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Membrane Disruption Mechanism by Antimicrobial Peptides

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Antimicrobial peptides (AMPs) are a class of small (less than100 residues) host defense peptides that induce selective membrane lytic activity against microbes. To understand the mechanism of membrane disruption by AMPs, we investigated, via atomic force microscopy, topological changes in supported phospholipid bilayers induced by protegrin-1 (PG-1). We have observed that PG-1 induces structural transformations, progressing from fingerlike instabilities at bilayer edges, to the formation of sievelike nanoporous structures and finally to a network of stripelike structures in a zwitterionic dimyristoylphosphatidylcholine (DMPC) model membrane in buffer, with increasing PG-1 concentration. Our results suggest that AMPs act to lower the interfacial energy of the bilayer in a way similar to detergents. By varying the lipid composition, temperature and using AMPs with different secondary structures, we are able to identify factors other than electrostatics that are important for the efficacy of AMPs.