

Report on the Proceedings of  
*Stem Cell Research  
Opportunities and Challenges*

15 October 2003  
Scotland House, Brussels

A Discussion Forum Organised by



in collaboration with



# PROGRAMME

## Objectives:

- to provide an opportunity for MEPs, Council staff and Commission staff to develop their understanding of stem cell science, and its social and economic implications.
- to inform the debate about the ethics of stem cell research and development and to inform the discussion on the guidelines for FP6 funding of this area of research.
- to raise the profile of Scottish achievements in stem cell research.

## Programme

### 12:30 Introduction/Overview (subject and key speakers)

Sir David Carter, Vice-President, The Royal Society of Edinburgh  
Chairman, Scottish Stem Cell Network

### 12:40 Lunch and networking

### 13:40 Session 1 – *Clinical Aspects and Science of Stem Cell Research*

- *Clinical:* Dr Marc Turner, Senior Lecturer/Clinical Director, Scottish National Blood Transfusion Service, Royal Infirmary of Edinburgh
- *Science:* Professor John Ansell, Head of Oncology Division, University of Edinburgh
- *Clinical:* Professor Bernat Soria, Director, Institute of Bioengineering, University Miguel Hernandez, Alicante, Spain

### 14:40 Discussion

### 15:10 Break for refreshments

### 15:30 Session 2 – *Ethical/regulatory/legal issues and social/economic implications*

- *The Swedish perspective on stem cell research*  
Professor Jan Carlstedt-Duke, Dean of Research, Karolinska Institute, Sweden
- *Regulatory:* Dr Marc Turner, Senior Lecturer/Clinical Director, Scottish National Blood Transfusion Service, Royal Infirmary of Edinburgh
- *Innovation and Ethics:*  
Professor Joyce Tait, Director, INNOGEN, University of Edinburgh
- *Legal:* Dr Graeme Laurie, AHRB Research Centre for Studies in Intellectual Property and Technology Law / INNOGEN, University of Edinburgh

### 16:30 Discussion

### 17:10 Closing Remarks – Sir David Carter

### 17:30 Reception – A Taste of Scotland

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*This report reflects opinions expressed by participants in a specific event. It does not, however, necessarily represent the views of the RSE Council, nor of the Society's Fellowship.*

## EXECUTIVE SUMMARY

The current state of stem cell research from the perspectives of science, clinical application, law and ethics was presented by a delegation representing the field from Scotland, Sweden and Spain.

The potential benefits arising from human embryonic stem cell research were outlined from a clinical perspective. Additionally, it was acknowledged that this would provide insight into disease mechanisms generally and how adult stem cells could be used.

A broader use of stem cells was highlighted; therapeutic applications in the treatment of cancer and their use in drug discovery were discussed.

Suggestions were made for formulating the regulatory framework for stem cell research based on a forward-looking model considering the requirements of future stringent testing for therapeutic approval.

The need for a constructive engagement with public opinion was emphasised. The role of the media across Europe will be important in this and clear lessons can be learnt from the GM crop debate.

It was suggested that the objective of the European Directives in stem cell research should be to reduce variability across countries and to provide a consistent system of accreditation and licensing. In this way an enabling framework for stem cell research to move into therapeutic benefit could be realised.

The role of industry and commercial ownership of stem cell technology was briefly addressed and identified as a key area in the future development of the field.

## INTRODUCTION

This Discussion Forum was organised by The Royal Society of Edinburgh (RSE), Scottish Stem Cell Network and Scotland Europa as a follow-on event to the meetings organised by the RSE, the Royal Swedish Academy of Sciences and the Karolinska Institute during the *Scotland in Sweden* programme in 2002 (copies of the report available from International Activities Manager, RSE or on the Society's website).

This event brought European scientists and other experts in the field of stem cell research together with officials of European Institutions and Member States governments. The Discussion Forum was held in the light of current discussions in Europe, namely on the proposed "Tissue Directive" (*'Medicine: standards of quality and safety of human tissues and cells'*) and on guidelines for the future EU funding of stem cell research under

FP6. In the summer of 2002, the European Commission published the special programme: *'Detailed FP6 implementing provisions concerning research activities involving the use of human embryos and human embryonic stem cells'*, to be finalised by the end of 2003.

To help inform the debate about these pieces of legislation and to allow expert views to be heard, this meeting was held on 15 October 2003 at Scotland House, Brussels. The programme covered three aspects of Stem Cell Research, namely: clinical and scientific issues, social/commercial issues and ethical/legal/regulatory issues. The Discussion Forum enabled further understanding of the science and issues involved to be discussed at a European level, as well as contact between officials and experts in different Member States to be made.

# CLINICAL ASPECTS AND SCIENCE OF STEM CELL RESEARCH

## ABSTRACTS

**Stem Cells and Regenerative Medicine: A Clinical Perspective.** Dr Marc Turner, Senior Lecturer/Clinical Director, Royal Infirmary of Edinburgh

Degenerative conditions such as ischaemic heart disease, cerebrovascular disease, chronic lung, liver and renal disease and diabetes mellitus are among the most important causes of morbidity and mortality in Europe, leading to a major loss of high quality and productive life for individuals and engendering a high social and economic burden on health care systems. Most current therapeutic approaches provide symptomatic control or reduce disease progression, but little can be done to reverse tissue damage and organ failure. Organ transplantation provides a solution in renal, liver, heart and lung failure and significant improvements have been made in graft survival and the quality and duration of patients' lives. However, a number of problems remain, particularly insufficiency of organ donation and the long-term immunosuppression required to prevent graft rejection. Stem cell transplantation could potentially circumvent the problems of organ shortages, avoid the need for major surgical procedures and allow repair of tissues not amenable to organ transplantation.

**In-Vitro Differentiation of Pancreatic B-Cells from Embryonic Stem Cells: New Strategies in Cell Therapy for the Treatment of Diabetes Mellitus.** Professor Bernat Soria, Instituto de Bioingeniería, Universidad Miguel Hernández, Alicante, Spain

Lack of insulin creates a devastating disease (Type 1 diabetes) which requires insulin administration during the whole of the patient's life. Islet transplantation as a potential treatment for diabetes has been investigated extensively over the past ten years. Recent results from the Edmonton group have yielded, for the very first time, insulin-independence in the totality of Type 1 diabetic patients receiving enough islets. However, such an approach will always be limited, mainly because of the difficulty in obtaining sufficiently large numbers of purified islets from cadaveric donors. One alternative to organ or tissue transplantation is the use of a renewable source of cells. *Stem cells* are clonogenic cells capable of both self-renewal

and multilineage differentiation. Recent studies have produced well-defined differentiation protocols, which can be used to guide stem cells into specific cell lineages as neurons, cardiomyocytes and insulin-secreting cells. Moreover, these derived cells have proven to be useful in different animal models. In this regard, insulin-secreting cells derived from R1 mouse embryonic stem cells normalise blood glucose when transplanted into streptozotocin-induced diabetic animals.

**Human Stem Cells.** Delivered by Professor John Ansell, University of Edinburgh, on behalf of Professor A. John Clark, OBE, FRSE, Roslin Institute, Roslin, Midlothian

A wide variety of human diseases result in end-stage tissue or organ failure. At present the options for clinical management of such patients are limited. Although in some conditions, such as end-stage renal failure, patients can be sustained indefinitely through artificial means, end-stage cardiac, hepatic, neurologic or haematopoietic damage is either rapidly fatal or leads to severe impairment of the quality of life. Organ transplantation is an option for some patients, but chronic shortage of donor organs, the hazards and complexity of transplantation surgery and the difficulties of managing immunological incompatibility between donor and recipient, preclude the use of this approach for many patients. Although xenotransplantation offers the promise of unlimited availability of donor tissues and organs, problems of immunological incompatibility have not yet been overcome and concerns over the possible transmission of zoonoses to the recipient or the wider community have yet to be resolved.

Recent advances indicate that it may be possible to generate cells for transplantation without recourse to conventional donors. This is based on findings that early development is both more "plastic" and "directable" than was previously thought. In particular pluripotent embryonic stem cells (ES) have been isolated and shown to be able to differentiate down a variety of developmental pathways. We now understand how to control the development of these ES cells to produce, for example, neuronal cells and heart muscle cells. Most of this work has been pioneered in the mouse,

but in 1998 similar human ES cells were isolated from early human embryos and grown in culture, a development that has opened up the possibility of repairing or replacing cells or tissues in such devastating diseases as Parkinson's, diabetes, and chronic heart disease. Furthermore, it now appears that the developmental pathways that stem cells and their progenitors follow are not irrevocably programmed and they can be changed or reversed. Important new information is being revealed about stem cells in adult tissues and recent findings have identified such stem cells to be much more widely distributed in other tissues than was at first thought. Surprisingly, it appears that these adult stem cells can develop into cells characteristic of other tissues under certain circumstances. Finally, the cloning of Dolly and other animals clearly shows just how plastic mammalian development is, in that differentiated adult nuclei can be completely reprogrammed after transfer into a recipient oocyte. These advances in our understanding of developmental biology set the scene for the development of new, stem cell-based "regenerative" therapies to treat tissue and organ damage in a variety of human diseases.

