie Leach Scully took her PhD in molecular biology at the University of Cambridge, and did postdoctoral work in oncogenesis and neurodegeneration in Lausanne and Basel. Since 1996 she has worked at the Arbeitsstelle für Ethik in den Biowissenschaften at the University of Basel. Her research interests include the ethics of genetic medicine, feminist bioethics, disability, and the use of empirical research in bioethics. Her current research projects, at Basel and the University of Newcastle, are investigating the moral evaluation by non-professionals/patients of genetic testing and of prenatal sex selection.

# EMBO Award for Communication in the Life Sciences 2003



2003 Winner:  
Peter Csermely

The European Molecular Biology Organization launched this award in 2002 in order to give recognition to the huge efforts that some scientists make to communicate their science to the public while remaining fully active in research.

The winner of the 2003 edition of the Award is Peter Csermely, professor of biochemistry at the Semmelweis University in Budapest, Hungary. The prize is awarded to prof. Csermely for his extensive efforts in interesting and engaging young people in science.

In 1996 he established a programme in Hungary to help motivated and gifted high school students (aged between 14 and 20) to find mentors and introduce them to scientific research in Hungarian universities or research institutes. The network started with one hundred students, but now includes 1260 and an additional 3800 working in student research teams. 620 high school teachers help in recruiting students and 660 mentor volunteers help in the organisation. Besides giving free top-level research opportunities to talented students at their most receptive age, the programme has already promoted the establishment of two hundred scientific research clubs in high schools in Hungary, the Ukraine, Romania, Slovakia, Croatia and Serbia, hence promoting Central-Eastern Europe cooperation. The students also participate in exchange programmes with German, Israeli, Irish, and American institutions.

Beside the organisation of this successful project, professor Csermely is also a key figure in the communication of the Life Sciences in Hungary. He has written several reviews for national popular science magazines, and is also the author of a book on stress proteins, which is a favourite among students and teachers interested in molecular studies. He pursues a very active research career studying the proteins that help other proteins to fold correctly in the cell or stabilize them in times of cellular stress.

For more information please visit: <http://www.chaperone.sote.hu>

# Social activism in science: a personal account



## Jon Beckwith

Department of Microbiology and Molecular Genetics, Harvard Medical School, Boston, USA

I describe a chance meeting on a train in France that leads me to a reunion with a long-lost scientific colleague (now a quail farmer in Normandy) and raises questions about the different choices the two of us have made. He has quit science and I remain in science and am a social activist. Both of us were influenced by the societal turmoil of the 1960's and 70's, but were unprepared by our scientific training to confront that turmoil when it spread to the scientific community. I will describe this era of social ferment in science, including the activist organizations that formed and their effects on the scientific community. Joining this movement I, as a geneticist, became determined to confront the misrepresentations and misuse of genetics sometimes promoted by scientists themselves and sometimes by social movements and institutions. Learning of the role of geneticists in the evolution of the eugenics movement led me to focus on the misrepresentation of genetic theory and research to support this movement. Historically, claims emanating from the field of human behavior genetics played a major role in eugenics theory. I chose mainly to devote my activism to exposing the scientific flaws and distortions in current research areas such as sociobiology, studies on IQ and genetics, genetics and criminality and others. These activities often brought me into conflict with leaders of the scientific community.

However, my involvement in the analysis of the social impact of genetics led to my appointment to the U.S. Government's Working Group on Ethical, Legal and Social Implications (ELSI) of the Human Genome Project. The ELSI Working Group was commissioned to anticipate the potential negative social impact of Human Genome research and propose the means for avoiding these problems. While I was initially optimistic about the potential of ELSI, the disappointing response of genome scientists to ELSI efforts led to the demise of the committee. The conflicts between the ELSI group and the scientific wing of the Human Genome Project appeared to reflect the long-standing "Two Culture" gap between scientists and those working in the social sciences and humanities.

I will talk about the lessons I have learned from my experiences. The increasing impact of fields such as genetics requires, in my opinion, greater social involvement of scientists in these issues. It is possible to be an active scientist and also participate in efforts to deal with the social consequences of science. Success in these efforts is often limited by the lack of communication and the distrust between the "Two Cultures." I will point to efforts such as the Boston-based Genetic Screening Study Group as one model for surmounting the cultural differences between scientists and those working in other fields. This group consists of scientists, sociologists, ethicists, lawyers and others representing levels from student to professor. Finally, in order for any significant increase in this important social activism to take place, scientific institutions must recognize it as a valuable component of a scientific career and reward it accordingly.

