

Uses of stem cells in gynecology

ESSAY

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Abbreviations

ABMTR	autologous blood and marrow transplant registry
ADAC	Adult stem cells
ADSCs	Adipose-derived stem cells
ART	Assisted reproductive technologies
ASC	American cancer society
BM	Bone marrow
BMP	Bone morphogenetic protein
BMT	Bone marrow transplantation
CFU	Cell forming unit
CIHR	Canadian institutes of health research
DLI	Donor lymphocyte infusion
EB	Embryoid body
EC	Embryonal carcinoma cells
EFP	Green fluorescent protein
EG	Embryonic germ cells
ESC	Embryonic stem cells
EST	Embryonic stem cells test
F1K-1	The receptor of VEGF
FBS	Fetal bovine serum
FDA	Federal drug administration
G 0	Grade 0
HDCT	High dose chemotherapy
HESCs	Human embryonic stem cells
HLA	Human leucocytic antigen
HSC	Haematopoietic stem cells
ICM	Inner cell mass

IVF	Invitro fertilization
MDCs	Muscle-derived stem cells
MEF	Murine embryonic fibroblast
mES	Mesenchymal embryonic stem cells
MSCs	Mesenchymal stem cells
MUD	Marrow unrelated donor
NIH	National institute of health
OS	Overall survival
PBCT	Peripheral blood cell transplantation
PBPC	Peripheral blood progenitor cells
PG	Primordial germ cells
RT-PCR	Reverse transcriptase polymerase chain reaction
SCNT	Somatic cell nuclear transfer
SUI	Stress urinary incontinence
TA	Transit-amphifying cells
TBI	Total body irradiation
TTGF-B	Transforming growth factor-B
TUUS	Trans-urethral ultrasound
VEGF	Vascular endothelial growth factor

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INTRODUCTION
&
Aim of the
work

INTRODUCTION

A stem cell is a special kind of cell that has a unique capacity to renew itself and to give rise to specialized cell types. Although most cells of the body, such as heart cells or skin cells, are committed to conduct a specific function, a stem cell is uncommitted and remains uncommitted, until it receives a signal to develop into a specialized cell. Their proliferative capacity combined with the ability to become specialized makes stem cells unique. Researchers have for years looked for ways to use stem cells to replace cells and tissues that are damaged or diseased (*Ruth and Lana 2001*).

In 1998, for the first time, investigators were able to isolate pluripotent stem cell from early human embryos and grow them in culture (pluripotent, meaning the cells have the potential to develop almost all of the more than 200 different known cells). In the few years since this discovery, evidence has emerged that these stem cells are, indeed, capable of becoming almost all of the specialized cells of the body and, thus, may have the potential to generate replacement cells for a broad array of tissues and organs, such as the heart, the pancreas, and the nervous system. Thus, this class of human stem cell holds the promise of being able to repair or replace cells or tissues that are damaged or destroyed by many of our most devastating diseases and disabilities (*Ruth and Lana 2001*).

At about the same time as scientists were beginning to explore human pluripotent stem cells from embryos and fetal tissue, a flurry of new information was emerging about a class of stem cells that have been in clinical use for years-so-called adult stem cells. An adult stem cell is an

undifferentiated cell that is found in a differentiated (specialized) tissue in the adult, such as blood. It can yield the specialized cell types of the tissue from which it originated. In the body, it too, can renew itself. During the past decade, scientists discovered adult stem cells in tissues that were previously not thought to contain them, such as the brain. More recently, they reported that adult stem cells from one tissue appear to be capable of developing into cell types that are characteristic of other tissues. For example, although adult hematopoietic stem cells from bone marrow have long been recognized as capable of developing into blood and immune cells, recently scientists reported that, under certain conditions, the same stem cells could also develop into cells that have many of the characteristics of neurons. So, a new concept and a new term emerged-adult stem cell plasticity. Current science indicates that, although both of these cell types hold enormous promise, adult and embryonic stem cells differ in important ways. What is not known is the extent to which these different cell types will be useful for the development of cell-based therapies to treat disease (*Ruth and Lana 2001*).

Aim of the work

This work aim to show the advanced application of stem cells derived either from adults or embryos in the management of some gynecological disorders.

