

This project contains proposal of execution of complex, interdisciplinary studies concerning rational design, synthesis and determination of biological properties of conjugates of organic low molecular weight carriers with inhibitors of bacterial and fungal enzymes (antimetabolites), containing in their structures linkers cleavable by enzymes present in microbial cells but stable in blood serum. Components of the conjugates will be as follows: cell penetrating peptides, molecular umbrellas and lipidic molecules as molecular nanocarriers, linkers cleavable by esterases and  $\beta$ -glycosidases and inter alia, 5-fluorocytosine and inhibitors of bacterial alanine racemase as antimetabolites. The main goal of the proposed studies is verification of reality and applicability of a novel concept of construction of potential antifungal and antibacterial drugs based on conjugation of effective molecular nanocarriers with antimetabolites through the linkers selectively cleaved in microbial cells. Expected results include: determination of molecular basis and factors determining biological activity of novel conjugates and formulation of guidelines for further optimization of conjugate structures in terms of their penetrability through biological membranes, stability in blood serum and selective toxicity.