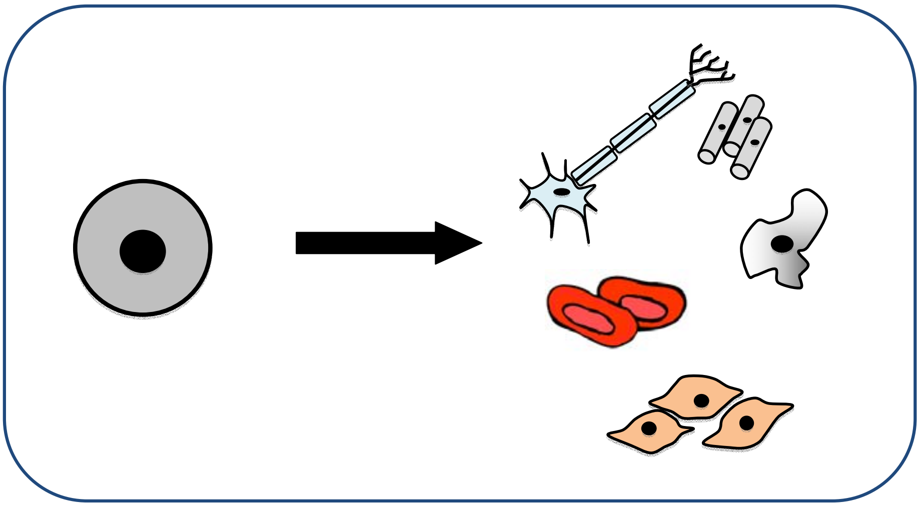
Introducing stem cells



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Dear speaker…

This presentation is intended as a flexible tool for scientists, science communicators and educators. Not all the slides will be useful for any one occasion. Choose the ones most suitable for your audience, mix them with your own slides, or just use the diagrams.

Contents

- **Stem cell biology basics:** For school students aged 16+, or adult public with little or no scientific knowledge
- **Cloning**: For adult public with little or no scientific knowledge; initial slides also suitable for students aged 16+
- **Stem cell biology in more detail**: For informed non-specialist audiences, e.g. clinicians, scientists working in fields other than stem cell biology.

Presenter's notes

Each slide in the Basics and Cloning sections includes notes that give a simple, jargon-free explanation of the key points. The more detailed slides in the last section have much briefer notes and assume some knowledge of stem cell science.

Further information and resources

The 15-minute film, "A Stem Cell Story" provides an excellent introduction to stem cells and covers many of the concepts presented here. See www.eurostemcell.org/films
Got a question or a comment? Contact us at http://www.eurostemcell.org/contact

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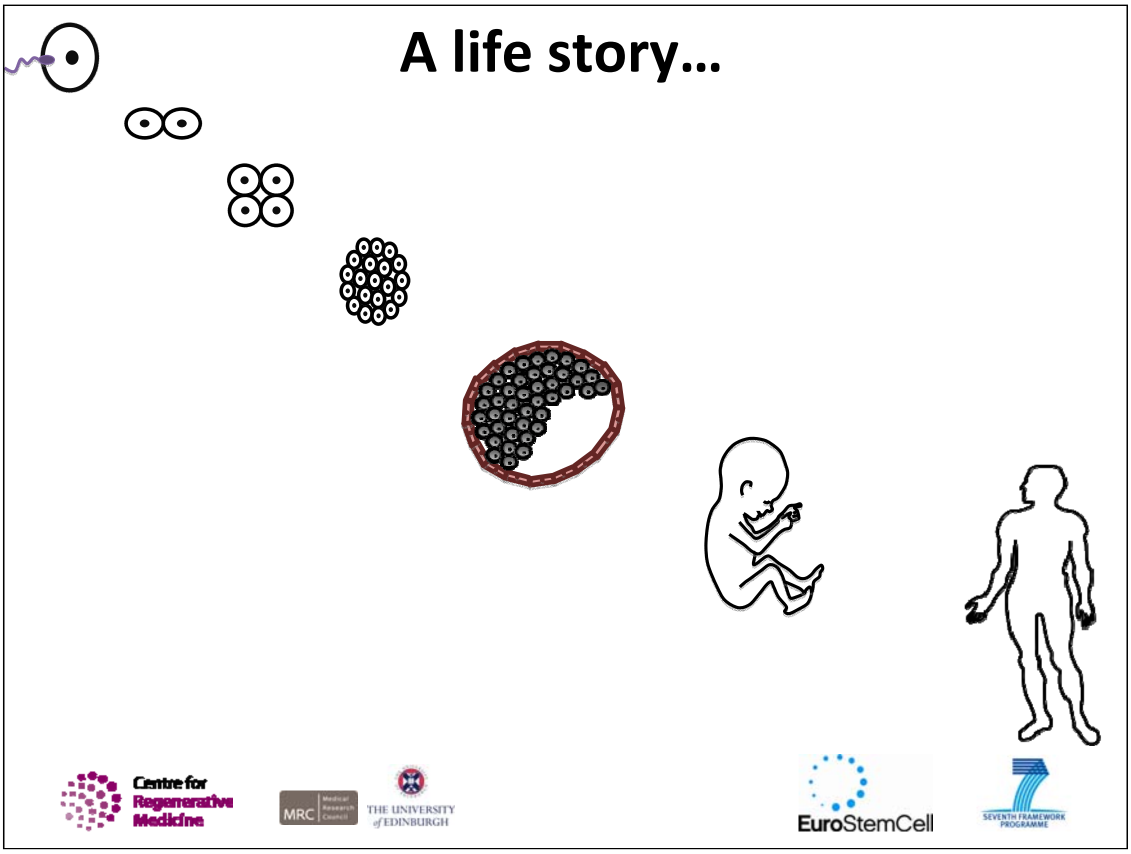
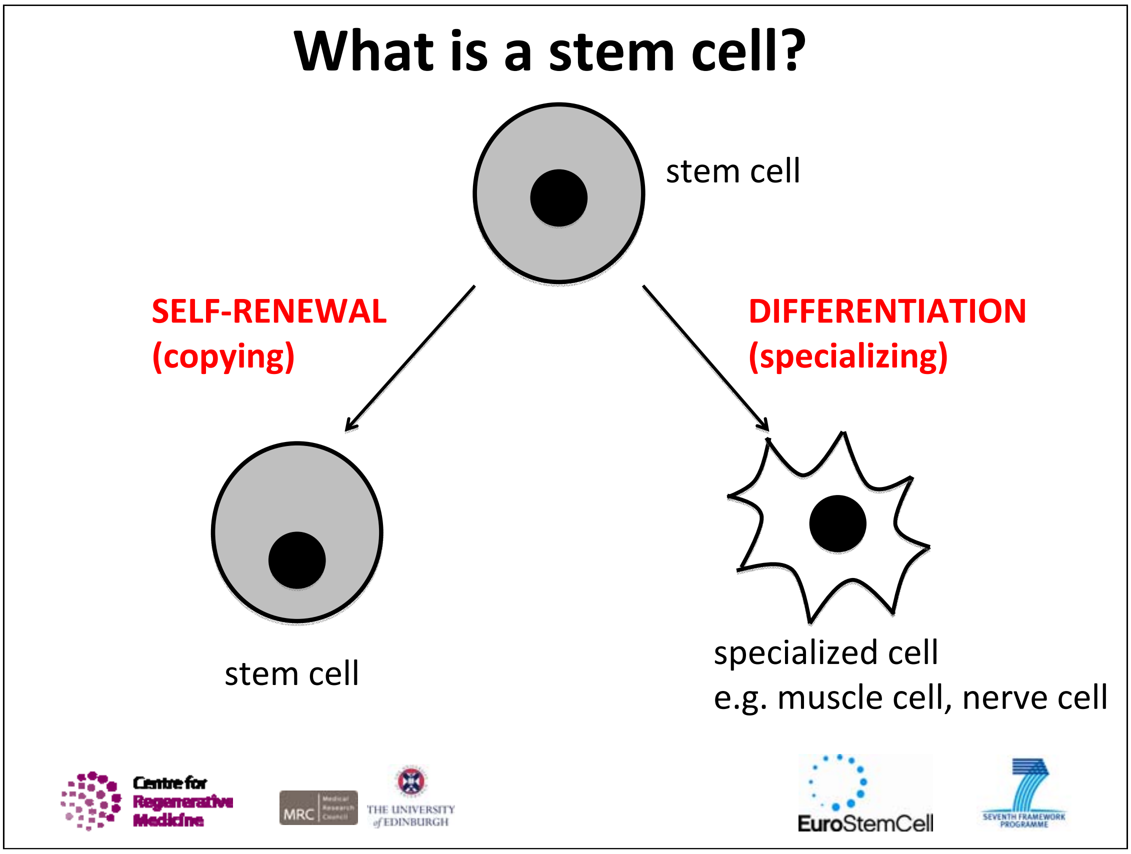
Stem cell biology basics



A life story…

Human development starts with just 1 cell – the fertilized egg. This cell divides to produce 2 'daughter cells'. These daughters divide, and their daughters divide again, and so on. There are a great many steps needed to form an adult body, or even a baby. Along the way, lots of different types of cells must be made.



What is a stem cell?

Note: The next slide provides an alternative version of this diagram that some younger audiences may find easier to understand. It aims to avoid the misconception that a stem cell always makes one copy of itself and one specialized cell when it divides (see below). The concept of a stem cell is very well explained in the short film, "A Stem Cell Story" at www.eurostemcell.org/films

What the diagram shows

Stem cells are different from other cells of the body because stem cells can both:

1) Self-renew: Make copies of themselves

AND

2) Differentiate: Make other types of cells – specialized cells of the body.

