Polymer- and Peptide-membrane interactions in model systems

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Antimicrobial peptide/membrane interaction is the initial event leading to membrane lesion or cell penetration. Synthetic peptides and polymers can target both the external membrane and/or cell interior. Here we describe the interaction of a peptide (BP100) and three high molecular weight amphipathic diblock copolymers of with large unilamellar vesicles, LUVs, prepared with phosphatidylcholine, PC, and phosphatidylglycerol, PG. The copolymers consisted of two separated blocks of poly(methylmethacrylate), PMMA, and poly(N,N-dimethylaminoethylmethacrylate), PDMAEMA. The general structures of the polymers were (PMMA₁₋₃-PDMAEMAₙ). Molecular weights ranged from 20,000 to 42,000 kD and PMMA/PDMAEMA ratios were 1/1; 1/3 and 1/6. The copolymers aggregate in aqueous solution at a critical aggregation concentration (CAC), depending of the pH and ionic strength, as evidenced by NMR spectra, fluorescence and light scattering. These polymers, as BP100, permeabilized LUVs containing PG, leading to aggregation and decreasing the LUVs zeta potential. Unlike that observed with BP100, the kinetics of LUVs permeabilization did not show a lag time, i.e., it was all or none phenomena. The polymer induced permeabilization of LUVs was strongly dependent on pH, reaching a maximum near pH 9. Copolymer titration curves showed that the apparent pKas of the amino groups were in the 6 to 10 range. The interactions of the copolymers with giant vesicles, GUVs, were similar to those observed with BP100. Since the copolymers do not have the same flexibility of the short peptide BP100, it seems that the organization on the membrane is a very slow process and the initial binding is so strong that led to fast and complete LUVs leakage. The mechanisms of induced leakage may be different from that of low molecular weight peptides due to the high molecular weight of the copolymers which hinders reorganization at the LUV interface.

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