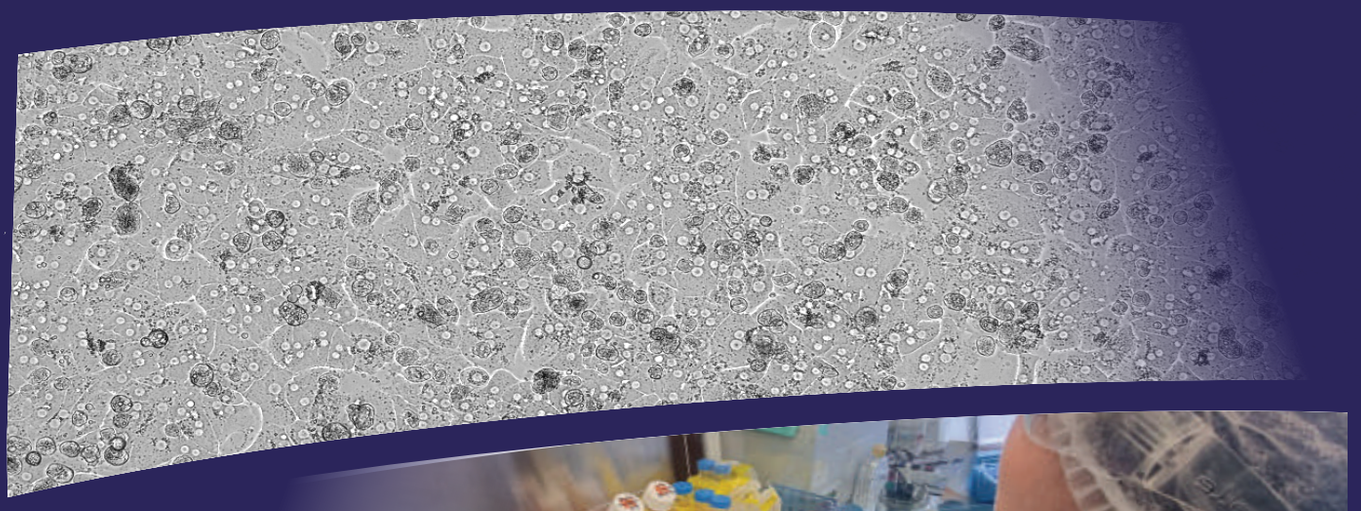
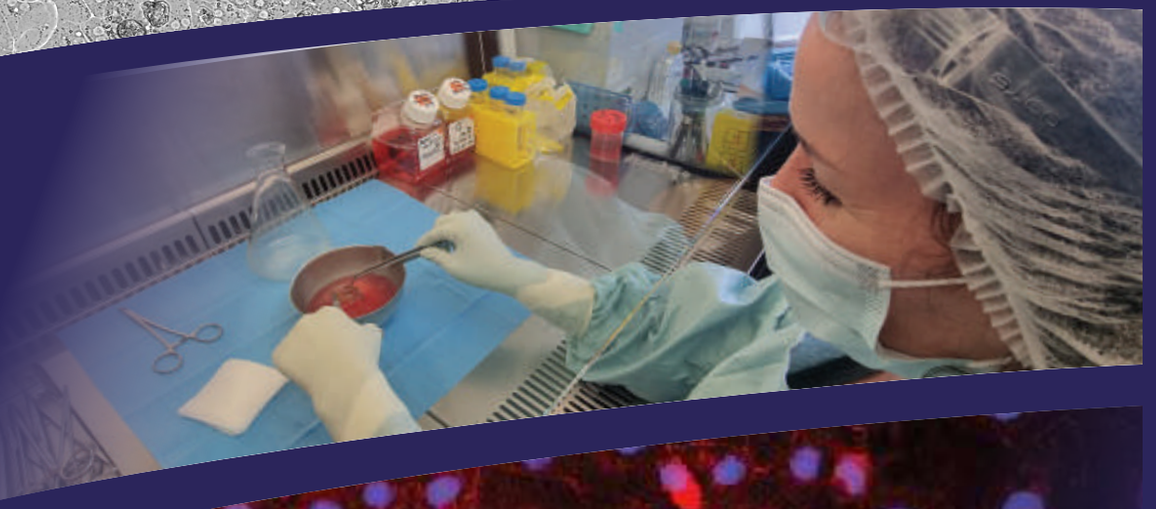
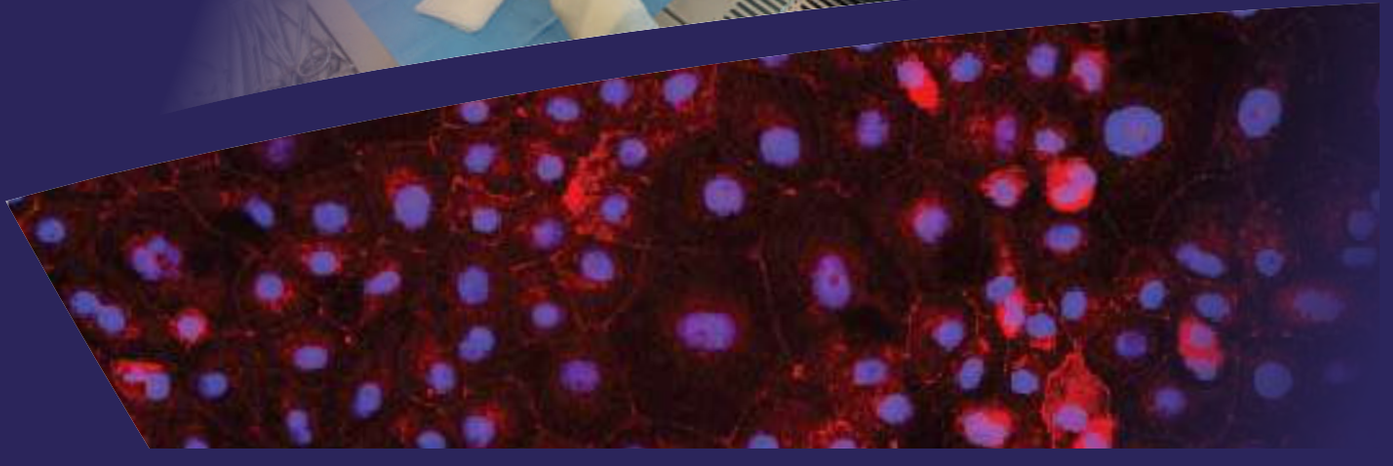
ICAN BioCell - Human Liver Biology

