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Blockade of PD-1/PDL-1 axis impair the development and effector function of CD8+CXCR5+ follicular T cells in chronic Hepatitis B patients

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Classical CD8 T cells are implicated for protective and pathogenic roles in chronic hepatitis B (CHB) infection. Recently, a new subset of CD8 T cells expressing CXCR5 and exhibiting features of follicular T cells has been identified during chronic viral infections. However, in CHB, their roles have not yet been well defined. Here, we characterized circulating CD8+CXCR5+ and CD8+CXCR5- T cells and their association with clinical and viral factors in CHB. We found that CHB infection did not influence the overall frequencies of CD8+CXCR5+ cells but CD8+CXCR5- cells were increased. However, among CHB, CD8+CXCR5+ cells were higher in patients with low HBsAg and HBV DNA level, patients who were HBeAg negative and had high fibrosis scores. Importantly, these cells showed significant association with HBsAg and HBV DNA reduction. Contrarily, CD8+CXCR5- T cells were expanded and positively associated with patients having high HBsAg, HBV DNA and ALT levels.

CD8+CXCR5+ T cells constituted higher frequencies of Tc1, Tc2, Tc17 and Tc22 subsets and overexpressed PD-1. Interestingly, PD-1+CD8+CXCR5+ cells exhibited higher CD69 and secreted more IFN-γ, IL-21 and IL-22 than PD-1- population, which illustrate effector phenotype of these cells; whereas, CD8+CXCR5- population displayed lower CD69 and secreted less cytokines irrespective of PD-1 expression, suggesting a phenotype of overall exhaustion. Importantly, blockade of PD1/PD-L1 pathway significantly impair the development of both CD8+CXCR5+/- cells and reduced effector cytokine production. In addition, HBcAg- specific cytolytic function measured by CD107a, perforin and granzyme B expression was higher in CD8+CXCR5+ than CD8+CXCR5- cells; however, HBsAg-specific cytolytic activity was impaired in both cell types. In conclusion, CD8+CXCR5+ cells are enriched in effector phenotypes with HBV-specific cytokine producing abilities and lytic function, despite increased PD-1 and associate with HBsAg and HBV DNA reduction, which may serve them as potential therapeutic target for CHB.

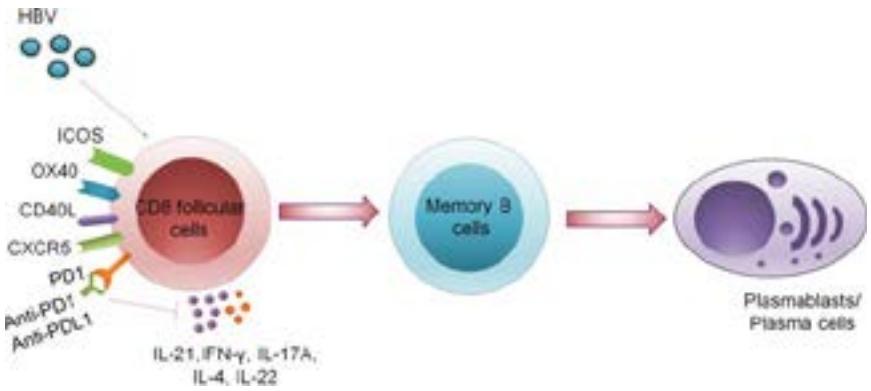

Figure: Role of CD8+CXCR5+ folliclar cells in chronic hepatis B infection. PD-1 Expressing CD8+CXCR5+ follicular T cells functions as effector cells in chronic hepatitis B patients. Blockade of PD1/PD-L1 axis impair the development and effector function of these cells which may contribute to viral persistence.

Biography

Arshi Khanam has her expertise in viral infections, especially in chronic hepatitis B. Her current area of research is to identify the immunological mechanisms of viral persistence and target immunological molecules for therapeutic purpose to eradicate the infection.