cooperation with the flavoprotein, NADH oxidase. Here we report the crystal structure of *A. xylanus* AhpC in its oxidized form. The enzyme forms a ring-like (α2)5-decamer, the structure of which is similar to those of the previously reported Prxs, and especially to that from *Salmonella typhimurium*. The dimer-dimer interface of the decamer exhibits moderate and conserved hydrophobic interactions, which have been proposed to dissociate at the physiological ionic strengths. In the crystal, electron densities of small molecules were observed between the decamers and were shown to play a unique role in the crystallization by bridging the decamers via the hydrogen bonds.

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Keywords: protein structures, antioxidants, oligomers

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Structures of CFTR NBD1 Suggest a Molecular Mechanism for Cystic Fibrosis

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Cystic fibrosis (CF) is caused by genetic defects in the cystic fibrosis transmembrane conductance regulator protein (CFTR), most commonly through omission of residue Phe-508 (ΔF508) in the first nucleotide-binding domain (NBD1), resulting in misfolded, non-functional CFTR chloride channel. The structure of NBD1 was solved in order to better understand the effect of this deletion.

Initially, the structure of wild-type (WT) mouse NBD1 was determined [1]. This revealed a largely conventional NBD fold, compared with those of similar bacterial proteins, with the exception of additions in the N- and C-terminal regions of the protein with phosphorylatable and potentially regulatory function. Residue Phe-508 was seen to be surface exposed in a loop region and not of obvious importance to the NBD1 fold.

Recently, the structure of human NBD1 with ΔF508 present was determined [2], which revealed that the deletion did not alter or disrupt the fold of this domain. This observation was supported by thermodynamic measurements on WT and ΔF508 protein that showed the stability of NBD1 is unaffected as well. The effect of the deletion then appears to be the disruption of interactions of NBD1 with other domains of CFTR, most likely with the first membrane spanning domain (MSD1). This new understanding of the molecular mechanism of dysfunctional ΔF508 CFTR will lead to improved drug discovery efforts for CF.

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Keywords: disease-related structures, cystic fibrosis, nucleotide-binding domain

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Amyloidosis: Structure of a λ 6 Light Chain Antibody Fragment

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It has been well evidenced the preferential association of the lambda VI antibody light chain subgroup with antibody light chain amyloidosis. We have generated an engineered light chain variable region domain (rVL6aJL2) whose 99 amino terminal residues are encoded by the germline VI gene segment 6a and the complementary segment of 12 residues encoded by the gene segment JL2. *In vitro* fibril formation assays demonstrated that the rVL6aJL2 is able to slowly aggregate itself as amyloid-like fibrils under physiological conditions. The recombinant protein expressed in *E.coli*, was purified and crystallised using 1.4 to 2.0 M sodium acetate, 100mM MES pH 6.5. Crystals diffracted up to 1.9 Å resolution. The crystals grew in three different space groups and all contained fibrilar structures assembled into the crystal. These structures have helicoidal shape with a 93 Å long pitch, and a section perpendicular to the axis, 45 Å wide, with a squared shape. The molecule that generates this structure through a 4_1 symmetry, is a dimer built as that formed by light and heavy chains in functional antibodies. These dimer-dimer contacts found, comprises a surface larger than 1600 Å^2 and the amino acids involved has been shown to participate in fibrillogenesis. As in other structures from fibrillogenic antibody light-chains, no significant conformational changes have been observed. The question we have so far is: have or not the helicoidal structures we found over 3 different space groups relation with the atomic structure of amyloidotic fibers?

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Keywords: amyloidosis, fibres, crystallographic structure

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Structural and Functional Study of the Bloom Syndrome Protein

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Bloom Syndrome (BS) is an autosomal recessive human disorder characterized by genomic instability and a predisposition to a wide variety of cancers. The gene mutated in BS encodes a three domains enzyme, the Bloom Syndrome Protein (BLM), which C-terminal extension can be divided in two subdomains: RecQ-Ct and HRDC.

We report herein that the RecQ-Ct domain, responsible for DNA unwinding, contains a zinc finger motif. In order to understand the role of this motif in BLM, we constructed a series of mutations altering its highly conserved residues. Experiments done with these mutants showed that they were severely impaired in DNA binding and for the subsequent ATPase and helicase activities, revealing the importance of the zinc finger motif for all the functions of the enzyme. We computed the three dimensional structure of the RecQ-Ct domain by homology modeling using the template structure of the RecQ helicase from *E. coli*. This model allowed us to study the consequences of mutations observed in the Bloom Syndrome Protein when associated to a cancer. The mutant enzymes have been expressed in *E. coli* and their activities have been compared to the wild type enzyme. In order to get new insight in the molecular basis of Bloom Syndrome disease, we underwent the crystallization of the RecQ-Ct and HRDC domains in presence of various DNA substrates.

Keywords: cancer, DNA-protein interactions, structure-function

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Molecular Basis for Antitumor Effect of Actin-aplyronine A Complex

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Aplyronine A is a promising candidate of anticancer agent isolated from *Aplysia kurodai*. The complex structure of actin-aplyronine A is determined via a synchrotron X-ray analysis at 1.45Å resolution. Aplyronine A binds to actin in the similar manners with the trisoxazole toxins and gelsolin segment 1 around its aliphatic tail part which should play an important role for F-actin depolymerizing activity. In contrast, the structural aspects relating to peculiar interactions between aplyronine A and actin can be found around the macrolide ring part which should be a key to the potent antitumor effect of aplyronine A. Actin-aplyronine A complex structure should suggest that each complex comes to have ability to effect other biological reactions which are essential for deaths of cancer cells. The precise charge density map was also visualized with the maximum entropy method to construct the structure model of a disordered stereoisomer of a peculiar side-chain of aplyronine A as well as to