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PROJECT TITLE - STEM CELLS RESEARCH

BENG102P – TECHNICAL REPORT WRITING

Submitted by

SNEHA VEJJU (21BIT0647)

Submitted to

Prof. Christopher Rajasekaran Wilson

School of Social Sciences & Languages (SSL)

VIT, Vellore Tamil Nadu – 632 014

Introduction and Abstract:

What is Stem Cell Research?

- These are the blood cell-forming adult stem cells found in bone marrow.
- Every type of blood cell in the bone marrow starts as a stem cell. Stem cells are immature cells that are able to make other blood cells that mature and function as needed.
- These cells are used in procedures such as bone marrow transplants.

Stem cells are a population of undifferentiated cells characterized by the ability to extensively proliferate (self-renewal), usually arise from a single cell (clonal), and differentiate into different types of cells and tissue (potent).

There are several sources of stem cells with varying potencies.

Pluripotent cells are embryonic stem cells derived from the inner cell mass of the embryo and induced pluripotent cells are formed following reprogramming of somatic cells.

Pluripotent cells can differentiate into tissue from all **3 germ layers** (endoderm, mesoderm, and ectoderm).

Multipotent stem cells may differentiate into tissue derived from a single germ layer such as mesenchymal stem cells which form adipose tissue, bone, and cartilage.

Tissue-resident stem cells are oligopotent since they can form terminally differentiated cells of a specific tissue.

Stem cells can be used in cellular therapy to replace damaged cells or to regenerate organs.

In addition, stem cells have expanded our understanding of development as well as the pathogenesis of disease.

Disease-specific cell lines can also be propagated and used in **drug** development.

Despite the significant advances in stem cell biology, issues such as ethical controversies with embryonic stem cells, tumor formation, and rejection limit their utility.

However, many of these limitations are being bypassed and this could lead to major advances in the management of disease as well as applications of these cells in regenerative medicine.

Stem cells are undifferentiated cells that are present in the embryonic, fetal, and adult stages of life and give rise to differentiated cells that are building blocks of tissue and organs.

In the post-natal and adult stages of life, tissue-specific stem cells are found in differentiated organs and are instrumental in repair following injury to the organ.

The major characteristics of stem cells are:

(a) self-renewal (the ability to extensively proliferate)

(b) clonality (usually arising from a single cell

(c) potency (the ability to differentiate into different cell types).

These properties may differ between various stem cells.

For example: embryonic stem cells (ESCs) derived from the blastocyst have a greater ability for self-renewal and potency while stem cells found in adult tissue have limited self-renewal since they would not proliferate extensively and can only differentiate into tissue-specific cells.

Specific organs arise from the germ layers. Some of the progenitor cells that have contributed to organ formation do not terminally differentiate but are retained as tissue stem cells and can be found in bone marrow, bone, blood, muscle, liver, brain, adipose tissue, skin, and the gastrointestinal tract.
The tissue stem cells may be called progenitor cells since they give rise to terminally differentiated and specialized cells of the tissue or organ.

The dynamics of tissue stem cells or progenitor cells varies from tissue to tissue; for example, in bone marrow, liver, lung, and gut, stem cells regularly proliferate to supplement cells during normal turnover or injury, while in the pancreas, the heart, or the nervous system they proliferate to replace damaged cells following injury.

Stem Cell Classification Based on Differentiation Potential:

The ability to differentiate, one of the two main characteristics of stem cells, varies between stem cells depending on their origin and their derivation.

