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SCOTLAND
IN SWEDEN

**REPORT ON THE PROCEEDINGS OF
REALISING THE POTENTIAL
OF LIFE SCIENCES AND
BIOTECHNOLOGY**

**17 OCTOBER 2002
STOCKHOLM**

**A SEMINAR ORGANISED BY THE ROYAL SOCIETY OF
EDINBURGH, THE KAROLINSKA INSTITUTE AND
THE ROYAL SWEDISH ACADEMY OF SCIENCES.**

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From 16 - 19 October 2002, the **SCOTTISH EXECUTIVE** held, in Sweden, a programme of events to promote and position Scotland in areas such as arts, culture, governance, science and tourism.

The Executive commissioned the **ROYAL SOCIETY OF EDINBURGH** to organise and implement the science pillar of the programme on its behalf. As Scotland's National Academy of Science, the Society was pleased to do so.

In partnership with the **KAROLINSKA INSTITUTE** and the **ROYAL SWEDISH ACADEMY OF SCIENCES**, the Society developed and organised

Realising the Potential of Life Sciences & Biotechnology¹

a one-day event which focused on stem cell research and biotechnology, ethics and society. It was held in Stockholm on 17 October and brought together leading Scottish and Swedish scientists, researchers, commentators and academia; the Scottish Executive Minister for Enterprise & LifeLong Learning; and people from the Scottish and Swedish biotechnology sectors.

The event was the centrepiece of the whole ***Scotland in Sweden*** programme and served as a platform for the further development and strengthening of scientific collaboration between Scotland and Sweden. In that respect, the Society intends to host a follow-up collaborative event with the Karolinska Institute and the Academy, in Edinburgh during 2004.

This report provides a summary of the event and acknowledges the considerable input by the partners, and others, in organising it.

ACKNOWLEDGEMENTS

The Royal Society of Edinburgh is extremely grateful to the Karolinska Institute and the Royal Swedish Academy of Sciences for their contributions to making ***Realising the Potential of Life Sciences & Biotechnology*** the success that it was. In particular, the Society would like to thank the staff of the Karolinska Institute and the Royal Swedish Academy of Sciences, whose inputs were pivotal to this, and to enabling the event to be organised and managed in the true sense of co-operation.

The Society would also like to thank others, namely staff in the United Kingdom Embassy in Stockholm, the Scottish Executive, Scottish Enterprise and Scottish Development International, all of whom made valuable contributions to the event's success.

STEM CELL RESEARCH - CHALLENGES, SOLUTIONS AND VALUES

This session covered the morning of the event and was held in the Nobel Forum at the Karolinska Institute. Its objective was to facilitate discussion between eminent Scottish and Swedish scientists and commentators on issues concerning stem cell research and cloning. Its broad structure was a round-table discussion, jointly chaired by Professor Hans Wigzell, President, Karolinska Institute and Sir William Stewart, President, Royal Society of Edinburgh. Participants are listed in Annex B.

The session comprised two parts. Firstly, it focused on issues surrounding control of propagation and differentiation mechanisms, and on improved understanding of the biology of cells that would underpin therapeutic application.

Presentations¹:

The Origin and Potential of Embryo Derived Stem Cells by Professor Austin Smith, Director, Institute of Stem Cell Research, University of Edinburgh.

Regeneration of Nerve Cells From Stem Cells in the Adult Brain by Professor Jonas Frisen, Department of Cell and Molecular Biology, Karolinska Institute.

These were followed by a round-table discussion involving all participants.

The second part focused on current progress in human stem cell research, the prospects for isolating human cells from cloned embryos, and therapeutic and other applications of human stem cells.

Presentations²:

Opportunities Created by the Development of Human Embryonic Stem Cells by Professor John Clark, Head, Division of Gene Expression & Development, Roslin Institute.

Stem Cell Research in Sweden - A Recent Survey by Professor Harriet Wallberg-Henriksson, Secretary General for Medicine, Swedish Research Council.

These were also followed by a round-table discussion.