**J**on Beckwith is the American Cancer Society Professor at Harvard Medical School and a member of the U.S. National Academy of Sciences. His laboratory studies the mechanism of protein secretion, structure and function of membrane proteins, disulfide bond formation in proteins, and cell division.

Professor Beckwith has been engaged since 1969 in activities related to the social impact of genetics. He was a leader of Science for the People, an organization that worked to demystify scientific issues for the public, describing the social and political influences on scientific research and its uses. He has been critical of biological determinist thinking in such research areas as sociobiology and human behavioral genetics. He was appointed to the NIH's Working Group on Ethical, Legal and Social Implications of the Human Genome Project. Beckwith has recently published a memoir of his social activism entitled "Making Genes, Making Waves: A Social Activist in Science".

WHAT, BRAD? MY RED HAIR IS ONLY REAL IF I'VE A GENETIC ACCREDITATION TO PROVE IT?



## *Session III:*

# Use and abuse of genetic information in justice, security and the information society

One aspect of the rapid progress of human genetics, and its application in medicine, is the creation of databases containing genetic information. The issue of genetic databases has raised many difficult questions and new problems. We face, for instance, the question concerning the nature of genetic information. Genetic information is not entirely intimate, but rather contains both obvious information about us that is accessible to everyone, as well as information of a more sensitive nature. Another fact about genetic information is that it contains not only information about our present health condition, but it could say something about our future medical conditions as well. How are we supposed to react to such information? Finally with genetic information we do not only acquire information about a particular individual, but her/his relatives as well. An individual might, therefore, not only be consenting to the probing of her/his own genetic information, but that of others as well.

The ethical questions regarding genetic databases are many and diverse. In this case we have a tension between the issues of the common good that these databases are serving, and the individual rights such as the right to respect for the individual and the protection of personal data. Many have, for instance, questioned security and protection of privacy in this setting. Genetic databases have also challenged the common views on the subjects' consent for participation in scientific research, especially since many genetic databases are not created for a single research project, but are intended to be a dynamic resource for as yet unspecified scientific research. Do we have to think differently about consent in this context? In order to answer these questions some have argued that we need to analyse the effects of science and technology on ethical frameworks. Old style concepts of informed consent may, for example, not apply to this new

setting. Then we face difficult questions on the issue of genetic discrimination. A central concern here is with the definition of the term “genetic discrimination”, and how it differs from other kinds of discrimination. Should genetic information be available to and usable by insurance companies? What about employers? What are the possibilities for the use and abuse of genetic information in the evolving landscape of the information society?

Salvör Nordal, session chair

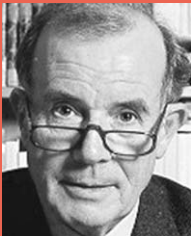


# Salvör Nordal

Center for Ethical Studies of the University of  
Iceland, Reykyavik, Iceland

**S**alvör Nordal has been director of the Centre for Ethics at the University of Iceland since 2001. She obtained a B.A. in Philosophy from the University of Iceland in 1989, and a M.Phil in Social Justice from the University of Stirling in 1992. Since 1998 she has been teaching various courses in philosophy and ethics, and has published essays in ethics and social philosophy. She is currently working on the issue of privacy in connection with genetic research and is working within the European research project, ELSAGEN - Ethical Legal, and Social Aspects of Human genetic databases - coordinated by The Centre for Ethics in Iceland and funded by the European Commission.

# The use of human genetics in health care, forensics and the private sector; ethical aspects and limits



## Ludger Honnfelder

Director, Section of Biomedical Ethics, Institute of Science and Ethics, University of Bonn, Germany

The core question underlying the general topic of this conference is what impact new scientific developments in the field of genetics may have on the old philosophical question of free will. Even if we choose to resist the concept of strong genetic determinism, the precise function of genes in the development of a human being requires clarification. This gene function creates the anthropological relation of the individual genome to that individual's personality, which as a result also needs clarification. These clarifications are important in order to assess to what degree the individual genome may be involved in a consideration of the protective rights that each person is entitled to.

Our session on the "Use and abuse of genetic information in justice, security and the information society" focuses on very special fields of societal activity where the possibility of affecting and possible offending of individual rights in the context of genetics exists: namely, the rights to informational self-determination.