2D/3D human liver models in primary culture to assess

the efficiency of your molecules







IHU ican

BioCell

Human Liver Biology

IHU

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Foundation for Innovation
in Cardiometabolism
and Nutrition

Key assets

INNOVATION

In vitro and ex vivo models to study chronic liver diseases

EXPERTISE

An expert scientific and technical team at your service

COLLABORATION

The platform is designed to support large-scale academic or industrial projects

ENVIRONMENT

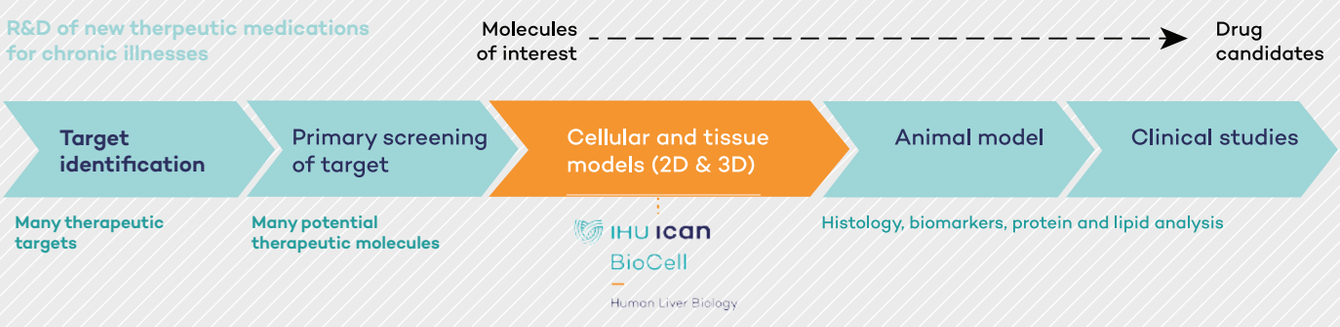
Located within a university hospital environment, ICAN BioCell Human Liver Biology has been collaborating with the AP-HP for 10 years