Sir David Carter, FRSE, Vice-President, Royal Society of Edinburgh, concluded the morning session by summarising the key messages of the discussions. These were:

- ◆ Stem cell research has opened an exciting era for scientific research, and it is encouraging that both Sweden and the United Kingdom (UK) have sanctioned the use of embryonic stem cells derived from the pre-implantation embryo. It is important that scientists remain fully alert to the fact that this is a very sensitive issue and a cause of disquiet for significant sectors of populations. There is a need to be judicious and progress in a measured fashion. It will be vital to avoid making any mistakes that could inflame and alienate public opinion, avoid building up inappropriate expectations, and continue to engage the public in an appropriately involved way.
- ◆ The research must be appropriately safeguarded. The UK was helping to lead in this respect through the activities of its Human Embryology and Fertility Authority, without whose authority embryonic stem cell research cannot take place. So far only two centres in the UK are licensed to undertake this research, one of which is the Institute of Stem Cell Research, University of Edinburgh. The UK has also recently established a Stem Cell Bank, the function of which will be overseen by a Steering Committee. Issues under ongoing consideration include the 'ownership' of stem cells and the associated Intellectual Property Rights.
- ◆ There was consensus that stem cell research has immense potential to produce key cells that could transform disease and disability. For example, dopamine-producing cells for Parkinson's disease, beta cells of the islets of Langerhans for diabetes mellitus. It may also provide insights that will allow the function of existing failing cells to be conserved; and have potential in relation to biopharmaceutical drug discovery. It is, however, vitally important to guard against over-optimistic projections. The general expectations of the public were already high, arguably too high.
- ◆ We should not be too simplistic and see stem cells as the sole saviour in disease. The benefits and disadvantages of these cells needs to be balanced against those of alternative therapies. It is also important to appreciate that stem cells may not work well if introduced in isolation and in the 'wrong place'. For example, insulin-producing beta cells normally live in the islets of Langerhans surrounded by other endocrine cells that influence intermediate metabolism and in immediate proximity to the exocrine cells of the pancreas that produce digestive enzymes. The beta cells are not there by accident and their function is closely integrated with that of the cells around them.
- ◆ Great care will be needed to avoid undesirable consequences of the therapeutic use of stem cells. Oncogenic transformation is a potential, albeit unlikely, hazard. Immune rejection needs to be considered, although there may be 'privileged' sites such as the central nervous system where it is less problematic. We also need to remember that new cells engineered so that they are identical to those of the original failing population may be less effective when the disease being treated is an auto-immune disease.
- ◆ The potential of cell cloning is considerable in the fields of diagnostics and therapeutics. As with all aspects of stem cell research, the work must be taken forward with care and sensitivity that recognises and respects fundamental values. It cannot be overemphasised that stem cell research is not about the future cloning of human beings, an activity that would be an anathema and as abhorrent to the current research community as it is to the majority of the general public.
- ◆ In comparison to the UK, the level of public debate in Sweden seemed more mature and non-confrontational. Particularly impressive has been the positive role played by the media in helping to attain consensus in Sweden. Similar maturity and greater consensus would be a desirable within the UK but will not be attained overnight. Transparency and openness will remain vital to the future development of stem cell research and its diagnostic and therapeutic application.



Sir David Carter, Vice-President; RSE, Sir William Stewart, President, RSE; Professor Hans Wigzell, President, Karolinska Institute; and Professor Jan Carlstedt-Duke, Dean of Research, Karolinska Institute, participating in one of the round-table discussions.

[Photo by Janet Jeppsson, Karolinska Institute.]

NETWORK LUNCH

The lunch was held in the Nobel Forum at the Karolinska Institute. The morning participants were joined by Iain Gray, MSP, Scottish Executive Minister for Enterprise & Lifelong Learning; and invited guests from the United Kingdom Embassy in Sweden, the Swedish Government, Swedish academia, and interests within the Scottish and Swedish biotechnology sectors.

The objective was to provide an informal opportunity for discussion between key players on areas of common scientific interest.

Introduced by Professor Jan Carlstedt-Duke, Dean of Research, Karolinska Institute, Iain Gray made a short speech to conclude the lunch.

The attendees at lunch were:

Barbro AHLSTROM, Information Officer, Karolinska Institute

Dr. Katarina BJELKE, Head of Research and Postgraduate Education Department, Karolinska Institute

Agneta BLADH, Under-Secretary of State for Research, Swedish Ministry of Research

Professor Patrik BRUNDIN, Dept of Physiological Sciences, Lund University

Stuart BROWN, RSE Public Relations Officer

Roisin CALVERT, RSE Events Manager

Professor Jan CARLSTEDT-DUKE, Dean of Research, Karolinska Institute

Professor John CLARK, FRSE, Head, Division of Gene Expression & Development, Roslin Institute

Sir David CARTER, FRSE, RSE Vice-President

Professor Peter ERICSSON, Dept of Clinical Neurosciences, Gothenburg University

Professor Ingemar ERNBERG, Microbiology & Tumor Biology Centre, Karolinska Institute

