

Crystal Structure of Get4-Get5 Complex and Its Interactions with Sgt2, Get3 and Ydj1

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The tail-anchored (TA) proteins are a typical class of membrane proteins, which present a single transmembrane domain (TMD) located near their C-termini. By anchoring the single TMD into the phospholipid bilayer surrounding cellular organelles, the N-terminal cytosolic portion of TA proteins can be properly arranged to cytosol for particular functional purposes. In cell, TA proteins are broadly found in the nuclear envelope, peroxisome, mitochondria, endoplasmic reticulum (ER), and Golgi apparatus for conducting diverse important functions, such as regulating apoptosis (Bcl-2 family), operating vesicular transport by intracellular membrane fusion (SNAREs), translocating proteins into Mitochondria (Tom5, Tom6, Tom7, Tom22) or across ER (Sec61 β , Sec61 γ), and assisting the folding or degradation of membrane proteins. However, in the beginning of biogenesis of all types of TA proteins, the translations are completed by the soluble-form ribosomes in the cytosol. The post-translational targeting mechanism is then occurred on TA proteins for inserting them onto correct membrane locations. During the targeting, one of the signals which helps determining the destinations for various TA proteins is the characteristics of the C-terminal TMDs and flanking regions. Wherein, the variations of length and hydrophobicity on the TMDs can be distinguished by different protein trafficking systems which are responsible for targeting specific TA proteins onto distinct cellular organelles.

The machinery for TA protein trafficking to ER is previously identified to conduct by the Get1-3 (Golgi ER trafficking 1-3) proteins. Wherein, the membrane proteins Get1 and Get2 act as receptors for recruiting the cytosolic ATPase Get3 onto the ER surface, and the TA protein carried by Get3 can be consequently targeted to ER. More recently, the Get4 and Get5 are discovered to be responsible for delivering TA protein to Get3. The

cooperation among Get3-4-5 is therefore turning into one of the major subjects in the TA protein trafficking. Hence, in order to elucidate the communicating manner among Get3-4-5, we have solved the crystal structure of a full-length Get4 complexed with the Get4 binding domain of Get5. Together with the mutual interaction analysis among Get3 and different fragments of Get4 and Get5, this study provides significant insights for TA protein trafficking.

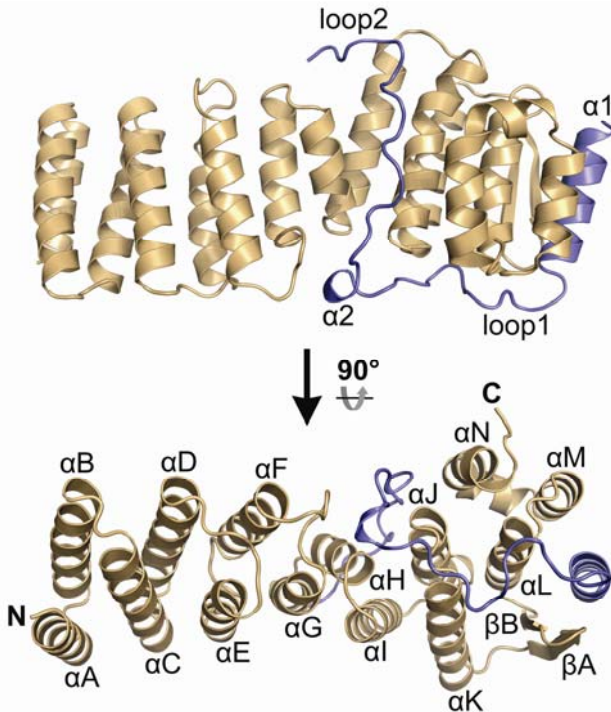


Fig. 1: Ribbon diagrams for the Get4/Get5N complex structure. The structure of Get4 in the complex (gold) and Get5N (blue) is shown. The upper and lower panels are the front orthogonal view and top orthogonal view, respectively.

Reference

- [1] Y.-W. Chang, Y.-C. Chuang, Y.-C. Ho, M.-Y. Cheng, Y.-J. Sun, C.-D. Hsiao, and C. Wang, J. Biol. Chem. (2010 in press)