Chapter (1)

The stem cell

Review of Literature

The stem cell

A stem cell is a cell that has the ability to divide (selfreplicate) 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) to the many different cell types that make up the organism. That is, stem cells have the potential to develop into mature cells that have characteristic shapes and specialized functions, such as heart cells, skin cells, or nerve cells (*Ruth and Lana, 2001*).

The Differentiation Potential of Stem Cells: Basic Concepts and Definitions

Many of the terms used to define stem cells depend on the behavior of the cells in the intact organism (in vivo), under specific laboratory conditions (in vitro), or after transplantation in vivo, often to a tissue that is different from the one from which the stem cells were derived. For example, the fertilized egg is said to be totipotent-from the Latin totus, meaning entire-because it has the potential to generate all the cells, and tissues that make up an embryo and that support its development in utero (*Ruth and Lana, 2001*).

Most scientists use the term pluripotent to describe stem cells that can give rise to cells derived from all three embryonic germ layers-mesoderm, endoderm, and ectoderm. These three germ layers are the embryonic source of all cells of the body (**Fig. I**). (Differentiation of Human Tissues). All of the many different kinds of specialized cells that make up the body are derived from one of these germ layers. Thus, pluripotent cells have the potential to give rise to any type of cell, a

property observed in the natural course of embryonic development and under certain laboratory conditions (*Ruth and Lana, 2001*).

