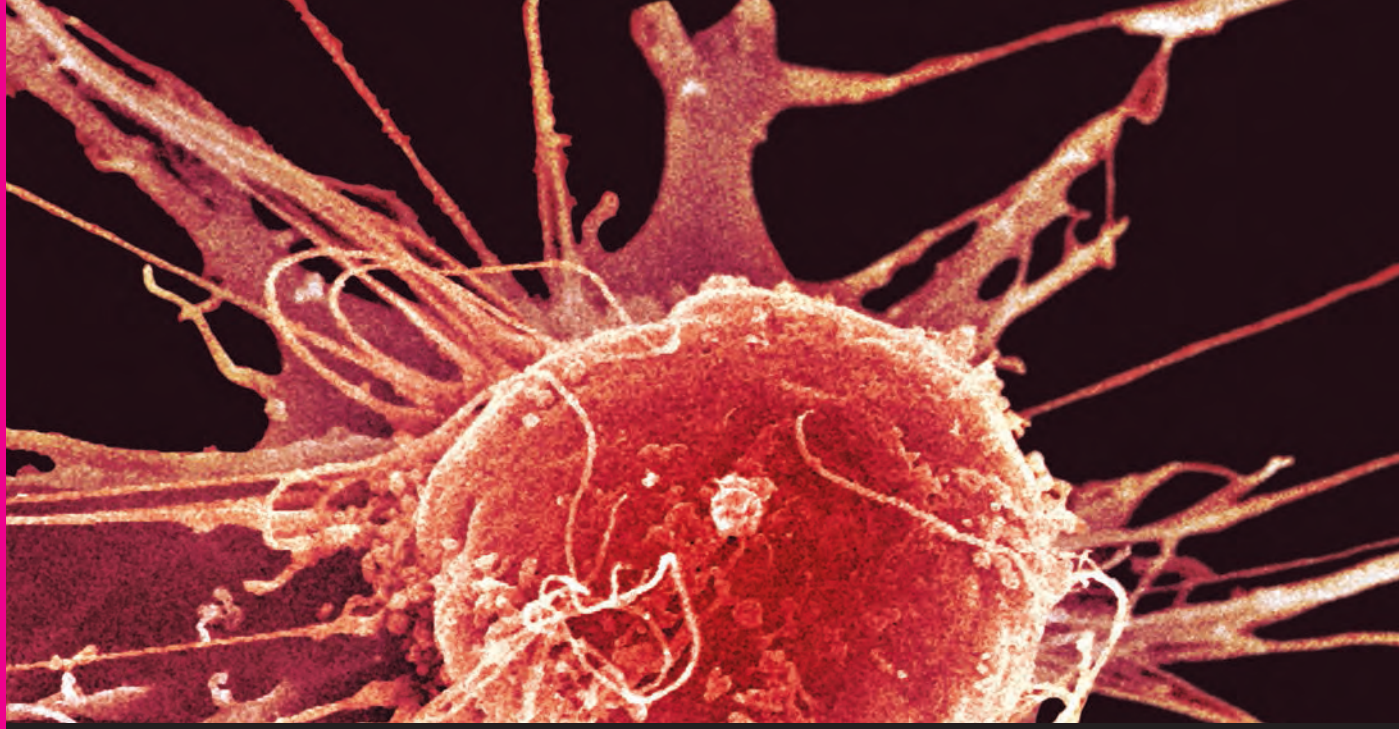

Edited by contributors:
Jan Barfoot, Donald Bruce, Graeme Laurie,
Nina Bauer, Janet Paterson and Mary Bownes

Stem Cells

science and ethics

Stem Cells

science and ethics

Acknowledgements

The Biotechnology and Biological Sciences Research Council (BBSRC), the UK's leading funding agency for research in the life sciences, commissioned this booklet to help 'A' level and Higher/Advanced Higher students gain access to accurate and up-to-date information on stem cell research.

The project was co-ordinated by Dr Jan Barfoot, the Scottish Initiative for Biotechnology Education through collaboration with the Institute of Stem Cell Research, MRC Centre for Regenerative Medicine and the School of Law (SCRIPT), all based at the University of Edinburgh.

The editors would like to express their thanks to the following people for their kind assistance with, and support of, the project:

Authors: Dr Jan Barfoot, Dr Nina Bauer, Dr Donald Bruce, Professor Graeme Laurie, Dr Janet Paterson and Professor Mary Bownes (see 'about the authors');

Funders: BBSRC;

In kind support: The Darwin Trust of Edinburgh and the University of Edinburgh;

Reviewers: Dr Clare Blackburn, Ms Ingrid Heersche and Dr Emma Longridge;

Research: Ms Kaija Allikmets, Mrs Kathleen Pullen, Ms Tara Sarwal and Mr Fu Yang;

Scientists who provided case study material: Dr Lesley Forrester, Professor Anthony Hollander, Dr Keisuke Kaji, Dr Sara Rankin, Professor Paul Sharpe and Dr Anna Williams;

Support with glossary definitions: Ms Emma Kemp, Mrs Kathleen Pullen and the EuroStemCell and EuroSyStem Consortia;

Development of activities: Dr Jan Barfoot, Dr Kate Millar (Ethical Matrix) and Dr Cathy Southworth (Stem cells, the heart of the matter);

Images: Pictures in case studies courtesy of Dr Sara Rankin, Dr Lesley Forrester, Dr Anna Williams, Dr Keisuke Kaji and Professor Anthony Hollander. Special thanks to Ms Ingrid Heersche.

Design and production:
Pax-studio www.pax-studio.com

BBSRC

THE UNIVERSITY of EDINBURGH

Scottish Initiative for Biotechnology Education

MRC Centre for Regenerative Medicine

contents...

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Introduction

Why was this booklet written and what is it about? Find out here.

1. Stem cells: the science

What are stem cells, what can they do and why are they important scientifically? This chapter will introduce you to the science of stem cells and the work of several scientists in this field.

2. Stem cells: legal and global perspectives

How can the law help us explore the ethical and social issues surrounding stem cell research? Discover what the law says about stem cell research in the UK and other countries.

3. Stem cells: ethical issues

Stem cell research has been extremely controversial. This thorough explanation of the ethical debate will get you thinking.

Glossary

Words in pink are further described in the glossary.

Look out for

Throughout this booklet look out for the following boxes:
A question to help you stop and consider an issue for yourself.
An activity to be done on your own or with friends.
An information box further describing a topic.
A real-life case study.

About the authors

Jan Barfoot

Jan Barfoot did a PhD in cancer genetics at the University of Edinburgh before starting work with the Scottish Initiative for Biotechnology Education (SIBE) in 2002. There she worked as a science communicator developing and delivering hands-on biotechnology and bioethical workshops, events and talks to a diverse range of audiences. She has facilitated several collaborative public engagement projects including a large interdisciplinary event at the Edinburgh International Science Festival, Signing Biotechnology, Making Tremors and the first two editions of Stem Cells: Science and Ethics. She now co-ordinates public engagement projects for the University of Edinburgh (most recently Researchers in Residence) and is a lecturer in Science Communication.

Nina Bauer

Nina did her undergrad studies in biology at the Carl-von-Ossietzky University in Oldenburg, Germany, and then moved to Stony Brook University in New York, USA, for a Masters in Neurobiology. In 2002, she returned to Oldenburg for a PhD in molecular neurobiology in the laboratory of Professor Christiane Richter-Landsberg. Her project investigated the formation of protein aggregates as they occur in neurodegenerative diseases like Alzheimer's and Parkinson's. Following her graduation, she broadened her background in clinical aspects of neuroscience during short post-doctoral projects at the Weizmann Institute of Science, Rehovot, Israel, and at the Salk Institute for Biological Studies, San Diego, USA. Finally, in 2008, she joined the Multiple Sclerosis Centre at the Centre for Regenerative Medicine in Edinburgh, UK, to investigate the molecular aspects of myelin formation in the laboratory of Professor Charles ffrench-Constant.

Mary Bownes

Mary Bownes is currently Vice Principal (Pro-VC) at the University of Edinburgh with responsibility in postgraduate affairs, widening participation, recruitment, admissions, scholarships and bursaries, community relations and sustainability. Science communication is a particular interest, especially the development of materials for use in schools and at science festivals to encourage people to take an active interest in biotechnology and how it affects everyday life. She is also very active in encouraging and enabling researchers to engage with the public about their research. Mary moved to the Department of Cell and Molecular Biology at the University of Edinburgh in 1979 to set up a group investigating the genetic and molecular basis of ovarian development in *Drosophila*. She is a Professor of Developmental Biology and Director of the Scottish Initiative for Biotechnology Education. Mary has published over 100 research papers in peer-reviewed journals and supervised the training of more than 27 PhD students. Mary is a Fellow of the Institute of Biology, the Royal Entomological Society and the Royal Society of Arts. She is also a member of the Royal Society of Edinburgh, where she chairs the Young People's Committee.

Donald Bruce

Donald Bruce is director of the consultancy Edinethics Ltd., addressing ethical and social issues in emerging technologies. He holds doctorates in chemistry and theology. He was Director of the Church of Scotland's Society, Religion and Technology Project (SRT) from 1992-2007, where he played a prominent role in the ethical debates on cloning and stem cells in the UK and Europe for many years, and also in encouraging public engagement with Democs card games. He is currently doing ethical work in EC projects on human enhancement and on the use of stem cells for toxicity testing of pharmaceuticals.

Graeme Laurie

Graeme Laurie is Professor of Medical Jurisprudence in the School of Law at the University of Edinburgh and Director of the SCRIPT research centre which examines the relationship between law and technologies. SCRIPT is also based in the School of Law and is sponsored by the Arts and Humanities Research Council.

Janet Paterson

Janet Paterson has a PhD in plant biology and spent five years as a research scientist at University of Edinburgh. Throughout this time, she was involved in many voluntary science communication activities. She joined the Scottish Initiative for Biotechnology Education (SIBE) in 2007 as Development Officer, becoming Deputy Director in January 2009. Janet is involved in many SIBE activities such as resource development, organising Discover Science at the Edinburgh Science Festival, training researchers in science communication, and running biotechnology workshops in schools.

Today, stem cells offer they could potentially we still need to learn a

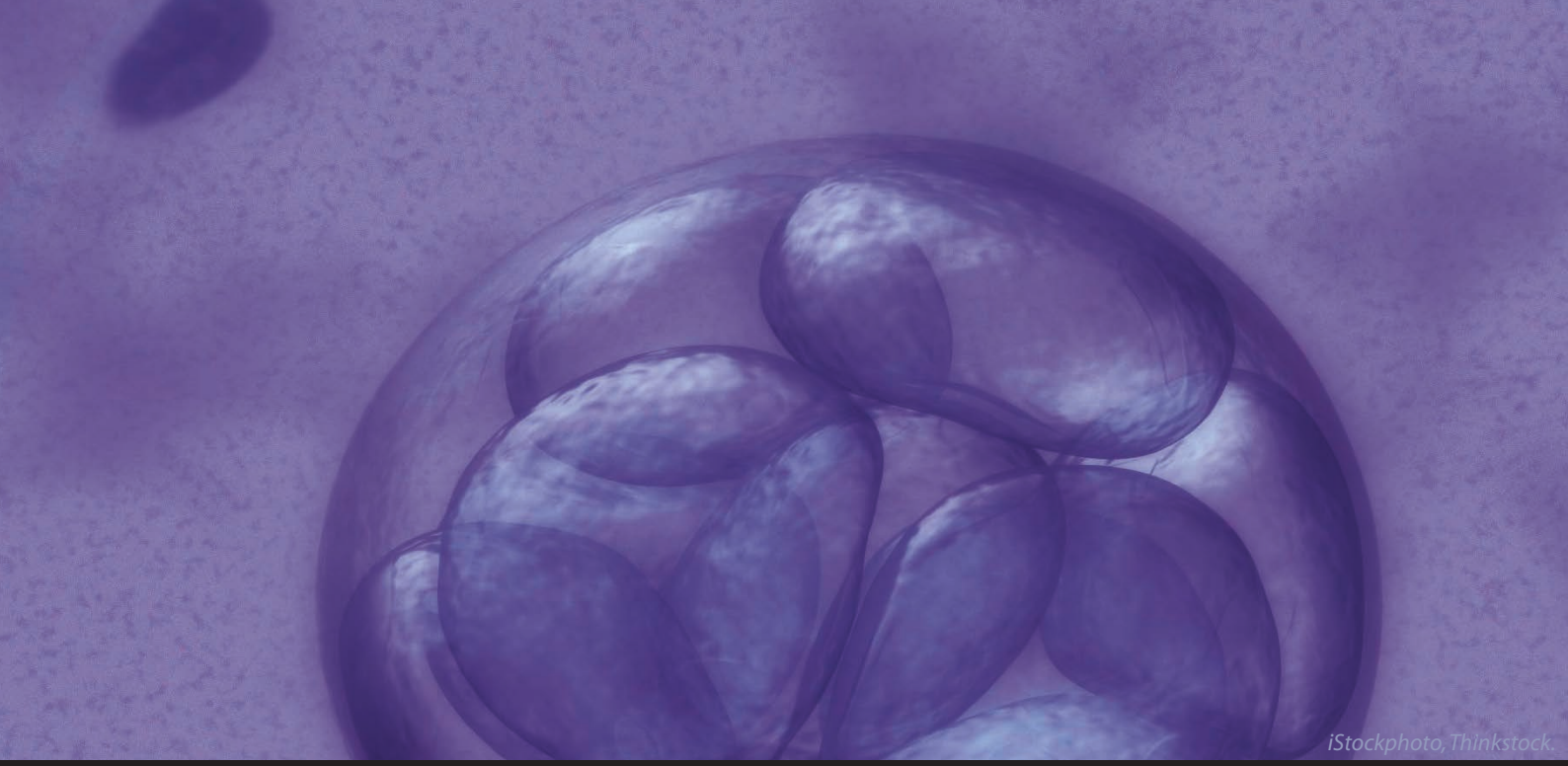
Clockwise from top left: Sally Lowell, University of Edinburgh; Courtesy of Dr Anna Williams; Copyright Dennis Kunkel Microscopy. Inc.; Yorgos Nikas, Science Photo Library; Courtesy of Professor Anthony Hollander; Steve Gschmeissner, Science Photo Library.

Introduction

If you do an online search for 'stem cell research' you will retrieve over 5 million hits world-wide from sources such as research organisations, media, governments, companies, lobby groups and patient charities. There is a huge amount of opinion and information on stem cells and their use in research and medicine - from both scientific and ethical perspectives. The aim of this booklet is to provide a clear overview of the science of stem cells and of the legal and ethical aspects of the subject. Chapter 1 covers the science of stem cells and includes several case studies from stem cell scientists. This is followed by a section on the legal aspects of stem cell research, both from a national and international perspective (Chapter 2). Chapter 3 is an in-depth exploration of the ethical issues, especially those concerning the early human embryo. The Ethical Matrix activity in this chapter gives an opportunity to explore the issues from different stand points.

This booklet is designed to be used in secondary school classrooms (in particular by 'A' level and Higher/Advanced Higher students) but could be read by interested individuals, or used with specific groups of people who have some pre-existing knowledge of biology. Throughout, there are included discussion questions, activities and sources of online materials or further reading. If used in the classroom please refer to the accompanying 'Teachers' Notes'. Throughout the booklet the terms that can be found in the glossary on page 46 are highlighted in pink.

a great model for research; in the long run, be used to cure diseases, but for that to happen, lot about their biological characteristics. *Dr Nina Bauer, Clinical Neuroscientist.*



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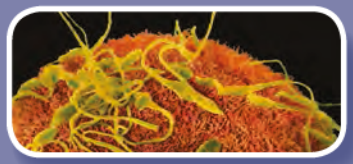
Chapter 1 Stem Cells: the science

Chapter 1 Stem Cells: the science

Human development

Understanding what stem cells are and where they are found is much easier with a little knowledge of how a human develops from a fertilised egg into an embryo, and then a fetus. Here are some basics:

START



Fertilisation

A male sperm and female egg fuse to form a zygote (fertilised egg).
When? 0-24 hours

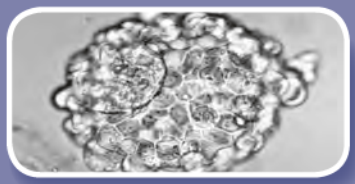
What else?

The zygote is totipotent: it can produce all the cell types needed to make a complete human.

Cleavage

The zygote divides (cleaves) into two identical cells. These cells then cleave and the process repeats to form a ball of around 100 cells.
When? 1-4 days

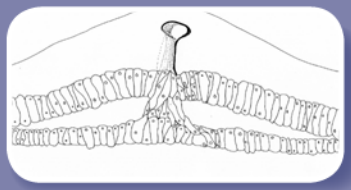
This happens while the zygote passes down the fallopian tube towards the uterus (womb). The ball of about 100 cells has formed by the time it gets there.



Blastocyst formation

The ball of cells begins to specialise forming an outer layer of cells with a cluster of cells inside (inner cell mass). It is now called a blastocyst.
When? 3-8 days

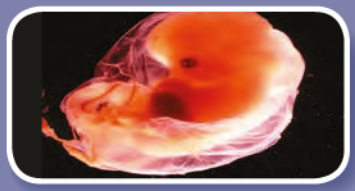
Cells of the inner cell mass are pluripotent: they can form all cell types of the human body except tissues which support the embryo, such as the placenta. The inner cell mass is the source of one type of stem cell, embryonic stem cells.



Gastrulation

The cells in the inner cell mass move to form three layers, each of which will become different areas of the embryo. The whole structure is now called a gastrula.
When? Week 3

The 3 layers are the ectoderm, mesoderm and endoderm. The first sign of the nervous system appearing (the primitive streak) occurs at gastrulation.



Organogenesis

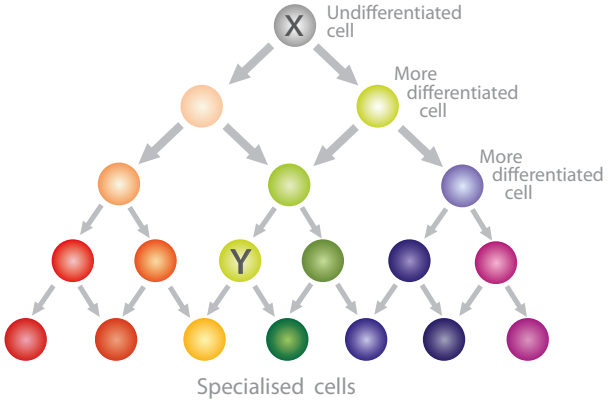
The formation of body organs. The embryo is called a fetus at 8 weeks when the structures which will give rise to all major organs are present.
When? Week 3-8

The ectoderm forms the skin, brain and nervous system; the mesoderm forms muscle and the skeletal and circulatory systems; and the endoderm forms the gut lining and many of the internal organs.

