Letter to the editor:

TGR5 REGULATES PORTAL PERFUSION PRESSURE OF THE LIVER

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Dear Editor,

Recently, Klindt and colleagues from the University of Düsseldorf published a study on the role of the bile acid receptor TGR5 in modulating portal pressure (Klindt et al., 2019). TGR5 is activated by bile acids, leads to an intracellular increase of cAMP (Kawamata et al., 2003; Keitel et al., 2019; Maruyama et al., 2002) and mediates cytoprotective effects (Keitel et al., 2009, 2015; Merlen et al., 2020; Perino and Schoonjans, 2015; Perino et al., 2014; Guo et al., 2016). In their present study, the authors present a concept according to which activation of TGR5 in sinusoidal endothelial cells of the liver blocks the release of endothelin-1. Endothelin-1 is known to cause contraction of hepatic stellate cells via the ET_A receptor. Therefore, endothelin-1 leads to a narrowing of the liver sinusoids and an increase of portal pressure (Klindt et al., 2019). Moreover, activation of TGR5 in hepatic stellate cells leads to internalization of the $ET_A R$ that also reduces the responsiveness to the contractile effect of endothelin-1.

The prevalence of liver diseases currently increases (Jansen et al., 2017; Ekhlasi et al., 2017; Hudert et al., 2019) and a better understanding of the responsible mechanisms is urgently needed to identify better strategies for therapeutic intervention (Svinka et al., 2017; Godoy et al., 2016; Ghallab et al., 2016; Gogiashvili et al., 2017). A particular challenge is that different cell types in the liver communicate in a complex manner, which leads to a situation, where the result of interventions is difficult to predict (Hoehme et al., 2010; Hammad et al., 2014; Schenk et al., 2017). The present study of Klindt and colleagues represents an important milestone in understanding the pathophysiology of increased portal pressure.

Conflict of interest

The author declares no conflict of interest.

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