At first sight, the question of the legitimate gathering and proper handling of genetic data can basically be answered within the sectors of medical

treatment and medical research, by appealing to and properly extrapolating central principles guiding both of these fields: the principle of informed consent and the principle of medical teleology (consideration of the ends for which a means can be justified). Surely not all ethical aspects in this connection have been investigated in full detail. However, of paramount importance is the fundamental idea that only the free and explicit consent of a person and the undeniably medical aim of treatment or research can justify gathering and using any bodily information from a patient or research subject. This is crucial in the 'genetic dimension' both of the physician-patient-relation and of the researcher-subject-relation, and thus will guide more specific regulations necessary in this field.

Less clear, however, is the overall balance concerning the gathering and use of genetic data by governmental and other public organs. On the one hand, there is basic agreement on the use of genetic information for forensic purposes, provided that the reliability of genetic evidence is not over-estimated, and that courts and judges are well informed and cautioned as to its possible failings. On the other hand, there is concern that citizens have to be protected against the storage of their genetic information and its accessibility to others. Obviously, there is a deep tension between both requirements, and an adequate balancing will depend on the proper identification of all individual rights involved.

However, it seems that the most intricate problems with the use of genetic data appear with respect to the private market, especially the job and insurance markets. Here, a straightforward appeal to principles of voluntary decision-making and free agreement may be just as misplaced as sweeping prohibitions. The two competing elements are legitimate rights to informational parity between contract partners in private insurance, and adequate precautionary measures against discrimination and one-sided power structures in the labour market. The proper evaluation of these will require a deeper insight into the quality of genetic information as well as into the general character of a free market from the perspective of societal justice.

**B**orn in Cologne, 1936, Ludger Honnefelder obtained a Doctor of Philosophy in 1971, and in 1981 a Habilitation in Philosophy. From 1972 to 1988 he was Professor of Philosophy in Trier and Berlin, and from 1988 to 2001 at the Seminar for Philosophy at the University of Bonn. He is currently Executive Director of the Institute of Science and Ethics at the University of Bonn (IWE), and Managing Director of the German Reference Centre for Ethics in the Life Sciences (DRZE) in Bonn. In addition, Professor Honnefelder is a member of the Steering Committee on Bioethics (CDBI) of the Council of Europe. His main research areas are ethics and applied ethics, with emphasis on biomedical ethics, metaphysics and the history of medieval philosophy.

# The spectre at the wedding feast: the Use and Abuse of genetic information, justice, security and the information society



## Alastair Kent

Director, Genetic Interest Group, United Kingdom

The “genetic revolution” holds great promise for future well being of mankind and of society. The imagery and rhetoric of genetic research has gone far beyond the laboratory and the consulting room and now permeates widely throughout society, with the iconic representation of DNA’s double helix being used to sell cars and cosmetics, to underpin fiction and science fiction, and to boost political aspirations as people from many walks of life claim a familiarity with genetic ideas, and invoke the (alleged) power of this new knowledge to support and promote their own agenda.

Clearly some genetic information is very powerful, and what an analysis of one’s DNA may reveal can be highly sensitive, and as a result a powerful mythology has emerged which may, if not carefully handled, make the proper ethical use of genetic information more difficult than it needs to be without necessarily preventing possible abuses, particularly when these arise from outcomes which may be socially undesirable, but which are biologically improbable – at least given the time scale over which it is usually claimed that they are likely to happen (or indeed may be happening already).

In my talk I will speak mainly from the perspective of patients and families living with genetic disease – whether resulting from mutations of large effect in known single genes, or as a result of the additive effects of a number of genes working together, mediated by environmental factors. I shall explore the issues raised by the use of genetic information in a range of different medical and non-medical contexts, the role of public perceptions of genetics and the need for a proper regulatory framework that puts this new knowledge in a proper context.

Amongst the topics I hope to address are the use and abuse of genetic information in the following areas (inter alia), and the conflicting demands that we face as a result:

- Research
- Clinical medicine (the planning and delivery of services)
- Insurance
- Policing
- Paternity/Genealogy
- Reproduction and reproductive technology

The stated aim of much (human) genetic research is to do good in some way. Achieving this will not be easy. Protecting this potential, whilst at the same time avoiding either abuse or the derailment of the genetic “adventure” by those who fear its consequences will be a challenge for all of us.

