Glycosomes are organelles characteristic for several organisms, including *Trypanosoma* parasites. Glycosomes are related to human peroxisomes, however they play most distinct roles in parasite cells. An important example is glycolysis, which is the only source of Energy-rich adenosinetriphsphate (ATP) for *T. brucei*, the main causative of Human African Trypanosomiasis (HAT). While glycolysis may be a less important energy source in *T. cruzi*, the causative of a neglected Chagas disease, the parasite cell uses glycosomes for compartmentalization of other important processes, such as sterol and pyrimidine synthesis or trypanothione reduction.

As glycosomes themselves are unable to express the enzymes responsible for the mentioned metabolic processes, these proteins have to be brought from the cytosol. Small proteins referred to as peroxins take part in this routing. Among them, PEX14 and PEX5 play the most important roles. It is postulated that binding of this peroxins allows for translocation of the enzymes through the glycosomal membrane. Hence, blockade of PEX14-PEX5 complex formation impairs enzyme transport into the organelle, resulting in severe metabolic consequences. It has been proven that inhibition of the individual glycolytic enzymes with ‘drug-like’ molecules results in parasite death. Consequently, impairing function of all of these enzymes at once by blocking their routing to target organelle should have at least comparable consequences for the cell.

This project aims in development of novel chemical entities, small-molecule inhibitors that would disable PEX14-PEX5 complex formation. By this, import of matrix enzymes into the glycosomes is impaired, resulting in death of parasite cell. So far only one class of such inhibitors was developed. These molecules were characterized by inappropriate pharmacological properties, resulting in low activity in biological systems. The ultimate goal of this project is development of novel classes of inhibitors that would possess at least comparable binding affinity to PEX14 and pronounced antiparasitic activity, having better solubility and pharmacokinetics at the same time. We plan to achieve this by combining medicinal and synthetic organic chemistry with chemical biology and biophysical and cellular experiments. The results of these investigations would not only help to understand biochemical processes in glycosomes but can be important for design of new therapeutic strategies deadly tropical diseases related do *Trypanosoma*.