Getting personal with hep B vaccines

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Therapeutic vaccines that boost antiviral immunity provide an attractive alternative to drug therapy for people who are infected with the hepatitis B virus (HBV). Yet, the large amount of genetic diversity found in circulating HBV strains has hindered the development of a 'one-size-fits-all' post-exposure vaccine.

A*STAR scientists from the Singapore Institute for Clinical Sciences

(SICS) and the Singapore Immunology Network have now devised a more personalized approach to HBV therapeutic vaccination. In collaboration with researchers from Singapore and Europe, the A*STAR team isolated and manipulated a type of white blood cell known as a monocyte to produce an HBV-specific immune response in cell culture. If this can be replicated in the body, the same transformation could form the basis of a simple and effective vaccine therapy for individuals infected by HBV.

To find cells that stimulate HBV-targeted immunity, the researchers investigated whether various immune cells that commonly capture and store viral proteins—a mechanism that enables the subsequent activation of virus-killing T cells through a process known as 'antigen presentation'— captured a particular protein called the hepatitis B surface antigen (HBsAg). They extracted six different types of 'antigen-presenting cells' (APCs) from 28 people chronically infected with HBV, all of whom carried large quantities of HBsAg in their bloodstreams. Of all the APCs, they found that only one distinct population of monocytes—CD14-expressing monocytes—tested positive for HBsAg.

Yet these monocytes did not activate HBV-specific T cells on their own; first, the researchers had to manipulate the HBsAg-containing monocytes to form another type of immune cell called a dendritic cell. The dendritic cells, when mixed together with patient-derived blood samples, then stimulated the expansion of virus-killing T cells. "This means that we may be able to directly stimulate the antigen-presenting cells of patients to start an immune response that can be beneficial to clear the virus infection," says team member Adam Gehring, now at the St Louis University Medical Center in the United States.

Achieving the same feat in the human body remains a challenge, however. In cell culture, the dendritic cells were differentiated using a combination of immune-stimulating proteins called cytokines. If taken

by people, this cytokine combination could have undesired effects on the immune system, says Antonio Bertoletti from the SICS, who led the research. But a safer method that only uses cytokines to promote HBV-specific immunity could provide something akin to "therapeutic vaccination without the vaccine," Bertoletti notes.

More information: Gehring, A. J., Haniffa, M., Kennedy, P. T., Ho, Z. Z., Boni. C. et al. "Mobilizing monocytes to cross-present circulating viral antigen in chronic infection." *The Journal of Clinical Investigation* 123, 3766–3776 (2013). dx.doi.org/10.1172/JCI66043

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