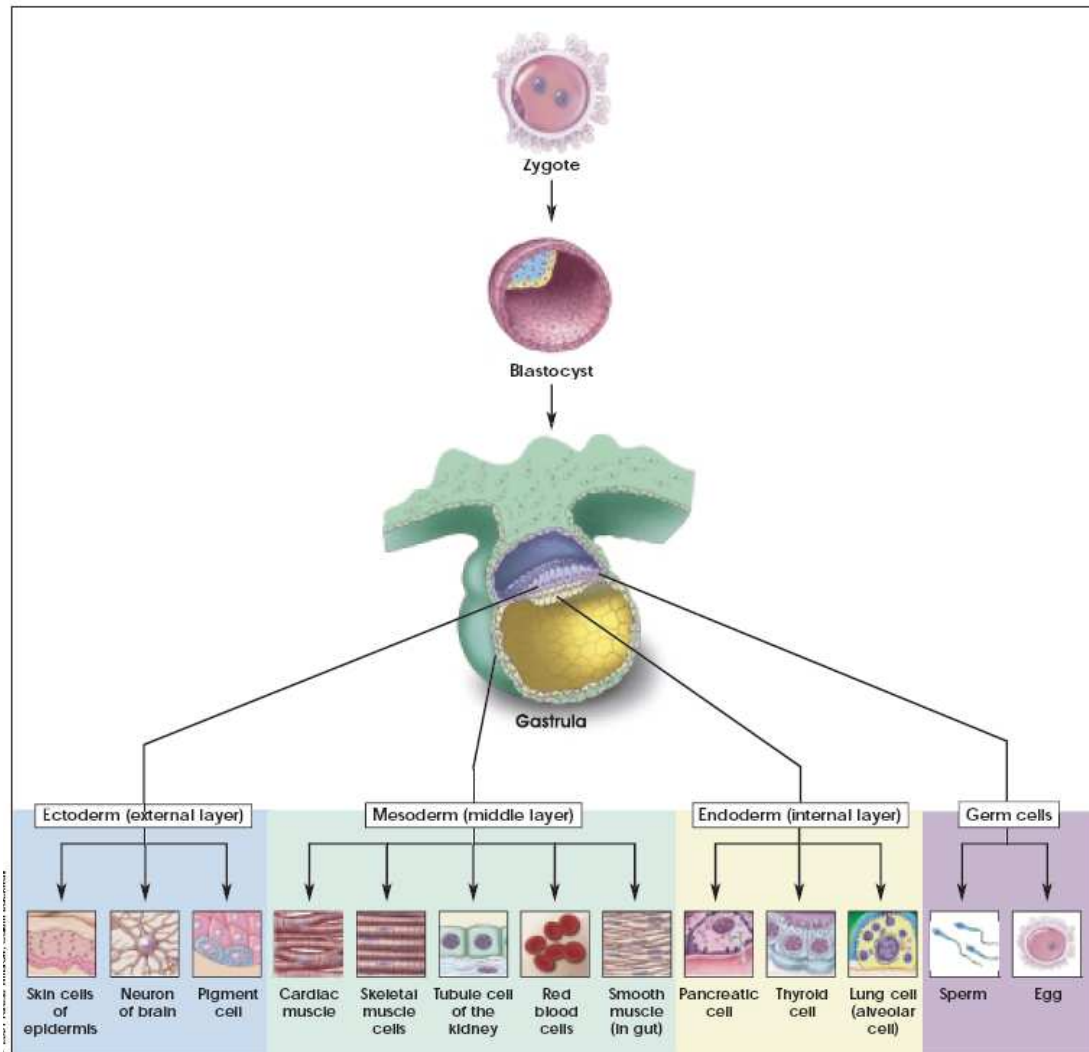


Fig. (I): Differentiation of human tissues (*Ruth and Lana, 2001*)

Unipotent stem cell, a term that is usually applied to a cell in adult organisms, means that the cells in question are capable of differentiating along only one lineage. Also, it may be that the adult stem cells in many differentiated, undamaged tissues are typically unipotent and give rise to just one cell type under normal conditions. This process would allow for a steady state of self-renewal for the tissue. However, if the tissue becomes damaged and the replacement multiple cell types is required,

pluripotent stem cells may become activated to repair the damage (*Slack, 2000*).

The embryonic stem cells are cells derived from the early embryo that can be propagated indefinitely in the primitive undifferentiated state while remaining pluripotent they share these properties with embryonic germ cells (EG) candidate embryonic stem cells (ES) and EG cells lines can differentiate into multiple types of somatic cells (*Pera et al., 2000*).

Adult stem cells are rare undifferentiated cells present in many adult tissues and organs (*Shostak, 2006*). Rather, adult stem cells are defined by their functional properties: high proliferative potential, substantial self renewal capacity and ability to differentiate into at least one type of mature functional progeny (*Morrison et al., 1997 and Eckfeldt et al., 2005*). That is, there is no evidence, at this time, of an adult stem cell that is pluripotent tissue; it can renew itself and become specialized to yield all of the specialized cell types of the tissue from which it originated. Adult stem cells are capable of self-renewal for the lifetime of the organism. Sources of adult stem cells include bone marrow, blood stream, cornea and retina of the eye, dental pulp of the tooth, liver, skin, gastrointestinal tract, and pancreas. Unlike embryonic stem cells, at this point in time there are no isolated adult stem cells that are capable of forming all cells of the body (*Ruth and Lana, 2001*).

The Embryonic Stem Cell

An embryonic stem cell (ES cell) is defined by its origin. It is derived from the blastocyst stage of the embryo. The blastocyst is the stage of embryonic development prior to implantation in the uterine wall. At this stage, the preimplantation embryo of the mouse is made up of 150

cells and consists of a sphere made up of an outer layer of cells (the trophectoderm), a fluid-filled cavity (the blastocoele), and a cluster of cells on the interior (the inner cell mass) (*Ruth and Lana, 2001*).

Embryonic-like stem cells, called embryonic germ (EG) cells, can also be derived from primordial germ (PG) cells (the cells of the developing fetus from which eggs and sperms are formed) of the mouse and human fetus (*Shamblott et al., 1998*).

Properties of embryonic stem cells:

ES cells derived from a pluripotent cell population (the inner cell mass of the blastocyst). It is diploid and karyotypically normal in vitro, it can be grown in vitro and expanded in number indefinitely in the primitive undifferentiated state characteristic of the embryonic cells from which they derived, and throughout long periods of cultivation. They retain a key property of these embryonic cells, pluripotency or the ability to develop into any cell types in the body (*Pera et al., 2000*)

ES cell can be induced to continue proliferating or to differentiate, also it is clonogenic that is a single ES cell can give rise to a colony of genetically identical cells (*Ruth and Lana, 2001*).

How does embryonic stem cell stay undifferentiated?

A true stem cell is capable of maintaining itself in a self-renewing, undifferentiated state indefinitely. The undifferentiated state of the embryonic stem cell is characterized by specific cell markers that have helped scientists better understand how embryonic stem cells (under the right culture conditions) replicate for hundreds of population doublings and do not differentiate. To date, two major areas of investigation have