**Research Theme**
Metabolic Disorders

**Research Project Title**
Peroxisome Proliferator-Activator Receptor beta/delta (PPARβ/δ) in Hepatocellular Carcinoma (HCC)

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**Project Description**
Peroxisome proliferator-activator receptors (PPARs) are nuclear receptors that function as cis-regulators modulating gene transcription activity. PPARs play essential roles in various biological processes including lipid and glucose metabolism as well as inflammation. Deregulation of PPAR signaling has been reported in diseases such as obesity, type 2 diabetes and various cancers.

Hepatocellular carcinoma (HCC) is a poor prognosis and high mortality disease; 80-90% of the HCC patients also have liver cirrhosis, which makes this cancer even harder to treat. We intend to investigate the role played by PPARbeta/delta (PPARβ/δ) in the progression of HCC in non-alcoholic fatty liver disease (NAFLD). Our aim is to assess whether PPARβ/δ could serve as drug target (agonists, antagonists) in HCC patients.

There is a growing body of evidence for a link between obesity and liver cancer in which PPARβ/δ might be involved. In fact, PPARβ/δ is suspected to participate in liver steatosis and fibrosis induced by either chemical injury or obesity via a role in the activation of Hepatic Stellate Cells (HSCs), a process that is key in disease development. However, the role of PPARβ/δ in carcinogenesis is still debated. We aim to unveil the molecular mechanism by which PPARβ/δ participates in HCC formation, especially during liver fibrosis, and whether modulation of its activity...
by agonists or antagonists impacts HCC progression in mouse models. Mice receiving the
carcinogen Diethylnitrosamine (DEN) will be fed with different diets and we will monitor the
progression of steatosis, fibrosis and HCC formation. The roles of PPARβ/δ in the different liver cell
types (hepatocytes, HSC, Kupffer cells) will be studied after isolation of these cells in in vitro
primary cultures. In parallel, cell-type specific deletions of PPARβ/δ will be used to unveil its role in
vivo in the different cells types of the liver as the disease develops.

Contact Us
If you have questions regarding this project, please email the Principal Investigator.
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