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Conformational Flexibility in Protein Function

Dynamics of S100A4, Photosynthetic Reaction Centre and the Prenylating Enzymes UbiA and MenA

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Abstract

Proteins are the most versatile macromolecules and they are essentially involved in the biological processes throughout all living organisms. The three dimensional structure of proteins and their dynamical properties underlie their biological function and knowledge about protein structure and dynamics contributes to a detailed understanding of biochemical processes. In this work various structural and dynamical methods were applied in the investigation of different protein systems, and in addition the stabilization of two membrane proteins for structural studies was explored.

The first X-ray structure of human S100A4 in complex with a non-muscle myosin IIA (NMIIA) fragment was solved to 1.9Å and contributed to our understanding in the structural mechanism of S100A4 mediated filament assembly which is believed to promote metastasis. The X-ray structure shows that the binding mechanism differs from that of other S100 proteins and that S100A4 adapts its conformation to the chemical properties of the ligand. Further studies on a C-terminal deletion mutant of S100A4 with combined structural high and low resolution methods unveiled a role of the conformational flexible C-terminus in the Ca^{2+}-affinity to S100A4. The results suggest that the reduced metastasis properties that were previously observed in C-terminal deletions mutants of S100A4 might be due to an impaired Ca^{2+}-control.

The nature and the extent of conformational dynamics in photosynthetic reaction centers during the electron transport processes are still not well understood. Differences in the THz absorption spectra of photosynthetic reaction centre from *Rhodobacter sphaeroides* were measured upon light activation and indicate a change in molecular vibrations that occur most probably in LM subunit and are independent of the environment.

Conformational flexible regions influence the formation of protein crystals for structural studies negatively and the structural stabilization of proteins is often applied in protein crystallization. A library of the polyprenyltransfeases UbiA and MenA with rational stabilized, predicted exposed surfaces was produced and eight mutants and the wild type proteins were recombinant overexpressed and purified. Homology models indicate that the mutations of potent mutants are situated in regions that are involved in the formation of crystal contacts. However additional exploration of the buffer environment of UbiA and MenA is required in order to stabilize the proteins for further studies and crystallization.