Recent Advances in Andrology-related Stem Cell Research

Essay

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Mohamed Osama Elbagory

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LIST OF ABBREVIATION

- **AR:** Androgen receptor.
- **ARL:** AIDs related lymphoma.
- **ASC:** Adult stem cells.
- **AVN:** Avascular necrosis.
- **bFGF:** basic fibroblast growth factor.
- **BMSC:** Bone marrow stem cell.
- **BPH:** Benign prostatic hyperplasia.
- **BTB:** Blood testicular barrier
- **CD:** Cluster of differentiation.
- **cGMP:** cyclic guanine monophosphate.
- **CMV:** Cytomegalovirus.
- **DNA:** Deoxyribonucleic acid.
- **EB:** Embryoid bodies.
- **EBV:** Epstein bar virus.
- **E-BMT:** Embryonic bone marrow transplantation.
- **ED:** Erectile dysfunction.
- **EGFP:** Enhanced green fluorescent protein.
- **eNOS:** endothelial nitric oxide synthase.
- **ER:** endoplasmic reticulum
- **ESC:** Embryonic stem cell.
- **FSC:** Fetal stem cell.
- **GCNA1:** Germ cell nuclear antigen 1.
- **GCT:** Germ cell tumors.
- **GDNF:** Glial cell derived neurotrophic factor.
- **GFP:** Green fluorescent protein.
- **GnRH:** Gonadotrophin releasing hormone.
- **GVHD:** Graft versus host disease.
- **Gy:** gray the unit of energy absorbed from ionizing radiation, 1Gy=1000 rad.
- **HIV:** Human immune deficiency virus.
- **HLA:** Human leukocytic antigen.
- **hMSC:** human mesenchymal stem cell.

- **hNCSC:** human neural crest stem cell.
- **HSC:** Hematopoietic stem cell.
- **HSV:** Herpes simplex virus.
- **H&E:** Hematoxline and eosine.
- **iPSC:** induced pluripotent stem cell.
- **IVF**: In-vitro fertilization.
- **ICSI:** Intra cytoplasmic sperm injection
- **LIF:** Leukemia inhibitory factor.
- **MHC:** Major histocompitability complex.
- **MPOA:**Medial preoptic area
- **MR:** Magnetic resonance.
- **MSC:** Mesenchymal stem cell.
- **NESC:** Neural embryonic stem cell.
- **NO:** Nitric oxide.
- **PAP:** Prostatic acid phosphatase.
- **PCR:** Polymerase chain reaction.
- **PDE5:** Phosphodiestrase E5.
- **PGC:** Primordial germ cell.
- **PSA:** Prostatic specific antigen.
- **PTLD:** Post transplantation lympho-proliftative disorder.
- **RA:** Retinoic acid.
- **RBC:** Red blood cell.
- **REM :** Rapid eye movement
- **ROS:** reactive oxygen species
- **SSC:** Spermatogonial stem cell.
- **SYCP3:** Synaptonemal complex protein.
- **TGCT:** Testicular germ cell tumor.
- **Thy-1:** Glycosyl phosphatidyl inositol anchored glycoprotein.
- **VOD:** Veno-occlusive disease.
- **UCSC**: Umbilical cord stem cell
- **WBC:** White blood cell.
- **ZP:** zona pellucida

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INTRODUCTION

Stem cells are human body's master cells, with the ability to grow and differentiate into various cell lines. Knowing the criteria of stem cell allows scientists to look for cell-surface molecules, or markers that distinguish stem cell from specialized cell. This allows scientists to isolate stem cell from specialized cells and investigate ways of taking advantage of their ability to make new specialized cells ***(Bondnar et al, 2004).***

There is a great interest in the biology of adult stem cell because of their capacity to self-renew and their high plasticity. These advantages enable adult stem cell to produce mature progenitors that actively participate in the maintenance of homeostasis process ***(Brittan and Wright, 2002).***

Because of their regenerative potential, stem cells are ideal therapeutic agents for degenerative diseases such as erectile dysfunction and defective conditions such as male infertility. In animal studies stem cells have shown promise for treating those andrological diseases. The potential of stem cell research is that it identify how it can be differentiated to male germ cells thus treat male infertility together with it's ability to transform into neuronal and endocrinal cells to treat erectile dysfunction ***(Yu et al, 2007; Hanna et al, 2007).***

