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Redistribution of Cholesterol in Model Lipid Membranes in Response to the Membrane-Active Peptide Alamethicin[1] WILLIAM HELLER, SHUO QIAN, Oak Ridge National Laboratory — The cellular membrane is a heterogeneous, dynamic mixture of molecules and macromolecules that self-assemble into a tightly-regulated functional unit that provides a semipermeable barrier between the cell and its environment. Among the many compositional differences between mammalian and bacterial cell membranes that impact its physical properties, one key difference is cholesterol content, which is more prevalent in mammals. Cholesterol is an amphiphile that associates with membranes and serves to maintain its fluidity and permeability. Membrane-active peptides, such as the alpha-helical peptide alamethicin, interact with membranes in a concentration- and composition-dependent manner to form transmembrane pores that are responsible for the lytic action of the peptide. Through the use of small-angle neutron scattering and deuterium labeling, it was possible to observe a redistribution of the lipid and cholesterol in unilamellar vesicles in response to the presence of alamethicin at a peptide-to-lipid ratio of 1/200. The results demonstrate that the membrane remodeling powers of alamethicin reach beyond the membrane thinning effect to altering the localization of specific components in the bilayer, complementing the accepted two-state mechanism of pore formation.

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