MS12-P1  Structural studies on the metastasis associated S100A4 using x-ray crystallography and small angle x-ray scattering (SAXS)  Annette Duelli, Bence Kiss, László Nyitray and Gergely Katona.  aDepartment of Chemistry and molecular Biology, University of Gothenburg,  bDepartment of Biochemistry, Eötvös Loránd University, Budapest  Email: annette.duelli@chem.gu.se

S100 proteins are a group of low molecular mass proteins that belong to the largest subgroup of the EF-hand Ca\(^{2+}\)-binding protein family. Altered expression levels of S100 protein members have been associated with a number of disorders, such as cancer, inflammatory diseases, cardiomyopathy and neurodegenerative conditions [1]. S100A4 also known as metastasin is mainly expressed in the nucleus, cytoplasm and extracellular space and is involved in angiogenesis, cell survival and cell motility. The interaction of S100A4 to non muscle myosin IIA (NMIIA) upon Ca\(^{2+}\)-binding causes filament disassembly resulting in increased cell motility. In order to understand how the binding and the disassembly of NMIIA occurs, we investigate the structural basis of the binding of two NMIIA fragments, f1 and pT (a part of f1) to S100A4. The three-dimensional crystal structure of a S100A4 mutant complexed to a pT-fragment was solved to 1.9 Å resolution and revealed an asymmetric binding of the peptide to a S100A4 dimer [2]. In order to get a deeper understanding of the binding of NMIIA to S100A4 different mutants and solution structures are investigated with x-ray crystallography and SAXS.


Keywords: S100A4, metastasin, Ca\(^{2+}\)-binding

MS12-P2  The N-terminal domain of the CI repressor from bacteriophage TP901-1 in complex with DNA.  Kristian H. Frandsen, Kim K. Rasmussen, Malene R. Jensen, Margit Pedersen, Jens-Christian N. Poulsen, Lise Arleth and Leila Lo Leggio.  aDepartment of Chemistry, University of Copenhagen, DK-2100 Copenhagen Æ, Denmark,  bDepartment of Physics, University of Copenhagen, DK-2100 Copenhagen Æ, Denmark,  cInstitut de Biologie Structurale Jean-Pierre Ebel, F-38027 GRENOBLE Cedex 1, France  E-mail: wvb875@alumni.ku.dk

Temperate bacteriophage TP901-1 has the option of either of two lifecycles, the Lysogenic lifecycle or the Lytic Lifecycle. The choice is made at the transcriptional level where the bistable genetic switch is controlled by a hexameric form of the CI repressor binding to operator sites hindering transcription. The CI protein consists of an N-terminal domain (NTD) responsible for DNA binding through a helix-turn-helix (HTH) motif, and a C-terminal domain (CTD) involved in oligomerization of the monomers [1][2][3].

Here, the X-ray crystal structures of NTD and an NTD-DNA complex were solved both by molecular replacement using a low sequence homology search model from the related bacteriophage P22 C2 repressor. The structures revealed an extension in one of the helices of the HTH motif, not previously observed in related phages. The extension are speculated to be involved in protein-protein interactions and thus to hold a functional role in the control of the genetic switch. Numerous closely genetically related pathogenic species are expected to possess a similar genetic switch, so structural studies of CI and the bistable genetic switch of TP901-1 can provide useful insight into bacterial control.


Keywords: bistable genetic switch; X-ray protein structure; DNA.