Science4U School Science Conference 2022: RCPath workshop

http://science4u.info/
www.rcpath.org/SSC2022

Date and venue: 27 April 2022 at the University of Westminster
Theme: Science for Regeneration
Title of workshop: Totally Stem-azing Cells

Introduction:

Welcome to the Royal College of Pathologists' event, Totally Stem-azing Cells!

Pathology is the branch of medicine involved with the study and cure of disease. Pathologists are disease experts and by knowing how a disease works, they can make the right diagnosis and treat the patient. Pathology is central to modern healthcare – 70% of diagnoses involve pathology.

Watch our short video: What is a Pathologist?

NHSBT or NHS Blood and Transplant are involved in everything around blood and transplant services, from safely collecting and processing donations and caring for transfusion patients to supporting and caring for tissue and stem cell donors and patients. Today we'll be learning more about stem cells through a hands-on activity and discussing their use in treating a wide range of blood cancers and disorders.

Stem cells are cells that are capable of cell division and specialisation into different types of cells. This means they have the potential to be transplanted into patients to treat various medical conditions, replacing cells that have been damaged or destroyed. Examples of disorders include: cancers such as leukaemia, type 1 diabetes, multiple sclerosis and spinal cord injury.

For some people, a stem cell transplant (also known as a bone marrow transplant) is the only hope of survival. But matching donors to patients isn't easy. Between 65-75% of those patients in need won't have a sibling match, so will need to find a kind stranger - i.e. someone who has registered on the British Bone Marrow Registry. We (NHSBT) work closely with other stem cell registries in the UK (Anthony Nolan) and globally (Bone Marrow Donors Worldwide and the World Marrow Donor Association).

Cord blood is another source of stem cells. This is the blood that remains in the placenta and umbilical cord following the birth of a baby, and is usually thrown away. It is rich in blood stem cells similar to those found in bone marrow and can be used to treat many different cancers, immune deficiencies and genetic disorders.

You will be finding out a bit more about stems, where you can find them and how they are classified in the first hands on activity.

ACTIVITY 1 – Understanding Stem Cells

Key learning points

1. What are stem cells?
2. Stem cells are classified by their potential to different
3. They are found in embryos, cord blood, and in human tissues such as bone marrow and the brain and muscles.

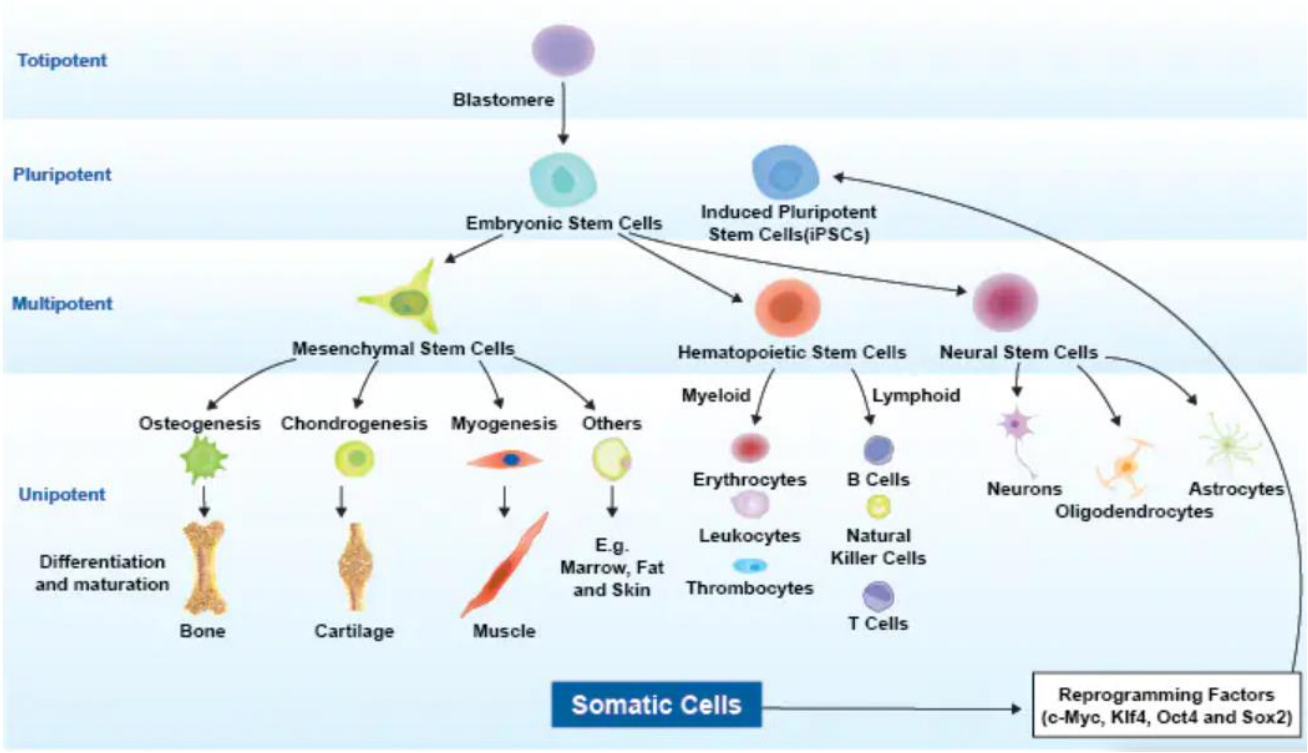
In this activity participants will learn that stem cells are the precursors to all other cells in our bodies, but some types can turn into many different cell types, whereas others can't.