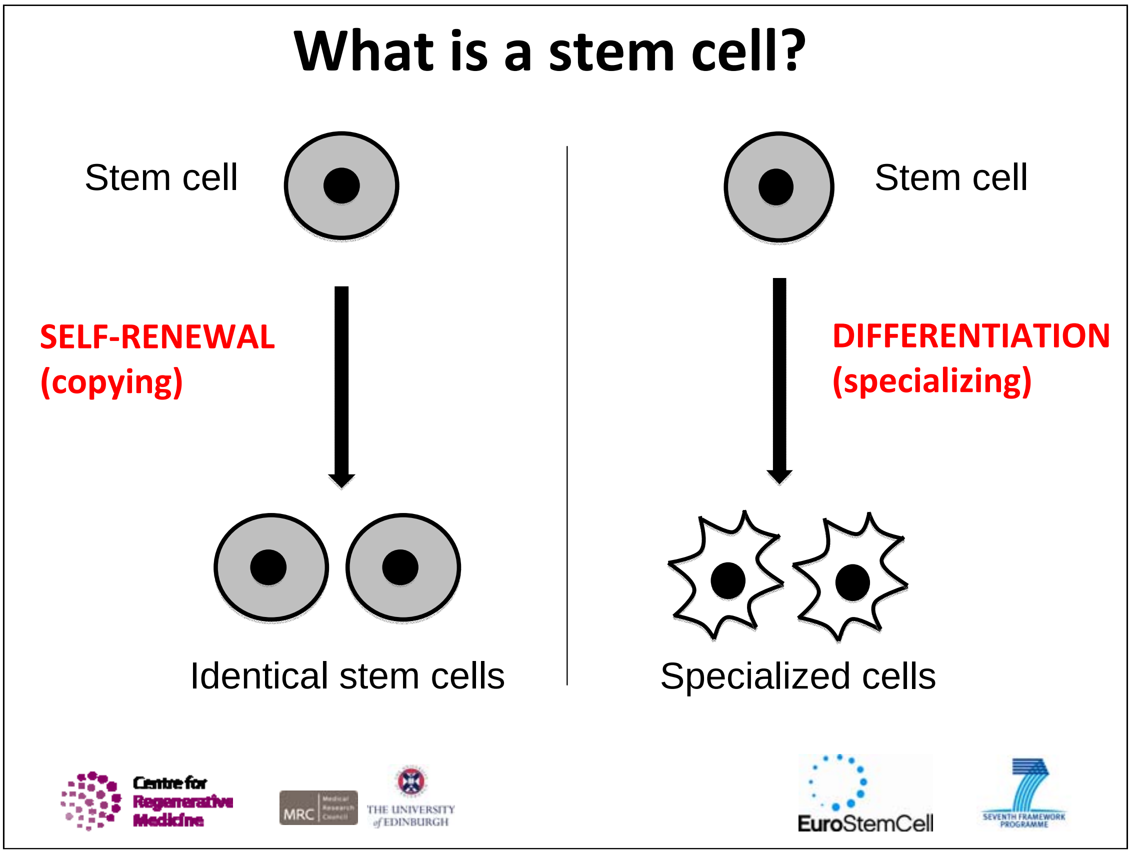
'Specialized' or 'differentiated' cells play particular roles in the body, e.g. blood cells, nerve cells, muscle cells. Specialized cells cannot divide to make copies of themselves. This makes stem cells very important. The body needs stem cells to replace specialized cells that die, are damaged or get used up.

Cell division - possible questions

1) 16+ year old students may remember learning about 2 kinds of cell division – mitosis and meiosis. They may have learnt that mitosis happens in wound healing or to replace short-lived cells, but probably won't have discussed stem cells in this context. You might therefore need to explain that most specialized cells cannot undergo mitosis. There are a few exceptions (e.g. liver cells or T-cells) but in general specialized cells can no longer divide. Skin cells, red blood cells or gut lining cells cannot undergo mitosis. Stem cells do divide by mitosis and this makes them very important for replacing lost or damaged specialized cells.

2) Should mitosis be discussed, you may wish to note the following: In mitosis, the DNA in the daughter cells is identical to the DNA in the dividing cell. This is true for dividing stem cells, both in self-renewal and in differentiation. In differentiation, the daughter cells are more specialized than the original stem cell. So, the daughter cells behave differently even though they have the same DNA as the stem cell. This is because there are lots of other molecules inside and around the cells that can change the way the cells behave.

3) Scientists think that when human stem cells divide they probably make EITHER two stem cells, OR two more specialized cells. In fruit flies, stem cells can divide to make one stem cell and one more specialized cell in a single division.



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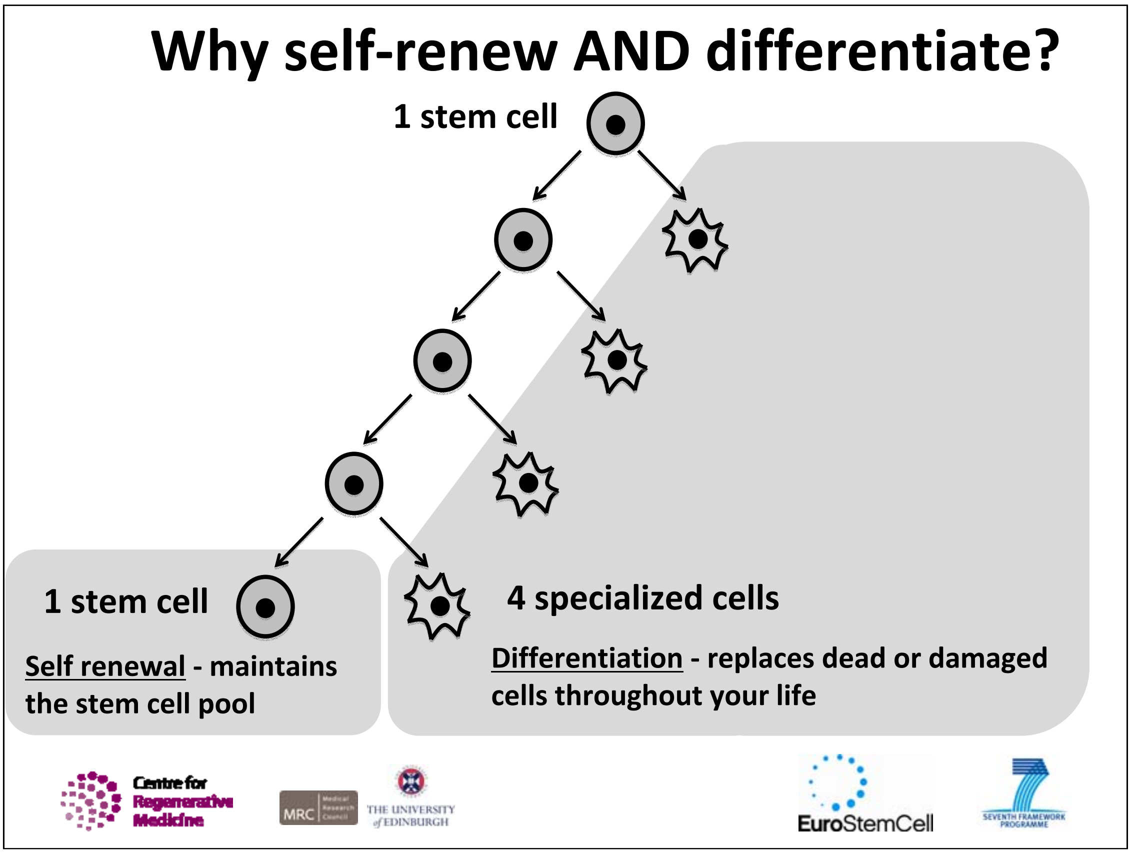


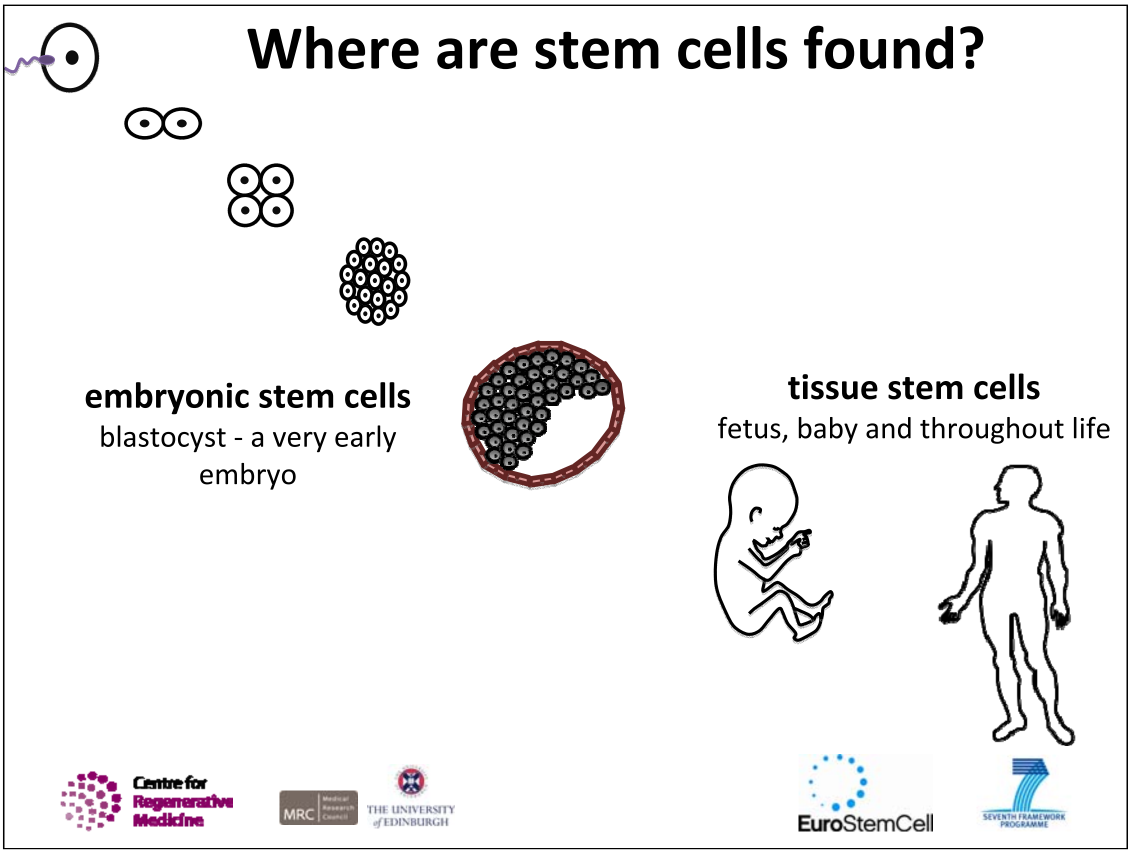
Why self-renew AND differentiate?

1) Self renewal is needed because if the stem cells didn't copy themselves, you would quickly run out. It is important for the body to maintain a pool of stem cells to use throughout your life.
2) Differentiation is important because specialized cells are used up, damaged or die all the time during your life. Specialized cells cannot divide and make copies of themselves, but they need to be replaced for your body to carry on working. For example, your body needs 100,000 million new blood cells every day. Of course, differentiation is also important for making all the different kinds of cell in the body during development of an embryo from a single fertilized egg.

