



Title	Solution structure of the dimerization domain of the eukaryotic stalk P1/P2 complex reveals the structural organization of the eukaryotic stalk
Author(s)	Lee, KM; Wu, WH; Chiu, YH; Sze, KH; Shaw, PC; Wong, KB
Citation	The 2011 Croucher Advanced Study Institute Conference on Structure-Based Screening and Design of Ligands for Protein Targets, Hong Kong, 12-15 December 2011.
Issued Date	2011
URL	http://hdl.handle.net/10722/169359
Rights	Creative Commons: Attribution 3.0 Hong Kong License

SOLUTION STRUCTURE OF THE DIMERIZATION DOMAIN OF THE EUKARYOTIC STALK P1/P2 COMPLEX REVEALS THE STRUCTURAL ORGANIZATION OF EUKARYOTIC STALK COMPLEX

Lee KM¹, Yu WH¹, Chiu YH¹, Sze KH², Shaw PC¹, and Wong KB¹

¹School of Life Sciences, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong, China.

²Department of Chemistry, The University of Hong Kong, Hong Kong, China.

leekaming@cuhk.edu.hk

The lateral ribosomal stalk is responsible for the kingdom-specific binding of translation factors and activation of GTP hydrolysis during protein synthesis. The eukaryotic stalk consists of the scaffold P0 protein which binds two copies of P1/P2 hetero-dimers to form a P0(P1/P2)₂ pentameric P-complex. The structure of the eukaryotic stalk is currently not known. To provide a better understanding on the structural organization of eukaryotic stalk, we have determined the solution structure of the N-terminal dimerization domain (NTD) of P1/P2 hetero-dimer. Helix-1, 2 and 4 from each of the NTD-P1 and NTD-P2 form the dimeric interface that buries 2200 Å² of solvent accessible surface area. In contrast to the symmetric P2 homo-dimer, P1/P2 hetero-dimer is asymmetric. Three conserved hydrophobic residues on the surface of NTD-P1 are replaced by charged residues in NTD-P2. Moreover, NTD-P1 has an extra turn in helix-1, which forms extensive intermolecular interactions with helix-1 and 4 of NTD-P2. Truncation of this extra turn of P1 abolished the formation of P1/P2 heterodimer. Systematic truncation studies suggest that P0 contains two spine-helices that each binds one copy of P1/P2 heterodimer. Modeling studies suggest that a large hydrophobic cavity, which can accommodate the loop between the spine-helices of P0, can be found on NTD-P1 but not on NTD-P2 when the helix-4 adopts an “open” conformation. Based on the asymmetric properties of NTD-P1/NTD-P2, a structural model of the eukaryotic P-complex with P2/P1:P1/P2 topology was proposed.