Project 1.2 The bile acid receptor as treatment in liver disease

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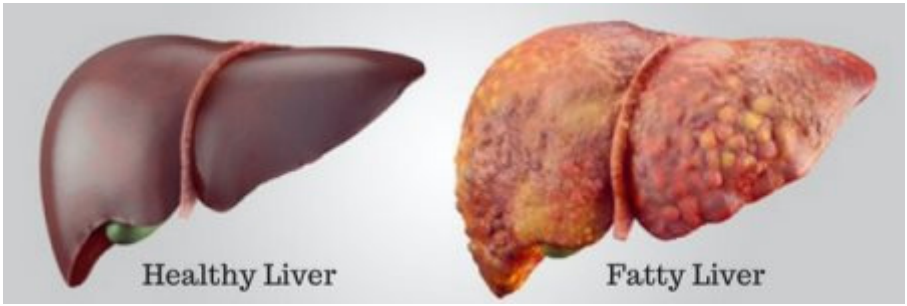

Clustered disorders associated with disrupted nutrient/energy homeostasis, including obesity, type II diabetes and non-alcoholic fatty liver disease (NAFLD), are increasing worldwide. Susceptibility to develop these diseases may originate from early life (programming). In NAFLD, a progressive subtype exists, designated as non-alcoholic steatohepatitis (NASH), that is recognized as an increasing cause of liver cirrhosis and hepatocellular carcinoma. Disturbed signaling of de bile acid receptor FXR in the gut-liver axis appears to contribute to the pathogenesis of NAFLD. Standard therapeutic interventions have not been established for NAFLD, but some new agents that modulate FXR signaling have shown promise as possible therapeutics. Yet, many steps, involving mechanistic studies in relevant animal models, are still required for tailoring pharmacotherapy to the dominant pathogenic pathways in a given patient, possibly with use of combination therapy. The ESR (PhD student) on the current project will contribute to the future direction in (personalized) treatment of patients with NAFLD and NASH, through application of newly developed mouse models generated by CRISPR-Cas technology, amongst others mice with humanized bile acid metabolism, and innovative methodologies to quantify metabolic fluxes in order to allow rapid and more accurate translation to the human situation.

Desired Disciplines

Biochemistry, Molecular biology, Pharmacy

Supervisors

Prof. Folkert Kuipers, PhD, Pediatrics and Laboratory Medicine, University Medical Center Groningen

Prof. Henkjan Verkade, MD PhD, Pediatrics, University Medical Center Groningen

Potential secondments

Mayo Clinic, Rochester MN, USA

Pasteur Institute, Lille, France