Possible questions or misconceptions

1) School students may have learnt simply that 'cells undergo mitosis to make copies of themselves to heal wounds or replace blood cells'. You may need to explain that specialized cells like skin, red blood or gut cells cannot undergo mitosis, which is why you need stem cells. There are a few exceptions (e.g. liver cells or T-cells) but in general specialized cells can no longer divide. For adult audiences, this could be expanded to cover the idea that there are intermediate cells (progenitors) between stem cells and specialized cells that divide to allow a large number of new cells to be made (see slide 26 on renewing tissues)

2) Scientists think that stem cells in the human body don't generally divide to produce one stem cell and one specialized cell at the same time. They probably divide to make EITHER two stem cells, OR two more specialized cells. In fruit flies, stem cells can divide to make one stem cell and one more specialized cell.



Where are stem cells found?
There are different types of stem cells:
-Embryonic stem cells: found in the blastocyst, a very early stage embryo that has about 50 to 100 cells;
-Tissue stem cells: found in the tissues of the body (in a fetus, baby, child or adult).

(Tissue stem cells are sometimes referred to as adult stem cells, even though they are found in the fetus and in babies, as well as in adults.)

Types of stem cell:
1) Embryonic stem cells

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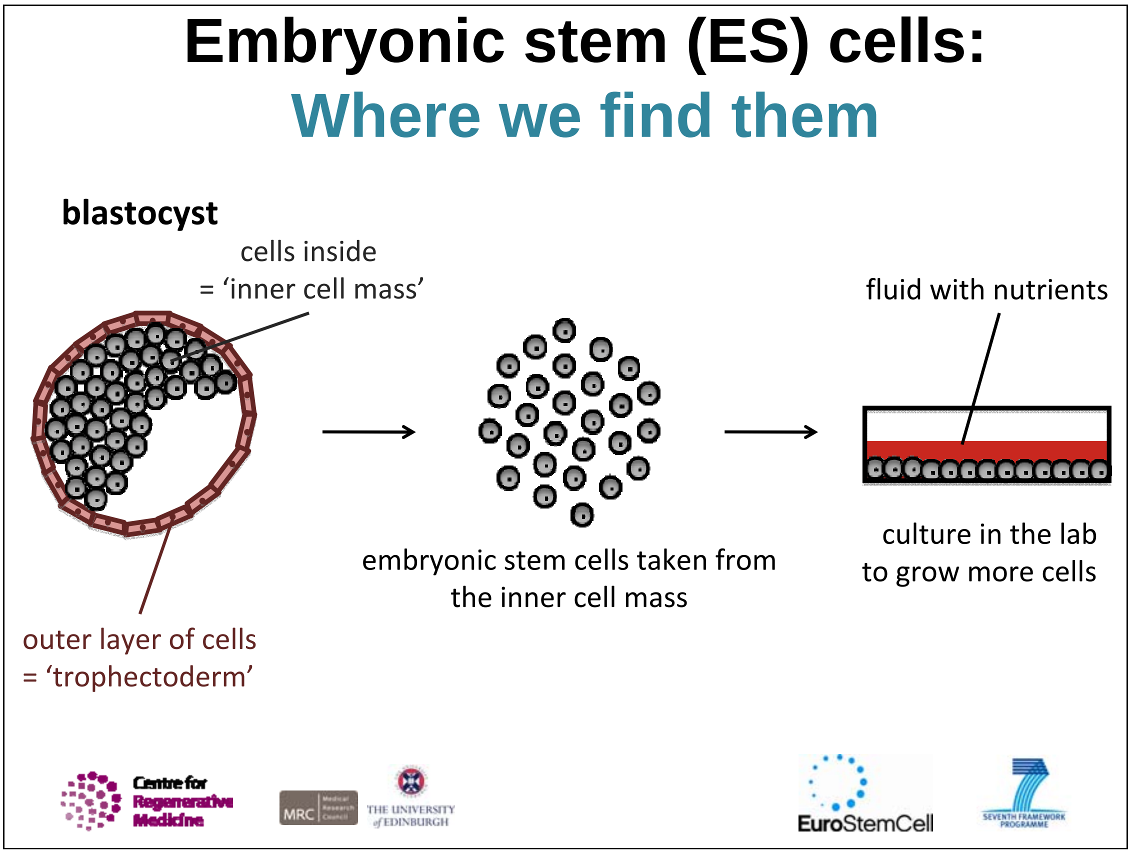
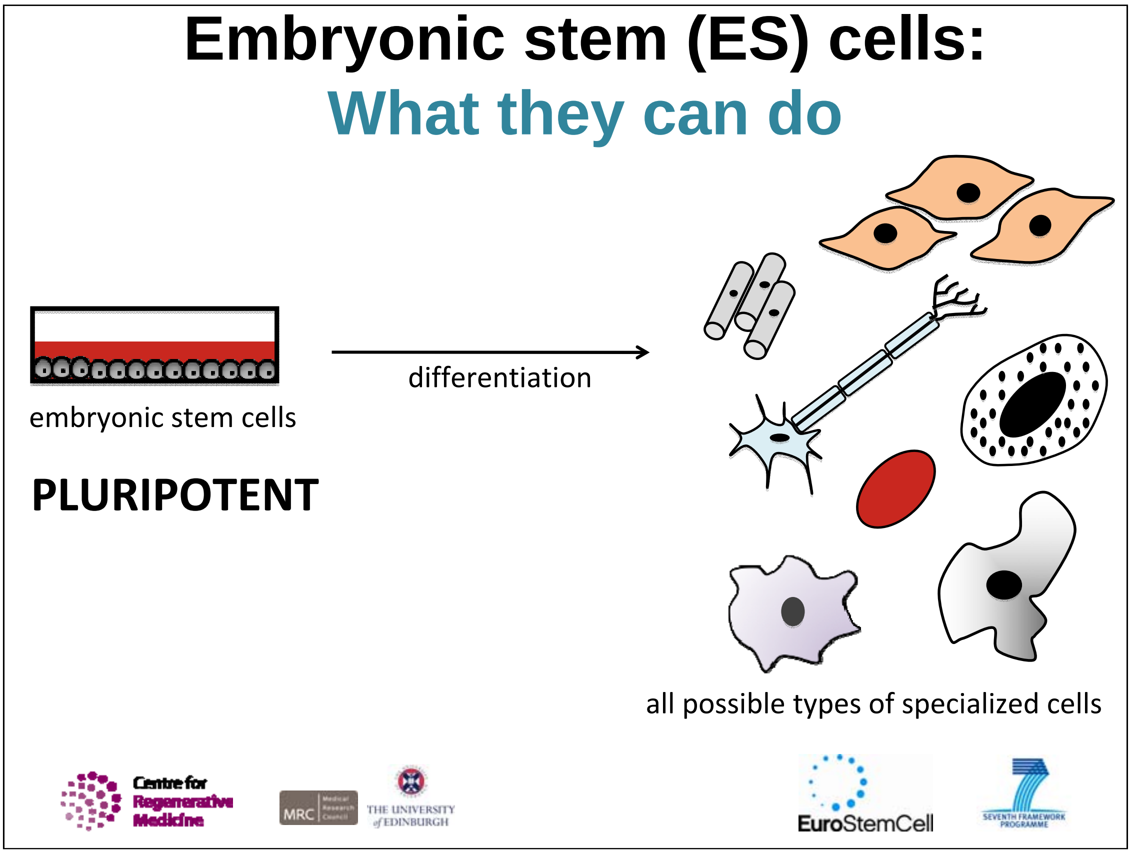


Embryonic stem cells: Where they come from

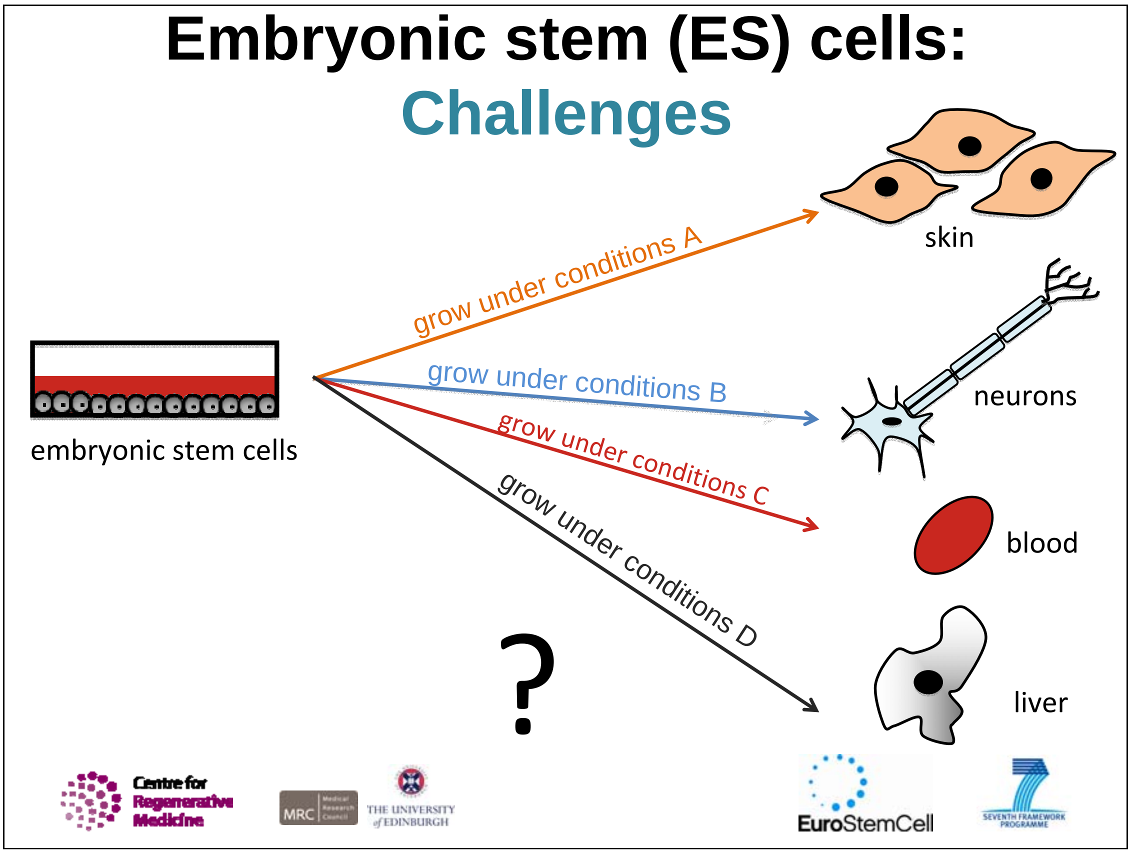
Embryonic stem (ES) cells are taken from inside the blastocyst, a very early stage embryo. The blastocyst is a ball of about 50-100 cells and it is not yet implanted in the womb. It is made up of an outer layer of cells, a fluid-filled space and a group of cells called the inner cell mass. ES cells are found in the inner cell mass.

