

**Project title:** Novel therapeutic approaches for primary liver cancer

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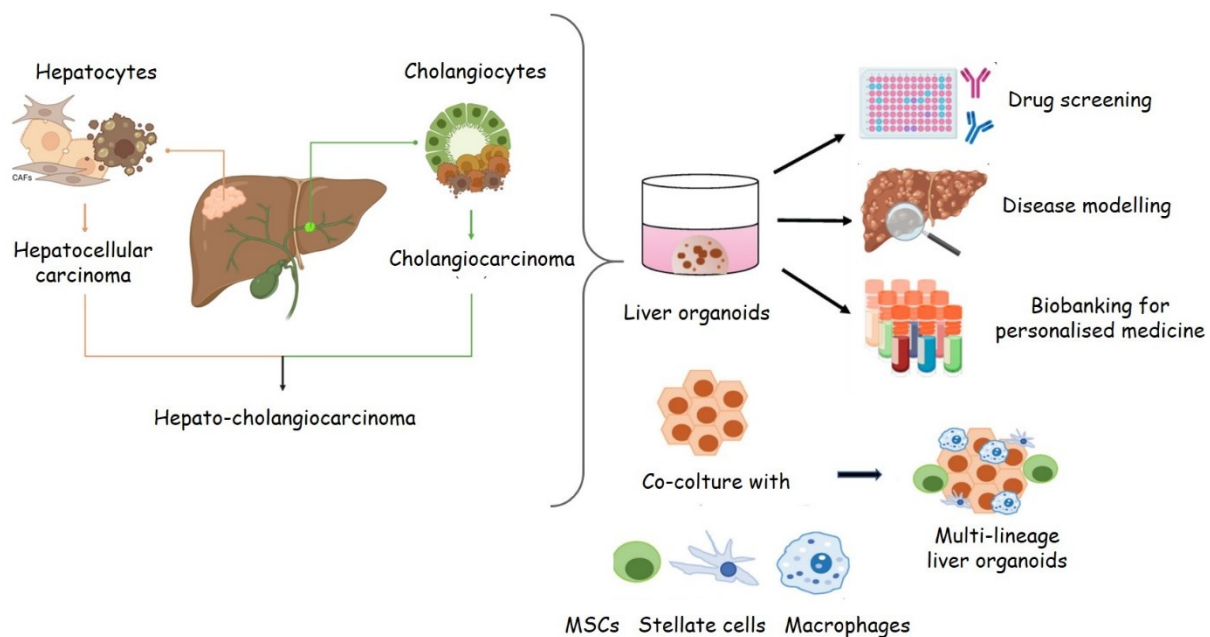
**Laboratory:** Molecular Hepatology laboratory; Department of Molecular Medicine.

Primary liver cancer (PLC), including hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (iCCA), is one of the leading causes of cancer-related mortality worldwide. HCC and iCCA are unique in terms of epidemiology and risk factors. While HCC mostly develops in the context of chronic liver diseases and cirrhosis, iCCA usually arises in the absence of underlying liver fibrosis. Usual risk factors for HCC include HCV and HBV infections; excessive alcohol intake; and non-alcoholic fatty liver disease. PLC still lacks perfect clinical treatment methods; finding an effective platform for liver cancer study and drug screening is of paramount importance. Bi-dimensional in vitro models are unable to recapitulate the key PLC features; consequently, the development of liver organoids a self-organising, self-renewing three-dimensional cell culture model that preserves all the morphology and genetic heterogeneity of the originating tumors has greatly improved cancer research, including the study of liver cancer.

In order to identify the molecular mechanisms involved in tumour progression of primary liver cancer and evaluate new preclinical therapeutic strategies, the candidate in this PhD project will:

- 1) investigate new molecular targets involved in HCC and iCCA;
- 2) develop a patient-derived organoids model to assess the tumourigenic potential of liver cancer, including a co-culture with stromal cells, immune cells, and other components to better reflect the heterogeneity of human liver cells and allow generation of multilineage liver organoids;
- 3) perform a high-throughput drug screening assay for new potential liver cancer drugs.

The successful development of this PhD project will help identify new molecular networks in primary liver cancer and, ideally, define an effective platform for personalised therapeutic strategy of liver cancer.



**Techniques:** Liver cell isolation, human primary liver cancer-derived organoid cultures, drug screening, transcriptome and proteomic analysis, live-cell imaging, confocal immunofluorescence microscopy.