Cell differentiation

It is amazing to think that a single fertilised egg can develop into an entire human body with hundreds of different cell types, each in the correct place and working together in a co-ordinated way. The different cell types are produced from an embryo in a process called cell differentiation. Cells which are differentiated have a specific job in the body, e.g. a brain cell transmits electrical signals as part of the nervous system and a liver cell helps remove toxins from the blood. An undifferentiated cell has no specific job, but may have the potential to become many different cell types.

How does cell differentiation happen? A cell changes gradually from being completely unspecialised to having a specific job. Cells in the embryo undergo many divisions and become slightly more specialised each time. The figure below explains further.



Cells differentiate gradually. Over several rounds of cell division, a new (and more differentiated) cell type arises. As cells become differentiated, the variety of different cells they could become is reduced. In the figure above, cell X has the potential to become seven different cell types, whereas cell Y only has the potential to become two. Cell Y is said to be more differentiated than cell X.

Genetic control of cell differentiation

So, there is a hierarchy of cells from undifferentiated, to partially differentiated, to highly differentiated. It is important to remember that cell differentiation is not random, it is highly controlled and happens in a precise sequence at the correct time and place; otherwise we would be in danger of having liver cells in our heart or lung cells in our pancreas. As cells differentiate, the pattern of genes which are switched on and off in them changes, which in turn changes the proteins which are present and active in the cell. Such genetic control of the process is accompanied by a number of other factors which alter the expression of genes and how the proteins function in the cell. Many stem cell scientists are investigating this complex area.

At the end of the differentiation process, cells which can no longer divide or change any further are said to be specialised cells; they now have a role in the body which cannot change. Not all cells reach this end point though. Some cells in the adult body retain the ability to divide and differentiate, so that they can replace cells when needed. For instance, cells in some organs such as blood and skin live for a relatively short time and constantly need to be replaced. This process of replacement is also necessary for repairing the body after injury. In most tissues and organs, there is a type of stem cell called a tissue stem cell which is responsible for generating these new cells. It is this ability to replace cells and repair tissue that makes stem cells so interesting to scientists and medics.

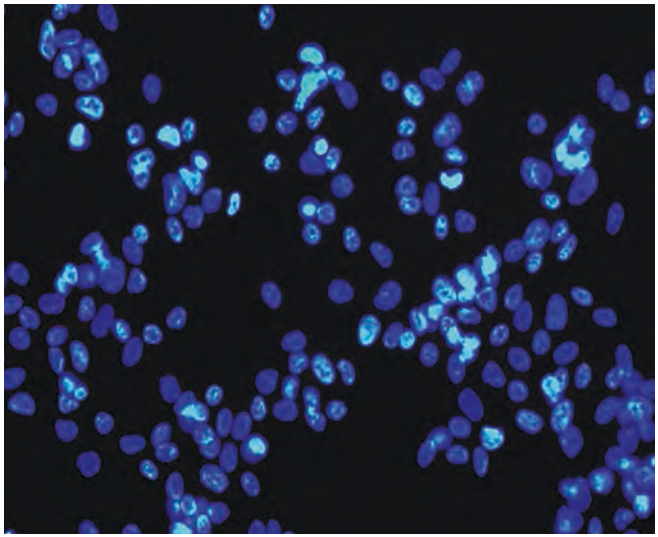
Task: Visualising embryo development

The development of an embryo is difficult to visualise through just reading. Explore some of the following sources of online movies about development in different organisms and consider these tasks.

1. Try to identify the following stages: fertilisation, cleavage, blastocyst formation, gastrulation and organogenesis.
2. Which processes are similar across different organisms and which are different? Make a list.
3. Consider at which points in the movies you might find totipotent, pluripotent or multipotent stem cells.

Sources:
Dynamic Development: [Reference/webpage no longer available – Feb 2016]
Nova Online (human):
http://www.pbs.org/wgbh/nova/miracle/program.html
Nova Online (different organisms):
http://www.pbs.org/wgbh/nova/odyssey/clips/

Conduct your own online research to find other movies.



Human stem cells. Fluorescent micrograph, iStockphoto, Thinkstock.

Stem cells

Definition of stem cells

Stem cells are cells that can:

- Generate more specialised cell types through the process of cell differentiation.
- Divide to make identical copies of themselves, a process called self-renewal.

Why do scientists carry out research on stem cells?

In most cases our bodies use tissue stem cells to replace damaged or worn cells. This repair mechanism is so efficient that, even though it occurs on a daily basis, we hardly notice it. However, where the damage is extensive, this repair mechanism can fail. Also, not all of the tissues in our body, for example brain tissue, can repair themselves efficiently, and many degenerative diseases are not yet treatable by modern medicine. Transplantation of organs such as the heart can be an option, but it relies on a plentiful source of transplant organs, and many are in short supply. Over the past decades, stem cell research has gained a lot of attention because it has the potential to fill this gap in human medical therapies. It is hoped that stem cell research may lead to new therapies for disorders like diabetes, motor neuron disease, cancer and heart disease.

Stem cells have many different uses in the laboratory. This is because they can self-renew indefinitely, whilst keeping their potential to develop into specialised cell types. This means that they could provide an unlimited source of new human tissue. One goal is to use stem cells grown in the laboratory to generate cells or organs which can be transplanted into patients in order to repair or replace damaged tissue. Millions of cells can be produced in the lab over many months from a small starting number of cells. However, knowledge of how the growth and behaviour of stem cells is controlled and how they are turned into, for example, brain cells, heart cells or muscle cells, remains limited. Another important application is the use of stem cells to produce representations (models) of human diseases. These models could be used to further understand why some diseases occur, to provide sources of cells for identifying new treatments and drugs and for testing those drugs for effectiveness and safety. In the UK, research using human stem cells is regulated by legislation, see chapter 2.

Summary of possible uses of stem cells:

- To provide lab-grown human or animal tissue for identifying new treatments for disease, including new drugs and other substances, rather than using animals.
- To produce new human tissue and organs to replace those lost in injury or disease. **See box, Organ regeneration.**
- To repair tissue by stimulating stem cells already in the body.
- To use stem cells from patients with inherited genetic diseases (such as cystic fibrosis or some forms of Parkinson's disease) to study how the disease develops.
- To investigate human development.
- To better understand diseases like cancer.

Organ regeneration

The use of stem cells to regenerate organs is exceptionally complex. This is due to the three-dimensional structure of organs and the fact that they contain many different cell types working together to create a functional organ. Two exceptions to this are the liver, which is predominantly made up of one cell type (hepatocytes) and has some in-built capacity to regenerate itself, and the epidermis of the skin which is essentially a two-dimensional organ.

Some of the questions that stem cell scientists are trying to answer are:

- How can stem cells be instructed to become a specific cell type, or in some cases even an entire organ, in the laboratory?
- How can stem cells grown in the laboratory be stopped from specialising before scientists want them to?
- How can differentiation be controlled such that the lab-grown cells are safe for clinical use?
- How can stem cells be used to create models of human diseases that drugs can be tested on?

Different types of stem cells

Scientists use three main types of stem cells: pluripotent stem cells, tissue stem cells and induced pluripotent stem cells.

Pluripotent stem cells

Pluripotent stem cells can generate all of the different cell types found in the body. The best known type of pluripotent stem cell is the embryonic stem cell (ES cell). As their name suggests, ES cells are obtained from early-stage embryos (see Human Development on page 5 of the booklet). Specifically, they are obtained from the inner cell mass of the blastocyst the ball of cells which, in humans, develops from the fertilised egg after 3-8 days.

CASE STUDY

Dr Sara Rankin,
National Heart and Lung Institute
Imperial College London

My work
My research is in the new field of regenerative pharmacology. Essentially I investigate how we can use drugs to stimulate endogenous adult bone marrow stem cells to repair the body. My group has recently identified a new drug combination that releases stem cells from the bone marrow into the blood. We are currently investigating the impact of increasing stem cell numbers in the blood on tissue regeneration.

My research goals
To understand the role of stem cells in disease. To work out the mechanisms that regulate the movement of stem cells from the bone marrow to sites of tissue damage and use this knowledge to develop drugs that could be used in humans to treat diseases such as heart disease or broken bones.

My typical kind of day
I enjoy the diverse range of activities that my job now involves, which includes teaching Pharmacology in tutorials for the undergraduate medical students and running training workshops for the postgraduates. I also have intense research meetings with my group of Masters, PhD and postdoctoral scientists to discuss results of experiments and plan the next set of experiments. This is very exciting, particularly when we get completely unexpected results that lead to new discoveries. I also run stem cell workshops for pupils and teachers which are great fun. I always loved the creative arts at school and so I have started a collaborative project with an artist. We hope to create a series of interesting and beautiful sculptures influenced by stem cell science that can be read and interpreted in multiple ways, breaking down the barriers between art and science. In addition to these activities I spend a lot of time travelling to give talks about my work and meet up with scientists who we collaborate with across the world, both in academia and in the pharmaceutical industry.

> *Being a scientist stretches your imagination and allows you to be creative. Every day you will learn something new and fascinating and one day you will discover something that could change the way we live.*

http://www.imperial.ac.uk/medicine/about/divisions/nhli/

To generate an ES cell line, the inner cell mass is placed in a petri-dish and supplied with specific nutrients, vitamins and hormones that enable the cells to survive and divide. If these cells keep self-renewing for many months when grown in these conditions, and can still differentiate when tested, they are called a stem cell line. Such cell lines can produce almost unlimited numbers of pluripotent ES cells for research.

Stem cells: drug discovery and toxicity testing

The discovery and development of pharmaceutical treatments (drugs) for diseases currently involves cell culture models usually made from tumour cells. Multiple drugs are tested to see if they might have a potential therapeutic use and, if so, whether they are toxic. Once a candidate drug has been selected, *in vivo* testing begins (testing within a living organism). However over 90% of the drugs tested in clinical trials are not approved for use, making this lengthy process costly and inefficient. One reason for the high failure rate could be that the cell culture models used are not very similar to the tissue of interest, that is the tissue that the disease affects.

Human embryonic stem cells (ES cells) can be made to differentiate into different cell types which will retain more similarity (in terms of genetics, phenotype and function) to the tissue of interest. They offer a better (more accurate and efficient) model with which to discover and test new drugs. Further, if a disease has a genetic component, ES cells could be generated with the particular genetic mutation. These cells could be made to differentiate into diseased tissue before drugs are tested on them.

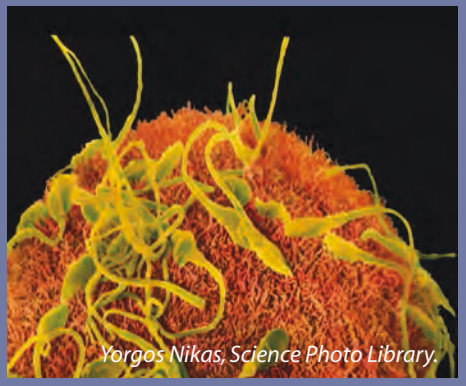
These ES cell-derived models could reduce the number of candidate drugs that fail at the final stages of testing and so reduce the number of *in vivo* experiments needed. Some scientists suggest that it is this application of stem cell technology that will be available first. It is estimated that in as little as 10 years, stem cells will be replacing current methods of drug discovery [1,2].

Sources of human embryonic stem cells in the UK:

- Most human ES cell lines are generated from unused embryos from *in-vitro* fertilisation (IVF) clinics. These embryos were created as part of fertility treatment, but were not needed for a pregnancy, and were donated for research. **What's IVF? See box**.
- In some cases, embryos can be created specially for stem cell research from donated eggs and sperm, using IVF methods. In the UK, permission to create embryos for research is granted only for very specific reasons, for instance in cases where scientists are trying to use ES cells to study a particular inherited disease.
- Embryos have also been created specially for stem cell research by activating donated human eggs without the use of sperm (parthenogenesis).

The generation of human ES cells has been controversial due to ethical issues concerning the status of the embryo. Such ethical issues are explored in chapter 3. Many UK researchers now use a number of well-established human ES cell lines in their experiments and do not isolate new ES cells from an embryo for each set of experiments. These ES cell lines are held in the UK Stem Cell Bank. **What's the Stem Cell Bank? See box on page 11.**

In-vitro fertilisation (IVF)


Yorgos Nikas, Science Photo Library.

Developed in the 1970s, this is a process where eggs are fertilised outside of the womb. A woman has to take fertility drugs to help produce eggs, which are then harvested and fertilised with sperm in the laboratory. The fertilised eggs can be implanted into the womb, and hormone treatment given to the woman to promote a successful pregnancy. The first 'test tube baby' was born in 1978 [3].

ES cells used in the laboratory can be of human or animal origin. Animal ES cells are used because they can be generated more easily than human ES cells. In the case of the mouse, they are easier to grow and are better understood than the human cells. As their general properties are similar, many of the findings made in mouse ES cells can be directly related to human ES cells, so work on these animal cells plays an important role in stem cell research.

Many scientists are excited about ES cells because of their capacity to generate so many different types of cell. ES cells are well suited to be used by scientists to help them understand which specific hormones and growth factors are needed to maintain the ability to self renew and to differentiate into other cell types. Through years of experimentation, mostly using mouse ES cells, some basic methods have now been established to induce ES cells to form some specific cell types. Once scientists work out how to generate a particular tissue from human ES cells, this method could, if the appropriate safety tests were passed, be used to produce cells for transplantation and medical therapies. However, as the tissue generated this way would be genetically different from that of a patient, the risk of tissue rejection by the patient's immune system would be high and so the patient may need drugs to suppress their immune system after transplantation. **What's Immune rejection? See box on page 11.**

Tissue stem cells

Tissue stem cells (sometimes less accurately termed adult stem cells) are found in many organs and tissues in the body, including bone marrow, blood, cornea, retina, intestine, muscle, nervous system, brain, and skin. They are also found in developing organs in the fetus, umbilical cord and placenta. More precisely, they occur

CASE STUDY

Dr Lesley Forrester
University of Edinburgh,
MRC Centre for Regenerative Medicine

My work
Blood consists of many different cell types that have diverse functions from carrying oxygen round the body to fighting infections. The cells are short lived and so they have to be constantly replenished from stem cells in the bone marrow.

My research goals
I want to understand the genetic mechanisms that ensure we make just the right number of blood cells. These mechanisms go wrong in patients with blood disorders so my research will help to understand these diseases.

Current challenges
We can produce blood cells in the laboratory from embryonic stem cells. This system can be used to study the genes involved in blood cell production and might provide a source of cells to treat patients. Our main challenge at the moment is to increase the efficiency of blood cell production and to ensure that the cells produced in the lab can function in the same way as normal blood cells.

My typical kind of day
It is difficult to describe my 'typical day' because no two days are the same. I spend as much time as possible talking to the people in my lab about their projects. Sometimes they are keen to tell me about a new result but, more often than not, we discuss why the result of an experiment is not as we expected. Have we discovered something really exciting or was there just a technical problem? Research scientists need to raise the funds to do the research by applying for grants, so much of my time is also spent writing and reviewing grant applications and research papers.

> *We are constantly problem solving, with the answer to one question often raising many more.*

http://www.crm.ed.ac.uk

in specific regions of an organ, the so-called 'stem cell niche'. Their role in the body is to replace cells which die throughout life due to wear and tear or injury and disease. For example, stem cells in bone marrow replace blood cells.

An important feature of tissue stem cells is that their capacity to generate other cell types is usually limited. For example, a brain stem cell can become any cell type of the brain, but not a muscle cell. Hence they are termed multipotent; capable of producing many cell types but not all cell types in the body (in contrast to pluripotent stem cells).

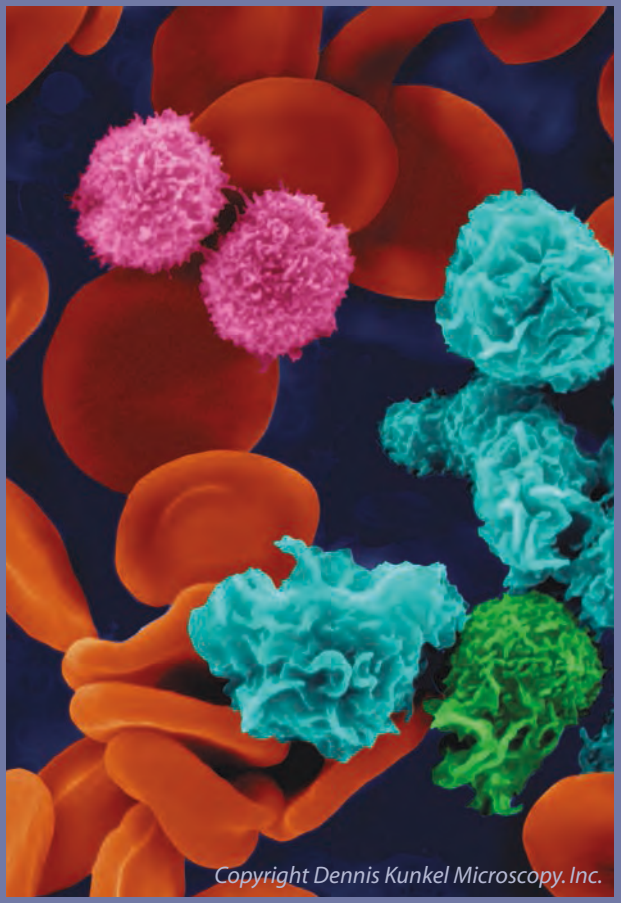
Tissue stem cells are obtained directly from the organ or tissue in which they are found. They are ideal to use to investigate questions around cell differentiation that are specific to a certain tissue. Currently there are some effective treatments that use tissue stem cells from donors but these treatments carry a risk that donated cells will be rejected. However, tissue stem cells have the advantage that, if they can be obtained from the patient in whom they will eventually be used, they will have the same genetic make-up as that person and therefore will not be rejected by the immune system. However, they are difficult to isolate and are usually found in very small numbers. Also, at the present time it is still not possible to grow enough tissue stem cells in the laboratory to be useful in treatments.

UK Stem Cell Bank

The UK Stem Cell Bank helps reduce the use of embryos in research. It is a centralised resource which stores quality-controlled stocks of ES cell lines that are provided free to researchers (although permission must first be sought from the UK Steering Committee). Having a central repository ensuring quality and safety testing is essential if the cell lines will eventually be used to produce a clinical treatment. It can also make sure that stem cell lines have been ethically sourced, for example with rigorous consent processes.