For a simple, clear explanation of how embryonic stem cells are obtained, watch the film, "A Stem Cell Story", at www.eurostemcell.org/films



Embryonic stem cells: What they can do

Embryonic stem cells are exciting because they can make all the different types of cell in the body – scientists say these cells are **pluripotent.**



Embryonic stem cells: Challenges

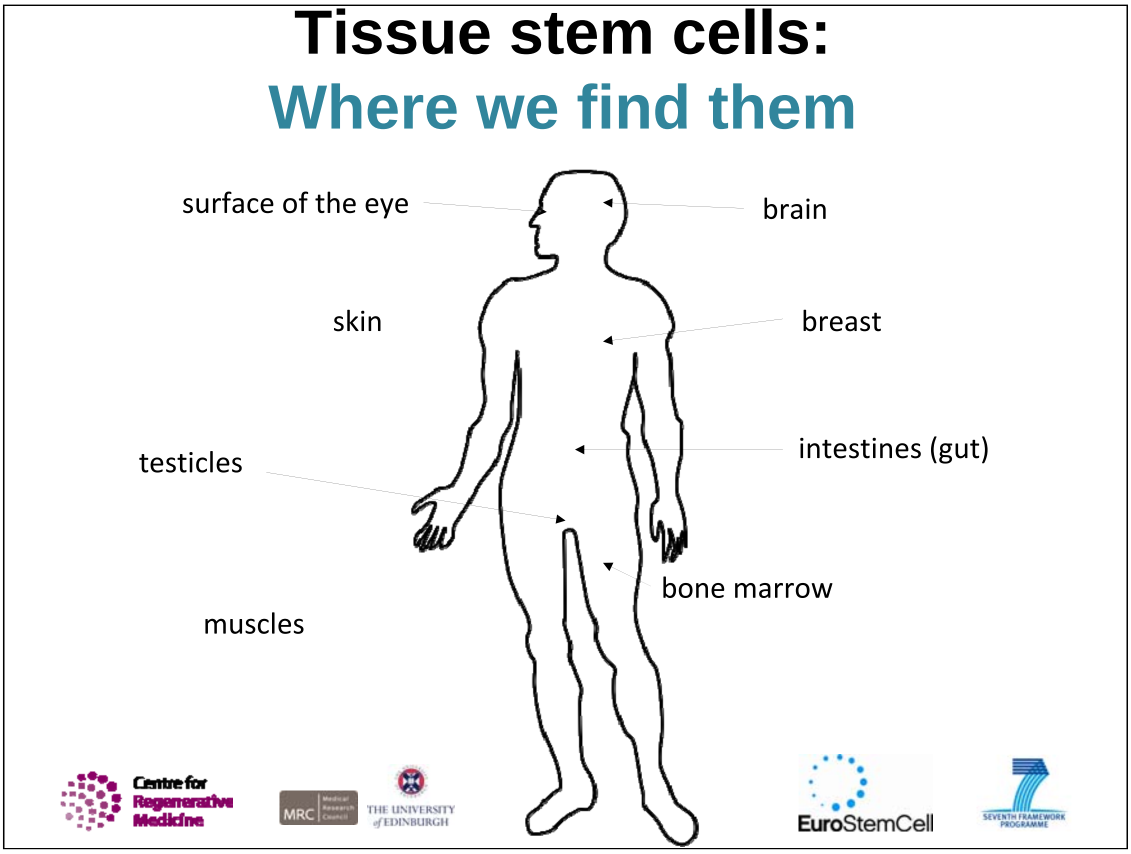
Scientists around the world are trying to understand how and why embryonic stem cells produce skin, blood, nerve or any other particular kind of specialized cell. What controls the process so that the stem cells make the right amount of each cell type, at the right time?

The big challenge for scientists is to learn how to control these fascinating cells. If we could force embryonic stem cells to make whatever kind of cell we want, then we would have a powerful tool for developing treatments for disease. For example, perhaps we could grow new insulin-producing cells to transplant into a patient with diabetes. But there is a great deal to learn before such therapies can be developed. Scientists also want to use stem cells to:

•Understand how diseases develop (disease modelling)

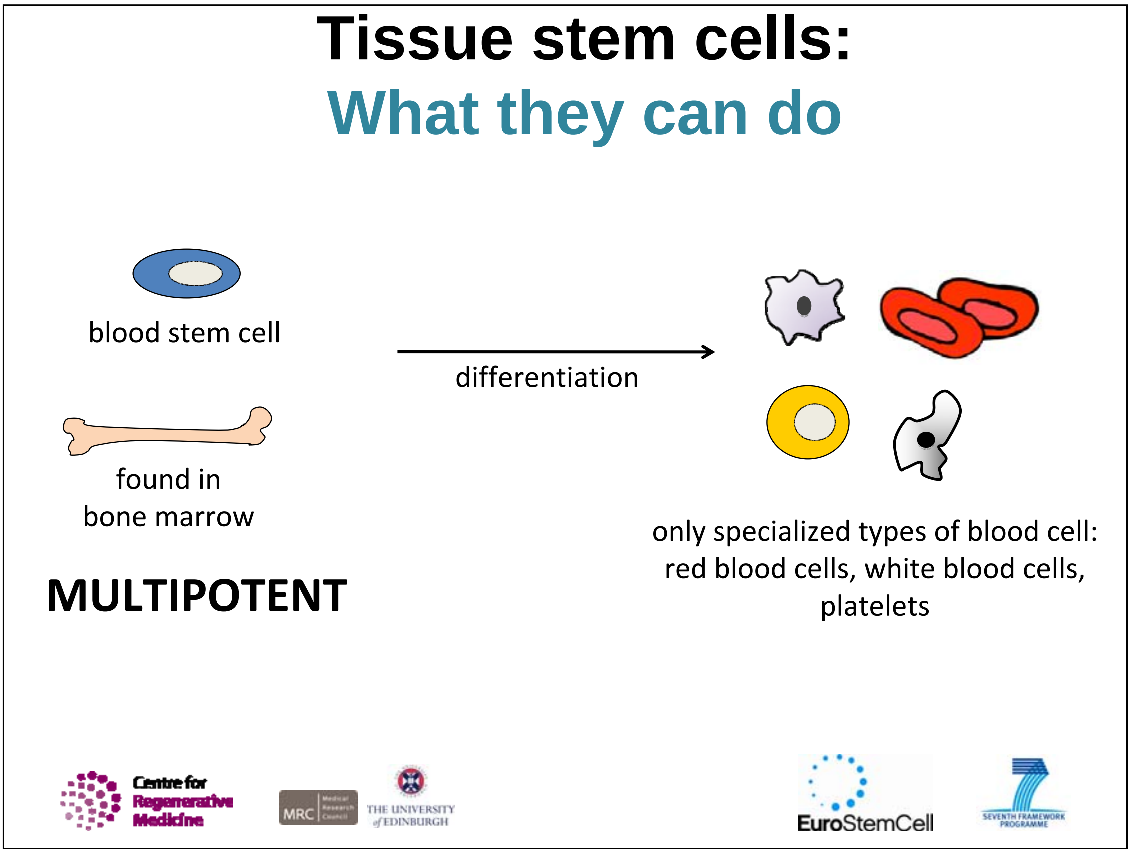
•Test drugs in the laboratory

Types of stem cell:
2) Tissue stem cells



Tissue stem cells: Where we find them

We all have stem cells in our bodies all the time. They are essential for keeping us fit and healthy. They replace cells that are damaged or used up. Scientists are still learning about all the different kinds of tissue stem cells found in our bodies and how they work.



Tissue stem cells: What they can do

Tissue stem cells can often make several kinds of specialized cell, but they are more limited than embryonic stem cells. Tissue stem cells can ONLY make the kinds of cell found in the tissue they belong to. So, blood stem cells can only make the different kinds of cell found in the blood. Brain stem cells can only make different types of brain cell. Muscle stem cells can only make muscle cells. And so forth.

Scientists say that tissue stem cells are **multipotent** because they can make **multiple** types of specialized cell, but NOT all the kinds of cell in your body.

Types of stem cell:
3)Induced pluripotent (iPS) stem cells

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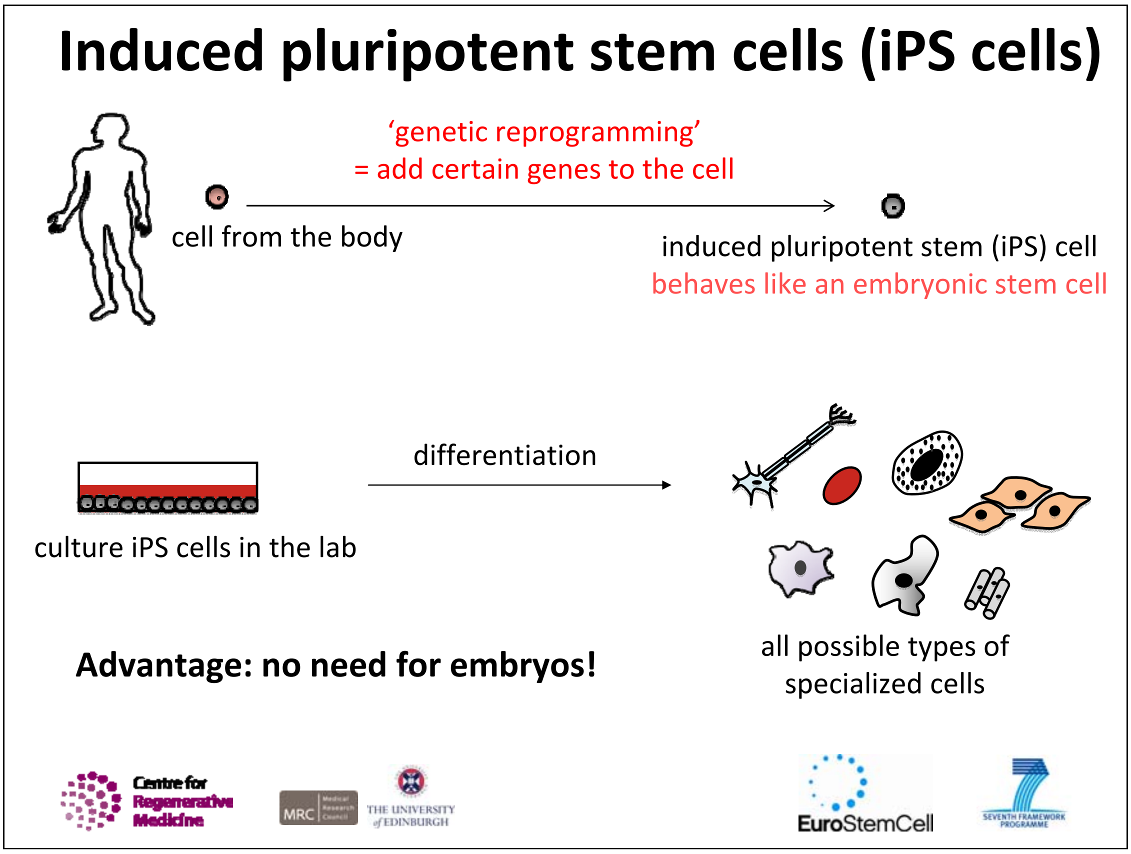


Induced pluripotent stem cells (iPS cells)

Note: This slide contains a lot of information and may be too complex for some audiences unless there is plenty of time for explanations and discussions.

