

# Hepatic Stellate Cells and Liver Disease

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Liver injury is a constant thread for the liver because it face many substances that enters human body through intestine which in most condition can not be screened adequately by mechanisms in the digestive system. Once the liver injury happened, the liver exerts several mechanisms to eliminate the substance and or limit the injury such as activate molecular pump mechanism in liver cells, activate the Kupffer cells and stimulate the activity of stellate cells.

Hepatic stellate cells (HSC) is the most important cells that directly involved in the process of liver injury. This cell is actually sit in the middle between sinusoids epithelium and liver cell. Any process that trigger the mechanism of inflammation also trigger the HSC to be active. The most important activity of HSC is in the process of fibrosis (fibrogenesis).HSC contribute to hepatic inflammation by their ability to secrete and respond to a wide range of growth factors.<sup>1,2</sup>

Immunohistochemical markers for HSC in animal liver tissues included desmin and muscle actin (alpha-SMA).<sup>3-6</sup>A study form Sandra et al identified cluster of differentiation 38 (CD38) as a novel membrane molecule of HSC and characterized its expression in rat HSC in vitro and in vivo. The study indicated that CD38 may be a key regulator of HSC activation and effector functions.<sup>7</sup> CD38 is a membrane-bound protein first identified by monoclonal antibody typing of lymphocytes and thus thought of as a lymphocyte-specific antigen.<sup>8</sup> CD38 also known as cyclic ADP ribose hydrolase is a glycoprotein found on the surface of many immune cells (white blood cells), including CD4<sup>+</sup>, CD8<sup>+</sup>, B lymphocytes and natural killer cells. CD38 also functions in cell adhesion, signal transduction and calcium signaling.<sup>9</sup>

CD38 is also present in many tissues such as brain and pancreas other than haematopoetic cells.<sup>10</sup> Abdeen et al did a study to find out if CD38 can be demonstrated immunohistochemically on HSC in liver biopsies from patients with chronic hepatitis and to find out if such labeling correlated with fibrosis score (METAVIR).

This study concluded that CD38 positive HSC can be demonstrated immunohistochemically and the count is highly predictive of moderate to severe hepatic fibrosis.<sup>11</sup> Another study from El-Gendi et al showed that CD38 HSC can be observed immunohistochemically in human liver core biopsies and the count is predictive of degree of hepatic fibrosis.<sup>12</sup> Study from Titos et al in this journal showed that number of CD38+ HSC is associated with degree of fibrosis. Whereas, this study also found that there is no correlation between CD38+ HSC with inflammation.<sup>13</sup> Thus, CD38+ HSC is more likely to be a specific marker for liver fibrosis because it is not influenced by inflammation.

The used of CD38 is more specific to identify HSC and the process of hepatic fibrosis compared to alpha-SMA. However, not all active HSC contains smooth muscles antigen. CD38 is may be more useful in giving information regarding total number of active HSC. The more precise immunohistochemical features should have advantage in the study of liver fibrosis especially the role of HSC. The study of HSC is important to understand and eventually may have therapeutic implications in the future.

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