Skin Stem Cells

Essay

Submitted for Partial Fulfillment of Master Degree in Anatomy

By

Heba Ramadan Eid Sorour
M.B, B.Ch

Under Supervision of

Prof. Dr. Kariman Abd El-Fattah Al Gohari

Professor of Anatomy
Faculty of Medicine, Ain Shams University

Prof. Dr. Fatma Ibrahim El Rakhawy

Professor of Anatomy
Faculty of Medicine, Ain Shams University

Ass. Prof. Dr. Dalia Fawzi Kallini

Assistant Professor of Anatomy
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
2011

الخلايا الجذعية فى الجلد

رسالة
توطئة مقدمة للحصول علي درجة الماجستير في **التشريح**

مقدمة من
الطبيب /هبة رمضان عيد سرور
بكالوريوس الطب والجراحة

تحت إشراف
الأستاذ الدكتور /كريمان عبد الفتاح الجوهري
أستاذ التشريح
كلية الطب - جامعة عين شمس

الأستاذ الدكتور /فاطمة إبراهيم الرخاوى
أستاذ التشريح
كلية الطب - جامعة عين شمس

الأستاذ مساعد دكتور/ داليا فوزى قلينى
أستاذ مساعد التشريح
كلية الطب - جامعة عين شمس

كلية الطب
جامعة عين شمس
2011

Stem cells are known by their capacity of self-renewal and multilineage differentiation, which make them suitable in treating a broad spectrum of human diseases.

Stem cells have been categorized as (1) Embryonic stem cells (ESCs), (2) Adult stem cells (ASCs), (3) Fetal stem cells (fSCs), and (4) Cord blood stem cells (CB-SCs)

The inner cell mass is the source of embryonic stem (ES) cells. These cells have the ability of going through numerous cycles of cell division and maintain the undifferentiated state. ES cells are pluripotent, and are capable of differentiating into cells representing the three primary germ layers endoderm, ectoderm and mesoderm.

Adult stem cells are multipotent stem cells that possess the characteristic of plasticity and the ability to specialize and develop into other tissues of the body. Beginning in an unspecialized and undeveloped state, they can be differentiated to become heart tissue, neural matter, skin cells, and a host of other tissues.

Fetal stem cells (fSCs) are derived from the placenta, amniotic fluid or fetal tissues. FSCs are higher in number, expansion potential and differentiation abilities if compared with SCs from adult tissues.

CONTENTS

Page

List of Abbreviations

ASCs	Adult stem cells
B	Bulge
BL	Basal layer
BM	Bone marrow
BMZ	Basement membrane zone
BrdUrd	Bromodeoxyuridine
CB	Cord blood
CB-SCs	Cord blood stem cells
CFE	Colony-forming efficiency
CNS	Central nervous system
COL7A1	Collagen, type VII, alpha 1
COL17A1	Collagen, type XVII, alpha 1
CSCs	Cardiac stem cells
DEB	Dystrophic Epidermolysis Bullosis
DP	Dermal papilla
DPCs	Dermal papillae cells
DS	Dermal sheath
DSCs	Dermal sheath cells
E	Epidermis
EBs	Embryoid bodies
EBS	Epidermolysis Bullosis simplex
ECM	Extracellular matrix
EGFP	Enhanced green fluorescent protein
EMI	Epidermal -Mesenchymal interaction
EPU	Epidermal proliferative unit
ES	Embryonic stem
ESCs	Embryonic stem cells
FACS	Fluorescence-activated cell sorting

List of Abbreviations (Cont.)

fSCs	Fetal stem cells
FSCs	Follicle stem cells
GE	Germinative epithelial
G protein	Guanine nucleotide-binding protein
GvHD	Graft-versus-host disease
H	Hair
^{3}H	Tritiated thymidine
HDMSCs	Human dermis-derived MSCs
HESCs	Human emberyomic stem cells
HF	Hair follicle
HF-SMPCs	Hair follicle-Smooth muscle progenitor cells
HG	Hair germ
HSCs	Hematopoietic stem cells
HSDSCs	Human skin-derived stem cells
ICM	Inner cell mass
IFE	The interfollicular epidermis
Ifs	Intermediate filaments
IPS	Induced pluripotent stem cells
IRS	Inner root sheath
IVF	*In vitro* Fertilization
JEB	Junctional Epidermolysis Bullosis
K	Keratins
K5	keratins 5
K14	keratins 14
Klf4	Kruppel-like factor 4
KSCs	Keratinocyte stem cells
Lgr5	Leucine-rich repeat-containing heterotrimeric guanine nucleotide-binding protein (G protein)- coupled receptor 5

List of Abbreviations (Cont.)

