Uncovering how intestinal transporter dysregulation and architectural changes contribute to malabsorption in cirrhosis.

Liver cirrhosis is a serious condition that damages the liver, weakening its function. Up to half of patients with cirrhosis suffer from malnutrition, even though many are not underweight. This may seem paradoxical, but increasing evidence suggests that the issue lies not in food intake, but in the impaired absorption of nutrients in the small intestine.

The goal of my project is to understand how liver cirrhosis affects the structure and function of the small intestine. I will focus on two main aspects: whether the architecture of the intestine changes (i.e., its length and the structure of the villi), and whether the expression and localization of membrane transporters responsible for absorbing most of the nutrients are altered.

To explore this, I will perform experiments on mice with chemically induced liver cirrhosis and compare them to healthy mice. I will measure the length of their intestines and examine their structure under a microscope. Then, using single cell RNA sequencing, I will identify which genes involved in nutrient absorption are active, where exactly they are active, and how strongly.

Finally, I will test whether these changes affect the levels of nutrients in the blood. I will collect blood from the portal vein of healthy and cirrhotic mice and measure the concentrations of selected amino acids, sugars, and vitamins.

This project will help us understand why patients with liver cirrhosis are malnourished and guide the development of more effective nutritional interventions to improve their health and quality of life. Additionally, this approach may also prove useful in examining transcellular transport disruptions in a range of conditions where malnutrition is a contributing factor.