STEM CELLS IN ANDROLOGY

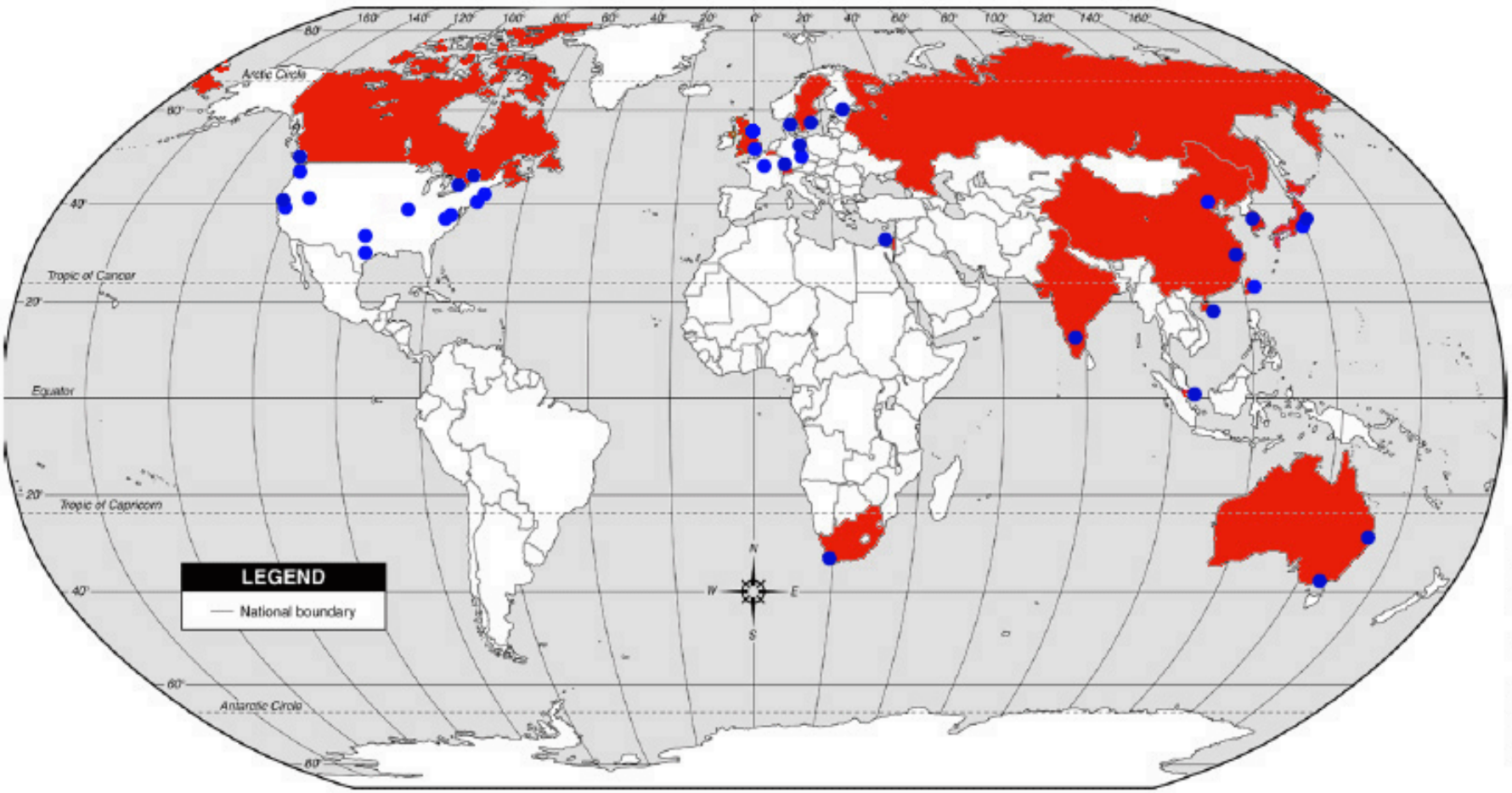
BY

Khalid M. Gharib

Lecturer of Dermatology and Venreology

Zagazig Univeristy

Stem Cell Research Worldwide



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.*

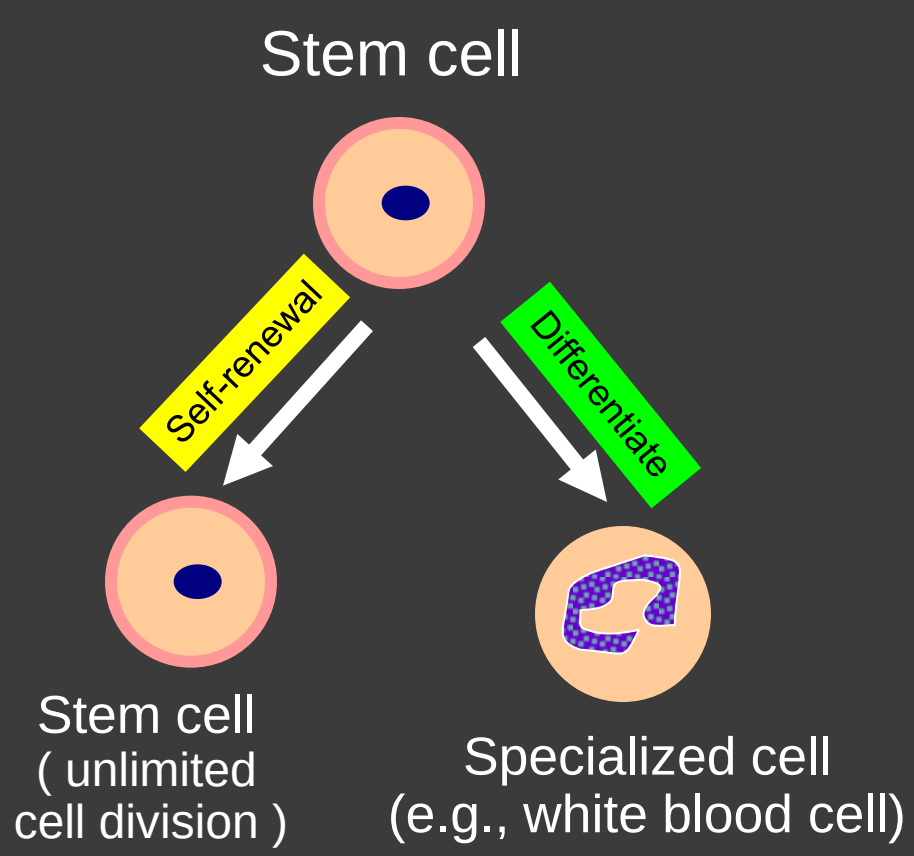
The unique properties of all stem cells

- *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)

