

Control of protein-protein-interactions through conformational changes induced by light: photoswitchable ligand molecules for PDZ domains

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Cytoplasmatic proteins involved in signal transduction are commonly constructed of modular domains which either have a catalytic function (e.g. kinases) or belong to the protein interaction domains (PIDs). The latter play a critical role in the assembly of protein complexes which control the complex cellular behaviour. One PID of great interest is the PDZ domain, a 100 amino-acid-residue domain. It frequently occurs as multiple copies in cytoplasmatic proteins and is often involved in the assembly of molecular complexes near the plasma membrane. While most PDZ domains recognize short, C-terminal peptide motifs, some do also recognize internal binding motifs like loops. The project aims at the design of ligands for both types of PDZ binding modes, using the syntrophin PDZ domain as the protein partner. The ligands will be cyclic peptides which contain a photosensitive, artificial amino acid. This will allow a control of conformation and thus activity of the peptide ligands via the irradiation of light. The artificial amino acids as well as the peptides will be synthesized, the PDZ domain will be expressed in *E. coli*, the binding of the ligands to the PDZ domain will be quantified and the structures of the free ligands and the ligand-protein complexes will be determined using NMR spectroscopy.

Projektbeteiligte

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