Immune rejection

Immune rejection is when the immune system of a patient recognises cells or tissues as foreign or 'non-self'. When this happens the immune system mounts an attack on the foreign cells which damages or kills them. This is a big problem for cell or organ replacement therapies, including classical organ transplantation and existing and proposed stem cell therapies. Whilst immunosuppressive drugs can be used, their use is complicated and has side effects. The only way to totally avoid immune rejection is to match a donor and recipient/patient perfectly, and this situation only occurs between identical twins or if the donor cells originate from within the patient.



CASE STUDY

Dr Anna Williams
University of Edinburgh,
MRC Centre for Regenerative Medicine

My work
I work on Multiple Sclerosis (MS), which affects young adults causing problems with walking, vision, balance and sensation.

Current challenges
Scotland has the highest rate of MS in the world. Nerves in the brain are normally protected with fatty myelin sheaths formed by oligodendrocytes which protect them and allow the fast conduction of electrical impulses. In MS, this myelin sheath is damaged (demyelination). Oligodendrocyte precursor cells in the brain try to repair the damaged sheath (remyelination), but they cannot do this very well and scars form causing permanent disability.

My research goals
I am interested in what makes the precursor cells try to repair the damaged sheath and how we could encourage them to do this better.

I work together with a lab assistant and a PhD student. We use models of MS to investigate these questions. We grow oligodendrocyte precursor cells in culture, let them mature and test the way they move, and make myelin sheaths under different conditions.

My typical kind of day
I work as a researcher and as a neurologist. As a researcher I oversee and plan experiments in the lab, attend seminars, write scientific papers and grant applications. As a neurologist, I look after my patients on the neurology ward and run outpatient clinics in the hospital. Sometimes I have to combine my two jobs on the same day, and work in the lab in the morning and see my patients in the afternoon. That keeps me busy!

> *Clinical work reminds me of the importance of my lab research to try and find ways to repair the brain, even if we are unsure of the cause of MS.*

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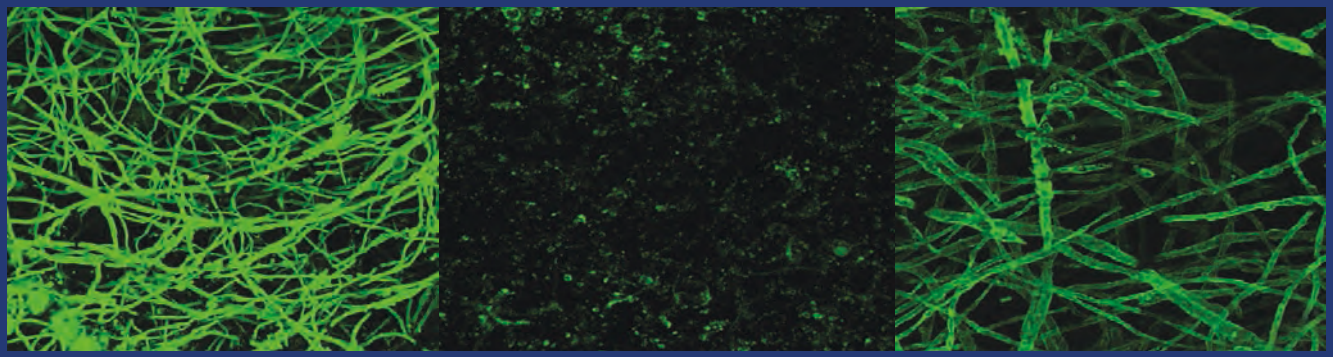

Images show myelinated nerves (green), then demyelinated nerves (green myelin debris) then remyelinated. Myelin is highlighted using immunohistochemistry for Myelin Basic Protein (MBP.) Fluorescent micrograph. Images: Anna Williams.

	Embryonic stem cells	Tissue stem cells
Differentiation ability	• They are pluripotent: capable of becoming any cell in the human body except cells needed to support the embryo, such as the placenta.	• They are multipotent: typically only give rise to the cells of the tissue in which they are found.
Role in body	• To develop the embryo into an entire human.	• To replace cells in the body which die throughout life due to wear and tear or injury and disease.
Sources for research	• Unused IVF embryos which have been donated, or embryos created for the purpose from donated eggs and sperm.	• Mature adult tissues such as bone marrow, muscles and skin; and from the fetus, umbilical cord, placenta and amniotic fluid.
Advantages in research and therapy development	• Have a strong ability to self-renew in the laboratory, resulting in a constant supply of ES cells. • Pluripotency means that ES cells have the potential to produce any cell type in the body.	• If taken from the patient's own body for use in therapies, cells would be genetically identical to that of the patient, avoiding the problem of immune rejection. • There are less ethical considerations compared with using embryonic stem cells.
Disadvantages in research and therapy development	• Genetically different to cells of potential patients, so immune rejection could occur. • Ethical issues over embryo destruction.	• They usually only produce a limited number of different cell types. • Conditions supporting self-renewal in the laboratory have only been identified for a few tissue stem cell types, for instance skin and cornea. • Are found in small numbers and are difficult to isolate.

Induced pluripotent stem cells

Scientists have more recently found another way of producing pluripotent stem cells without using embryos. In 2006-7, scientists discovered how to 'reprogramme' some specialised cells to become pluripotent so that they lose their specialist functions and behave in virtually the same way as embryonic stem cells [4,5]. The starting cells are reprogrammed into a pluripotent stem cell state. Pluripotent cells generated in this way are called induced pluripotent stem cells (iPS cells). iPS cells were first produced in mice, and it was quickly shown that the same method could be used to make human iPS cells. Importantly, once the conditions for making iPS cells had been worked out, it proved very easy for other scientists to make them. They can be made using any kind of cell in the body, but most often skin cells are used as they are easy to obtain.

This has been a very important advance, as it is now possible to generate human pluripotent stem cells without using human embryos. Additionally, as iPS cells could be generated from any individual, this technology opens the possibility of generating lots of patient-specific cells, which will not be rejected by the immune system upon transplantation. Further, it also allows the generation of pluripotent stem cell lines from patients with inherited diseases, in order to better understand why the diseases develop.

Making iPS cells

Initially the method for generating iPS cells required the use of viruses to insert four specific genes (*c-Myc, Klf4, Oct4* and *Sox*) essential for reprogramming specialised cells into a stem cell. However, the use of viruses greatly increased the risk of these cells becoming cancerous and they were therefore considered unsafe for transplantation into patients. Very recent developments

Task: Stem Cells, the heart of the matter

Your group will research and design a four-page A5 leaflet about stem cells for the British Heart Foundation. The leaflet should include what stem cells are, information about the three different types of stem cells and details of current research of the use of stem cells in the treatment of heart disease. The leaflet is aimed at adults who may have very little knowledge of biology or stem cells.

To achieve this task you need to:

1. Research the area.
2. Decide what information is important and interesting and should therefore be included in the final leaflet.
3. Find images/take photographs/produce illustrations.
4. Design the final layout.
5. Produce the leaflet.
6. Evaluate the leaflet by showing it to family and friends. How well have you communicated the science and applications?

show that reprogramming can also be achieved by providing the cells with specific proteins without the need to use viruses in the process [6]. The genetic information of the cells remains intact reducing the risk of the cells becoming cancerous. Even so, research is still ongoing to improve the safety and efficiency of this technology, and more work is needed before scientists will know whether stem cell therapies can be developed using iPS cells and whether they are a useful alternative to ES stem cells.

Which to use: embryonic, tissue or induced pluripotent stem cells?

All of the stem cell types outlined above are each invaluable for different reasons. While embryonic stem cells are pluripotent and can have a great ability to self-renew, they may not suit a patient due to immune rejection (although, advances in transplantation immunology are moving fast). In contrast, stem cells that have been derived from a patient's own body (i.e. both induced pluripotent and tissue stem cells) could avoid problems with this. The issue remains as to whether the time needed to harvest cells,

CASE STUDY

Dr Keisuke Kaji
University of Edinburgh,
MRC Centre for Regenerative Medicine

My work
I generate stem cells from specialised cells. Normally, specialised cells cannot produce different types of cells. For example, skin cells cannot make new muscle cells. But recently scientists developed a strategy to change these skin cells into stem cells that have the potential to make any type of cell in the body. These stem cells are called 'induced pluripotent stem (iPS) cells'. We expect that these new cells will revolutionise medicine because iPS cells have the potential to be used for drug screening, toxicology tests, disease modelling and regenerative medicine.

Current challenges
The efficiency by which skin cells can be turned into iPS cells is still extremely low and not sufficient for routine use. I'm trying to understand the mechanism of reprogramming and what hampers the process, to improve the technology.

My research goals
If we know how reprogramming happens, we will be able to use the knowledge not only to improve the technology but also to develop strategies to produce the desired types of cells.

My typical kind of day
Most of my time I spend in the lab doing experiments, but I also have to write up my experiments and publish scientific papers. Often it is hard to predict what I will do one week in advance, because it depends on the results I get from my experiments. I often have to work at the weekends, as I have to take care of my cells. I don't have a 9 to 5 job, but enjoy deciding what to do every day.

> *Doing science is fun!*

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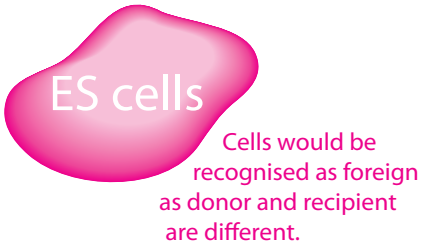
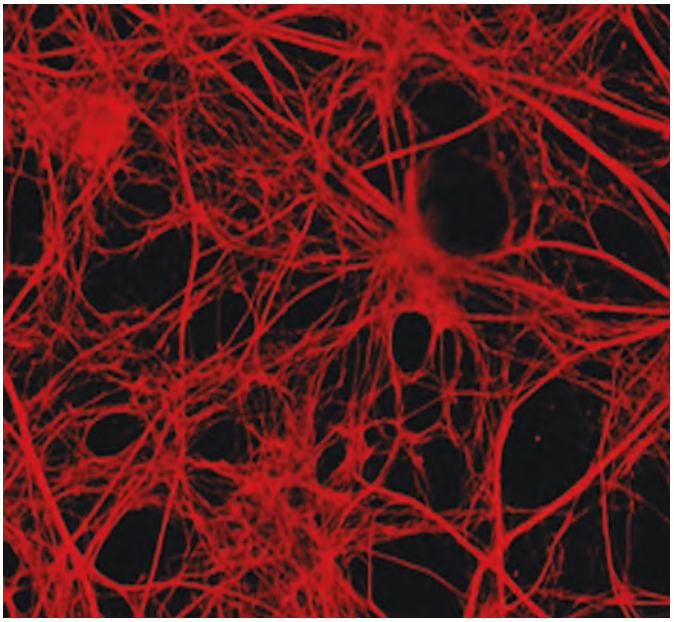
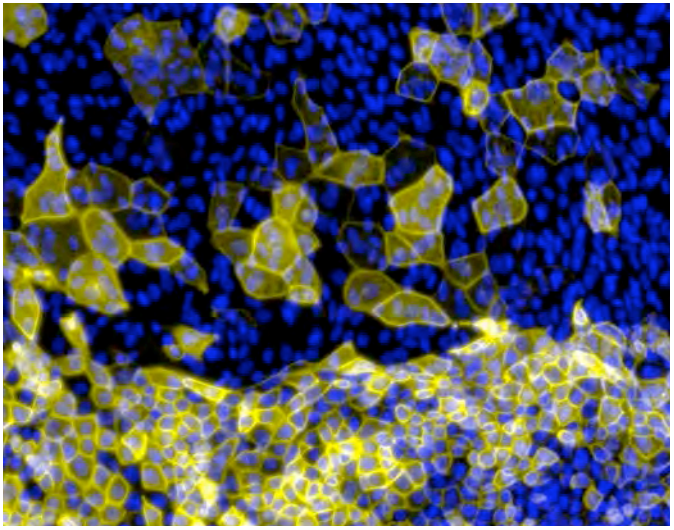
prepare them for treatment and place them back into the patient will be fast enough. Further, in the case of genetic diseases, stem cells from the patient's body may carry the same genetic defect and may therefore not be able to repair and cure the patient. For all of the different types of stem cell it will be important to ensure that lab-grown cells can be used safely in therapies. A lot of research still needs to be done; ultimately one stem cell type may be chosen for a particular therapy, while another may be more efficient in a different case.

This diagram summarises the properties of stem cells in terms of immune rejection.





Newly formed neurons from neural stem cells.
Image: Sally Lowell, MRC Centre for Regenerative Medicine, University of Edinburgh. www.crm.ed.ac.uk.



Newly formed skin cells (yellow) emerging from embryonic stem cells in culture. Cell nuclei are shown in blue.
Image: Sally Lowell, MRC Centre for Regenerative Medicine, University of Edinburgh. www.crm.ed.ac.uk.

Progress in stem cell therapy research

In many cases, research is focused on working with specific cell types for replacement therapies in specific situations. When whole organs are damaged, this poses a unique and difficult challenge for stem cell scientists. Organs generally have many different cell types, precisely co-ordinated and structured to achieve the desired function. This illustration summarises some of the progress in stem cell therapy research.

Teeth

Teeth are a useful test case for using stem cells for replacement of an organ that is not life-threatening to the patient. Professor Paul Sharpe leads a team at King's College London investigating tooth regeneration. This group is developing methods of producing an early stage of human teeth (primordia) for transplantation into the adult mouth to replace lost teeth. In animal studies they have shown that embryonic and tissue stem cell populations can be identified that can all form tooth primordia that are themselves able to develop into complete teeth in the adult mouth [7]. One very attractive source of dental stem cells, are cells derived from the pulp of teeth that are lost naturally by children.

Trachea

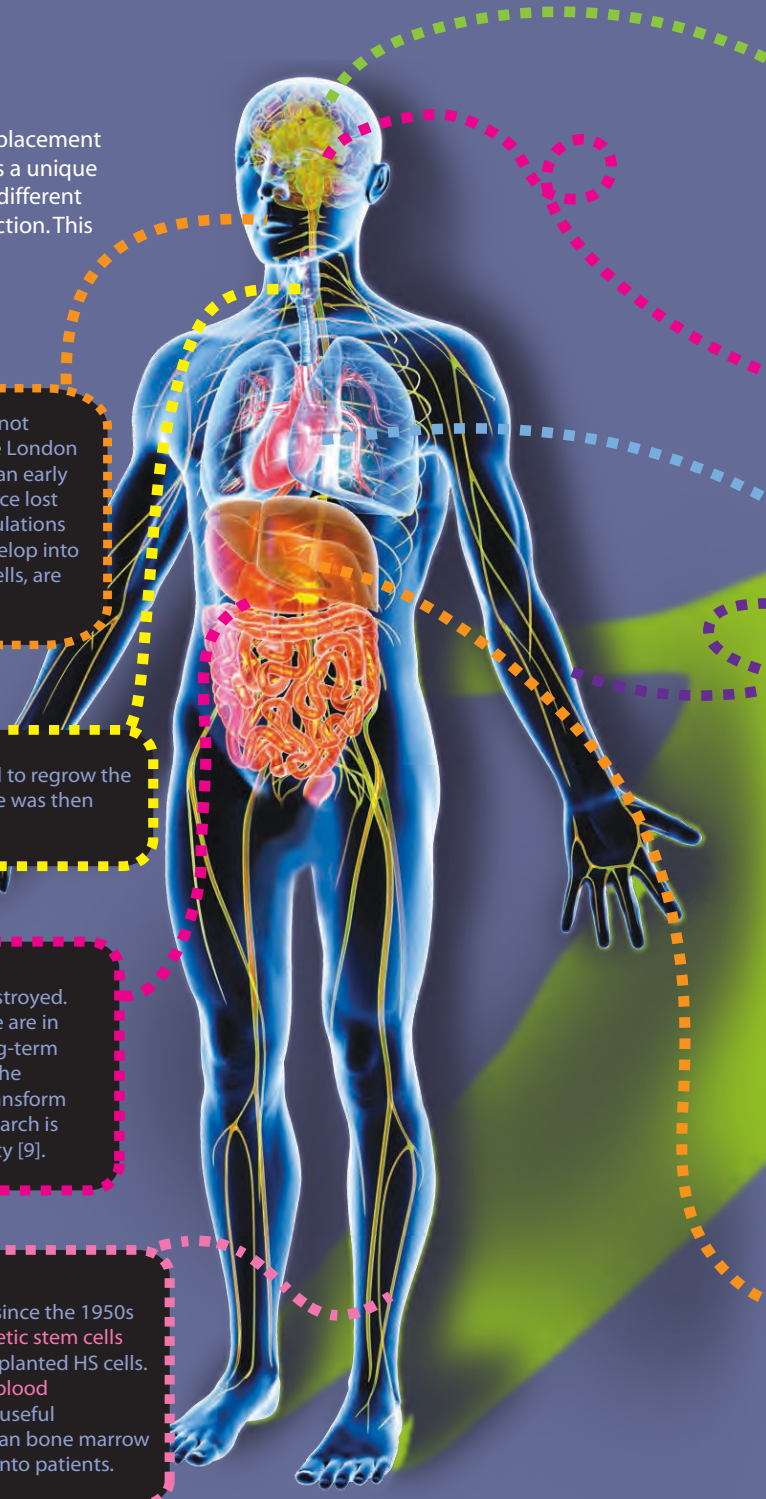
Using a scaffold windpipe from a donor, a patient's own stem cells were used to regrow the cellular part of the windpipe outside of the patient's body. The new windpipe was then transplanted into the patient [8].

Pancreas

In type I diabetes patients, the insulin-producing beta-cells of the pancreas are destroyed. Currently, these cells can be replaced by beta-cells from donated organs, but these are in short supply. Therefore, the generation of beta-cells is a major objective in the long-term goal of curing this condition. Embryonic stem cells, existing pancreatic cells from the patient, and cells from other tissues such as liver could potentially be guided to transform into beta-cells for transplantation into a patient to repair pancreatic function. Research is still ongoing and it will take some time before such a treatment may become reality [9].

Blood/Immune system

Stem cell therapy in the form of bone marrow transplants has been around since the 1950s to treat immune disorders [10]. Bone marrow is a rich source of haematopoietic stem cells (HS cells). A patient's own immune cells are destroyed and replaced by transplanted HS cells. Those cells proliferate to replace the immune system. Since the 1980s, cord blood transplantations from related and unrelated donors have been shown to be useful treatments for various blood disorders [11]. Cord blood is easier to obtain than bone marrow and contains HS cells which can be grown in the lab before transplantation into patients.



Brain

Animal models have shown that pluripotent stem cells can relieve symptoms of Parkinson's disease and restore the damage done by this neurodegenerative disease. This could be a promising new strategy for humans too [12].