All of us are made of cells.

- How many types of cell can you name?
- Where do all these cells come from?

Although there are hundreds of different types of cells, they all come from a basic undifferentiated/unspecialised cell called a stem cell. Stem cells are the precursors to every cell in our bodies.

https://www.novusbio.com/research-areas/stem-cells



Stem cells are characterised based on their potential to differentiate

- **Totipotent stem cells** can form all the cell types in a body, plus the extra-embryonic, or placental, cells. Embryonic cells within the first couple of cell divisions after fertilization are the only cells that are totipotent.

- **Pluripotent stem cells** can produce *all* of the types of specialised cells in the body, but not all cell types. Embryonic stem cells are pluripotent. Pluripotent stem cells are cells that have the capacity to self-renew by dividing and to develop into the three primary germ cell layers of the early embryo and therefore into all cells of the adult body, but not extra-embryonic tissues such as the placenta.

- **Multipotent stem cells** can produce a *multiple* types of specialised cells but not all types. They are more limited than pluripotent cells. Tissue stem cells (also sometimes called adult stem cells) are multipotent. e.g. brain cells and liver cells.

- **Unipotent stem cells** can only produce *one* cell type e.g. a muscle cell

Easy ways to remember the terminology: 'uni-' means 'one', 'multi-' means 'several/multiple', 'pluri-' means 'many' and 'toti-' means 'all'.

Examples of different cell families. See also the stem cell characterisation grid.

Blood cell family (multipotent)
Blood/haematopoietic stem cell
Red blood cell
White blood cell
Platelets

Brain cell family (multipotent)
Brain/neural stem cell
Neuron
Oligodendrocyte
Astrocyte

Embryo (pluripotent)
Embryonic stem cells
Embryo

Embryo with placenta and sac (totipotent)
Zygote

Muscle cell family (unipotent)
Muscle stem cell
Muscle fibres

Discussion points:
- 'Have you ever cut yourself?' Unipotent skin stem cells aid in the repair of skin.
- You can introduce multipotency by asking them about different blood cells, and explaining that they all come from the same stem cell.
- Totipotent cells exist right at the beginning of life.
- Explain that, when we were only one cell, that cell needed the potential to turn into any type of cell, in order to make the rest of us.

ACTIVITY 2: Saviour Siblings

The potential of stem cells to regenerate has made them an attractive tool for research into regenerative treatments. From neuronal disorders to cancer, stem cells could be used to treat many diseases. However the ethics surrounding sources, combined with the limited supply of donations explains why they are not yet a standard medical treatment option.

