Dr Gehring obtained his Ph.D. in the Department of Pathology at Case Western Reserve University (2004) in Cleveland, Ohio, where he studied strategies employed by Mycobacterium tuberculosis to evade detection of the CD4 T cell response. From there Dr Gehring joined the UCL Institute of Hepatology (2004-2006) at University College London as a research fellow and shifted interests to viral immunology, which has been the focus of his research since. Dr Gehring moved to Singapore in 2006, joining A*Star as a research fellow, and continued his work on the T cell response to viral infection and how this can be exploited for clinical therapy. He is now assistant principal investigator at the Singapore Institute for Clinical Sciences.

Abstract

Virus-specific T cells capable of controlling HBV and eliminating hepatocellular carcinoma (HCC) expressing HBV antigens are deleted or dysfunctional in patients with chronic HBV and HBV-related HCC. The goal of our work is to determine if T cell receptor (TCR) gene therapy can reconstitute HBV-specific T cell immunity in lymphocytes of chronic HBV patients and investigate whether they can recognize HCC lines with natural HBV-DNA integration. Using vector mediated gene transfer we can introduce HBV-specific T cell receptors (TCRs) into T cells of chronic HBV patients. The introduced TCRs are expressed and result in HBV-specific T cells that can produce IFN-γ, TNF-α, IL-2, and lyse hepatocyte-like cell lines expressing cognate HBV antigens. Adoptive transfer of TCR-redirected T cells in a xenograft HCC model prevented formation of transplanted tumors. Furthermore, Hep3B and PLC-PRF5, human HCC lines with natural HBV-DNA integration, could be recognized by HBV-specific TCR-redirected T cells. Thus, we are able to generate large numbers of multifunctional HBV-specific T cells that are capable of recognizing HBV infected cells and HCC tumor cells expressing viral antigens from naturally integrated HBV DNA. These genetically modified T cells could be used to reconstitute virus-specific T cell immunity in chronic HBV patients and target tumors in HBV-related HCC.