ICAN BioCell - Human Liver Biology

Our ICAN BioCell - Human Liver Biology platform is a scientific platform entirely dedicated to the production of primary human liver cells and the development of liver models in vitro and ex vivo. Its objective is to study the molecular mechanisms of chronic liver diseases (steatosis, NASH, fibrosis, cirrhosis, liver cancer, etc.) and to test the efficacy and toxicity of lead molecules and drug candidates.

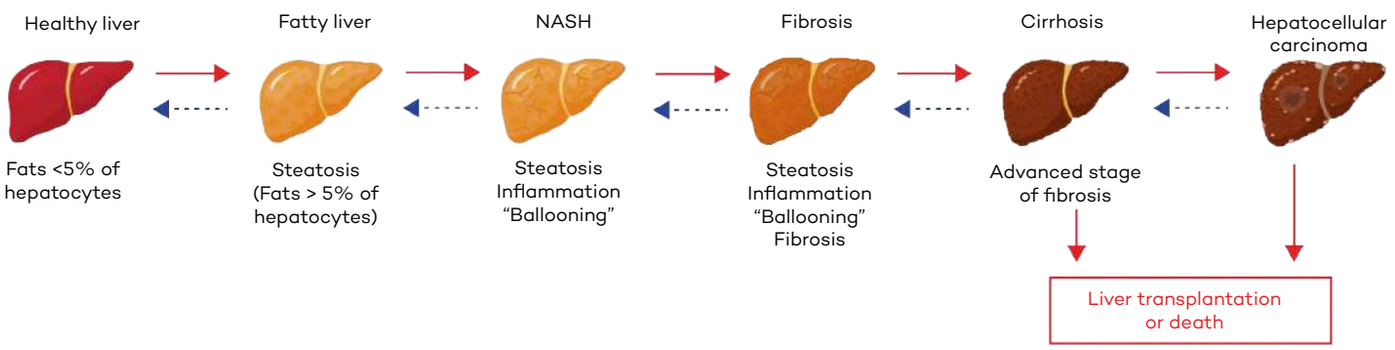
ICAN BioCell - Human Liver Biology offers innovative services for academic and industrial research projects in chronic liver diseases.

ICAN BioCell - Human Liver Biology in the industry value chain



Target diseases

Chronic liver diseases are a real public health problem. Controlling the aetiological factor (excessive alcohol consumption, viral infection, metabolic syndrome, autoimmune hepatitis) is currently the main strategy for limiting the progression of the disease to cirrhosis, constituting irreversible fibrosis of the liver parenchyma. At this stage, liver transplantation is often the only therapeutic alternative.



