

Principal Investigator Kim Ravnskjaer

Main Research Interests

YOU ARE AS HEALTHY AS YOUR LIVER, AND YOUR LIVER IS AS HEALTHY AS ITS BLOOD VESSELS

MISSION: In the Ravnskjaer lab we are devoted to exploring how cross-talk between liver cell types determines function and gene expression of the liver itself and other organs in our body. We therefore use advanced functional genomics and bioimaging to learn how hepatic inflammation, fibrosis, and microvascular dysfunction shape the course of other cardiometabolic diseases such as obesity, diabetes, atherosclerosis, and brain disorders.

IMPORTANCE: Despite weight-loss medicines, cardiometabolic diseases remain the main cause of death worldwide. Common drivers are the early deterioration of microvascular function and fibrosis disrupting tissue homeostasis and repair. Microvascular changes affect metabolism, inflammation, and tissue crosstalk across organs. Specifically, the breakdown of liver microvasculature and fibrogenesis in **MASH** (metabolic dysfunction-associated steatohepatitis), is linked not only to liver failure and cancer but also inflammatory processes elsewhere in the body and an increased risk of ischemic heart disease and stroke.

CHALLENGE: Most human tissues are composed of specialised parenchymal cells, vascular and perivascular cells, fibroblasts, neurons and local immune cells. These cells constantly interact with each other and the surrounding tissues while receiving signals from the blood. Deeply fascinating to study.

STRATEGY: To overcome this challenge, we apply single-cell and spatial transcriptomics to patient biopsies and animal disease models to dissect molecular disease mechanisms one cell at the time. We study signaling pathways and transcriptional networks and validate our findings by advanced microscopy and genetic or pharmacological perturbation in cells and animals.

We combine clinical analyses with experimental studies and computational modelling.

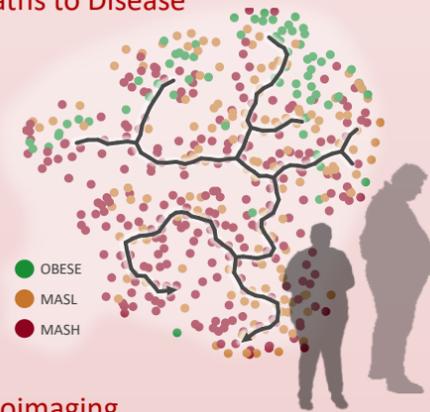


✉ ravnskjaer@bmb.sdu.dk

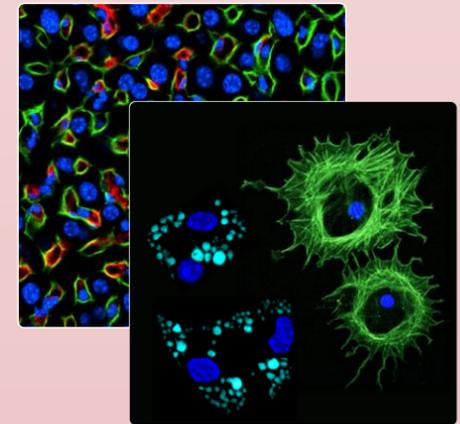
🦋 @ravnskjaer-lab.bsky.social

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Paths to Disease



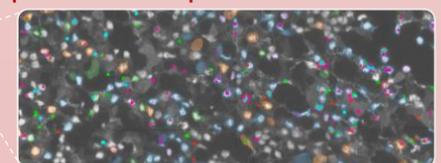
Bioimaging



Single cell transcriptomics



Spatial transcriptomics



HUMAN
LIVER

MOUSE
LIVER

Project examples Description

Single-cell and spatial analyses of cell populations during MASH development and resolution

We use single-cell RNA sequencing and spatial transcriptomics to study the development and resolution of MASH in human obesity. Through bioinformatics analyses and machine learning algorithms we resolve the transcriptional plasticity of liver cells and use this to discover, investigate, and target the transient cellular interactions that drive progression and regression of liver disease.

TOOLS: Patient biopsies, bulk transcriptomics, single-cell transcriptomics, spatial transcriptomics, histopathology, flow cytometry, light-sheet & confocal microscopy, mouse models, bioinformatics.

Microvascular control of tissue metabolism, signal transduction and gene expression

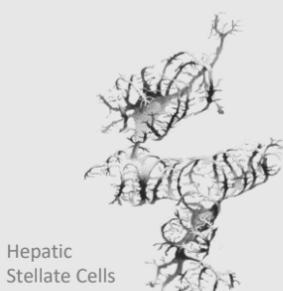
Hepatic Stellate Cells are deeply implicated in the development of MASH and liver fibrosis but as microvascular pericytes they also play fundamental roles in healthy liver function. We study how stellate cells and other pericytes in corporation with endothelial and immune cells regulate metabolism, signaling pathways, and gene expression.

TOOLS: Knockout mice, CRISPR/Cas9, liver cell isolation, bulk transcriptomics, single-cell transcriptomics, spatial transcriptomics, ELISA, tissue clearing, confocal microscopy, bioinformatics.

Microvascular G-Protein-Coupled Receptor profiling and targeting

Cell identity, plasticity and decision-making are important for homeostasis and disease development. In healthy tissues, cells undergo constant transitions to adapt to their environment. These changes become larger and often permanent in disease. G-protein-coupled receptors (GPCRs) is a main way by which cells in the liver and elsewhere sense their tissue environment and signals from the blood and brain. The family of GPCRs counts 826 receptors, and the dynamic expression of them across cell types is mostly unexplored. We here use single-cell and spatial transcriptomics to explore the *GPCRome* of the liver and other organs and try to understand receptor function. GPCRs are good drug targets and half of all approved drugs modulate GPCR function. The identification of *new* GPCRs associated with liver health or disease could therefore enable novel ways to treat cardiometabolic diseases.

TOOLS: Patient biopsies, transgenic mice, viral vectors, CRISPR/Perturb-Seq, spatial transcriptomics, single-cell transcriptomics, histopathology, light-sheet & confocal microscopy, culture of cells and tissue slices, bioinformatics.



Hepatic
Stellate Cells