Antimicrobial polycations: how different molecules cause different membrane perturbations

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The interaction of polycations such as antimicrobial peptides or biomimetic polymers with membranes of various lipid compositions can cause a variety of physical-chemical membrane perturbations. These effects depend on the molecular properties of synthetic of natural polycations. Systematic investigations are therefore crucial for the selection or modification of natural peptides or rational design of biomimetic compounds in the search for alternatives to classical antibiotics or therapeutic compounds. To date, the role of certain types of membrane perturbations in antimicrobial killing is still unclear. My team investigates the principles of activity and selectivity of various types of membrane-active antimicrobial polycations for membranes of different lipid composition (representing different species or microbes). The central perturbation is membrane permeabilization or leakage. However, many observations cannot be explained with leakage alone, even when considering the many different leakage mechanisms. I will show that selectivity for certain lipid compositions depends on properties of the polycation, such as hydrophobic and charged side chains, but also on the predisposition of the lipid composition for certain leakage mechanisms. Additionally, membrane fusion and aggregation can both influence membrane leakage or cause unnoticed measurement artefacts. This type of mechanistic understanding can be used not only in the search and design of antimicrobial compounds, but also for creating drug delivery systems.