*“For evil to triumph it is first necessary for good people to do nothing”*  
Dietrich Bonhoeffer

**A**lastair Kent is the Director of the Genetic Interest Group (GIG) – the UK Alliance of charities and support groups for people affected by genetic disorders. GIG's mission is to promote the development of the scientific understanding of genetics and the part that genetic factors play in health and disease, and to see the speedy transfer of this new knowledge into improved services and support for the treatment of currently incurable conditions.

Prior to joining GIG Alastair worked for a number of voluntary organisations on issues concerning policy, service development and disabled people.

# Panel discussion

- Participants:
- Salvör Nordal (chair)
  - Ludger Honnefelder
  - Alastair Kent
  - Bob Bramley
  - Regine Kollek



## Bob Bramley

Chief Scientist, Forensic Science Service,  
United Kingdom

**B**ob Bramley has a degree in chemistry and a doctorate in organic reaction mechanisms. He has been a forensic scientist for 33 years. From 1970-1985, he specialised in the examination of contact traces in offences against property; the investigation of traffic accidents, fire and explosions; alcohol analysis; and the provision of a wide range of analytical services. During this time he also examined scenes of crime and gave evidence in court as an expert witness.

From 1985-1996 he held various senior management posts as Assistant Director, Business Manager and Regional Operations Manager of the Birmingham laboratory, providing services in chemistry, biology, drugs/toxicology and document examination. In 1995 he was given the responsibility for running the new National DNA Database. In 1996 he moved into his current post as Chief Scientist of the Forensic Science Service, with overall responsibility for professional standards, and Custodian of the National DNA Database.



# Regine Kollek

Research Center for Biotechnology, Society and the Environment, University of Hamburg, Germany

Regine Kollek, PhD, received her doctoral degree in molecular biology from the University of Würzburg in 1979, and then spent two years as a postdoctoral fellow at the medical school of the University of California, San Diego. From 1981 through 1984 she was senior researcher at the Heinrich-Pette Institute, University of Hamburg, before joining the scientific staff of the Enquete-Commission on „Chances and Risks of Gene-Technology“ of the German parliament. In 1988 she became a member of an interdisciplinary working group at the “Hamburg Institute for Social Research”. Since 1995 she has been professor for Biomedical Technology Assessment and head of a research group dedicated to the study of the social and ethical implications of modern biotechnology in medicine at the University of Hamburg. Since June 2001, she has been vice chair of the German National Ethics Council. In March 2002, she also became a member of the UNESCO International Ethics Committee.



BRAD, I LOVE YOUR GENETIC MAKE-UP!

I WANT TO SHARE  
MY GENOME WITH YOU!

## *Session IV:*

# Fast forward: human trait modulation, “Genomes’R’us”, designer babies and genetic identity cards

Looking into the future and making predictions is dangerous. This is because we cannot know the impact of a discovery that science has not yet made. In the session "Fast Forward" distinguished speakers and panelists will nevertheless take the risk of trying to separate science facts from science fiction in the area of human trait modulation. Science can be viewed as the art of the soluble in the domain of the possible. Technically speaking, the ability of scientists to influence human life is expressed not by what is natural but by what is naturally possible. Ian Wilmut talks about the "age of biological control" that started with the birth of the first cloned mammal. But seen in the context of what is naturally possible, the creation of Dolly the sheep was not so much reproductive cloning as proof that nuclear reprogramming of cells is not prohibited by the laws of nature (even if, at present, it can only be achieved imperfectly). The stem cell revolution, on the other hand, really is about changing an individual's fate.

Scientists are trying hard to understand the reprogramming of genomes, cells and animals, and the coming age of genetic and epigenetic reprogramming opens up huge domains of possible manipulations. Some visions, such as genetic enhancement, are well beyond traditional medical reasoning. Germline modification, homologous recombination in stem cells, artificial chromosomes, therapeutic cloning and epigenomic reprogramming are just a few concepts that have attracted much attention recently, and rightly so. Will all this science lead to us producing "designer babies"? Or humans with novel traits? Gregory Stocks predicts that some humans in 2050 will carry something like a "Chromosome 47 Version 2.0". To others this is pure science fiction. The answer to questions like this in my view will not come from science alone, but from developments in the social domain.

Trait modulation need not be genetic in the sense that it will be fixed in the genetic make-up of following generations. One rapidly emerging field is the prediction of individual life futures. Proponents of "consumer genetics" are already proposing the advent of the 1000 Dollar genome, a future in which people should start listening to their personal genomes and adapt their lifestyle and therapy accordingly. A combination of genetic information and tailored pharmaceutical or other interventions into neurological processes may be able to modulate traits and trait development in humans. What success science will have in the reprogramming of developmental pathways in humans is still an open question – at least if we are talking about complex traits. Maybe after all the recent developments in the biological sciences we simply have expectations and fears that are exaggerated and premature. Then again, this should come as no surprise: faced with prophecies, modern societies are much faster to react with alarm as to what might happen than with reflection as to what will probably happen...

Volker Stollorz, session chair

---

# Volker Stollorz

Free Lance Science Writer, Frankfurter  
Allgemeine Sonntagszeitung, Cologne,  
Germany

Volker Stollorz was born 1964 and trained as a molecular biologist at the University of Cologne. As early as the 1980s he was keeping an eye on the complex relationship between science and society, as he witnessed the Institute of Genetics becoming heavily involved in the debate about the field testing of transgenic plants. As a result, he decided to add philosophy to his scientific interests, which at the time, strangely enough, was met with scepticism in the genetics department. In 1989 he finished his diploma in genetics, developmental biology and philosophy. After doing experimental research at the Nederlands Cancer Institute in Amsterdam, he rapidly developed a calling in presenting and discussing first rate science. Starting in 1991 as a science writer with a fellowship from the Robert-Bosch-Foundation, he has since helped to shape several innovative science sections in major German newspapers, both as a science writer and editor (Die Zeit 1992, Die Woche 1993-1998, Frankfurter Allgemeine Sonntagszeitung since 2001).

# Epigenesis, selective stabilization and biological identity



## Antoine Danchin

Genetics of Bacterial Genomes, Institut Pasteur,  
Paris, France

In contrast with the popular small-talk emphasizing inheritance of many traits in plants or animals, we know that there is no one-to-one correspondence between the genome of an organism and its existence as an individual entity. At least three overall processes possessing heritable properties superimpose on each other to make the individual as we see it. All are modulated by interaction with the environment of each individual cell that make up the organism as a whole.

Genes are transmitted from generation to generation. However the way they are expressed is not "transmitted", or, rather, not in a straightforward purely mechanistic way. During their expression, selective processes retain those states that are stable enough during the time course of expression. This first results in the development of the individual from an egg to an adult form (ontogeny). Selective processes (such as apoptosis) decide the final form of the individual. Other processes incorporate an image of the environment into a time-dependent form of the individual, corresponding to an epigenetic selective stabilization of relevant relationships (for example in the immune system, or in the central nervous system).

The role of the genome is to provide a "genetic envelope" of potentialities (that may differ from person to person) but that can, in no way, determine the final individuality of the person. Emphasis on the pure genetic make-up of an organism neglects most of the understanding of what makes life. Indeed, the

main lesson we can come away with from genome programmes is not that living organisms are mechanistic automata, but, rather, that they are constructed in such a way that, even if one could consider them as submitted to purely deterministic processes, they are poised to be innovative. Living organisms are those material systems that were able to produce the unexpected for survival in an unpredictable future. In this framework it is easy to understand why the loss of a gene can sometimes be beneficial to an individual, that individuals that have the same genetic make-up and the same environment can nevertheless be recognized as different, and that it is not possible to establish a hierarchy of “good” and “bad” characters to predict the future of organisms.

**T**rained as a mathematician and a physicist, Antoine Danchin became an experimental microbiologist in the early seventies. The main goal of his research has always been to try and understand how genes can function collectively in the cell. To this end, he started in 1985 a collaboration with computer scientists to evaluate the potential use of artificial intelligence techniques in the study of integrated problems in molecular genetics. This convinced him that it was time to investigate genomes as wholes, provided that an important effort in computer sciences was initiated in parallel.

Early in 1987 he proposed that a sequencing programme should be undertaken for *Bacillus subtilis*. This proposal was brought to life by an European joint effort on this genome, starting in 1988. The complete sequence was published in 1997. The first significant and unexpected discovery of this work was, in 1991, that many genes (at that time, half of the genes) were of completely unknown function. Furthermore, it was discovered that genomes are structures that are much more ordered than previously suspected, and that there probably exists a strong interaction between the organisation of the genes in the genome and the cell's architecture.