Professor Jonas FRISEN, Dept of Cell and Molecular Biology, Karolinska Institute

Iain GRAY, MSP, Scottish Executive Minister for Enterprise & LifeLong Learning

John GRANT, UK Ambassador to Sweden

Anders Haegerstrand, M.D., NeuroNova AB, Stockholm

Professor Mats G HANSSON, Dept of Public Health and Caring Sciences, Research Program Ethics in Biomedicine, Uppsala University

Professor Carl-Henrik HELDIN, Ludwig Institute for Cancer Research

Graeme HERBERT, RSE International Committee Secretary

Professor Outi HOVATTA, Obstetrics and Gynaecology, Dept of Clinical Sciences, Karolinska Institute

Brad HOY, Geron Biomed Ltd, Roslin

Olof JANTZE, VD, In Vitro Sweden AB

Janet JEPSSON, Principal Administrative Officer, Research and Postgraduate Education Department, Karolinska Institute

Eva KRUTMEIJER, Head of Information, Royal Swedish Academy of Sciences

Sir David LANE, FRS, FRSE, Director of CRC Cell Transformation Unit, Department of Molecular Oncology, Ninewells Hospital & Medical School, Dundee

Dr. Katarina LeBLANC, Centre for Allogeneic Stem Cell Transplantation, Huddinge University Hospital

Professor Urban LENDAHL, Dept of Cell and Molecular Biology, Karolinska Institute

Ragnar LINDER, MD, Amgen AB

Malin LINDGREN, Information Officer, Royal Swedish Academy of Sciences

Professor Alexander McCALL SMITH, FRSE, Professor of Medical Law, University of Edinburgh

Kjell NILSSON, Percell Biolytica

Professor Stefan NORDLUND, Dept of Biochemistry and Biophysics, Stockholm University

Professor Ulf PETERSSON, Dept of Genetics and Pathology, Uppsala University

Professor David PORTEOUS, FRSE, Head, Medical Genetics Section & Director of Genetics Core, Wellcome Trust Clinical Research Facility, University of Edinburgh

Damion POTTER, Head of Information and Public Relations, British Embassy

Professor Wilson SIBBETT, FRS, FRSE, Chairman, Scottish Science Advisory Committee

Professor Austin SMITH, Director, Institute of Stem Cell Research, University of Edinburgh

David SMITH, Director, Scottish Development International, Europe, Middle East, Asia

Ken SNOWDEN, Acting Director, Scottish Enterprise Biotechnology Team

Sir William STEWART, FRS, FRSE, RSE President

Sarah THOMSON, Marketing Manager, Scottish Development International, Europe

Professor Harriet WALLBERG-HENRIKSSON, Secretary General for Medicine, the Swedish Medical Research Council

Erik WALUM, Head of Pharmacology II, Biovitrum AB

Michael WHITE, Science Officer, British Council Scotland

Professor Hans WIGZELL, President Karolinska Institute

Nicola WILLIAMS, Scottish Enterprise Biotechnology Cluster Team



Left to Right. Professor Jan Carlstedt-Duke, Dean of Research, Karolinska Institute; Iain Gray, MSP, Scottish Executive Minister for Enterprise and Lifelong Learning; Sir William Stewart, President, RSE and Professor Janne Carlsson, President, Royal Swedish Academy of Sciences during a break in the Biotechnology, Ethics and Society Session.

This session covered the afternoon and early evening of the event, and was held at the Royal Swedish Academy of Sciences. Its objectives were to provide an opportunity for Scotland and Sweden to: learn about and from each other's biotechnology expertise; discuss issues relating to achieving the advancement and exploitation of biotechnology; and to discuss the ethical, political and societal issues relating to the advancement of genetic knowledge, and in particular population genomics.

The broad structure was a series of presentations¹ followed by plenary discussion. It was jointly chaired by Professor Janne Carlsson, President, Royal Swedish Academy of Sciences and Sir David Carter, Vice-President, Royal Society of Edinburgh.

The session was open to the public and was attended by Iain Gray, MSP, Minister for Enterprise and Lifelong Learning and all of the Scottish participants involved in the morning's round-table discussion.

The session comprised three parts. Firstly, following welcoming remarks by Professor Janne Carlsson and Sir William Stewart, Iain Gray² made a keynote address which focused on the importance of the life sciences and biotechnology sectors to both Scotland and Sweden, and Scotland's approach to realising the potential of these.

This was followed by **Translational Aspects of Cancer Research**, with presentations by Sir David Lane, CRC Cell Transformation Unit, Department of Molecular Oncology, Ninewells Hospital & Medical School, Dundee; Professor Carl-Henrik Heldin, Ludwig Institute for Cancer Research, Uppsala University and Professor Ingemar Ernberg, Microbiology & Tumour Biology Centre, Karolinska Institute.