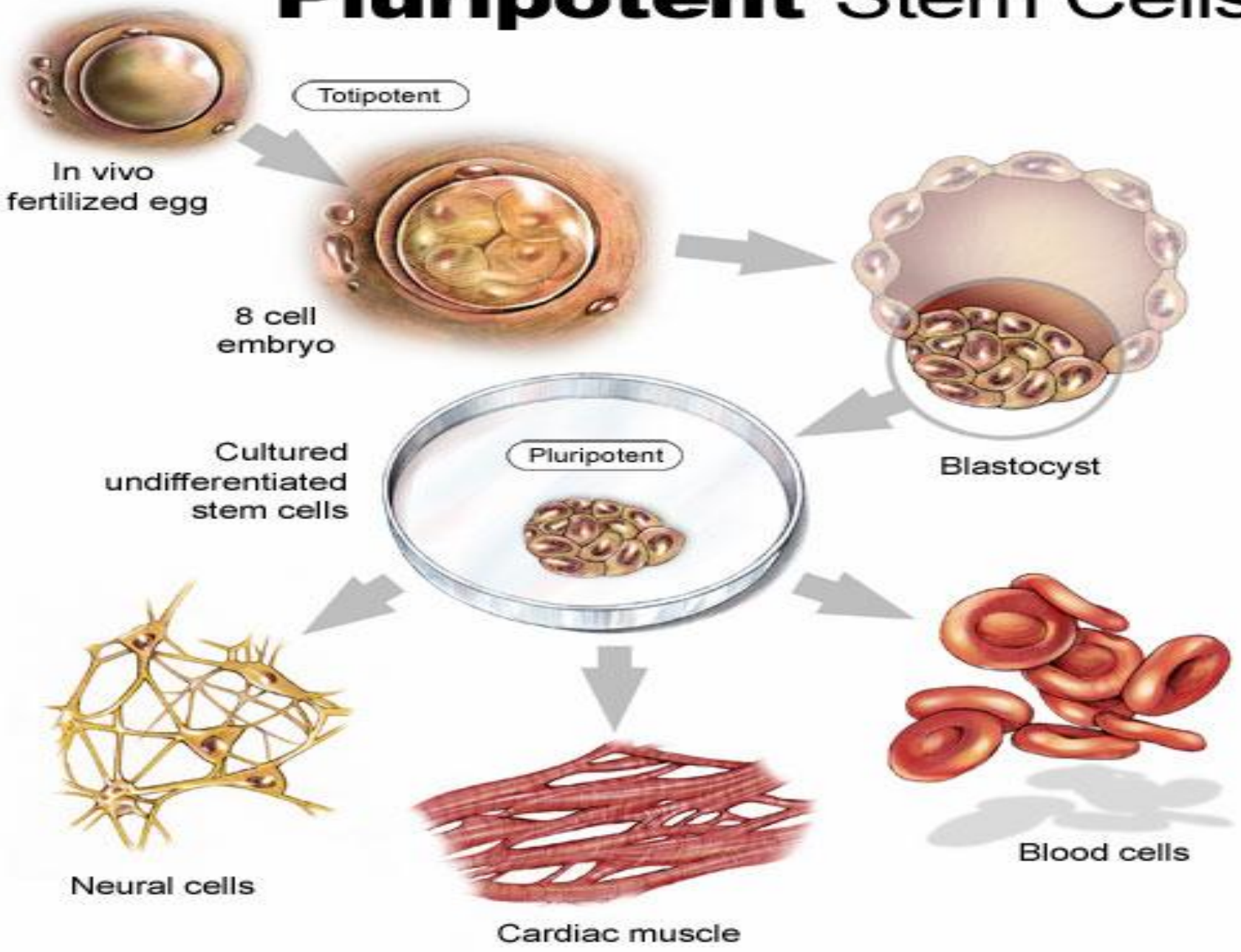
POTENCY DEFINITIONS OF STEM CELLS

- *Totipotent : can differentiate into an entire organism , result from fusion of egg and sperm*

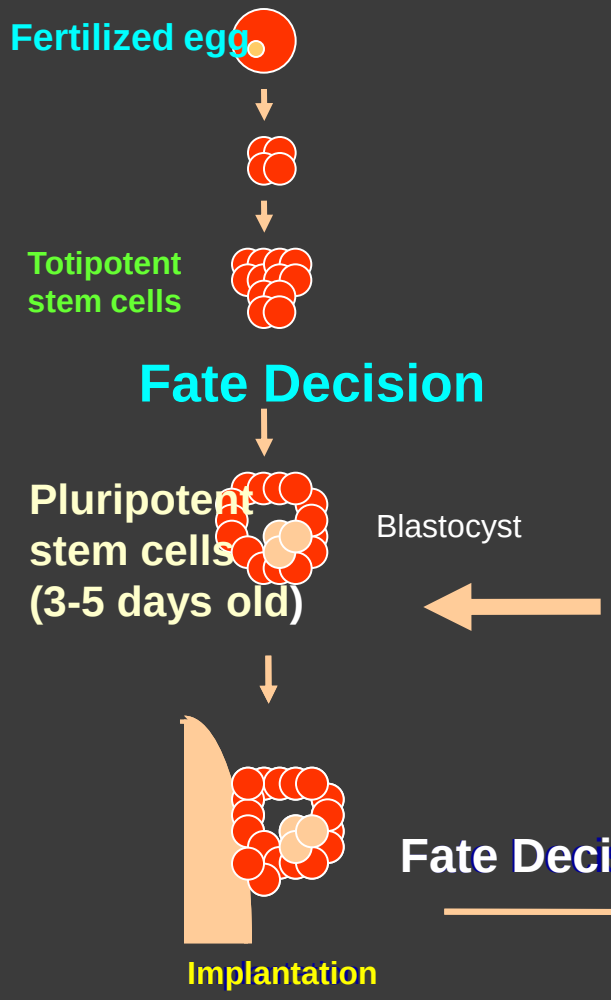
  - can form any cell of the embryo as well as the placenta.

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

Pluripotent Stem Cells



An Overview of Early Development



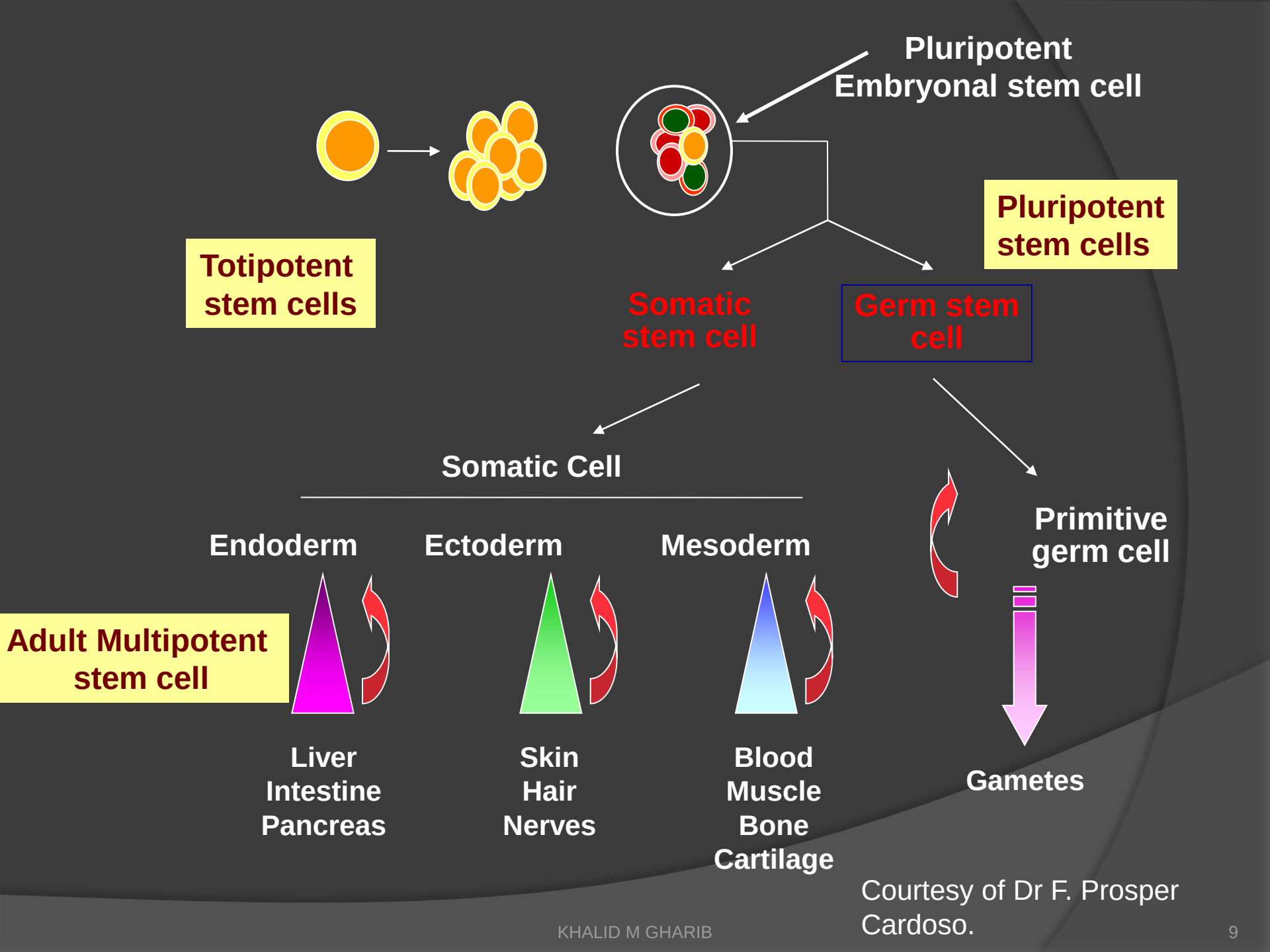
Totipotent: Can become any cell in body or placenta