Haematopoietic stem cell transplantation has been shown to slow the progression of Multiple Sclerosis in 70% of cases. The cells slowed progression of brain atrophy [13].

Eyes

Degenerative diseases of the retina are a major cause of incurable blindness worldwide. It is hoped that stem cell therapies may be used to replace retinal cells lost through disease. For example, retinal cells produced from human embryonic stem cells have shown success in the treatment of age-related macular degeneration in animal models and clinical trials are planned [14].

Skin

The prospect of faster wound healing or repair of serious burns, is driving researchers to find a stem cell therapy for damaged skin. Currently, patients with serious burns can be treated using a technique which grows new skin in the lab from their own skin cells. However, this can take weeks, with the patient at risk of dehydration and infection meanwhile. Recently, researchers have used human embryonic stem cells to attempt to produce skin grafts. The technique could potentially provide an unlimited supply of temporary skin for patients with large burns who are awaiting grafts of their own skin [15]. So far the skin grafts have been trialled successfully in mice and human trials are planned.

Heart

Cardiovascular disease, which includes coronary heart disease, hypertension and stroke, can cause the blood supply to part of the heart muscle to be cut off, depriving it of oxygen. This can cause significant damage and scarring to the affected area of tissue and may lead to heart failure. At the moment there are no cures, but it is hoped that stem cell therapy may in the future allow the replacement of damaged heart cells with healthy ones. So far, hundreds of clinical studies have examined the potential therapeutic effects of heart stem cell therapy. However, the bulk of the data suggests that it is still early days for this possible therapy [16].

Liver

Currently, the only effective treatment for serious liver disease is liver transplantation, and this is limited by a shortage of donor organs. However, research is being carried out to see if liver-like (hepatocyte-like) cells can be produced from stem cells. Although successful techniques have been developed, it has been found that the stem cell-derived hepatocytes cannot perform all of the functions of liver-derived hepatocytes, so more research is required to see if this could be a potential therapy for humans [17].

Human male anatomy, artwork. Pasieka, Science Photo Library.

CASE STUDY

Professor Anthony Hollander
Department of Cellular and Molecular Medicine
University of Bristol

My work

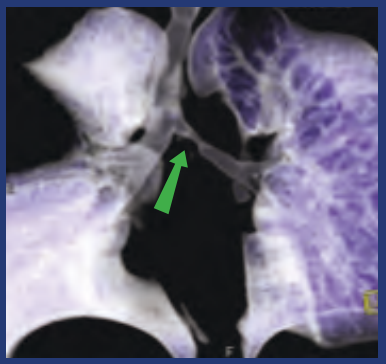
I am the Arthritis Research Campaign Professor of Rheumatology & Tissue Engineering as well as Head of the Department of Cellular & Molecular Medicine. I am also Scientific Director of a small University spin-out company, Azellon Cell Therapeutics, that is turning one of our scientific discoveries into a cellular medicine for knee injury.

Current challenges

Doing high quality scientific research is always challenging in an exciting way; but exploiting the results of your research so as to make it relevant to people in everyday life is perhaps the biggest challenge. This is because of the enormous care you have to take before treating patients with a new treatment you have invented. There are many regulations to conform to as evidence that the therapy is safe and effective. But turning research into treatments is essential if, as I do, you want to use your research to make a difference.

My research goals

I have spent the past 20 years researching the causes of, and possible treatments for, osteoarthritis. This work has led me into the fascinating fields of stem cell biology and tissue engineering. Figuring out how to use stem cells to create tissues such as cartilage and bone is now my primary goal.



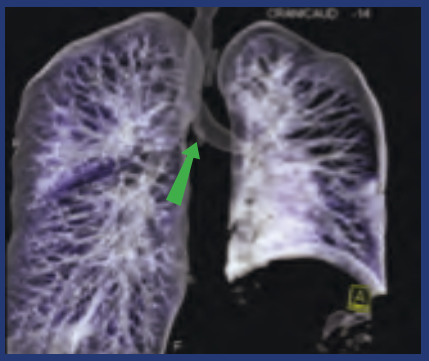
Before: Tracheal tissue engineering: A patient with a narrowed left bronchus...

My typical kind of day

Because I effectively have three jobs my day is both busy and varied. I am usually in work by 7:30am but try to have left before 6pm if I can. Running a large research department requires many meetings, documents to be written, discussions to be had and this takes up a lot of my time. I manage my research team through a weekly meeting where we all get together to share data and explore the next steps and then separate meetings with individual staff and research students when they are needed. My research also requires a lot of time writing grant applications, papers for publication and attending conferences all over the world (a nice aspect of the job, though a lot of travel can get tedious). I will sometimes spend time talking with journalists about my work and occasionally give interviews on television or radio.

> *If you know what your goals are in science and are prepared to work hard to achieve them, then you have a chance of making a big difference to the world we live in and you will have enormous fun along the way.*

http://www.bristol.ac.uk/cellmolmed/staff/hollander.html

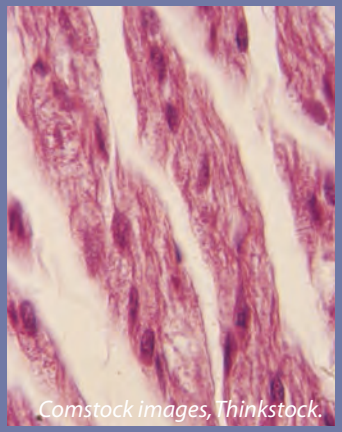


After: The same organ after implantation of the tissue engineered airway. The new airway was made using stem cells that were turned into cartilage cells. Images: Courtesy of Hospital Clinic of Barcelona.

Activity

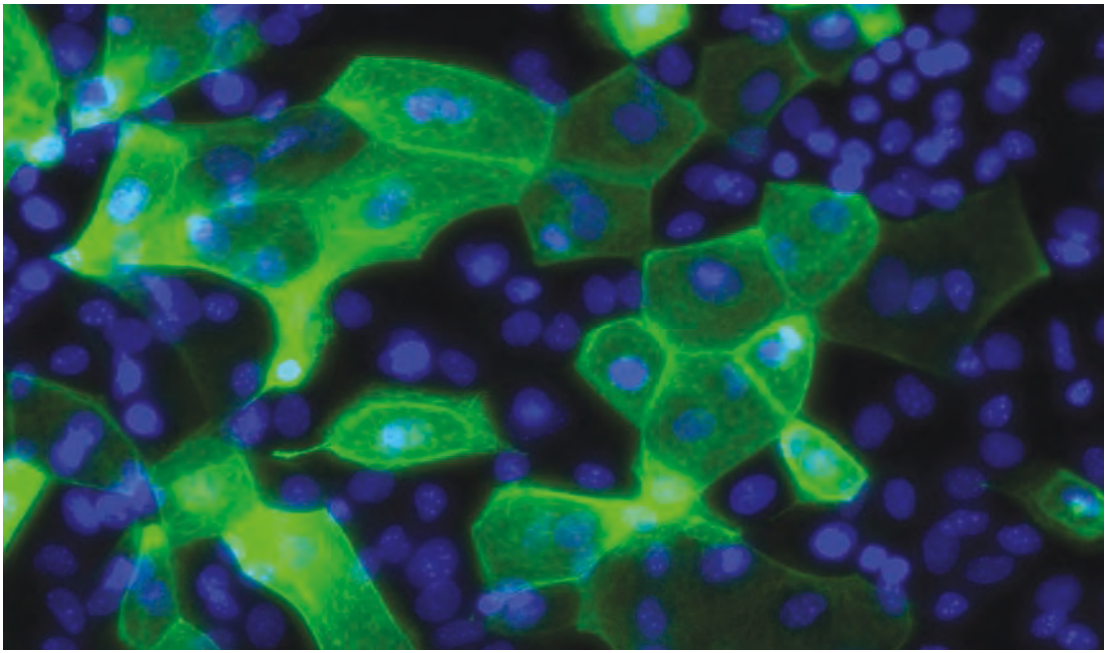
The MRC Centre for Regenerative Medicine, University of Edinburgh, has developed a role play exercise which looks at an application for a clinical trial that would use stem cells to treat spinal injury. Participants play the roles of scientists and members of the public at an open hearing about the proposed trial. The activity is an informal way to learn about and discuss the issues surrounding stem cell therapy and clinical trials.

Spinal muscular atrophy and iPS cells



Comstock images, Thinkstock.

Spinal Muscular Atrophy (SMA) is a genetic disease in which patients exhibit loss of motor neurons leading to muscle weakness, paralysis and in many cases death. A team of researchers in USA reprogrammed skin cells from a SMA sufferer and produced iPS cells which had many of the characteristics of the disease. They were differentiated to generate diseased motor neurons with similarities to those found in the patient. Finally, and importantly, these iPS-derived motor neurons were used to test the effect of a drug, valproic acid, which reversed some of the disease characteristics of the motor neurons [18].



Newly formed skin cells (green) emerging from embryonic stem cells in culture. Cell nuclei are stained with DAPI and show in blue.
Image: Sally Lowell, MRC Centre for Regenerative Medicine, University of Edinburgh. www.crm.ed.ac.uk

Conclusion

The vast possibilities of what stem cell research could achieve mean that the expectations for this research from both the public and scientific community are huge. However, whilst there are some clinical trials with stem cell therapies in the UK, few stem cell treatments are currently commonplace in UK hospitals. It would be misleading for this publication to suggest that stem cell therapies from iPS cells will be available soon in UK hospitals. Most scientists would acknowledge that much work is needed to investigate the characteristics, control, safety and reliability of iPS cells. In particular, what the similarities and differences are between iPS cells and ES cells. These issues must be considered before the research can be turned into medical treatments.

Some feel that the use of iPS cells to model human diseases will be the technology that is available first [19]. This would allow treatments and drugs to be tested for their effect on diseased human cells and whether or not they are toxic to the cells. Some early experiments have already been carried out that demonstrate this potential. **See box Spinal muscular atrophy and iPS on page 19.**

Various challenges must be overcome before many stem cell treatments become a reality, but there is optimism about the potential and scope for this. Furthermore, there is support from the Government. The UK Government has given high priority to the funding of stem cell research in the last few years and a wide range of stem cell science is supported by the Research Councils, medical charities and companies. The research ranges from basic research that informs our understanding of developmental biology and the way that stem cells function in healthy bodies, to research aimed at developing clinical applications of stem cells to treat disease. It is hoped that from a detailed understanding of stem cell behaviour, safe and reliable stem cell-based treatments will emerge.

Much has been achieved but much more remains to be done.

Key messages in this chapter

- Stem cells have two main characteristics: they can specialise into other cell types and they can self-renew.
- There are three main types of stem cells which are being researched: embryonic stem cells, tissue stem cells and induced pluripotent stem cells.
- Each of these three types of stem cell has advantages and disadvantages when it comes to using them for research or for stem cell therapies.
- There are several different ways in which stem cells are being used for research and in medical treatments, for example, cell replacement therapies, drug discovery or drug toxicity testing. Immune rejection is an important consideration for all cell replacement therapies.
- Injury or disease in many different parts of the body could in the future be treated through stem cell therapies. Different strategies may be needed for different problems.

Activity

True or False

Review your understanding of stem cells by reading the following statements and deciding whether you think they are true or false.

Statement	T/F
Embryonic stem cells are taken from the embryo at the blastocyst stage.	
There are no stem cells in an adult human.	
Embryonic stem cells and tissue stem cells are both pluripotent.	
Cell replacement therapies derived from embryonic stem cells would not cause an immune reaction.	
A pluripotent cell is capable of specialising into any cell type found in the body.	
Embryonic stem cells are the only type of stem cells under investigation by scientists.	
The role of tissue stem cells in the body is to provide replacement cells to repair damaged or worn out cells.	
Cell differentiation is random.	
One of the two main characteristics of stem cells is that they can self-renew.	
A multipotent cell cannot differentiate.	
Cells in the inner cell mass of the embryo are unspecialised.	
Therapies using a patient's own tissue stem cells would have fewer problems with immune rejection than therapies derived from embryonic stem cells.	
Nerve cells are differentiated cells.	
Once a cell is differentiated it can never, under any circumstances, become a different cell type.	
Pluripotent stem cells are found in most tissues of the adult body.	
Induced pluripotent stem cells can be made from skin cells which are reprogrammed to behave similarly to embryonic stem cells.	
Tissue stem cells are not as versatile as embryonic stem cells.	

Activity

True or False - How did you get on?

Statement	T/F
Embryonic stem cells are taken from the embryo at the blastocyst stage. **True**	TRUE
There are no stem cells in an adult human. **False**: There are tissue stem cells in adult humans which are used to repair worn or damaged tissues.	FALSE
Embryonic stem cells and tissue stem cells are both pluripotent. **False**: Only embryonic stem cells are pluripotent; tissue stem cells are multipotent.	FALSE
Cell replacement therapies derived from embryonic stem cells would not cause an immune reaction. **False**: As the embryonic stem cells would have been taken from an embryo with a different genetic make up to the patient then an immune reaction would occur.	FALSE
A pluripotent cell is capable of specialising into any cell type found in the body. **True**	TRUE
Tissue stem cells provide replacement cells to repair damaged or worn out cells. **True**	TRUE
Cell differentiation is random. **False**: Cell differentiation is a complex and precisely controlled process	FALSE
One of the two main characteristics of stem cells is that they can self-renew. **True**	TRUE
A multipotent cell cannot differentiate. **False**: A multipotent cell can differentiate into many cell types.	FALSE
Cells in the inner cell mass of an embryo are unspecialised. **True**	TRUE
Therapies using a patient's own tissue stem cells would have fewer problems with immune rejection than therapies derived from embryonic stem cells. **True**	TRUE
Nerve cells are differentiated cells. **True**	TRUE
Once a cell is differentiated it can never, under any circumstances, become a different cell type. **False**: Induced pluripotent stem cells are differentiated cells that have been manipulated to become a different cell type.	FALSE
Pluripotent stem cells are found in most tissues of the adult body. **False**: Pluripotent stem cells are only found in the inner cell mass of the blastocyst. Multipotent stem cells are found in most tissues of the adult body.	FALSE
Induced pluripotent stem cells can be made from skin cells which are reprogrammed to behave similarly to embryonic stem cells. **True**	TRUE
Tissue stem cells are not as versatile as embryonic stem cells. **True**	TRUE

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Further reading

The following reviews are good sources of more in-depth scientific information and opinion on stem cell research. The full text of all these articles can be found free of charge by using Google scholar.

1. Type in the title and authors' surnames as a search.
2. Remember the search is case sensitive so use the capitals as written below.
3. Change the drop-down menu from 'anytime' to 'since 2009'.
4. In some cases the document will just appear but in others you will need to click on the 'Full Text' or 'PDF' links. Alternatively you might find you need to click on the 'ScienceDirect' link and then the 'PDF' or 'download' links.
5. Finally, please note that in order to view PDFs you will need to have the free Adobe Reader software installed on your computer (http://get.adobe.com/uk/reader/).

Stem cells (general):
Binas, B. (2009) Embryo-derived stem cells - a system is emerging. BMB Reports 42 (2): 72-80.

Adult stem cells/Tissue stem cells:
Walker, M.R., Patel, K.K., Stappenbeck, T.S. (2009) The stem cell niche. Journal of Pathology 217 (2): 169-80.

iPS cells:
Rossant, J. (2009) Reprogramming to pluripotency: from frogs to stem cells. Cell 138 (6): 1047.

Genetic basis of pluripotency:
Chambers, I., Tomlinson, S.R. (2009) The transcriptional foundation of pluripotency. Development 136 (14): 2311-22.

Stem cells in therapeutics
Trounson, A. (2009) New perspectives in human stem cell therapeutic research. BMC Medicine 7: 29.

Prockop, D.J., Olson, S.D. (2007) Clinical trials with adult stem/progenitor cells for tissue repair: let's not overlook some essential precautions. Blood 109 (8): 3147-51.

Interested to know more?

http://www.eurostemcell.org/films
The European Consortium for Stem Cell Research has made four films looking at different aspects of stem cell research. This website also provides information and activities on stem cell research in several languages.

http://stemcells.nih.gov
A website providing comprehensive information on the basics of stem cells. It also provides a lot of research resources covering scientific, social and ethical aspects of stem cell research.

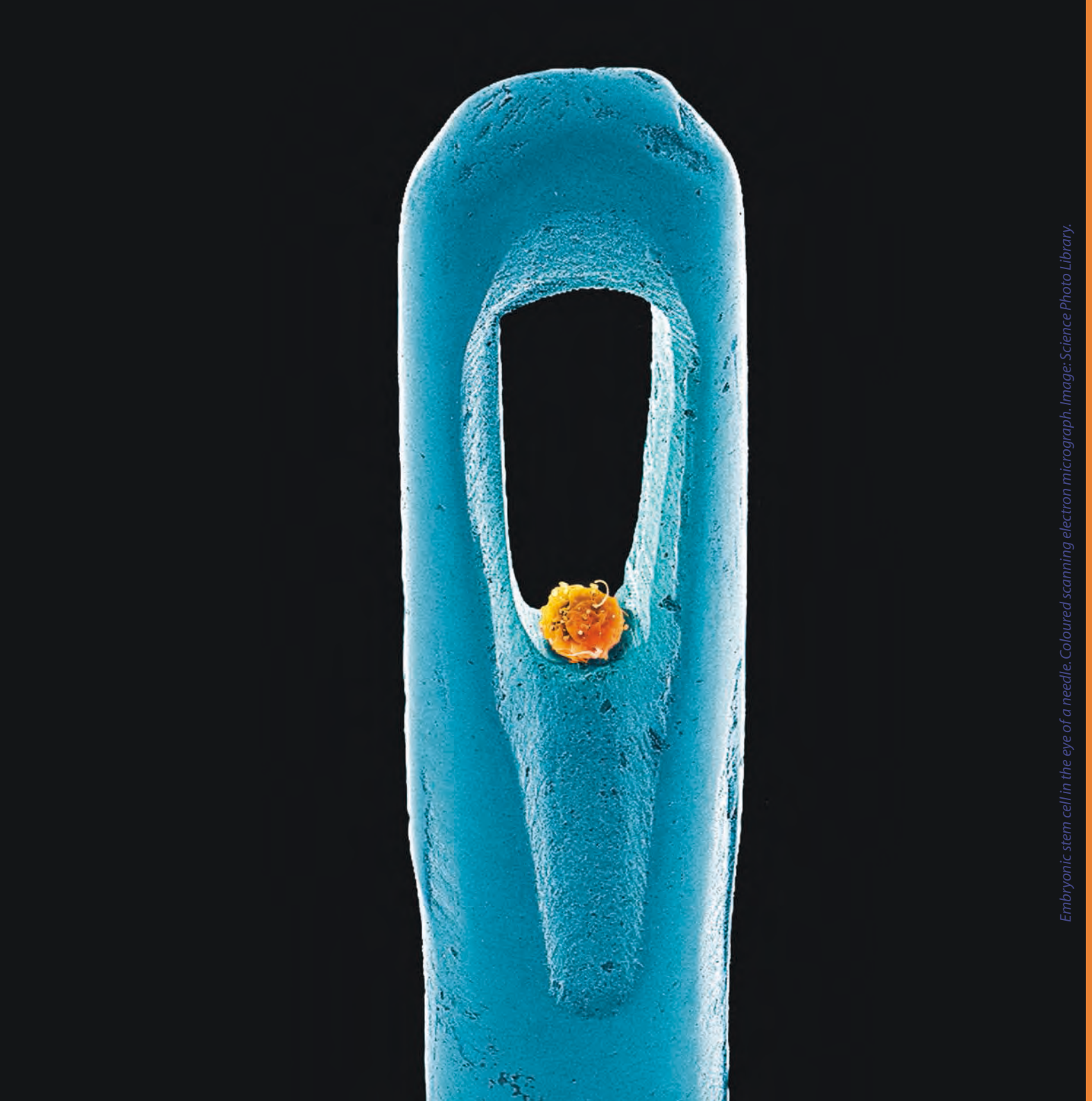
http://www.explorestemcells.co.uk
A UK website about stem cells, highlighting some developments in stem cell research in the UK.

http://www.medicalnewstoday.com/sections/stem_cell/
Updates on stem cell research.

