Master 2 research internship in Integrated Structural & Cell Biology in Grenoble

Supervisor(s):
Aurélien Deniaud, aurelien.deniaud@cea.fr

Host laboratory:
LCBM cbm-lab.fr/

Host group/team:
Met&Or

Title of the M2 research internship:
Correlative microscopy to explore the Canal of Hering

Project summary:
The liver is a major organ for metabolism that possesses a very complex architecture. It is organized in hexagonal lobules mainly composed of hepatocytes arranged in cords. Besides, within each cord, bile canaliculi are formed between hepatocytes and constitute a network of micrometer-sized channels where hepatocytes secrete the bile. Bile is then collected in bile duct thanks to connection with bile canaliculi at the periphery of the lobule. This connection between the liver and the biliary tree, named canal of Hering, is enigmatic but should be the source of liver progenitor cells. The study of the architecture of the Hering's canal remains a challenge since it is expected to be positioned every ~10 µM along the bile duct. Our aim is to locate and reconstruct in 3D the Hering's canal.
In the last years, we have developed the use of FIB-SEM, which is an electron microscope in which a sample is cut slice by slice by gallium ions, and each new surface is imaged in series. It enabled us to reconstruct at nanometer resolution specific ultrastructures within liver samples such as bile canaliculi. To be able to obtain the first ultrastructural reconstruction of the Hering's canal, we now need to combine FIB-SEM with a method of lower resolution to obtain, first, the overall structure of the liver lobule and, second, the high-resolution information on the Hering's canal. To reach these goals, we want to couple X-ray tomography with FIB-SEM and use our expertise in 3D image analysis to obtain the structure of the Hering's canal.
The obtained data will enable to confirm or not the presence of progenitor cells in the Hering's canal and will provide the first information on the connection between bile canaliculi and bile duct. Moreover, this work will provide a methodology for future multiscale ultrastructural studies.

Keywords:
correlative X-ray tomographyt with 3D electron microscopy, liver canal of Hering, 3d image analysis

Relevant publications of the team:
1. Deciphering silver nanoparticle fate in liver up to biliary excretion using HepG2/C3A spheroids in scenarios mimicking different exposure pathways.

Rekik Y, Tardillo Suárez V, Sharma V, Chevallet M, Gallet B, Falconet D, Charbonnier P, Kieffer I, Tucoulou R, Jouneau PH*, Veronesi G*, Deniaud A*. Environmental Science: Nano. 2023; 10:1842-57. doi: 10.1039/D3EN00177F.

2. Structures of Silver Fingers and a Pathway to Their Genotoxicity.

Kluska K, Veronesi G, Deniaud A, Hajdu B, Gyurcsik B, Bal W*, Krężel A*. Angewandte Int. Ed. Chemie. 2022; 134, e202116. doi: 10.1002/anie.202116621.

3. Correlative transmission electron microscopy and high-resolution hard X-ray fluorescence microscopy of cell sections to measure trace elements concentrations at the organelle level.

Tardillo Suárez V, Gallet B, Chevallet M, Jouneau PH, Tucoulou R, Veronesi G*, Deniaud A*. J Struct Biol, 2021; 213 (3). doi: 10.1016/j.jsb.2021.107766.

4. Nuclear Translocation of Silver Ions and Hepatocyte Nuclear Receptor Impairment upon Exposure to Silver Nanoparticles.

Tardillo Suárez V, Karepina E, Gallet B, Cottet-Rousselle C, Chevallet M, Charbonnier P, Moriscot C, Michaud-Soret I, Fuchs A, Tucoulou R, Bal W, Jouneau PH, Veronesi G, Deniaud A*. Environmental Science: Nano. 2020; 7:1373-87. doi: 10.1039/C9EN01348B.

5. Canalicular domain structure and function in matrix-free hepatic spheroids.

Raj Sharma V, Shrivastava A, Gallet B, Karepina E, Charbonnier P, Chevallet M, Jouneau PH*, and Deniaud A*. Biomaterials Science. 2020; 8:485-96. doi: 10.1039/C9BM01143A.