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Assessing how membrane curvature alters protein recruitment

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Cellular membranes exhibit a diversity of curvatures that serve to recruit or sort proteins to certain regions within the cell. Due to the complexity of the process that occurs at sites of curvature in cells, it is difficult to determine what molecular interactions are essential to the sorting process. In order to identify individual interactions, our lab has created a biophysical assay that mimics a cellular membrane with areas of curvature. The design of this in vitro assay allows for specific and separate adjustments of the lipid composition and the membrane curvature, which is provided by a nanopatterned substrate under a supported lipid bilayer. In our work, fluorescent, polystyrene nanoparticles were placed on a glass surface to form the nanopatterned substrate, upon which liposomes were deposited to create a supported lipid bilayer, and then proteins of interest were allowed to interact with the lipids and/or curvature. Both laser scanning confocal and total internal reflection fluorescence microscopy were used to characterize curvature binding events. Colocalization analysis of the images using an object-oriented method provides a precise evaluation of the areas around each fluorescent nanoparticle to determine whether or not a protein is recruited to curved membranes. The applications of this assay are broad due to its ability to evaluate the interactions of either lipids or proteins with curvature. Using this assay, we have evaluated if C-Reactive Protein (CRP) preferentially binds to curved membranes. CRP is known to bind to small mimics of LDL particles that contain highly curved membranes, but it is not clear whether the conformational state affects binding. CRP has a native, anti-inflammatory, pentameric (pCRP) form and a pro-inflammatory, modified (mCRP) form. The mechanism for converting pCRP to mCRP remains elusive. Our results show that the conformational state of mCRP binds preferentially to sites of curvature and this binding is enhanced with the presence of specific lipids.