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Catherine Postic is a research group leader in the Department of Endocrinology Metabolism and Diabetes at the Cochin Institute, INSERM U1016, CNRS UMR 8104 Université de Paris Cité.
Catherine Postic earned her doctorate at the University Paris Diderot in Paris. She completed post-doctoral work at Vanderbilt University in Nashville, TN USA. During this post-doctoral fellowship she was trained in the field of molecular biology and achieved the making of a conditional locus for the glucokinase (gck) gene, a key gene of glucose metabolism.
With this approach she has explored the cell-specific function of glucokinase in liver and pancreatic ß-cells and demonstrated the importance of this enzyme in the sensing of glucose. Her long time interest in the control of hepatic metabolism prompted her to study the function and the regulation of the transcription factor ChREBP. Using both physiological and metabolic approaches her group made significant advance in understanding the regulation of ChREBP by glucose and assessing its function in metabolic diseases such as Non Alcoholic fatty Liver Disease (NAFLD).She recently got interested in another important glucose sensor, the O-GlcNAc transferase (OGT), and is currently studying its role in liver physiology.

Glucose sensing and lipid metabolism in NAFLD

Glucotoxicity is a phenomenon that initiates a vicious cycle in which chronic hyperglycemia leads to the development of type 2 diabetes. Among the mechanisms involved, it is described that a fraction of glucose, metabolized in the hexosamine biosynthetic pathway, induces O-GlcNAcylation of intracellular proteins. O-GlcNAcylation is a reversible post-translational modification controlled only by two enzymes, OGT, which adds a molecule of N-Acetyl Glucosamine (GlcNAc) to serine or threonine, and OGA, which removes it. Our laboratory reported that O-GlcNAcylation of key effectors of metabolism contributed significantly to gluco-lipotoxicity in liver (Kuo 2008, Guinez 2011) and pancreatic β cells (Fardini 2014). In order to determine the metabolic consequences of a targeted deletion of the OGT enzyme in in the context of NAFLD, our laboratory generated mice constitutively deficient for OGT in the liver (OGTLiverKO). Surprisingly, these mice do not exhibit major disruption of metabolic homeostasis but show a severe liver phenotype with the presence of numerous regeneration nodules visible after weaning. RT-PCR and western blot analyzes showed that the expression of cyclins A2, B1 and D1 was significantly increased in the liver of OGTLiverKO mice compared to controls, suggesting an exacerbated proliferative state. Immunohistological analyzes revealed the presence of pro-inflammatory cells and signs of fibrosis in the spans surrounding the regeneration nodules. This was associated with a significant increase in markers of inflammation (TNFα) and fibrosis (TGFβ), suggesting significant liver injury in OGTLiverKO mice. Full characterization of this novel mouse model is currently ongoing.