# Inhibition of aquaporin-3 in macrophages by a monoclonal antibody as potential therapy for liver injury

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Aquaporin 3 (AQP3) is a water and hydrogen peroxide ($H_2O_2$)-transporter expressed in various epithelial cells and in macrophages. Here, we developed an anti-AQP3 monoclonal antibody (mAb) that inhibited AQP3-facilitated $H_2O_2$ transport and prevented liver injury in an experimental animal model. Using AQP3 knockout ($AQP3^{-/-}$) mice in a $CCl_4$-induced model of liver injury and fibrosis, we found that AQP3-facilitated $H_2O_2$ uptake into macrophages was responsible for nuclear factor-κB (NF-κB) cell signaling and macrophage activation during acute liver inflammation. The hepatic inflammation, oxidative stress, and stellate cell activation caused by activated macrophages was dependent on macrophage AQP3 expression. Administration of an anti-AQP3 mAb, which targeted an extracellular epitope on AQP3, prevented liver injury by a mechanism involving inhibition of AQP3-mediated $H_2O_2$ transport and macrophage activation. These findings implicate the involvement of macrophage AQP3 in liver injury, and provide evidence for mAb inhibition of AQP3-mediated $H_2O_2$ transport as therapy for macrophage-dependent liver injury.

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