Pluripotent: Can become any cell in body

Multipotent: Can become any cell within a specific germ layer or cell lineage

Embryonic stem cells come from inner cell mass of blastocyst.

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

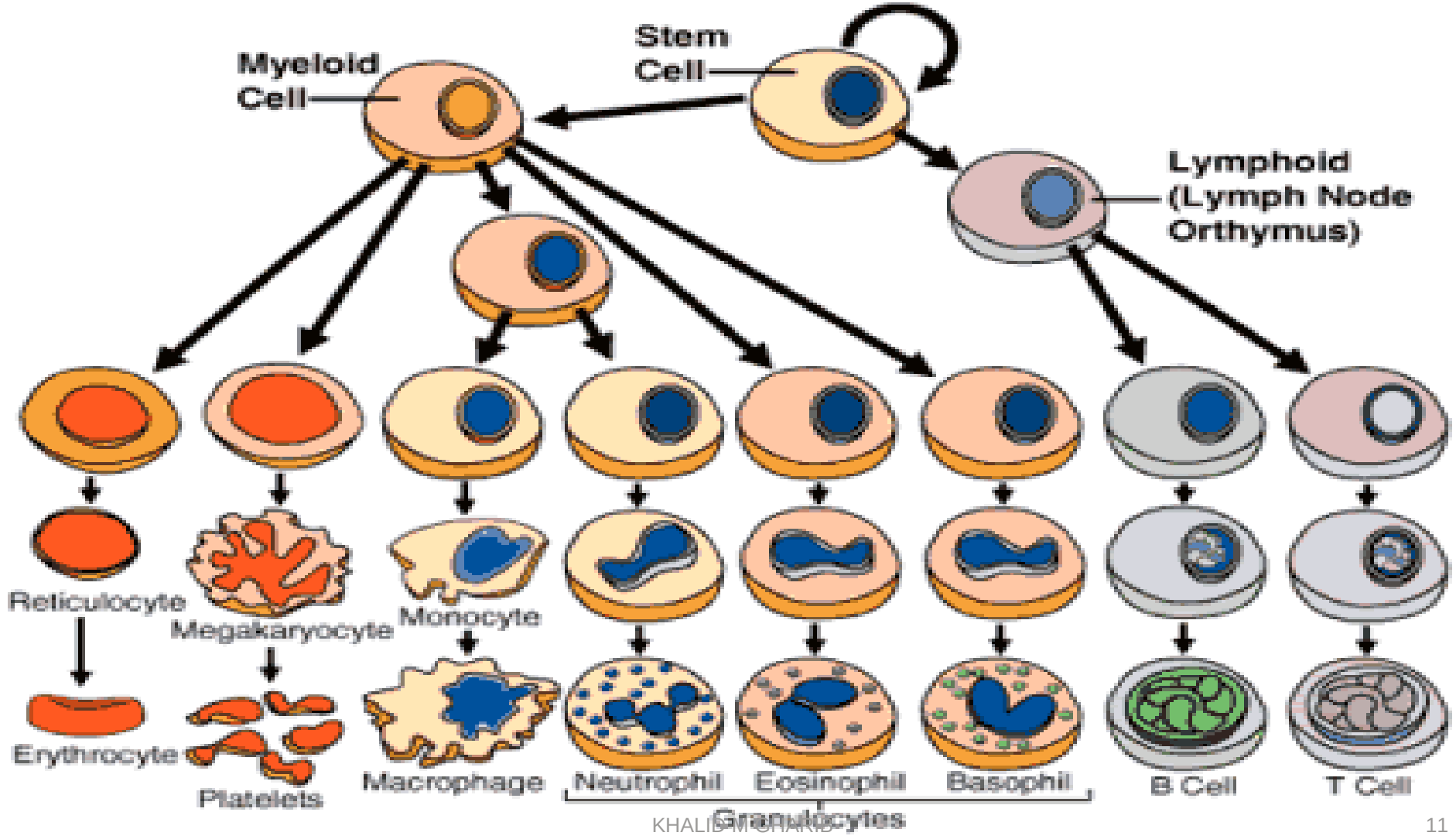


Courtesy of Dr F. Prosper Cardoso.

