Introduction

Stem cells are primal cells found in all multicellular organisms that retain the ability to renew themselves through mitotic cell division and can differentiate into a wide range of specialized cell types ***(Becker et al., 1963 and Siminiovitch et al., 1963)***.

The rigorouis definition of a stem cell requires that it possesses two properties:

- **Self-renewal:** the ability to go through numerous cycles of cell division while maintaining the undifferentiated state.
- **Unlimited potency:** the capacity to differentiate into any mature cell type. In a strict sense, this makes stem cells either totipotent or pluripotent, although some multipotent and/or unipotent progenitor cells are sometimes referred to as stem cells.

Potency specifies the differentiation potential (the potential to differentiate into different cell types) of the stem cell.

- **Totipotent** stem cells are produced from the fusion of an egg and sperm cell. Cells produced by the first few divisions of the fertilized egg are also totipotent. These cells can differentiate into embryonic and extraembryonic cell types.
- **Pluripotent** stem cells are the descendants of totipotent cells and can differentiate into cells derived from the three germ layers.
- **Multipotent** stem cells can produce only cells of a closely related family of cells (e.g. hematopoietic stem cells differentiate into red blood cells, white blood cells, platelets, etc.).

- **Unipotent** cells can produce only one cell type, but have the property of self-renewal which distinguishes them from non-stem cells.

(Friedenstein et al., 1974 and Friedenstein et al., 1976)

The three broad categories of mammalian stem cells are: embryonic stem cells, derived from blastocysts, adult stem cells, which are found in adult tissues, and cord blood stem cells, which are found in the umbilical cord ***(Tuch, 2006)***.

Embryonic stem cells are cultures of cells derived from the epiblast tissue of the inner cell mass (ICM) of a blastocyst. A blastocyst is an early stage embryo – approximately 4 to 5 days old in humans and consisting of 50-150 cells. ES cells are pluripotent, and gives rise during development to all derivatives of the three primary germ layers: ectoderm, endoderm and mesoderm.

Because of their unique combined abilities of unlimited expansion and pluripotency, embryonic stem cells (ES) are a potential source for regenerative medicine and tissue replacement after injury or disease. To date, no approved medical treatments have been derived from embryonic stem cell research. However, many nations currently have moratoria on either ES cell research or the production of new ES cell lines ***(Thomson et al., 1998)***.

Adult stem cells are undifferentiated cells found throughout the body that divide to replenish dying cells and regenerate damaged tissues. Also know as somatic (from Greek, of the body) stem cells, they can be found in children, as well as adults.

A great deal of adult stem cell research has focused on clarifying their capacity to divide or self-renew indefinitely and their differentiation potential. Many adult stem cells may be better classified as progenitor cells, due to their limited capacity for cellular differentiation ***(Gardner, 2002)***.

Umbilical cord blood is human blood from the placenta and umbilical cord that is rich in hematopoietic stem cells. Cord blood is collected after the umbilical cord has been detached from the new born, and utilized as a source of stem cells for transplantation ***(Cbr systems, 2006)***.

Lineage

To ensure self-renewal, stem cells undergo two types of cell division. Symmetric division gives rise to two identical daughter cells both endowed with stem cell properties. Asymmetric division, on the other hand, produces only one stem cell and a progenitor cell with limited self-renewal potential. Progenitors can go through several rounds of cell division before terminally differentiating into a mature cell. It is possible that the molecular distinction between symmetric and asymmetric divisions lies in differential segregation of cell membrane proteins (such as receptors) between the daughter cells, however, there is no evidence for this mechanism.

An alternative theory is that stem cells remain undifferentiated from environmental cues in their particular niche. Stem cells differentiate when they leave that niche or no longer receive those signals. Studies in Drosophila germarium have identified the signals dpp and adherins

junctions that prevent germarium stem cells from differentiating***(Song and Xie 2003).***

The signals that lead to reprogramming of cells to an embryonic-like state are also being investigated. These signal pathways include several transcription factors including the oncogene c-Myc. Initial studies indicate that transformation of mice cells with a combination of these anti-differentiation signals can reverse differentiation and may allow adult cells to become pluripotent ***(Takahashi and Yamanaka, 2006)***. However, the need to transform these cells with an oncogene may prevent the use of this approach in therapy

Medical researchers believe that stem cell therapy has the potential to radically change the treatment of human disease. A number of adult stem cell therapies already exist, particularly bone marrow transplants that are used to treat leukemia ***(Gahrton and Bjorkstrand, 2000)***.

In the future, medical researchers anticipate being able to use technologies derived from stem cell research to treat a wider variety of diseases including cancer, Parkinson's disease, spinal cord injuries, and muscle damage, amongst a number of other impairments and conditions ***(Lindvall, 2003 and Goldman & Windrem, 2006)***.

Key events in stem cell research

- **1960s** - Joseph Altman and Gopal Das present evidence of adult neurogenesis, ongoing stem cell activity in the brain; their reports contradict Cajal's "no new neurons" dogma and are largely ignored
- **1963** - McCulloch and Till illustrate the presence of self-renewing cells in mouse bone marrow

- **1968** - Bone marrow transplant between two siblings successfully treats Severe combined immunodeficiency disease (SCID)
- **1978** - Haematopoietic stem cells are discovered in human cord blood
- **1981** - Mouse embryonic stem cells are derived from the inner cell mass
- **1992** - Neural stem cells are cultured *in vitro* as neurospheres
- **1997** - Leukemia is shown to originate from a haematopoietic stem cell, the first direct evidence for cancer stem cells
- **1998** - James Thomson and coworkers derive the first human embryonic stem cell line at the University of Wisconsin-Madison.
- **2000s** - Several reports of adult stem cell plasticity are published
- **2003** - Dr. Songtao Shi of NIH discovers new source of adult stem cells in children's primary teeth ***(Shostak, 2006)***.
- **2004-2005** - Korean researcher Hwang Woo-Suk claims to have created several human embryonic stem cell lines from unfertilised human oocytes. The lines are later shown to be fabricated.
- **07 January, 2007** - Scientists at Wake Forest University led by Dr. Anthony Atala and Harvard University report discovery of a new type of stem cell in amniotic fluid.[Becker AJ, McCulloch EA, Till JE (1963).] This may potentially provide an alternative to embryonic stem cells for use in research and therapy ***(Calif in Stem Cell Grants Associated Press, 2007)***.