

DYNAFLOW

Title Dynamic bile flow modelling and cellular sensing in primary sclerosing cholangitis.

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Project partners



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Abstract Primary sclerosing cholangitis (PSC) is a progressive liver disease characterized by fibrobliterative destruction of the intraand/or extra-hepatic bile ducts, leading to liver cirrhosis. There is no effective medical therapy for PSC, and the majority of patients will eventually require liver transplantation. Following a primary immunological insult, biliary flow obstruction leads to pressure damage to the biliary epithelium and hepatocytes and drives disease progression. We will use a systems biology approach to model the hydrodynamic and signalling consequences of the altered biliary flow. We will:

- i. experimentally map and model the 3D structure and cellular interactions of small bile ducts in well characterized and long-term followed patients and animal models of PSC,
- ii. perform 3D geometry-based hydrodynamic modelling,
- iii. calibrate models on intravital imaging of biliary flow in murine models,
- iv. look at the consequences on cellular programming using in-situ functional genomics and;
- v. mechanistically analyse and model biliary pressure sensing and it's signalling consequences.

The resulting spatiotemporal model of altered bile flow and signalling will allow A) to identify targets for the utterly needed pharmacological intervention to prevent biliary pressure damage and B) pave the way for personalized pharmacological biliary pressure optimization in affected patients.

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