Crystal structure of the core domain of human HspBP1, a novel nucleotide exchange factor for Hsp70

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Molecular chaperones of the Hsp70-type are key components of the protein folding machinery in all living cells [1]. Protein folding occurs in an nucleotide-dependent manner. Substrate proteins and Hsp40-type co-chaperones stimulate the ATPase activity of Hsp70; nucleotide exchange factors (NEF) like GrpE (in bacteria and mitochondria) and BAG-1 (in the eukaryotic cytosol) trigger the release of ADP. Although structurally not related, GrpE and BAG-1 trigger a conserved molecular switch in the ATPase domain of their associated Hsp70 chaperones [2]. Human HspBP1 belongs to a third family of NEFs, which is conserved from yeast to humans [3]. Structural analysis of the core domain of HspBP1 alone and in complex with a fragment of Hsp70 revealed a reaction mechanism different from GrpE and BAG-1.

The crystal structure of the core domain of HspBP1, residues 84 – 359, was solved by Selenium SAD to 2.1 Å resolution using data from beamlines BW6, DESY, Hamburg, Germany, and ID14-4, ESRF, Grenoble, France. 16 (out of 20) Selenium sites of the selenomethionine derivative were identified in the peak wavelength (0.9793 Å) dataset using the program SnB [4]. The crystals were of space group C2 containing two monomers per asymmetric unit. Although the Se-substructure could be solved from the dataset collected at BW6, presumably overlap with a second diffraction pattern made resulting electron density maps difficult to interpret, and so we collected a second dataset from a different crystal with less overlap at ESRF which was used for model building and refinement [5].

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