STEM CELLS IN ANDROLOGY

BY

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Countries with a permissive or flexible policy on embryonic stem cell research (in red)

- Denotes Genome Sequencing Center
WHAT ARE STEM CELLS?

- Stem cells are “master cells “

- The raw material :- from which all of the body’s mature, differentiated cells are made.

- Stem cells give rise to brain cells, nerve cells, heart cells, pancreatic cells, etc.
The unique properties of all stem cells

- **Undifferentiated / unspecialized cells**
  
  Undifferentiated cells can differentiate to yield major specialized cell types or organs.

- **Self-renewal property** is to maintain and repair the tissue. Thus they have potential to replace cell tissue damaged by severe illnesses.

- **Potency**
Stem cell

- Self-renewal

- Differentiate

Stem cell (unlimited cell division)

Specialized cell (e.g., white blood cell)
POTENCY DEFINITIONS OF STEM CELLS

- **Totipotent**: can differentiate into an entire organism, result from fusion of egg and sperm - can form any cell of the embryo as well as the placenta.

- **Pluripotent**: can differentiate into any tissue type except placental tissue. Produced from inner cell mass of blastocyst.
Pluripotent Stem Cells

- Totipotent
  - In vivo fertilized egg
  - 8 cell embryo

Cultured undifferentiated stem cells

- Pluripotent
- Blastocyst

- Neural cells
- Cardiac muscle
- Blood cells
An Overview of Early Development

- **Fertilized egg**
  - Totipotent:
    - Can become any cell in body or placenta
  - Pluripotent: Can become any cell in body
- **Blastocyst**
  - Multipotent:
    - Can become any cell within a specific germ layer or cell lineage
      - Embryonic stem cells come from inner cell mass of blastocyst.

- **Implantation**
  - Gastrulation (day 14) leads to Primary Germ Cells
    - Endoderm (inner) → digestive tract, resp. track
    - Mesoderm (middle) → bones, blood cells, heart
    - Ectoderm (outer) → skin, CNS
Somatic Cell

- Endoderm
  - Liver
  - Intestine
  - Pancreas
- Ectoderm
  - Skin
  - Hair
  - Nerves
- Mesoderm
  - Blood
  - Muscle
  - Bone
  - Cartilage

Germ stem cell

- Pluripotent embryonal stem cell
- Pluripotent stem cells
- Totipotent stem cells

Adult multipotent stem cell

- Courtesy of Dr F. Prosper Cardoso.
Multipotent: can differentiate into multiple specialized cells of a closely related family of cells

Unipotent: these cells only produce one cell type, but have the property of self renewal which distinguishes them from the non stem cells.
One Cell - Several lineages
TYPES OF STEM CELLS (sources)

- **Embryonic**: derived from the inner cell mass of a blastocyst / human embryo

**Source:**

1. Excess fertilized eggs from IVF (in-vitro fertilization) clinics
2. Therapeutic cloning (somatic cell nuclear transfer)
- Adult: derived from mature organisms that can divide to form more differentiated cells
  - but are less versatile and more difficult to identify, isolate, and purify.

  Eg: Stem cells have been found in the blood, bone marrow, liver, kidney, cornea, dental pulp, brain, skin, muscle

- Fetal: derived from aborted fetal tissue

- Umbilical: derived from umbilical cords
  - All blood cell types (red blood cells, white blood cells, and platelets)
Adult Stem Cells
### ADVANTAGES OF EMBRYONIC STEM CELLS OVER ADULT STEM CELLS

<table>
<thead>
<tr>
<th>Embryonic S.C.</th>
<th>Adult S.C.</th>
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<tr>
<td><strong>“Pluripotent”</strong>&lt;br&gt;(can become any cell types present in the human body)</td>
<td><strong>“Multipotent”</strong>&lt;br&gt;(“can become many but not any”)&lt;br&gt;E.g., blood stem cells can develop into several blood cell types, but cannot develop into brain, kidney, or liver cells</td>
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<td>Easy to obtain but blastocyst is destroyed.</td>
<td>Difficult to isolate in adult tissue.</td>
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Recently, due to discovery of cell surface markers, it has become possible to characterize the hair follicle stem cells.

Cytokeratin15 is the best marker for bulge epithelial stem cells in human hair.

