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Membrane Active Peptides and Their Interactions with REVs Protein Corona

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Abstract: Extracellular vesicles (EVs) are lipid bilayer enclosed nanoparticles secreted by most cells and found in body fluids. They have the advantage of displaying native membrane proteins on their surface and with the ability to interact with other cells play important role in many biological processes like cellular uptake, immune response, and cancer progression. Furthermore, their size distribution makes them promising candidates to expand biophysical understanding of membrane active peptides (MAPs). To study the action mechanism of MAPs we used red blood cell-derived extracellular vesicles (REV) as a model membrane system. We selected well-known MAPs: KLA, PNC28, CM15 and Melittin, and their interaction was investigated using several biophysical techniques such as polarized light spectroscopy (Szigyártó et al. 2018), microfluidic resistive pulse sensing and freeze-fracture transmission electron microscopy. We observed that CM15 and Melittin efficiently remove the proteins from REV membrane surfaces even at lower 5 μM concentrations, resulting in smoothed membrane surface while leaving the vesicle intact (Singh et al. 2020). Whereas a similar effect was not detected in the case of KLA and PNC28 even at a higher concentration of 160 μM. The overall results indicate that REV as a complex model membrane provides an excellent platform to understand better their interactions with MAPs and reveals *novel* peptide functions. This further highlights their role in possible future applications for nanoparticle and surface engineering of EV-based therapeutics.