# الملخص العربى

تم إجراء هذه الدراسة على عشرة مرضى يعانون على جانبي الوجه من ندب ما بعد حب الشباب القابلة للتمدد. حيث تم علاج أحد جانبي الوجه بالحقن الموضعي للخلايا الجذعية المأخوذة من نخاع العظام لنفس الشخص في جلسة واحدة يليها حقن موضعي للخلايا الليفية التحفيزية كل أسبوعين خلال فترة ستة أشهر. بينما على الجانب الآخر من الوجه تم حقن الخلايا الليفية التحفيزية فقط كعنصر تحكم .

في نهاية الدراسة ، كانت نسبة الانخفاض في متوسط درجة الندب (١٦,٧٤٥ -/+٣٥,٢٨٢) في الجوانب المعالجة من الوجه مقارنة بـ (١٣,٣٥١-/+١٣,٣٠٣) في الجوانب المتحكم بها والمسيطر عليها بحقن الخلايا الليفية التحفيزية فقط كعنصر تحكم .

على الرغم من أن العلاج بالخلايا الجذعية يبدو واعداً في علاج الحالات الضمورية والتنكسية في مختلف أعضاء الجسم بما في ذلك الجلد ، فإن معدل التحسن من خفيف إلى معتدل كما هو موضح في هذه الرسالة تكشف عن أن استخدام هذه التقنيات يحتاج إلى مزيد من التوحيد والصقل. و الأكثر أهمية هو اختيار المريض المناسب وذلك لضمان النتائج المرجوة من استخدام الخلايا الجذعية للحث على التمايز في الاتجاه الصحيح.

# استخدام الخلايا أحادية النواة المستخلصة من النخاع العظمى لعلاج نفس الشخص من ندب الجلد الصُمورية ما بعد حب الشباب

رسالة

توطئة للحصول على درجة الماجستير في الأمراض الجلدية والتناسلية وأمراض الذكورة


مقدمة من

الطبيبة/ سهـــام محمد حسنين سليم

تحت اشراف

**أ.د/ علاء الدين إسماعيل عبد المطلب**

أستاذ الجراحة العامة

كلية الطب-جامعة عين شمس

**أ.د/ أحمد إبراهيم رشـيد**

أستاذ الأمراض الجلدية والتناسلية وأمراض الذكورة

كلية الطب-جامعة عين شمس

**د/ الحسن محمد حسن الحفناوى**

مدرس الأمراض الجلدية والتناسلية وأمراض الذكورة

كلية الطب-جامعة عين شمس



**كليه الطب**

**جامعه عين شمس**

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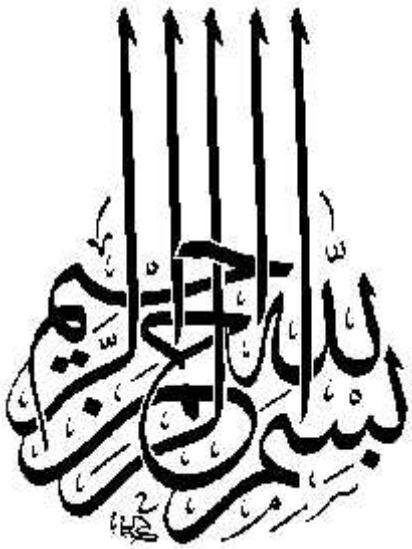

﴿قالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا

إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ﴾

صدق الله العظيم

سورة البقرة آية (٣٢)

# Introduction

In the last two decades, skin stem cell biology has been a rapidly advancing field in life sciences ***(Snyder and Teng, 2012*).**

To utilize stem cells for grafting and skin tissue regeneration, we must develop well-defined and efficient resources e.g of embryonic stem cells derived from the inner cell mass of embryos at the blastocytes stage, putative epidermal stem cells located at the bulge of hair follicles, or even adult stem cells of non-epidermal origin, such as those derived from the bone marrow and peripheral blood circulation ***(Fu and Sun, 2009).***