LRCs	Label retaining cells
MKTP	Melanocyte keratinocytes transplantation
MSCs	Mesenchymal stem cells
NC	Neural crest
NPCs	Neural precursors
NSCs	Neural stem cells
NT	Nuclear Transfer
Oct4	Octamer 4
OLCs	Oocyte-like cells
ORS	Outer root sheath
P 63	Protein 63
PGC	Primordial germ cells-like cells
PSC	Pluripotent stem cells
PUVA	UVA + Psoralen
S	Sebaceous gland
SCs	Stem cells
SCNT	Somatic cell nuclear transfer
Sec Germ	Secondary Germ
SKPs	Skin-derived precursors
SMCs	Smooth muscle cells
SMPCs	Smooth muscle progenitor cells
Sox2	SRY box–containing protein 2
SVZ	Sub-ventricular zone
TA cell	Transit amplifying cell
TES	Tissue-engineered skin
TSCI	Traumatic spinal cord injury
UCB	Umbilical cord blood
UVA	Ultra violet A
VSEL	Very small embryonic-like
V-SMCs	Vascular smooth muscle cells

List of Figures

List of Figures (Cont.)

Introduction

Stem cells are known by their capacity of self-renewal and multilineage differentiation, which make them uniquely situated to treat a broad spectrum of human diseases **(Cui-ping and Xiao-ping, 2008)**.

Mammalian stem cells are divided into two major categories: (1) Embryonic stem cells that may differentiate into all of the specialized tissues and (2) Adult stem cells that are present in tissues and are capable to regenerate and maintain the normal tissue turnover and repair by providing new specialized and differentiated cells **(Falabella, 2009).**

The inner cell mass is the source of embryonic stem (ES) cells, which have the ability of going through numerous cycles of cell division maintaining the undifferentiated state. ES cells are pluripotent, and are capable of differentiating into cells representing the three primary germ layers endoderm, ectoderm and mesoderm **(Zouboulis et al., 2008).**

Adult stem cells are the regenerative cells of the human body that possess the characteristic of plasticity and the ability to specialize and develop into other tissues of the body. Beginning in an unspecialized and undeveloped state, they can be differentiated to become heart tissue, neurones, skin cells, and other tissues **(Sharpless and Dephnho, 2007).**

Mammalian skin serves a number of vital physiological functions to maintain homeostasis. Skin provides a moisture barrier, regulates body temperature via hair follicles, sweat

glands, and dermal capillaries, and provides lubrication via sebaceous gland **(Cui-ping and Xiao-ping, 2008).**

Skin consists of two layers: the epidermis, a stratified squamous keratinized epithelium and an underlying thick layer of collagen-rich dermal connective tissues providing support and nourishment. Appendages, such as hair follicles and glands are derived from and linked to the epidermis but extend deep into the dermal layer **(Zheng et al., 2005).**

Significant advances have been made in identifying and locating the stem cells that inhabit the skin including epidermal stem cells, dermal stem cells and hair follicle stem cells **(Fernandes et al., 2004).**

The outermost, cornified layers of the epidermis are continually shed from the surface of the skin and are replenished through proliferation of cells in the basal layer (BL) that contained putative stem cells (SCs) in addition to the transiently amplifying (TA) cells, which give rise to terminally differentiating suprabasal layers **(Watt and Jensen, 2009).**

Epithelial stem cells are identified in the hair follicle bulge as quiescent "label retaining cells". Bulge cells possess stem cell characteristics, including multipotency and high proliferative potential .After wounding or transplantation; bulge cells give rise to epidermis, follicles, and sebaceous glands **(Tumbar et al., 2004)**.

Hair follicle dermal stem cells reside in the dermal papillae (DP) at the base of the follicle and the dermal sheath

(DS) that surrounds the outside of the hair follicle. These cells exhibit some properties of stem cells, including regenerative potential, wound healing and ability to produce a functional dermis **(Cui-ping and Xiao-ping, 2008)**.

Moreover, non-follicular mesodermal (mesenchymal) stem cells isolated from the dermis proved to be able to differentiate to endoderm and ectoderm due to their ability to synthesize nestin, fibronectin and vimentin as well as other marker proteins **(Zouboulis et al., 2008).**

ES cells can be derived by somatic cell nuclear transfer (SCNT). Somatic cells can be reprogrammed to an embryonic-like state by injection of the nucleus of a somatic cell into enucleated oocyte. Researchers report the use of nuclei from hair follicle stem cells and other skin keratinocytes as nuclear transfer (NT) donors to clone mice, revealing skin as a source of readily accessible stem cells **(Cui-ping and Xiao-ping, 2008)**.

Expression of defined factors in human fibroblasts of the dermis of the skin generates induced pluripotent stem cells (iPS) morphologically and physiologically highly similar to human embryonic stem cells (HESCs) **(Lowry et al., 2008).**

The study of skin stem cells may lead to the treatment of skin loss, skin disease and hair loss **(Cui-ping and Xiao-ping, 2008).**

Aim of the Work

The aim of the present study is to make a review about the concept of stem cells, its exact site in skin (epidermal, dermal and follicular) and its clinical importance in different dermatological and non-dermatological disorders.