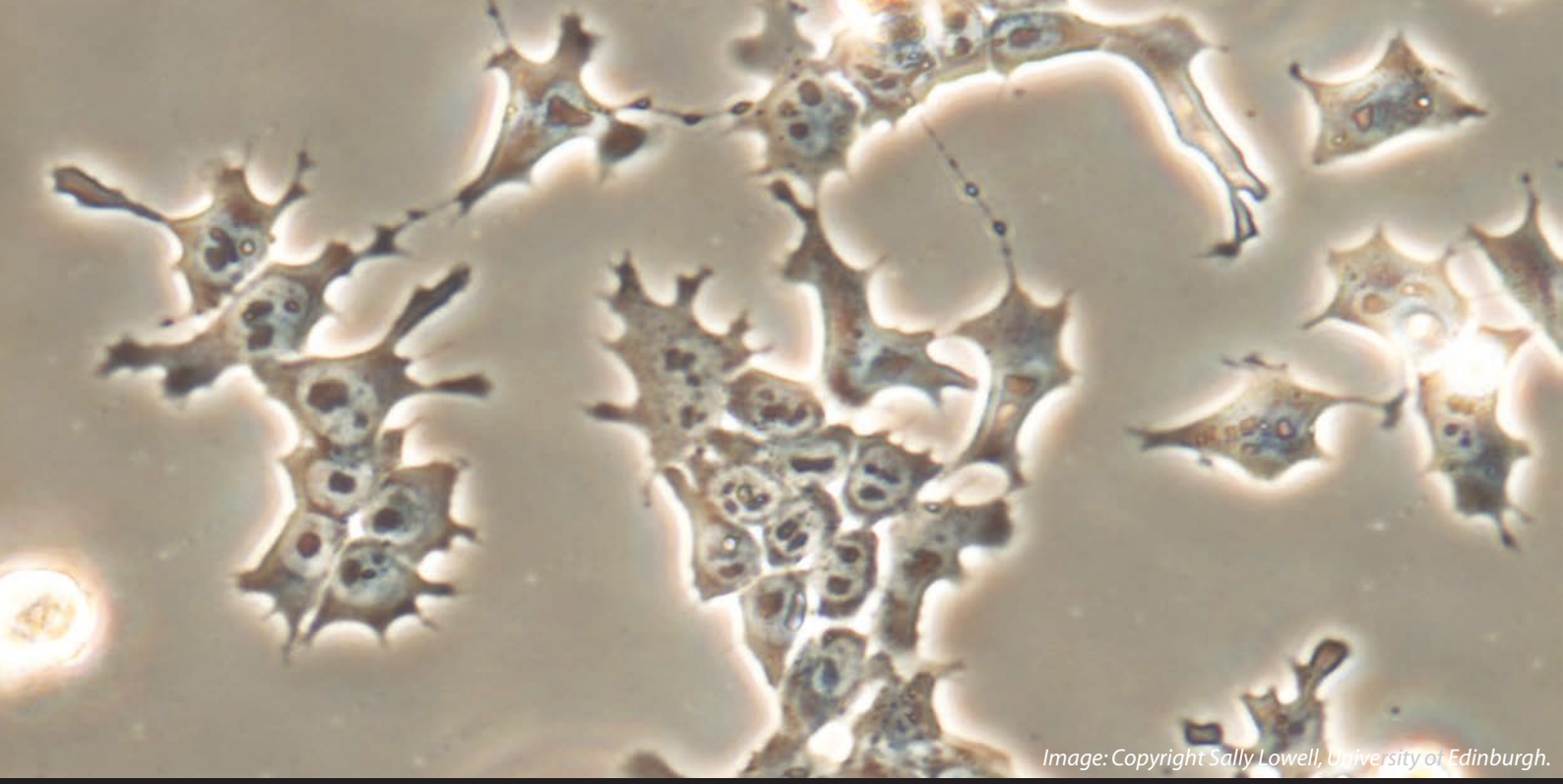
[Reference/webpage no longer available – Feb 2016]
A series of online lessons provided by the University of Michigan about stem cell research.

http://www.centreofthecell.org/interactives/bioengineering/index.php
An online interactive game generated by the Centre of the Cell where the player has to decide how to repair the damaged cartilage of Ben.

www.bbsrc.ac.uk
Website for the Biotechnology and Biological Sciences Research Council.



Embryonic stem cell in the eye of a needle. Coloured scanning electron micrograph. Image: Science Photo Library.



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Chapter 2 Stem Cells: legal and global perspectives

Chapter 2 Stem Cells: legal and global perspectives

What is the role of the law in tackling the ethical and social issues raised by stem cell research? How do we decide if we should ban research completely, allow it or attempt to control it? Who decides these things? What if we disagree? And what should happen internationally when different countries, cultures and peoples have different attitudes towards something as controversial as stem cell research? Is international agreement possible or desirable?

What does law do?

Law serves many purposes. It tells us that some behaviours are acceptable or unacceptable in society and if it is important enough to make a rule about it. It gives us rights to protection against harm from other people and from the state. It aims to protect us from harming ourselves, especially before we become adults. It also offers protection to those who cannot protect themselves, like very young children and those with mental incapacity. Many argue that it should also protect the unborn.

Law can help to shape a society that is better for all of us. It can work to promote certain social goods, such as human welfare, social development and economic growth. But we do not all agree about the kind of society in which we want to live or what counts as 'better'. For example, should we encourage industrial development for the jobs and wealth it will bring even if this means an increase of risk of harm to the environment? Similarly, should we encourage medical research that involves the use and destruction of human embryos even if this might one day lead to cures for diseases such as cancer and Alzheimer's? There is a lot to agree and disagree about when it comes to stem cell research. What is the role of law in all of this?

> *Although the law struggles to keep up with advances in embryonic research, I believe that the UK's position strikes an acceptable balance between the interests of society in promoting research and the protection of embryos.* *Professor Graeme Laurie, Professor of Medical Jurisprudence*

Activity

In small groups, consider the list of laws below and add 4 or 5 more examples of your own. Then group them into:

1. Laws that the whole group agree with.
2. Laws that the whole group disagree with.
3. Laws that some of the group agree with and others disagree with.

Discuss the list your group has drawn up.

Why do you hold the view that you do?

What would you say to someone who disagrees with you?

Who should decide what laws there should be?

Pick one of the laws that have fallen into category 3. Try and rewrite it so that everyone agrees with it.

- Compulsory wearing of seatbelts in cars.
- Compulsory wearing of crash helmets on motorcycles – should this be extended to bicycles?
- The ban on selling (rather than donating) an organ, like a kidney, to someone who needs a transplant.
- The permission to create embryos for research purposes.
- The ban on burning domestic waste.
- The ban on buying or being bought alcohol until over the age of 18.
- The ban on marrying more than one person.
- Compulsory education for children and young people of school age.

How easy was it to write a law so that everyone agreed?

How is law made?

There are many different types of laws. There are national laws that only apply in the country where they are made, but there are also international laws which apply in all the countries that

have agreed to follow them. For example, the criminal law in Scotland only applies in Scotland, but there are also international laws (Treaties and Conventions) which regulate the laws of war between countries and a whole host of other subjects.

Governments propose national laws but these must be passed by Parliament before they have the force of law. A parliament exists to reflect the will of the people and includes members of parliament (MPs) who are democratically elected representatives of the people. It is the role of the courts to interpret the law and to settle disputes about the law. Citizens can influence law-making by lobbying their local MP and/or by bringing petitions to parliament or cases to court arguing that the law should adopt a particular position. Another way for citizens to express their views is in response to a public consultation. A government will often hold a consultation on its ideas for a new law or a change to the law before it makes the proposal to parliament. This is an opportunity for citizens to make a difference. But the degree of citizen awareness and participation can be variable.

Activity

As a group, discuss how valuable the role of public consultation is in your opinion.
List the pros and cons of this approach. Here are some points to consider:

1. Should we hold a public consultation every time a new law is proposed?
2. How should Government deal with a range of different views?
3. Is there a risk that those who shout loudest will be heard over others?
4. Should we necessarily introduce laws supported by the majority?

(Remember: it is often suggested that the majority of the public think we should bring back hanging. Is this a good enough reason to do so?)

Public consultation took place before the British Government changed the law in 2000 and 2008 about the creation and use of embryos for research purposes. The Government said that: "This consultation is part of a process of re-establishing a framework that is broadly acceptable to society".

What does the law say in the United Kingdom about stem cells?

The UK was the first country in the world to regulate artificial reproduction and embryo research. It did so in the Human Fertilisation and Embryology Act 1990, and this was partially revised in 2000 to allow human embryonic stem cell research and was updated in 2008 after public consultation (see above). This law *(known as legislation)* imposes a strict system of controls on the creation, storage and use of embryos outside the human body. It is a criminal offence to do any of the above activities without permission *(a licence)* from a body known as the Human Fertilisation and Embryology Authority (HFEA). The written consent of the donors of the embryos must also be given and this must clearly show that they have consented to the uses to which their embryos will be put.

The HFEA receives applications from all scientists who want to conduct embryo research in the UK, including embryonic stem cell research. The 1990 Act only allows embryos to be used (and destroyed) for a number of specific purposes. Examples include fertility treatment or scientific research into human illnesses. No embryo can be kept or used after 14 days of its development. It is possible to receive a licence to create embryos solely for the purpose of medical research, including their use to develop embryonic stem cell lines. In this way, it is argued, the law in the UK creates a 'balanced' approach: it operates a framework that protects the embryo as a human organism while permitting research under strict controls.

STOP AND CONSIDER:

- What is the significance of the 14-day period beyond which embryos cannot be kept or used?
- How is it possible to argue that the UK position 'protects the embryo as a human organism' when it allows – and some would argue encourages - research which invariably results in its destruction?

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What happens in other countries?

Different countries take different approaches to stem cell research regulation. In many ways, this reflects the different attitudes held by different peoples around the world towards the human embryo. For example, a recent survey of nine European countries showed that views varied considerably. The spread of opinions went from countries like Austria and Germany where there is a strong view that the human embryo should be treated the same as you and me, i.e., like a human person with all the rights and protections that we enjoy, to countries like Denmark and the UK where there is a strong view that the human embryo is not developed enough to enjoy such protections.

Such views are often – although not always – reflected in the laws of these countries. For example, while the UK allows both the creation and importation of embryos for research purposes (and the production of cloned and hybrid embryos, Ireland does not allow either use and is generally strongly opposed to any uses of embryos. In other countries which display a moral discomfort about this kind of research, the creation of embryos is illegal but their importation and use is allowed; examples include Germany and Italy. Many countries in Europe and elsewhere, such as Canada and Denmark, only allow embryos to be used for stem cell research when they were originally created for fertility treatment (but not implanted).

In yet other countries, it seems that money is what matters. In the United States of America (USA), former President Bush prohibited the Federal Government from funding embryonic stem cell research with public money and this position has also been adopted by a number of states around the USA. But they do not go as far as banning the research completely; that is, if private investors are willing to pay for the research they will be left alone to conduct it. Most recently, President Obama reversed the Bush policy on federal funding but each state in the Union is still at liberty to regulate stem cell research as it sees fit.

Finally, there are some countries, such as Argentina and Iceland, which have no regulation. The result of this is not that the research is outlawed but rather that anything is potentially permitted, free of controls and protections. The reason for this is an old rule about law: ***Anything that is not illegal is legal.***

Activity

1. Using the examples of Ireland, Italy and Canada, how many factors can you think of that might have played a part in shaping the laws in these countries?
2. How many different roles for the law can you imagine when it comes to stem cell research?

For countries who wish to encourage research, there are programmes which try to assist the sharing of materials. An example is the UK Stem Cell Bank. This resource was set up to act as a central reserve for high-quality research materials and also to help reduce the number of embryos that would have to be created and destroyed in the name of research. It aims to make international sharing easier. Another example is the European Human Embryonic Stem Cell Registry which exists to help the free flow of information and to foster international co-operation.

Money changes everything

No one really knows how much it will cost to bring stem cell therapy to patients. A good guess, however, would put the bill at over £300 million for each type of therapy. This is because the research process in such uncharted waters is slow and costly and also because there will have to be so many safety checks and double-checks before we can be sure that a therapy works and will do more good than harm. But who pays for this work? Who is entitled to profit from any breakthroughs that are made? Once again, should the law have a role to play in answering these questions?

At the moment most basic stem cell research in the UK is publicly funded, but the point is likely to come when major companies get seriously involved, because they have the financial and other resources to turn a laboratory result into a clinical product. The reality is that most drugs and therapies that make a daily difference to the lives of millions of people around the world are produced by companies. They are not charities. They expect a decent profit from their work. One of the best ways to secure a profit is by taking out a patent on any new invention, and this is also true for medical inventions. A patent allows its owner to have exclusive control over his invention in the market. This means that, within limits, the owner can set the price.

The problem is that while no one is likely to die if they do not get their hands on the latest i-phone, this could very well be true of new medicines. Should patents be allowed to restrict access to vital medicines? Indeed, should patents be granted over embryonic stem cell lines when these have involved the destruction of embryos? In other words, should profits be allowed from activities that many consider to be unethical or immoral?

Once again, we see different attitudes in different countries. The USA considers that free competition is a 'good thing' and that it should not attempt to put limits on what inventors do with their inventions. In Europe, however, a different attitude exists. The European Parliament directive and the legal protection of biotechnological conventions (1998) says that a patent should not be given for inventions which are "immoral" or, more specifically, which involve "uses of embryos for industrial or commercial purposes". This means that patents are unlikely to be given for embryonic stem cell inventions that involve the destruction of the embryo in the process. Some fear that a consequence of this will be that research in this area will go to other countries where there is no such rule and that this could have a negative impact on Europe.

Activity

In small groups, discuss the pros and cons of the European Parliament directive. In addition to the potential economic impact, you might consider:

(a) whether it is legitimate to have one rule for the whole of Europe when we see that different countries have different approaches in allowing research, or

(b) whether this is an appropriate rule because of the important moral status of the embryo and because we need more consistency between countries.

As a group, design, write and conduct an anonymous poll of your classmates as to whether or not they feel patents of embryonic stem cell inventions should be permitted in Europe. Discuss the results of the poll.

International considerations

STOP AND CONSIDER:

- Would it be better to have international legal agreement on stem cell research and commercialisation?

There have been attempts to reach international agreement on how we should treat embryos and how embryonic research should be regulated by the law. Two examples are relevant.

The *European Convention on Human Rights and Biomedicine* (1997) states in Article 18 that: "The creation of human embryos for research purposes is prohibited." The Convention is an instrument to which 47 European countries can sign up and be bound by its terms. More than 10 years after its inception, however, less than half of these countries have done so. The UK has not signed

because it is already in direct breach of the Convention. The 1990 Act allows the creation of embryos for research purposes. Without a country's signature no action can be taken against it.

The United Nations has also sought international agreement. The UN General Assembly adopted a *Declaration on Human Cloning* in 2005 (which applies also to genetic engineering techniques). While this might look like an international success, it is important to consider the terms of the Declaration; "...Member States were called on to adopt all measures necessary to prohibit all forms of human cloning inasmuch as they are incompatible with human dignity and the protection of human life". But what is human dignity? Who defines this and how? The reason this text was put forward was precisely because countries could not agree; 84 countries voted in favour, 34 against and 37 abstained. This text at least leaves it to each country to argue that its own measures are compatible with human dignity. But it is far from an international agreement on how we should proceed in this area.

Final thoughts

- Do you think the law has an important role to play in addressing the issues raised by stem cells?
- If you were a law-maker, what approach to regulation would you take and why?
- Should we continue to push for international agreement in this area?