Since the first report of the isolation and culture of human ES cells there have been a number of significant advances. The first cultures of these cells were isolated by growing them on so-called mouse feeder cells, to provide the necessary factors to prevent them differentiating. Now it is possible to grow them on media conditioned by these cells, which greatly facilitates their handling and manipulation in culture. When these cells are removed from the conditioned medium they spontaneously differentiate and produce a wide variety of different cell types. Much of our current research is focused on how to control this differentiation and produce more defined populations of a given cell type. For example, we are studying how to generate so-called TH-neurons in culture. These are the neurons that produce dopamine; their degeneration in a

specific part of the brain called the *substantia nigra* leads to Parkinson's disease. The current protocols which have been developed involve modifying the culture conditions by adding a variety of mitogenic and differentiation factors in a stage-wise fashion and now yield populations of cells containing quite high proportions of these neurons. The next phase will be to carry out detailed proof-of-principle studies in animals to show that engraftment of such hES-derived cells can reverse the symptoms of Parkinson's. We are also learning how to differentiate hES cells to produce human liver cells. At this stage the reason for this is not so much to produce cells for transplantation but, rather, to produce human liver cells that can be used for drug discovery and testing the toxicological properties of new drugs under development. Human ES cell technology has great potential to provide large amounts of human cells types that are otherwise very difficult to obtain for this kind of research. Indeed, it may also be able to produce genetically-defined hES cells and their differentiated counterparts by combining nuclear transfer with hES isolation. Nuclear transfer could be used to generate ES cell lines from patients with complex genetic diseases that are present in tissues such as the brain or the liver. These genetically-tailored hES cell lines could then be differentiated to the cell type of interest to provide a *bona-fide* model in cell culture to study the genetics and biochemistry of the disease.

In summary, despite the complex technical, regulatory and ethical issues of working with human ES cells, this technology is at a most exciting stage. Much of the preliminary work has now been done and we are now learning how to specifically differentiate these extraordinary cells to make specific human cells for both medicine and research. Nevertheless there is still a long way to go and it will take a concerted effort from the scientists, the medical profession and the regulators before the promise of this technology can be fully realised.

## DISCUSSION

**Sir David Carter.** Are there are questions from the audience?

**Professor Carlstedt-Duke.** Is transplantation a good model for development in stem cell biology? You are going from cell function to complex tissue in degenerative conditions such as Parkinson's disease or diabetes; conditions which are not really principal targets for transplantation.

**Dr Marc Turner.** That is right. Transplantation is not a model for potential stem cell work but my presentation showed the limitations of transplantation, drawing out the nature of the problems and defining the avenues open to researchers, including the limitations of those avenues. I cannot personally see the scenario when you grow a liver in a test-tube and the notion of whole organ development does not seem a very sensible scenario.

**Professor Carlstedt-Duke.** Future targets might include congenital conditions where there are specific lesions amenable to treatment within a reasonable limit.

**Sir David Carter.** I think if I can just say something about the potential for liver cells to regenerate that provides useful context for liver transplantation. If you are a normal individual involved in a road traffic accident in which, for example, you lose 80% of your liver, and you have serial scans over the next 10–14 days, you can see the remaining 20% grows back to almost the original volume. This shows the capacity of normal liver cells to regenerate, but of course the organ remains plumbed in and works well. You might still be able to use hepatocytes for people with a failing liver, in whom hepatic structure, blood supply and drainage remains.

**Professor Carlstedt-Duke.** Or to understand the processes so that one can turn the key quickly to ensure the regeneration or optimal usage of the potential within the remaining cells.

**Professor Bernat Soria.** I would like to make a comment. If we are talking about regenerating tissues we should distinguish between cell transplantation (for example, bone-marrow transplantation) and solid organ transplantation (for example, liver or kidney transplantation). Solid organ transplantation is very different from cell transplantation. During

solid organ transplantation vessels are connected by the surgeon in order to re-establish vascularisation. Cell transplantation does not need vessel connections; that will be the option in the case of Parkinson's disease. In the case of diabetes, we need islets, a middle way between a solid organ and cells. So it is a vascularised micro-organ that contains different sub-types. The advantage of the stem cells is that you can also regenerate micro-vascular structures. It is simple in the way that the stem cell generates a structure that is assembled. In addition, you can generate different cell types such as hemopoietic stem cells and use them to induce immune tolerance by hemopoietic chimeras. In certain cases, you could use the stem cells to generate a micro-organ and with the same stem cells induce tolerance to ensure that this organ be accepted.

**Sir David Carter.** That is an important point. Another question.

**Professor Rona MacKie.** I would like to go back to diabetes. Obviously, there is a lot to understand about why our islet cells burn out, the auto-immune phenomenon in the first place, the overuse if you like. At what point do individual beta cells become an islet? There is obviously a critical point there in terms of growth and cell interaction; it seems to me that there is not much understanding. The process does not yet seem to be terribly well described.

**Professor Bernat Soria.** In the last 15 years we have studied the sociobiology of different cell types in the islet and of how the different cells arrange themselves. If you separate the islet cells, and you leave them to re-aggregate, they form an islet again; they re-establish the same connections. So it seems this property is in the cells. If we can generate different cell types, and get them to re-aggregate, then we can form an islet. From our working knowledge of the islet we even know the size of the aggregate that we need (about 50–100 cells) that will solve the oxygenation problem in the first period before vascularisation. So there are several strategies to generate an islet that could work, at least, in animal experiments. The problem is more complex than just one single cell. The case is different between Type I and Type II diabetes. In the

case of Type I, more than 50% of patients have an auto-immune disease and the rest do not have an auto-immune disease. In the case of auto-immune disease, you also have to solve auto-immunity, as these patients have antibodies against the cells. There is no one single treatment for all diabetic patients, but I am convinced that in the future we may provide different treatments for different profiles of patients, and the stem cells can help us to define the different profiles.

**Dr Donald Bruce, Science and Technology**

**Project, Church of Scotland.** I have a comment rather than a question. When people give statistics for people that suffer from diseases, and we then talk about therapy or potential therapy, what no one ever says is that, for example, instead of dying from diabetes, a patient will die from colon cancer; i.e. no one says they will still die. My second point is that stem cell technology is a new technique, and we really do not know at this stage how effective it could be. What percentage of people suffering from, say, diabetes would you expect to treat effectively if things went reasonably well, not exceptionally well? Are we talking about 5%? 80%? Just where are we?

**Sir David Carter.** You have to have a timescale on that.

**Dr Donald Bruce.** Let us say 20 years time.

**Professor Carlstedt-Duke.** Yes, Parkinson's disease rather than diabetes represents one of the nicest models that has been studied in this respect in that foetal tissue has been used to treat patients with advanced Parkinson's disease. More than 50% of these patients have shown significant improvement and these

patients have been followed for various periods, up to 10 years or more, and they have had continued benefit from the foetal transplant in the brain. I think this really shows the potential of this sort of cell-based therapy and what can be done in the future. We are still just scratching on the surface.

**Sir David Carter.** I think to address your first comment, Donald, a partial answer is provided by Finland. This country used to have the highest incidence of death from coronary heart disease, higher even than Scotland. From a variety of interventions, Finland has reduced its incidence of premature death from coronary heart disease dramatically. However, the Finns still die of coronary heart disease but they do not do so at 55, they do so much later in life.

**Professor Bernat Soria**

To return to diabetes and islet transplantation: with the new protocols from Edmonton, 80-90% of the patients are free of insulin more than one year after treatment.

**Professor John Ansell.** Can I add a comment? I wonder, Donald, if that is not a misleading question anyway. If you go back to when Michael Woodruff did the first kidney transplants in Edinburgh, would you have asked the same question about how good kidney transplantation was going to be? And with what we know now about kidney transplantation, would you have said that it is still a relevant question?

**Sir David Carter.** Well, we can park this. If you have further issues please talk to our speakers over tea. Let us break for 15 minutes. Thank you very much to our three speakers for getting us off to a fascinating start.

## ETHICAL, REGULATORY & LEGAL ISSUES AND SOCIAL & ECONOMIC IMPLICATIONS

### ABSTRACTS

#### **The Swedish Perspective on Stem Cell**

**Research.** Professor Jan Carlstedt-Duke, Dean of Research, Karolinska Institute, Stockholm, Sweden

Following the "Measures for Purposes of Research and Treatment involving Fertilised Human Ova" Act 1991, embryo research is legally permitted until 14 days after conception in Sweden. After a review by the Swedish Research Council, the act permits human embryonic stem cell research. A number of experiments have been conducted at different Swedish research institutions. Some of these cell lines are included in the NIH list of approved cell lines announced in 2000. Most reaction has been positive, but one donor couple subsequently requested the cell line to be removed, a request which raises the ethical issue about how to define a cell line, as an original or new cell preparation. The possibility of carrying out research on both embryonic and somatic stem cells will give rise to future solutions which may not be found by using either type of cells in isolation. The advantage of using stem cells over transplantation will be less rejection and stem cells may also offer a better alternative to gene therapy.