AIM OF ESSAY

This work outline the future challenges in andrology-related stem cell applications and using it as a novel technique in treating male-related disorders

STEM CELL BASICS

Stem cell and its characters:

Stem cells are unspecialized cells that can differentiate into more mature ones with specialized functions. In humans, they have been identified in the inner cell mass of the early embryo (Blastocyst), in some tissues of the fetus, the umbilical cord, the placenta, and in several adult organs ***(Blau et al, 2001).***

Stem cells have the ability to divide for indefinite periods; often throughout the life of the organism. Under the right conditions, or given the right signals, stem cells can give rise (differentiate) into many different cell types that make up the organism. These are the properties that make stem cells unique, the fact that they can divide thousands of times without error and without breaking down, and that they can differentiate into a variety of different kinds of cells that have characteristic shapes and specialized function such as heart cells, lung cells, skin cells, or nerve cells ***(Blau et al, 2001).*** (Fig.1)

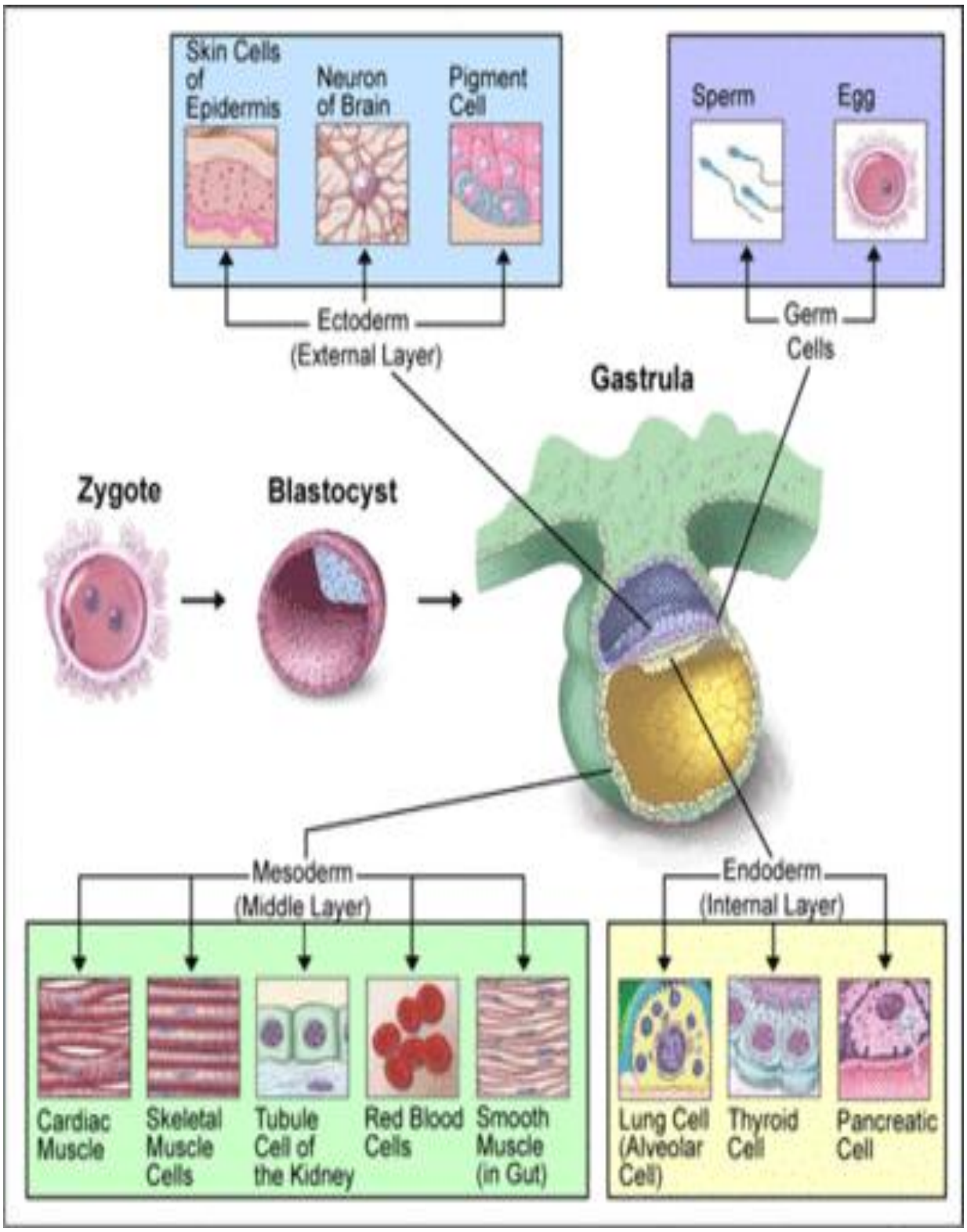

Figure 1: Differentiation potential of stem cells ***(Winslow, 2001).***

The differentiation potential of stem cells is classified to totipotent, pluripotent, multipotent and unipotent. A fertilized egg (zygote) istotipotent and can differentiate into any cell type. An embryonic stem cell (ESC) is pluripotent and can differentiate into any cell type, except a fertilized egg. An adult stem cell (ASC) is multipotent and can differentiate into most cell types of its tissue origin. Erythroidproginator cell is a unipotent stem cell and can differentiate to one cell type which is red blood cells. However, numerous studies have shown that ASC can differentiate into cell types beyond their tissue origin e.g. bone marrow stem cells (BMSC) differentiating into cardiomyocytes therefore, ASC appear to possess a certain degree of pluripotency***(Woodward et al, 2005; Kolf et al, 2007; Satija et al, 2007).***

Types of stem cells:

1-Embryonic stem cells (ESC):

ESC is defined by its origin. It is derived from the blastocyst stage of the embryo. The blastocyst is the stage of the embryonic development prior to implantation in the uterine wall. At this stage, the pre-implantation embryo consists of a sphere made up of an outer layer of cells (Trophectoderm), a fluid-filled cavity and clusters of cells on the interior ***(Thomson et al, 1998).*** (Fig. 2)

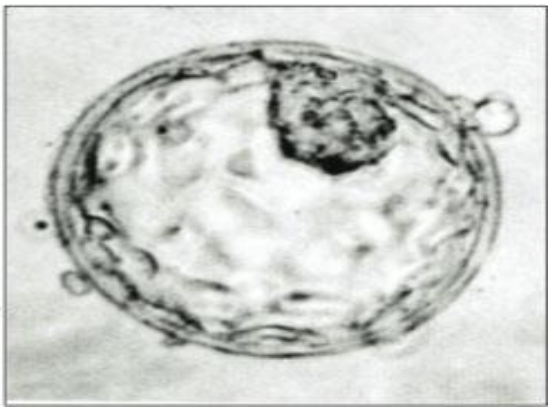

Figure 2: Human blastocyst showing inner cell mass and trophectoderm ***(Winslow, 2001).***

Smith in 2001 defined Properties of ESC as: (All of these criteria have been met by mouse ESC)

- Derived from the inner cell mass of the blastocyst.
- Capable of undergoing long term self-renewal.
- Exhibit a stable diploid number of chromosomes (karyotype).
- Give rise to cells that are derived from all three primary germ layers of the embryo (endoderm, mesoderm and ectoderm).
- Capable of integrating into all fetal tissues during development.

- Capable of colonizing and giving rise to a colony of genetically identical cells, which have the same properties as the original cell.
- Can be induced to proliferate or to differentiate ***(Smith, 2001).***

Technique of growing human ESC in-vitro:

Human ESC can be generated by culturing cells from the inner cell mass of a human blastocyst in a multi-step process as follows:

- Separation of the pluripotent cells of the inner cell mass from the surrounding trophectoderm by immuno-surgery or antibody mediated dissolution of the trophectoderm.
- Plating the inner cell mass in culture dishes containing growth medium supplemented with fetal bovine serum on feeder layers of mouse embryonic fibroblasts that had been gamma irradiated to prevent their replication.
- Inner cell masses divides and form clumps of cells after 9 to 15 days.
- Dissociation of cells from the periphery of the clumps chemically or mechanically and replanting them in the same culture conditions.
- Colonies of apparently homogeneous cells are selectively removed, mechanically dissociated, and replanted thus creating a cell line ***(Thomson et al, 2000).*** (Fig. 3)