A number of factors would favor the use of embryonic stem cells over adult stem cells for the repair and regeneration of skin tissues. The most obvious are their capacity for immortality and self renewal, which enables them to provide an unlimited supply of differentiated keratinocytes or keratinocytes progenitors for treating skin injury. However, since the 1970s, embryonic stem cell-related research has raised a host of difficult ethical issues and has sparked great public interest and controversy. By contrast, adult stem cells derived from the skin, bone marrow or peripheral blood and in

spite of their limited capacity for self-renewal and proliferation, which may decrease with age, would be more acceptable for therapeutic application in human skin tissues ***(Fu and Sun, 2009).***

Significant progress has been made in the regeneration of the dermis in wound healing through transplantation of bone marrow-derived mesenchymal stem cells (BM-MSCs). **Badiavas and co-workers** tracked green fluorescent protein (GFP)-labeled bone marrow transplanted into non-GFP-transplanted mice to determine the participation of bone marrow stem cells in cutaneous wounds With wounding, bone marrow-derived cells could be induced to incorporate into and differentiate into non-hematopoietic skin structures ***(Badiavas et la., 2003).***

These BM-MSC treated wounds showed significantly accelerated wounding closure, with increased re-epithelialization, cellularity and angiogenesis ***(Kim et al., 2012).***

***Korbling et al., (2002)*** argue that stem cells in mobilized peripheral blood and marrow have similar in vivo characterisation. Actually, normal skin is a target organ for bone marrow-derived cells from both the hematopoietic and mesenchymal stem-cell pool. The bone marrow contribution to

normal skin and to healing cutaneous wounds is substantially greater than previously recognized ***(Sasaki et al., 2008).*** After tissue injury, hematopoietic and multipotent progenitor cells mobilize from the bone marrow into the pool of circulating cells. These cells migrate to the site of injury, where they regulate the proliferation and migration of epithelial cells and dermal mesenchymal cells during the early inflammatory phase. However, the roles of bone marrow-derived hematopietic and mesenchymal cells differ little in skin biology: wound healing involves local cutaneous cell reconstituting the epiderms, as well as distant bone marrow-derived cells and adjacent uninjured dermal mesenchymal cells reconstituting the dermal fibroblast population ***(Fu and Sun, 2009).***

# Aim of the Work

The aim of the present study was to assess the utility of autologous adult bone marrow stem cells in the management of atrophic distensible post acne scars.

# Stem Cells

## 1-Definition

The word "stemness" defines a series of properties which distinguish a heterogeneous variety of cell population. However, in the absence of a current consensus on a gold standard protocol to isolate and identify stem cells, the definition of "stemness" is in a continuous evolution ***(Pittenger et al., 1999; Fortier, 2005 and Mayhall et al., 2004).***

Biologically, stem cells (SCs) are characterized by self renewability ***(Zhong, 2008)*** that is the ability not only to divide themselves rapidly and continuously, but also to create new SCs and progenitors more differentiated than the mother cells. The asymmetric mitosis is the process which permits to obtain two intrinsically different daughter cells. After that, the mitotic spindle aligns itself perpendicularly to the cell axis polarity. At the end of the process two different cells are obtained as shown in **(Figure 1)** ***(Doe, 2008; Zhong and Chia, 2008; Knoblich, 2008).***