Professor Danchin has published many scientific articles and four books, including one on the origin of life, one on genomes (*The Delphic Boat*, Harvard University Press, 2003). He has a continuing interest in philosophy, in exchanges with other civilisations (formation of a Chinese-European University Without Walls in 1990), and has published many articles on subjects in epistemology and ethics. This was at the root of his interest to promote genome research in Hong Kong, where he created the HKU-Pasteur Research Centre in 2000. He stayed in Hong Kong for three years, where he set up a working seminar with the Department of Mathematics of Hong Kong University to discuss epistemological and ethical problems raised by the recent status of Biology in human knowledge.

# Fast forward: human trait modulation, fact and fantasy



## Steven Rose

Brain and Behaviour Research Group, The Open University, United Kingdom

Maintaining a balance between the gung-ho press releases from biotech companies and university geneticists on the one hand, and the hyperbolic fantasies about designer babies, cloned geniuses, brains on chips and the rest that fuel popular anxiety is becoming increasingly difficult. This is partly because both sides in the debate about ethics and the ambiguities of scientific progress have a vested interest in exaggeration. But we need to try to draw a line between science fact and science fiction. Both advocates and opponents of gene technology tend to make the same basic scientific error: that there is a direct line between genome and phenotype unmodified by developmental contingences, and that many important human 'behavioural traits' are determined by one or a few genes. I will exemplify this by looking specifically at concerns over the genetics of 'intelligence' and 'aggression.' In opposition to the claims of genetic determinists I will argue that both are abstractions, meaningless except in the context of specific social and cultural environments, and that therefore neither is a phenotype in the classical sense. Thus attempts to identify 'genes for' such complex aspects of human interaction are simply obscurantist. Naïve counterpositions of 'the environment' to 'the gene' is a false dichotomy and both the hopes and fears invested in current and potential gene technology are misplaced.

Instead, I will argue that we need to understand living organisms, and especially humans, as autopoietic – self-creating. In the long route from fertilised ovum to adult the raw materials of genes, physical, social, cultural

and technological environment are employed in the creation of a conscious human being possessed of agency. There is no opposition between human biology and human freedom; rather, it is implicit in the nature of living processes that we are free to create our own futures, though in circumstances not of our own choosing.

It would nonetheless be a mistake to under-rate the potential of current developments in both genetics and the neurosciences in providing new opportunities for control and manipulation of nature, including human nature. Genomes are certainly not 'us' and we are unlikely to see any 'designer babies' if that is taken to mean babies whose genes have been technologically manipulated to enhance desirable or reduce undesirable traits. However we are likely to see increasing uses of genetic information to attempt to predict individual life futures. The combination of genetics and neuroscience offers the development of tailored psychopharmaceuticals, and increasing physical, chemical and biological interventions into brain and mind processes. Overwhelmingly the direction and pace of such research is in the hands of large multinational companies and the US military, and this presents civil society within and outside the US with huge challenges. How we overcome them, how we find as a society ways to control and direct such scientific 'advance' to ensure that need is placed before profit and power is a challenge that confronts us all.

Following a degree in biochemistry at Cambridge, a PhD in neurochemistry in London and post doc periods in Oxford, Rome and London, Steven Rose was appointed Professor of Biology and Director of the Brain and Behaviour Research Group at the Open University in 1969, a post he has held ever since. He is also visiting professor at University College London. His research centres on the neurobiology of learning and memory concerning which he has published more than 300 papers and reviews. He has received a variety of medals and international awards. He has written or edited 15 books including most recently *The Making of Memory* (science book prize 1993, new edition 2003), *Lifelines* and *Alas Poor Darwin* (with Hilary Rose). He is currently writing a book on the future of the brain. He has wide experience of radio and television in the context of interviews, discussion, debate and science programmes and is a regular panel member of Radio 4's *The Moral Maze*. BBCTV4 transmitted a filmed profile of him in 2003.

# Panel discussion

- Participants:
- Volker Stollorz (chair)
  - Antoine Danchin
  - Steven Rose
  - Ruth Chadwick
  - John Durant
  - Peter McGuffin



## Ruth Chadwick

ESRC Centre for Economic and Social Aspects of Genomics, Lancaster University, United Kingdom

Ruth Chadwick is Professor of Bioethics and Director of the ESRC Centre for Economic and Social Aspects of Genomics (CESAGen), Lancaster University. She has co-ordinated a number of projects funded by the European Commission, including the Euroscreen projects (1994-6; 1996-9) and co-edits the journal *Bioethics*. She is a member of the Human Genome Organisation (HUGO) Ethics Committee (Vice-Chair since 1999), the Food Ethics Council, the Medical Research Council Advisory Committee on Scientific Advances in Genetics and the Advisory Committee on Novel Foods and Processes (ACNFP). She was editor-in-chief of the award winning *Encyclopedia of Applied Ethics* (1998) and edited the *Concise Encyclopedia of the Ethics of New Technologies* (2001). In addition to CESAGen, which is a partnership with Cardiff University, current research grants include (with Oxford and Sheffield) the Wellcome Trust Electronic Bioethics Resource and partnership in the North West Genetics Knowledge Park (NoWGeN).



