The role of PCSK9 in the pathogenesis of non-alcoholic fatty liver disease

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Statin treatment exhibits a beneficial effect in patients of cardiovascular diseases (CVD) and non-alcoholic fatty liver disease (NAFLD). Statins are common treatments for such conditions.

The role of pro-protein convertase subtilisin kexin type-9 (PCSK9) in the pathogenesis of NAFLD is summarized in this review. The authors also review the effects of the new hypolipidaemic drugs—PCSK9 inhibitors—on NAFLD. Increments in high intrahepatic or circulating PCSK9 levels in muscle and liver lipid storage was indicated by research data. The increment was also observed in adipose energy storage and hepatic fatty acids, as well as triglycerides storage and secretion, thus contributing to the pathogenesis of NAFLD.

These findings were the basis of a number of animal and human studies, aimed at reducing PCSK9 with inhibitors (human IGG antibodies, antisense particles against PCSK9 mRNA, and small anti PCSK9 antibodies). The results of these experiments point towards liver protection from NAFLD through inhibition of PCSK9 expression in the induction of degradation of hepatic HNF1a protein, insulin resistance (IR), and other mechanisms. The use of PCSK9 inhibitors ameliorates NAFLD, aside from beneficial effects on CVD and independently of low density lipoprotein cholesterol level reduction.

More information: Eleni Theocharidou et al, The Role of PCSK9 in the Pathogenesis of Non-alcoholic Fatty Liver Disease and the Effect of PCSK9 Inhibitors, *Current Pharmaceutical Design* (2018). DOI:

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