Hepatocyte Growth Factor Ameliorates Adenovirus-induced Hepatitis

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Hepatocyte growth factor (HGF) is a pleiotropic molecule with anti-inflammatory properties, and its concentration increases during bacterial and viral infection. Our aim was to determine the effects of HGF on viral hepatitis and to further explore potential therapeutic strategies in viral hepatitis. In mice infected with adenovirus, we found HGF expression and concentrations increased in the liver and were accompanied by a similar rise in the expression of bcl-2, a gene downstream of the HGF action. To further investigate HGF’s effects, we hydrodynamically delivered the HGF plasmid to C57BL/6 mice and injected 5 x10⁹ pfu adenovirus i.v. 3 days later. Animals were sacrificed and analyzed 6 days later. The HGF-transfected group, when compared to the control animals, had less infiltration of intrahepatic lymphocytes (IHL) and necrosis, as well as lower levels of serum ALT. The HGF-transfected group had a higher percentage of c-Met⁺ (HGF receptor) dendritic cells and Kupffer cells, but a lower percentage of granzyme B⁺ CTL and γδ T cells. The HGF-transfected group had lower percentages of CD44⁺ T cells, but higher percentages of CD44⁺CD62L⁺ cells. In vitro stimulated CTL from HGF-transfected mice displayed higher IFN-γ and IL-17 levels. The hepatic expression of IFN-α, IFN-β, TGF-β, IL-6 and CXCL9 was lower in the HGF-transfected group. This group also had lower serum concentrations of IL-6, IL-12(p70), IL-10, and IL-2. Interestingly, hepatic expression and serum levels of IL-7 were higher in this group. In conclusion, while HGF exerts protection by suppressing the expression and secretion of pro-inflammatory cytokines during viral hepatitis, HGF seems to promote CTL functions with high levels of IL-17 and IFN-γ, but with lower granzyme B levels. Thus, more studies are needed to determine the effects of HGF on viral replication.