DESCRIPTION FOR THE GENERAL PUBLIC

Foldameric mini-proteins - structure and catalytic function

Foldamers are oligomers with a strong tendency to form well-defined three-dimensional structures in solution. They constitute a field of science that has grown rapidly in recent years due to the numerous exciting features of such molecules. One of the most widely studied branches of this research concerns peptides with incorporated beta-amino acid residues. The mimicking of native secondary structures (in particular helices) has been the main focus until now. The possibility of the rational structural design of peptidic foldamers has led to the discovery of compounds showing desirable properties, such as inhibitors of protein-protein interactions for cancer treatment.

This research proposal is related to studies on foldamers that will be able to form protein-like three-dimensional structures. Basing on known alpha-peptidic mini-protein templates and the toolbox of previously studied foldameric secondary structures, we plan to present a rational strategy for the construction of extended protein-like foldameric structures (foldameric mini-proteins). Subsequently, we plan to use the discovered scaffolds for the development of enzyme mimetics. The grafting of the chosen enzyme active sites on elaborated molecular architectures will lead to catalytically active molecules. Four enzyme classes (metallohydrolases, serine hydrolases, aldolases and epoxide hydrolases) are planned to be mimicked.

The possibility of rational construction of structurally extended molecules gives chance to develop materials with various functionalities. In particular, development of molecules with chosen catalytic activity could be of high importance for a wide range of scientific fields. Importantly, the proposed methodology of artificial enzyme construction shows numerous advantages in comparison to other approaches (rational design, efficient synthetic methods, possibility structural studies by CD and NMR spectroscopies). We hope that studies on peptidic foldamers will give an insight into the rules governing the construction of the native proteins, in particular enzymes.