Transfer of MHC-class-I molecules among liver sinusoidal cells facilitates hepatic immune surveillance.

Abstract:

In the liver, antigen-presenting cell populations such as Kupffer cells, liver dendritic cells, and liver sinusoidal endothelial cells (LSECs) participate through cross-presentation to CD8 T cells (CTLs) in hepatic immune-regulation and immune-surveillance. The participation of hepatic stellate cells (HSCs) in immune regulation is controversial. Here we studied HSC's contribution to antiviral CTL immunity. Flow cytometric analysis of MHC-I molecules at the cell surface of liver cells from mice with cell-type restricted MHC-I expression. Mice with HSC-restricted MHC-I expression were infected with a hepatotropic virus and analyzed for development of viral hepatitis after CTL transfer. HSCs transferred MHC-I molecules to LSECs and these molecules were employed for LSEC cross-presentation to CTLs. Such transfer of MHC-I molecules was sufficient to support in vivo LSEC cross-presentation of soluble antigens to CTLs. Importantly, this transfer of MHC-I molecules contributed to anti-viral CTL immunity leading to development of immune-mediated hepatitis. Our findings demonstrate transfer of MHC-I molecules among sinusoidal liver cell populations as a potent mechanism to increase anti-viral CTL effector function. The transfer of MHC-I molecules from HSCs supplies LSECs with additional MHC-I molecules for their own
cell-intrinsic cross-presentation. Such cross-allocation of MHC-I molecules in liver cell populations is distinct from cross-dressing that occurs among immune cell populations in lymphoid tissues where peptide-loaded MHC-I molecules are transferred. Our findings thus reveal a novel mechanism that increases local cross-presentation and CTL effector function in the liver, which may be instrumental for immune-surveillance during viral infection of antigen-presenting liver cells.