

Peptides are involved in numerous biological processes. They may interact with receptors, enzymes and modify protein - protein interactions. Dynamic combinatorial chemistry is recently developed method which allows for discovering new molecules interacting with defined target. This approach has proven to be efficient way to design new molecular receptors as well as enzyme inhibitors. However, dynamic combinatorial chemistry requires labile molecules forming reversible systems which can react on external factors by shift of chemical equilibrium. Reactions of peptide bond formation were for long time considered as irreversible, which excluded their applications in combinatorial chemistry. However the results of recent studies reveals that modified peptides may undergo reaction of reversible cleavage of peptide bond resulting from the transfer of acyl group from nitrogen atom onto sulfur atom. The consequence of this process is a metathesis of peptide bond, which opens new possibilities in dynamic combinatorial chemistry. The subject of research proposed in this project is an exploration of the reversible opening of peptide ring in transformations of cyclic peptides. These experiments will be performed on systems known as lasso peptides. Characteristic feature of these compounds is their unique topology - the linear peptide chain is threaded through macrocyclic lactam ring and mechanically interlocked. The lasso peptides are a new group of natural products characterized by antibacterial activity. They are formed biosynthetically and currently there is no chemical method of synthesis of these compounds. In this project we will attempt to convert cyclic peptide with attached linear peptide chain into folded lasso peptide at high pressure conditions.