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Acceleration of TAA-Induced Liver Fibrosis by Stress Exposure Is Associated with Upregulation of Nerve Growth Factor and Glycopattern Deviations

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Abstract

Liver fibrosis results from many chronic injuries and may often progress to cirrhosis and hepatocellular carcinoma (HCC). In fact, up to 90% of HCC arise in a cirrhotic liver. Conversely, stress is implicated in

liver damage, worsening disease outcome. Hence, stress could play a role in disrupting liver homeostasis, a concept that has not been fully explored. Here, in a murine model of TAA-induced liver fibrosis we identified nerve growth factor (NGF) to be a crucial regulator of the stress-induced fibrogenesis signaling pathway as it activates its receptor p75 neurotrophin receptor (p75NTR), increasing liver damage. Additionally, blocking the NGF decreased liver fibrosis whereas treatment with recombinant NGF accelerated the fibrotic process to a similar extent than stress challenge. We further show that the fibrogenesis induced by stress is characterized by specific changes in the hepatoglycocode (increased β1,6GlcNAc-branched complex N-glycans and decreased core 1 O-glycans expression) which are also observed in patients with advanced fibrosis compared to patients with a low level of fibrosis. Our study facilitates an understanding of stress-induced liver injury and identify NGF signaling pathway in early stages of the disease, which contributes to the established fibrogenesis.

Keywords: NGF; hepatoglycocode; liver fibrosis; mouse model; stress-induced fibrosis.

Figures

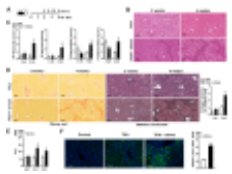

Figure 1 (**A**)
Experimental murine...

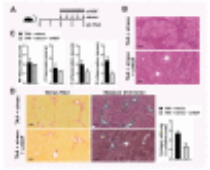

Figure 2 (**A**)
Experimental murine...

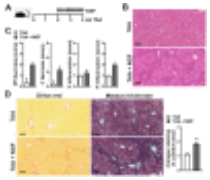

Figure 3 (**A**)
Experimental murine...

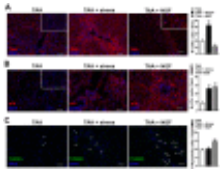

Figure 4 Representative images and number of...

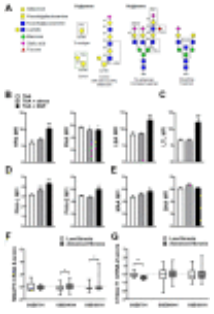

Figure 5 (**A**) For an...

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