What are iPS cells?

In 2006, scientists discovered that it is possible to make a new kind of stem cell in the laboratory. They found that they could transform skin cells from a mouse into cells that behave just like embryonic stem cells. In 2007, researchers did this with human cells too. The new stem cells that are made in the lab are called **induced pluripotent stem cells**. Just like embryonic stem cells, they can make all the different types of cell in the body – so we say they are **pluripotent**.

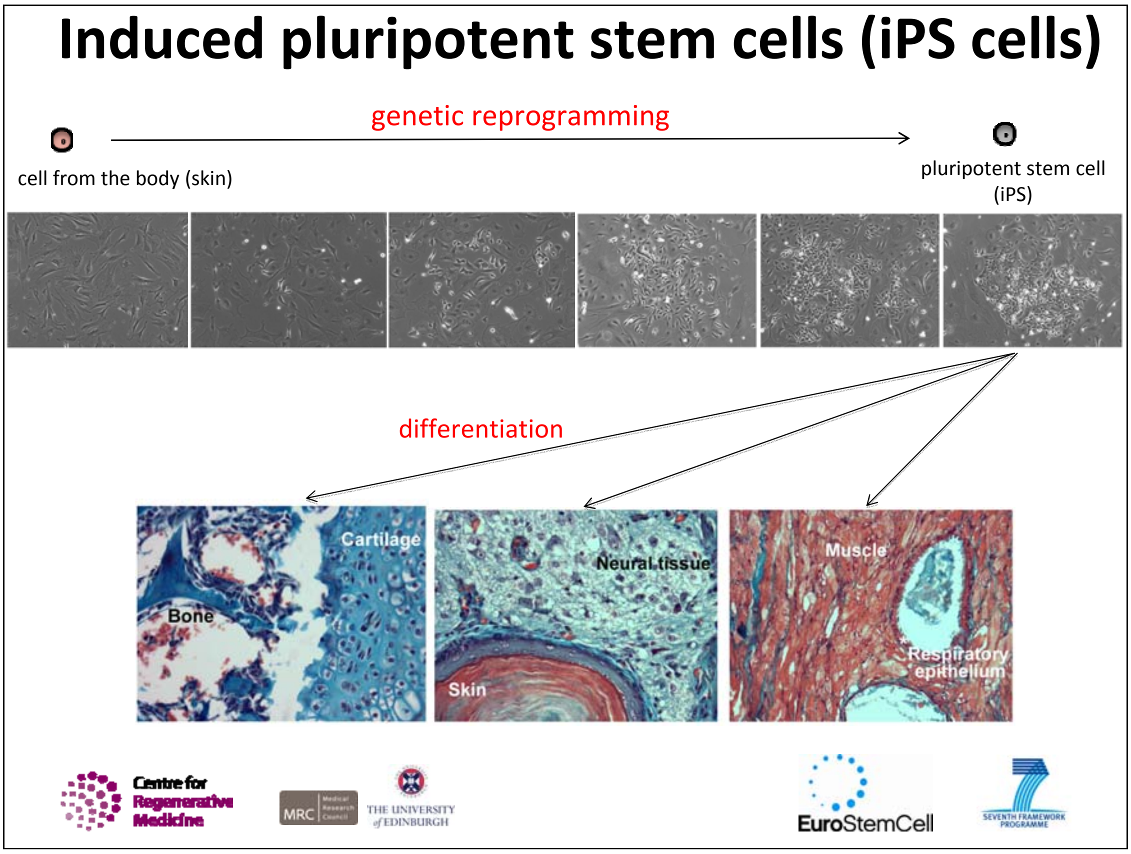
Making induced pluripotent stem (iPS) cells is a bit like turning back time. Scientists add particular genes to cells from the body to make them behave like embryonic stem cells. Genes give cells instructions about how to behave. So, this process is a bit like changing the instructions in a computer programme to make the computer do a new task. Scientists call the process they use to make iPS cells 'genetic reprogramming'.

Why are they exciting?

Researchers hope that one day they might be able to use iPS cells to help treat diseases like Parkinson's or Alzheimer's. They hope to:

1) Take cells from the body - like skin cells - from a patient
2) Make iPS cells
3) Use those iPS cells to grow the specialized cells the patient needs to recover from the disease, e.g. certain brain cells. These cells would be made from the patient's own skin cells so the body would not reject them.

There is a long way to go before scientists can do this, but iPS cells are an exciting discovery.



Induced pluripotent stem cells (iPS cells)

This is an alternative representation of the same information as on the previous slide. Please see the previous explanatory notes.

Stem cell jargon

Potency	**A measure of how many types of specialized cell a stem cell can make**
Pluripotent	**Can make all types of specialized cells in the body** **Embryonic stem cells are pluripotent**
Multipotent	**Can make multiple types of specialized cells, but not all types** **Tissue stem cells are multipotent**

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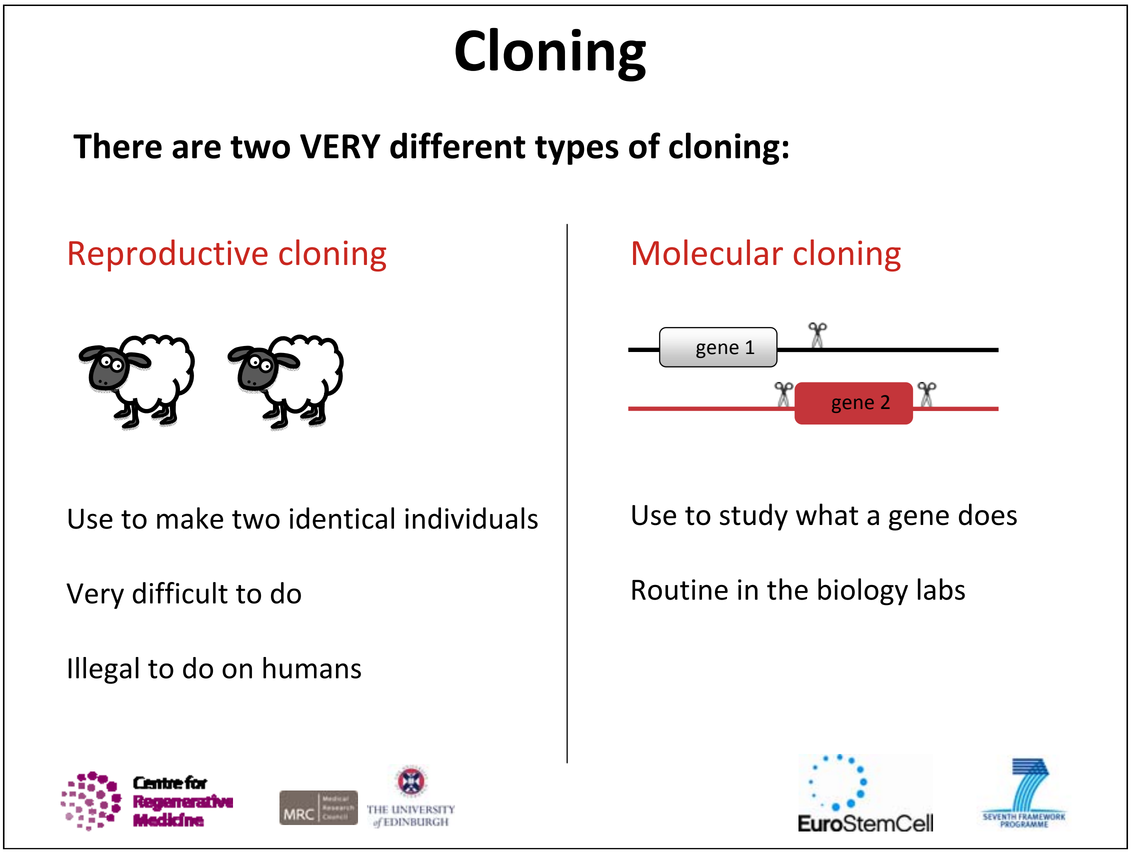
Stem cell jargon
Scientists use the words **pluripotent** and **multipotent** to help them describe stem cells. ALL stem cells can both self-renew and differentiate, BUT some stem cells can make more kinds of specialized cells than others. The terms on the slide are the key ones to remember. There are also stem cells that are:

TOTIPOTENT: can differentiate into all types of specialized cells in the body PLUS cells that are needed during development of the embryo only: placenta, yolk sac, umbilical cord.

UNIPOTENT: can only differentiate into one type of specialized cell. For example, spermatogonial stem cells (found in the testicles) are unipotent because they can only form sperm cells.