The Swedish Biobank Law came into effect in January 2003; it covers the stem cell preparations, not the stem cells themselves. The preparations cannot be used for commercial purposes and the law requires informed consent from patients, among other stipulations. From 1 January 2004, there will be a new system for reviewing the ethics of research in Sweden. There will be six independent regional Ethical Boards and a Central Board to co-ordinate ethical standpoints. These Boards' decisions will be compulsory; the Chairmen will be legally qualified and the Boards will consist of scientists and laymen.

In Sweden, there is consensus that restrictive legislation must be avoided. With the new law, the ethics will be considered on a case-by-case basis within the framework laid down by the Ethical Boards. Embryos are required for stem cell experiments and IVF research. Reproductive cloning will not be permitted in Sweden.

With the help of the Swedish media, there is support from Parliament, the general public

and the scientific community for research on stem cells to go ahead.

#### **Challenges in Bringing Stem Cell Therapies to the Clinic.** Dr Marc Turner, Senior Lecturer and Clinical Director, Royal Infirmary of Edinburgh

Stem cell research raises the prospect of regenerative therapy for some of the degenerative disorders which give rise to widespread morbidity and mortality amongst the ageing European population. However, a number of issues will have to be addressed, even at this early stage, if stem cells or their derivatives are ever to be used as human therapeutics. Much can be learnt from the development of other human therapeutics such as blood components, plasma products, bone and tissues. Haematopoietic stem cell processing and banking is particularly germane in this regard. Key issues include the provenance of the source materials and the implementation of validated process control and quality assurance systems in GMP-grade clean-room facilities. The national, European and international regulatory environment is complex and continues to evolve with regard to the quality standards and systems required to provide human therapeutics. A balanced approach will be required if we are to ensure that the development of this field is not inhibited by the very policies put in place to ensure its eventual clinical applicability.

#### **Promoting and Governing Stem Cell Research and Development in Europe.** Professor Joyce Tait, Director, INNOGEN, University of Edinburgh, Scotland, UK

Fundamental research in life sciences, particularly in areas like stem cells, is opening up new possibilities for products and services that could deliver major benefits to society. However, experience has shown that we are not good at judging the outcomes that will eventually be available, commercially or through health services, from new scientific discoveries. We tend to make linear predictions, ignoring the twists and turns and changes of direction that characterise development pathways, and the competing technologies that can arise from other areas of scientific discovery.

Despite our poor record in technology Foresight, we are now adding a further set of

linear predictions, attempting to foresee the risks and societal costs of presumed technological outcomes and to regulate research and development pathways so as to avoid them. Such a strategy is likely to close off many potentially useful development pathways and skew the scientific and technological future in ways that we will never even be aware of, whilst failing to avoid many real costs and risks.

We need new forms of governance and new rules of engagement for stakeholder groups to cope with this level of complexity. In addition to our conventional focus on science/technology, policy/regulation, and public/stakeholder concerns as separate compartments, we need to pay much more attention to the interactions amongst these constituencies. We should focus more on policies that are enabling rather than constraining – promoting desirable choices rather than closing down options. We also need to find better ways of dealing with vested interests and entrenched positions, whilst maintaining a maximum degree of choice for citizens. An important consideration is the extent to which the choices open to some citizens should be constrained because of the deeply held, and often loudly expressed, views of others.

A society where there is open competition of ideas and informed choice for citizens is more likely to be successful than one which is restrictive and fearful of novelty.

#### **The Legal Aspects and Social Consequences of Patenting the Products of Stem Cell**

**Research.** Dr Graeme Laurie, Co-director of the Arts and Humanities Research Board Centre for Research Studies in Intellectual Property and Technology Law, and Associate of the ESRC Centre for Social and Economic Research on Innovation in Genomics (INNOGEN), University of Edinburgh, Scotland, UK.

The European Commission's first report on the implementation of the Directive for the legal protection of biotechnological inventions indicates that all is not well in the Union. The majority of member states had failed to implement the provisions by December 2002, and eight members were referred to the European Court of Justice in July 2003 when further negotiations came to nothing. Many concerns relate to the uncertainty that surrounds the bioethical aspects of the law, although there is on-going confusion about what the Directive can realistically achieve, given that its remit is in the field of patents and not in the regulation of science more generally. Nonetheless, even the express aim of the Directive to provide greater legal clarity has been questioned, in particular regarding the morality provisions in Article 6. Notably absent from these provisions is any mention of human stem cells - a subject which has provoked global ethical and legal debate about whether research should take place at all, and if so, how it should be governed.

This paper considers the robustness of the current European patent provisions to meet the ethical and legal challenges posed by the prospect of patenting stem cells of human origin, with particular emphasis on embryonic stem cells. The conclusion is that the European Patent Office is embarking on a dangerous and unprincipled path in its interpretation of the morality provisions as these relate to embryonic stem cell patents. This is to the detriment of stem cell technologies and researchers alike. Guidance from the European Group on Ethics and the UK Patent Office fails to uphold the stated underlying rationale of the morality terms as these relate to embryos, namely, to respect the dignity of the embryo and guard against its instrumentalisation. All of this confusion stems from a failure to distinguish between challenges to advances in science – which should be properly dealt with through regulatory regimes – and concerns about the grant of patents – which should only relate to the impact of a monopoly on the marketplace.

## DISCUSSION

**Sir David Carter.** We have plenty of time for discussion. Questions and comments please.

**Dr Donald Bruce.** I am going to speak on the religious situation. In the European debate that is currently going on, there is the assumption that religious views on this issue are, by definition, all negative towards the use of embryos.

The Church of Scotland became involved with the embryo issue in stem cells right from the outset, and we have a more plural view of the issue. This reflects our culture in that some would say *certainly* do not use embryos for any purpose in research, others who would say that we would *rather* you did not. In a sense, this says to me, in regard to how the scientists are operating, are you hearing the public, even when the law says that you can undertake research involving embryonic stem cells? As Joyce says, there is a substantial minority in those countries which say, "do not do it at all".

Culturally, you have got to try to hold society with you. In the UK, a two-thirds majority voted for embryonic stem cell research in the Houses of Parliament, so clearly we have a mandate. But on the other hand, the regulatory authority has got to work out whether using an embryo is so important, and whether there is really no other way of doing it, as against you can use this thing any time you like. One might use the use of mice as a model for dealing with it. Where the use of animals is shooting up, is one in danger of the same problem of open season on the use of embryos, just because the law says so, without reference to the culture?

**Sir David Carter.** Jan, do you want to answer that?

**Professor Jan Carlstedt-Duke.** I think this is actually central to the whole issue of how we can work with an interplay of approaches. The idea of the use of embryonic stem cells, the use of embryos or fetuses in research is not a means *per se*; it must be a process which is productive and can not be carried out in any other way. I think this is always going to be a dynamic process. It must be an interaction between society and science. And because of that, the only way I can see that that can be carried out is through ethical boards and related means, which has a very active

process of anchoring this out in society and maintaining a dialogue with society. This is not something which can just be carried out within regulatory bodies, within parliament or within the scientific community; this is something in which society, on a broad scale, has to be engaged.

**Sir David Carter.** Joyce, you might want to come in on this.

**Professor Joyce Tait.** Yes, I do not think I was saying what Donald implied, i.e. that you have to carry all of society with you. I think I was saying rather the reverse, that there are going to be very few issues in the future that are worth bothering with, where you will carry all of society with you. And we actually have to find ways of handling the situation, where there are some quite deep divisions within society, and defining how we should go forward. I think we have to handle this potential divide between science and society more competently than we are doing at the moment. I think it should involve not allowing the views, even strongly held views, of a significant minority to over-ride the options open to the rest of society. As long as you can arrange things so that you are not imposing choices on that minority which would be ethically unacceptable to them. This means that it would not be sensible or valid, for example, to require somebody who objected ethically to donate an embryo for scientific research or to benefit from the results of that research if they objected to that. But, I think it is also not acceptable in a democracy, to allow that view to dominate the options open to the rest of society. And I think we have to begin to act much more strongly than in the past.

**Dr Donald Bruce.** But we have to be careful of the law of society.

**Professor Joyce Tait.** I think there are some fundamental norms which one must not violate and I think that is where you would have to have a discussion.

**Dr Donald Bruce.** The choice is to come in law but almost the one thing we must not do is a collection of it all in religious views. There are new laws in order to ...

**Professor Joyce Tait.** There is also a choice of

religions and I know there are some religions that do not object to choices.

**Sir David Carter.** I am anxious to bring others in on this issue.

**Professor John Ansell.** From the scientist's perspective what we need is to be able to work within a long-term decision, because science is not quick and easy. We cannot answer some of these questions within the next six months, so we need to have regulation that allows us to work within an area for some time to come. And that is what worries me, Jan, about the issue in Sweden, where you have an ethical body making regulatory decisions. The personnel on that ethical body will change, and sitting on one of these things myself, I know what a difference a different individual can make to the flavour of decisions that are made. So it would worry me, that a body like that taking a regulatory decision could overturn its own regulatory decision within six months. In the meantime, the scientists have got some money to start off what they want to do, and suddenly find they have to stop again. That is not an environment in which we are all going to prosper.

**Sir David Carter.** I was struck by the fact that you have got six different groups with an overarching group, so presumably there are checks and balances. Do you want to enlarge on this issue?

**Professor Jan Carlstedt-Duke.** In the law there is hopefully a process built in to cope with this, a process in which there should be a normalising of the ethical approach, and in which key ethical questions should always be passed up to the over-riding group. This group has a primary function to set norms for key questions, such as where the acceptable limit is today for the use of embryos, or where can you set the limit in the processes we use today. That is the big difference compared with the ethical committees that we have at present which are very independent and where much depends on which group of people sit there, or if you happen to apply to the committee in the north of Stockholm compared with the south of Stockholm. I believe that this structure will improve on the process that we do have today.

**Professor Wilson Sibbett.** I was just wondering,

listening to the various comments, whether you think that the complex multinational structure of the UK and the EU might limit some of the progress you could be making in terms of really developing robust legal systems. Such systems could promote Europe as a particularly strong area in stem cell research and might represent a process that patients could go with?

**Professor Jan Carlstedt-Duke.** I think that it is very much dependent upon what is being discussed in all four talks in this second session. Are we able to establish a system that is permissive but sets clear boundaries while not being restrictive? If we can at least agree on those conditions, I think that we can maintain plurality, accommodating the various viewpoints within different countries, within different groups based on various beliefs and so on, and have the opportunity to develop and adapt ourselves to the developments. I think you can look at what is happening in the States, where there is one over-riding and complex legal system. They do have Federal law, and despite a unified law defining certain limits, you see also there, a plurality at the State level with very diverse opportunities and possibilities of developing science.

**Sir David Carter.** I am interested in Bernat's view on this. I was very struck by the fact that you said you had to go to Singapore to do the sort of work that you wished to do. Is this still the situation for you?

**Professor Bernat Soria.** It will be for the next few years. My experience was one of frustration because after we published the first results, I applied for a grant from the Juvenile Diabetes Foundation, and won more than US\$ 600,000 (which is a big grant if you are not in the USA). So as I am from Spain, this was the biggest grant we could get. Once we had the money, we were advised that using human embryonic stem cells could be something that was not regulated, and that I could even lose the status of public servant if I pursued this work. So I began to look for a solution and, Singapore was the best thing I could find at that time. I do not know how long it will take for Spain to change the regulations and to make everything easier.

**Sir David Carter.** Other questions from the floor.

**Elizabeth Mitchell, Medical Research Council.** I

would like to ask Marc Turner (who was quite sanguine about the Tissues Directive) whether he has any comments on the amendments put forward?

**Dr Marc Turner.** If I gave the impression of sanguinity it was not intended. I think the question of regulation is quite interesting, because there are two quite separate things we are discussing here and my main concerns are that the Tissues Directive has tended to confuse the issue. One concern is that we have had quite an active debate about the regulation of *in vitro* research surrounding embryos and stem cells and related issues. Personally, I think we need to look at issues of plurality within and around Europe. The other issue is regulation as it applies to therapeutic products for safe and effective use, and there is already enough plurality around that, more than we need. My main concern about the European Tissues Directive is that, like the Blood Directive, its main or appropriate focus should be the regulation of therapeutic products. In my opinion, the ethical issues surrounding embryonic stem cells, the fundamental ethical questions about stem cell research, are a bit *ultra vires*, in the same way as they are in the patent issue, if you see what I mean. I think a good piece of legislation set up for one particular purpose has been dragged into an entirely different kind of debate. That does concern me, because it might end up that we do not get a much-needed European Tissue Directive because it has got bogged down in these difficult ethical issues surrounding human embryonic stem cells.

**Sir David Carter.** I wonder if I could get the panel to speculate on what is going to happen about funding of embryonic stem cell research in Europe? It seems to me that in the States there has been no logic. I wonder what is going to happen in Europe and what the time scale is going to be?

**Professor John Ansell.** A comment. I have a feeling that it is going to be pragmatically decided. If I can be slightly flippant, if Christopher Reeve were to stand up and make Superman IV as a result of some of this technology, I think President Bush would be forced, both commercially and through public opinion, to change his stance. Similarly, if the technology for curing diabetes became

common and accessible across Europe, most States in Europe would be for stem cell research. I just have a feeling that that is how it is going to go, with the ethical debate becoming a secondary issue to the public wanting these treatments.

**Professor Bernat Soria.** I have a more general comment. It is difficult to discuss ethics, but as scientists we have to provide information; basically that is our commitment. However, we are also citizens and we have ethical values; most of us have been educated in the ethical and cultural values that we share all over Europe. But Europe is changing, it is becoming multi-cultural; for example, the percentage of Muslim people is increasing and we have to accommodate multi-culturality in the decisions. So the question is, can we generate a framework that is acceptable and usable for everybody? There is a broad consensus in the scientific community, patients' organisations and medical associations that stem cell research is very important. We have a long tradition of ethical boards that analyse clinical issues, so I would pass some of the decisions to these boards as one way to solve the problem. There is one final consideration: the field is exploding now. We are discussing what has been published in the last few months; we do not know what will be published in the next two months even. I have said previously that human stem cells are not totipotent, but there is one paper describing how you can go from embryonic stem cells to germ cells and at least you should be able to generate parthenogenetic embryos from these stem cells. I enjoyed the last presentation about patenting, but if you consider the novel biological entities that will be created, it will probably be more useful and acceptable to have an experienced ethical board that incorporates different ethical viewpoints.

**Dr Graeme Laurie.** I think we have some examples which demonstrate that we tend to stumble forward in what is quite an unprincipled way and we tend to fall back on legal sophistry or other political fudges. For example, look at the reaction to cloning, where we came up with this very convenient distinction between therapeutic and reproductive cloning. In the Article 6 that I

talked about, we have this list of specific inventions that will not be patented. It is my firm belief that the reason we came up with that list was that the Directive had taken ten years to get to the stage it had. So, the question was what are the most controversial issues at the moment? Cloning and interfering with the germ line? They were put on the list specifically and without thinking forward as to what it might mean for new technologies that arise. So we end up with these fudges. Yes, the funding comes forward and the regulatory process stumbles on but I think it is a really unsatisfactory way to proceed.

**Sir David Carter.** Jan, did you want to comment?

**Professor Carlstedt-Duke.** Yes, I think you asked about the funding. I think the moratorium that we have just now, if it was made permanent, is a very dangerous track to go down. We are in danger of changing the whole basis of the Framework programme, in which one has set up a guideline for the Programmes that allows research as long as it is permitted in the country or institution where it is carried out. We must have the potential to develop a situation where an individual or a minority is going to dictate what is not allowed or is allowed. And you can appreciate that this can be extended into many other areas of research in which there is controversy, such as psychiatry or *in vitro* fertilisation, contraception and the like. There are many other issues in which we do not have consensus in society and in which it will be possible, if we follow this principle, to block research using the Framework Programme. I think that it would be a very dangerous track using a restrictive point of view rather than an open point of view with an active process of acceptance or not of individual experiments.

**Carole McKinlay, UK Research Office (UKRO).** I attended a talk on Monday that was about ethics in medical research. Octavi Quintana Trias of the DG Research in the European Commission, who has as part of his remit research dealing with stem cells, said that it was not an issue of whether or not stem cell research will be funded, but rather the conditions that would be required to satisfy everyone to allow it to be funded. So I think it is not a question of whether it will go ahead, it is just a question of how.

At the same talk though, there was a big focus on the issue of consent, and active and informed consent for stem cell research. One of the speakers today mentioned that there has been a cell line developed but the donors had withdrawn their consent. He said that the cell line had to be destroyed and that this had caused a bit of a problem because of a lack of information collected from donors in the first place. However, surely that is a fundamental part of the system to allow that to happen subsequently? There was also an issue that Marc Turner mentioned, in relation to patient administration, namely that it is difficult to follow patients over thirty years or so and know where they are. One of the debates that went on for quite a long time at the event on Monday, focused on the fact that we can have informed consent for donation, but should you go back to the donors later on if you are changing the research that you are doing and find out if they still consent? Obviously the two choices are, do you have to follow the donor or do you have to have a really complex consent form in the first place? I wonder if any of the speakers have any thoughts on these issues?

**Professor Carlstedt-Duke.** Yes, and the reason why I raised that point is to stress that it is very difficult to set the limit. What is it that has been donated? Is it the embryo, is it the primary cell extract, is it the cell line, is it the modified cells and so on - where do we set the limit? And this is something that has to be addressed. This problem was not addressed in this particular case and I would contend that if it is an established cell line, something that has undergone scientific development, that is not the original donation and that it should not be withdrawn.

**Sir David Carter.** Marc, do you have a comment on this?

**Dr Marc Turner.** Yes, I think it is an extremely tricky issue. Actually, we treat research in clinical consent slightly differently from consent to conventional treatment. You are quite right, for a research project, for example, if you are putting a patient through a clinical study or if they are donating a sample, we take consent for that specific study. You are not entitled to then use those samples for some other study that comes into your head

subsequently. And you are quite right, the patient has the right to withdraw their consent at any stage. Of course, we do not actually do that for therapeutic products. If you are a blood donor, you consent to the donation, you cannot then decide ten days later that you want your blood back. Also, if you come into A&E (accident and emergency) bleeding to death, the hospital does not ring up all the donors to confirm their consent. It seems to me just hearing about this specific consent issue for the first time, that if the donation was made in full knowledge of the range of things that could be done with it, this decision to destroy a cell line might be unreasonable.

