Inactivated Orf virus (Parapoxvirus ovis) elicits antifibrotic activity in models of liver fibrosis.

Abstract:
Inactivated Orf virus (ORFV, Parapoxvirus ovis) demonstrates strong antiviral activity in animal models including a human hepatitis B virus (HBV)-transgenic mouse. In addition, expression of interferon (IFN)-? and interleukin-10 (IL-10) was induced after administration of inactivated ORFV in these mice. IFN-? and IL-10 are known to elicit antifibrotic activity. We therefore aimed to study antifibrotic activity of inactivated ORFV in models of liver fibrosis. We characterized ORFV-induced hepatic cytokine expression in rats. We then studied ORFV in two models of liver fibrosis in rats, pig serum-induced liver fibrosis and carbon tetrachloride (CCL4)-induced liver fibrosis. ORFV induced hepatic expression of IFN-? and IL-10 in rats. ORFV mediated antifibrotic activity when administrated concomitantly with the fibrosis-inducing agents in both models of liver fibrosis. Importantly, when CCL4-induced liver fibrosis was already established, ORFV application still showed significant antifibrotic activity. In addition, we were able to demonstrate a direct antifibrotic effect of ORFV on stellate cells. These results establish a potential novel antifibrotic therapeutic approach that not only prevents but also resolves established liver fibrosis. Further studies are required to unravel the details of the mechanisms involved.