INTRODUCTION

Stem cells are unspecialized cells having two important characteristics that distinguish them from other cell types. First, these unspecialized cells can renew themselves for long periods through cell division. The second is that under certain physiologic or experimental conditions, they can differentiate into specialized cell types such as the beating cells of the heart muscle or the insulin-producing cells of the pancreas ***(Wagers et al., 2002).***

There are two main kinds of stem cells; adult stem cell which are undifferentiated cells found among differentiated cells in a tissue or organ and have a major role in tissue repair ***(Robey, 2000),*** and embryonic stem cells which could be isolated from the blastocyst of the embryo *(**Andras et al., 2006**).*

In adults, stem cells reside in a physiologically limited and specialized microenvironment, or niche, that supports stem cells but varies in nature and location depending on the tissue type. Maintaining a balance between the proliferation signal and antiproliferation signal in such microenvironment, is the key to homeostatic regulation of stem cells, allowing stem cells to undergo self-renewal while supporting ongoing tissue regeneration ***(Linheng and William, 2006)***.

Examples for that regenerative stem cells are intestinal stem cells that are present between differentiated Paneth cells ***(He et al.;2004)*** and skin stem cells, which are located in the bulge area of the hair follicle ***(Silva et al.,2005).*** Adult hematopoiesis occurs in bone marrow in which

hematopoietic stem cells are primarily located in the osteoblastic niche on the bone surface ***(Kiel et al., 2005).***

"Cancer stem cells" are recently identified. They are a sub-population of tumor cells that possess characteristics normally associated with stem cells. They may be responsible for tumor relapse and metastasis ***(Clarke, et al., 2006).*** Any genetic mutation that leads stem cells to become independent of growth signals, or to resist antigrowth signals, will cause the stem cells to undergo uncontrolled proliferation and possible tumorigenesis **(*Linheng and William, 2006)***.

Owing to their high self renewal capacity and differentiation potency, stem cell based therapy is now a promising approach in treating many diseases as stem cells can be directed to differentiate into specific cell types. So, they can be used to replace damaged cells and tissues and treat different diseases including Parkinson's and Alzheimer's diseases, spinal cord injury, stroke, burns, heart disease, diabetes, osteoarthritis, and rheumatoid arthritis ***(Mason and Dunnill, 2008).***

However, There is a wide spread controversy over the use of stem cells. Besides the ethical problem of embryo destruction to get embryonic stem cells ***(Kaunas, 2005),*** uncontrolled cell proliferation causing tumors ***(Philippe et al., 2008)*** and the immunological challenges of embryonic stem cells rejection ***(Abdelkrim et al., 2009)*** are major problems.

Various immunohistohemical markers are used to detect pluripotent stem cells as stem cell factor (cKIT ligand) that stimulates stem cell proliferation ***(Kakurai et al.,2002***), alkaline phosphatase that is expressed in embryonic

stem cells (***Skotheim et al.,2003)*** and OCT4 which is a transcription factor that is unique for pluripotent cells ***(Gerrard et al.,2005)***.

As regard for the liver; it is now generally accepted that liver contains cells with stem-like properties and that these cells can be activated to proliferate and differentiate into mature hepatic epithelial cells under certain pathophysiologic circumstances ***(Chen et al., 2001).***

The origin of hepatic stem cell population has been a controversial topic. A hypothesis suggests that they are activated bone marrow stem cells that migrate to the liver in response to injury **(Lemaigre *and Zaret, 2004)***.

However, there is a growing body of work suggesting that hepatic stem cells are an independent stem cell population, distinct from hematopoietic stem cell ***(Nierhoff et al., 2005).***

Epidemiological studies indicate that hepatocellular carcinoma (HCC) is one of the most common human visceral malignancies. The risk of hepatocellular carcinoma is significantly increased in chronic liver diseases especially when cirrhosis is present. As cirrhosis develops, hepatocyte necrosis is followed by an attempted secondary proliferative response of mature hepatocytes, but this proliferative response is often impaired in chronic liver disease. An alternative mechanism for hepatocyte regeneration in chronic liver disease may involve stem cell proliferation and differentiation into hepatocytes ***(Kym et al .,1999) .***

Using hepatic/stem progenitor cells may provide an alternative therapy to liver transplantation for patients with liver failure ***(Maggie et al.,2006).***They

may repopulate damaged liver cells after transplantation either through intravenous or intrasplenic route ***(Kuo et al.,2008).***