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IMMUNOLOGY

Viral hepatitis—a critical role for T-bet in viral clearance?

New research published in *The Journal of Experimental Medicine* supports a crucial role for the transcription factor T-bet —a regulator of T-cell immunity—in viral clearance of HBV and HCV. Moreover, the findings suggest that deficient T-bet induction in virus-specific $CD8^+$ T cells might be a factor in viral persistence and chronic infection.

Peter Kurktschiev and colleagues used flow cytometry to determine the expression of T-bet in virus-specific $CD8^+$ T cells during HBV and HCV infection and examined whether its expression correlated with clinical outcome. Peripheral blood mononuclear cells from a wide range of individuals were isolated: those with acute resolving, chronic or resolved HBV infection; those with long-term chronic, acute resolving, chronic-evolving or spontaneous resolution HCV infection; and, as controls, those with acute Epstein–Barr virus infection or healthy individuals.

The researchers found that T-bet was highly expressed in virus-specific $CD8^+$ T cells in the context of acute HBV and acute HCV infection, with high expression levels maintained for at least 4–6 months in acute resolving cases. Strong T-bet expression correlated with spontaneous resolution of HCV infection. By contrast, T-bet deficiency early in the infection (within 1 month after onset of symptoms) in acute HCV infection seemed to be characteristic of a chronic-evolving disease course, with T-bet expression levels remaining low at all time points analysed.

> “...T-bet was highly expressed in ... acute HBV and acute HCV infection...”

T-bet expression correlated with IFN-γ production and proliferation of virus-specific $CD8^+$ T cells. Interestingly, induction of T-bet by antigen and IL-2 stimulation partially restored immune functions in previously dysfunctional T-bet-deficient $CD8^+$ T cells.

“Our most important observation is that T-bet expression in virus-specific $CD8^+$ T cells has shown a strong correlation with the clinical outcome of HCV infection,” says Kurktschiev, adding that T-bet could prove useful as a biomarker to monitor activation of the cellular immune system during infection. “Our results describe the immune response and not the virus so it is highly possible that these mechanisms could have a role in other viral infections.”

“Whilst we are not the first to report the effects of T-bet on $CD8^+$ T cells, there were no data on its role in HBV and HCV infection,” he notes. Further work is needed to replicate the findings in larger patient cohorts and to determine whether T-bet induction could be a potential therapeutic target.

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Original article Kurktschiev, P. D. *et al.* Dysfunctional $CD8^+$ T cells in hepatitis B and C are characterized by a lack of antigen-specific T-bet induction. *J. Exp. Med.* doi:10.1084/jem.20131333