Redistribution of Cholesterol by Membrane Active Peptides

Alamethicin and Melittin

SHUO QIAN, WILLIAM HELLER, Oak Ridge National Lab — Many membrane active peptides are found to disrupt lipid bilayer of membrane in a concentration-dependent manner and form transmembrane pore over threshold concentrations, as depicted in Two-State Model. However, at low concentration, the interaction between peptide and lipid bilayer remains less understood beyond the thinning effect. Here we present small-angle neutron scattering studies of the interaction of two well-known membrane active peptides (melittin and alamethicin) with lipid bilayers made of dymyristoyl phosphatidylcholine (DMPC) and cholesterol (Chol). Through the use of deuterium-labeled DMPC, changes in the distribution of the lipid and cholesterol in unilamellar vesicles were observed for peptide concentrations well below those that drive pore formation. We have found the binding of the peptides have profound impact on the distribution of cholesterol residing inside the lipid bilayer. Those results point the existence of a possible secondary mechanism of action against cellular membranes as metabolic inhibitors that affect cellular machinery by redistributing cholesterol.

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