A useful place to look up other words and phrases to do with stem cells is the EuroStemCell online glossary: www.eurostemcell.org/glossary

Cloning



Cloning

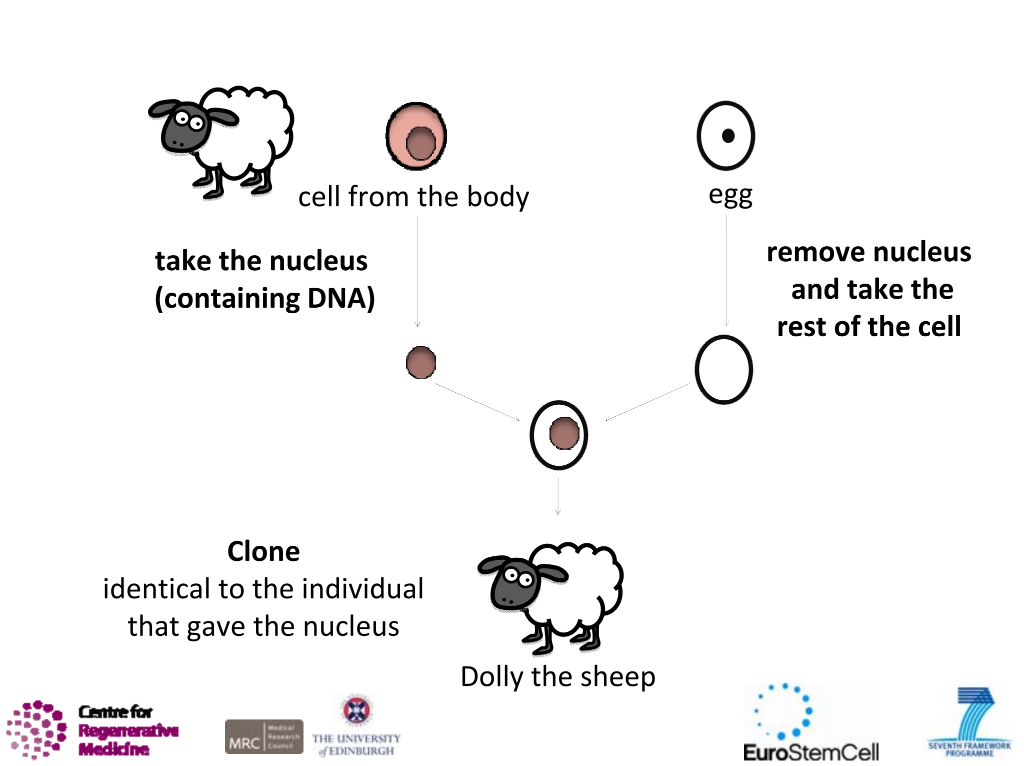
When most people think of cloning, they think of the idea of making a copy of an individual – an animal or even a person. This is called **reproductive cloning**. It hit the headlines in the late 1990s when 'Dolly the sheep' was cloned. She was the first mammal ever to be cloned.

In fact, this kind of cloning is very difficult to do and it is illegal even to try to clone a human being.

There is another type of cloning that many biologists do every day: **molecular cloning**. This is a technique used to help scientists investigate what particular genes do and how they work.

The following slides explain these processes in more detail.

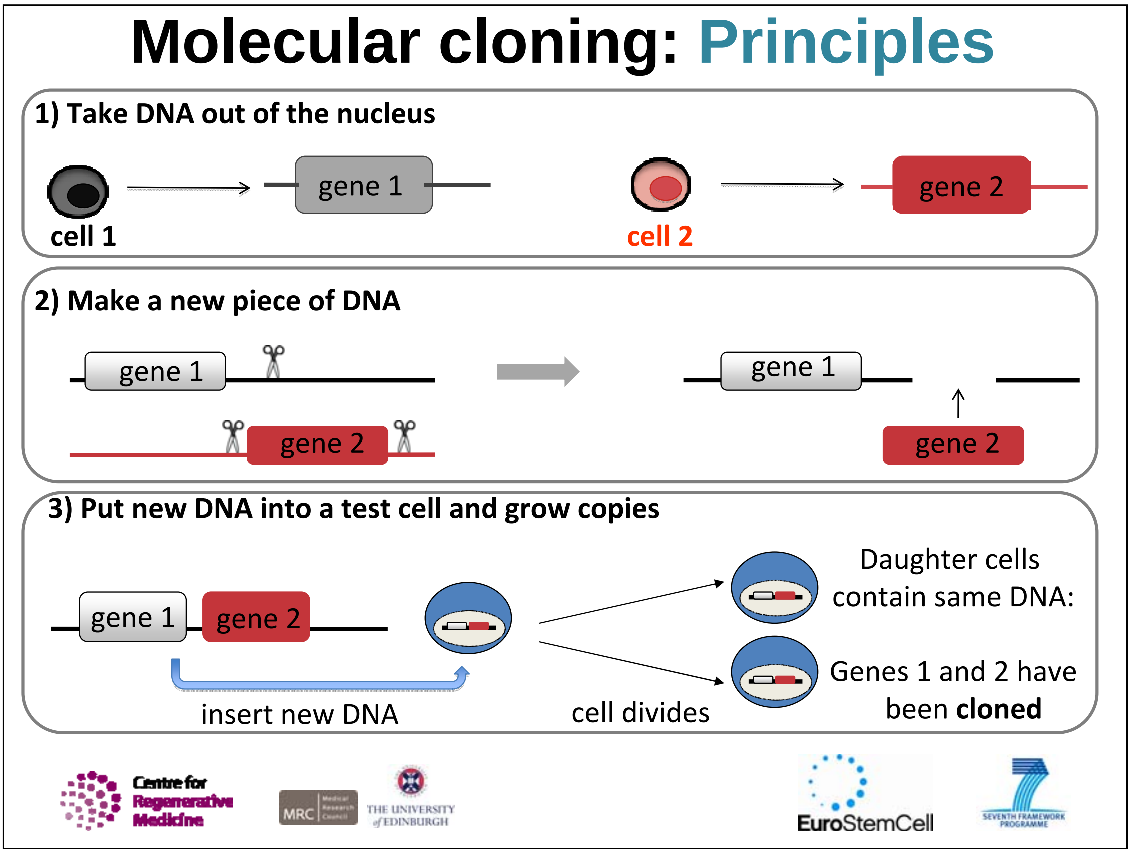
Reproductive cloning



Reproductive cloning

Dolly the sheep was the first cloned mammal. To make Dolly, scientists took the nucleus out of a normal cell from a sheep. They put that nucleus into an egg cell that had no nucleus. They then had a new cell. To make the new cell start to divide and grow, they gave it an electric shock. Then it started to divide and develop into an embryo. When it had grown into a very early stage embryo called a blastocyst – a ball of just 50-100 cells – it was implanted into the womb of another sheep so that it could grow into a lamb and be born. The new sheep is a clone of the sheep from which the nucleus was taken at the start of the process. Both sheep have the same DNA.

Not only sheep have been cloned. Scientists have now cloned many different animals, including mice, cats, dogs, frogs, goats, horses, pigs, rabbits and others. However, it is a difficult process and does not always work. It is illegal to clone a human being in this way.

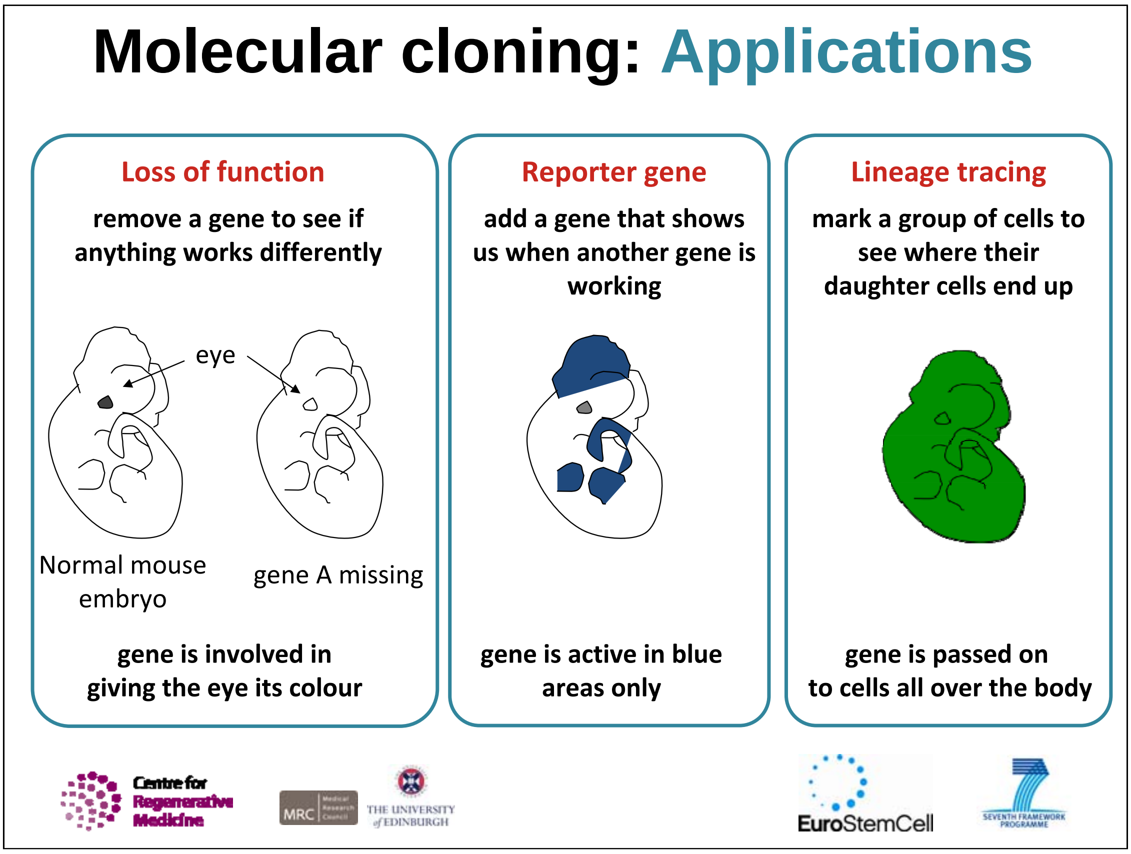


Molecular cloning: Principles

Molecular cloning is a process used by scientists to make copies of a particular gene or genes inside a cell. They use the technique to find out more about what certain genes do or how they work. Molecular cloning is done routinely in laboratories today. It involves several steps:

1) Take the DNA out of a cell.
2) Cut out the gene you are interested in (gene 2 in this example). Insert it into a strand of DNA taken from another cell. The gene is not literally cut out with a knife or scissors – carefully chosen enzymes break the DNA chain at particular points. More enzymes are used to insert the gene into another piece of DNA at exactly the right place (in this example, next to gene 1).
3) Once you have made a piece of DNA containing the gene you want to study, put your new DNA into a test cell. When the cell divides, it makes copies of itself. Each new daughter cell contains an exact copy of the DNA in your test cell, including genes 1 and 2. The genes have therefore been copied and we say they have been cloned.

This is a simplified description of the technique. There are some intermediate steps involved and the details of the technique can vary, but this scheme illustrates the key principle, i.e. we are able to make cells containing particular genes in order to find out what those genes do. Some examples of how this technique can be used are given on the next slide.



Molecular cloning: Applications

Molecular cloning is an important tool used by scientists to learn more about the roles of genes in development and disease. Some examples of how molecular cloning can be used in the lab are:

Loss of function (often called "gene knockout"): a common technique that has been very useful in helping scientists understand how particular genes are involved in disease. A gene is removed or blocked so that it does not work, and then scientists watch to see what happens. This has been of such wide benefit for science and medicine that the scientists who developed this technology were awarded the Nobel Prize for Medicine in 2007.