**Carole McKinlay.** My point was not so much about clinical practice, it was about the research surrounding it. If it is difficult in clinical practice to monitor the patient for thirty years and know where they are, then doing it for donors in research projects must be equally difficult.

**Ben Turner, UK Representation to the European Union (UKREP).** I wanted to make a comment because the impression is often that this young science is in danger of being snuffed out by ignorant regulation in this area, and I can see why some would want to present that picture. Can I just go back to the exact words you used on the Framework Programme? People need to understand that the issue that is being discussed at present by the European Union is a very specific issue about how the Framework Programme, and how a specific part of that is funded, something in the order of 40M euros. It is not an issue of European regulation dictating to Member States what they can and cannot do. That has clearly been ruled out. So we are not talking about a Directive in that case. Even when we are talking about a Directive, such as the Tissue and Cell Directive, the Member States have clearly taken a common position, against those amendments where ethical considerations are being brought in.

There is a particular MEP who is very keen to bring ethical amendments into this, but let us wait and see what happens is my point. I would not want people to go away from here thinking that European regulation is about to ban stem cell research, or even the funding of it throughout Europe. A lot of this is about presentation and that is why the UK government, whom I represent, is very very interested in this set of stem cell research guidelines. But the practical effect of these decisions would be marginal on biotech science in the UK. I think people in the know should not therefore overstate the case either way.

**Professor Carlstedt-Duke.** Could I make a rebuttal? I agree that the guidelines today are very clear: that this is not the case, this is not allowed. What I said was that there was a seminar in April in which governments were asked to define their standpoint on the ethical aspects of stem cell research. There were a number of government representatives who put forward the particular point that because stem cell work was not allowed in their country, they considered that it should not be allowed to be funded within in the Framework Programme. That would create a completely new precedent. That is not the case today, but this is a precedent that has been raised within the discussions of funding stem cell work within the Framework Programme.

**Ben Turner.** The UK government agrees with you. However, the current issue with the Framework Programme is not an issue of harmonisation, it is about internal guidelines for the European Community funding. With any kind of EU spending that is done, like structural funds or whatever, there will be criteria and financing rules or rules about the qualifications needed, etc. I think these are very different issues, and people need to keep that distinction firmly in their minds.

## SUMMARY AND CONCLUDING REMARKS

**Sir David Carter.** I have certainly learnt a great deal today.

The take-home messages for me are as follows:

- ❖ If we could really understand the biology of embryonic stem cells it would transform our ability to do things with adult stem cells, and it would transform our understanding of biology in general. I am not just thinking about normal processes but also about disease states such as neoplasia.
- ❖ Before I came, I was clear about some of the issues surrounding the use of stem cells in tissue or cell regeneration, and in drug development and toxicity. I was not clear about the possibility of the use of stem cells as adjuvant therapy in the treatment of metastatic cancer. That is something that has intrigued me today, and I will take it away as an important issue.
- ❖ In today's presentations we deliberately used transplantation as a good working example of some of the predicaments that clinical medicine finds itself in. And as someone who has worked in transplant surgery, there is one point I would like to make to you in the context of discussing graphs that show duration of survival. If you transplant somebody's liver, when they wake up the next morning from the anaesthetic, they will tell you they feel immeasurably better, and the quality of life that that transplantation brings about must not be understated. I think that we have learnt today, again, that our ability to continue solid organ transplantation is limited, even in Spain with an impressive track record of organ donation. In general, it is clear that organ donation is going to fail even further to keep pace with demand and we do have a huge problem.
- ❖ One of the impressive things about today is that we have aired some of the negative experiences. We have not talked about the possibility of malignant transformation in any detail but we have mentioned it as an issue demanding further study. The question of the Swedish couple who wanted their cell line destroyed raised a lot of issues that I am sure we are all going to go away and think about.
- ❖ I was very taken with Marc Turner's point that just because you bring in good manufacturing practice now, do not assume that this will take care of all the cell lines that have been or will be produced. It seems that certain that many lines will not pass the stringent tests that we now require. We have got to be clear and explicit about the negatives that surround stem cell technology. We also have to accommodate the point that we might get things passed in a country but there are still going to be significant minorities who are uneasy about the direction of travel. I see these as challenging but not insuperable issues.
- ❖ Returning to this distinction between adult and embryonic stem cells, the question of scalability is very important, the point that Bernat Soria made very strongly. You can convince adult stem cells that they should differentiate but you cannot necessarily get them to proliferate. That, for me, goes back to the starting message: if we understood more of the mechanisms that control these processes (and we are able to pursue that research), then it might transform our ability to use cells other than embryonic stem cells in the future.
- ❖ The regulatory question, I suppose, is one of the key issues for people sitting in this room. I was very impressed when, as representatives of the RSE, we were in Sweden last year. We got a taxi from the airport and were going to a joint meeting with the Karolinska Institute and the Swedish Academy of Sciences. The taxi driver spoke very good English and enquired why we were there. We replied that we are scientists and we were reluctant to bother him with the details. But he insisted and upon being informed we were there to discuss stem cells, he asked if we would be discussing embryonic stem cells or other forms of stem cells. We then went to the meeting, and Professor Harriet Wallberg-Henriksson from the Swedish Medical Research Council gave us a excellent paper on how Sweden had engaged its public in the debate about the ethicality of stem cells. She showed a slide with a range of

organisations that had been unhelpful to them and at the other end of the spectrum, organisations which had been most helpful in ensuring a measured debate with the public. The organisations which had been most helpful to them were the media. You certainly could not display that slide in Britain! So we took a very big message away from that. I like the clarity of Sweden's proposals for regional Ethical Boards and the over-arching Board. We will all be very interested to see how this arrangement develops.

- ❖ One of the key unanswered questions today was, who do cell lines belong to if you are in industrial partnership? This will prove important, as most of this work is conducted in partnership with industry. That could be the subject of another meeting.
- ❖ Regarding the question of the Directives, I think we all appreciate the laudable aim of trying to reduce variability and close gaps. We accept that we have to have a mandatory system of accreditation and licensing. But I take the point that we are not looking for a restrictive legislation, we are looking for a framework that is enabling and not constraining. I was very taken by the point that Joyce Tait was making, namely that stem cell research could be the next GM, and I share her anxiety. I think that in Britain, the debate surrounding stem cell research could very easily become similar to the GM debate. The debate on GM in the UK has been seriously distorted and I would have real concerns that unless we engage more constructively with the public (one of the things the Network (SSCN) wants to do) we are in for a very difficult time.

I think Joyce Tait's point about innovation not being linear is one of the messages that came across very clearly. I think she is absolutely right to stress the degree of unpredictability; you do not necessarily know what is going to happen with science over the next weeks or months that might change an apparently linear prediction. And I like the point that she was making about the carrot and the stick, to the need to enable rather than constrain.

- ❖ I thought the final paper about patents gave us clarity regarding what will remain a complex issue. I take the point that we need consistency, and we need to draw the distinction between the ethics and the science, and the concerns about patenting and the commercial issues that surround it.

I hope you agree that it has been a superb day. We are grateful to our panel, some of whom have had to step in at the last minute. I think they have acquitted themselves well. We have been delighted to have you all join us, you have been a great audience. I hope you feel that today has been useful and that you have made some contacts that will be useful to you and useful to us, as we take forward the work of Scottish Stem Cell Network. We would like to see our Network not only as something that is good for us in Scotland, in developing this science objectively in concert with public opinion and the other commercial and business issues, but also as a means of developing active partnerships in Europe.

So my final thanks to you all for coming, and, in particular, to the panel of speakers. I thank those that have organised this meeting from the Royal Society of Edinburgh, the Scottish Stem Cell Network and our hosts, Scotland Europa. It has been a really enjoyable day. Thank you all very much.

## PARTICIPANTS

Ms Annagrazia Altavilla, Marseille University

Ms Karin Altenberg, British Council Sweden

Professor John Ansell, University of Edinburgh

Professor Jane Bower, Glasgow Caledonian University

Dr Donald Bruce, Church of Scotland

\* Mr George Calder, Scottish Executive EU Office

Professor Jan Carlstedt-Duke, Karolinska Institute

Sir David Carter FRSE, The Royal Society of Edinburgh

Ms Katrien Devolder, Centre for Environmental Philosophy & Bioethics, Ghent University

Mr Donald Ellis, Secretariat of the EU Council of Ministers

Ms Sarah English, Scotland Europa

Ms Jean Finlayson, The Royal Society of Edinburgh

Mrs Liliana Galetescu, European Commission

Mr Herve Gouget, British Council

Mr Paul Harris, Scotland Europa

Mr Roland Hein, Permanent Representation of Germany to the EU

Dr Anne Hicks, Biotechnology & Biological Sciences Research Council

Professor Outi Hovatta, Karolinska Institute

Mrs Barbara Humphreys-Zwart, Secretariat of the EU Council of Ministers

Ms Maria Johansson, European Parliament

Ms Gwennael Joliff-Botrel, European Commission

Mr Charles Kessler, European Commission

Dr Graeme Laurie, AHRB Research Centre for Studies in Intellectual Property and Technology Law/INNOGEN, University of Edinburgh

\* Professor Sir Neil MacCormick, MEP, FRSE, European Parliament

\* Mr Donald MacInnes, Scotland Europa

Mr Colin Mackay, Weber Shandwick Adamson

Professor Rona MacKie FRSE, Department of Public Health, University of Glasgow

Ms Carole McKinlay, UK Research Office

Ms Elizabeth Mitchell, Medical Research Council

Dr Marilyn Moore, Scottish Stem Cell Network

Mr Kandelberger, Stagière to Frau Angelika Niebler MEP, European Parliament

Dr Frank Niggemeier, Permanent Representation of Germany to the EU

Mr Jonathan Orr, Permanent Representation of the United Kingdom to the EU

Dr Anne Marie Schleich, Auswaertiges Amt

Professor Wilson Sibbett FRSE, Scottish Science Advisory Committee

Professor Bernat Soria, Institute of Bioengineering, University Miguel Hernandez, Alicante, Spain

Ms Elisa Stefani, Assistant to Mr Fiori, MEP, European Parliament

Ms Sandra Steinhauer, Vienna Business Agency

Professor Joyce Tait, University of Edinburgh

Ms Sally Taylor, European Parliament

Dr Ralf Toenjes, Paul Ehrlich Institut (Langen, Germany)

Mr Ben Turner, Permanent Representation of the United Kingdom to the EU

Dr Marc Turner, Scottish National Blood Transfusion Service

Mr Michael White, The Royal Society of Edinburgh

Ms Marta Yanci Serrano, Madrid Regional Representation Brussels Office

Mr Leo Zonneveld, British Embassy, The Hague

\* Attended lunch or reception only

## BIOGRAPHIES

### CHAIR

#### **Sir David Carter, FRSE**

Sir David was Vice-President of The Royal Society of Edinburgh until 27 October 2003 and is Chairman of the Scottish Stem Cell Network. He was Regius Professor in Clinical Surgery in the University of Edinburgh (1988-96), Chief Medical Officer in Scotland (1996-2000) and Vice-Principal of the University of Edinburgh (2000-2003). He is currently chairman of the BMA Board of Science, the Health Foundation and the Queens Nursing Institute (Scotland). He was Chairman of the Scientific Advisory Committee of the Cancer Research Campaign prior to the formation of Cancer Research UK and is a member of the new Scientific Executive Board of the new charity. He is a Fellow of the Royal College of Surgeons Edinburgh and England, Royal College of Physicians of Edinburgh, Royal College of Physicians and Surgeons of Glasgow and the Faculty of Public Health Medicine. He is an honorary fellow/member of various international colleges and of the Deutsche Gesellschaft für Chirurgie, Society of Surgeons of Nepal and American Surgical Association.

Surgical interests centred on hepatobiliary and pancreatic disease and he was President of the International Hepato-biliary and Pancreatic Association in 1989. He established the Scottish Liver Transplant Unit in Edinburgh. He served as Surgeon to Her Majesty the Queen in Scotland from 1993-1997.

### SPEAKERS

#### **Professor John Ansell**

Professor of Experimental Haematology, University of Edinburgh. Head of Division of Oncology, School of Molecular and Clinical Medicine, College of Medicine and Veterinary Medicine, University of Edinburgh. Director, University of Edinburgh, Leukaemia Research Fund, John Hughes Bennett Laboratory. Deputy Director, Edinburgh University Cancer Research Centre. Co-Director, Scottish Instrumentation and Research Centre for Advanced Mass Spectrometry (SIRCAMS). Secretary and Co-founder of the Scottish Stem Cell Network. He is also a Member of the Roslin Institute Ethics Committee and on the Editorial Board of *Cloning and Stem Cells*.

John Ansell has had a major interest in haematopoietic stem cell differentiation for approximately 20 years and was a founder member of the Centre for Genome Research (now Institute for Stem Cell Research). More recently he has helped to establish SIRCAMS as a resource for proteomic studies in biomedical research.

**Professor John Clark, OBE, FRSE** was unable to attend the meeting due to illness. Professor Ansell delivered Professor Clark's presentation on his behalf at short notice.

John Clark was educated at Barton Grammar School, Lincolnshire, UK. In 1973 he gained a BA (Hons) degree from Christ's College, Cambridge and in 1975 an MSc in Zoology

from the University of W. Ontario, Canada. He was awarded a doctorate in Genetics from the University of Edinburgh in 1982.

He has had a distinguished scientific career beginning with a Post-doctoral Research Fellowship in the Department of Genetics at the University of Edinburgh. This research involved the cloning and characterisation of the mouse major urinary protein (MUP) genes.

From 1986 to the present he has been a Scientist at the Roslin Institute. He was appointed Head of Division, Gene Expression & Development in 1993, conducting research which involves the application of gene technologies to mice and farm animals. He became Director of the Roslin Institute in 2003.

He is leading a personal research programme focused on the development of novel transgenic technologies and the development of human stem cells. He is founder and consultant to Geron BioMed.

In 1997, Professor Clark was awarded an OBE and in 1999 he was elected a Fellow of the Royal Society of Edinburgh.

#### **Professor Jan Carlstedt-Duke, MD, PhD**

Medical training at Karolinska Institutet, Stockholm. Licensed physician 1984. PhD in medical chemistry 1979, Karolinska Institutet. Docent in molecular endocrinology 1983. Professor of molecular endocrinology 1996. Vice-Dean of Research at Karolinska Institutet

1999. Dean of Research since 2001. Area of focus in research has been the mechanism of action of steroid hormones, particularly glucocorticoids. Clinically active in paediatric endocrinology until 1999.

#### **Dr Graeme Laurie**

Graeme Laurie is Senior Lecturer in Law at the University of Edinburgh and co-Director of the Arts and Humanities Research Board Centre for Research Studies in Intellectual Property and Technology Law. He is also an Associate of the ESRC InnoGen Centre for Social and Economic Research on Innovation in Genomics, also at Edinburgh University. His research interests include the role of law in promoting and regulating science, medicine and technology. He has provided advice to, and been consulted by, a number of bodies on matters of technology and law. These include the House of Commons Science and Technology Committee (1995), the Governments of Lesotho (1997) and the Faroe Islands (1999), the Massachusetts State Legislature (1999), the World Health Organisation, WHO (2000), and the Human Genetics Commission (2001). In 2001 he convened a WHO Working Group that produced international guidelines on the establishment and maintenance of genetic databases. He is a member of the Interim Advisory Group on Ethics and Governance for Biobank UK and the Privacy Advisory Committee for Scotland and serves as an Associate Editor (Law) on the Journal on Medical Ethics. His publications include the monograph *Genetic Privacy: A Challenge to Medico-legal Norms*, published by Cambridge University Press in 2002.

#### **Professor Bernat Soría Escoms, MD, PhD MD (Valencia, 1974); PhD (Valencia, 1978)**

Since 1988, full Professor of Physiology and Director, Institute of Bioengineering, University Miguel Hernández, Alicante, Spain. Full Professor of Physiology and Biophysics, University of Alicante (from 1986). Chairman of the Department of Physiology, University of Alicante (1990-1997). Vice-Dean and Acting Dean of the University of Alicante, School of Medicine (1985-1986). Co-ordinator of the National Agency of Evaluation, Comisión Interministerial de Ciencia y Tecnología (Madrid, 1991-1993). Associate Professor, Dept Biochemistry and Physiology, University of

Alicante School of Medicine (1984-85). Vice-Dean of the School of Medicine, University of Valencia (1983-1984). Associate Professor, Dept Biochemistry and Physiology, University of Valencia School of Medicine (1982-1984). Senior Research Associate, Dept. of Biophysics, School of Biological Sciences, University of East Anglia, Norwich (1980-1982). Postdoctoral fellow, Max Plank Institut für Biophysikalische Chemie, Göttingen (1979-1980). Membranebiophysik gruppe (Drs Neher and Sakmman, Nobel Laureates 1991).

*Membership and Duties in Scientific Societies, Editorial Work:* President of the Spanish Society of Diabetes (2000-2004); President of the Spanish Society of Biophysics (1999-2003); President of the European Association of Biophysical Societies (2003-2004); President of the Spanish Society of Physiological Sciences (1998-2000); Member of the Council and Convenor of the Biomedical Engineering Task Force of the International Union for Pure and Applied Biophysics (IUPAB); Secretary of the Board of Fundación Valenciana de Investigaciones Biomédicas (1992-95); Consultor of the European Parliament, STOA Committee (1995-97); Associate Editor of *Pflügers Archiv-European Journal of Physiology* (1996 to date); Founding Member of the Instituto de Neurociencias de Alicante (1990-); Founding Member of the Sociedad Española de Neurociencias (1983-); Sociedad Española de Bioquímica (Ordinary Member, 1984-); European Association for the Study of Diabetes (Ordinary Member, 1988-); Biophysical Society USA (Ordinary Member, 1987-); Cell Transplant Society (Ordinary Member, 1991-); Pancreatic Islet Study Group (Member of the Council, 1993-); Physiological Society (Ordinary member, 1996).