ICAN BIOCELL - HUMAN LIVER BIOLOGY

- Toxicity
- HBV / HCV infection
- Induction of steatosis
- Induction of fibrosis/NASH
- Evaluation of the impact of molecules (antiviral, antifibrotic, anti-NASH

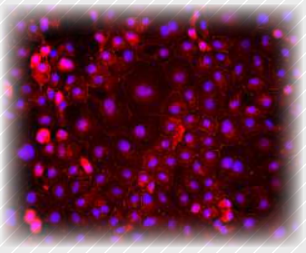
* Precision Cut Liver Slices

Expertise

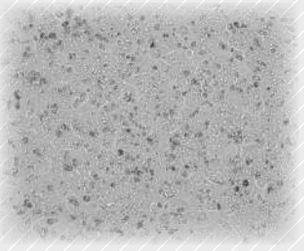
1. A service for human liver cell isolation

- Fresh human hepatocytes (HH) plated or in suspension format
- Hepatic non-parenchymal cells (NPC)
- Biliary epithelial cells
- Human liver myofibroblasts (HLMF) from normal liver, fibrosis and cirrhosis
- The platform has a biobank of 72 batches of frozen characterised HLMFs

Human hepatocytes (HH)

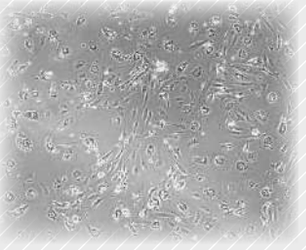


HH in immunoflorescence

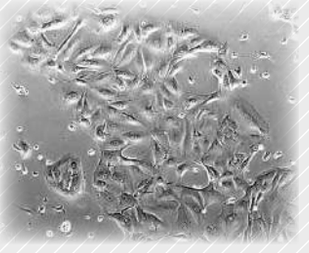


Primary culture of HH

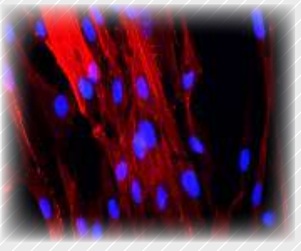
Non-parenchymal cells



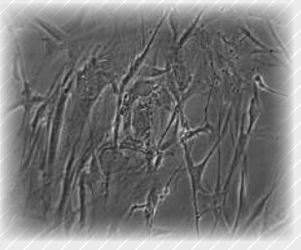
Biliary epithelial cells isolated from a gallbladder



Human liver myofibroblasts (HLMF) from either a normal, fibrotic or cirrhotic liver.



HLMF in immunofluorescence



Primary culture of HLMF

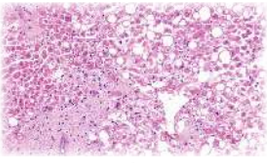
2. 3D models

The platform offers 3D models that present several types of liver cells in a physiological context. These preclinical models are relevant to study the NASH and liver fibrosis.

PCLS model (thin liver slices 250-300 µm)

The team has developed a 3D ex vivo Precision Cut Liver Slices (PCLS) model prepared from steatotic livers and demonstrated the efficacy of an innovative defatting "cocktail" called D-FAT on this model (L. Aoudjehane et al, DMM, 2020).

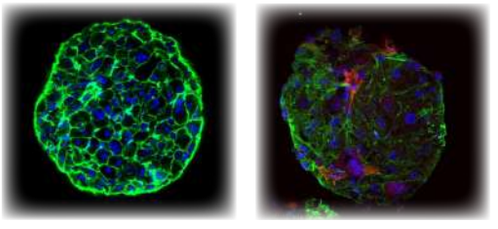
PCLS (precision cut liver slices) model in culture



Cross-section of steatotic PCLS with H&E staining

Hepatic spheroid model HH+NPC

In order to better understand the progression of NASH and evaluate therapeutic targets, the team developed a 3D liver spheroid model developed from primary human cells to mimic the architecture of the human liver and the NASH environment.