# John Durant

At-Bristol, United Kingdom

John Durant is Chief Executive of At-Bristol, the UK's largest independent science and natural history centre. At-Bristol attracts more than 500,000 visitors a year to its 3 main attractions: Explore, a hands on science centre; Wildwalk, a multi-media natural history centre; and IMAX, a large format science film theatre. Since opening in 2000, At-Bristol has won a dozen different awards for its buildings, exhibitions and public programmes.

John has 25 years experience as a science communicator – first, in Continuing Education; and second in science museums and science centres. For 11 years, John held the twin appointment of Assistant Director (Head of Science Communication) at the Science Museum and Professor of Public Understanding of Science at Imperial College, London. At the Science Museum, John led the practical reform of the Museum's exhibitions and public programmes, culminating in his appointment in 1996 as Director of the UK£50 million Wellcome Wing at the Science Museum project. At Imperial College, he launched a Science Communication programme embracing direction of an international collaborative research programme on public perceptions of biotechnology, the supervision of doctoral students and the creation of the UK's first MSc Course in Science Communication. He also launched the peer review quarterly journal, Public Understanding of Science.

John joined At-Bristol in 2000. He is Past President of ECSITE, the European science centre network and is currently Chairman of ECSITE-UK, the UK science centre network.



# Peter McGuffin

MRC Social Genetic and Developmental  
Psychiatry Centre, Institute of Psychiatry,  
Kings College London, United Kingdom

**P**eter McGuffin was born in Belfast and emigrated with his parents at the age of 10 to the Isle of Wight. He first decided that he wanted to be a psychiatrist at the age of 16 after coming across (something he'd never heard of before) Freud's 'Introductory Lectures on Psychoanalysis', in a local public library. He later went to medical school at the University of Leeds, England where he graduated in 1972 and then received postgraduate training in internal medicine. It was at this stage that he became interested in genetics and had his first publications on immunogenetic aspects of coronary heart disease. He transferred this interest to psychiatry and (with his wife Anne Farmer, also now a professor at the IoP) carried out one of the first genetic marker association studies on schizophrenia. He completed his training as a psychiatrist at the Maudsley Hospital, London, and was awarded a Medical Research Council Fellowship to study genetics at London University and at Washington University, St Louis Missouri. He subsequently became an MRC Senior Clinical Fellow at the Maudsley and the Institute of Psychiatry and then took up the Chair of Psychological Medicine at the University of Wales College of Medicine in Cardiff in 1987. He succeeded Prof Sir Michael Rutter as Director of the MRC Centre at the Institute of Psychiatry in October 1998. Despite his very early Freudian leanings Peter McGuffin's research, his books and papers have been mainly on the genetics of normal and abnormal behavior.

# acknowledgments

Conference book layout and editing  
Alessandra Bendiscioli, Andrew Moore

Cover design  
Petra Riedinger, Uta Mackensen

Illustration  
Uta Mackensen

Printed by  
MeraDruck, Sandhausen

Conference organisation  
Alessandra Bendiscioli, Andrew Moore

Technical support  
EMBL Photolab, Luis Vacs

Database support  
Björn Kindler

For more information on the EMBO and EMBL Science and Society activities,  
please contact:

EMBO  
Meyerhofstr. 1  
69117 Heidelberg, Germany  
Tel. +49 6221 8891 109/119  
Fax +49 6221 8891 200  
Email: [scisoc@embo.org](mailto:scisoc@embo.org)  
<http://www.embo.org/projects/scisoc/index.html>

EMBL  
Meyerhofstr. 1  
69117 Heidelberg, Germany  
Tel. +49 6221 387 493  
Fax +49 6221 387 525  
Email: [info@embl.de](mailto:info@embl.de)  
<http://www.embl.org>

# notes

# notes

# notes

# notes

# notes