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Master Thesis:
PBPK Modeling of Oral Bioavailability of beyond Rule of Five Compounds.

Lipinkski's rule or rule of five (Ro5) was formulated in the late 1990s to qualitatively assess the likelihood of oral bioavailability of synthetic molecules. The majority of the currently marketed drugs comply with this rule. However, pharmaceutical industry's quest to address unmet medical needs in complex diseases requires modulation of novel targets with highly innovative treatment modalities, that are beyond classical small molecules and therefore beyond the chemical space outlined by the Ro5 (beyond Ro5: bRo5).
This MSc thesis aims to assess a fitness of the drug metabolism and pharmacokinetics (DMPK) *in vitro* screening cascade for optimization/selection of bRo5 compounds with oral bioavailability. With this goal 50 bRo5 compounds already studied in the clinical trials were already selected. Literature databases were mined to extract *in vivo* pharmacokinetic properties of these substances. These substances were also profiled in selected DMPK *in vitro* assays.

The goal of your master thesis will be to:

- establish *in vitro*/*in vivo* correlations for the bRo5 compounds;
- compare it with *in vitro*/*in vivo* correlations for the Ro5 compounds;
- investigate formulation effects on oral bioavailability;
- integrate diverse *in vitro* data into a PBPK model to improve *in vivo* PK prediction;

You:

- are a highly motivated individual with an interest in drug discovery and development, in particular, drug metabolism and pharmacokinetics;
- have a quantitative mindset and experience with modelling and/or statistical analysis in a scripting environment (R, Matlab, etc.);
- have basic experience or an interest in physiologically based pharmacokinetic modelling;

This master thesis will be jointly supervised by:

- Prof. Dr. Lars Kuepfer, Uniklinik RWTH Aachen;
- Dr. Denis Menshykau, Bayer AG, Wuppertal;

If you are interested, please contact: **Lars Küpfer, lkuepfer@ukaachen.de.**