Intravital visualization of dynamic hepatic microenvironment in nonalcoholic steatohepatitis mouse model

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KEY WORDS : Intravital imaging, Steatosis, LD, NASH, infiltration

1. Abstract

Nonalcoholic fatty liver disease (NAFLD) has rapidly prevailed as the most common chronic liver disease worldwide. Whereas simple steatosis revealed with accumulation of lipid droplets (LD) in hepatocyte normally does not affect liver function, more progressed form of NAFLD, nonalcoholic steatohepatitis (NASH), can potentially progress to cirrhosis and hepatocellular carcinoma, which results in irreversible liver failure. Yet current understanding of underlying mechanism in the transition from simple steatosis to NASH is very limited. In this work, we longitudinally visualized hepatic microenvironment during the progression from simple steatosis to NASH in the methionine and choline-deficient (MCD) diet-induced NASH mouse model. Using a custom-built intravital confocal laser-scanning microscope, we successfully visualized lipid droplet (LD) in hepatocyte, liver vasculature and mononuclear phagocytes expressing CX3CR1-GFP or CSF1R-GFP *in vivo*. 2 days of MCD diet induced simple steatosis with microvesicular LD accumulation in hepatocytes without sign of inflammation. Continued 1-2 weeks of MCD diet induced severe steatosis with increased volume and size of LD in hepatocyte and progression to NASH with increased macrophage infiltration and foci formation. In addition, apoptosis or necrosis of parenchymal cells and vascular disintegrity were observed with increased number of mononuclear phagocytes engulfing sub-cellular debris. In summary, we achieved intravital visualization of dynamic hepatic microenvironment in diet-induced NASH mouse model correlated with disease progression in longitudinal manner.

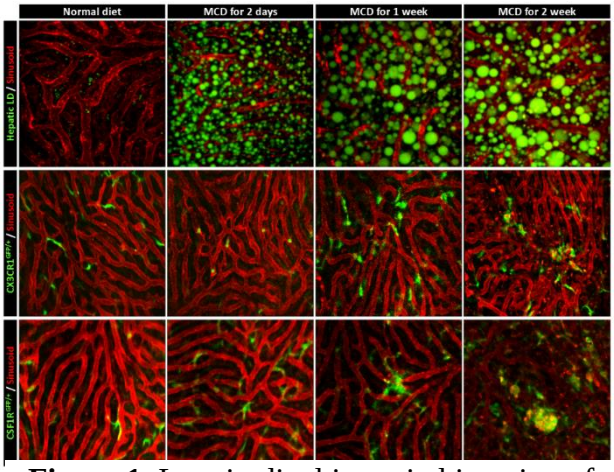

Figure 1. Longitudinal intravital imaging of NASH progression in MCD diet-induced

2. References

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