ID: MSCA-2020-LVGrunsven02

Title: Liver fibrosis initiation revisited

Liver fibrosis is the pathological condition of the liver resulting from sustained wound healing in response to various causes of liver injury, including chronic alcohol abuse, viral infections or obesity. Liver disease remains a global issue, with an estimated death toll of over 1.3 million deaths due to liver cirrhosis, the advanced form of liver fibrosis. Fibrosis, or scarring of the liver, constitutes the deposition of excessive amounts of extra-cellular matrix, which is produced mostly by hepatic stellate cells (HSCs) that upon liver damage switch from a quiescent state to an activated myofibroblastlike state. Although extensively investigated, the initiating events that trigger and orchestrate HSC activation are still not entirely understood. In this project we would create a detailed transcriptomic landscape of HSC activation in vitro and in vivo with a focus on the first 24 hours. To get insight into the chromatin landscape and dynamics of quiescent- and activated HSCs, ATAC- and ChIP- sequencing at the population level, and super-resolution microscopy at the single cell level will be carried out. Finally, newly developed in vitro liver fibrosis models will be used to validate the importance of key transcription factors and histone modifiers identified during liver injury-induced HSC activation in vitro.

Supervisors: Leo.van.Grunsven@vub.be, Inge.Mannaerts@vub.be

Research Group: https://livr.research.vub.be/

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