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VIRAL HEPATITIS

Biomarker for HBV therapy discontinuation

> an HBV-specific T cell biomarker can predict the safe discontinuation of NUC therapy

Lifelong nucleoside or nucleotide analogue (NUC) therapy is the current treatment of choice for patients with chronic hepatitis B (CHB). However, a new study has shown that an HBV-specific T cell biomarker can predict the safe discontinuation of NUC therapy.

NUC compounds can suppress HBV replication but cannot fully eradicate the virus. Accordingly, this therapy is maintained for life in most patients with CHB, and discontinuation can lead to virological relapse and hepatic flare. However, some patients are able to control the infection without ongoing treatment, and there is evidence that components of immunity, particularly T cells, are necessary for HBV control and avoidance of liver damage.

"We decided, therefore, to test whether we can identify immunological biomarkers predicting the safe discontinuation of antiviral therapy in patients with CHB," explains author Antonio Bertoletti. The researchers longitudinally studied the immune profiles of two cohorts of patients ($n = 19$ and 27) with CHB who controlled HBV or relapsed upon NUC antiviral therapy discontinuation. The functional profiles of antigen-specific T cells were characterized before and after the discontinuation of NUC therapies using standard immunological assays, along with analyses of global non-antigen-specific immune cell populations.

"We show that patients who do not relapse upon therapy withdrawal are characterized, during treatment, by an increased frequency of $PD1^+$ HBV-specific T cells directed against nucleocapsid and polymerase proteins of HBV," reports Bertoletti. "In addition, our study highlights the neglected beneficial role that inhibitory molecules play in the long-term persistence of partially exhausted T cells specific for chronic antigens."

As their current method is too complicated for routine clinical use, the investigators are now looking to develop alternative methods to directly quantify $PD1^+$ HBV-specific T cells. "Our findings could lead to a change in the clinical management of patients with CHB," concludes Bertoletti. "The possibility to better define which patients can safely stop treatment will allow studying the virological and immunological consequences of treatment withdrawal in more detail."

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