Title: Role of the hepatic microenvironment in liver fibrosis related to chronic hepatitis C

Supervisor: Eve-Isabelle Pecheur

Duration: 3 months

Project Context:
Currently, 25% of the cases of hepatocellular carcinoma are due to a chronic infection with the hepatitis C virus (HCV). This end-stage complication of liver pathology can occur after liver fibrosis and cirrhosis. Recently released antivirals do not seem to reduce the occurrence of liver cancer at advanced stages of cirrhosis. A better comprehension of the early stages of chronic hepatitis C is therefore needed. Liver fibrosis is a hallmark of a massive remodeling of the hepatic extracellular matrix (ECM), contributing to subsequent carcinogenesis. The molecular details of the occurrence of this fibrosis remain obscure.

Project Objectives:
We recently showed that the expression and trafficking of syndecan-1, a heparan sulfate proteoglycan (HSPG) of the liver ECM, were altered during chronic infection. We also identified major HCV-induced defects of the global metabolism of HSPG.

Our project aims at dissecting the molecular mechanisms underlying HCV-induced fibrogenesis and early carcinogenesis, by analysing the expression and activity of enzymes of hepatic HSPG metabolism, by studying the potential infection-related alterations of glycosylation profiles of HSPG, and by identifying new effectors able to propagate signals throughout the hepatic microenvironment during various stages of chronic infection. These studies will combine approaches of sugar and protein biochemistry, of molecular biology, and will be conducted in cell culture systems and in patients samples (liver biopsies or resections, serum).
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**Bibliography**