- *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

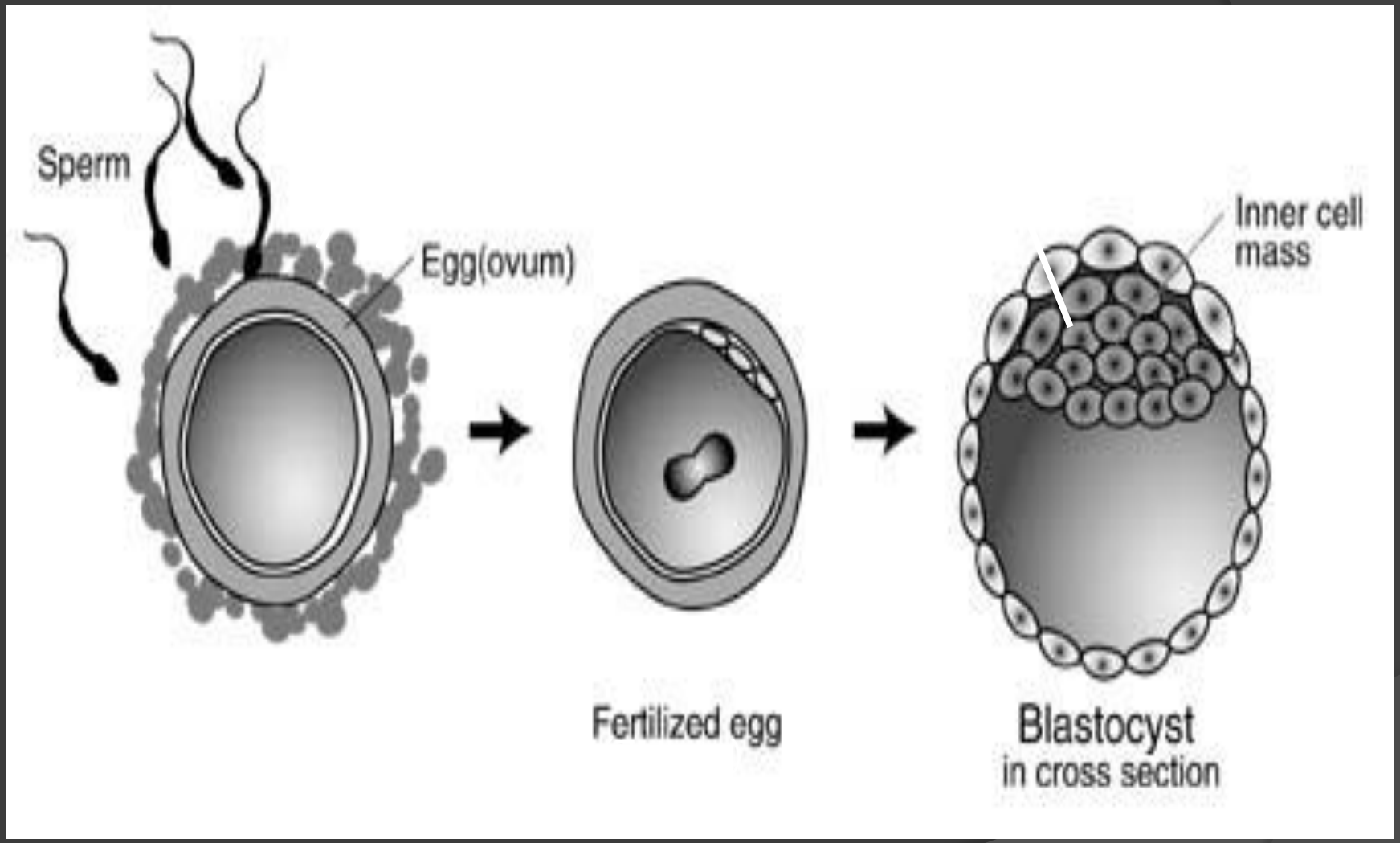


TYPES OF STEM CELLS (sources)

- *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)*


Sperm
Egg(ovum)
Inner cell mass
Fertilized egg
Blastocyst
in cross section

- *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.

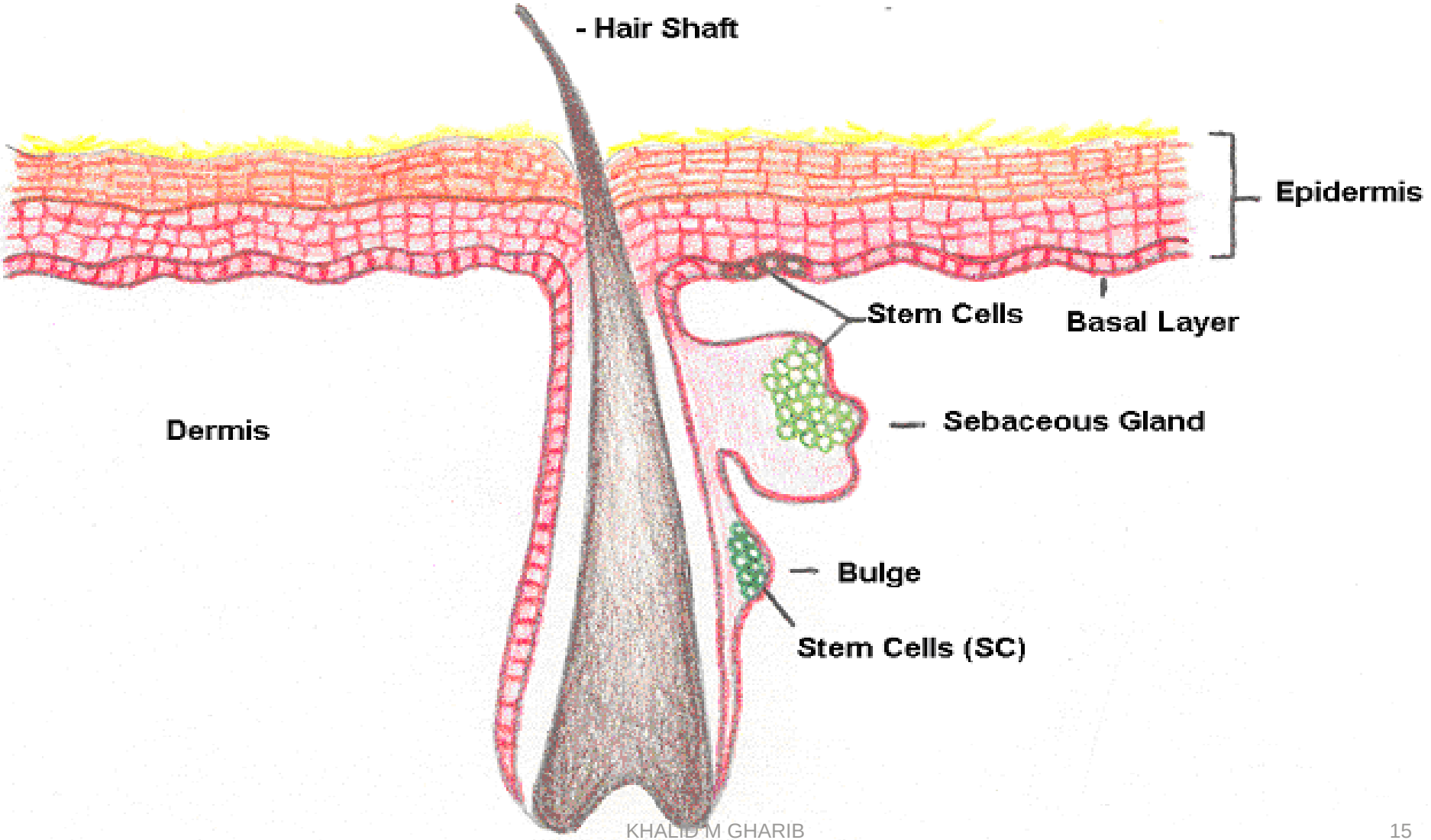
  Eg: Stem cells have been found in the blood, bone marrow, liver, kidney, cornea, dental pulp, brain, skin, muscle

