Letters to the Editor

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Reply to the Letter to the Editor ‘Effect of treatment with polyunsaturated fatty acids on HCV- or diet-induced fatty liver’

This is a reply to the Letter to the Editor by Comparcola et al.

We appreciate Comparcola and colleagues for their comments on our findings about the pathogenesis of lipid metabolism disturbances in hepatitis C virus (HCV) infection [1]. The pathogenesis of hepatic steatosis in hepatitis C has been enthusiastically investigated [2]. Several pathways have been described as mechanisms underlying steatogenesis in hepatitis C: the core protein of HCV inhibits the secretion of very low density lipoprotein (VLDL) from the liver by suppressing the function of microsomal triglyceride transfer protein (MTP) [3], increases the production of fatty acids by upregulating sterol regulatory element binding protein (SREBP)-1c gene expression [4], and induces hepatic insulin resistance resulting in the increased uptake of fatty acid into the liver [5]. The combination of these events would lead to a frequent development of steatosis in hepatitis C.

We thank Comparcola et al. for noting that NADH accumulation is a characteristic feature of mitochondrial dysfunction in a NAFLD model [6]. We propose that the accumulation of NADH due to dysfunction in the mitochondrial electron transfer system (ETS) may be responsible for steatogenesis in HCV infection [1]. Interestingly, tacrolimus, an immunosuppressive agent, reverses the influence of the core protein, including hepatic steatosis and insulin resistance, simultaneously with the restoration of mitochondrial ETS function, as indicated by reduction of NADH accumulation, in a mouse model [7]. This pathway may be a common one in the pathogenesis of NASH and hepatitis C, and could be a target for treatment. Hepatitis C should be recognized as a metabolic disease as well as a hepatic disease that manifests as insulin resistance and lipid metabolism disorder, resembling NASH, as previously proposed by our team [8] and Balsano et al. [9].

Of importance, exogenously administered polyunsaturated fatty acids (PUFAs) improve the accumulation and altered composition of lipids caused by HCV [1], as well as those in non-alcoholic fatty liver disease [10]. However, we would like to withhold our consent for its application in hepatitis C patients, because PUFAs did not reduce the NADH accumulation in our model system, while pyruvate did [1].

Lastly, it is crucial for hepatologists to identify hepatitis C as a metabolic disease, not only to guide patients toward improving their life style, but also to invent a measure to reverse the metabolic disorders, which are the essential aggravating factors for hepatitis C.

Conflict of interest

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References


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