

Direct visualization of phase behavior of model lipid membrane induced by cell-penetrating peptides

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Cell-penetrating peptides (CPPs) are short cationic peptides that can transverse the plasma membranes along with various cargo molecules. Although successful intracellular delivery of many bioactive compounds has been achieved using CPPs, their internalization mechanisms is poorly understood. Here, we directly visualized the action of the cationic peptides on planar freestanding model lipid membrane composed of DOPC/DMPC/DMPG /cholesterol, to investigate the influence CPP on the phase behavior of the membrane containing anionic lipid DMPG. We showed that the synthesized CPP, poly-5-trimethylammoniumpentoxybenzoyl-L-lysine, preferentially binds to the anionic lipid DMPG-rich domains, and causes dissolving of DMPG-rich domains by steric interaction between the bound peptides. At the same time, in DOPC-rich phase, new DMPG-rich domains were formed as a consequence of lateral segregation of lipids by electrostatic interaction between lipids and peptides. These results suggest that the peptide-induced phase behavior can be influenced not only by the peptide properties but the local composition of the membrane.