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Study of Membrane-Bound Conformation and Pore Formation of Magainin2 using Vacuum-Ultraviolet Circular-Dichroism Spectroscopy

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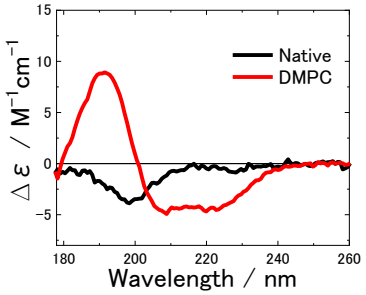
Magainin2 (MG2) is an antimicrobial peptide consisting of 23 amino acids, and its antimicrobial activity occurs due to the interaction with membranes followed by the formation of transmembrane pores. The activity closely relates to the membrane-bound conformation of MG2 and it largely depends on the characteristics of constituents of membrane or lipid molecules. Recently, it found that the characteristics such as the void-space within membrane and the fluidity of membrane contribute to the membrane interaction of proteins [1, 2]. Hence, to clarify the contribution of these membrane characteristics to the MG2-membrane interaction, the membrane-bound conformations of MG2 in the presence of four types of membranes which were prepared from DLPC, DMPC, DPPC, or DSPC lipid molecules were analyzed by a vacuum-ultraviolet circular dichroism spectroscopy.

MG2 formed a random coil structure in native state (without membrane) and its structure altered the helical structure in the presence of DLPC and DMPC lipid membranes at 25°C (**FIGURE1**), meaning that MG2 interacted with the both membranes. On the other hand, MG2 retained its random coil structure in the presence of DPPC and DSPC lipid membranes, implying non-interaction. Since the phase transition temperature (T_m) of these lipid molecules are -2°C for DLPC, 24 °C for DMPC, 41 °C for DPPC, and 55 °C for DSPC, it was suggested that MG2 could interact with the membrane of liquid state. To enhance the fluidity of DPPC and DSPC lipid membrane or to get their liquid states, the temperature was raised above T_m of the both lipid molecules. After decreasing the temperature until 25°C, we found that MG2 formed helix structure in the DPPC lipid membrane but retained the random structure in the DSPC lipid membrane. The differences of DPPC and DSPC lipid molecules were their spontaneous curvatures (positive for DPPC and negative for DSPC), which affected the void-space within membrane (internal void-space for DPPC and external void-space for DSPC). Since DLPC and DMPC lipid membranes had the internal void-space, the internal space would be key factor for promoting the membrane-interaction of MG2.



FGURE1 VUVCD spectra of MG2 in the presence and absence of DMPC lipid membranes at 25°C.

These results suggest that the internal void-space in membrane and the increment in the membrane fluidity would be driving force of MG2-membrane interactions.

REFERENCES

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