The project TopFUNG contains a proposal of complex interdisciplinary studies aimed at evaluation of molecular basis for the rational design of novel antifungals targeting fungal topoisomerase II (topoII). The high biochemical similarity between fungal and mammalian cells and the generation of resistance to already used chemotherapeutic agents make it desirable to search for new molecular targets. Topoisomerases belong to the family of enzymes involved in the processes related to DNA metabolism: transcription, replication, recombination and chromosome condensation. Although those enzymes are significant molecular targets in antibacterial and anticancer chemotherapy very little is known about the possibilities to target fungal topoII. Nevertheless, research indicates that fungal topoisomerases are crucial for the survival of some fungal strains, mammalian and fungal enzymes show diversity in terms of molecular structures and properties as well as differences in sensitivity to some inhibitors. Our preliminary results also strongly support the hypothesis of possible selective fungal topoII inhibition. The crucial goal of the project will be verified in consequence of the execution of three lines of research actions: a combined structure and docking based virtual screening, yeast topoisomerase II inhibition studies and final evaluation of biological properties of synthetized inhibitors.

Completion of all planned studies should help to answer the question, whether compounds inhibiting fungal topoisomerase II, could be applied in the future for the treatment of disseminated mycoses.