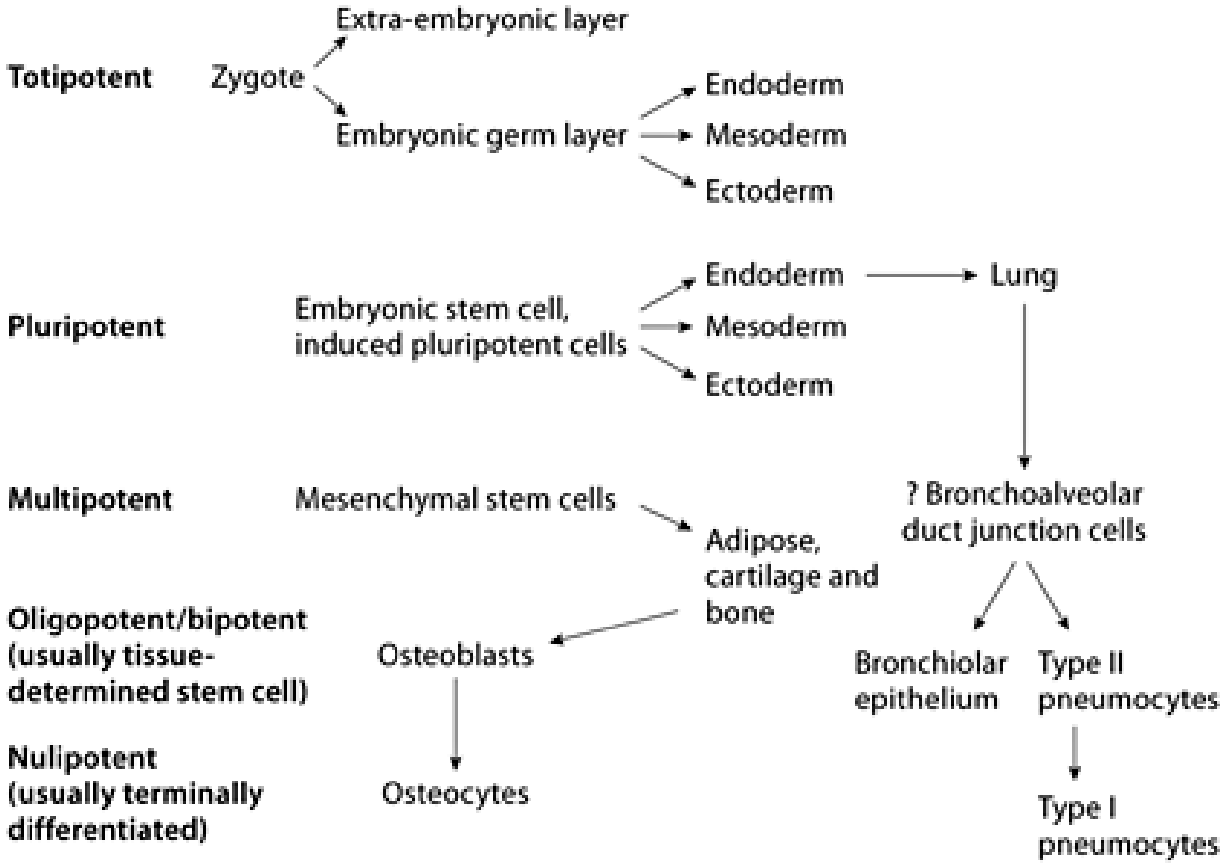
All stem cells can be categorized according to their differentiation potential into 5 groups:

- totipotent or omnipotent
- pluripotent
- multipotent
- oligopotent
- unipotent

Differentiation potential	Origin
Totipotent or omnipotent	
Pluripotent	ESCs, iPSCs
Multipotent	Fetal stem cells
Oligopotent	Adult or somatic stem cells
Unipotent	

The hierarchy of stem cells. Totipotent cells form embryonic and extra-embryonic tissue. Pluripotent cells form all **3** germ layers while multipotent cells generate cells limited to **1** germ layer.

