The liver plays a key role in numerous metabolic processes, and its dysfunction affects the entire body. When the liver is affected by disease, not only the metabolism of lipids, proteins, and carbohydrates changes, but also the storage of important nutrients. Liver disorders can lead to secondary health problems, such as hormonal imbalances, reduced immunity, and improper functioning of other organs. Liver damage is associated with impaired metabolic processes, including the detoxification (removal of toxins) of the body. Therefore, liver diseases may lead to imbalances in the elemental composition. Well-documented examples of such conditions include the effects of iron or copper imbalance. Additionally, new studies suggest that imbalances in other elements may also have similar importance. These imbalances directly contribute to disruptions in enzyme activity, where trace elements act as key cofactors (non-protein chemical compounds essential for proper enzyme activity). Such enzymes include molybdenum-containing proteins e.g. xanthine oxidase (XO), as well as enzymes where zinc serves as a cofactor, such as superoxide dismutase (SOD-1).

The potential hepatic relationships between XO and SOD-1 are of particular interest. XO helps break down certain molecules involved in DNA building and energy production, converting them into uric acid. A natural consequence of XO-catalysed reactions is the production of harmful oxygen species. Superoxide dismutase 1 catalyses the conversion of superoxide radicals into oxygen and hydrogen peroxide. Zinc is a key component of the active site of the SOD-1 molecule. It enables the enzyme to neutralize harmful superoxide radicals and alleviate oxidative stress in cells. SOD-1 plays a crucial role in maintaining the balance of harmful oxygen species, protecting cells from oxidative damage associated with various disease processes. Their balance helps protect liver cells from damage, especially during liver disease. For this reason, among other enzymes, XO and SOD-1 were selected for the proposed study.

Moreover, our previous pilot studies demonstrated significant differences in the concentrations of silver and copper between healthy and cirrhotic livers. We also found that patients with alcoholic liver disease or primary sclerosing cholangitis had much lower XO enzyme activity than healthy individuals.

These results encouraged us to design this study, which aims to expand knowledge about liver physiology and pathophysiology through ***a series of experiments***: 1) **analysis of gene expression**, 2) **determination of protein concentration**, and 3) **assessment of XO and SOD-1 activity in liver tissue, peripheral blood, and portal blood**. We will compare these parameters between liver transplant recipients with diagnosed end-stage liver failure and deceased donors without diagnosed liver pathology. To best conduct the proposed project – determining the above **parameters** – we are currently performing some of the necessary steps to qualitatively examine XO and SOD-1 and analyse the obtained data. To date: 1) we have completed patient recruitment, selected study groups, and collected complete sets of liver tissue and blood samples from both liver transplant recipients and healthy donors for ***the series of experiments***, and 2) before starting the proposed project, we will additionally determine the levels of selected elements in this biological material using atomic absorption spectrometry. All results concerning gene expression, protein concentration levels, XO and SOD-1 activity, as well as the concentration of selected trace elements, will be analysed to identify relevant relationships in human tissues.

This is the first study to compare liver, peripheral blood, and portal blood to understand how trace elements affect liver function. The results may expand our knowledge of liver disease mechanisms and improve diagnostic and therapeutic strategies. Our interdisciplinary project combines molecular biology, liver pathology, and clinical aspects to uncover complex relationships between trace elements and enzyme function in both healthy individuals and those with liver disease. By identifying specific trace element deficiencies and their impact on enzyme function, we hope to identify changes that could help develop better blood tests or new treatments for liver disease in the future.