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Key messages in this chapter

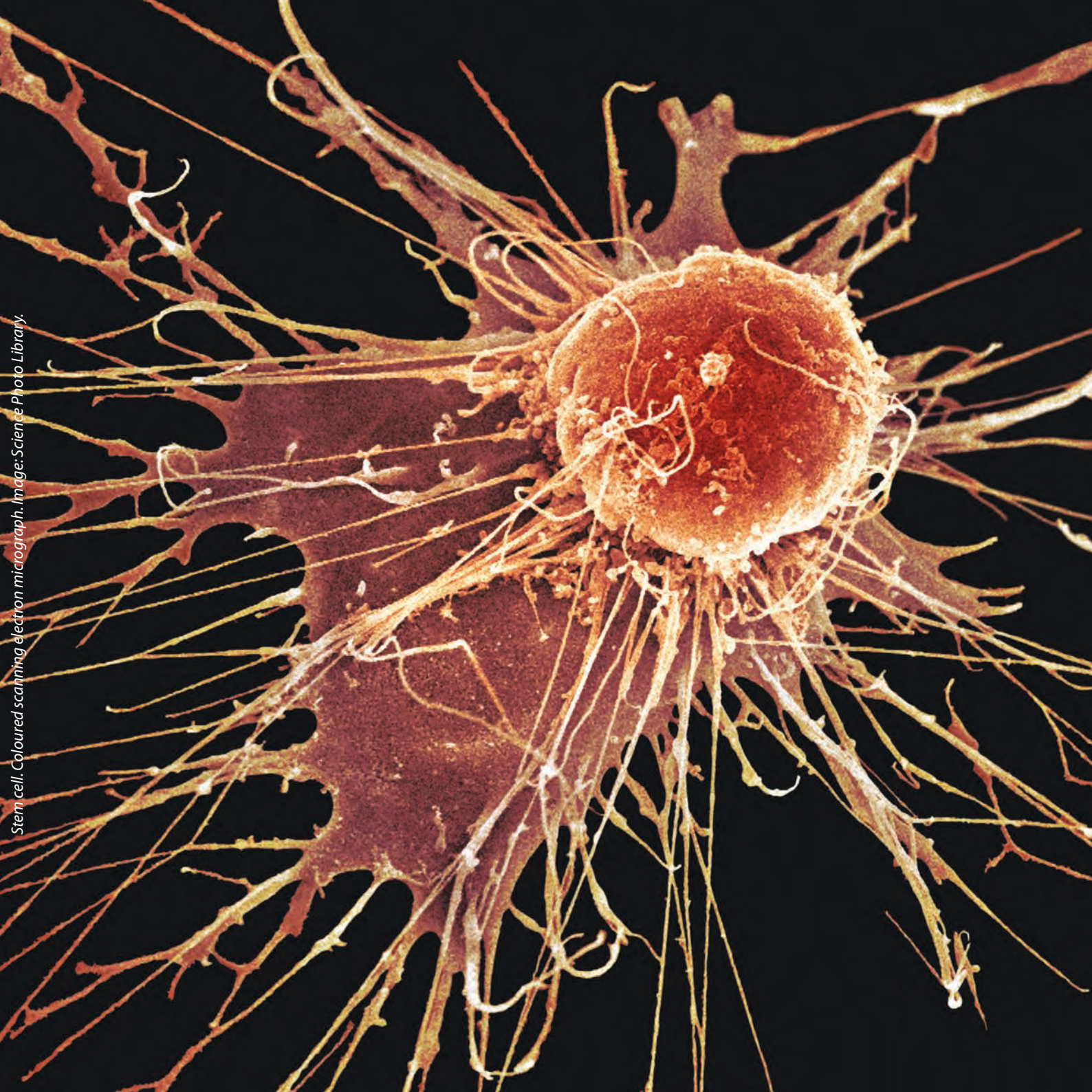
The law serves many purposes and can help shape society for the better. There are international laws and national laws.

In the UK, all parties who wish to create, store or use embryos outside the human body are governed by strict controls contained in the Human Fertilisation and Embryology Act 1990. This act has been modified twice since its inception. In addition a licence must be granted by the Human Fertilisation and Embryology Authority (HFEA) to conduct embryonic stem cell research.

There are no international laws regarding stem cell research but many differing national laws and regulations. These could be seen as reflecting the different attitudes held by people around the world towards the human embryo.

Stem cell research and therapies are costly and consideration must be given as to who will pay for these. Companies rely on patents to help secure profit, however in Europe, patents are unlikely to be granted for embryonic stem cell inventions that involve the destruction of the embryo.

There have been attempts to reach international agreement on stem cell research and commercial exploitation but so far this has not been successful.



Stem cell. Coloured scanning electron micrograph. Image: Science Photo Library.

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Review of the Human Fertilisation and Embryology Act: A public consultation.

UK Stem Cell Bank.

UN General Assembly Declaration on Cloning (2005).

European Directive on the legal protection for Biotechnological inventions (Directive 98/44/EC) (1998) Official Journal of the European Communities 41: L213/13.

Interested to know more?

[Reference/webpage no longer available – March 2019]
An article (with various links to the related issue) from CNN featuring Barack Obama's view on stem cell research, providing an overall outlook of stem cell research in the USA in the coming few years.

[Reference/webpage no longer available – December 2016]
A fact sheet summarising laws governing stem cell research in USA, EU and UK.

[Reference/webpage no longer available – Feb 2016]
Constantly updated news and guidance on recent UK policies on stem cell research and related ethical issues.

http://www.hinxtongroup.org/wp.html
Updated information on world policies on stem cell research.

http://www.law.ed.ac.uk/ahrc
Website for SCRIPT, the University of Edinburgh law and technology research centre under the directorship of Professor Graeme Laurie (the author of this section).

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Chapter 3 Stem Cells: ethical issues

Chapter 3 Stem Cells: ethical issues

> *For me, stem cells show how important it is to consider what wider human values are affected, as science digs ever deeper into human biology. So that we do not just say "Wow!" but we also ask ourselves "But what is right?"* *Dr Donald Bruce, Ethicist*

Introduction

Few people doubt the medical potential of stem cell research. But ethically it has proved extremely controversial. As with other new areas of medical research, there are issues like proving the effectiveness and minimizing the risks, personal questions about donation and consent, and social issues like whether everyone can afford the therapies and how much health service resources they would consume. But what makes this area especially contentious is the source of the cells, and in particular the use of human embryos. Different European countries vary greatly in their laws about stem cell research, reflecting the deep ethical conflicts which exist about the nature of the human embryo, and what are, or are not, permissible uses.

Why is this so controversial?

To illustrate the point, in Edinburgh, late night walking tours of the Old Town feature among their scary tales the deeds of Burke and Hare in the early nineteenth century, who murdered people and sold their bodies as anatomical specimens to the medical school. Most people would recoil at the idea of killing another human being in cold blood in order to provide spare parts or cells for another. Yet, some people consider that this is what we are doing if we allow the use of an early embryo to provide stem cells for replacement therapy, because in terms of its moral status, the embryo is as much a human being as a new-born baby.

Others are equally deeply troubled that concerns about the status of a few cells in the earliest stage of human development should be allowed to hold back the prospect of what can be done to treat terminal disease and chronic human suffering. Day after day, doctors and nurses can offer only temporary relief for people they cannot cure; relatives and friends give devoted care and support but know there is only one tragic outcome. Many people feel that we should not make the status of embryos a constraint on finding a way that might address so much suffering.

Many people, however, fall somewhere in between these opposite poles. They see the human need, but they think the human embryo is more than just nameless cells, and yet it is not the same as a baby. So it presents an ethical dilemma without easy answers.

These represent three classic viewpoints of a complex ethical debate about embryos which underlies much of this area of research. We will look at these in more detail in the next section. Later, we will also look at some other ethical questions like cloned embryos, animal-human hybrid cells, producing human sperm from stem cells, and using stem cells to test future pharmaceutical drugs for toxic effects.

The status of the early human embryo

Do early embryos fall into the same class as people, or are they a ball of cells and nothing more? Or does the answer lie somewhere in between?

No moral status at the blastocyst stage

One pole of the argument emphasises a scientific way of viewing the embryo in terms of its composition, properties and functions. At the blastocyst stage, a human embryo created by IVF expresses no bodily characteristics, it is not conscious and it cannot feel anything. It could not survive outside the womb. At this stage, it could split to produce twins, so we cannot yet say for sure that this is a single individual. It has not implanted in the womb. The mother would not yet be aware that she is pregnant. Faced with the scientific case, a philosophical judgment is made that at this stage the embryo has no moral significance. At this point it is not a human person; it is just a ball of cells.

Those who hold this view say that medical research on early human embryos is not only permissible but desirable, subject to the normal conditions of research. Some even say it is a moral duty of humanity, if it provides a potential means to find treatments for otherwise serious and incurable suffering. Only at some later stage of development, perhaps where certain human characteristics are manifested, should there be ethical restrictions on research. This is a "yes … provided" position.

Philosophy vs Morals and Ethics?

Philosophy can be defined as a study and investigation of questions about ethics and existence. It can be used when talking about one's 'world view' or personal belief about how to live. For example, someone might say "my philosophy is to live and let live".

However, can you define the difference between morals and ethics?

One useful definition states that a person's moral values are what they believe to be right or wrong. One moral might be; "It is right to tell the truth". Ethics is how these morals are worked out in a real life circumstance. They are all about how you apply your morals to a situation, and, as such, your morals and ethics affect each other. For example, some ethical decisions you might make mean that you end up telling a lie, even though morally you believe lying to be wrong.

Can you think of any examples where that might happen?

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The same moral status as a baby

The opposite view says that we should not judge the status of the embryo by its state of development, but by what it will become, namely a human person. We must therefore look at it in the wider philosophical or theological context by which we understand the meaning of a human life. From the completion of fertilisation onwards we should see the embryo as having the status of the human being which it should become. We have a special duty to protect the most vulnerable of the human community, and nothing is as vulnerable as an early embryo. Some would admit that there is uncertainty about the status of a developing embryo, but we must give the embryo, as we would to any vulnerable person, the benefit of the doubt and protect it as one would a human life.

Those that hold this view believe that no research should therefore be allowed that is not for the benefit of that particular embryo. No matter what the potential might be for life-saving treatments, medical research can never justify us taking the life of an embryo, denying it the chance of becoming a fully developed human. Once a human life has been created, even in an embryo, it is not for other humans to destroy it or cause it to be destroyed. Those holding this position advocate only the use of stem cells derived from adult tissue or placental cord blood. If it turned out that some cell therapies could only be achieved using ES cells, those holding this view make the judgment that those therapies should not be used, since it would amount to destroying some human lives in order to save others.

This is an "under no circumstances" position. Although it is perhaps best known as the formal position of the Catholic and Orthodox churches, and of some (but by no means all) Protestant Christians, it is not a view shared by all religions.

People with the second view criticise the first view as reducing the 'being' of the embryo to a scientific description. The latter criticise the second position as giving a significance to the embryo for which, at that stage, there is no scientific basis. For these two polar positions, their ethical responses to embryonic stem cells are straightforward: all or nothing.

Intermediate views

But many people think that neither of these radically opposed views do justice to the complexity of the developing embryo. They hold a position somewhere between the two. They may recognise

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some of the scientific arguments in position one. But they consider that the human embryo nonetheless has more moral status than mere cells of the body. But they would not agree that this is as much status as we would give to a new-born baby in position two. This is much less clear-cut than the two polar positions, and can be expressed in a variety of ways. Some argue that the moral status of the embryo increases as it develops.

Some people make a distinction between those embryos which lead to a successful pregnancy, and the majority of conceptions in which the body spontaneously aborts at a fairly early stage. Whereas it is unreasonable to ascribe human status to those conceptions which never succeeded, successful embryos would have full human status from conception.

The upshot is that there would be limited circumstances under which research on human embryos might be allowed. The seriousness of certain medical conditions would justify the action. Many Jews, Muslims and Protestant Christians fall broadly within this category, and also many non-religious people. A very influential statement of this way of thinking was the 1984 Warnock Report on fertility and embryo research, which argued that "the embryo of the human species ought to have a special status and that no one should undertake research on human embryos the purposes of which could be achieved by the use of other animals or in some other way" [1].

This has been the philosophical basis of UK legislation on embryo research since 1990. It might be called a "no … unless" view. There are several implications:

- The researcher is obliged to look for alternatives to embryo research, use them where possible, and only use embryos where there is no alternative.
- If an alternative is established, the implication is that human embryo research can no longer be morally justified.
- The research would be for one of an agreed set of significant medical goals, like the treatment of serious disease or crippling injury, and the underlying biological understanding needed to develop such treatments.
- Some areas of research should not be allowed to use human embryos.
- Research should only be allowed up to a certain point in the development of the embryo.
- There must be some formal system to regulate, control and license research.

Those who hold the "yes … provided" view would agree on the last two points, perhaps the middle two, but not the first two. Those who hold an "under no circumstances" position would agree with none of them, because they consider that research using embryos would never be justified.

Some ethical questions about limited embryo research

14 day rule

After what point in the development of an embryo should no research be allowed? You could say that any limit is arbitrary because it is a continuous process of development. But legally a line has to be drawn somewhere between conception and birth, unless you hold the view that human embryos should not under any circumstances be used in research. After consulting professional medical bodies, the Warnock Committee recommended 14 days, because at about this time there are several ethically significant biological changes. Shortly after this the 'primitive streak' begins to appear, which will make the three germ layers including the cells that will become the central nervous system, which in turn will lead to consciousness and sensory feeling. After this, twinning is no longer normally

Task: A stem cell story

The following group task will help you consolidate and further consider your knowledge and views on stem cell research. These films were produced by the EuroStemCell network which is a European consortium for stem cell research.

1. Watch 'A stem cell story' at the following web address: http://www.eurostemcell.org/films
2. As a group consider the following questions:
   - What did you think of the film?
   - List three things that were new to you.
   - List three things that were familiar to you.
   - Discuss the examples given of producing skin for burns patients, neurons for testing possible drug treatments for neurological diseases and developing insulin-producing cells to treat diabetes. Do you think these are appropriate applications for the research?
3. Now watch 'Conversations: ethics, science, stem cells' also available online at http://www.eurostemcell.org/films
   - Discuss your initial response to the film.
   - List three things that were new to you.
   - List three things that were familiar to you.
   - At the end, each of the speakers give their opinion. What would you say if you were interviewed for this film?
4. As a group, design and present a 10 minute talk to help a group of 13yr olds consider the science and ethics of stem cells. You should consider:
   - What further research you need to do to gather the information for your presentation.
   - How you would present the science to this audience in a creative and clear way.
   - Whether or not you will include information about induced pluripotent stem cells (see page 13).
   - What the key points are that you wish to cover and how to make those points clearly and concisely.
   - How to present the information in an accurate and balanced way.

possible, so we know that it is indeed one particular individual. Implantation in the womb is normally complete by then. Some see an important moral significance to this beginning of the physical relationship between mother and the eventual baby.

Using embryos as a means to an end?

Some object to the fact that extracting stem cells from an embryo to make replacement body cells is treating the embryo as just a source of spare parts. At least fertility research still treats the embryo as a reproductive whole. Embryonic stem cell research takes a purely utilitarian view of the embryo, as a means to an end. This cannot be squared with regarding the embryo as having a 'special status'. In response, the Chief Medical Officer's report argued that human embryonic stem cell research did not lack respect towards the moral status of the embryo, provided it was to gain benefits for human health [2]. The two views differ on whether respect for an embryo is measured by what you do not allow to be done to it, or the uses to which it is put.

Limited or unlimited research?

As stem cell science develops, there are increasing pressures from scientists to expand what is allowed ethically into new and controversial fields, like mixed animal-human embryos, creating sperm from stem cells, and using embryonic stem cells for testing chemicals for toxic effects. In this intermediate position, it is not enough to evaluate such potential new developments based on a purely scientific view of the human embryo or medical research. You must ask if this is justified bearing in mind it involves the use of human embryos of special moral status. Some have expressed concern that any sense of 'special status' for the early human embryo is being eroded in what has been allowed by the UK authorities and Parliament.

Alternatives to using human embryos?

As long as important medical aims could be achieved in no other way, an ethical argument could be made for carefully specified human embryo research, in parallel with research from tissue stem cells. Opponents of embryo research have stressed the untapped potential of stem cells derived from adult tissues or placental cord blood, and argued that research should focus on these and not on embryos. Until recently, this seemed a weaker scientific case, but induced pluripotent stem (iPS) cells (see page 13) may now provide a genuine alternative. The new field is developing fast but for the time being, neither the science of embryonic stem nor

iPS cells is advanced enough to know what each might achieve. Maybe iPS cells will be good for some things but embryonic stem cells better for others? Or maybe they will turn out to be essentially the same. No one knows for certain yet. If, in future, iPS cells can fulfil safely in a clinical context the range of functions anticipated for embryonic stem cells, at what point might it then become a moral obligation to stop embryo research? This question strikes to the heart of the present UK ethical compromise over embryo research. For those who consider embryos to have no moral status until 14 days or later, to stop embryo research would never be an option. But the logic of the special status of the human embryo implies the obligation to use alternatives where these exist. If it comes to a choice, which view should prevail? This may become a real question sooner than we expect, so it is worth thinking about.

STOP AND CONSIDER:

- Consider the three main views of the moral status of human embryos. Where would you stand, and why do you think so?
- Can we say we respect an embryo and allow it to be used for research which ends in its destruction?
- Are there limits to what sort of research we should allow on embryos? If so, what?
- If at some point in future, induced pluripotent stem cells are shown to be viable and safe alternatives to human embryonic stem cells, is there a moral obligation to abandon embryo stem cell research? How should society decide?

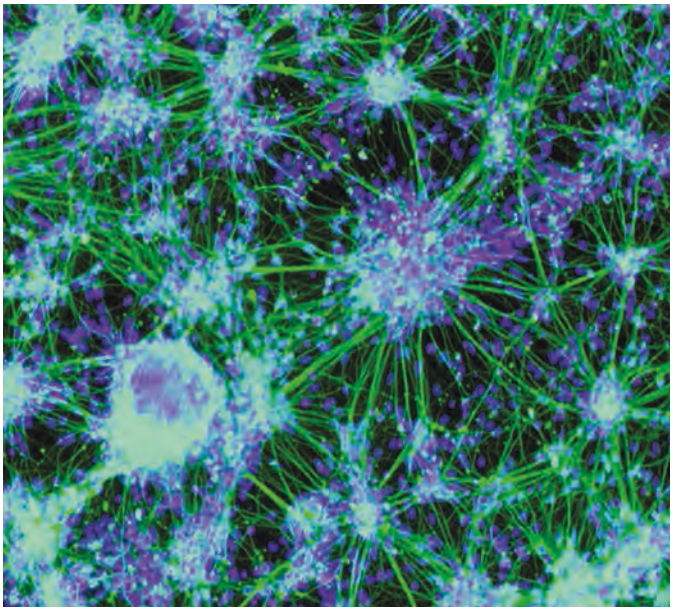
Ethical questions about creating new types of embryo for research

Creating embryos or using surplus IVF embryos?

Many who might have serious reservations about the idea of using embryos for stem cell research accept it nonetheless where the source is surplus embryos left over from IVF treatments, which would otherwise be destroyed. This is perhaps the most commonly held justification. If these embryos would not now have any chance to develop into babies, because the couple who created them does not wish to attempt further pregnancies, why not use them for potentially very beneficial medical research? Some regard this as 'the lesser of two evils'. Many European countries allow this but forbid creating embryos. The UK is unusual in allowing both. It was recommended by the Warnock committee, but only by the narrowest of majorities. Many authorities see an important ethical distinction here [3], but those in favour of creating embryos for research do not agree and fear that research would be held back. Those objecting think that to create an embryo just for research treats it purely instrumentally, inconsistent with its special moral status. This issue remains controversial.

