

**Samenvatting toegekende MUMC+/FHML TKI-LSH subsidie projecten 2023**

**LSHM202302: Improving our understanding and detection of lung cancer cachexia.**

**Public summary**

Lung cancer is a common form of cancer and responsible for the majority of cancer deaths. Cachexia is a syndrome often associated with lung cancer, in which patients experience involuntary loss of muscle and fatty tissue (mass). This syndrome often accelerates during chemoradiotherapy (CRT), the standard treatment for stage III non-small cell lung cancer (NSCLC) patients. Conversely, the presence of cachexia increases the risk of cancer therapy side effects, requiring discontinuation and reducing its efficacy. This project aims to unravel cellular processes and dynamics of tissue loss during CRT in lung cancer, as a necessary step towards a better understanding of lung cancer cachexia and more sensitive methods to detect it at an early stage.

Because obtaining tissue from patients with cachexia is very difficult, in this project we also use mice in which lung cancer is induced. In this mouse 'model', research can be done on tissue, and it is possible to painlessly monitor lung tumor growth and muscle mass reduction - which has great similarities with the patient - using special imaging techniques ('microCT scans'). The first goal of the project is to use the latest laboratory analysis techniques to measure changes in tissue cells that precede tissue loss. In addition, artificial intelligence will be applied to the CT scan analysis to visualize tissue loss over the entire body (goal 2), and to detect changes in tissue characteristics on CT scans that correspond to the tissue analyses from the lab (goal-3). Finally, these newly developed artificial intelligence 'networks' will be adapted for sensitive detection, and possibly prediction, of cachexia from patient CT scans (goal-4).

The new insights and imaging technology resulting from this project will allow cachexia to be measured more sensitively and in an early phase, which will contribute to better treatment for patients with NSCLC.

**Consortium partners**

Maastricht University, NUTRIM and GROW Institutes

Maastro Clinic

SmART Scientific Solutions BV

**LSHM202303: Inflammatory Bowel Disease: improving disease monitoring with volatile metabolites**

**Public summary**

Patients with chronic inflammatory bowel diseases or inflammatory bowel diseases (IBD) experience periods of inflammation in the gastrointestinal tract, leading to abdominal complaints and intestinal damage. There are also periods of disease remission. Close monitoring of intestinal inflammation is crucial because early treatment can alleviate symptoms more rapidly and improve the long-term course of the disease. Currently, this often requires invasive procedures such as colonoscopy, which are expensive and carry certain risks. The main objective is to identify substances in the exhaled breath and stool of IBD patients, known as volatile organic compounds (VOCs), and gut microbiota, and compare them with colonoscopy findings. Our hypothesis is that the characteristic intestinal inflammation of IBD produces specific VOCs that can be measured in breath and stool samples. These VOCs could serve as markers for better disease monitoring and potentially aid in the diagnosis of IBD. Furthermore, these VOCs may provide insights into the activity of gut microbiota, which plays a significant role in IBD. Exhaled breath and stool samples will be collected from 250 IBD patients. The aim is to identify VOCs and characteristics of gut microbiota that distinguish IBD patients with mucosal inflammation from those without it. Using a multi-omics approach, complex machine-learning techniques, and creating digital twins (a specific method), the project aims to develop a more patient-friendly and accurate way to measure inflammation in IBD, improve IBD patient care, and make healthcare costs more affordable. The outcomes of the project will contribute to social participation and functioning via early diagnosis. The breath/faecal test, as a non-invasive approach, also fits with the vision of health that is focused on functioning in the living environment and less invasive approaches.

**Consortium partners**

Maastricht University

Owlstone Medical

**LSHM202307: Data-driven improvement of Chronic Pain Care**

**Public summary**

Chronic pain affects various aspects of daily life, causing physical or social decline, psychological problems, and reduces quality of life. In the Netherlands, over two million people suffer from chronic pain, with an estimated cost of around €20 Billion per year, including 700,000 people with severe pain and 33,000 patients with complex problems. Additionally, there are challenges in treating chronic pain, such as over- and under-treatment of patients, fragmented care, and moderate to poor treatment outcomes. There are (national) approaches addressing these challenges; National Care Standard for chronic pain, Value-based healthcare and the Integrated Care agreement (IZA). Nevertheless, concrete tools are still lacking. The Value4Pain consortium (V4P) aims to address major issues in chronic pain by accelerating value-based pain care. V4P consists of public and private frontrunners: Maastricht University Medical Center+ Pain Medicine, University Maastricht, and Medtronic Integrated Health Solutions. The goals are achieved through three work packages; 1) provide insights into the complex care process by a comprehensive data platform, 2) develop tools for goal-setting and shared decision-making, and 3) create predictive models to determine treatment outcomes and assess the benefit of treatment or care plan. V4P objectives are to improve the treatment of chronic pain patients, particularly those from low socio-economic backgrounds and those with high levels of pain, anxiety, depression and catastrophizing. V4P aims to provide personalized pain management and contributes to social and economic wellbeing of chronic pain patients. Much of the annual costs of chronic pain is due to patients seeking the right treatment without success. If the V4P initiative leads to a 1% more efficient chronic pain care system, it could save 200 million euros annually and improve the quality of life for 100,000 people. The consortium hypothesizes that a data-driven approach is essential for maintaining accessible, high-quality healthcare at affordable costs.

