Stem Cells

Definition

- Undifferentiated and unspecialised cells
- Capable of extensive proliferation and self-renewal via mitosis ⇒ Maintains constant pool of stem cells
- Able to differentiate into specialised cells due to differential switching on of genes upon receiving the appropriate molecular signals ⇒ Stem cells carrying normal functional allele can differentiate into the specialised cell type of damaged tissue + Specialised cell will carry normal functional allele which can produce normal levels of functional protein ⇒ Treats genetic diseases

Types of cell division:

- Symmetrical (proliferation)
    - Produces 2 identical daughter stem cells to maintain a constant pool of stem cells
- Asymmetrical (self-renewal)
    - Produces 1 daughter stem cell → Ensure constant pool of stem cells
    - Produces 1 progenitor daughter cell → Increase/renew population of specialised cells in a specific tissue
        - Progenitor daughter cell = Partially specialised cell which can differentiate into related specialised cell

Types of stem cells/differentiation potential

Totipotent	Pluripotent	Multipotent
Ability to differentiate into all cell types that make up an organism **including extra-embryonic tissue** such as the placenta which nourishes the embryo	Ability to differentiate into all cell types that make up an organism **except extra-embryonic tissue** such as the placenta	Ability to differentiate only into **several related** cell types
Able to form the entire organism	Cannot form the entire organism alone	-
Zygotic stem cell derived from a fertilised egg. Cells produced within the first 3 divisions (8 cell stage) after	**Embryonic stem cell** derived from cells of inner cell mass of blastocyst at about 4-5 days post	**Adult stem cells** e.g. Haematopoietic stem cells found in bone marrow/Neural stem cells

the egg is fertilised	fertilisation	found in the brain

Explain the normal functions of stem cells in a living organism

- Stem cells are **undifferentiated** and **unspecialised** cells
- Capable of extensive proliferation and **self-renewal** to ensure a constant pool of stem cells with the same development potential
- Stem cells divide by **mitosis** to produce genetically identical daughter cells
- For growth and development
- To regenerate/replace cells that are lost due to normal cell death and injury
- Able to **differentiate** into specialised cells due to differential switching on and off of genes upon receiving the appropriate molecular signals
- Zygotic stem cells are **totipotent** and can differentiate into all cell types that make up an organism including extra embryonic tissue
- Embryonic stem cells are **pluripotent** and can differentiate into all cell types except the extra-embryonic tissue
- Adult stem cells are **multipotent** and can differentiate into a limited range of related cell types
- e.g. Haematopoietic stem cells differentiate into red and white blood cells only

e.g. Haematopoietic stem cell in bone marrow

- Divide asymmetrically after stimulation by molecular signals ⇒ Produce stem cells for maintenance of stem cell pool + Progenitor cells to increase/renew population of specialised blood cells
- B and T lymphocytes (white blood cells) from lymphoid progenitor cell
- Red blood cells and platelet producer cells from myeloid progenitor cell

Stem Cell Transplant
E.g. Bone marrow haematopoietic stem cell transplants to leukaemia patients

- Leukaemia = Cancer of the blood/bone marrow leading to abnormal increase in number of immature white blood cells (blast cells) which are non-functional and crowd the bone marrow, preventing production of functional white blood cells
- Treatment:
    - Patient irradiated to remove existing haematopoietic stem cells and white blood cells from the body
    - Bone marrow from haematopoietic stem cells from normal, healthy bone marrow donors multiplied and infused into patient
    - Haematopoietic stem cells can then populate the bone marrow and differentiate into normal blood cells
    - Stem cells capable of self-renewal, ensuring a constant pool of stem cells ⇒ no need for repeated transplants

Explain why stem cells can continuously divide mitotically

- Each round of cell division involves DNA replication which results in the shortening of telomeres at the ends of the chromosome due to end replication problem
- When telomeres are shortened to a critical length, cells undergo programmed cell death/apoptosis
- However, stem cells are able to express the telomerase gene to produce telomerase that lengthens the telomeres, allowing them to proliferate continuously
- In other cells, the expression of this gene is switched off

Reasons for weaker expression of normal allele

- Donated stem cells likely to have 2 copies of normal functional allele and hence, likely to have higher levels of expression than transduced cells that have at most 1 copy of normal functional allele integrated into its genome
- Normal functional allele may be linked to and regulated by weaker promoter
- Normal functional allele may not be stably integrated into genome and hence is gradually lost with each subsequent cell division
- Low success rate of gene therapy ⇒ few successfully transduced stem cells
- Normal functional allele may be under the influence of enhancer element while the other is not
- Normal functional allele may be under the influence of silencer element