CHARACTERISATION OF KUPFFER CELL AND INFILTRATING MONO-MACROPHAGE POPULATIONS IN CCl4 INDUCED LIVER DAMAGE model

Ananya Ajith[1], Jonathan Evraerts[1], Davide Brusa[2], Caroline Bouzin[3], Etienne Sokal[1],

Mustapha Najimi[1]

Université Catholique de Louvain, ananya.ajith@uclouvain.be

Background-

Kupffer cells (KC) are embryonically derived liver resident macrophages, responsible for maintaining liver homeostasis. Apart from KCs, infiltrating mono-macrophages of bone marrow origin also make up a small proportion of the hepatic macrophage population. During chronic liver diseases, the Kupffer cell population is largely replaced by the infiltrating mono-macrophage populations. Thus, the hepatic macrophage populations differ in their origin, phenotype, and characteristics. So, maintaining a balance between the different hepatic macrophage populations determines the outcome of the progression of chronic liver diseases.

Aim-

To study the miRNA-based epigenetic dysregulation of KCs and infiltrating macrophages during chronic liver diseases.

Methods-

C57BL/6 mice were intraperitoneally injected with carbon tetrachloride (CCl4) twice a week for 4 and 18 weeks to induce progressive liver damage. Enzymatic digestion of the liver using collagenase was performed to isolate non-parenchymal cell fractions (NPF). Cell sorting using specific surface antibodies was performed to isolate KCs and infiltrating mono-macrophages from the NPF of digested livers.

Results-

The overall leukocyte cell population was found to be slightly increased in the CCl4 groups than oil-treated group. The overall frequency of the myeloid cell population remained the same between the vehicle and CCl4-treated groups. The frequency of KCs is decreased in both CCl4-treated mice liver groups (20%-25% of total myeloid cell population) in comparison to the vehicle-treated group (60% of myeloid cell population), while the frequency of mono-macrophages was found to be initially increased in the 4 weeks CCl4 treated group (25% of myeloid cells) and then decreased in the 18 weeks CCl4 treated group (10% of myeloid cells).

Conclusion-

Our preliminary results suggest a dynamic change in the hepatic macrophage populations during chronic liver disease conditions. During the initial stage of CCl4-induced liver disease, the loss of the KC population is replenished by the infiltrating mono-macrophages. Our next step is to fully characterize the sorted KCs and infiltrating mono-macrophages, at the epigenetic level, and potentially correlate these alterations with the chronic progression of liver disease toward hepatocellular carcinoma.