A question and answer session involving the speakers followed. This gave rise to a consensus that better integration, both within academic/research organisations and between them and commerce, was essential if cancer, and indeed other research, was to maximise its potential in terms of translation for the benefit of human wellbeing. Differing pressures on academia and commerce made it difficult to achieve better integration. Creating the right environment for that to happen was vital, but that too was difficult to achieve. Issues such as aligning individual and collective needs and expectations, and removing barriers had to be addressed. For example, a culture whereby quests for individual distinction are not detrimental to, but complement the wider research picture; commercial involvement and investment that recognises and accepts that in many cases research means more medium-to-long-term returns rather than short-term results; and removing organisational barriers, so that working structures support an integrated work ethos. None of this should, however, undermine issues of quality and integrity. The challenge is great, but failure to properly integrate would mean that considerable potential would not be realised.

Genetics and Society was the theme of the final part of the session.

Presentations were given by Professor David Porteous, Wellcome Trust Clinical Research Facility, University of Edinburgh and Professor Ulf Pettersson, Department of Genetics & Pathology, Uppsala University.

A question-and-answer session involving the speakers and Professor Sandy McCall Smith, Professor of Medical Law, University of Edinburgh, followed. A wide range of issues were raised and discussed, including

- The need to engage the public and to explore ethical and societal issues at early stages and throughout processes.
- Addressing tensions between individual choice and societal interests.
- Changing attitudes towards public health - one suggestion was that public health information is perhaps largely ignored on the grounds of low-risk assessment by individuals.
- Concerns about commercial genetic testing and its wider consequences, and in that context the impact on jurisdictional regulations of the internet - through which genetic tests can easily be sought world-wide.
- Tackling ever-increasing patient demands on General Practitioners to provide quicker and better-quality medical advice, and in that context the utilisation of modern informatics technology.
- Consequences for the insurance industry, and insurance purchasers, of information being available on an individual's genetic predisposition.
- Concerns about wider access to such information being obtained by, for example, the police for the purposes of prosecution.

Following the conclusion of the afternoon session, an informal early evening reception was hosted by Professor Carlsson in the Session Hall and adjoining rooms of the Royal Swedish Academy of Sciences.

STOCKHOLM: 17 OCTOBER 2002
EVENT PROGRAMME

STEM CELLS AND CLONING - CHALLENGES, SOLUTIONS AND VALUES at the Nobel Room, Karolinska Institute (KI)

0900 **Opening and Welcome** - Professor Hans Wigzell, President of KI

0905 **Stem Cell Research** - Chaired by Sir William Stewart, FRS, FRSE, President, Royal Society of Edinburgh (RSE)

Presentations by: Professor Austin Smith, Director, Institute of Stem Cell Research, University of Edinburgh and Professor Jonas Frisen, Dept of Cell and Molecular Biology KI, followed by a round-table discussion

1040 **Human Stem Cell Technology** - Chaired by Professor Wigzell

Presentations by: Professor John Clark, FRSE, Head, Division of Gene Expression & Development, Roslin Institute and Professor Harriet Wallberg-Henriksson, Secretary General for Medicine, the Swedish Medical Research Council, followed by round-table discussion

1150 **Discussion Summary** - Sir David Carter, FRSE, Vice-President, RSE

NETWORK LUNCH at the Nobel Forum, Karolinska Institute.

1200 Buffet Lunch

1330 **Concluding remarks** by Iain Gray, MSP, Scottish Executive Minister for Enterprise & LifeLong Learning

BIOTECHNOLOGY, ETHICS AND SOCIETY at the Royal Swedish Academy of Sciences (KVA)

1400 **Welcome** by Professor Janne Carlsson, President, KVA

1405 Sir William Stewart, FRS, FRSE, President, RSE

1410 **Keynote Address:** Iain Gray, MSP, Scottish Executive Minister for Enterprise & Life-Long Learning.

1430 **Translational Aspects Of Cancer Research** - Chaired by Sir David Carter, FRSE, Vice-President, RSE

1440 Sir David Lane, FRS, FRSE, Director of CRC Cell Transformation Unit, Department of Molecular Oncology, Ninewells Hospital & Medical School, Dundee

1500 Professor Carl-Henrik Heldin, Ludwig Institute for Cancer Research, Uppsala

1520 Professor Ingemar Ernberg, Microbiology & Tumour Biology Centre, KI

1540 **Q&A Session** with speakers

1610 Coffee Break

1630 **Genetics and Society** - Chaired by Professor Janne Carlsson, President, KVA

1640 Professor David Porteous, FRSE, Head, Medical Genetics Section & Director of Genetics Core, Wellcome Trust Clinical Research Facility, University of Edinburgh

1700 Professor Ulf Pettersson, Department of Genetics & Pathology, KI

1720 **Q&A Session** with speakers and Professor Sandy McCall Smith, Professor of Medical Law, University of Edinburgh

1750 **Concluding Remarks**, Professor Janne Carlsson, President, KVA

1800 **Reception at KVA**

1 Annex F - Abstracts. Abstract for presentation by Professor Ulf Pettersson not provided.

2 Annex E - Keynote Address abstract

Professor Patrik BRUNDIN, Dept of Physiological Sciences, Lund University
 Professor Jan CARLSTEDT-DUKE, Dean of Research, Karolinska Institute
 Professor John CLARK, FRSE, Head, Division of Gene Expression and Development, Roslin Institute
 Sir David CARTER, FRSE, RSE Vice-President
 Professor Peter ERICSSON, Dept of Clinical Neurosciences, Gothenburg University
 Professor Jonas FRISEN, Dept of Cell and Molecular Biology, Karolinska Institute
 Professor Mats G HANSSON, Dept of Public Health and Caring Sciences, Research Program Ethics in Biomedicine, Uppsala University
 Professor Outi HOVATTA, Obstetrics and Gynaecology, Dept of Clinical Sciences, Karolinska Institute
 Sir David LANE, FRS, FRSE, Director of CRC Cell Transformation Unit, Department of Molecular Oncology, Ninewells Hospital & Medical School, Dundee

Dr. Katarina LeBLANC, Centre for Allogeneic Stem Cell Transplantation, Huddinge University Hospital
 Professor Urban LENDAHL, Dept of Cell and Molecular Biology, Karolinska Institute
 Professor Alexander McCALL SMITH, FRSE, Professor of Medical Law, University of Edinburgh
 Professor David PORTEOUS, FRSE, Head, Medical Genetics Section & Director of Genetics Core, Wellcome Trust Clinical Research Facility, University of Edinburgh
 Professor Wilson SIBBETT, FRS, FRSE, Chairman, Scottish Science Advisory Committee
 Professor Austin SMITH, Director, Institute of Stem Cell Research, University of Edinburgh
 Sir William STEWART, FRS, FRSE, RSE President
 Professor Harriet WALLBERG-HENRIKSSON, Secretary General for Medicine, the Swedish Medical Research Council
 Professor Hans WIGZELL, President, Karolinska Institute

The Generation of Neurons from Stem Cells in the Adult Brain - Professor Jonas Frisen

Neurons are continuously generated in certain regions of the adult mammalian brain. They integrate into the synaptic circuitry and can be activated by physiological stimuli. These neurons derive from multipotent, self-renewing neural stem cells. Such stem cells can be cultured from the walls of the ventricular system of the adult rodent and human brain. Under certain conditions, adult neural stem cells can generate a large number of different non-neural cell types. We have found, by *in vivo* labeling experiments, cell sorting and *in vitro* cultures, that ependymal cells have neural stem cell

properties in the rodent. Ependymal cells divide rarely to give rise to subventricular zone progenitor cells which generate neuroblasts that migrate to the olfactory bulb. In response to a spinal cord injury, ependymal cells lining the central canal are induced to proliferate and generate migratory progeny which differentiate to astrocytes and contribute to scar formation. Further studies on the regulation of stem cell differentiation may allow the development of strategies to stimulate neurogenesis in the adult brain.

The Origin and Potential of Embryo Derived Stem Cells - Professor Austin Smith

Mouse embryonic stem (ES) cells are continuous cell lines derived directly from the pre-implantation embryo. ES cells have two key properties: (i) they can be multiplied without apparent limit in the laboratory, and (ii) they can be induced to develop into a wide range of well-defined fully differentiated cell types such as nerve, muscle, heart and blood cells. This has stimulated interest in the isolation of analogous cells of human origin. Such human pluripotent stem cells would constitute a renewable source of normal cells that could be employed in pharmaceutical and toxicological screening. They might also

be used to regenerate diseased or damaged tissues by cellular transplantation. Human stem cell lines can now be derived from supernumerary embryos produced during infertility treatments. These cells offer great hope of developing effective treatments for conditions such as Parkinson's disease, cardiomyopathies and diabetes. For these hopes to be realised, however, a major research effort is required to improve our current rudimentary understanding of stem cells and our ability to control their behaviour.