- *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

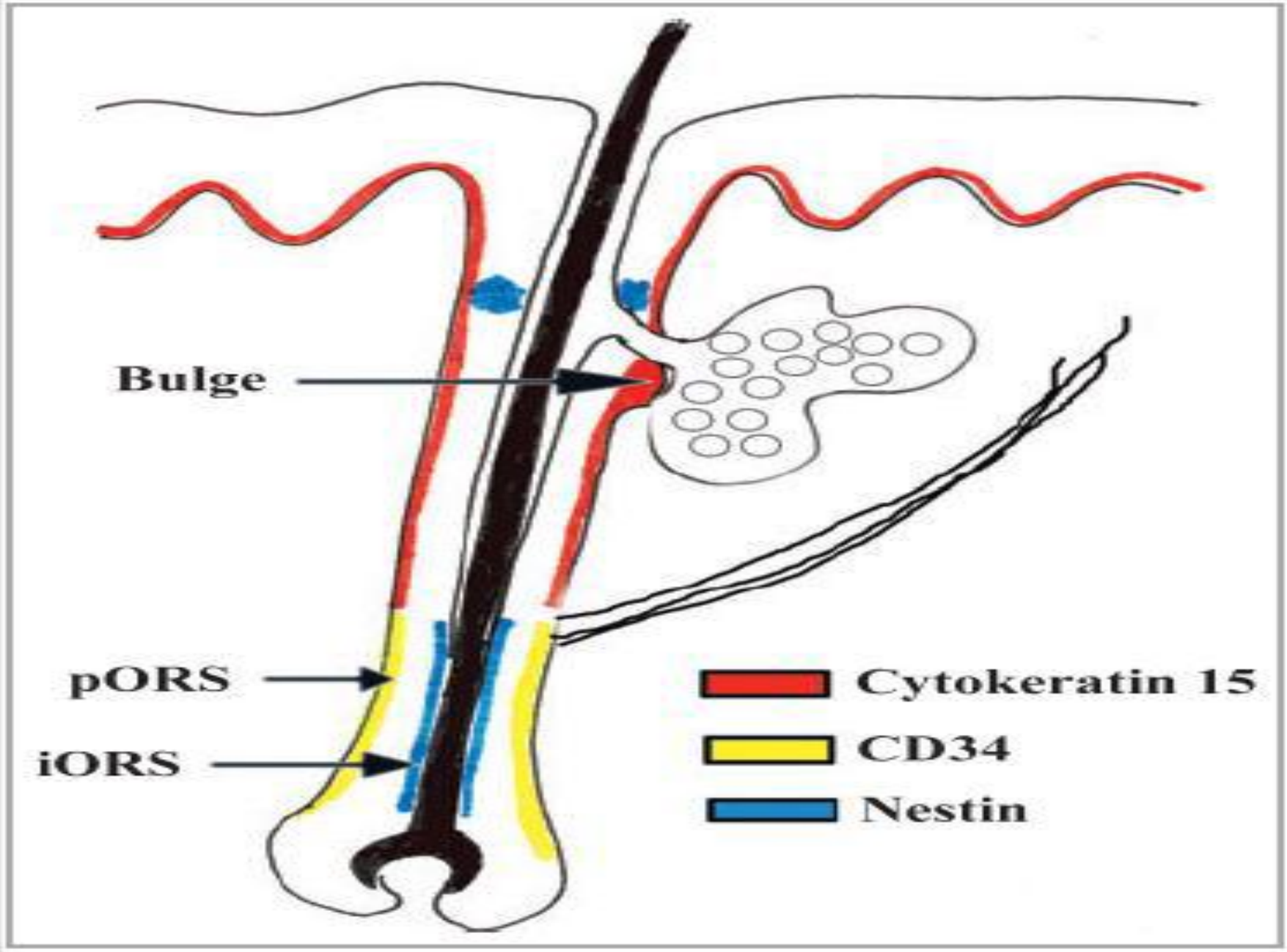


ADVANTAGES OF EMBRYONIC STEM CELLS OVER ADULT STEM CELLS

Embryonic S.C.	Adult S.C.
"Pluripotent" (can become any cell types present in the human body)	"Multipotent" ("can become many but not any") E.g., blood stem cells can develop into several blood cell types, but cannot develop into brain, kidney, or liver cells
Stable. Can undergo many cell divisions.	Less Stable. Capacity for self-renewal is limited.
Easy to obtain but blastocyst is destroyed.	Difficult to isolate in adult tissue.

STEM CELL MARKERS

- 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.

