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Journal of Autoimmunity

Volume 42, May 2013, Pages 19-28

Mouse liver-specific CD8+ T-cells encounter their cognate antigen and acquire capacity to destroy target hepatocytes ☆

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https://doi.org/10.1016/j.jaut.2012.10.002

Abstract

CD8+ T-cell immune response to liver antigens is often functionally diminished or absent. This may occur via deletion of these autoaggressive T-cells, through the acquisition of an anergic phenotype, or via active suppression mediated by other cell populations. We generated a double transgenic model in which mice express CD8+ T-cells specific for the lymphocytic choriomeningitis virus nucleoprotein (LCMV-NP) and LCMV-NP as a hepatic neo-autoantigen, to study the immunological response of potentially liver antigen autoaggressive CD8+ T-cells. Autoreactive transgenic CD8+ T-cells were analyzed for functionality and cytotoxic effector status. Despite severe peripheral deletion of liver-specific CD8+ T-cells, a fraction of autoreactive NP-specific CD8+ T-cells accumulate in liver, resulting in hepatocyte injury and production of auto-antibodies in both male and female mice. NP-specific intrahepatic T-cells showed capacity to proliferate, produce cytokines and up-regulate activation