Biomarker discovery and advanced monitoring of new cell and gene-based therapies for hereditary tyrosinemia type 1

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Hereditary tyrosinemia type 1 (HT1) is a lethal inborn error of liver metabolism due to a deficient fumarylacetoacetate hydrolase (FAH) enzyme. HT1 patients suffer from a chronic loss of hepatocytes leading to cirrhosis and hepatocelullar carcinoma, two prevalent pathologies with unmet diagnostic and therapeutic needs. New treatment options are needed as the widespread application of orthotopic liver transplantation is limited. Nowadays, most patients can be treated with the orphan drug nitisinone in combination with restricted protein intake. However, the use of nitisinone leads to tyrosine accumulation in the blood resulting in impaired cognitive functioning of the patients and sight problems. In this project, Haaike explores the HT1-associated plasma metabolome in Fah-deficient mice and HT1 patients, map the therapeutic and side-effects of nitisinone, and prioritize new metabolomic biomarkers to monitor current and novel therapies. In parallel, she will evaluate the therapeutic effects of novel gene- and stem cell-based therapies in an experimental mouse model of HT1 and compare it to standard nitisinone treatment, using known and novel biomarkers discovered in this project.

This research project is a joined PhD with the research group Pharmaceutical Chemistry and Drug Analysis (FASC; Prof. Dimitri De Bundel) of the Vrije Universiteit Brussel and in close collaboration with the Metabolomics Core Facility of the VUB/UZ Brussel (Prof. Geert Martens) and the University of Liverpool (Prof. J. Gallagher and Prof. L. Ranganath). This project receives support of the Willy Gepts Funds of the UZ Brussel and by a medical grant of Swedish Orphan Biovitrum (SOBI).