In this next part of the workshop, we're going to be looking at how stem cells can be used to treat a disease called Fanconi anaemia.

What is Fanconi anaemia?

Fanconi anaemia (FA) is a genetic disorder associated with

- physical defects (for example abnormal thumbs, short height, skin problems, organ defects etc)
- bone marrow failure with anaemia (due to low red blood cells), risk of infection (due to low white blood cells) and bleeding (due to low platelets).
- Patients with FA are also at risk of developing cancers particularly acute myeloid leukaemia (AML)

Is there a cure for Fanconi anaemia?

Hematopoietic stem cell transplantation (HSCT) is the only curative treatment option for the blood problems seen in Fanconi anaemia.

This treatment replaces stem cells from another healthy person (known as a donor).

These stem cells make their way to the bone marrow, where they begin to grow and make healthy red blood cells (which carry oxygen around the body), white blood cells (which prevent and fight infections) and platelets (which stop you bleeding).

Who can the donor be?

https://www.anthonynolan.org/patients-and-families/understanding-stem-cell-transplants

Stem cells can be donated from someone else (a donor) who has the matching tissue type (HLA type) collected from blood or from bone marrow. The donor can be:

1. **Family member** – Even if the patient has a brother or sister then there is less than a 30% chance that they will be a tissue match to allow them to be the donor

2. **Unrelated donor.** Anthony Nolan, a UK charity that works in the areas of leukaemia and hematopoietic stem cell transplantation, has a register of willing volunteers who are ready to donate their stem cells to someone in need of a transplant.

If you have an HLA tissue type that's rare or less common, it may be harder to find a matching donor, because there may be fewer people with your tissue type.

Patients are more likely to find a matching donor from someone with a similar ethnic background because our HLA tissue types are inherited. Anthony Nolan is hard at work, both in the UK and internationally, to encourage people from minority ethnic backgrounds to join their country's stem cell registers.

3. **Some people may be given stem cells from an umbilical cord.** Cord blood is found in an umbilical cord which connects a baby in the womb to the placenta. The placenta and umbilical cord are a rich source of stem cells.

A cord blood transplant can be an alternative option if a brother, sister or matched unrelated donor is not available. Stem cells found in cord blood are 'immature', which means they can develop to suit the patient and may not need to be an exact match.

What is a saviour sibling and what are the ethical issues?

A saviour sibling is a child who is conceived in order to provide an organ or cell transplant to a sibling that is affected with a fatal disease, such as cancer or Fanconi anaemia, that can best be treated by haematopoietic stem cell transplantation.

The saviour sibling is conceived through in vitro fertilization. Fertilized zygotes are tested for genetic compatibility (using a process called human leukocyte antigen (HLA) typing), using preimplantation genetic diagnosis (PGD), and only zygotes that are compatible with the existing child are implanted. Zygotes are also tested to make sure they are free of the original genetic disease.

Upon birth, umbilical cord blood is taken and used for haematopoietic stem cell transplantation.

In the United Kingdom, the Human Fertilisation and Embryology Authority (HFEA) has ruled that it is lawful to use modern reproductive techniques to create a saviour sibling to be considered by a case by case basis.

ACTIVITY 2 - TASK

In the case we're considering today, Sibling A, has Fanconi anaemi. Their parents have decided that they like to try and create a baby via IVF (sibling B) - they will select an embryo that is matched with the older sibling, so that they can help treat Sibling A.

