Progression of MASLD goes along with significant changes of a recruited and TGFb sensitive macrophage population

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Autoren

Stephanie D. Wolf Moritz C. Malms Sophia Müller-Dott Tobias Lautwein Seddik Hammad Karl Köhrer Julio Saez-Rodriguez Steven Dooley Tom Lüdde Johannes G. Bode

Abstract

The course of fatty liver disease progresses from liver steatosis to chronic inflammation, potentially leading to development of liver cirrhosis, the major risk factor for hepatocellular carcinoma. Cells of innate immunity, especially macrophages, play an important role in this context, although the detailed mechanisms of cell communication are incompletely understood.

The results of the study of a high temporal resolution feeding series prove that the development of fibrosis is accompanied by accumulation of macrophages and formation of so-called crown like structures (CLS) that contain recruited macrophages. A detailed analysis of changes in the composition of immune cell populations during disease progression using CITE Seq Analyzes showed that there is a significant increase in a recruited macrophage population that highly expresses CD11b and CD14. The activation state of this population is substantially controlled by TGFb. The increase in this population is accompanied by a decrease in other macrophage populations in the liver, particularly sessile macrophages. Interestingly, the gene expression of the CD11b-high-CD14-high macrophage population is significantly more influenced by signals via the TGFbRII than the gene expression of the other macrophage populations. This suggests that CD11b-high, CD14-high expressing macrophages play an important role in responses to increased concentrations of active TGFb. These data suggest that the progression of MASLD is accompanied by significant changes in the composition of the liver's macrophage populations, with accumulation of a recruited CD14-high expression macrophage population in particular, whose activation state is relevantly determined by TGFb.