Bronchoalveolar duct junction cells in the lung may be multipotent while type II pneumocytes are oligopotent and differentiate into type I pneumocytes of the alveoli.



i. Totipotent:

Totipotent or omnipotent cells are the most undifferentiated cells and are found in early development. A fertilized oocyte and the cells of the first two divisions are totipotent cells, as they differentiate into both embryonic and extraembryonic tissues, thereby forming the embryo and the placenta.

ii. Pluripotent:

Pluripotent stem cells are able to differentiate into cells that arise from the 3 germ layers – ectoderm, endoderm, and mesoderm – from which all tissues and organs develop.
Pluripotent stem cells called ESCs were first derived from the inner cell mass of the blastocyst.
These cells are called induced pluripotent stem cells (iPSCs) and share similar characteristics with ESCs. Notably, there has been no pluripotent cell population isolated from the lung.

iii. Multipotent:

Multipotent stem cells are found in most tissues and differentiate into cells from a single germ layer.
Mesenchymal stem cells (MSCs) are the most recognized multipotent cell. They can be derived from a variety of tissue including bone marrow, adipose tissue, bone, Wharton's jelly, umbilical cord blood, and peripheral blood.
These cells can differentiate into mesoderm-derived tissue such as adipose tissue, bone, cartilage, and muscle.

iv. Oligopotent:

Oligopotent stem cells are able to self-renew and form 2 or more lineages within a specific tissue; for example, the ocular surface of the pig, including the cornea, has been reported to contain oligopotent stem cells that generate individual colonies of corneal and conjunctival cells.

v. Unipotent:

Unipotent stem cells can self-renew and differentiate into only one specific cell type and form a single lineage such as muscle stem cells, giving rise to mature muscle cells and not any other cells. In the lung, type II pneumocytes of the alveoli give rise to type I pneumocytes.

Stem Cell Classification Based on Origin:

Stem cells can be grouped into 4 broad categories based on their origin: ESCs, fetal and adult stem cells, and iPSCs. In general, ESCs and iPSCs are pluripotent, whereas adult stem cells are oligopotent or unipotent.

- Embryonic Stem Cells
- Adult Stem Cells
- Tissue Resident Stem Cells
- Induced Pluripotent Stem Cells

i. Embryonic Stem Cells:

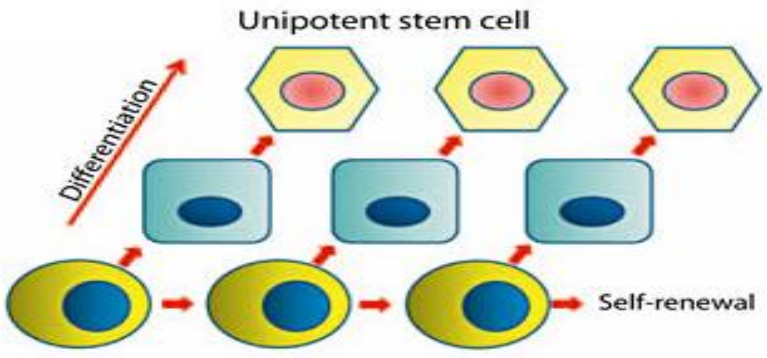
ESCs are pluripotent, derived from the inner cell mass of the blastocyst, a stage of the pre-implantation embryo, 5–6 days post-fertilization.
ESCs are identified by the presence of transcription factors such as Nanog and Oct4.
These factors maintain the stem cells in an undifferentiated state, capable of self-renewal.

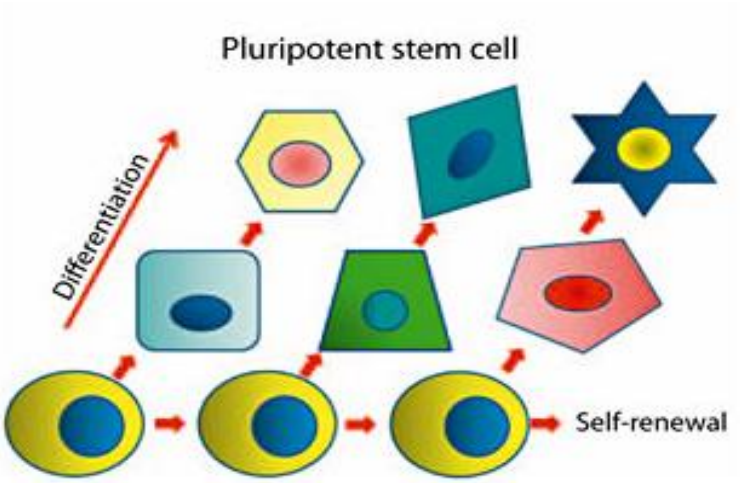
ii. Adult Stem Cells:

Adult stem cells are derived from adult tissue.
These cells have been shown to be anti-inflammatory and augment repair of animal models of injury.
Adult stem cells are of advantage since autologous cells do not raise issues of rejection or ethical controversies. Adult stem cells could be obtained from all tissues of the 3 germ layers as well as placenta.

iii. Tissue Resident Stem Cells:

The ability of some tissues and organs in the adult to renew and repair following injury is critically dependent on tissue-resident stem cells that generate tissue-specific, terminally differentiated cells.
Tissue-resident stem cells reside in a ‘stem cell niche’.
The majority of tissue-resident stem cells are dormant but are activated by specific signals during **injury** and **repair**.
Symmetrical cell division by a stem cell results in identical daughter cells, which provides new cells to rectitude damaged cells following injury
Asymmetric division occurs when a stem cell generates an identical daughter cell and a second differentiated daughter cell.
This process allows for organ repair and regeneration while maintaining a population of stem cells





iv. Induced Pluripotent Stem Cells:

iPSCs are produced from adult somatic cells that are genetically reprogrammed to an 'ESC-like state'.
Transducing mouse fibroblasts with 4 genes:

- Octamer-binding transcription factor 3/4 (OCT3/4)
- SRY-related high-mobility group box protein-2 (SOX2)
- oncoprotein c-MYC
- Kruppel-like factor 4 (KLF4).

Then, adult human dermal fibroblasts with the same 4 factors:

- Oct3/4
- Sox2
- Klf4
- c-Myc.

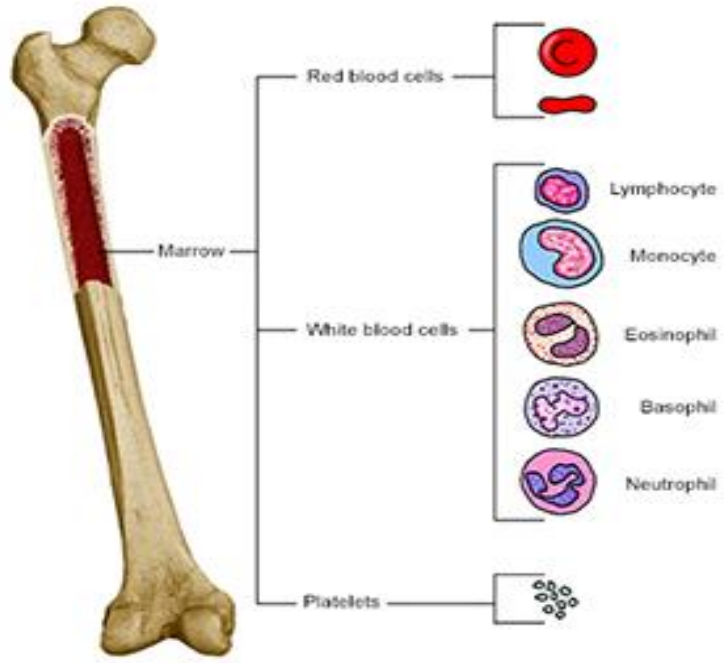
To avoid the use of oncoproteins c-MYC and KLF4 they have used one factor (OCT3/4 or KLF4) or they have substituted them with combinations of other factors, including the use of non-retroviral vector approaches, such as chemical compounds, plasmids, adenovirus, and transposons.
Despite the **safety** issues, this innovative discovery has created a powerful tool to reprogram somatic adult cells 'sending them back' to earlier undifferentiated stages and generating iPSCs, thereby creating an identical match to the cell donor and thus avoiding issues of rejection.

