Master project description for students 2025

Impact of long-term erlotinib treatment on intestinal CYP content and activity - a study comparing the data from *Slco2b1*$^{-/-}$ vs *hSLCO2B1*$^{+/+}$ rats

Erlotinib (sold under brand name Tarceva) is a tyrosine kinase inhibitor used for the treatment of non-small cell lung (NSCL) cancer. This molecule is a substrate of the drug uptake transporter Organic Anion Transporting Polypeptide (OATP) 2B1 and it is known to be metabolized by CYP3A4, CYP1A2 and CYP1A1, respectively. Recent findings from our lab show that the level of CYP3A1, which is the rat orthologue of CYP3A4, is significantly increased in the liver of *hSLCO2B1*$^{+/+}$ rats. These animals are genetically modified to express the human version of the transporter. In our study we intend to determine the expression and activity of the enzymes involved in erlotinib metabolism in the intestine of *hSLCO2B1*$^{+/+}$ rats and of *Slco2b1*$^{-/-}$ rats that lack the gene encoding for the uptake transporter. In addition we will determine the metabolic activity of CYP3A and CYP1A in animals chronically treated with erlotinib.

In detail, the master student will work on intestinal specimens previously collected from animals treated with erlotinib for 8 days and prepare microsomal fractions from them. This will be followed by performing CYP specific reactions using substrates like testosterone (for CYP3A activity assessment) or caffeine (for CYP1A activity assessment). The data gathered on CYP activity in the small intestine will be compared to data we already have on hepatic specimens. The master student will be trained in the state-of-the-art methods of UPLC and LC-MS/MS and learn how to establish, optimize and validate the UPLC analytical method. Other *in vitro* methods that will be used are: Western blotting and immunohistochemistry for detection of proteins. The data and statistical analysis will be performed based on comparison between solvent-treated and erlotinib-treated animals. The master student will also gain an advanced knowledge of Graph Pad and Excel software.

Interested applicants should contact Marta Rysz (marta.rysz@unibas.ch)