Stem Cell Research in Sweden: a Recent Survey - Professor Harriet Wallberg-Henriksson

In December 2001, the Swedish Research Council adopted ethical guidelines for human stem cell research. Prior to the decision, an intense ethical debate in the media took place among politicians, policy makers, scientists and experts on ethics. The guidelines allow for research on stem cells derived from left-over embryos from *in vitro* fertilization treatment. Furthermore, the procedure of somatic cell nucleus transfer was found ethically acceptable, but the procedure cannot be utilized in Sweden today due to legal aspects.

In a recent survey of stem cell research in Sweden, Professor Jan Lindsten and Professor Lennart Enerbäck concluded that there is at present a great potential for further development of stem cell research in Sweden. At

least eighty senior researchers are active today in the areas of haematopoietic, mesenchymal, neural and embryonic stem cell research. Clusters of stem cell scientists can mainly be found in Lund, Göteborg and Stockholm. Although the competence is substantial and the state of knowledge is sound, the Swedish scientists in this area produce fewer papers than in other biomedical areas. The reason for this could be that stem cell research is a fairly young area. However, in terms of citation, the Swedish stem cell papers are cited to a greater extent compared to papers from the whole world. Finally, it appears that utilising the knowledge and research resources in collaboration with prominent bordering areas have not been fully exploited as yet.

Opportunities Created by the Development of Human Embryonic Stem Cells - Professor John Clark

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 impediment in 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 haematopoietic

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. In this forward-looking presentation I shall discuss the opportunities created by the development of human ES cells, not only for cell therapy, but also for other important applications such as drug testing and drug discovery.

I very much welcome today's event, which brings together practitioners from the life sciences and biotechnology sectors to discuss key issues and share experiences. It is an excellent opportunity for key Scots in these fields to meet with their Swedish counterparts, and for both to forge collaborative and productive partnerships that will maximise scientific and economic benefit in the long term.

Both Scotland and Sweden can be justifiably proud of the expertise in their biotechnology industries. In Scotland the sector has been identified as a key economic driver and our economic development agency, Scottish Enterprise, has implemented a £40 million biotechnology action plan. This seeks to build on our key strengths of a world-class research base, a highly skilled workforce, and innovative companies and organisations.

The Scottish biotechnology sector is growing rapidly, supported by necessary infrastructure developments in new manufacturing and research facilities. It is developing advances in cancer therapies, antibiotics and protein development to fight diseases such as cystic fibrosis. It also recognises the value in creating knowledge based on international strategic partnerships, which are essential to Scotland's full participation in the global marketplace and to its future economic well being.

This morning's stem cell research and cloning discussion is evidence of the academic excellence and vibrant economies in both countries. Stem cell research is being conducted in a number of research institutions across Scotland:

- The Beatson Institute for Cancer Research in Glasgow is researching stem cells and chemokines.
- The Medical Research Council Human Genetics Unit, based at the Western General Hospital, Edinburgh, is researching Stem cell differentiation; the MRC has recently awarded 11 studentships in Stem Cell Research. The Western General Hospital is also conducting research into the differentiation of haematopoietic stem cells.

Research at the Roslin Institute is focusing on genetics, specifically research into the development of a test for 1GF2R Gene - the gene that causes animals to be born abnormally large. The Institute was recently successful in a £2 million plus bid for a Faraday Partnership in Farm Animal Genetics and Genomics, partly supported by the Scottish Executive.

The Institute of Stem Cell Research, University of Edinburgh is focusing on genetics and genomics and has approximately 70 people working in stem cell research in the areas of neural, Hematopoietic, thymus and bone stem cells.

Scotland's reputation for commercial exploitation of this academic excellence is less of a cause for celebration. Recently published statistics show that this continues to be the case, but encouragingly also show that Scotland has increased its investment by 30% in real terms in the past six years. We are therefore moving in the right direction.

The development of pharmaceuticals is an area of large R&D expenditure growth in Scotland. Alongside electrical machinery and apparatus, these two sectors account for about half of the total Scottish R&D expenditure in businesses. The sectors are serious about their future significance. Last week a number of companies from Scotland participated in the major Biotech Forum, held in Malmo - an area which I hope to visit next year to see at first hand the infrastructure and commercial activity which have made it so successful, both in its own right, and as part of the Medicon Valley, one of Europe's major life sciences regions.

There is huge global potential for both Scotland and Sweden, and biotechnology offers us enormous opportunities, not only to create wealth and high quality jobs, but also to improve the quality of our lives. I look forward to seeing how the alliance between Scotland and Sweden in this develops.

