The Journal of Immunology, 2013, 190, 202.4
Copyright © 2013 by The American Association of Immunologists, Inc.

202.4

Increased IL-22-producing cells contribute to liver fibrosis through promoting Th17 migration in chronic HBV patients (P3363)

Zheng Zhang,[1] Juanjuan Zhao,[1] Yangxin Fu,[2] and Fu-Sheng Wang[1]

[1]Research Center for Biotherapy, Beijing 302 Hospital, Beijing, China [2]Center for Infection and Immunity, Institute of Biophysics, Chinese Academy of Science, Beijing, China

Interleukin-22 is markedly upregulated in chronic HBV (CHB) infection; however, its functional role in patients with liver fibrosis (LC) remains obscure. We screened mRNA expression in HBV-infected liver tissue vs normal control and found IL-22-associated pathway was significantly changed. We further found that intrahepatic IL-22+ cell counts were significantly increased in HBV-infected patients, especially in LC patients. Further analysis indicated that IL-22 could be produced by various liver-infiltrating lymphocytes, but preferentially produced by IL-22+IL-17a+IFN-γ- Th17 cells in LC patients, which was also positively associated with liver fibrosis severity in CHB patients. We also found human HSCs express high levels of IL-22R. IL-22 exposure increased pSTAT3 expression and fibrotic protein production, and also prevented soluble TRAIL-mediated HSC apoptosis in vitro. Blockade of IL-22 in a HBV-transgenic mice model with T cell-mediated liver fibrosis significantly restricted liver fibrosis progression, and Th17 migration and CCL20 expression. IL-22-treated HSCs secreted CCL20, and blockade of CCL20 preferentially reduced the migration of Th17 cells in vitro. These data suggest that the increased IL-22-producing cells contribute to liver fibrosis through promoting Th17 migration in chronic HBV patients, and may facilitate the rational development of immunotherapeutic strategies targeting IL-22 for the amelioration of liver fibrosis in chronically HBV-infected subjects.