3D in vitro hepatic spheroid model

3. Specialised services for the study of fibrosis and NASH

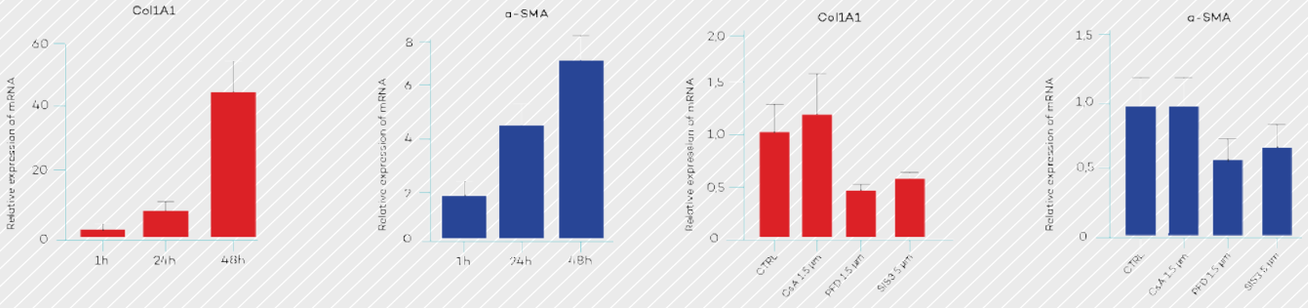
Fibrosis

- Quantifibrosis to evaluate the activity of anti-fibrotic molecules in a model:

2D: Primary human liver myofibroblasts (HLMF)

3D: PCLS and/or spheroids

- Fibrotic markers: analysis of a-SMA, type I collagen and other markers expression by QPCR, ELISA, WB, etc.



Study of liver fibrosis in a 3D PCLS model, L. Aoudjehane et al; AASLD (2015)-EASL (2016) communication

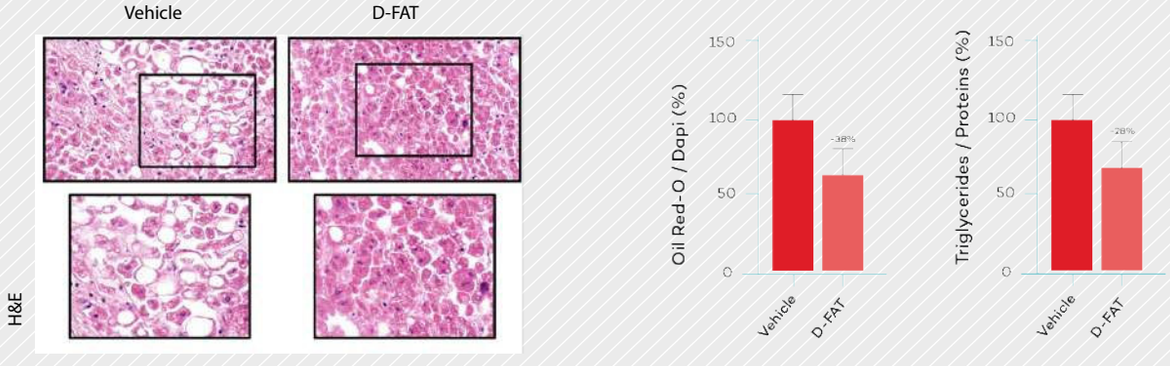
NASH

- Study the NASH mechanism and evaluate the therapeutic molecules efficacy in models:

2D: Steatotic hepatocytes (HH) or normal HH with induced steatosis (+FFA)

3D:
- Steatotic PCLS
- Multicellular liver spheroids (HH+NPC)

- Lipid metabolism (triglyceride assay, RedOil staining, genes involved in lipid metabolism: CPT1, PGC-a1, MTTP, APOB100, etc.)
- Liver functional metabolism (albumin, CYP3A4 activity, ABC transporters, etc.)
- Viability and toxicity (MTT, ATP and HDL) and oxidative stress (ROS detection)
- Inflammatory cytokines (QPCR and ELISA)