Advantages and Disadvantages of Stem Cells:

	Adult Stem Cells	Embryonic Stem Cells	Induced Pluripotent Stem Cells
Pros	• Trans differentiate and and reprogramming of these cells is possible but is not well studied • Thought to be less likely to be rejected if used in transplants • Success has already been demonstrated in various clinical applications	• Can maintain and grow for 1 year or more in culture • Established protocols for maintenance in culture • ESCs are pluripotent cells that can generate most cell types • By studying ESCs, more can be learned about the process of development	• Abundant somatic cells of donor can be used • Issues of histocompatibility with donor/recipient transplants can be avoided • Very useful for drug development and developmental studies • Information learned from the "reprogramming" process may be transferable for *in vivo* therapies to reprogram damaged or diseased cells/tissues
Cons	• Limitations on ASC ability to differentiate are still uncertain; currently thought to be multi or unipotent. • Cannot be grown for long periods of time in culture • Usually a very small number in each tissue making them difficult to find and purify • Currently there is no technology available to generate large quantities of stem cells in culture	• Process to generate ESC lines is inefficient • Unsure whether they would be rejected if used in transplants. • Therapies using ESC avenues are largely new and much more research and testing is needed • If used directly from the ESC undifferentiated culture prep for tissue transplants, they can cause tumors (teratomas) or cancer development	• Methods for ensured reproducibility and maintenance, as differentiated tissues are not certain. • Viruses are currently used to introduce embryonic genes and has been shown to cause cancers in mouse studies

Stem Cells in Clinical Practice and Regenerative Medicine:

The contribution of stem cells in modern medicine is of paramount importance, both for their broad use in basic research and for the opportunities they give us to develop new therapeutic strategies in clinical practice.
Stem cells such as iPSCs will be critical in the investigation of new and safe therapies.
In addition, stem cells may be able to **replace damaged tissue** or even **regenerate organs**.
Cell therapy has been investigated in almost every degenerative disorder.
Promising results from preclinical studies and clinical trials have already been described in several diseases, such as diabetes mellitus, chronic myeloid leukaemia, cirrhosis, pulmonary fibrosis, Crohn's disease, heart failure, and disorders of the nervous system, and the immunomodulatory effects of stem cells have found their utility in several conditions characterized by predominant inflammation.



There are issues to consider in cell therapy and **regenerative medicine**.
Genetic instability can give rise to tumour formation. Indeed, the plasticity and self-renewal that characterize stem cells could lead to carcinogenesis in the host tissue, while spontaneously occurring teratomas and related tumours could develop from the use of ESCs or iPSCs in therapeutic cell transplantation.

Uses of Stem Cells:

- Grow new cells in a laboratory to replace damaged organs or tissues.
- Correct parts of organs that don't work properly.
- Research causes of genetic defects in cells.
- Research how diseases occur or why certain cells develop into cancer cells.

Facts about Stem Cells:

- Stem cells are highly adaptable
- Studies were first conducted on mouse embryos
- There is a lot of potential for diseases that could be cured
- Test new drugs for safety and effectiveness

Outcome and Conclusion:

Data reveal the importance of improving knowledge and information about the therapeutic and research potential of stem cells

Stem cells are an important tool for understanding both the organogenesis and the continuous regenerative capacity of the body.

They could be a model for the study of pathogenetic mechanisms and could assist researchers in understanding the pathophysiology of various diseases.

They also offer the possibility of developing biological models for the study of new pharmacological agents.

However, the most important potential of these cells is to replace damaged tissue and even regenerate organs.

To date, a large number of research protocols, preclinical studies, and clinical trials have been published.

Although, several clinical studies have already reported encouraging results for the development of new therapeutic strategies in cell-based medicine, there are a number of risks and obstacles.

Despite this, there is ongoing research and development that gives us great optimism about regenerative medicine.

Information about cryopreservation of cordonal stem cells is especially critical in gynaecologists and paediatricians since they are the main stem informer from physicians to future mothers. Sadly, the Italian percentage of cryopreserved cordonal stem cells is particularly low.

In conclusion, we believe that human beings have the right to be informed in order to take decisions concerning their body parts, their biological tissues collection, and their relative destination and utilization.

References/Bibliography/Citation:

- Wikipedia
- Verizon
- VIT Faculties
- Students (both from and outside VIT)