Heart failure (HF) occurs when the heart is unable to pump sufficiently to sustain the blood flow required to meet body's metabolic demands. Despite rapidly developing therapy strategies, HF has still a poor outcome with nearly 25% to 50% mortality rate in 5 years after diagnosis.

Moreover, a disrupted pumping activity of the heart can affect the hepatic circulation triggering an altered liver function and, thus, heart failure and liver function are strictly correlated.

The liver is major organ involved in the metabolism, storage of e.g. glycogen or iron, the detoxification of the body and protein production. Liver sinusoidal endothelial cells (LSECs) belong to non-parenchymal cells lining the lumen of the hepatic sinuses and constitute a unique blood - hepatocyte barrier. If liver function disorders occur, LSECs among all liver cells are most exposed to the components transported with the blood, and their proper function may be impaired. LSECs play a key role in liver, and therefore a liver dysfunction is always associated with impaired LSECs function.

Although the co-existence of heart failure and liver dysfunction is known, knowledge about role of LSECs in the pathogenesis of HF is limited.

Thus, the aim of the project is to investigate liver function during progression of HF in Tgαq*44 mice, which are considered a reliable and unique model for studying the progression of this disease. In fact, Tgαq*44 mice mimic pathophysiology of human chronic HF. **A particular attention will be dedicated to the role of LSECs, as they are a master regulator of the hepatic circulation, and could be responsible for the activation of mechanisms involved in development of the liver dysfunction accompanying HF.**

The aim of the project will be accomplished following tasks:

1) studying changes in liver morphology and function along the progression of heart failure in Tgαq*44 mice.

2) studying the changes that occur on LSECs in the progression of heart failure in Tgαq*44 mice (status of metabolism and oxidative stress, expression of pro-inflammatory, endothelial and mesenchymal markers).

3) exploring the role of LSECs in the heart failure pathology and their influence on hepatocytes (co-cultures system).

Given the LSECs key role in a maintaining normal liver function, the impairment of their activity might play a pivotal role in the development of liver pathology observed in HF patients. Results of this project may suggest new therapeutic strategies for the liver dysfunction in the context of HF, thereby ameliorating the outcome of the HF patients which is known to be poor in case of co-existence of the liver disease.