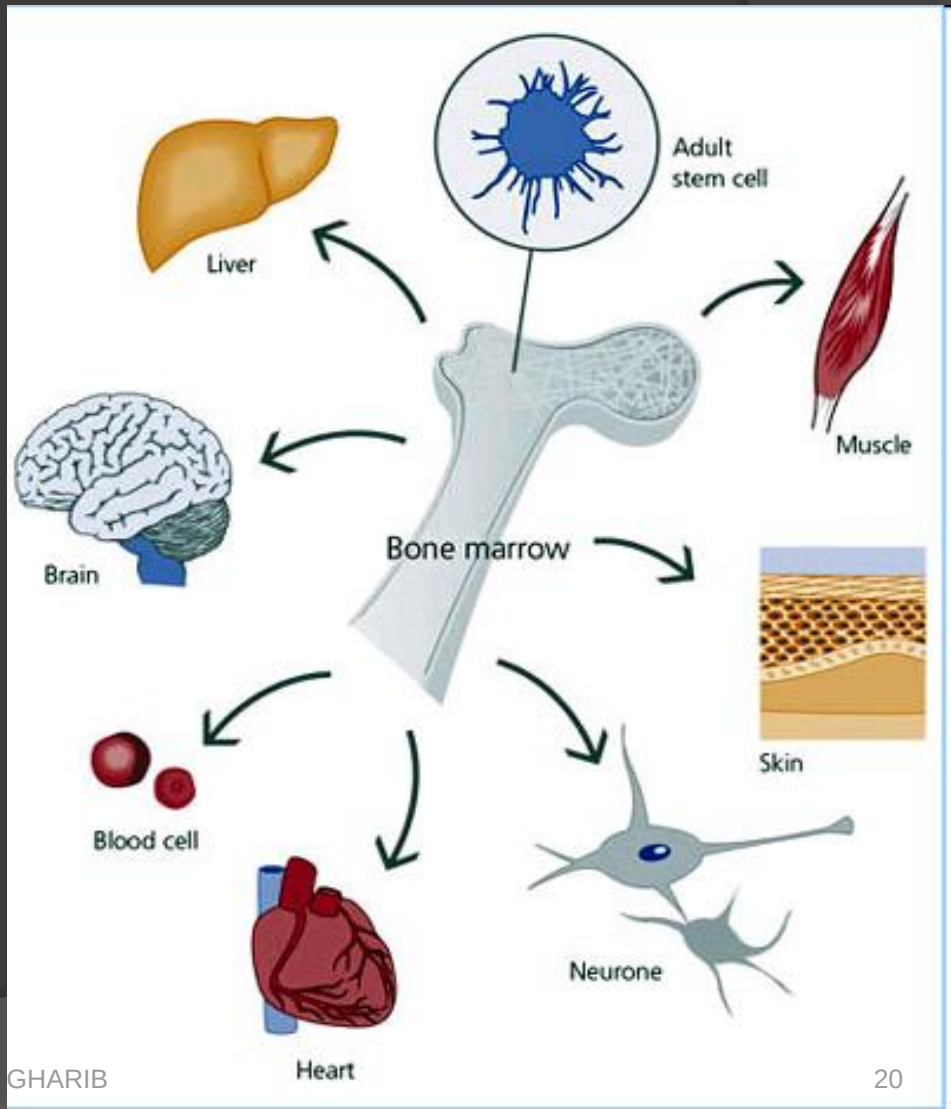

Bulge
pORS
iORS
Cytokeratin 15
CD34
Nestin

Stem cells from patient's plucked hair can be grow into skin

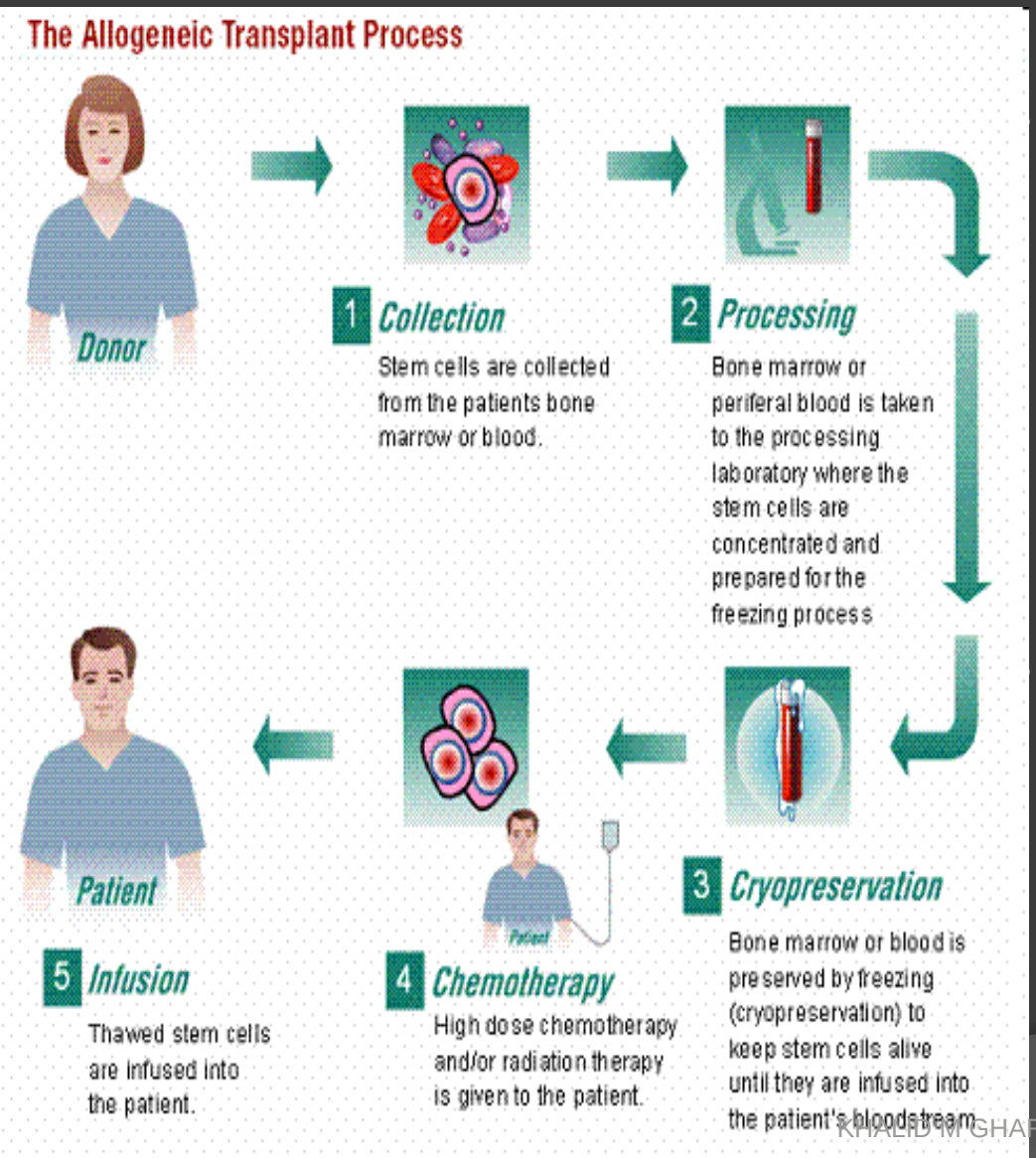
- *Hair follicles contain skin stem cells (keratinocyte)*
- *Pluck the patient's hair*
- *Cultured to form epidermal cells equivalents of the patients own skin*
- *This is autologous graft thus bypassing the problem of rejection*
- *Used for venous ulcers and burn victims*

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.



Allogeneic – Stem Cells

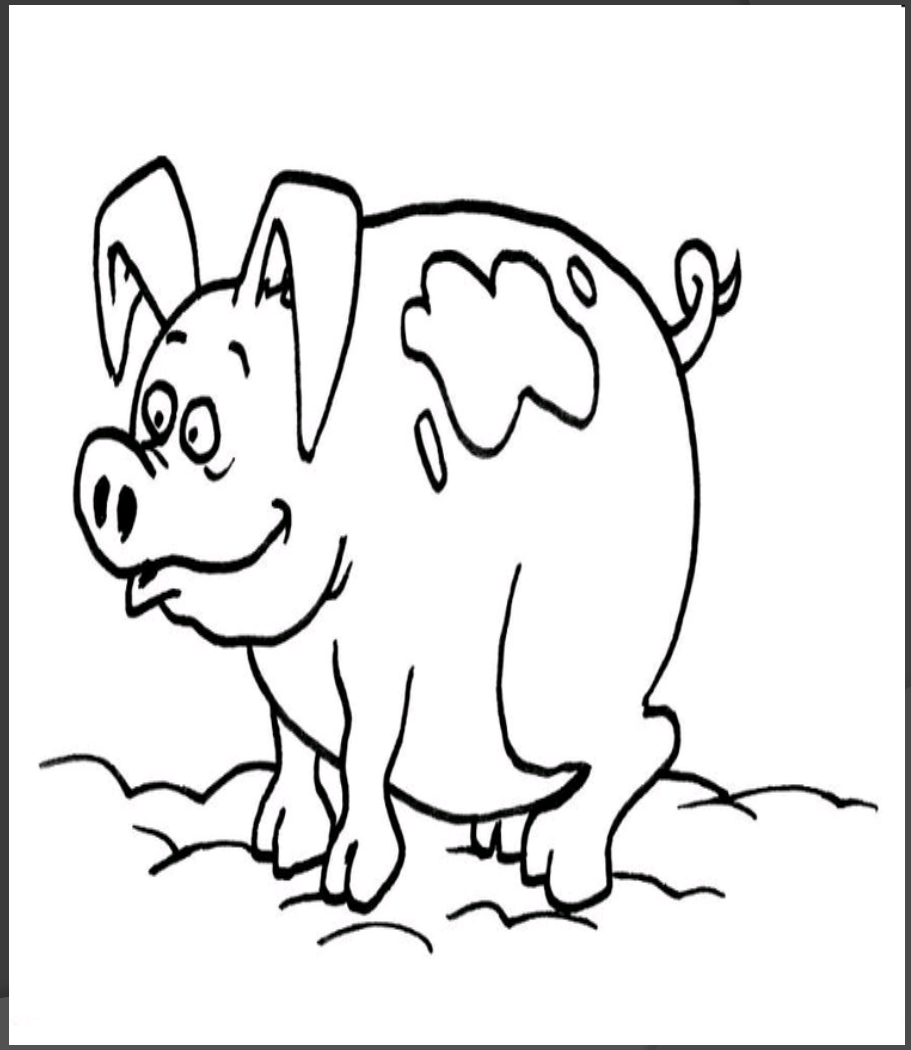


Sources of stem cells from another donor (allogeneic) are primarily relatives (familial-allogeneic) or completely unrelated donors (unrelated-allogeneic).