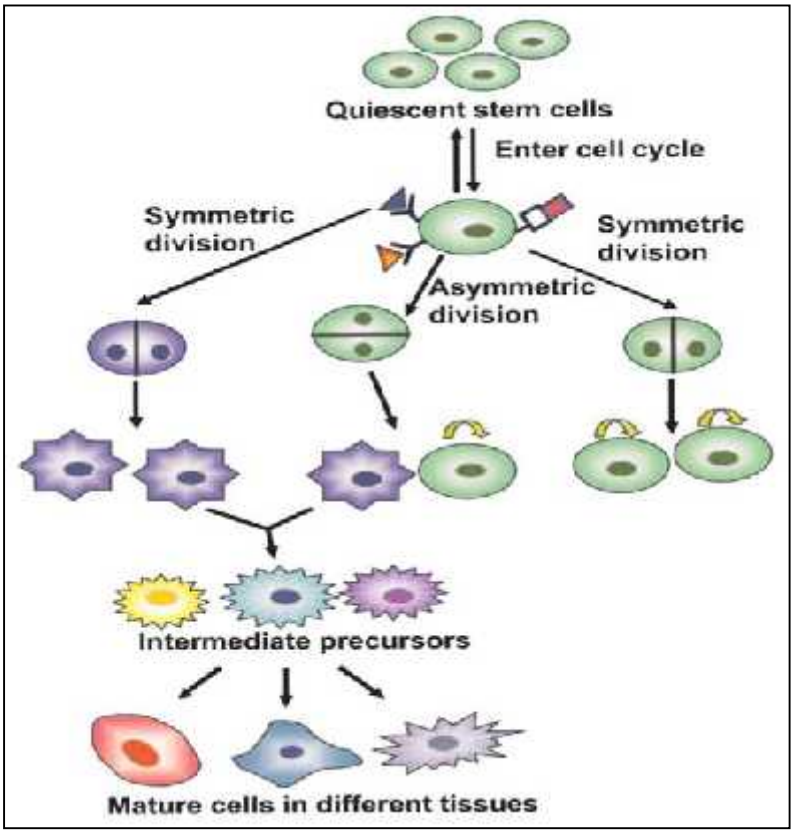


**Figure (1):** Possible stem cell division pathways: Stem cells can remain quiescent or enter cell cycling in three ways: asymmetric division gives rise to a stem cell daughter and a precursor daughter; two kinds of symmetric division will generate twin daughter cells of either stem cell or progenitor properties ***(Cai et al., 2004).***

Stem cells morphology is usually simpler than that one of the committed cells of the same lineage. It has often got a circular shape depending on its tissue lineage and a low ratio cytoplasm/nucleus dimension, i.e. a sign of synthetic activity. Several specifics markers of general or lineage "stemness" have

been described but some, such as alkaline phosphatase, are common to many cell types ***(Pittenger et al., 1999; Baksh et al., 2004; Baharvand et al., 2004; Barry and Murphy, 2004 and Thomson et al., 1998).***

From the physiological point of view, adult stem cells (ASCs) maintain the tissue homeostasis as they are already partially committed. ASCs usually differentiate in a restricted range of progenitors and terminal cells to replace local parenchyma ***(Ladurner et al., 2000),*** damaged cells or sustaining cellular turn over ***(Fang et al., 2004).***

Stem cells derived from early human embryos (Embryonic stem cells) (ESCs) are pluripotent and can generate all committed cell types ***(Pera et al., 2000; Pessina and Gribaldo, 2006).*** Fetal stem cells (FSCs) derive from the placenta, membranes, amniotic fluid or fetal tissues. FSCs are higher in number, expansion potential and differentiation abilities if compared with SCs from adult tissues ***(Gucciardo et al., 2009).***

Naturally, the migration, differentiation and growth are mediated by the tissue, degree of injury and SCs involved. Damaged tissue releases factors that induce SCs homing. The tissue, intended as stromal cells, extracellular matrix,

circulating growth and differentiating factors, determines the exact way of gene activation and a functional reaction on SCs, such as moving in a specific district, differentiating in a particular cell type. These factors can alter the gene expression pattern in SCs when they reside in a new tissue ***(Blau et al., 2001).***

## 2-Plasticity of Stem Cells

Plasticity is the ability of an adult stem cell from one tissue to generate the specialized cell type(s) of another tissue. For example, adult stem cells from bone marrow generated "under specific experimental conditions" cells that resemble neurons and other cell types that are commonly found in the brain as shown in **(Figure 2)**. The concept of adult stem cell plasticity is new, and the phenomenon is not thoroughly understood. Evidence suggests that, given the right environment, some stem cells are capable of being "genetically reprogrammed" to generate specialized cells that are characteristic of different tissues ***(Slack, 2000).***