Using somatic cell nuclear replacement to produce stem cells

In 2000 the UK Government voted controversially to allow the use of somatic cell nuclear replacement to make 'cloned' embryos from which stem cells could be produced. There were several reasons in favour. The original idea was to make replacement cells that were genetically matched for a patient, so the body should not reject them. It was thought that this could be done by first making a cloned embryo using cells from the patient. This so-called 'therapeutic cloning' was criticised as impractical and costly [4]. And it was hit by a big scandal. Korean scientists claimed to have done all this, but the main results were shown to have been faked. So far no one has yet made a confirmed stem cell line from a cloned human embryo, generated by nuclear replacement.



Neurons (green) derived from embryonic stem cells. Cell nuclei are shown in purple. Fluorescent micrograph.
Image: Sally Lowell, MRC Centre for Regenerative Medicine, University of Edinburgh. www.crm.ed.ac.uk.

A better argument is for basic research. The new discoveries about human iPS cells have used knowledge gained from cloning and gives scientists a way of making stem cell lines to model otherwise inaccessible disease state cells, for example to open up the understanding of motor neuron disease.

Using cloned embryos in stem cell research drew much criticism, notably in a vote of the European Parliament and a non-binding recommendation of the United Nations General Assembly. A House of Lords Select Committee, set up to clarify such issues in 2002, said cloned embryos "should not be created for research purposes unless there is a demonstrable and exceptional need which cannot be met by the use of surplus embryos" [5]. There are two main ethical objections. Firstly, it would again involve the deliberate creation of an embryo simply to use as a resource for cells (see the previous section). Secondly, there are widespread ethical and safety objections to reproductive human cloning. So if you created a cloned human embryo for research it would have to be destroyed, but the same technology could be used by some who seek the notoriety of creating cloned babies. Some consider it unwise to produce cloned embryos for research, in the absence of a global ban on reproductive cloning.

Animal-human mixed (hybrid) cells

There was further ethical controversy when a proposal was made in 2007, and passed in the 2008 HFE Act [6], allowing hybrid cloned embryos to be created for research, using animal eggs instead of human ones. In a highly politicised campaign, proponents argued that the shortage of donated human eggs was holding up stem cell research and potential treatments. Using animal eggs was hardly different from human eggs but would avoid pressures on women to donate. Its opponents criticised it on ethical grounds for mixing reproductive cells, and on scientific grounds that it was so speculative and limited in use that it would do little to speed up treatments. Many now think that advances in iPS cells may make this approach to making pluripotent cells largely irrelevant. Some observers consider that the real issue was not hybrids but the freedom of science.

STOP AND CONSIDER:

- If we allow spare IVF embryos to be used to make stem cells, should we also create IVF embryos solely for research, or is this treating human embryos as a means to an end?
- Is it a good thing that the UK has allowed controversial areas of research, like the creation of cloned human embryos or animal-human embryos to go ahead, if in most other European countries they would be illegal or seen as unethical?

New ethical challenges in stem cell research

Deriving sex cells (sperm and eggs) from human embryonic stem cells

Some research groups have claimed to have made human sperm cells from embryonic or bone marrow stem cells. Many would welcome this, if it gave us a better understanding of what sometimes goes wrong in male fertility. It will not be clear for some time if it could work well enough to enable an infertile man to produce sperm, but what ethical issues would it raise? If a man wanted sperm derived from his own body cells, using stem cells from spare IVF embryos would be no use. He would need a cloned embryo of himself created, say, from some of his skin cells, to make the stem cells and thus the sperm. But should the man produce one or more embryos that are 'twins' of himself, which must then be destroyed to 'create' his own sperm, hopefully to have a child that is biologically his and his partner's (using IVF)? Is there a contradiction if he creates and sacrifices a cloned embryo to create an 'ordinary' one? If iPS cells could be used, that ethical problem would be solved. A second issue is safety. There are risks that the sperm would be damaged during these very complex processes, risking deformed babies. For clinical safety, it would have to be proved first time and every time, that everything had worked. How could that be done without doing a procedure which treats the child to be born, in effect, as an experiment? This is quite different from a dying patient consenting to take the risk of an experimental therapy with her eyes open. These examples illustrate some of the dilemmas coming from new areas of stem cell research.

Using human embryonic stem cells to test drugs and chemicals for toxicity

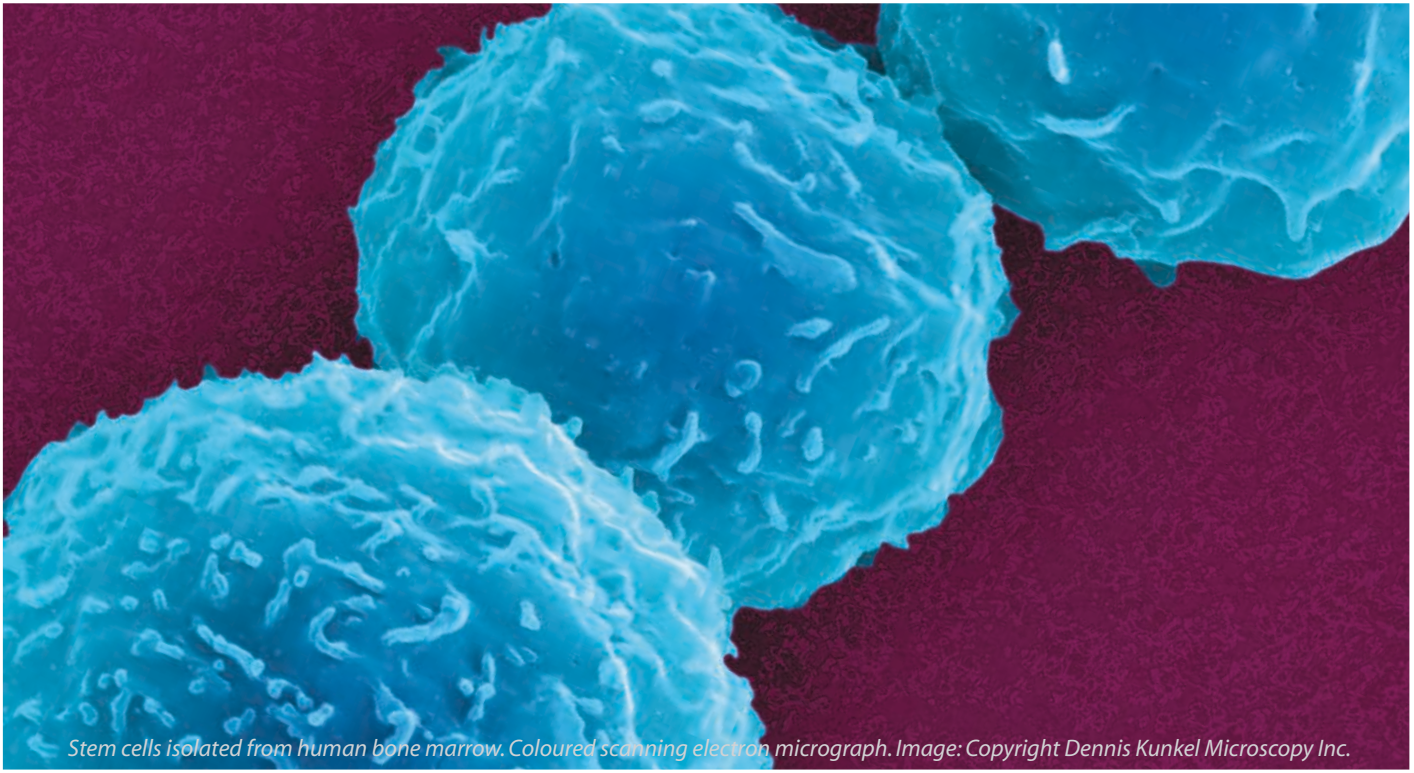
Most experts in the field acknowledge that cell replacement therapies based on human ES cells are a long way away. But another application is coming quickly, which has hardly been discussed publicly and which also raises difficult ethical issues. This is to use human embryonic stem cells (or cells derived from them) to test chemicals for possible toxic effects [7]. Pharmaceutical drugs have to be tested and under new EC REACH regulations so do all existing industrial and household chemicals. Toxicity testing is not on the list of permitted uses of human embryos under the

HFE Act [9]. But having created an embryonic stem cell line, say for diabetes research, can the same cells be used for purposes which would have been refused a licence, like drug screening or even testing cosmetics?

Some say that embryonic stem cells have no moral status. But others disagree because they were created by destroying a human embryo, arguing that the same limits on what the embryo can be used for must apply also to whatever uses the cells would subsequently be used for. It is also possible that scientists would sometimes need to use fresh human embryos to create stem cell lines for drug or chemical testing.

There are also issues about public accountability and who gets to benefit. When human ES cells research was first argued for, the big ethical case presented to the public was therapies to treat untreatable degenerative conditions, not for testing chemicals. If this indeed becomes the first major use, has the public been 'kept in the dark'? By law, pharmaceutical companies have to test all intended drugs anyway, but if they could use embryonic stem cells for the rapid screening of chemicals, it would reduce the time and cost of testing. But is a commercial benefit good enough reason for using cells derived from embryos?

Most present toxicity tests rely on using animals. Using human cells instead of animals may give a more reliable test, but would it be better ethically? Both animal research and embryo stem cell research oblige the researcher to look for an alternative. Can we replace one ethically controversial process (using animals) by another ethically controversial process (using cells derived from human embryos)? For example, say you disapproved of using animals to test cosmetics; would it be OK to use cells derived from human embryos instead?



Stem cells isolated from human bone marrow. Coloured scanning electron micrograph. Image: Copyright Dennis Kunkel Microscopy Inc.

STOP AND CONSIDER:

- Is it acceptable to allow human ES cells or iPS cells to produce human reproductive cells, sperm or (less likely) eggs? What are your reasons, either way?
- Should a man be allowed to produce a cloned embryo from a skin sample that is the 'twin' of himself, to create sperm, hopefully to have a child (by IVF) that is biologically his own? Does it matter that he is destroying the cloned embryo of himself to create a new embryo?
- Should we allow ES cells to be used to test the potential toxic effects in humans of pharmaceutical drugs, or cosmetics, or other chemicals?
- Is it allowable to use an ES cell line that was licensed on the basis of diabetes for testing the toxic effects of pharmaceutical drugs, or cosmetic products, given that a license would not have been granted for these directly?
- Should society have a voice in deciding, or is this something we leave to the Government or to the commercial companies?

Other ethical issues about stem cells

This summary of ethical issues has focused primarily on the special features relating to stem cells and embryos. There are other issues relating to stem cells which are common to other areas involving genetics or human tissues. These have not been covered in this booklet, however they are listed below as suggestions for further study for readers:

- Exaggeration and honesty-Exaggerated claims, either about the potential of 'breakthroughs' in stem cell science or its objections, can mislead people. The media have newspapers to sell. Scientists are enthusiastic about their discoveries and also want to secure further funding. Politicians and campaigners have causes to promote. People have deeply held beliefs. How do we handle this as a society?
- Patenting of stem cells - Is it in the public interest to allow the patenting of human stem cell lines [9]?
- Despite the claims made to promote them, will stem cell treatments be available (and affordable) for all? Will stem cell therapies only be pursued for commercially attractive illnesses?
- Donation and consent - For those people involved in donating eggs, embryos or tissues, there are issues of informed consent, non-directive counselling, understanding of research aims, privacy, and the separation of researchers from the donation process.
- Justice and equity - How far are we justified in this expensive research when so many in the world have shortened life spans because they lack the resources to tackle easily treatable diseases?

Ethics and the scientist

The turn of the twentieth century saw a noticeable change in Europe in public attitudes towards science and technology. While science is still held in high esteem, scientists are no longer regarded as a largely independent, elite group which periodically offers discoveries and finished products to an accepting society. People are now more critical [10]. The society, whose taxes and investments provide the research funds and infrastructure for scientific endeavour, now demands more accountability for what is done on its behalf. They want to know what and who is driving the research, how well its risks have been taken into account, or what alternative solutions there might be. People want to be able to voice their objections if what is proposed might go against their core values and beliefs. This is especially so in the area of stem cells because it touches on some very basic beliefs about what a human being is, when human life begins, and what is permissible in research in pursuit of medical treatments. As a result, not only the public but also funders of research now expect scientists to be able to show they are aware of, and understand, the ethical and social dimensions of their work. Scientists themselves are increasingly recognising that ethics is not just a matter for society as a whole, but is something they need to think about for themselves.

References for this chapter

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Interested to know more?

International forum for discussion of stem cells, also providing news about stem cell research.

http://www.topix.com/forum/tech/stem-cell-research
An open forum for discussions of stem cells.

http://www.beep.ac.uk
The Bioethics Education Project supports students in learning to discuss bioethical issues and teachers in planning lessons on them.

http://www.npr.org/templates/story/story.php?storyId=16493814
Radio interview on 'making embryonic stem cells without human embryos?' An attempt to eliminate the human embryo controversy.

Key messages in this chapter

The use of early human embryos in stem cell research is a complex and controversial ethical issue.

This section suggests three viewpoints regarding the moral status of human embryos. These are: no moral status, the same moral status as a baby and an intermediate view between these two poles.

Current UK legislation does not allow research on embryos more that 14 days old (the 14 day rule). Opinion is divided as to whether such a line can be drawn.

Currently in the UK, embryos can be created for research purposes under specific circumstances. Two ways in which embryos are created for research is through the generation of animal-human hybrid embryos and through using nuclear replacement to make embryos.

There are other ethical considerations to be taken into account with regard to using embryonic stem cells for drug and toxicity testing and the generation of sex cells (sperm and eggs).

An important aspect of being a scientist involves engaging with the social and ethical dimensions of research. Society and scientists alike must be involved in the discussions regarding using human embryos in stem cell research.

Activity

Introduction

In this activity you will first produce an ethical matrix and then use it as a tool to discuss some ethical issues surrounding stem cells.

The ethical matrix (designed by Professor Ben Mepham, Centre for Applied Bioethics at the University of Nottingham) is a tool to help people analyse an ethical issue and make informed choices. It can aid reflection and discussion about a topic and here it is used to help people explore for themselves the ethical issues surrounding using embryos in research. The strength of the ethical matrix is that it allows users of the matrix to 'put themselves in the shoes of others', appreciating the different perspectives on the issue and the different criteria people use to make their decisions.

The ethical matrix is based on three key ethical principles (for further information on these see Mepham, 2008):

1. wellbeing: that is, the safety, welfare and health of an individual or group;
2. autonomy: that is, an individual's right to be free to choose and make their own decisions; and,
3. justice: that is, to what extent a situation is just or fair for an individual or group.

These principles are very useful for exploring ethical concerns but it should be noted that there can be some crossover between them and they will not cover every ethical concern in all cases. Furthermore, they do not easily pose questions of principles, for example, that something is fundamentally right or wrong in terms of an individual's principles. In the blank ethical matrix below the three key principles form the headings of the columns. The first column contains a list of interest groups, individuals, groups of people or institutions which have an interest in or are affected by stem cell research using embryos. Completing the ethical matrix means that you apply these three ethical principles in order to consider and then map (e.g. list) the issues for each interest group.

Task

(this is described here as a group activity but note it is a useful individual activity as well):

1. Working in groups, give each person a photocopy of the blank ethical matrix.
2. Consider the interest groups (read through the list) and decide whether there are any additional groups which you would like to add (a blank space at the bottom of the 'interest groups' columns is provided, if needed).
3. For each interest group consider how stem cell research using embryos affects the group's wellbeing, autonomy and justice and list the key issues in the appropriate blank space in the table. When completing each row remember that you should do it as if you were a member of the interest group in question e.g. complete spaces on the 'patients' row as if you were a patient needing a treatment, complete the spaces in the 'scientists' row as if you were a scientific researcher using embryonic stem cells.
4. Once everyone has completed the ethical matrix consider these questions:

- What are the most significant issues or impacts for each interest group (e.g. the most significant for the patient group). Discuss your answers.
- How does your analysis of the significant issues or impacts for each interest group differ from your colleagues? Compare your matrix with those produced by your colleagues (or other groups involved in this activity), identify any similarities and discuss the differences. Would you change your matrix (e.g. edit the list of key issues for each interest group) based on this group discussion?
- By weighing up all of the issues for each interest group can you make a decision on the acceptability of this type of research? Does your decision allow all of the ethical principles (i.e. wellbeing, autonomy and justice) to be respected or upheld for all interest groups? Discuss your answer.
- Compare your final decision with your colleagues (or other groups involved in this activity). Does your decision differ? Discuss your decision-making, e.g. how did you weigh up the issues?
- Discuss how different people may weigh the ethical issues and come to a final decision on the acceptability of the research, such as pro-life groups (e.g. people or organisations who for religious or other reasons are interested in this issue), patient groups (e.g. promoting the benefits of research) or politicians.
- You have considered the overall issues raised by stem cell research using embryos. Now consider if your analysis would change if you were discussing a specific use or a specific research project. For example, identify the ethical issues raised by using embryonic stem cells to develop a specific cancer treatment. Does your analysis change if the research aims change, e.g. research related to diabetes rather than cancer, or research focused on understanding basic cellular processes rather than towards a medical treatment?

This activity is adapted from and has been reproduced with kind permission and assistance from Dr Kate Millar, Department of Ethical Engagement Methods developed by staff at the Centre for Applied Bioethics, University of Nottingham, UK (see http://www.nottingham.ac.uk/bioethics/).

Mepham, T.B. (2008) Bioethics: An introduction for the biosciences. Oxford, Oxford University Press.

The Ethical Matrix

Interest Groups	Wellbeing (safety, welfare and health)	Autonomy (freedom and choice)	Justice (fairness)
Patients - people who are hoping that stem cell therapies will treat an illness, disease or injury.			
Scientists - people working in stem cell research and developing stem cell therapies to treat patients.			
Embryo - the source of embryonic stem cells for research.			
Society - issues for wider society such as social priorities, research and medical priorities and how money should be allocated.			

Autonomy is concerned with the interests of an individual. 'Embryo' is included as an interest group as some might consider the embryo as an individual.