The stem cells in this situation are extracted from either the donor's body or cord blood

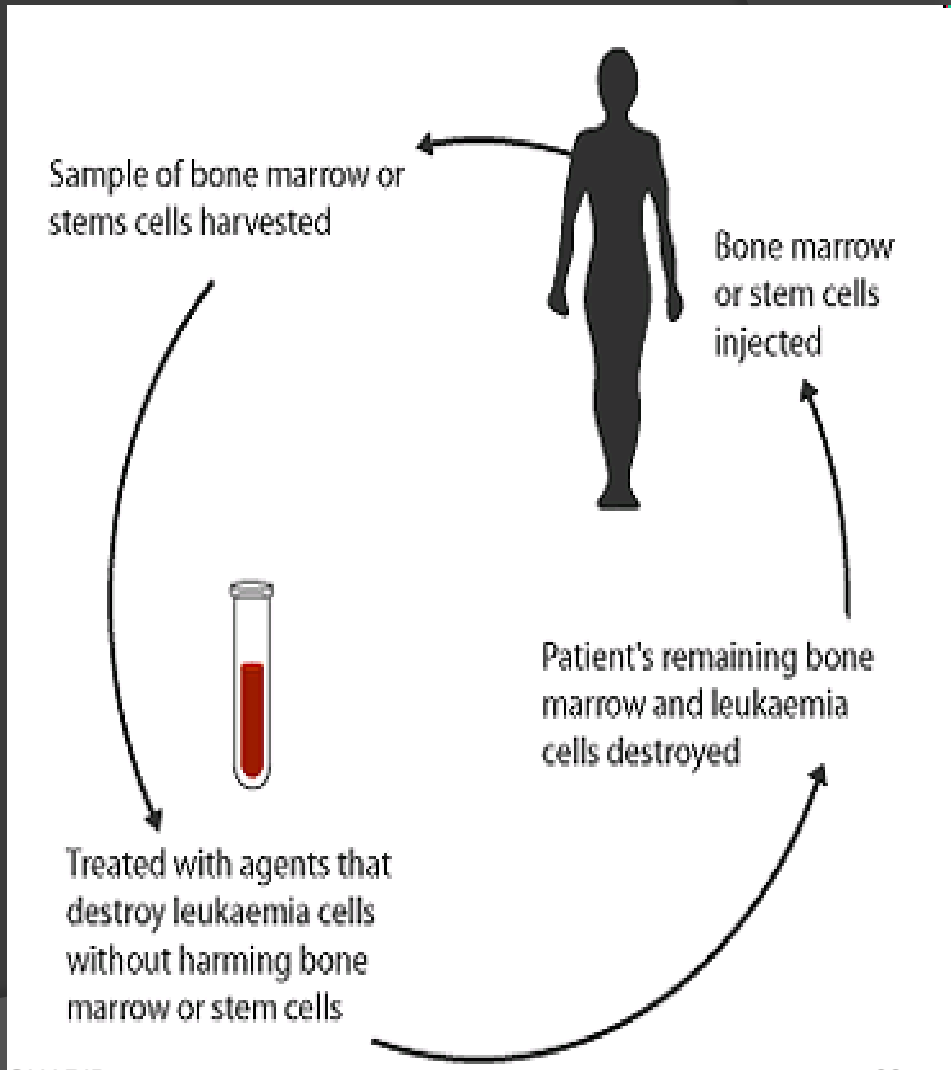
Xenogenic - Stem Cells

- 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?

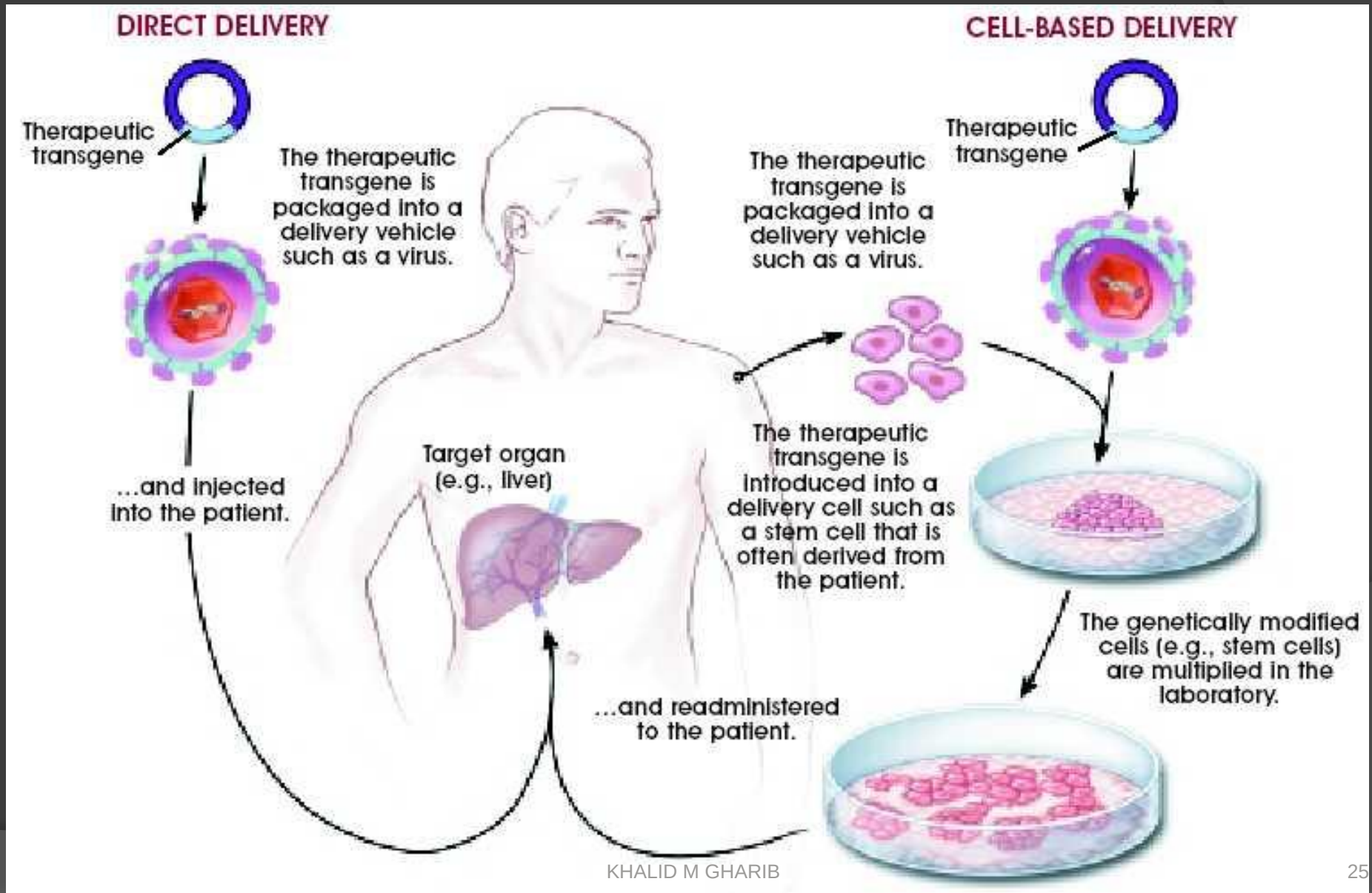
- Stem cells can be used to generate healthy and functioning specialized cells, which can then replace diseased or dysfunctional cells.
- It is similar to the process of organ transplantation only the treatment consists of **transplanting cells instead of organs**.



