

Time-Resolved Study on Folding Landscapes of SH3 Domain Proteins

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As we reported [1], src SH3 domain protein forms alpha-helix-rich transient intermediate on the folding pathway before forming the native beta-rich structure. Small angle x-ray solution scattering (SAXS) shows that the alpha-helix-rich transient intermediate is a compact globule state [1]. We have been studying folding of two other SH3 domains, Fyn SH3 domain mutant and phosphatidylinositol 3-kinase (PI3K) SH3 domain. There were observable alpha-helical burst phases in both two SH3 domains by circular dichroism (CD) combined with cryo-stopped flow method. SAXS results indicate that transient alpha-helix-rich intermediate in both proteins are also compact. However, there are significant differences on the three folding pathways; src SH3 folds via. a single step, Fyn SH3 via. two steps, and PI3K SH3 folds apparently via. a single step, but this seems to be similar to the slow process of Fyn SH3.

Thus, although the three SH3 domains are homologous and take the same topological tertiary structures, their folding pathways are so diversified.

We started new study on the folding of another SH3 domain, hNck2 SH3 domain. Results will be shown in the poster.

1. Li *et al.* (2007) *Biochemistry*, 46, 5072-5082