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Titel des Beitrags:
Chimeric antigen receptor (CAR)-engineered T cells redirected against hepatitis C virus (HCV) E2 glycoprotein.

Abstract:
The recent availability of novel antiviral drugs has raised new hope for a more effective treatment of hepatitis C virus (HCV) infection and its severe sequelae. However, in the case of non-responding or relapsing patients, alternative strategies are needed. To this end we have used chimeric antigen receptors (CARs), a very promising approach recently used in several clinical trials to redirect primary human T cells against different tumours. In particular, we designed the first CARs against HCV targeting the HCV/E2 glycoprotein (HCV/E2). Anti-HCV/E2 CARs were composed of single-chain variable fragments (scFvs) obtained from a broadly cross-reactive and cross-neutralising human monoclonal antibody (mAb), e137, fused to the intracellular signalling motif of the costimulatory CD28 molecule and the CD3? domain. Activity of CAR-grafted T cells was evaluated in vitro against HCV/E2-transfected cells as well as hepatocytes infected with cell culture-derived HCV (HCVcc). In this proof-of-concept study, retrovirus-transduced human T cells expressing anti-HCV/E2 CARs were endowed with specific antigen recognition accompanied by degranulation and secretion of proinflammatory and antiviral cytokines, such as interferon ?, interleukin 2 and tumour necrosis...
Moreover, CAR-grafted T cells were capable of lysing target cells of both hepatic and non-hepatic origin expressing on their surface the HCV/E2 glycoproteins of the most clinically relevant genotypes, including 1a, 1b, 2a, 3a, 4 and 5. Finally, and more importantly, they were capable of lysing HCVcc-infected hepatocytes. Clearance of HCV-infected cells is a major therapeutic goal in chronic HCV infection, and adoptive transfer of anti-HCV/E2 CARs-grafted T cells represents a promising new therapeutic tool.