MS03-P17 | Crystal And Solution Structures Of SH2 Domain Of Signaling Molecule In Complex With The Co-Stimulatory Receptor CD28

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In addition to the signalling produced by the binding of antigen-major histocompatibility complex to T-cell receptors, co-stimulatory signals from other receptor-ligand interactions are required for full activation of T-cells. One of co-stimulatory receptor, CD28, has no enzymatic activity and its cytoplasmic region consists of 41 amino acids that contain the sequence YMNM, in which the tyrosine residue is phosphorylated by kinase. The phosphorylated sequence, pYMNM, is recognized by SH2 adaptor proteins, such as Grb2, Gads, and PI3-kinase regulatory subunit, p85. We had reported the high resolution X-ray crystal structures of Grb2 SH2, Gads SH2, p85 nSH2, and p85 cSH2 in complex with the CD28 phosphopeptide, showing that the four SH2 domains had highly conserved secondary structure and overall structures in the complex states were similar to each other [1]. In this study, we evaluate the solution structures of those SH2 domain and its complex with CD28 phosphopeptide using small angle X-ray scattering connected to size exclusion chromatography (SEC-SAXS) and compered them with the crystal structures. The radius of gyration of SH2 domains in the free states are smaller than those in the CD28 phosphopeptide complex states, as well as the maximum values of distance distribution. The experimental scattering curves were well fitted to theoretical scattering curves calculated from the PDB information, indicating that the solution states are almost similar to crystal structures. We will discuss the protein dynamics in the solution with results obtained from another biophysical methods.

[1] Inaba et al., J. Biol. Chem., 292, 1052, 2017