Action of Antimicrobial Nylon-3 Polymers on Model Membranes

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Today, we face a dramatic increase in antibiotic resistance. Polymer-based synthetic mimics of antimicrobial peptides (smAMPs) such as Nylon-3 polymers offer a promising alternative to classical antibiotics through their action on membrane integrity. We examine the effect of nylon-3 smAMPs on model membranes of varying composition. For that, we use microcalorimetry, fluorescence spectroscopy and cryo-electron microscopy. Differential scanning calorimetry is used to detect electrostatic lipid clustering, i.e. the selection and recruitment of charged lipids from a mixed membrane. Isothermal titration calorimetry yields binding properties of the different nylon-3 smAMPs to lipid vesicles. In cryo-electron microscopy and dynamic light scattering, aggregation or/and fusion of vesicles induced by nylon-3 smAMPs was observed. It is still unclear, if those processes are relevant for the antimicrobial action in vivo or an artefact in our model studies. Time-Correlated Single Photon Counting fluorescence serves advanced leakage studies, and characterizes leakage events of nylon-3 smAMPs and model membrane. Taken together, our experiments show how the balance between electrostatic interactions and hydrophobically driven interactions determine the effect of smAMPs on membranes.