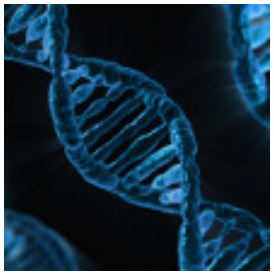

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Structural modelling of the DNAJB6 oligomeric chaperone shows a peptide-binding cleft lined with conserved S/T-residues at the dimer interface

The remarkably efficient suppression of amyloid fibril formation by the DNAJB6 chaperone is dependent on a set of conserved S/T-residues and an oligomeric structure, features unusual among DNAJ chaperones. We explored the structure of DNAJB6 using a combination of structural methods. Lysine-specific crosslinking mass spectrometry provided distance constraints to select a homology model of the DNAJB6 monomer, which was subsequently used in crosslink-assisted docking to generate a dimer model, revealing that a peptide-binding cleft lined with S/T-residues is formed at the monomer-monomer interface. Mixed isotope crosslinking showed that the oligomers are dynamic entities that exchange subunits. The purified protein is well folded and composed of oligomers with a varying number of subunits according to small-angle X-ray scattering (SAXS). Elongated particles (160x120 Å) were detected by electron microscopy and single particle reconstruction resulted in a 20 Å resolution density map into which the DNAJB6 dimers fit. The structure of the oligomer with the S/T-rich region is a large step forward in the understanding of the function of DNAJB6 and how it can bind aggregation-prone peptides and prevent amyloid diseases.

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Session Classification: Poster session with drinks & nibbles

Track Classification: Dynamics of proteins in crowded and confined geometry