Chapter (1):
Stem Cell Basics

Stem cells (SCs) are undifferentiated cells that are defined by their ability to self renew and multilineage differentiation, (Fig.1) **(Enver et al., 2009).**

Stem cells divide much slower than the more differentiated cell type which is often interpreted as protecting against mutations and cytotoxic agents **(Stiehl and Marciniak-Czochra, 2011).**

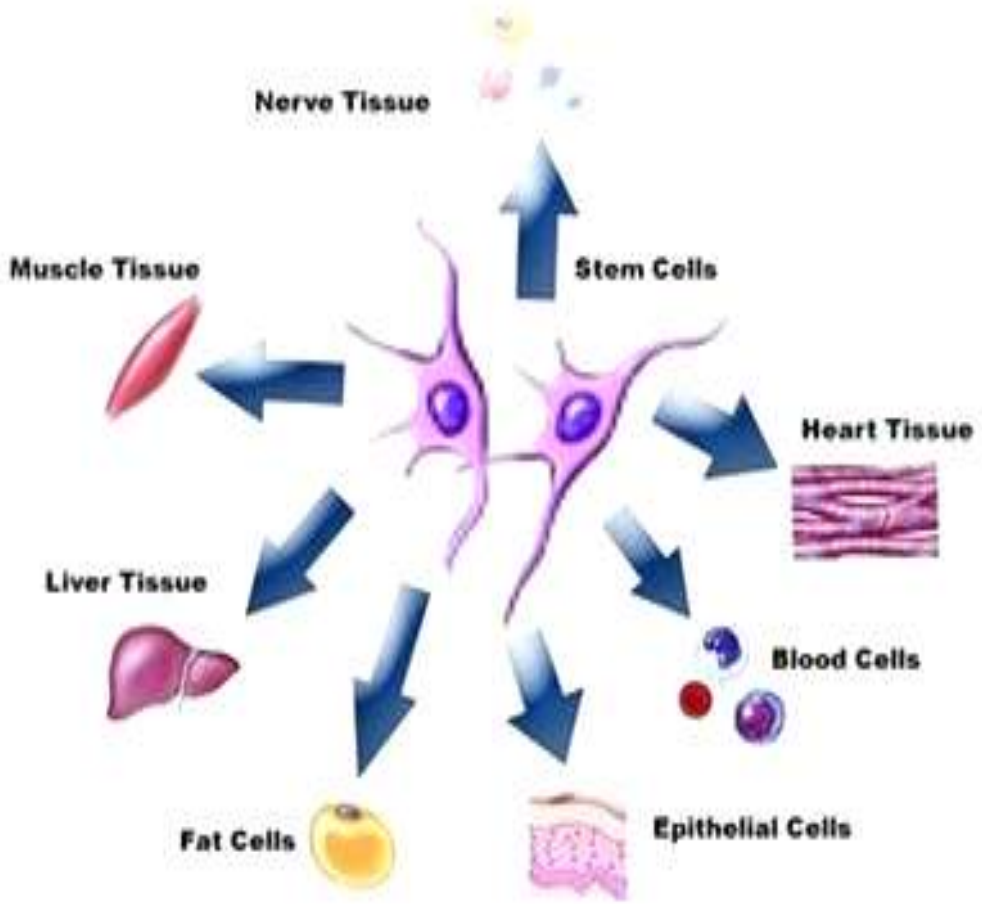

Figure (1)*:* Stem cell multilineage differentiation **(Enver et al., 2009).**

I- Properties:

Stem cells are characterized by the following properties: they are able to maintain the size of their population by producing offspring with stem cell properties (self renewal), able to give rise to cells with different biological properties (multipotency), are functionally non-specialized cells and their populations are morphologically and biochemically hetero-geneous **(Dick, 2003).**

Replication of stem cells can occur either symmetrically or asymmetrically (Fig.2) **(Moore and Lemischka, 2006 & Zouboulis et al., 2008).**

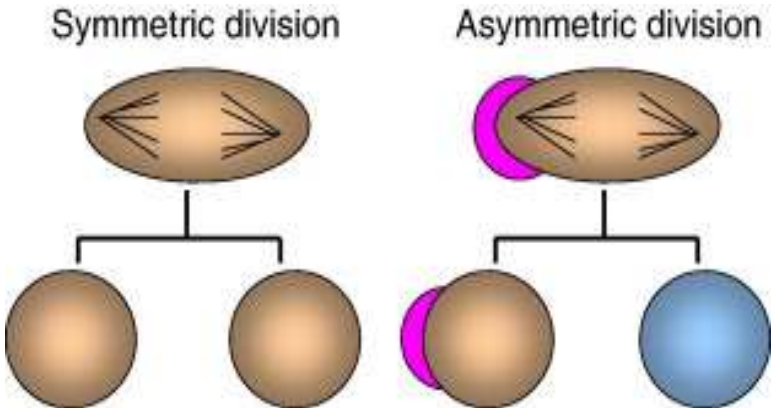

Figure (2): Symmetric and asymmetric cell divisions **(Zouboulis et al., 2008).**

Symmetric division occurs when a stem cell divide to gives rise to two identical daughter cells. That allows the stem cell pool to be regulated by factors that control the probability of self-renewing versus differentiation. Stem cells typically cycle slowly, being in a mitotically quiescent form most of the time **(Yu and Silva, 2008).**