Trypanosomatids are unique organisms because they couple glycolytic and peroxisomal function in a single organelle, the glycosome. As glycosome completely lacks genetic information, all enzymes that are active in this compartment need to be transferred there post-translationally. A family of proteins called Peroxins (small peroxisomal proteins, PEX#) orchestrate this routing. Among them, PEX5 and PEX14 have a pivotal role in this pathway because glycosomal import of matrix proteins is dependent on complex formation between these two proteins. Therefore, it has been postulated that breaking complex of these two proteins can be a viable strategy to combat deadly *Trypanosoma* infections as well as to study biochemical pathways in glycosomes.

As many other protein-protein interactions, PEX14-PEX5 interface utilizes mainly hydrophobic, aromatic interactions, with only two shallow, solvent exposed cavities present in a large interface area. Consequently, in order to compete for PEX14 binding site a ‘conventional’, ‘drug like’ chemical compound needs to include highly lipophilic moieties, which obviously makes it extremely challenging keep the pharmacochemical properties within desired ranges. Therefore, alternative strategies should be developed to target this difficult protein-protein interaction (PPI).

This project aims to investigate oxopiperazine helical mimetics as new PEX14-PEX5 PPI inhibitors with high Trypanocidal activity in cellular assays and favorable pharmacochemical profile. The multidisciplinary approach to achieve this goal will involve such methods as chemical synthesis, structure-based computational drug design as well as biophysical and cellular assays. The conclusion drawn from this studies may be important not only for future design of drugs for neglected tropical diseases caused by *Trypanosoma* parasites, but also for better understanding of biochemical processes that take place in glycosomes.