The life sciences sector is important to both Scotland and Sweden. Important not just in economic terms, but in terms of how society reacts to and copes with the impact of the potential offered by new discoveries in this area. Ethical, political and societal issues must be considered carefully.

In Scotland, as in Sweden, we have been aware for some time of the economic potential offered by the life sciences. In 1999 we launched a £40m biotechnology cluster action plan to help the sector realise its full potential. We have come a long way since then and are well on the way to exceeding ambitious headline targets of: doubling the number of biotech companies from 50 to 100; increasing the number of support and supply organisations from 180 to 290; and doubling employment in the cluster from 12,000 to 24,000. In total, Scotland's Biotech community has doubled in the last four years. A significant achievement – but only a beginning. We have had particular success with a number of specific companies. For example, two of the top three biotech venture capital investments in Europe during 2001 featured Scottish companies - £34 million for Dundee-based Cyclacel and £30.5 million for Straken in Galashiels.

We look at developments in biotechnology within our broader economic development policy. To succeed in a global economy, Scotland has to use and extend its competitive advantages. To be successful, Scotland must place science and skills at the heart of its economic agenda. Our strategy for the future, **A Smart Successful Scotland**, has three key priorities:

- Growing Businesses – encouraging entrepreneurship and supporting innovation and new companies.
- Global Connections – encouraging companies to increase their involvement in global markets.
- Skills and Learning - keeping skills and knowledge relevant within the modern workplace.

To meet the challenges of global competition, and to realise its potential, Scotland's goal is simple but challenging: more jobs, better jobs and shared prosperity.

The Science Base is one of our most important sources of new ideas, knowledge and techniques. It allows us to take part in, and gain from, scientific advances in other countries and to bring new knowledge to bear on Scottish problems. It supports efforts

to attract skilled workers and investment into the Scottish economy. We are committed to ensuring that it has internationally-recognised strengths and makes a significant contribution to our economic objectives.

Appropriate breadth is important, but no country can afford to provide public funds for unlimited scientific activity - no matter how good. Public money is therefore targeted on the most relevant parts of the science base - skilled people, resources and the physical infrastructure to work, and areas of current or future importance. This is vital if we are to recruit, retain and professionally develop sufficient high-quality scientists, and support staff, across a range of disciplines, and if we are to make Scotland attractive to scientists and investors.

We must also be clear about what we want the science base to do and how broad, how strong, and how specialised it should be. These decisions must be taken with an awareness of international as well as national developments. Maintaining an internationally-strong science base depends on support for good quality, effective scientific research activity in the Higher Education sector and in other publicly-funded bodies - supplemented by privately-funded research and development.

Achieving maximum benefit from investment in science requires effective partnership and co-ordination among those funding science, those undertaking scientific activity, those providing advice and those depending on scientific outputs.

Constraints of size mean Scotland cannot be a world leader in all areas of science, and cannot maintain an effective science base or take advantage of the benefits of scientific activity in isolation from the rest of the UK or the international community. The importance of ensuring that Scottish science is fully linked with UK, European and wider global activity cannot be overstated. We must maintain and enhance our international reputation; be part of international partnerships and collaboration.

We must also identify and concentrate on areas of science where we have the potential to be world leaders, which will benefit our economy and people. Scotland is one of the world leaders in a number of key scientific areas, including bioscience and genomics, medical research and e-science. It makes sense to maintain and build on these strengths, and to focus on areas where we

may be developing similar scientific potential – or where economic development considerations are paramount.

Scotland played a leading role in the formation of, and is actively involved in, the European Bioregions Network. This recently-formed group aims to develop closer interregional co-operation and build stronger networks of biotechnology clusters across Europe. Its common reference point is the European Commission communication paper "Life Sciences and Biotechnology – A Strategy for Europe" which will enable the identification of a range of common themes and issues which can be tackled collaboratively.

Scotland is also well placed to take advantage of the Genomics and Biotechnology for Health funding stream presented by the 6th Framework Programme. We have a proven track record of excellence in this area. We

are equally well placed to participate in the European Research Area through our world-class reputation with centres of excellence in Dundee, Edinburgh and Glasgow. Our Higher Education Institutes are traditionally skilled at accessing EU grants, but our businesses, especially SMEs, do significantly less well. We aim to address that.

Our **Science Strategy for Scotland** highlights the importance of building a greater European and international focus within our science base and encouraging cross-country collaborations, and increased mobility of researchers. I hope contacts made and renewed today will further that aim. I also hope it serves as a platform for even greater synergy and collaboration between Scotland and Sweden in the fields of life sciences and biotechnology.