At each of your tables, ask students to a go at listing some of the pros and cons of creating a saviour sibling. You may wish to consider the following points of view:

1. The parents
2. Sibling A
3. Sibling B

Questions/points to consider with students:

1. How would you feel if you were the
    a. Parents?
    b. Sibling A?
    c. Sibling B when they are older?
2. What happens to sibling A if a saviour sibling is not created?
3. What do the students think about the terms 'designer babies' and 'saviour siblings'? Would we need these 'special' babies to be born if enough people came forward to donate blood and register with the bone marrow registry, or if all new mothers donated umbilical cord blood?
4. Should a child be born primarily for the benefit of an existing child? Is this really the case for saviour siblings?
5. What is the impact on the life of the saviour sibling?
6. Is there a moral duty on the parents to do everything they can to protect the health of their existing child?
7. Does this moral duty include having another child?
8. Should the state fund the creation of another child in these circumstances?
9. The parents are capable of conceiving naturally, why does the state need to be involved?
10. Does this have an impact on the life of the pre-existing sibling?
11. If we think it's ethically acceptable, where should the line be drawn in relation to when a saviour sibling can be created?
12. What obligations can be placed on the saviour sibling once they have been born?
13. Collect cord blood at birth for use later on? Ongoing blood donations? Ongoing bone marrow donations? Donation of a solid organ? Where would you draw the line? Why?
14. If you want to take it further – why is this limited to saviour siblings? It's theoretically possible to clone people, so why don't we have a 'clone army' to provide society with a ready supply of healthy organs or bone marrow?

Extreme statements are the most useful to stimulate conversation:

1. 'It's never morally acceptable to create a person solely to benefit an existing person. The existing child should be allowed to die if there is no other treatment.'

    OR

2. 'The saviour sibling is being created to save the existing child, so their body should be used as much as necessary – blood donations, bone marrow donations, solid organ donations are all acceptable.'

Further information

There is quite a bit of information here, so feel free to use as much or as little as needed depending on time available.

Activity 1 – stem cells

Useful background links:

- STEM Cell page on the NHSBT website: https://www.nhsbt.nhs.uk/what-we-do/transplantation-services/stem-cells/
- Stem cell technology - The therapeutic use of cells - 4th level Science Revision - BBC Bitesize
- EuroStemCell page : Hope Beyond Hype comic: https://www.eurostemcell.org/hope-beyond-hype

RCPath events and competitions

Art of Pathology competition

Activity 2 – saviour siblings

There are not enough cord blood donations, especially from diverse donors (and many of the genetic conditions such as sickle cell anaemia and thalassaemia are seen more in those populations).

There are only four **public** cord blood banks in the UK (one in Scotland, one in Northern Ireland and two in England: NHSBT and The Anthony Nolan Trust). Only a small number of maternity hospitals within these areas can offer their mothers the opportunity to donate their cord blood to a public cord bank. Do the students think more people should be offered the opportunity to donate their cord blood, or do they not feel this is a good use of NHS resources?

There is extra information below on cord blood banking for students who wish to know more.

Background on umbilical cord banking

The umbilical cord connects the fetus/baby to the placenta. The cord supplies blood and nutrients to the fetus while it is in the uterus. At the time of delivery, the cord is clamped and cut, to separate the baby from the placenta. A short time later, the mother delivers the placenta and cord, which is discarded as clinical waste. In cord blood collection for banking, a needle is inserted into the cord (once the baby has been delivered and the cord cut) and the blood from the cord is collected into a cord blood pack. The cord blood is then processed back at the cord blood bank, frozen and stored at below -180^{0}C. It can be stored in the cord blood bank at this temperature for many years.

Cord blood is known to be very rich in ‘haemopoietic stem cells’. These are similar to stem cells found in the bone marrow but may be even more flexible in the type of cells and tissues that they can potentially become. Just like bone marrow, cord blood can be used to perform a stem cell transplant in a patient who requires replacement of their bone marrow e.g. in leukaemia, or in inherited blood disorders such as Thalassaemia or Fanconi’s anaemia. The first cord blood transplant was carried out in France in 1988 and the number of cord blood transplants taking place worldwide has increased year on year since then. Stem cell transplants have the best chance of success when there is a full tissue-type match between the donor and the patient.