#### **Professor Joyce Tait**

Director of the ESRC Centre for Social and Economic Research on Innovation in Genomics. She is a Professorial Fellow in the University of Edinburgh, with an interdisciplinary background covering natural and social sciences. She specialises in systemic approaches to complex issues, particularly in areas related to developments in chemical and biological sciences: strategic and operational decision making in companies and public bodies; policy analysis; risk assessment and regulation; Foresight;

technology management; sustainable development; public attitudes and communication; land use and management.

The InnoGen research programme will focus on three perspectives – scientists, industry and private interest groups; policy makers and regulators; and citizens and public interest groups. The analysis will explore the interactions amongst these constituencies and their implications for the evolution of the knowledge base, the structure and dynamics of the industry sectors involved (pharmaceuticals, health care, food and agro-biotechnology), the evolution of policy at UK, EU and global levels, and the development of processes of citizen and stakeholder engagement in innovation processes. Research projects will cover developed and developing countries.

**Dr Marc TURNER, PhD, FRCP(Ed), MRCPPath**  
Senior Lecturer in Immunohaematology and Transfusion Medicine at the University of Edinburgh and Clinical Director / Consultant Haematologist at Edinburgh and SE Scotland Blood Transfusion Centre. His research interests include immunohaematology, the risk of transmission of variant CJD by blood transfusion and he is leader of the SNBTS Cell Therapeutics Group focused on the translation of academic and preclinical research studies into the clinic in the fields of stem cell and regenerative medicine, adoptive immunotherapy and tissue engineering.

## DISCUSSANTS

**Professor Rona MACKIE, CBE, FRSE**

Professor of Dermatology, and Head of Department at the University of Glasgow from 1978 to 2000. Currently, she is a Senior Research Fellow at Glasgow University in the Department of Public Health and Medical Genetics. Professor MacKie's major research interest is in the field of skin cancer, particularly malignant melanoma. She currently holds grants for both epidemiological and molecular biological research in this area. She is an active member of the European Organisation for the Research and Treatment of Cancer, and of the World Health Organisation's Melanoma Programme. Professor Mackie is also International Convener for The Royal Society of Edinburgh.

**Professor Wilson SIBBETT, CBE, FRS, FRSE**

Chair of SSAC and Wardlaw Professor of Physics, University of St Andrews. Professor Sibbett was a member of the Joint Working Group of The Royal Society of London and The Royal Society of Edinburgh, which produced the highly influential report, *Devolution and Science*, published in April 1999. He is widely recognised as a world authority in laser physics and optoelectronics. Professor Sibbett's work has wide-ranging applications in the field of ultrafast science and technology, including optical communications and photobiology. He was the recipient of the Rank Prize for Optoelectronics in 1997, The Mitutoyo - NPL Frontier Science and Measurement Award in 1998 and the Rumford Medal of the Royal Society for "Research into Ultrashort-Pulse Laser".

## BACKGROUND INFORMATION

### News items, sources of background information

There is a wealth of information available on the subject of stem cell research. The following is given for reference and is by no means an exhaustive list; web addresses have been given where possible as an acknowledgement of the source of information. We accept no responsibility or liability whatsoever with regard to the information contained in the references below, and readers should respect copyright where appropriate.

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Creation of the International Stem Cell Forum (ISCF), August 2003: [http://europa.eu.int/comm/research/biosociety/news\\_events/news\\_genetics\\_networking\\_en.htm](http://europa.eu.int/comm/research/biosociety/news_events/news_genetics_networking_en.htm)

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EC Press release dated 7 April 2003, ref. IP/03/506 - report for EU Inter-Institutional seminar on bioethics, held on 24 April 03: [http://europa.eu.int/rapid/start/cgi/guesten.ksh?p\\_action.gettxt=gt&doc=IP/03/506|0|RAPID&lg=EN](http://europa.eu.int/rapid/start/cgi/guesten.ksh?p_action.gettxt=gt&doc=IP/03/506|0|RAPID&lg=EN)

Homepage for seminar 24 April 2003 - programme, speakers and web cast of speeches, requires Windows Media player to listen. [http://europa.eu.int/comm/research/conferences/2003/bioethics/index\\_en.html](http://europa.eu.int/comm/research/conferences/2003/bioethics/index_en.html)

Links to documents on bioethics: [http://europa.eu.int/comm/research/biosociety/bioethics/documents\\_en.htm](http://europa.eu.int/comm/research/biosociety/bioethics/documents_en.htm)

Links to documents about embryonic and foetal tissue. [http://www.europa.eu.int/comm/research/index/pages\\_en\\_731.html](http://www.europa.eu.int/comm/research/index/pages_en_731.html)

DG Research Science and Society web page. [http://www.europa.eu.int/comm/research/science-society/index\\_en.html](http://www.europa.eu.int/comm/research/science-society/index_en.html)

DG Research Biosociety webpage. [http://europa.eu.int/comm/research/biosociety/index\\_en.htm](http://europa.eu.int/comm/research/biosociety/index_en.htm)

Summary of the Council of Europe Oviedo Convention on Human Rights and Biomedicine – signed in 1997 following 20 years of debate. Referred to in the Ethical Rules for FP6 below. [http://www.coe.int/T/e/Communication\\_and\\_Research/Press/Topics/Bioethics.asp](http://www.coe.int/T/e/Communication_and_Research/Press/Topics/Bioethics.asp)

EU supports and co-ordinates stem cell research Brussels, 12 September 2001: <http://europa.eu.int/comm/research/press/2001/pr1409en.html>

Background note published 7 November 2002 - written in layman's terms with box on stem cells, called "Life sciences, genomics and biotechnology for health: the new picture of health". <http://europa.eu.int/comm/research/news-centre/en/med/02-11-ed01.html#box01>

### Extracts

**a) From Ethical Rules for FP6: Crucial information for the Sixth Framework Programme applicants who have identified ethical issues, in the "Guide for Proposers checklist"**

[http://europa.eu.int/comm/research/science-society/ethics/rules\\_en.html](http://europa.eu.int/comm/research/science-society/ethics/rules_en.html)

National legislation. Participants in FP6 projects must conform to current legislation and regulations in the countries where the research will be carried out. They must seek the approval of the relevant ethics committees prior to the start of the RTD activities, if there are ethical issues involved.

EC legislation. Participants must conform to relevant EU legislation such as:

- The Charter of Fundamental Rights of the EU.
- Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on

the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.

- Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data.
- Council Directive 83/570/EEC of 26 October 1983 amending Directives 65/65/EEC, 75/318/EEC and 75/319/EEC on the approximation laid down by law, regulation or administrative action relating to proprietary medicinal products.
- Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions.
- Directive 90/219/EEC of 23 April 1990 on the contained use of genetically modified micro-organisms.
- Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC.

#### **International conventions and declarations**

Participants should respect the following international conventions and declarations:

- Helsinki Declaration in its latest version
- Convention of the Council of Europe on Human Rights and Biomedicine signed in Oviedo on 4 April 1997, and the Additional Protocol on the Prohibition of Cloning Human Beings signed in Paris on 12 January 1998
- UN Convention on the Rights of the Child
- Universal Declaration on the human genome and human rights adopted by UNESCO

Participants should take into account to the opinions of the European Group of Advisers on the Ethical Implications of Biotechnology (1991 -1997) and the opinions of the European Group on Ethics in Science and New technologies (as from 1998).

#### **Protection of Animals**

In accordance with the Amsterdam protocol on animal protection and welfare, animal experiments must be replaced with alternatives wherever possible. Suffering by animals must be avoided or kept to a minimum. This particularly applies (pursuant to Directive 86/609/EEC) to animal experiments involving species which are closest to human beings. Altering the genetic heritage of animals and cloning of animals may be considered only if the aims are ethically justified and the conditions are such that the animals' welfare is guaranteed and the principles of biodiversity are respected.

#### **Ethical review at EU level**

An ethical review will be implemented systematically by the Commission for proposals dealing with ethically sensitive issues, in particular proposals involving the use of human embryonic stem cells in culture. In specific cases, further ethical reviews may take place during the implementation of a project.

Fields of research which are excluded from the programme:

- Research activity aiming at human cloning for reproductive purposes;
- Research activity intended to modify the genetic heritage of human beings which could make such changes heritable (research relating to cancer treatment of the gonads can be financed).
- Research activities intended to create human embryos solely for the purpose of research or for the purpose of stem cell procurement, including by means of somatic cell nuclear transfer.
- In addition during the year 2003 the Commission will not fund research involving the use of human embryos or embryonic stem cells except for banked or isolated human embryonic stem cells in culture.

#### **b) UKRO - European RTD Insight - September 2003**

*Common Position on Human Tissues and Cells*

The Council has formally adopted its common position on the proposed new law setting quality and safety standards for the handling of human tissues and cells.

The Agriculture Council adopted the political agreement (reached by the Health Council in June 2003) on a proposal for a Directive concerning human tissues and cells (see above). This legislation will introduce more stringent requirements on the suitability of donors, screening of donated substances, as well as the traceability from donor to patient and vice versa. Rules for third country imports will also be established ensuring equivalent standards of quality and safety. The legislative proposal will now be forwarded to the EP for a second reading.