Annex F BIOTECHNOLOGY, ETHICS, AND SOCIETY: ABSTRACTS

Translation in Cancer Research, from Bench to Bedside - Professor Sir David Lane

The completion of the human genome project and a rapidly enhanced understanding of the molecular mechanism of human disease are creating a wealth of new targets for drug discovery. Keeping pace with this is the development of novel technologies that can enhance the speed and accuracy of drug discovery at every level of the process. Importantly, these technologies have a great impact on the cost of drug development, enabling academic and small Biotech companies to make larger contributions to the process. Conversely, the recognition of molecular variation in the disease process and in the metabolic and toxicological response of individuals to therapeutic drugs implies the individualisation of treatment and care that may favour the development of a larger number of medicines to treat a particular disease. All of these processes are particularly clear in the development of new anti-cancer drugs.

Cancer Research UK in Britain and the NCI in the USA have both instituted schemes that

allow academic groups access to diverse chemical libraries and high throughput screening against validated targets emerging from basic research. Target validation has been greatly aided by the development of reporter cell lines, knock-out-mouse-derived cell lines and dominant negative mutant and anti-sense approaches. Commercially small biotech companies have access to large and diverse chemical libraries and success with *in silico* screening using molecular docking software to screen "virtual" libraries is greatly reducing the number of molecules that must be physically tested for activity. This critically depends on the increasing rapidity of 3D-structure determination. Exciting examples that have emerged from these new approaches include inhibitors and activators of the p53 response, signal transduction modifiers and pro-apoptotic agents. Downstream challenges include more rapid assessment of PK, metabolism and toxicology. The new drugs, tailored to specific molecular forms of disease, will also pose novel problems for the regulators, practitioners and patients.

Translational Aspects of Cancer Research - Professor Ingemar Ernberg

The new challenge in cancer research derived from the fact that fundamental mechanisms of cancer have been established during the latest 25 years. Together with the new

possibilities derived from new technologies in genomics, proteomics and systems biology the task is to select and transfer this knowledge for clinical use.

Generation Scotland – a Strategy for Health and Wealth Creation - Professor David Porteous

The health of the public is determined by biological, environmental, social, economic and political factors. The relative weights of these factors and the opportunities for risk modification or intervention vary greatly from disease to disease, individual to individual and country to country. Building upon the fruits of the Human Genome Project, the new genetics can identify key biological factors that underpin common causes of ill health. Genetic knowledge is essential if we are to make best use of existing healthcare resources, develop more effective treatments and treat patients optimally. This process depends upon access to personal genetic information. Informed consent and medical confidentiality *can and should* guard against inappropriate use of personal genetic information.

Genetic knowledge is a major driver for health and wealth creation. *Generation Scotland* is a proposed solution to health through genetic knowledge. *Generation Scotland* must forge an equitable partnership between the people of Scotland, the NHS Scotland, academia and industry.

Generation Scotland builds upon:

- an unhealthy, stable & supportive population;
- the NHS Scotland;
- a national clinical genetics network;
- registers of morbidity & mortality;
- 'Cradle to grave' electronic record linkage;
- excellence in biomedical, social and e-science in Scotland;
- a strong biotechnology industry base.

Generation Scotland aims to establish:

- a network of excellence in clinical science, genetic epidemiology, statistical genetics and bioinformatics;
- a centralised sample bank and high throughput genotyping facility;
- a commercialisation arm to build partnerships with the biotechnology and pharmaceutical sectors to develop the research outputs;
- a communications arm to develop awareness of, engagement in, support for and understanding of the requirements for success and the outcomes from *Generation Scotland*.

Targeting of Signal Transduction Molecules in Cancer Treatment - Professor Carl-Henrik Heldin

The growth, migration, differentiation and apoptosis of cells are regulated by signals the cell receives from its environment. Such signals are transduced over the cell membrane by specific receptors, the activation of which initiates a number of intracellular signaling pathways. Components of these signaling pathways are often perturbed in cancer, leading to the characteristic features of a cancer cell, *i.e.* lack of growth control,

invasiveness, dedifferentiation and inability to undergo apoptosis when appropriate.

Platelet-derived growth factor (PDGF) and transforming growth factor- β (TGF- β) are examples of important growth regulatory molecules. In certain tumors the signaling pathways of PDGF and TGF- β are perturbed. The development and use of antagonists for PDGF and TGF- β in the treatment of cancer, will be discussed.