Because of the complexities of human tissue-types, the best match will always come from a ‘HLA identical sibling’ – this is a brother or sister who has been shown to carry exactly the same tissue-type as the patient. However, successful transplants can also take place between a well-matched unrelated donor and the patient. In very general terms, the closer the match, the better the outcome. A further complication is that tissue-types can vary significantly between different racial groups. The number of Asian and African descent donors enrolled on the UK bone marrow panel

is significantly lower than the number of Caucasian (white) donors. Cord blood banking may help this issue as many cord banks seek to recruit antenatal patients from a wide variety of ethnic backgrounds. This enriches the diversity of tissue-types that they hold in the cord blood bank and may improve the chance of a patient from a non-Caucasian background of being able to find a match.

BBC report
This BBC report describes the first successful saviour sibling treatment in the UK for a child with Fanconi's anaemia in 2010. The patient was called Megan and the saviour sibling was called Max

https://www.bbc.co.uk/news/health-12055034

The BBC report includes the following consideration of ethical issues:

- Simon Fishel, managing director of Care Fertility, said: "This is fantastic and positive medial science.
- "The ethical issues are in favour of doing this work. We are trying to save the life of a child and achieve a family without the enormous burden of a child with this disorder who would die."
- But Josephine Quintavalle, Director of Comment on Reproductive Ethics said of Max: "He owes his life to his capacity to be of therapeutic use to his sick sister, otherwise he would not have been chosen in the first place. "This is the big ethical problem."
- The mother Kate Matthews said: "Max is loved for being him and not for what he has done. He has completed our family and now I have a bubbly and healthy girl."
- Megan's genetic disorder, Fanconi Anaemia, means that she may face long-term health problems. But her family say they will face those hurdles when and if they come to them.

Notes and resources to think about the ethics of saviour siblings (and questions 4-14 from discussion activity) - Ruth Stirton 21 April 2022

Saviour siblings are created using preimplantation genetic diagnosis (PGD) and in-vitro fertilisation (IVF). It is only available where there is a pre-existing child with a life threatening condition, for which there is no other treatment. The aim is to create an embryo which is a genetic match for the existing child, but which does not carry the genetic mutation which causes the life-threatening illness. In the case of Megan Matthews (2010), it was Fanconi Anaemia, in Charlie Whitaker's case (2003) it was Diamond Blackfan Anaemia, in Zain Hashmi's case (2003) it was Thalassaemia. Saviour siblings can only be created with the approval of the Human Fertilisation and Embryology Authority. This is considered on a case-by-case basis.

Useful links/resources

- https://www.hfea.gov.uk/treatments/embryo-testing-and-treatments-for-disease/pre-implantation-tissue-typing-ptt/
- https://www.dailymail.co.uk/health/article-1389499/I-know-I-born-save-Charlie-instead-born-just-Brotherly-love-saviour-sibling.html
- Zain Hashmi article
- https://www.bionews.org.uk/page_160806 - Compensation paid after IVF clinic used wrong embryo for 'saviour' sibling 2021
- https://www.bbc.co.uk/news/health-12055034 - First successful saviour sibling donation in the UK 2010

- Film/book: My Sister's Keeper, Jodi Picoult - https://www.imdb.com/title/tt1078588/ https://www.jodipicoult.com/my-sisters-keeper.html

- Clones: Never Let Me Go, Kasuo Ishiguro - https://www.imdb.com/title/tt1334260/ https://en.wikipedia.org/wiki/Never_Let_Me_Go_(novel)

- https://getrevising.co.uk/grids/arguments_for_and_against_saviour_siblings

- https://getrevising.co.uk/grids/saviour-siblings

- https://explorebiotech.com/pros-cons-designer-baby/

- https://sites.lib.jmu.edu/elsi-biotech/reproductive-biotechnology/savior-siblings-and-cloning/

- https://www.google.com/amp/s/www.bbc.co.uk/news/health-12055034.amp

- British Bone Marrow Registry: https://www.bbmr.co.uk/
- Anthony Nolan: https://www.anthonynolan.org
- Cord blood: https://www.nhsbt.nhs.uk/what-we-do/blood-services/cord-blood-donation/

- Virtual Careers Talk event where haematologist, Dr Mahesh Sharma, talks about bone marrow transplants: https://youtu.be/wn9IWQ3Ykew (His talk starts at 13 mins 45 seconds into the video.)