MS12-P1 **Structural studies on the metastasis associated S100A4 using x-ray crystallography and small angle x-ray scattering (SAXS)**
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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 NMAII 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.

[1] Schneider M, Hansen JL, Sheikh SP (2008) S100A4: a common mediator of epithelial-mesenchymal transition, fibrosis and regeneration in diseases? *J Mol Med 2008*, **86**:507-522.
[2] Bence Kiss, *et al.* (2012) Crystal structure of S100A4-NMIIA tail fragment complex reveals a novel target binding mechanism in the S100 protein family. *PNAS 2012,* **109** (16):6048-53.

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

MS12-P2 **The N-terminal domain of the CI repressor from bacteriophage TP901-1 in complex with DNA.**
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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.

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[2] Pedersen, M., M. Ligowska, et al. (2010). "Characterization of the CI Repressor Protein Encoded by the Temperate Lactococcal Phage TP901-1." *Journal of Bacteriology* **192**(8): 2102-2110.
[3] Pedersen, M., L. Lo Leggio, et al. (2008). "Identification of quaternary structure and functional domains of the CI repressor from bacteriophage TP901-1." *J Mol Biol* **376**(4): 983-996.

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