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Titel des Beitrags:
HCV-Induced Immune Responses Influence the Development of Operational Tolerance After Liver Transplantation in Humans.

Abstract:
Pathogen-induced immune responses prevent the establishment of transplantation tolerance in experimental animal models. Whether this occurs in humans as well remains unclear. The development of operational tolerance in liver transplant recipients with chronic hepatitis C virus (HCV) infection allows us to address this question. We conducted a clinical trial of immunosuppression withdrawal in HCV-infected adult liver recipients to elucidate (i) the mechanisms through which allograft tolerance can be established in the presence of an ongoing inflammatory response and (ii) whether anti-HCV heterologous immune responses influence this phenomenon. Of 34 enrolled liver recipients, drug withdrawal was successful in 17 patients (50%). Tolerance was associated with intrahepatic overexpression of type I interferon and immunoregulatory genes and with an expansion of exhausted PD1/CTLA4/2B4-positive HCV-specific circulating CD8(+) T cells. These findings were already present before immunosuppression was discontinued and were specific for
HCV infection. In contrast, the magnitude of HCV-induced proinflammatory gene expression and the breadth of anti-HCV effector T cell responses did not influence drug withdrawal outcome. Our data suggest that in humans, persistent viral infections exert immunoregulatory effects that could contribute to the restraining of alloimmune responses, and do not necessarily preclude the development of allograft tolerance.

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