

Guest editorial:

**HIGHLIGHT REPORT:
ROLE OF THE ATP-RELEASING PANX CHANNELS IN
LIVER FIBROSIS**

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Recently Sara Crespo Yanguas and colleagues from the University of Brussel published a study about the role of pannexin1 in the pathogenesis of liver fibrosis (Crespo Yanguas et al., 2018). Panx channels are known as mediators of ATP release (Dahl, 2015). After injury cells may release ATP and uridine-5'-triphosphate into the extracellular space. The released ATP attracts immune cells to the area of damage (Davalos et al., 2005; Chekeni et al., 2010). In cardiac fibrosis cardiomyocytes have been shown to release ATP via pannexin1 which contributes to activation of fibroblasts (Dolmatova et al., 2012). However, in liver the role of pannexin1 in liver fibrosis remains unknown. Therefore, the authors compared pannexin1 knockout and wild-type mice after CCl₄ treatment for 8 weeks and after bile duct ligation (Crespo Yanguas et al., 2018).

Interestingly, pannexin1 knockout mice showed reduced collagen content, stellate cell activation, and inflammation compared to wild-type mice. Therefore, the release of ATP seems to contribute to myofibroblast activation also in the liver. In contrast to the CCl₄-fibrosis model, bile duct ligation led to more hepatocellular injury and a stronger immune response in the pannexin1 knockout than in wild-type mice.

It is not surprising that different consequences are observed in the CCl₄ and the bile duct ligation models. CCl₄ is a model of pericentral liver damage where a fraction of approximately 40 % of hepatocytes in the centre of the lobule are killed (Hoehme et al., 2010; Hammad et al., 2017; Bartl et al., 2015). It seems plausible that the ATP released from these damaged hepatocytes activates stellate cells (Leist et al., 2017). In contrast, bile duct ligation leads to a ductular response with proliferation of cholangiocytes, branching and looping of bile ducts, leading to a denser mesh of interlobular bile ducts around portal veins (Vartak et al., 2016; Jansen et al., 2017). Simultaneously, periportal fibrosis occurs (Ghallab et al., 2018). It is interesting that this phenomenon is enhanced by the pannexin1 knockout, although the responsible mechanism still has to be elucidated.

Currently, hepatotoxicity *in vivo* (Stöber, 2016; Du et al., 2017; Reif et al., 2017; Hammad et al., 2018; Ghallab et al., 2016) as well as mechanistic studies in hepatocyte *in vitro* systems represent very active research areas (Ghallab, 2017; Godoy et al., 2013, 2015, 2016). In this rapidly progressing field Sara Crespo Yanguas and colleagues made an important contribution by revealing the role of ATP-release channels in the pathogenesis of liver fibrosis.

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