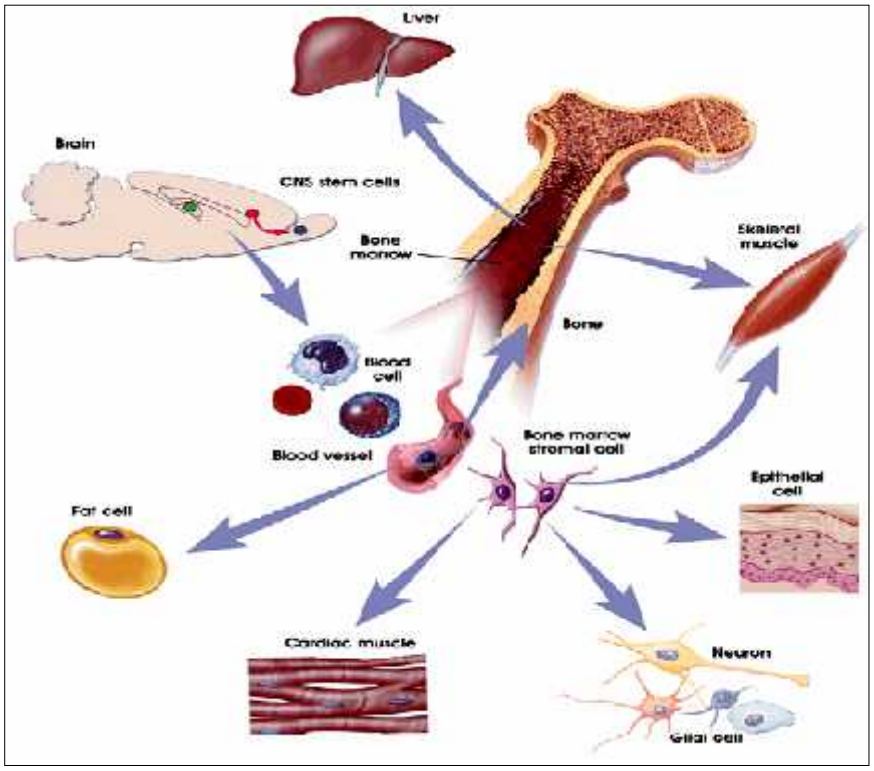


**Figure (2):** Plasticity of adult stem cells ***(Potten and Loeffler, 2001).***

## 3-Trans-differentiation

Is the acquisition of the identity of a different phenotype through the expression of the gene pattern of other tissue (direct) or through the achievement of a more primitive state and the successive differentiation to another cell type (indirect or dedifferentiation). By fusion with a cell of another tissue, a cell can express a gene and acquire a phenotypic element of another parenchyma ***(Fortier, 2005).***

## 4- Clonality or Clonally Derived Stem Cell

A cell is said to be clonally derived or to exhibit clonality if it was generated by the division of a single cell and is genetically identical to that cell. In stem cell research, the concept of clonality is important for several reasons. For researchers to fully understand and harness the ability of stem cells to generate replacement cells and tissues, the exact identity of those cells' genetic capabilities and functional qualities must be known. Human pluripotent stem cells from embryos and fetal tissue are by their nature clonally derived ***(Odorico et al., 2001).***

## 5- Progenitor or Precursor Cell

A progenitor or precursor cell occurs in fetal or adult tissues and is partially specialized; it divides and gives rise to differentiated cells. Researchers often distinguish precursor/ progenitor cells from adult stem cells in the following way: when a stem cell divides, one of the two new cells is often a stem cell capable of replicating itself again. In contrast, when a progenitor/ precursor cell divides, it can form more progenitor/ precursor cells or it can form two specialized cells, neither of which is capable of replicating itself as shown in **(Figure 3)**. Progenitor/ precursor cells can replace cells that are damaged or dead, thus maintaining the integrity and functions of a tissue such as liver or brain. Progenitor/ precursor cells give rise to

related types of cells for examples lymphocytes such as B cells, and natural killer cells but in their normal state do not generate a wide variety of cell types ***(Slack, 2000).***

