SUMMARY

The liver is the largest organ in the human body weighs 1200-1500g and formed anatomically from two lobes (right and left). The liver has a dual blood supply (portal vein and hepatic artery). The liver of mammals is made up of parenchyma and stroma the structural units of the liver are the lobules in the centers of which are central veins. The liver cells (hepatocytes) are arranged in the form of plates or cords usually one cell thick, and directed from the periphery to the center of the lobule.

Hepatic stellate cells are located in the subendothelial space, between the basolateral surface of hepatocytes and the anti-luminal side of sinusoidal endothelial cells. They comprise approximately one-third of the nonparenchymal cell population and about 15 % of the total number of resident cells in normal liver.

Hepatic stellate cells have many functions in normal liver:

A. Role in Liver Development and Regeneration:

Stellate cells can be found within the progenitor cell niche in normal and regenerating liver, which is situated near the canals of Hering. Stellate cells may also be vital to the development of intrahepatic bile ducts during development.

B. Retinoid Metabolism:

Under physiological conditions, about 50-80% of total retinoid of the body is stored in the liver, of which 80-90% is stored in

stellate cells. Loss of retinoid is prominent feature accompanying stellate cell activation both in vivo and in culture.

C.Immunoregulation:

Stellate cells can amplify the inflammatory response by inducing infiltration of mono- and polymorphoneuclear leukocytes.

Stellate cells also can function as professional antigen presenting cells that can stimulate lymphocyte proliferation or apoptosis.

D. Secretion of Lipoproteins, Growth Factors, and Cytokines:

1. Apolipoproteins and lipids:

Stellate cells secrete ma forms of lipoproteins such as apolipoprotein E and prostaglandins.

2. Production of growth factors and cytokines:

Stellate cells not only secrete cytokines but also respond to them. HGF is a more potent hepatocyte mitogen produced by stellate cells. Production of HGF by stellate cells diminishes during acute liver injury.

Stellate cells also secret many other growth factors which have important role in the proliferation of hepatic cells and stimulate mitosis in stellate cells. And also secrete cytokines effect in accumulation and proliferation of Kupffer cells.

E. Biology of Membrane and Nuclear Receptors:

There are many receptors founded on stellate cell membrane and nucleus to which many cytokines and growth factors bound and can affect the cell function and its secretion to different substances and also have many effects on the activity, proliferation and growth of stellate cells.

F. Adipogenic Features:

The transcriptional program required for adipocyte differentiation is nearly identical to that required for maintaining stellate cells in their quiescent state. There is also similarity between the substances secreted by stellate cells with those secreted by adipocytes.

G. Detoxifying and Antioxidant Enzymes, pH Regulation, and Generation of Oxidant Stress:

Several enzymes involved in both intermediary metabolism and detoxification of ethanol and xenobiotics have been identified in stellate cells.

Stellate cells also have tightly regulated systems for monitoring cellular pH, which are closely linked to cellular activation. Specifically, the Na^+/H^+ exchanger is the main intracellular (pH_i) regulator in rat stellate cells, and stellate cell activation is associated with an increase in pH_i and in PDGF-stimulated activity of the Na^+/H^+ exchanger.

H. Regulation of Blood Flow in Normal Liver:

Hepatic stellate cells help in controlling blood flow in liver through secretion of endothelin-1 which has constrictive effect on stellate cells also noticed that with inhibition of carbon monoxide secretion stellate cells contracts.

Role of hepatic stellate cells in disease:

The clarification of stellate cell response in hepatic injury and repair has been a significant turning point in understanding the basis of hepatic fibrosis.

Stellate cells activation is the central event in hepatic fibrosis and activation consists of two major phases: initiation and perpetuation, followed by resolution of fibrosis if injury subsides.

1. Initiation:

Initiation (also called a "preinflammatory stage ") refers to early changes in gene expression and phenotype that render the cells responsive to other cytokines and stimuli.

2. Perpetuation:

Perpetuation results from the effects of these stimuli on maintaining the activated phenotype and generating fibrosis. Perpetuation involves autocrine as well as paracrine loops. It is comprised of several discrete responses including proliferation, contractility, fibrogenesis, matrix degradation, retinoid loss, and inflammatory cell infiltration.

3. Resolution: