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Leo van Grunsven obtained his Biology degree in 1992 from the Utrecht University working on the identification of upstream regulatory regions of Cyclin genes. He went to Lyon (France) for a PhD on the regulation of NGF-dependent neural outgrowth in Pheochromocytoma cells and obtained his PhD in 1996 from the Ecole Normale Supérieure de Lyon. He had his postdoctoral training at the NINDS/NIH (Bethesda, USA) and the KU Leuven (Belgium) which focused on understanding the transcriptional regulation of neuronal differentiation. At the NIH the focus was on neuronal stem cells, while at the KU Leuven neuronal differentiation was studied during early neurogenesis in the mouse and frog with a strong emphasis on the transcriptional repressor SIP1/ZEB2. He joined the lab of the late Prof. Albert Geerts at the Vrije Universiteit Brussel (VUB, Belgium) in 2006 and became an assistant Professor in 2009 and heads the Liver Cell Biology research group since. His research group studies molecular mechanisms involved in liver -homeostasis, -fibrosis and –regeneration with a special focus on hepatic stellate cells. His group was the first to identify autophagy, AGE- and HIPPO-signaling as key mechanisms involved in hepatic stellate cell activation during liver fibrogenesis. His team pioneered in the establishment of an hepatocyte-injury dependent in vitro liver fibrosis model by using spheroid cultures of human hepatocytes and hepatic stellate cells (2016). The research efforts of his lab now also include induced pluripotent stem cell-derived hepatocytes and hepatic stellate cells as a cellular source for these spheroid cultures. The group continues to invest in further refinement of in vitro models of fibrosis and NAFLD based on primary mouse liver cells and investigates the regulation of stress pathways in hepatic stellate cells and sinudoidal liver cells during acute and chronic liver injury in mouse models.

More info: http://livr.vub.ac.be/ ResearchPortal VUB

Modeling fibrosis and NAFLD in 3D liver cultures

Liver fibrosis and cirrhosis can be caused by viral hepatitis, non-alcoholic fatty liver disease (NAFLD), alcoholic- (ASH) and non-alcoholic-steatohepatitis (NASH). Currently, no therapies are available in the clinic that can target fibrosis directly. Commonly used models for in vitro liver fibrosis consist of mono-layer cultures of rodent hepatic stellate cells (HSCs), thereby ignoring the role of hepatocyte injury, which usually triggers the switch of quiescent HSCs in a healthy liver to activated myofibroblastic HSCs in an injured liver. The presentation will give an overview of our progress on developing complex 3D liver cultures; from hepacotye-HSC cultures to primary- and iPSC-derived four cell-type cultures that can model fibrosis and NAFLD. Special attention will be given to a recenlty established multicellular in vitro spheroid culture model using primary mouse hepatocytes, HSCs, liver sinusoidal endothelial cells (LSECs) and Kupffer cells (KCs). These liver spheroids maintain the independent liver cell functionalities for two weeks and demonstrate the capacity to mount a fibrotic response upon drug-induced liver damage or fatty liver conditions. Importantly, the anti-steatotic and anti-fibrotic efficacy of anti-NAFLD compounds such as Elafibranor, Lanifibranor and Obeticholic acid as observed in mice, could be reproduced in these cultures. These culture models represent an important step forward towards in vitro compound testing for drug-induced liver fibrosis and NAFLD.