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EDITORIAL

Highlight report: adaptations of the biliary tree to cholestasis

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Recently, Peter Jansen and colleagues have published a comprehensive review article about the pathophysiology of cholestatic liver disease (Jansen et al. 2017). One of the central key messages of this article is that cholestatic liver disease typically evolves with anatomically an ascending course, where the early lesions occur 'downstream' in bile ducts, which later leads to 'upstream' bile salt mediated damage of hepatocytes. An interesting lesson learned from Jansen's article is that three topological domains of the biliary tree respond differently to cholestasis. Large bile ducts enlarge their diameter, which increases the capacity to conduct and accommodate biliary fluid (Strazzabosco 1997; Vartak et al. 2016). Upstream, the interlobular ducts undergo branching, and rejoining, which transforms a sparse mesh into a much denser mesh (Vartak et al. 2016). Moreover, the inner surface of the ducts becomes corrugated, which leads to a strong increase of the luminal duct surface and thereby increases bile resorption capacity. The bile canalicular network represents the most upstream domain of the biliary tract. In cholestasis, canaliculi show increased average diameters and an increase in the frequency of spine- or bleb-like protrusions into hepatocytes (Jansen et al. 2017). The causes of these changes are still controversially discussed and range from biochemically induced tight junctional remodeling and altered pericanalicular action to a possible consequence of increased canalicular pressure (Masyuk et al. 2001; Das et al. 2009; Liu et al. 2015).

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Recently, research on cholestatic liver disease has been a particular focus in toxicological sciences (Miszczuk et al. 2015; Deharde et al. 2016; Reif et al. 2015; Barosso et al. 2016; Crespo Yanguas et al. 2016) and imaging and image analysis pipelines have been established to study morphological and functional changes in liver disease (Hammad et al. 2014; Ghallab et al. 2016; Hoehme et al. 2010; Drasdo et al. 2014; Godoy et al. 2013). Interestingly, drug induced liver injury (DILI) shows a different pathophysiology (Jansen et al. 2017). While autoimmune disorders, such as primary sclerosing cholangitis and primary biliary cholangitis first damage the biliary tree followed by damage of hepatocytes, the opposite order of key events is observed for most hepatotoxic chemicals, where damage to the parenchyme precedes compromised functions of the biliary tract. The review of Jansen and colleagues gives an excellent overview for those interested in how the functionality and stress responses of the biliary tract and hepatocytes are interlinked.

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