Other markers as Nestin, p63 and CD34 allow assessment of stem and progenitor cell populations in human scalp.
Stem cells from patient’s plucked hair can be grown into skin

- Hair follicles contain skin stem cells (keratinocyte)
- Pluck the patient’s hair
- Cultured to form epidermal cells equivalents of the patient's own skin
- This is autologous graft thus bypassing the problem of rejection
- Used for venous ulcers and burn victims
Autologous – Stem Cells

- Sources of the patient’s own stem cells (autologous) are either the cells from patient's own body or his or her cord blood.
- For autologous transplants physicians now usually collect stem cells from the peripheral blood rather than the marrow.
- This procedure is easier, unlike a bone marrow harvest, it can take place outside of an operating room and the patient does not have to be under general anaesthesia.
Sources of stem cells from another donor (allogeneic) are primarily relatives (familial-allogeneic) or completely unrelated donors (unrelated-allogeneic). The stem cells in this situation are extracted from either the donor's body or cord blood.
Xenogenic - Stem Cells

- In this stem cells from **different species** are transplanted, e.g. striatal porcine fetal ventral mesencephalic (FVM) xenotransplants for Parkinson's disease. This has no major ethical concerns and a large amount of tissue is available, however life long immunosupression and risk of rejection are the major limitations.
How Does Cell Therapy Work?

- Stem cells can be used to generate healthy and functioning specialized cells, which can then replace diseased or dysfunctional cells.
- It is similar to the process of organ transplantation only the treatment consists of transplanting cells instead of organs.
How Does Cell Therapy Work?

- **Bone marrow transplants** are an example of cell therapy in which the stem cells in a donor's marrow are used to replace the blood cells of the victims of leukemia.

- Cell therapy is also being used in experiments to **graft new skin cells** to treat serious burn victims, and to **grow new corneas** for the sight-impaired.

- In all of these uses, the goal is for the healthy cells to become integrated into the body and begin to function like the patient's own cells.
Stem cells for Gene Therapy

**DIRECT DELIVERY**

- Therapeutic transgene
- The therapeutic transgene is packaged into a delivery vehicle such as a virus.
- ...and injected into the patient.

**CELL-BASED DELIVERY**

- Therapeutic transgene
- The therapeutic transgene is packaged into a delivery vehicle such as a virus.
- The therapeutic transgene is introduced into a delivery cell such as a stem cell that is often derived from the patient.
- The genetically modified cells (e.g., stem cells) are multiplied in the laboratory.
- ...and readministered to the patient.
What Diseases Can be Cured by Stem Cell Therapies

- Any disease in which there is tissue degeneration can be a potential candidate for stem cell therapies.

![Diagram of eye with normal retina and two types of macular degeneration: wet and dry.](image-url)
Speculation

Stem Cell Medicine

Discarded IVF embryos

Donated tissues (Brain)

Pluripotent stem cells

Tissue stem cells

Blood

Neurons

Heart

Muscle

Drug discovery

Transplantation

Multipotent
Obstacles of Stem Cell Research

- How to find the *right type* of stem cells?
- How to put the stem cells into the right *place*?
- Will the stem cells perform the *desired function* in the body?
- Differentiation *protocols* for many cell types have not been developed.
Review

Recent advances in andrology-related stem cell research

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Abstract

Stem cells hold great promise for regenerative medicine because of their ability to self-renew and to differentiate into various cell types. Although embryonic stem cells (BSC) have greater differentiation potential than adult stem cells, the former is lagging in reaching clinical applications because of ethical concerns and governmental restrictions. Bone marrow stem cells (BMSC) are the best-studied adult stem cells (ASC) and have the potential to treat a wide variety of diseases, including erectile dysfunction (ED) and male infertility. More recently discovered adipose tissue-derived stem cells (ADSC) are virtually identical to bone marrow stem cells in differentiation and therapeutic potential, but are easier and safer to obtain, can be harvested in larger quantities, and have the associated benefit of reducing obesity. Therefore, ADSC appear to be a better choice for future clinical applications. We have previously shown that ESC could restore the erectile function of neurogenic ED in rats, and we now have evidence that ADSC could do so as well. We are also investigating whether ADSC can differentiate into Leydig, Sertoli and male germ cells. The eventual goal is to use ADSC to treat male infertility and testosterone deficiency. (Asian J Androl 2008 Mar; 10: 171–175)
Using stem cells to treat andrological diseases

erectile dysfunction (ED) and male infertility.
THANK YOU