Reporter gene: this generally involves using colour to help scientists easily see when a particular gene is working. A 'reporter gene' is added to the DNA of cells. This reporter gene makes the cells produce a coloured protein – for example, a blue protein. The reporter gene is put into the cells' DNA right next to another gene (gene x) that scientists really want to investigate. Wherever gene x is active (or 'switched on') in a cell, the reporter gene is also active. This means the cell makes the blue protein and looks blue. So, it is easy to see which cells have an active gene x because those cells are blue.

Lineage tracing: this involves looking to see what happens to a cell's daughter cells, and their daughters, in a developing animal. First, some cells are marked by giving them a gene that scientists can easily see working, e.g. a gene to make a protein that is a fluorescent green colour. This makes the cells look green. Every time the cells divide, their daughter cells inherit the gene for the green protein, so the daughter cells are green too. This allows us to see when their marked cells divide and where they end up as an animal develops.

Stem cell biology in more detail

Tissue stem cell types and hierarchies

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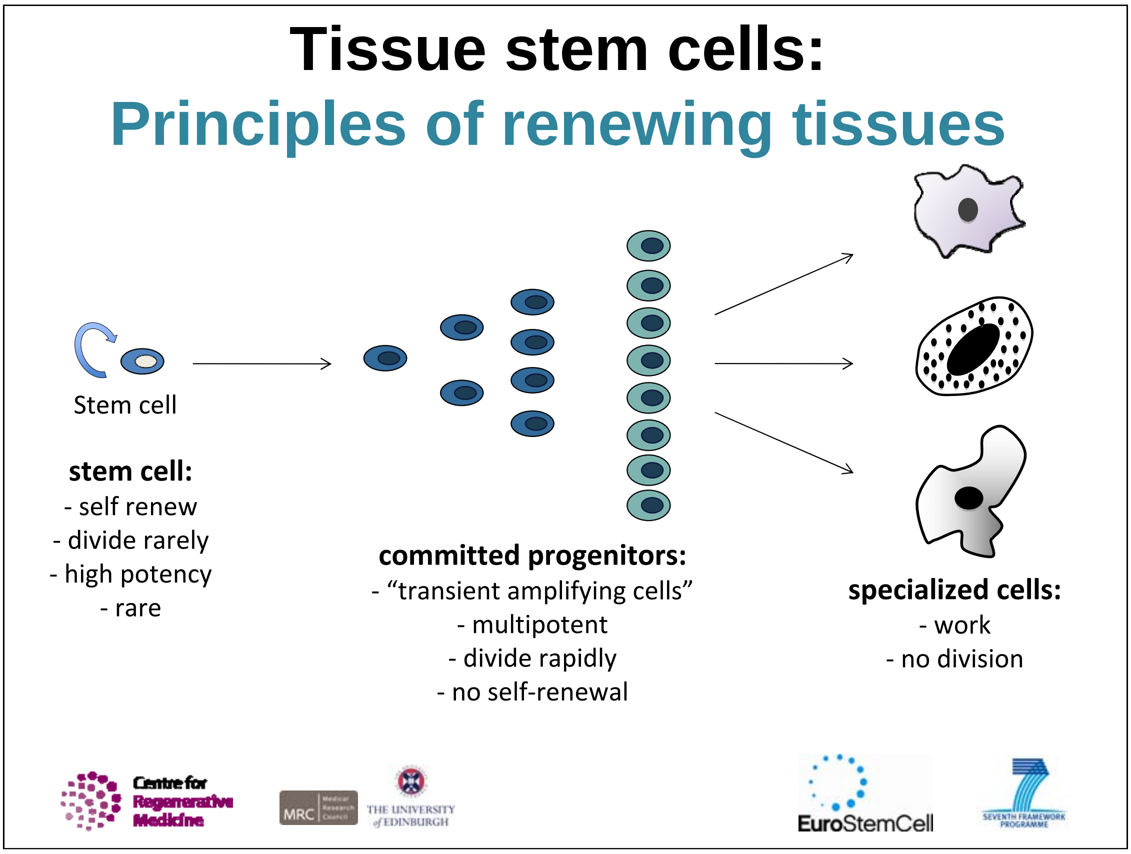


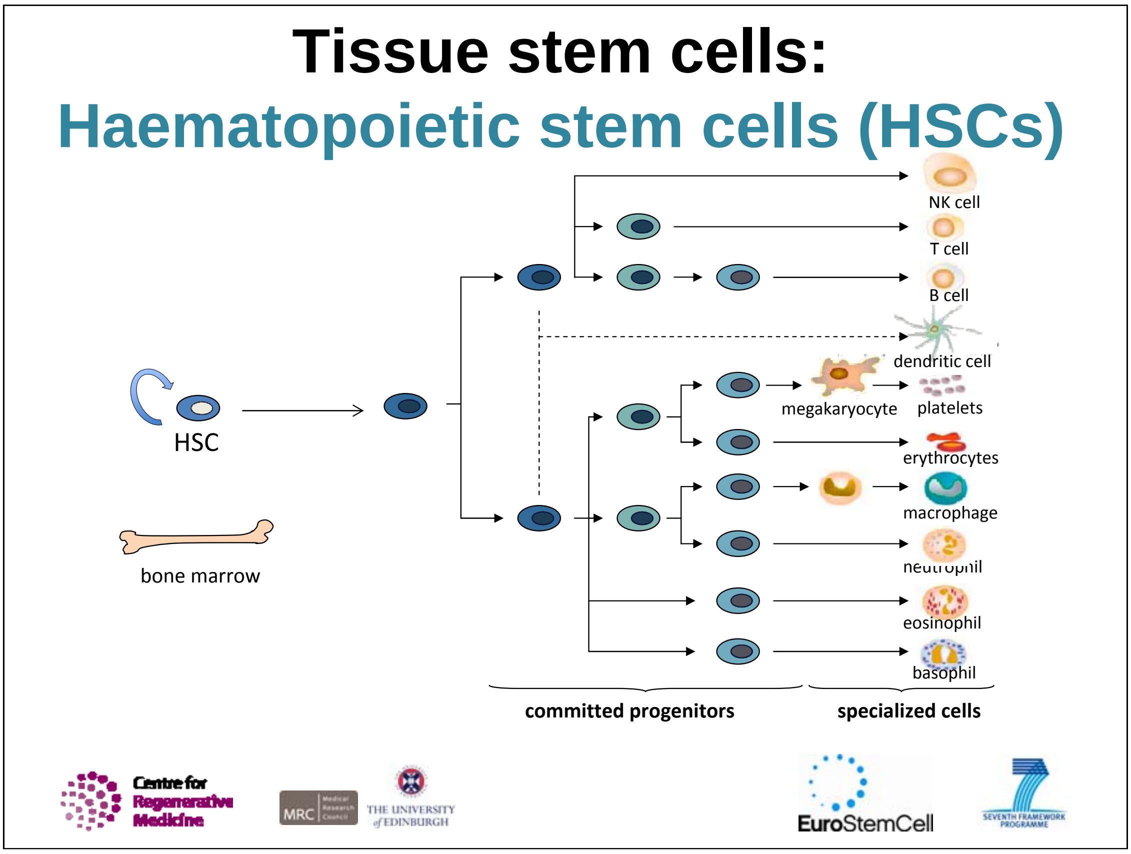
Tissue stem cells: Principles of renewing tissues

The slide shows the typical hierarchy of cells from tissue stem cell to specialized cell.

Stem cells give rise to committed progenitors. These are not fully differentiated cells but have different properties from stem cells – they are an intermediate cell type.

Committed progenitors will divide many times and will give rise to fully differentiated and functional cells via a series of steps.

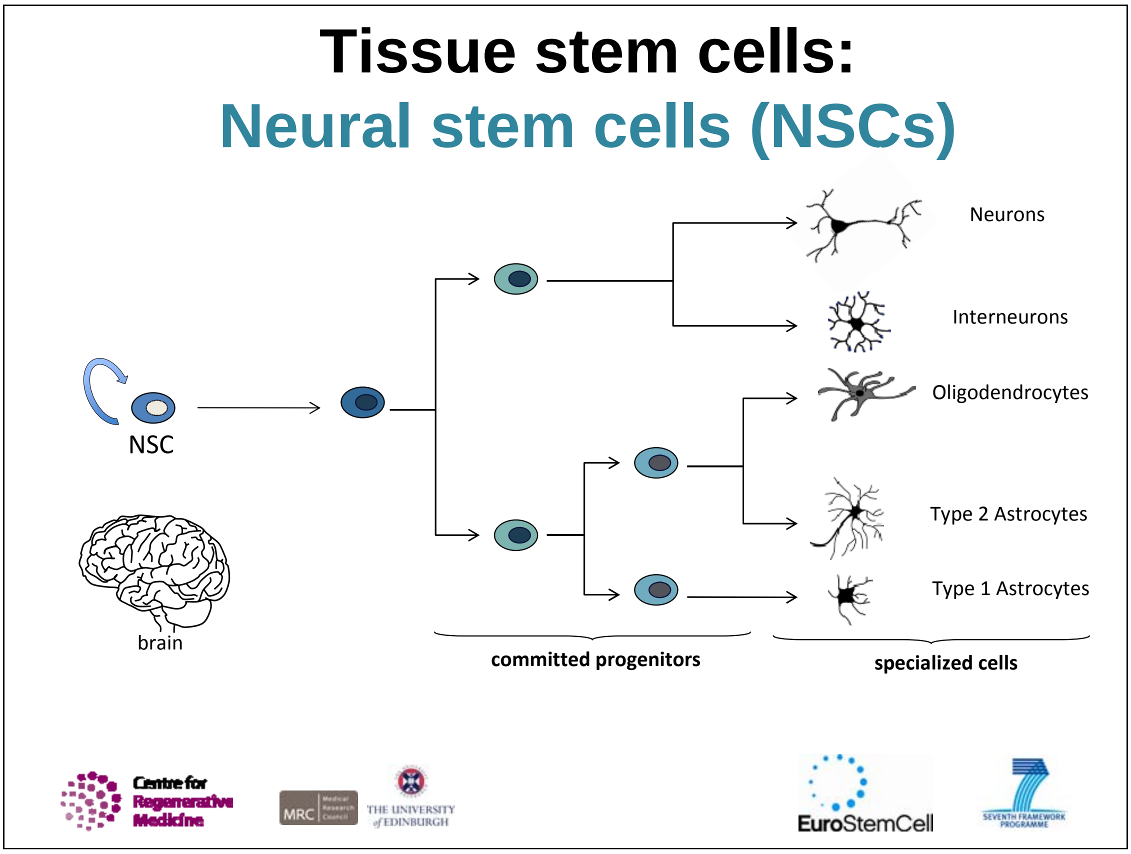
This typical hierarchy is applicable to many types of tissue stem cell (some examples are given in the following slides to illustrate this principle).