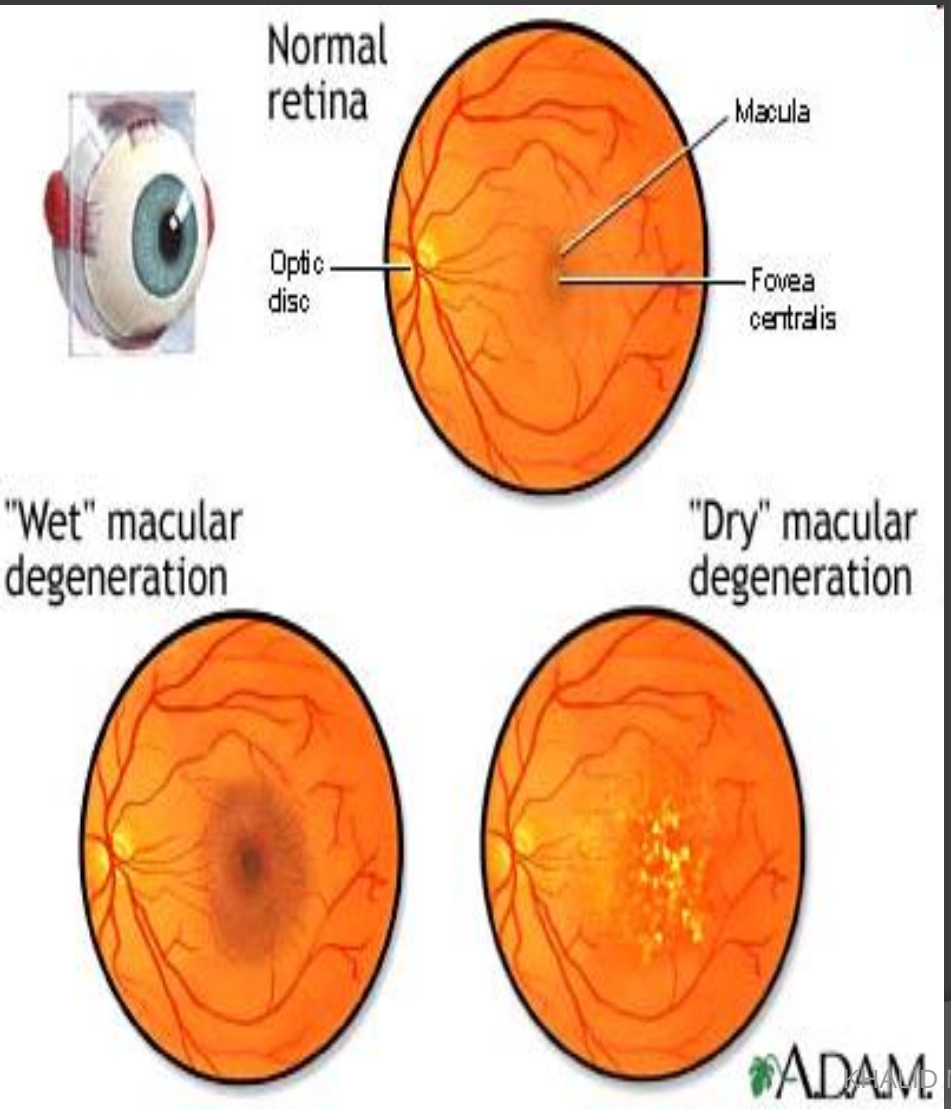
How Does Cell Therapy Work?

- **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

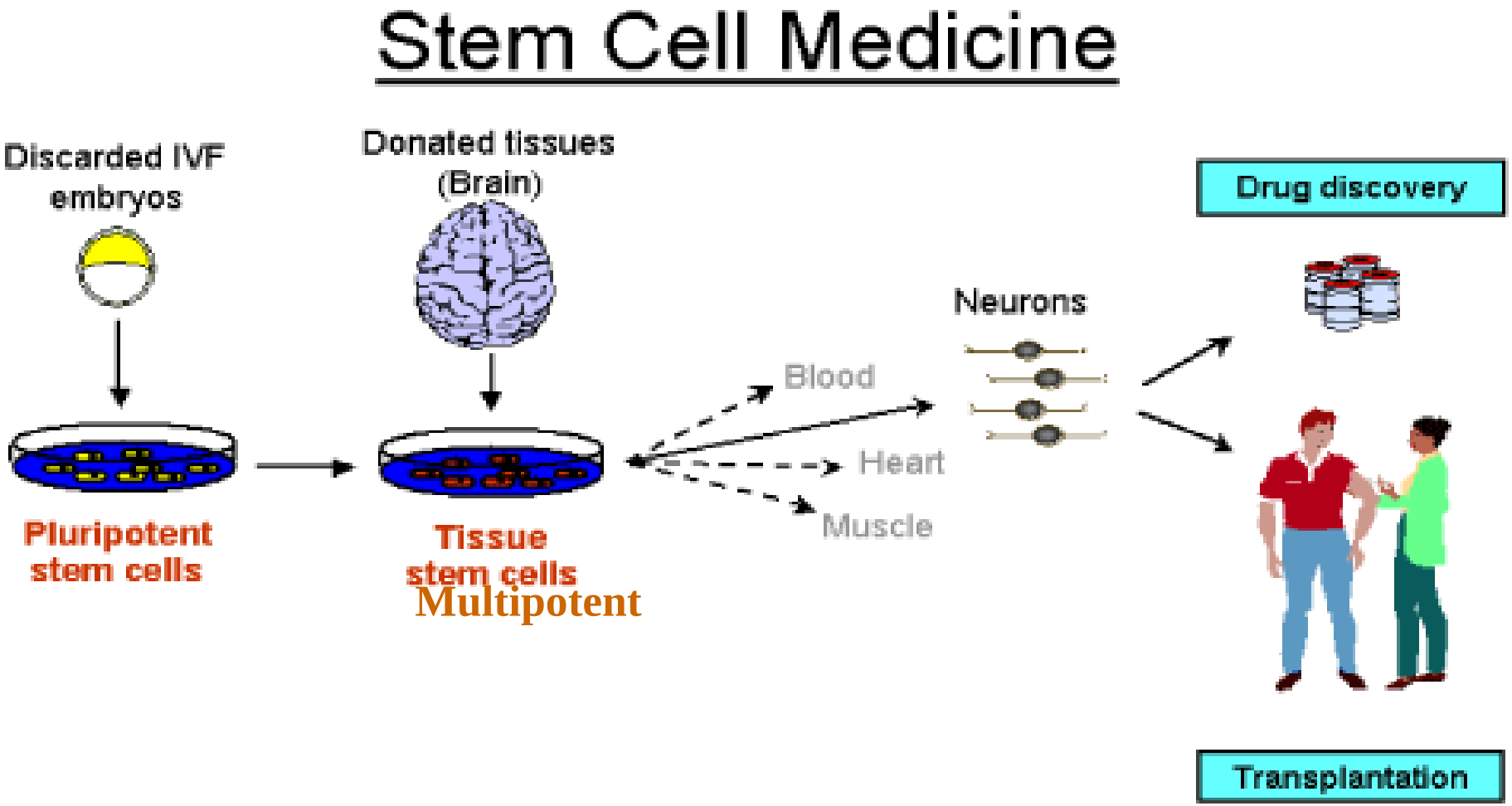


What Diseases Can be Cured by Stem Cell Therapies



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

Speculation



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.

Blackwell Publishing

Asian J Androl 2008; 10 (2): 171–175
DOI: 10.1111/j.1745-7262.2008.00389.x

AJA
www.asiaandro.com

·Review·

Recent advances in androlgy-related stem cell research

Ching-Shwun Lin[1], Zhong-Cheng Xin[2], Chun-Hua Deng[3], Hongxiu Ning[1], Guiting Lin[1], Tom F. Lue[1]

[1]*Knuppe Molecular Urology Laboratory, Department of Urology, School of Medicine, University of California, San Francisco, CA 94143, USA*
[2]*Andrology Center, Peking University First Hospital, Beijing 100009, China*
[3]*Urology Department, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou 510080, China*

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