분과발표-B

Solution Structure and Secondary Membrane Binding of Human Annexin I (2-26) by ^{1}H NMR Spectroscopy

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Annexin I fragment, residues from 2 to 26 which may play a key role for the secondary binding of the N-terminal domain of annexin I, was synthesized to investigate the solution structure and the activity of the secondary membrane binding. CD studies showed that annexin I (2-26) adopts mainly an a-helical conformation in membrane-mimic environments, while is randomized in an aqueous solution. The effects of membrane-mimetics on annexin I (2-26) were different; the peptide preferentially associates with zwitterionic DPC micelles than with negatively charged SDS micelles, as shown in fluorescence spectroscopy. The structure of annexin I (2-26) was determined both in 50% TFE/H_2O solution and 300 mM SDS micellar aqueous solution, showing a stable N-terminal helical conformation spanning residues from 4 to 15/16 in both solvents and a short C-terminal helix formed only in TFE with less significance. As shown in helical wheel projection, Trp12 is located in the interface of hydrophic/hydrophilic faces of the amphiphatic helix, and the hydrophobic cluster (AWFI) containing Trp12 plays an important role in the interaction with membrane. When Ca^{2+} was titrated, the helicity of the peptide in SDS micelles was increased, suggesting that the electrostatic repulsion was decreased between negatively charged head group of SDS micelles and side chains of glutamates of the peptide, mediated by Ca^{2+} as a salt bridge. These results leaded to a possible model for the secondary membrane binding of annexin I (2-26), which demonstrates that the peptide peripherally interacts with a negatively charged membrane in a partially Ca^{2+}-dependent manner.