**Consortium partners**

University Maastricht

Medtronic HIS

MUMC+ Pain Medicine

**LSHM202309: Reinforcing a healthy day-night rhythm in metabolism by nutrition in older people**

**Public summary**

We live in a 24-hour economy in which we use artificial lighting and digital screens, we sleep at varying time, and we have access to food 24 hours a day for 7 days a week. However, the human body is not naturally prepared for such a 24-hour culture. Our body has its own biological clock that is regulated, among other things, by the day and night cycle of the earth. This biological clock ensures that all kinds of processes in the body take place in a certain 24-hour rhythm. With aging and lifestyle diseases such as type 2 diabetes and obesity, it has been shown that our biological clock works less well and that our 24-hour behavior is no longer aligned with our internal clock, which can contribute to health problems. For example, we previously showed that older participants who are at risk of developing type 2 diabetes burn fewer carbohydrates during the day. Even more importantly, unlike healthy young people, these older participants did not switch to fat burning at night. This switch from carbohydrate to fat burning is typical of the transition from the fed to the fasted state. This lack of metabolic rhythm is important because low metabolic flexibility is linked to the development of a variety of age-related health problems. 3 In the current project, we want to test whether taking a mixture of specific nutrients in the evening can bring the body into a more 'fasted state' during the night. We do this in a group of older people who are overweight and have impaired (muscle) health. In this way we hope to strengthen the 24-hour feeding-fasting cycle and thus help the biological clock to achieve a healthy 24-hour rhythm of metabolism. At the same time, we test whether certain age-related health problems are reduced by this approach.

**Consortium partners**

Maastricht University

Danone Nutricia Research

**LSHM202310: Efficacy of a Novel Butyrate-Enriched Triglyceride in Diabetes Prevention**

**Public summary**

This project investigates the long-term effect of the gut bacteria product butyrate on metabolic health in individuals who are overweight or obese and at high risk of developing type 2 diabetes. Our gut bacteria may play a significant role in the development of obesity and type 2 diabetes. They affect our metabolism by fermenting undigested foods in our colon, producing short-chain fatty acids (SCFAs). These SCFAs influence the metabolism of our organs, potentially enhancing the function of the hormone insulin, which is beneficial in preventing obesity-related diseases such as diabetes and cardiovascular conditions. In a recent study, we demonstrated that SCFAs produced in the colon, particularly through slowly fermentation of complex carbohydrates, lead to higher concentrations of these SCFAs in the bloodstream. Based on this finding, we expect that dietary interventions resulting in high levels of SCFAs in the blood will have the most pronounced effects on our metabolism. The objective of this research project is to investigate whether a chronic increase (6-months) of the SCFA butyrate in the blood has positive effects on insulin sensitivity and metabolism. This increase will be achieved by administering an oil in which butyrate is bound to triglycerides. If we demonstrate positive effects, this could lead to the development of products enriched with SCFAs or specific fibers that help prevent obesity and type 2 diabetes. Ultimately, this project has the potential to provide seminal information that may contribute to our understanding of how diet and gut bacterial products influence insulin sensitivity in humans.

**Consortium partners**

Maastricht University

AAK Netherlands BV

**LSHM202312: Finding novel therapeutic targets and biomarkers for NonAlcoholic SteatoHepatitis**

**Public summary**

TranslATe-NASH will identify immune-related mechanisms involved in Non-Alcoholic SteatoHepatitis (NASH) for new diagnostic and treatment options. Currently, there are no treatments and no simple blood tests for diagnosis, leaving this condition often unrecognized and untreated. Together with the Dutch Obesity Clinic, we will obtain human tissues and blood samples to investigate the involvement of immune cells in NASH and how they are activated. With Flowview diagnostics, we will perform bioinformatics analysis to discover new markers and pathways that are important for developing liver inflammation, which is a crucial step in disease progression. Estimates suggest that 52 million people have a fatty liver with an annual cost of €35 billion (€1163 per patient). Finding novel means to diagnose NASH more early and identifying new therapeutic targets will significantly reduce the burden of this disease. Based on our experimental data and the fact that obesity is a strong risk factor for NAFLD, translate-NASH will focus on the role of immune cells in the adipose tissue-liver axis in obese individuals. Using our unique access to human paired tissue and blood samples, we will use flow cytometry and multivariate 4 bioinformatics analysis to find new immune-related mechanisms that underlie the development of NASH in humans and the important cross-talk with adipose tissue. The data generated will provide crucial information on the human adipose tissue-liver axis in NASH. The mechanisms, pathways and markers discovered in this project will directly feed the development of diagnostic tests and novel avenues for the design of treatment for NASH.

**Consortium partners**

Maastricht University

Flowview Diagnostics

Nederlandse Obesitas Kliniek

**LSHM202313: Improving How We Send RNA Treatments to Heart Cells Grown in a Lab**

**Public summary**

The DELIVERANCE project represents a pioneering effort in addressing the global health crisis of ischemic heart disease, the leading cause of mortality worldwide. This project is a collaboration between experts in the field of cardiac regeneration, focusing on innovative RNA therapeutics to boost cardiac self-regeneration. Ischemic heart disease has far-reaching societal and economic implications. According to the World Health Organization, it is responsible for over 9 million deaths annually. The current treatment methods, involving angioplasty and lifelong use of generic drugs, often fall short of providing a comprehensive solution. Hence, the need for groundbreaking concepts that stimulate cardiac self-regeneration to treat this disease is paramount. The DELIVERANCE project introduces a novel approach by harnessing the power of RNA therapeutics to stimulate cardiomyocyte proliferation. Specifically, it explores the potential of a specific microRNA target to achieve this objective. This innovative approach holds the promise of transforming the way ischemic heart disease is treated by addressing the root cause of the disease rather than merely managing its symptoms. The project's main objectives involve testing three formulation strategies to deliver the new RNA therapeutic to human heart muscle cells in advanced 3 dimensional laboratory models. Successful outcomes could lead to a safer and more effective treatment option that targets the underlying causes of the disease, ultimately improving patient outcomes and reducing the societal and economic burden associated with ischemic heart disease.

**Consortium partners**

Maastricht University

Summa Biotech