Tissue stem cells: Haematopoietic stem cells (HSCs)

HSCs = blood stem cells

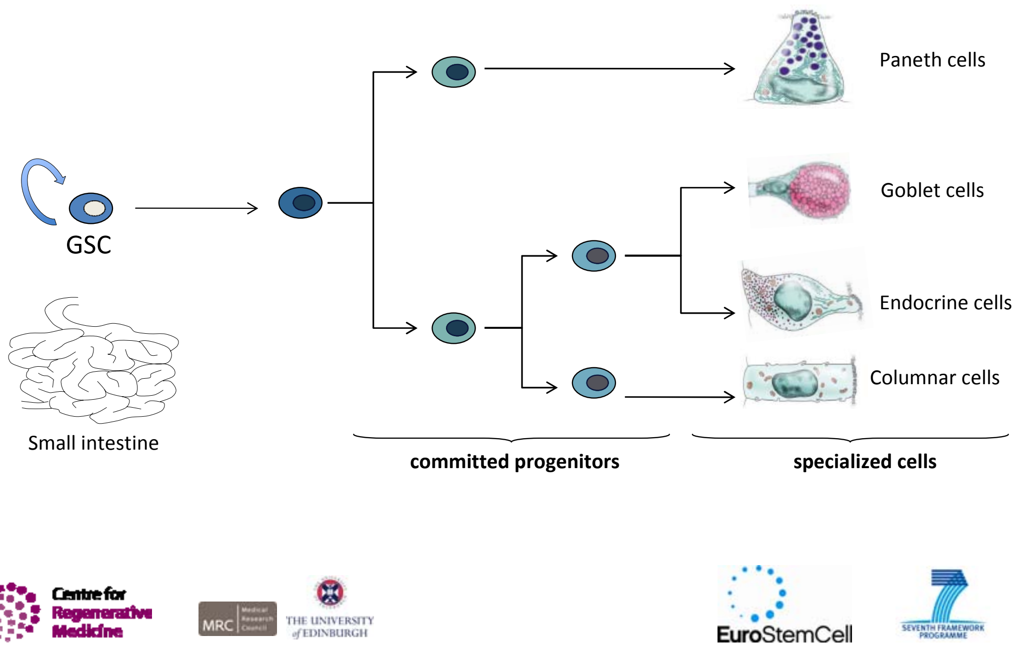
HSCs are isolated from the bone marrow. They give rise to committed progenitors, which then give rise to all specialized blood cell types.



Tissue stem cells: Neural stem cells (NSCs)

NSCs are isolated from specific areas of the brain. They give rise to committed progenitors, which then give rise to all specialized brain cell types.

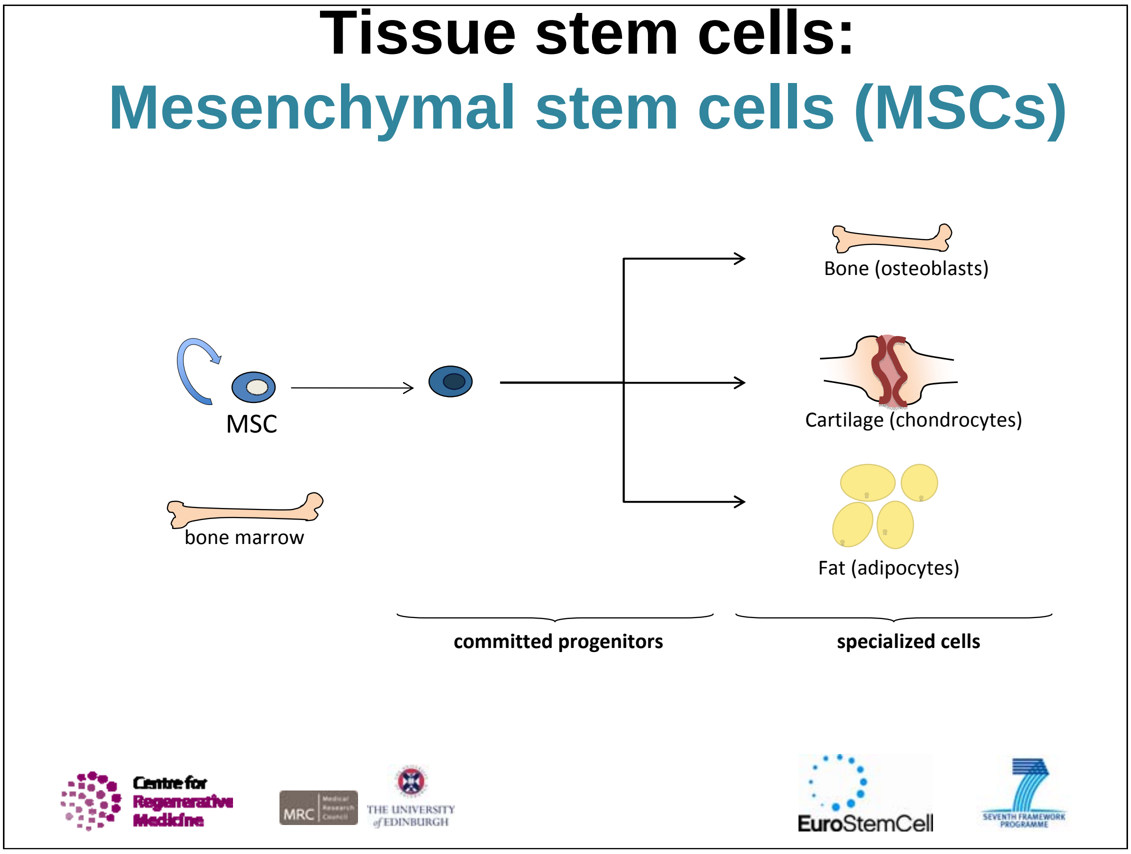
Tissue stem cells: Gut stem cells (GSCs)



Tissue stem cells: Gut stem cells (GSCs)

GSCs = intestinal stem cells

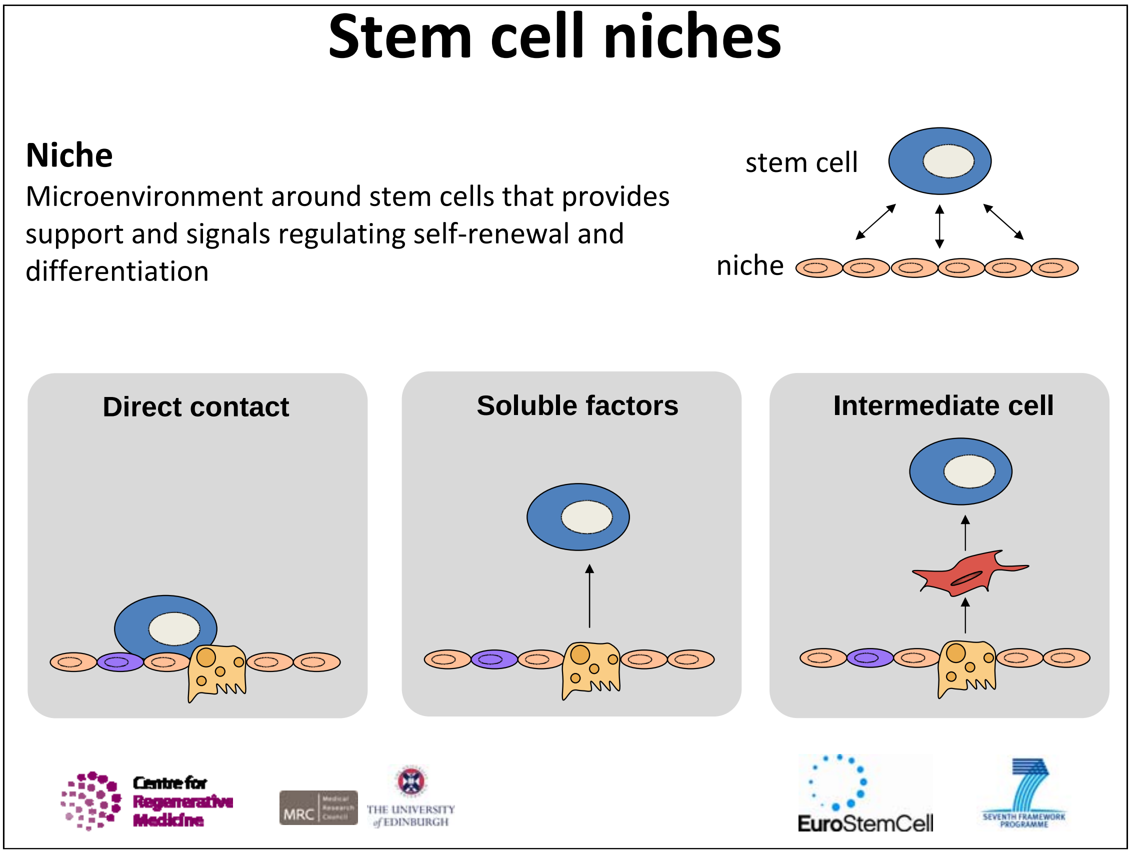
GSCs are present in the small intestine. They give rise to committed progenitors, which then give rise to all specialized intestinal cell types.



Tissue stem cells: Mesenchymal stem cells (MSCs)

MSCs are isolated from the bone marrow. They give rise to committed progenitors, which then give rise to all specialized mesenchymal cell types (bone, cartilage, fat).

Stem cells at home: The stem cell niche



Stem cell niches

The stem cell niche is a major concept in stem cell biology. Understanding the microenvironment around stem cells is as important as understanding stem cells themselves. The microenvironment regulates the behavior of stem cells and thus can teach us how to control stem cells in culture.

The niche can act on a stem cell by various mechanisms:

•Direct contact between the stem cell and the niche cells

•Soluble factors released by the niche that travel to the stem cell

•Intermediate cells that ‘communicate’ between the niche and the stem cell

Scientists are still working to understand exactly how niches work, and more is known about the niches of some kinds of stem cells than others.

Credits

Picture credits

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Slide 27, blood cell diagrams: Jonas Larsson, Lund Univeristy, Sweden
Slide 29, intestinal cell diagrams: Hans Clevers and Nick Barker, Hubrecht Institute, The Netherlands

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