Stem Cells Glossary

Term	Definition
Adult stem cells	See tissue stem cells.
Alzheimer's disease	A progressive neurological disease of the brain that leads to the irreversible loss of neurons and dementia.
Animal-human hybrid	An embryo which is a mixture of both human and animal tissue, created by inserting human DNA into an animal egg.
Asymmetric division	Cell division resulting in two daughter cells with different properties. Observed in some but not all stem cells.
Atrophy	A wasting or decrease in size of a body organ, tissue or part, owing to disease, injury, or lack of use.
Beta cell	A cell type found in the pancreas (specifically in the islets of Langerhans) that produces the hormone insulin.
Blastocyst	A ball of around 250 cells formed around five days after fertilisation.
Bone marrow	The tissue that fills the cavities in the centre of bones. The formation of blood cells (red blood cells, white blood cells and platelets) occurs in the bone marrow. Haematopoietic stem cells are also found in the bone marrow.
Cancer	Any malignant growth or tumour caused by abnormal and uncontrolled cell division.
Cell culture	The process by which live cells are grown in the laboratory. The cells are placed in a petri dish and given a mixture of nutrients so that they can survive and divide.
Cell line	A population of cells all carrying the same genes, grown in the laboratory through many cycles of growth and division over many generations of cells.
Cell replacement therapy	The replacement of cells damaged by disease or injury, with new healthy ones derived from stem cells. The ability of stem cells to self-renew and differentiate into particular cell types offers the potential to culture stem cells in the lab to become replacements. Where the original stem cells are derived from the patient, there is the potential to avoid immune rejection. Also referred to as cell transplantation therapy or stem cell therapy.
Cleavage	Division and resulting multiplication of cells in the early embryo.

Clinical trial	A research study in human subjects to answer specific questions about vaccines, new therapies or new ways of using known treatments. Clinical trials are used to determine whether or not new drugs or treatments are both safe and effective. Trials take place in four phases: Phase I tests a new drug or treatment in a small group; Phase II expands the study to a larger group of people; Phase III expands the study to an even larger group of people; and Phase IV takes place after the drug or treatment has been licensed and marketed.
Cloned embryo	A term used to describe an embryo produced using nuclear replacement.
Convention	An agreement between states or nations.
Cord blood	Blood from the umbilical cord of a new-born baby; a particularly rich source of stem cells, especially haematopoietic stem cells.
Demyelination	The removal of myelin, an insulating and protective protein which coats neurons.
Diabetes	A condition where the amount of glucose in the blood is too high, due to the pancreas not producing enough of the hormone insulin (which helps glucose get into the cells of the body) or insulin not working properly.
Differentiation	The process by which cells become specialised to perform certain tasks. When a cell can differentiate no more it is said to be terminally differentiated.
EC REACH	Acronym for European Community regulation for Registration, Evaluation, Authorisation and Restriction of Chemical substances. The law came into effect on 1st June 2007 and regulates chemicals and their safe use (EC 1907/2006).
Embryonic stem cells (ES cells)	Stem cells from the inner cell mass of the blastocyst which will go on to produce every cell in the human body.
Endogenous	Developing or originating within an organism.
Gastrulation	Stage of embryo development occurring in the third week following fertilisation when the inner cell mass forms three layers (the ectoderm, mesoderm and endoderm) which will become different areas of the embryo.
Germ cells	The reproductive cells in multicellular organisms such as the sperm and egg.
Haematopoietic stem cells (HS cells)	Stem cells found in the bone marrow or blood that give rise to all the blood cell types.
Hepatocyte	The main cell type found in the liver. Hepatocytes are the functional cell in the liver and constitute 70-80% of the cells found in the liver.
HFE Act 2008	Human Fertilisation and Embryology Act 2008 was an amendment to the Human Fertilisation and Embryology Act 1990 and the Surrogacy Arrangements Act 1985.

Term	Definition
Hybrid cloned embryos	See animal-human hybrid
Hypertension	High blood pressure.
Immune rejection	Where the immune system attacks foreign tissue introduced into the body, e.g. grafts and transplants.
In-vitro fertilisation (IVF)	A technique in which the process of fertilisation of an egg with a sperm is carried out in the laboratory. A resulting embryo is then placed into the womb to develop into a pregnancy.
Induced pluripotent stem (iPS) cells	A type of stem cell which is artificially made from an adult somatic cell (e.g. a skin cell) by switching on four specific genes. The non-pluripotent cell is therefore induced to become pluripotent.
Lobbying	The practice of influencing decisions made by the government (in groups or individually). It includes all attempts to influence legislators and officials, whether by other legislators, constituents, or organized groups.
Macular degeneration	An eye disease caused by the degeneration of cells in a part of the retina called the macula lutea. It results in blurred vision and in some cases blindness.
Model	A biological specimen which simulates the processes of, for example, a human disease, so that it can be used for research instead of a human with that disease. Models could be cultures of cells, animals or even computer-based.
Motor neuron disease (MND)	Motor neuron disease is a disease that causes damage to motor neurons. It can lead to wasting of muscles which in turn causes loss of mobility and difficulties with swallowing, speech and breathing. In most cases the cause of MND is unknown.
Multiple sclerosis (MS)	An auto-immune disease where the body's own immune system attacks the protective coating around nerves called myelin. MS can cause physical or cognitive (learning or reasoning) disability.
Multipotent cells	Stem cells which are able to give rise to a subset of fully differentiated cells.
Nuclear replacement	The process whereby the nucleus of an egg is removed and replaced with the nucleus of another cell, which could be a germ cell or a somatic cell.
Oligodendrocyte	A type of cell which sheaths the axons of neurons with myelin, an insulating and protective protein.
Organogenesis	The formation of specific organs in the developing embryo.
Osteoarthritis	A degenerative joint disease caused by gradual loss of cartilage.

Parkinson's disease	A degenerative disease of the brain.
Parthenogenesis	The activation of an egg without the involvement of sperm. So that the egg starts to develop as if it had been fertilised when actually it has not.
Patient-specific stem cell therapy	The name given to a proposed technique involving treating a patient by producing genetically matched somatic cells or stem cells. These replacement cells would be derived from an intermediate embryo or blastocyst, created for the purpose by nuclear replacement, using cells taken from the patient.
Phenotype	An observable characteristic (trait) of an organism or tissue.
Pluripotent cells	Capable of giving rise to all the cell types of a mature organism but not able to support the development of an embryo.
Primitive streak	A structure formed in the embryo during gastrulation which in humans signifies the start of development of the nervous system.
Primordia	Organs at their most early and basic stage of development.
Regenerative pharmacology	Reconstruction of diseased or injured tissue by activation of resident cells using pharmacological methods.
Remyelination	The re-generation of myelin, an insulating and protective protein which coats neurons, which have been damaged in diseases such as multiple sclerosis (MS).
Reprogramming	Altering the state of differentiation in a cell as happens in the production of iPS cells.
Self-renewal	The ability of a stem cell to divide and produce copies of itself for an indefinite period of time. This is the defining property of stem cells.
Somatic cell	Any cell in a plant or animal other than germ cells.
Specialised cell	A cell that is suited to a specific job. Skin cells, red blood cells, neurons, hepatocytes, beta cells are all types of specialised cells. Stem cells are unspecialised.
Stem cell	A cell that can divide indefinitely to either produce more stem cells or a variety of different cell types (specialised cells).
Stem cell line	The term used to describe a particular strain (or family) of constantly-dividing stem cells. Each stem cell line has its own unique name, such as 'Shef 1' or 'Nott 2', and will have been derived from an initial starter (or parent) culture of isolated ES cells, iPS cells or tissue stem cells. See cell line.
Stem cell therapy	See cell replacement therapy.

Term	Definition
Stroke	A stroke occurs when a blood clot forms and blocks the passage of blood to the brain. It can lead to loss of brain function.
Terminally differentiated	Cells which can no longer divide or change function any further.
Tissue stem cells	Stem cells found in some adult (and fetal) tissue, used to replenish cells in the body, replacing those which naturally wear out. Tissue stem cells are sometimes referred to as adult stem cells.
Tissue-specific cells	Cells which are specific to, or exclusively found in, a single tissue in the body.
Totipotent cells	Cells which possess the ability to develop into an embryo which can then develop into a complete organism (including generation of a placenta).
Treaty	An agreement under international law entered into by sovereign states and international organisations.
United Nations	An organisation of independent states formed in 1945 to promote international peace and security.
Zygote	A diploid, totipotent cell created when an egg and sperm fuse.

Image acknowledgements

Front Cover

Stem cell. Coloured scanning electron micrograph (Science Photo Library).

Page 1
Pipette tips (iStockphoto, Thinkstock).

Page 3
- Newly formed neurons from neural stem cells. Fluorescent micrograph (Sally Lowell, MRC Centre for Regenerative Medicine, University of Edinburgh).
- Courtesy of Dr Lesley Forrester.
- Embryonic stem cell in the eye of a needle. Coloured scanning electron micrograph (Steve Gschmeissner, Science Photo Library).
- Tissue macrophages (blue), monocyte (green), T lymphocytes (pink) and human red blood cells from a leg wound. Coloured scanning electron micrograph (Dennis Kunkel Microscopy, Inc.).
- Courtesy of Professor Anthony Hollander.
- Sperm on the surface of a human egg (ovum) during fertilisation. Coloured scanning electron micrograph (Yorgos Nikas, Science Photo Library).

Chapter 1

Page 4
Cleavage in human embryo. Light micrograph (iStockphoto, Thinkstock).

Page 5
- Sperm on the surface of a human egg (ovum) during fertilisation. Coloured scanning electron micrograph (Yorgos Nikas, Science Photo Library).
- Cleavage in human embryo. Light micrograph (iStockphoto, Thinkstock).
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Page 7
Human stem cells. Fluorescent micrograph (iStockphoto, Thinkstock.).

Page 9
Sperm on the surface of a human egg (ovum) during fertilisation. Coloured scanning electron micrograph (Yorgos Nikas, Science Photo Library).

Page 11
Tissue macrophages (blue), monocyte (green), T lymphocytes (pink) and human red blood cells from a leg wound. Coloured scanning electron micrograph (Dennis Kunkel Microscopy, Inc.).

Page 12
Myelinated nerves (green), demyelinated nerves (green myelin debris) and remyelinated nerves. Myelin is highlighted using immunohistochemistry for Myelin Basic Protein (MBP). Fluorescent micrograph (Anna Williams, University of Edinburgh).

Page 15
- Newly formed neurons from neural stem cells. Fluorescent micrograph (Sally Lowell, MRC Centre for Regenerative Medicine, University of Edinburgh).
- Newly formed skin cells (yellow) emerging from embryonic stem cells in culture. Cell nuclei are shown in blue. Fluorescent micrograph (Sally Lowell, MRC Centre for Regenerative Medicine, University of Edinburgh).

Page 16-17
Human male anatomy, artwork. Pasieka, Science Photo Library.

Page 18
Tracheal tissue engineering: a patient with a narrowed left bronchus (left panel) and the same organ after implantation of the tissue engineered airway (right panel). The new airway was made using stem cells that were turned into cartilage cells (Images courtesy of Hospital Clinic of Barcelona).

Page 19
- Human muscle cells magnified 200x. Light Micrograph (Comstock, Thinkstock).
- Newly formed skin cells (green) emerging from embryonic stem cells in culture. Cell nuclei are stained with DAPI and show in blue. Fluorescent micrograph (Sally Lowell, MRC Centre for Regenerative Medicine, University of Edinburgh).

Page 25
Embryonic stem cell in the eye of a needle. Coloured scanning electron micrograph (Steve Gschmeissner, Science Photo Library).

Chapter 2

Page 26
Embryonic stem cells. Light micrograph (Sally Lowell, MRC Centre for Regenerative Medicine, University of Edinburgh).

Page 29
Hemera, Thinkstock.

Page 31
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Page 32
Stem cell. Coloured scanning electron micrograph (Science Photo Library).

Chapter 3

Page 34
Robyn Mackenzie, iStockphoto, Thinkstock.

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Page 39
Neurons (green) derived from embryonic stem cells. Cell nuclei are shown in purple. Fluorescent micrograph (Sally Lowell, MRC Centre for Regenerative Medicine, University of Edinburgh).

Page 41
Hematopoietic stem cells isolated from human bone marrow (adult). Coloured scanning electron micrograph. (Dennis Kunkel Microscopy, Inc.).

Back cover

Haematopoietic stem cells isolated from human bone marrow (adult). Coloured scanning electron micrograph. (Dennis Kunkel Microscopy, Inc.).

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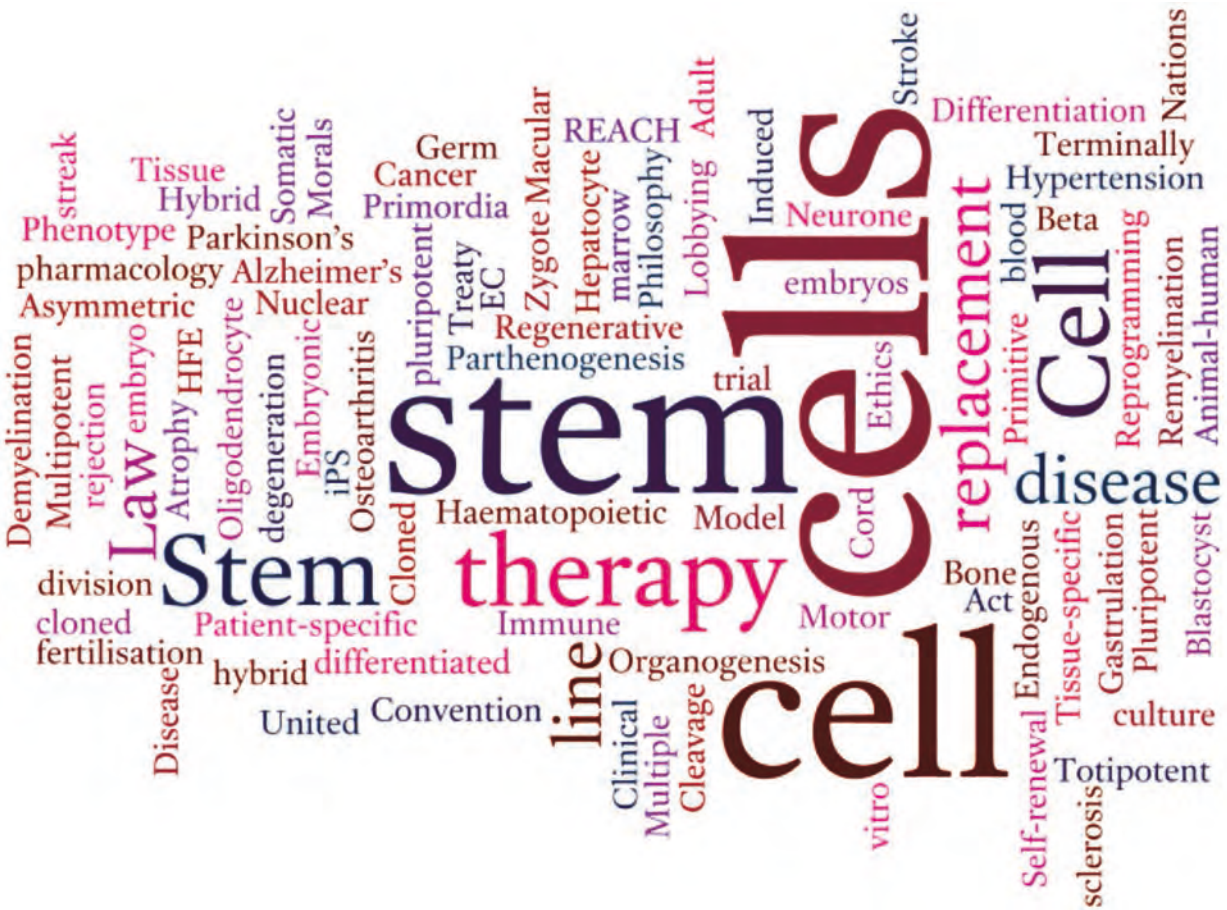

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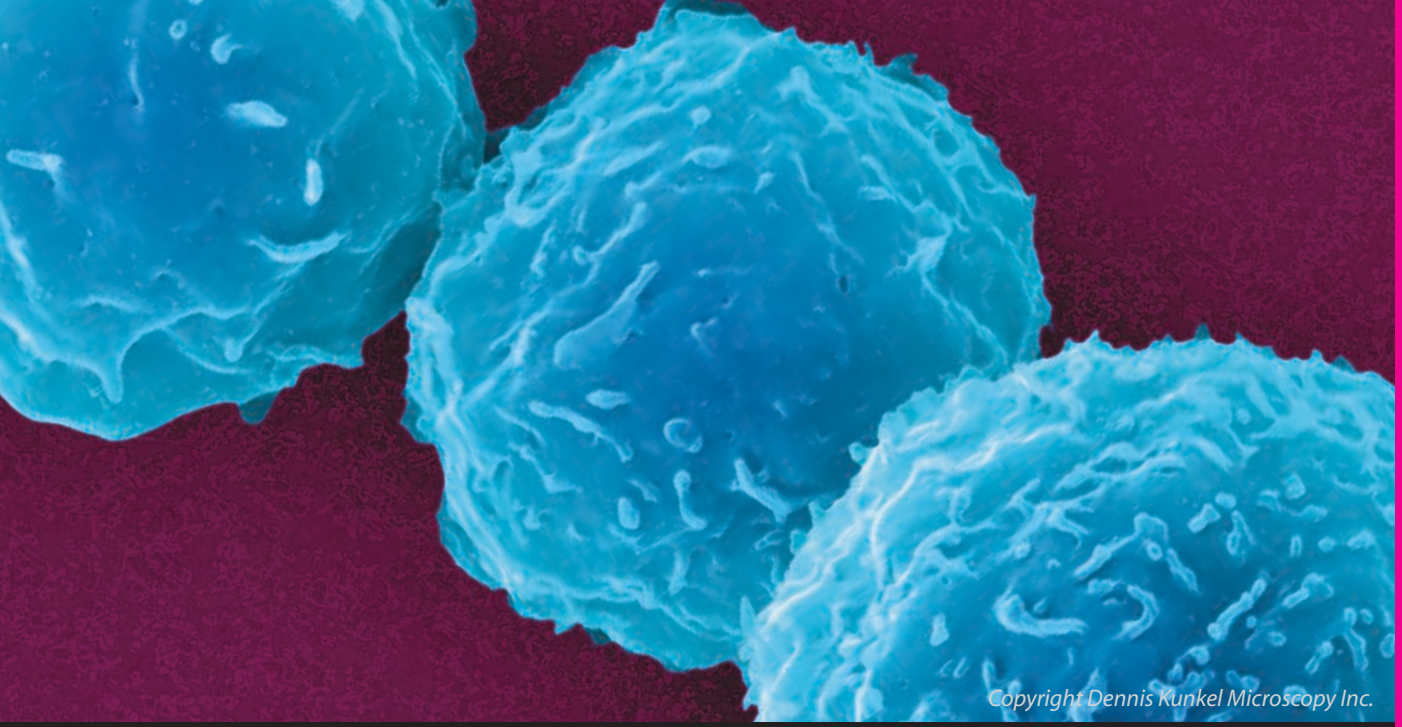

For more information and to request a copy of this booklet please visit:
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Stem Cells

science and ethics

It is the mark of an educated mind to be able to entertain a thought without accepting it.

Aristotle (384 BC - 322 BC)