

The Structure of Ykt6p reveals an auto-inhibitory mechanism for non-syntaxin SNARE proteins

Mingjie Zhang

*Department of Biochemistry, Hong Kong University of Science and Technology,
Clear Water Bay, Kowloon, Hong Kong*

Ykt6p is an essential, evolutionarily conserved non-syntaxin R-SNARE implicated in multiple intra-cellular membrane trafficking steps. Here we solve the structure of the N-terminal domain of Ykt6p (Ykt6pN, residues 1-140). The structure of Ykt6pN differs entirely from that of the Habc domain of syntaxin and resembles the overall fold of the actin regulatory protein, profilin. NMR spectroscopy, yeast two-hybrid and gel filtration studies reveal that like the syntaxins, full-length Ykt6p adopts a "closed" conformation. *In vitro* binding studies demonstrate that the auto-inhibited conformation of the protein serves as a kinetic switch controlling the incorporation of Ykt6p into SNARE complexes. Thus it appears that despite differences in three-dimensional structures, a common mechanism may be employed to regulate SNARE-SNARE interactions.