# Postnatal stem cell -based approaches for regenerative tissues

**Nesreen Ebrahim Ahmed Salem**

Types of stem cellsThere are 3 major types of stem cells ; embryonic, fetal, and adult, each come from different sources and has some different properties.A) Embryonic stem cellWhen a sperm fertilizes an egg it becomes what is known as zygote, many scientists view zygote as the ultimate stem cell because it can develop into any cell not only of embryo but also of surrounding tissues, such as placenta. Because the zygote has the highest degree of transdifferentiation, it is referred to as a totipotent stem cell. So totipotent cells are the first stage stem cells that can be found in zygote and develop into both embryonic and extraembryonic tissues. Thirty hours after fertilization, the zygote begins to divide, and by fifth or sixth day the cells form a blastocyst. These cells are somewhat less potential for differentiation and more specialized than totipotent zygote stem cell ; those on the outer surface of the blastocyst develop into placenta and other tissues that surround the fetus, while those inside, referred to as embryonic stem cells become the cells of the fetal organs and tissues. Such stem cells that can become any of the more than 200 types of cells in the body are called pluripotent stem cell (Tzukerman et al., 2003).B) Fetal stem cellAs embryo grows, it accumulates additional embryonic stem cells in the yolk sac; as the fetus grows from weeks 8 to 12, they accumulate (fetal stem cells) in the liver. Both embryonic and fetal stem cells generate the developing tissues and organs. At this stage, the stem cells are more tissue specific rather than generating all of the body’s 200 different cell types, for example, fetal stem cells in liver tend to generate liver and blood cell families. Such are generally designated as multipotent. Nevertheless, fetal cells may have an advantage over embryonic stem cells in that they may not form teratomas. Fetal liver tissue has been shown to be a rich source of stem cells. Indeed, in studies in which stem cells from human fetal liver tissue, cord blood or adult were transplanted into mice, fetal liver tissue was shown to be the richest source of very primitive progenitors. Up until week 12, fetal stem cells as embryonic stem cells, have very important property: they can be transplanted into an individual without being rejected. This is because they have little to know of certain type of protein on their surface (class II human leucocytic antigen ) which otherwise can trigger a rejection reaction if the cells are transplanted into other individual. After 12 weeks, fetal stem cells acquire these immune triggering proteins, and they remain from this point on, including adult stem cells (National Institute of Health, 2004).C) Adult stem cellAn adult stem cell is an undifferentiated cell found among differentiated

cells in a tissue or organ, can renew itself and can differentiate to yield the major specialized cell types of tissue or organ. The primary roles of adult stem cell in living organisms are to maintain and repair the tissue in which they are found. These cells have more limited differentiation potential so they are called multipotent stem cell (National Institute of Health 2005).Scientists have found adult stem cells in many tissues more than they thought possible. This finding has led scientists to ask whether adult stem cell could be used for transplants. Certain type of adult stem cells seems to have the ability to differentiate into a number of different cell types, given the right conditions. If this differentiation of adult stem cell can be controlled in the laboratory, these cells may become the basis of therapies for many serious common diseases. These adult stem cells are very small in number in each tissue and reside in a special area of each tissue where they remain quiescent (non dividing) for many years until they are activated by disease or tissue injury (National Institute of Health, 2005).Types of postnatal stem cellsPostnatal stem cells include, (1) umbilical cord , which contains hematopoietic stem cells and Wharton jelly cells (mesenchymal stem cells), (2) tissue specific stem cells, as many adult tissues contain populations of stem cells that have the capacity for renewal after trauma, disease, or aging. For example, the postnatal bone marrow has traditionally been seen as an organ composed of two main systems rooted in distinct lineages; the hematopoietic tissue proper and associated supporting stroma. The evidence pointing to a putative stem cell upstream of the diverse lineages and cell phenotypes comprising the bone marrow stromal system has made marrow the only known organ in which two separate and distinct stem cells and dependent tissue systems not only coexist, but also functionally cooperate . Originally examined because of their critical role in the formation of hematopoietic microenvironment , marrow stromal cells later come to center stage with the recognition that they are the stem /progenitor cells of skeletal tissues. More recent data pointing to the unexpected differentiation potential of marrow stromal cells into neural tissue or muscle grant them membership in the diverse family of somatic stem cells (Bianco et al., 2001).Side population (SP) stem cellsThere is a recent type called side population stem cells which is present in bone marrow as well as the other tissues. Although major advance in the murine hematopoietic stem cell field came with development of phenotypic strategies to physically purify transplantable activity from bone marrow and fetal liver (Jordan et al., 1990), other hematopoietic stem cell (HSC) purification strategies have taken advantage of differential staining with vital dyes such as Rhodamine 123 or Hoechst 33342 (Wolf et al., 1993).In the hematopoietic field, the Hoechst low ”side population” (SP) phenotype was originally described in murine bone marrow preparations, where this fraction was found to be greatly enriched for long-term repopulating hematopoietic stem cells. Transplantation activity enrichment of mouse bone marrow–derived SP cells varies from 1,000 to 3,000 fold, which is similar to the enrichment achieved by purification of HSCs using combinations of cell-surface markers (Goodell, 2002 ).These SP cells are identified according to their ability to efflux the dye at a greater rate than other cells within the bone marrow. Moreover, the degree of efflux activity seems to correlate with the maturation state, such that cells exhibiting the highest efflux activity are the most primitive or least restricted in terms of differentiation potential

(Goodell et al., 1997).The Hoechst efflux phenomenon has proven to be a highly useful primary purification strategy for isolating potential stem/progenitor cells from various tissues in the absence of cell-surface markers. Cells with an SP phenotype have now been described in many solid tissues, including the skeletal muscle, lung, liver, heart, testis, kidney, skin, brain, and mammary gland (Rietze et al., 2001).Molecular determinant of side population phenotypeHow and why do these cells efflux dyes? The supravital stain Hoechst 33342 stoichometrically binds to (adinine-thymidine) AT-rich regions of the minor groove of DNA (Lalande and Miller, 1979). Hoechst fluorescence intensity is an index of DNA content, chromatin structure and conformation, and discriminates between cells in different stages of cell cycle (Arndt-Jovin and Jovin , 1977).Origin of side population cells throughout developmentThere is accumulating evidence to suggest that hematopoietic cells are recruited to tissues such as muscle (Ferrari et al., 1998), liver (Lagasse et al., 2000, ) heart (Orlic et al., 2001 a`), and kidney (Kale et al., 2003) during regeneration from certain types of damage. If tissue SP cells represent resident stem cell populations, do the SP cells in particular organs originate from a common pool of cells in the bone marrow and adopt tissue-specific characteristics upon seeding within a specific local environment? There is some experimental evidence that supports this notion. In lethally irradiated recipients transplanted with bone marrow SP cells isolated from Rosa26 transgenic mice, 5 months after transplant, approximately 40% of host muscle SP cells were LacZ+ (marker gene), thus being derived from donor cells. Alternatively, organ- and tissue-specific SP cells may arise solely as a consequence of the normal development of that specific organ but share the SP phenotype as a function of their inherent biological characteristics (Kale et al., 2003).