INTRODUCTION

In normal liver, hepatic stellate cells (HSCs) are nonparenchymal, quiescent cells whose main functions is to store vitamin A (containing over 80% of total vitamin A in the body) and probably to maintain the normal basement membrane-type matrix. Hepatic stellate cells (HSCs) undergo an activation process in which they lose vitamin A, become highly proliferative, and synthesize fibrotic matrix rich in type I collagen **(Rifaat and Scott, 2002)**.

Hepatic stellate cells (HSCs) are located between parenchymal cell plates and sinusoidal endothelial cells, and extend well-developed, long processes surrounding sinusoids in vivo as pericytes. However, HSCs are known to be "activated" or "transdifferentiated" to myofibroblasts like phenotype lacking cytoplasmic lipid droplets and long processes in pathological conditions such as liver fibrosis and cirrhosis, as well as merely during cell culture after isolation **(Sato et al., 2003)**.

Stellate cell activation is the central event in hepatic fibrosis. Activation consists of 2 major phases: (1) initiation (also called apreinflammatory stage) and (2) perpetuation. Initiation refers to early paracrine mediated changes in gene expression and phenotype that render the cells responsive to other cytokines and stimuli. Perpetuation then results from the effects of these stimuli on maintaining the activated phenotype and generating fibrosis **(Rifaat and Scott, 2002)**.

Hepatic stellate cells (HSCs) do not descend from the neural crest as have been hypothesized but derive from the septum

transversum mesenchyme, from endoderm or from the mesothelial liver capsule **(Cassiman et al., 2006)**.

Activated human hepatic stellate cells (HSCs) contain (Ca+2) channels that modulate the contractile effect of endothelin-1 and mediate the inhibitory action of NO **(Gasull et al., 2001)**.

It is widely believed that DNA synthesis and expressions of alpha smooth muscle actin and transforming growth factor-beta are all together increased in activated hepatic stellate cells both in vitro and in vivo **(Osada et al., 2001)**.

Differentiation of hepatic stellate cells (HSCs) to extracellular matrix and growth factor producing cells supports liver regeneration through promotion of hepatocyte proliferation. The neurotrophin receptor p75NTR, a tumor necrosis factor receptor superfamily member expressed in hepatic stellate cells (HSCs) after fibrotic and cirrhotic liver injury in humans, is a regulator of liver repair **(Passino et al., 2007)**.

Adenosine reversibly inhibits Ca+2 fluxes and chemotaxis of hepatic stellate cells (HSCs) and upregulates TGF-beta and collagen I mRNA. Adenosine provides: 1) a "stop" signal to hepatic stellate cells (HSCs) when they reach sites of tissue injury with high adenosine concentrations and 2) stimulates transdifferentiation of hepatic stellate cells (HSCs) by upregulating collagen and transforming growth factor-beta (TGF-β) production **(Hashmi et al., 2007)**.