The main objective of the project is to investigate the impact of polymorphism of β_2-adrenergic receptor (β_2-AR) on the functionality of the receptor and its interaction with ligand molecules.

β_2-adrenergic receptor belongs to an important membrane receptors family called G-protein coupled receptors (GPCRs). β_2-AR is an extremely important molecular target for drugs used to treat heart failure, asthma and prevent premature miscarriages. The natural β_2-AR is present in over eighty different forms varying by the types of some of amino-acid residues (polymorphs). A genetic variation that occurs with a frequency greater than 1% is called polymorphism.

Clinical studies show a correlation of polymorphism with an increased risk of many chronic diseases (e.g.: heart failure, hypertension, obesity, concomitant asthma and polycystic ovarian syndrome), varying response to some drugs, more intensive course of disease as well as with faster development of tolerance to the medication.

Important issues of the effect of β_2-AR polymorphism on the above phenomena and, in particular, of the molecular basis of differences in the drug-receptor and G protein receptor interactions in the context of various polymorphs have not yet been elucidated. By conducting this project we are going to carry out a comprehensive experimental and theoretical research involving a large group of functionally different compounds (agonists, antagonists, inverse agonists) interacting with selected polymorphs of β_2-AR. By conducting advanced *in vitro* and *in silico* studies we plan to explain the differences in the interaction patterns between Val34Met, Thr164Ile, Arg175Gly, Ser220Cys polymorphs with functionally different ligands.

Due to the key role played by β_2-adrenergic receptor in the physiology of the human body, and as the molecular target for a large group of drugs available on the market, the scientific impact of this proposal can be very broad and cover biological, pharmaceuticals and chemical sciences. Moreover, from the perspective of targeted therapy, directed to a particular patient, carrying out our research is very important because it will help to answer the question of how patients with different genotypes of β_2-AR may respond to the beta-agonists treatment.