Introduction:
- Macrophages display a high plasticity and their polarization is strongly influenced by the local microenvironment.
- Own unpublished data indicate that hepatocyte-derived factors have a strong impact on macrophage polarization and function.
- The change of macrophage polarization and stage-dependent recruitment of neutrophils during development of HFD induced fatty liver disease (FLD) and its relevance for progression to non-alcoholic steatohepatitis (NASH) and development of acute on chronic liver failure (ACLF) is not fully understood.

Aim:
- Time resolved analysis of the recruitment of macrophages and neutrophils and changes of macrophage polarization as well as assessment of metabolic disturbance during development of HFD induced FLD and evaluation of its relevance for progression to NASH and/or ACLF development by a systems biology approach.

Progress and Results:
- **Experimental Model of HFD induced fatty liver disease (FLD) and metabolic disturbance**
  - Pre-Perfusion
  - Post-Perfusion
  - Chow
  - HFD
  - HFD leads to increased weight gain, increased liver weight and causes metabolic disturbance.
  - Changes of macrophage numbers and their morphological appearance
    - F4/80
    - CD14
    - CD11b
    - CD11c
    - CD163
    - CD206
    - Macrophages form like structures during development of FLD induced FLD and ACLF.

Ongoing work & Outlook:
- **Summarizing scheme of the ongoing pilot experiment:**
  - Recruitment of neutrophils and macrophages and characterization of macrophage polarization
  - Persistence of neutrophils
  - Circulating neutrophils and monocytes during development of FLD and ACLF
  - Changes of Cytokine/Chemokine Expression
  - Integration of data into mathematical models of the recruitment of macrophages and neutrophils during FLD development and:
    - Dependency of results analysis of genetically engineered mice: MK2-/Stat3ap/-Stat3ap+
    - Depending on the results analysis of genetically engineered mice: MK2-/Stat3ap/-Stat3ap+
    - PTEN+/PTEN--/PAR4--/LRP8--

Publications: