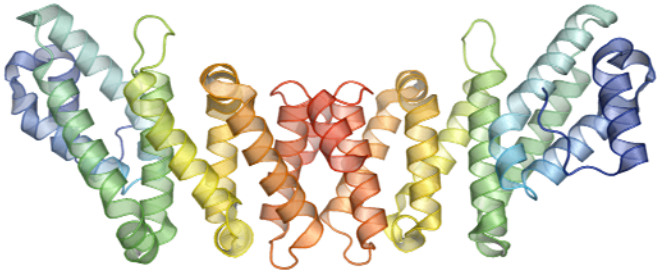
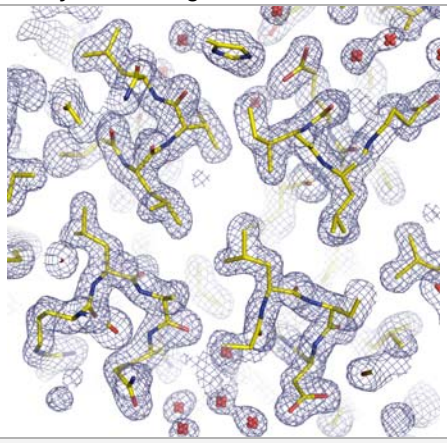
Center for Eukaryotic Structural Genomics

Protein Structure Initiative

Target ID	GO.79294	
Source Organism	*Brachydanio rerio*	
Target Name	BC090306	
PDB Entry	2I2O	Deposition: 16-Aug-2006
Function	eIF4G-like protein	
Produced From	*E. coli* B834 p(RARE2) pVP-33K	
Structure by X-ray	Resolution: 1.92 Å	R-value (R-free): 19.2% (23.5%)
	No. of Residues/ASU: 421	Monomers/ASU: 2
Data Collected At	Advanced Photon Source 22-ID 04-Aug-2006	
Authors	E. Bitto, G.E. Wesenberg, G.N. Phillips, Jr., J.G. McCoy, C.A. Bingman	





Structural Features

Crystal structure of an eIF4G-like protein from *Brachydanio rerio* (PDB ID code 2I2O) reveals a crescent shaped molecule consisting of ten α-helices arranged as five HEAT repeats with the order of helices 1a-1b-2a-2b-3a-3b-4a-4b-5a-5b. Each HEAT repeat consists of two antiparallel α-helices that are held together by hydrophobic interactions along their adjacent sides. The consecutive HEAT repeats are stacked upon each other and rotated along the superhelical axis to form a right-handed solenoid. The structure has an extended hydrophobic core that is stabilized by salt bridges and Van der Waals interactions between the conserved nonpolar residues. Tandem arrays of HEAT repeats (3-22) are found in a wide variety of proteins where they serve as scaffolding modules for assembly of large multi-protein complexes. They include Huntingtin, A and B subunit of protein phosphatase 2, importin β, elongation factor 3, and many others. The closest structural neighbor of 2I2O identified by VAST search is the middle segment of eukaryotic initiation factor 4GII (eIF4GII). eIF4G superimposes onto 2I2O structure with Z-score 15.5, 2.7 Å RMSD and 24% sequence identity over 167 aligned residues. The comparison of these structures reveals the same overall fold with slight differences in the orientation of the N-terminal and C-terminal helices. eIF4G is a modular adaptor protein that recruits all the components necessary for the initiation of protein synthesis in eukaryotes. The middle portion of eIF4G binds eIF4A and viral RNA IRES (internal ribosome entry site) and represents a minimal functional module required for initiation of translation. Extensive mutagenesis studies identified several surface residues of eIF4G involved in eIF4A and IRES binding. The eIF4A-binding residues are clustered on the surface of helix 1a, 1b, and 2b and in the adjacent loops. IRES binds to positively charged/hydrophobic region mapped to helix 2b, 3b, and the connecting loops. Although some of these residues are also present in 2I2O, it is hard to make a prediction about eIF4G-like function of 2I2O since the ligand-binding residues are poorly conserved even among the eukaryotic eIF4G homologues.

Percent Identity with Nearest PDB Structure at Time Solved	22% (1HU3)
Pfam Cluster	MIF4G
Sequence Cluster Size	136

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