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ALCOHOLIC HEPATITIS

Potential role of cytokine CCL20 in alcoholic hepatitis

The cytokine CCL20 might have a role in the pathogenesis of alcoholic hepatitis (AH), and has potential as a new therapeutic target in this devastating disease, according to a new study.

AH is the most severe form of alcoholic liver disease (ALD), and is associated with high rates of mortality. Poor understanding of the pathophysiology of this condition, lack of appropriate experimental models and limited interest from pharmaceutical companies have combined to mean that very few drugs have been developed for ALD and AH.

Previous studies identified CCL20 as the most upregulated cytokine in the liver of patients with AH. "For this reason, we decided to further investigate the potential role of CCL20 in the pathogenesis of AH," explains Silvia Affò. "To investigate if CCL20 could represent a new potential target for therapy, we decided to use a translational approach."

The team assessed hepatic expression and serum levels of CCL20 in patients with AH, and found these levels to be associated with key clinical features of the disease, such as grade of fibrosis, severity of portal hypertension and endotoxaemia. The researchers also investigated the cellular sources of CCL20 and its biological effects *in vitro* and *in vivo*. Macrophages and hepatic stellate cells (HSCs) were found to be the main cell types that produce CCL20, and the cytokine demonstrated proinflammatory and profibrogenic effects on HSCs.

Finally, the researchers knocked-down CCL20 expression *in vivo* after inducing liver damage using lipopolysaccharide (LPS). The results suggest that CCL20 mediates LPS-induced hepatocellular damage and modulates the hepatic inflammatory infiltrate.

"Further pre-clinical studies in future models of AH are required to determine if targeting CCL20 is an effective and safe therapeutic strategy to modulate the inflammatory response and liver injury in AH," concludes Affò.

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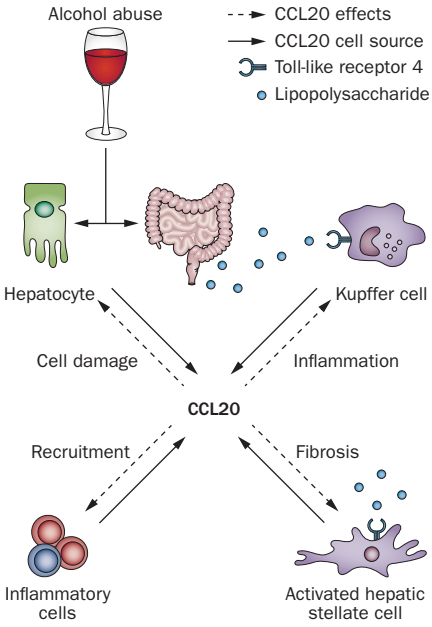

Original article Affò, S. *et al.* CCL20 mediates lipopolysaccharide induced liver injury and is a potential driver of inflammation and fibrosis in alcoholic hepatitis. *Gut* doi:10.1136/gutjnl-2013-306098