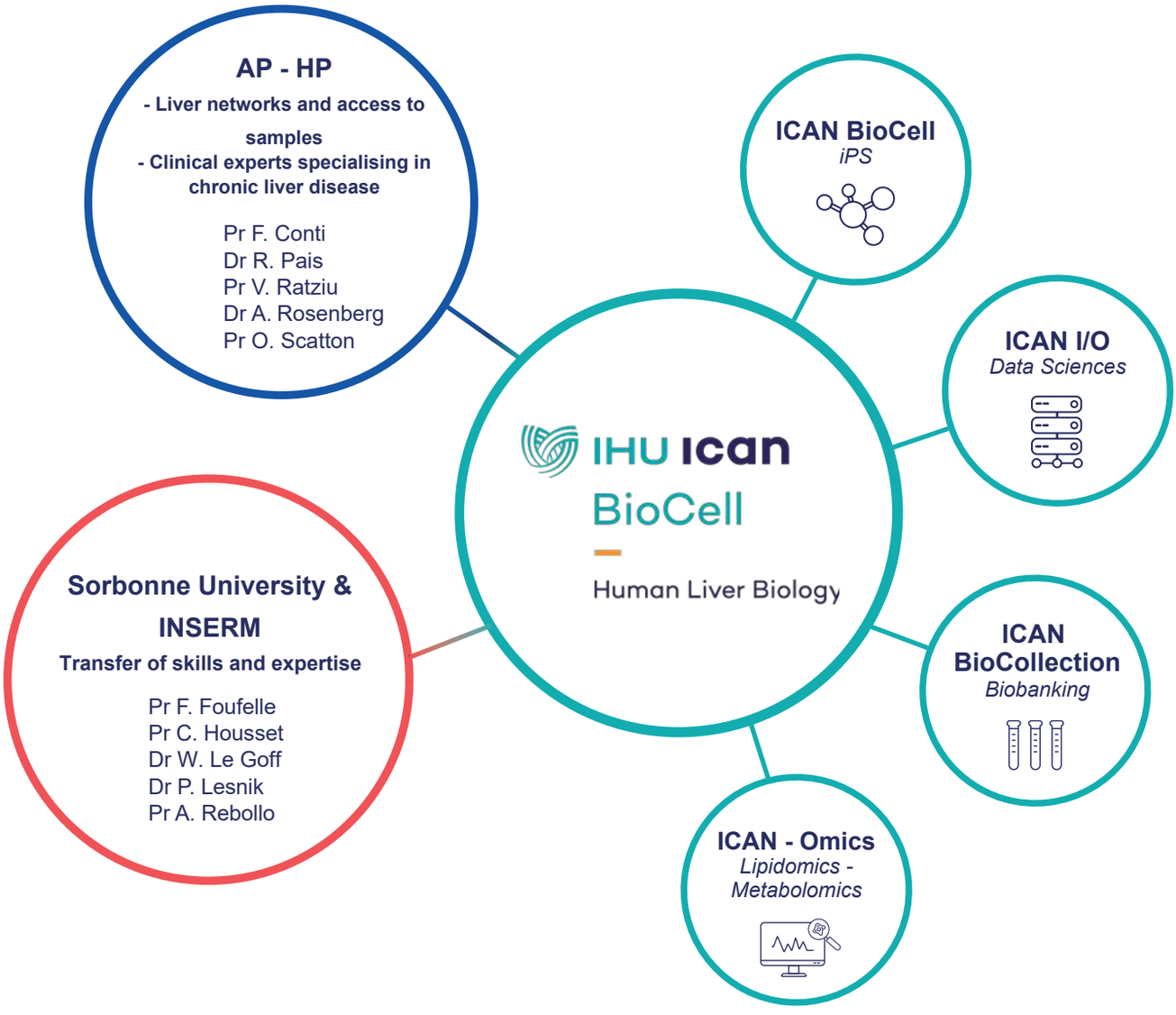
Study of hepatic steatosis in a 3D PCL model, L. Aoudjehane et al; Disease Models & Mechanisms (2020)

REGULATORY ASPECTS

CODECOH, DC-2020-3900 and AC2020-3861

- Preparation of human cells for research and scientific collaboration
- Authorisation to store, process and sell human cells

Outreach and partnerships



THE TEAM

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