**c) UKRO - European RTD Insight - August 2003 - as background context**

*Research Priorities of the Italian Presidency (second half of 2003)*

The Italian Minister for Education, Universities and Research, Letizia Moratti, and Research Commissioner Philippe Busquin have presented the research priorities for the Italian presidency of the EU, under the broad umbrella of developing the ERA and the Lisbon and Barcelona objectives. The aims are to increase the volume of investment in RTD, with a clear focus on the role of SMEs, to develop and diversify the centres and networks of excellence, and to focus on the development and mobility of human resources.

Six broad policy areas are to be addressed. These are:

- The 3 per cent objective (implementing the measures set out in the Communication 'Investing in research: an action plan for Europe');
- Measures aimed at attracting and retaining researchers (see 'Researchers in ERA Communication' article, below);
- Discussion between ministers, at the Competitiveness Council in September 2003, on the European candidate site for the International Thermonuclear Experimental Reactor (ITER);
- Defining and implementing a coherent set of rules for collaboration between the EC and the European Space Agency (ESA);
- Reaching an agreement with Member States on an EC proposal for establishing criteria for EU funding of research projects involving the use of human embryonic stem cells; and
- Organisation of a follow-up conference in Trieste in November to assess progress of European co-operation on research infrastructures, and stimulate further initiatives.

**Further Information**

- [http://www.cordis.lu/italy/priorities\\_busquin.htm](http://www.cordis.lu/italy/priorities_busquin.htm)

**d) UKRO - European RTD Insight - August 2003**

Stem Cell Research in FP6

Given the sensitive nature of human embryonic stem cell research, the Council of Ministers and the EC agreed before signing off on FP6 that further ethical guidelines on governance and monitoring of such research would have to be adopted before the end of 2003, and before any such research projects would be funded. The EC proposal on this has now been published. This does not aim to set universal ethical principles, nor does it aim to provide guidelines for EU Member States, since this is not within the remit of the EU, merely the conditions for FP6 research involving the derivation of stem cells from human supernumerary embryos. The proposal is fully in line with the various opinions of the European Group on Ethics (EGE). With proposals to set up a European registry of stem cells, and to establish public stem cell banks, the EU hopes to provide optimal access to, and use of, stem cells for public research purposes.

Research Commissioner Philippe Busquin said that 'The decision to fund human embryonic stem cell research from the Sixth Framework Programme was already taken by Council and Parliament last year. By funding this research and by setting strict ethical rules for such funding, the EU contributes in a responsible way to advancing this science for the benefit of patients across the world, while at the same time ensuring that it takes place within a clear ethical framework.'

**Further Information**

- EC Press Release number IP/03/969 of 09/07/03, listed above
- European Group on Ethics, in particular Opinions No. 15 [http://europa.eu.int/comm/european\\_group\\_ethics/docs/avis15\\_en.pdf](http://europa.eu.int/comm/european_group_ethics/docs/avis15_en.pdf) and No. 16 <http://europa.eu.int/comm/>

[european\\_group\\_ethics/docs/avis16\\_en.pdf](http://european_group_ethics/docs/avis16_en.pdf)

- The EC Proposal Document, COM (2003) 390 final  
[http://europa.eu.int/smartapi/cgi/sga\\_doc?smartapi!celexapi!prod!CELEXnumdoc&lg=EN&numdoc=52003PC0390&model=guichett](http://europa.eu.int/smartapi/cgi/sga_doc?smartapi!celexapi!prod!CELEXnumdoc&lg=EN&numdoc=52003PC0390&model=guichett)

**e) UKRO - European RTD Insight - July 2003**

**Council Position on Human Tissues and Cells**

EU health ministers have reached political agreement on a new directive proposing quality and safety standards for dealing with human tissues and cells. The directive aims to establish standards for the donation, procurement, testing, processing, storage and distribution of human tissues and cells.

Several delegations expressed concerns over the ethical and health implications of the use of tissues and cells. However, the Presidency reminded Member States that they will be able to introduce more rigorous protective measures under the new directive than they could have under the original draft directive. In particular, Member States will be able to set requirements for voluntary unpaid donation, and for the prohibition of tissues and cells from embryonic origin.

The legislation will introduce more stringent requirements on the suitability of donor and the screening of donated substances, as well as the traceability from donor to patient and vice versa. Rules for third-country imports will also be established in order to ensure equivalent standards of quality and safety. The common position will be formally adopted at a future Council meeting, after which the proposal will be forwarded to the European Parliament for a second reading.

**Further Information**

- Common Position of the Council of the European Union on the Tissue Directive  
[http://register.consilium.eu.int/scripts/utfregisterDir/WebDriver.exe?Mlang=EN&key=REGISTER&ssf=DATE\\_DOCUMENT+DESC&fc=REGAISEN&srm=25&md=400&what=simple&ff\\_TITRE=common+position+human+tissues+cells&ff\\_FT\\_TEXT=&ff\\_SOUS\\_COTE\\_MATIERE=&dd\\_DATE\\_REUNION=&rc=8&nr=9&Mlval=detail](http://register.consilium.eu.int/scripts/utfregisterDir/WebDriver.exe?Mlang=EN&key=REGISTER&ssf=DATE_DOCUMENT+DESC&fc=REGAISEN&srm=25&md=400&what=simple&ff_TITRE=common+position+human+tissues+cells&ff_FT_TEXT=&ff_SOUS_COTE_MATIERE=&dd_DATE_REUNION=&rc=8&nr=9&Mlval=detail)
- Council of the European Union Press Release, Health Council June 2003, please refer to page 7 of report <http://ue.eu.int/pressData/en/lisa/75977.pdf>
- Amended proposal for Tissue Directive: [http://europa.eu.int/smartapi/cgi/sga\\_doc?smartapi!celexapi!prod!CELEXnumdoc&lg=en&numdoc=52003PC0340&model=guichett](http://europa.eu.int/smartapi/cgi/sga_doc?smartapi!celexapi!prod!CELEXnumdoc&lg=en&numdoc=52003PC0340&model=guichett).

**f) UKRO - European RTD Insight - May 2003**

**Move to Ban Stem Cell Research**

The European Parliament has backed a plan to regulate the use of human tissues and cells in the EU, but added amendments that ban therapeutic cloning and limit research into human embryonic stem cells. The EP adopted in April a report by MEP Peter Liese on the EC proposal setting quality and safety standards for the donation, procurement, testing, processing, storage and distribution of human tissues and cells. More than 80 amendments were adopted to the report in the first reading under the co-decision procedure; these mainly concerned the scope of the directive, ethical considerations, compensation for tissue and cell donation, anonymity and donor consent.

MEPs rejected two amendments that would have banned research involving the destruction of human embryos. The proposal was to be discussed by the Health Council on 2 June.

**Further Information**

- The draft report on the proposal for a directive on setting standards of quality and safety for the donation, procurement, testing, processing, storage, and distribution of human tissues and cells, tabled at ENVI meeting on 19 February 2003, <http://www.europarl.eu.int/meetdocs/committees/envi/20030219/470384en.pdf>

## PARTNER INFORMATION

**The Royal Society of Edinburgh** (RSE) is Scotland's National Academy of Science & Letters. An independent body with charitable status, its multidisciplinary fellowship of 1200 men and women of international standing represents a knowledge resource for the people of Scotland. Committed to its Royal Charter of 1783 for the "advancement of learning and useful knowledge" the Society recognises the important role it can play in today's Scotland. Working as part of the UK and within a global context, the RSE seeks to contribute to Scotland's social, economic and cultural wellbeing by:

- organising conferences and lectures for the specialist and for the general public on topics of national and international importance
- providing independent, expert advice to key decision makers in Scotland
- awarding over £1.5million annually to Scotland's top young academics to promote research in Scotland
- enabling leading Scottish-based researchers to collaborate with the best of their international counterparts
- inspiring school children in classrooms from the Borders to the Northern Isles and promoting their interest in science, society and culture
- producing academic journals of international standing

The aim of the **Scottish Stem Cell Network** is to encourage and develop the interdisciplinary relationships that will enable advances in stem cell biology to be rapidly translated to deliver new treatments for degenerative diseases :

- Develop and consolidate Scotland's reputation as a key player in the stem cell biology sector of the global biotechnology industry.
- Create an environment where there will be regular exchanges of scientific and clinically relevant information on stem cells.
- Foster collaborative links between research scientists and clinicians.
- Engage the private sector in the development of stem cell technology.
- Lobby government and regulatory authorities in support of stem cell technology.
- Develop national and international links with other centres of excellence.
- Realise the benefits to patients from effective treatments of degenerative diseases.

The Network was launched on 9 May 2003.

**Scotland Europa** ([www.scotlandeuropa.com](http://www.scotlandeuropa.com)) is an innovative alliance of public, private and civil society bodies networking Scotland in Europe. Its aim is to promote Scotland's interests to the key institutions of the European Union and to the regions of the EU and beyond. Scotland Europa forms part of the International Operations directorate.

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