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Patrick Rensen received his PhD (cum laude) in 1992 at Leiden University, and is professor Metabolic Aspects of Vascular Disease at Leiden University Medical Center, Leiden, The Netherlands, and guest professor at Xi'an Jiaotong University, Xi'an, China. He is Established Investigator of the Dutch Heart Foundation, chairman of the European Lipoprotein Club (ELC), board member of the Scandinavian Society for Atherosclerosis Research (SSAR), and board member of the Leiden University Fund (LUF) Committee for Academic Expenditure. His research group studies the role of lipid and glucose metabolism in cardiometabolic diseases, with a main focus on modulation of energy metabolism as a strategy to prevent and treat obesity and associated diseases including NAFLD, type 2 diabetes and atherosclerotic cardiovascular disease. He currently investigates novel strategies to target NAFLD, including lifestyle-related approaches (e.g., exercise, dietary fiber intake) and pharmacological approaches (e.g., FGF21, incretins, DHCR24 inhibitors), taking account the role of thermogenic adipose tissues, the gut microbiome and the biological clock. To this end, he combines mechanistic experiments in a humanized mouse model for cardiometabolic diseases (i.e., APOE*3-Leiden.CETP mice) with human intervention studies in metabolically compromised individuals. Current grant support includes the Dutch Research Council (NWO), Dutch Heart Foundation (DHF), Dutch Diabetes Research Foundation (DFN), European Federation for the Study of Diabetes (EFSD), NovoNordisk Foundation, Dutch Digestive Foundation (MLDS) and the Chinese Scholarship Council (CSC). He currently co-authors approx. 340 publications (H-index 58) in peer-reviewed scientific journals (e.g., Cell, Cell Metab, Nat Med, Nat Commun, Eur Heart J, Circulation, Gut), and is Editorial Board member of Atherosclerosis.

Adipose-liver crosstalk in NAFLD

Cong Liu, Robin van Eenige, Zhixiong Ying, Yanan Wang, Sander Kooijman, Milena Schönke, Patrick C.N. Rensen

The main research focus of our group is modulation of energy metabolism to target obesity and related cardiometabolic diseases. We recently set out to evaluate experimental strategies to combat NAFLD, via lifestyle-targeted and pharmacological approaches, mainly by employing APOE*3-Leiden.CETP transgenic mice. Using this well-established model for human cardiometabolic diseases including NAFLD, we recently studied biological mechanisms underlying protective effects of various recombinant hormones (e.g., FGF21, GLP1 and GIP) in NAFLD. By combining extensive metabolic phenotyping with immune cell profiling, we revealed that FGF21R agonism and GLP1R/GIPR agonism strongly inhibit diet-induced NAFLD progression, involving activation of thermogenic adipose tissues. In addition we evaluated a novel strategy to target NAFLD by inhibition of DHCR24, the enzyme that mediates the conversion of desmosterol into cholesterol, using our selective DHCR24 inhibitor SH42. Treatment with SH42 increased hepatic desmosterol to selectively activate LXR in macrophages without inducing lipogenesis in hepatocytes. As such, this novel strategy appeared very successful in reducing hepatic inflammation as well as lipid accumulation. Results of these ongoing studies will be presented, and relevance for treatment of NAFLD in humans will be discussed.