STEM CELL TRANSPLANTATION IN CHRONIC LIVER DISEASE

An Essay
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General Surgery

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List of Abbreviations

Abb.	Full term
Sc	Stem cell.
OLT	Orthotopic liver transplantation.
rHSPC	Resident hepatic stem cell-progenitor cells.
GFP	Green fluorescence protein.
HSCs	Hematopoietic stem cells.
EpCAM	Epithelial cell adhesion molecule.
FACS	Fluorescence – activated cell sorting.
NASH	Non –alcohol steatohepatitis.

INTRODUCTION

The liver is one of the most important organs in human body, being responsible for functions such as detoxification, excretion, metabolism and regulation of various constituents in the blood.

The liver has a tremendous regenerative potential and both hepatocytes and stem cells within the organ are able to repair the liver during injury.

Cirrhosis represents a late stage of progressive hepatic fibrosis characterized by distortion of the hepatic architecture and the formation of regenerative nodules.

Orthotopic liver transplantation (OLT) is the standard treatment modality in patients with decompensate cirrhosis. However, it has several limitations such as shortage of organ donors, rejection, high cost and surgical complications ***(Nejad et al., ٢٠٠٧).***

For example in Iran the minimum number of patients who need liver transplant year is around ١٠٠٠ or more but the maximum number of Orthotopic liver each trans- plantation (OLT) is only ١٠٠ per year, therefore the majority of patients with end stage liver disease in Iran are presently dying at the end of natural history of liver disease.

Living donor liver transplantation provides one means to expand organ availability. However there is a real need for an alternative therapies for end stage liver disease ***(Nejad et al., ٢٠٠٧).***

Preliminary experience with clinical hepatocyte transplantation during past decade has provided proof of concept that cell therapy can be effective for the treatment of some liver diseases ***(Maurizio Muraca et al., ٢٠٠٦).***

Recent progress in cell biology resulting in the isolation and characterization of bone marrow stem cells and progenitor cells further increases the expectation for a new approach to the treatment of genetic and chronic liver diseases.

Cell therapy can be defined as the use of living cells to restore, maintain or enhance the function of tissues and organs. The use of isolated, viable cells has emerged as an experimental Therapeutic tool in the past decade due to progress in cell biology and particularly in techniques for the isolation and culture of cells derived form several organs and tissues. However, experimental cell therapy has a longer tradition in hepatology, since it has been known for more than ٣٠ years that isolated hepatocytes infused into the portal vein engraft into the liver cords and express the normal cell function such a therapeutic strategy was put

forward as an alternative to Orthotopic liver transplantation (OLT) which requires major surgery and is limited by the availability of donors ***(Maurizio Muraca et al., ٢٠٠٦)***.

There are at least two types of stem cells in the human bone marrow: mesenchymal stem cells and haematopoietic stem cells (HSCs). HSCs:- are CD٣٤+ and CD١٣٣+ and they can give rise to all lineages of blood cell differentiation).

Recently, intracoronary infusion of bone marrow stem cells was reported to be safe and effective in patients with acute myocardial infarction Furthermore in vivo transdifferentiation of human HSCs to functional hepatocytes has been demonstrated, also it has been shown that infusion of bone marrow stem cells to animal models of liver cirrhosis can lead to regression of liver fibrosis. ***(Nejad et al., ٢٠٠٧)***.

Recently, it was reported that portal administration of autologous CD١٣٣+ HSCs accelerated liver regeneration. We hypothesized that infusion of HSCs may help to reverse liver failure in patients with decompensated cirrhosis.

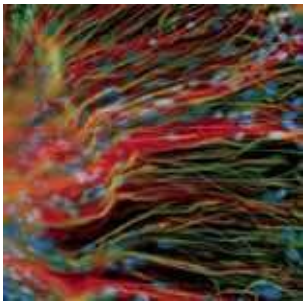
In the present essay we put the cell therapy (stem cell transplantation) in the lime- light as an alternative to (OLT) and during this essay we well be answer the questions about stem cell transplantation; what is the stem cell; what are the sources, types, techniques of isolation and purification then routes of administration and then we evaluate rates of success in this field.

AIM OF THE WORK

In the present essay we aim to put the cellular therapy in treatment of chronic liver disease under vision as an effective alternative treatment than liver transplant (surgically).

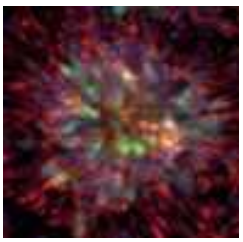
Chapter (١)

UNDERSTANDING STEM CELLS



For centuries, scientists have known that certain animals can regenerate missing parts of their bodies. Humans actually share this ability with animals like the starfish and the newt. Although we can't replace a missing leg or a finger, our bodies are constantly regenerating blood, skin, and other tissues. The identity of the powerful cells that allow us to regenerate some tissues was first revealed when experiments with bone marrow in the ١٩٥٠s established the existence of *stem cells* in our bodies and led to the development of bone marrow transplantation, a therapy now widely used in medicine. This discovery raised hope in the medical potential of regeneration. For the first time in history, it became possible for physicians to regenerate a damaged tissue with a new supply of healthy cells by drawing on the unique ability of stem cells to create many of the body's specialized cell types ***(Almeda et al., ٢٠٠٤).***

Once they had recognized the medical potential of regeneration through the success of bone marrow transplants, scientists sought to identify similar cells within the embryo. Early studies of human development had

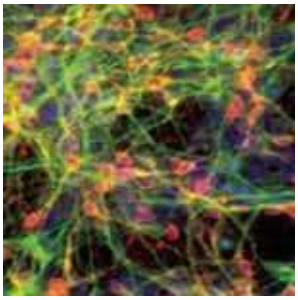


demonstrated that the cells of the embryo were capable of producing every cell type in the human body. Scientists were able to extract embryonic stem cells from mice in the ١٩٨٠s, but it wasn't until ١٩٩٨ that a team of scientists from the University of Wisconsin–Madison became the first group to isolate human embryonic stem cells and keep them alive in the laboratory. The team knew that they had in fact isolated stem cells because the cells could remain unspecialized for long periods of time, yet maintained the ability to transform into a variety of specialized cell types, including nerve, gut, muscle, bone and cartilage cells ***(Bulte et al., ٢٠٠١).***

Stem cell research is being pursued in the hope of achieving major medical breakthroughs. Scientists are striving to create therapies that rebuild or replace damaged cells with tissues grown from stem cells and offer hope to people suffering from cancer, diabetes, cardiovascular disease, spinal-cord injuries, and many other disorders. Both adult and embryonic stem cells may also provide a route for scientists to develop valuable new methods of drug discovery and testing. They are also powerful tools for doing the research that leads to a better understanding of the basic biology of the human body ***(Cantz et al., ٢٠٠٤).***

What Is A Stem Cell?

Ultimately, every cell in the human



Body can be traced back to a fertilized egg that came into existence from the union of egg and sperm. But the body is made up of over ٢٠٠ different types of cells, not just one. All of these cell types come from a pool of *stem cells* in the early embryo. During early development, as well as later in life, various types of stem cells give rise to the *specialized* or *differentiated* cells that carry out the specific functions of the body, such as skin, blood, muscle, and nerve cells.

Over the past two decades, scientists have been gradually deciphering the processes by which unspecialized stem cells become the many specialized cell types in the body. Stem cells can regenerate themselves or produce specialized cell types. This property makes stem cells appealing for scientists seeking to create medical treatments that replace lost or damaged cells.

Stem cell are unspecialized cells that have two defining properties: the ability to differentiate into other cells and the ability to self –regenerate.