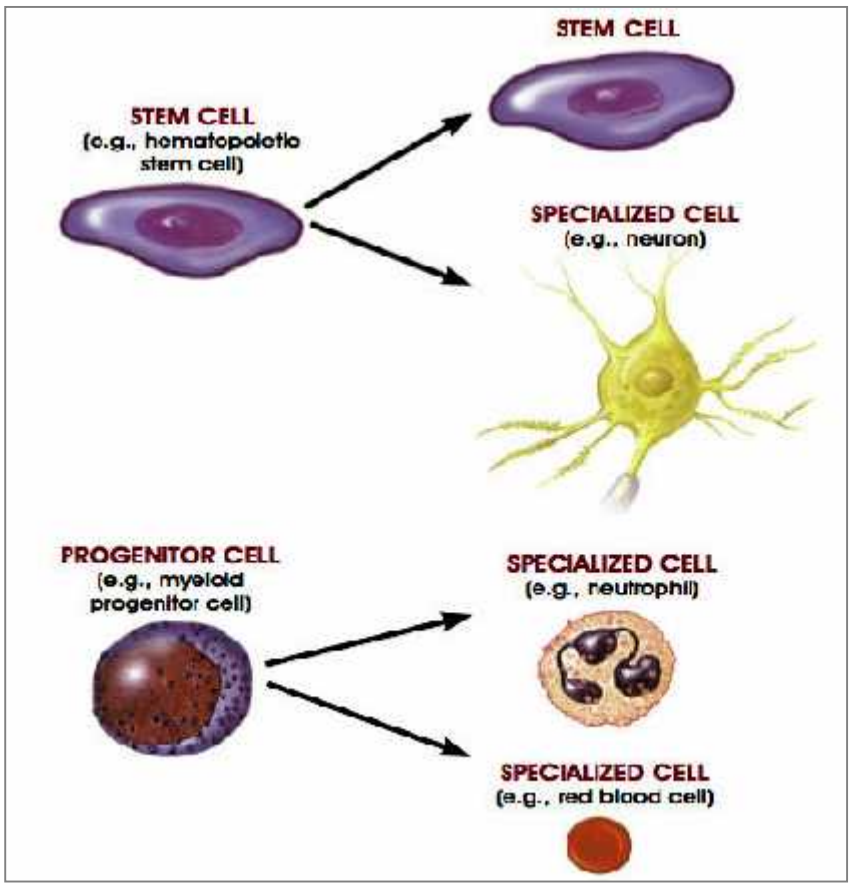


**Figure (3):** Distinguishing features of Progenitor/Precursor cells and stem Cells. A stem cell is an unspecialized cell that is capable of replicating or self renewing itself and developing into specialized cells of a variety of cell types. The product of a stem cell undergoing division is at least one additional stem cell that has the same capabilities of the originating cell. Shown here is an example of a hematopoietic stem cell producing a second generation stem cell and a neuron. A progenitor cell (also known as a precursor cell) is unspecialized or has partial characteristics of a specialized cell that is capable of undergoing cell division and yielding two specialized cells. Shown here is an example of amyeloid progenitor/precursor undergoing cell division to yield two specialized cells ***(Robey, 2000).***

## 6-Classification of Stem Cells

Stem cells can be classified by the extent to which they can differentiate into different cell type:

"Totipotent": can differentiate into any cell type in the body plus the placenta, which nourishes the emberyo. A fertilized egg is a type of totipotent stem cell. Cells produced in the first few divisions of the fertilized egg are also totipotent ***(Woodward et al., 2005).***

"Pluripotent": The "pluripotent" cells, are descendants of the totipotent stem cells of the embryo. These cells, which develop about four days after fertilization, can differentiate into any cell type, except for totipotent stem cells and the cells of the placenta ***(Woodward et al., 2005).***

"Multipotent": "multipotent" cells are descendants of the pluripotent stem cells and antecedent of specialized cells in particular tissues. For example, hematopoietic stem cells, which are found primarily in the bone marrow, give rise to all of the cells found in the blood, including red blood cells, white blood cells, and platelets ***(Woodward et al., 2005).***

"Oligopotent": stem cells can differentiate into only few cells, such as lymphoid or myeloid stem cells ***(Hans R. Scholer, 2007).***