The liver is one of the most important organs in the human body. It contributes not only for digestion and storage of nutrients but also for regulating glucose levels, fat metabolism, and producing various hormones. Proper liver function is crucial for maintaining metabolic health. However, the liver is increasingly damaged due to modern lifestyle factors. Low physical activity and diets high in sugars and saturated fats lead to obesity, which in turn causes non-alcoholic fatty liver disease (NAFLD). In NAFLD, fat begins to accumulate in liver cells, which can lead to inflammation, fibrosis, and even cirrhosis. It is estimated to affect about one-third of adults worldwide.

In recent years, researchers have increasingly focused on the role of peptide hormones molecules that can influence appetite, energy metabolism, blood glucose levels, and inflammation.

Neuronostatin (NST) is one such peptide hormone. It was discovered in 2008 using bioinformatics methods. Studies to date indicate that NST may affect fat and carbohydrate metabolism by acting on the pancreas and adipose tissue. However, the role of this peptide in liver function remains unknown. Preliminary studies conducted by our team have shown the presence of neuronostatin receptors in liver cells (hepatocytes), suggesting that this hormone may directly affect the liver.
The liver regulates blood sugar and fat levels. When it becomes insulin resistant, it can no longer properly control blood glucose, leading to metabolic problems such as obesity and diabetes. In our studies, obese mice treated with neuronostatin showed decreased insulin sensitivity, indicating that this hormone may influence the development of hepatic insulin resistance.

The project aims to investigate how neuronostatin affects liver function and metabolism in both normal-weight and obese conditions. The study will include experiments on mice with normal body weight as well as mice with obesity induced by a high-fat diet. Importantly, already available tissues from a previously conducted project titled focused on the effects of neuronostatin on adipose tissue will be used, to align with the 3R principle (Replacement, Reduction, Refinement). It will allow for a reduction in the number of experimental animals used.. The analyses will include liver fat content, inflammation status, liver enzyme activity, and expression of genes involved in carbohydrate and fat metabolism. These studies will help determine whether neuronostatin influences metabolic changes and liver damage caused by obesity.

To further elucidate the mechanism of neuronostatin action, experiments will be conducted on AML12 mouse hepatocyte cell lines. It will be assessed whether NST protects liver cells from damage caused by excess fats (lipotoxicity), cellular stress, and apoptosis (cell death). Additionally, the signaling pathways activated by NST in these cells will be investigated.

The primary expected outcome of the project is to deepen the understanding of neuronostatin’s role in regulating liver metabolism under both physiological and obesity conditions. The results will clarify whether neuronostatin plays a significant role in mechanisms leading to liver steatosis, metabolic disorders, and inflammation triggered by excess adipose tissue. Consequently, these studies may contribute to identifying neuronostatin as a potential therapeutic target for treating obesity-related liver diseases such as non-alcoholic steatohepatitis (NASH) and insulin resistance.