

Poster Presentation

MS77.P05

Crystallographic studies for the folding of an extending peptide

Y. Hanazono¹, K. Takeda¹, K. Miki¹

¹*Kyoto University, Graduate School of Science, Kyoto, Japan*

Full-length proteins can fold into thermodynamically stable structures at an exceptionally fast rate as shown by in vitro experiments. In contrast, it takes much more time to finish nascent protein folding than full-length protein folding, because nascent protein folding depends on the rate of ribosome biosynthesis in the living cell. Therefore nascent polypeptide chains in vivo fold co-translationally in different manners from the full-length proteins. However, the transient structures and the co-translational folding pathway are not well understood. In order to reveal the atomic details of nascent protein folding, we studied the hPin1 WW domain, which consists of two beta-hairpins between the three-stranded beta-sheets. Here we report a series of WW domain N-terminal fragment structures with increasing amino acid length by using circular dichroism spectroscopy and X-ray crystallography. In crystallization, maltose-binding protein was fused just behind the WW domain fragments to fix the C-terminus as nascent proteins are anchored to the ribosome. Co-translational folding of beta-sheet-rich proteins is discussed based on our finding that intermediate-length fragments unexpectedly take a helical conformation, even though the full-length protein has no helical regions. Furthermore, in a region of one of the loop structures of the full-length protein, these fragments take different formations. Our results suggest that the newly synthesized polypeptides adopt the most stable conformation during the course of peptide extension and fold into the native structures, eventually.

Keywords: co-translational folding, transient structure, WW domain