Nanoscale membrane-curvature as an allosteric modulator of protein localization and function.

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To date we have established exhaustive correlations between the lipid composition of membranes and its impact on membrane properties and protein function. In addition to composition the shape of cellular membranes appears to be a well-conserved phenotype in evolution. Nevertheless we largely ignore what are the consequences of membrane shape/curvature to biological functions that make it so critical for sustaining life. The lack of information on the significance of membrane shape has predominantly been due to the absence of reliable assays that allow us to perform systematic experiments as a function of membrane shape/curvature. We have recently demonstrated the possibility to construct a high throughput array of unique nanoscale membrane curvatures. The assay is based on unilamellar liposomes of different diameters (30 nm to 700 nm), and therefore curvature, that are immobilized on a surface at dilute densities allowing for imaging of single liposomes with fluorescence microscopy.

Here I will discuss published and unpublished data on several important classes of biomolecular interactions that exhibited dramatic curvature dependence including i) BAR domains and amphipathic helical peptides, ii) membrane anchoring of lipidated proteins, iii) SNARE-mediated docking of single lipid vesicles iv) the conformation of transmembrane proteins.

Selected References

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2 **Nature Chemical Biology, 2009.** 5 (11): p. 835 *How Curved Membranes Recognize Amphipathic Helices and Protein Anchoring Motifs*. N. S. Hatzakis*, V. K. Bhatia*, J. Larsen, K. L. Madsen, P. Y. Bolinger, A. H. Kunding, J. Castillo, U. Gether, P. Hedegård and D. Stamou.

3 **EMBO Journal,** 2009, 28 (21), p. 3303 *Amphipathic motifs in BAR domains are essential for membrane curvature sensing.* V. K. Bhatia, K. L. Madsen, P. Y. Bolinger, P. Hedegård, U. Gether, D. Stamou.

4 **Proceedings of the National Academy of Sciences. 2009**. 106 (30): p. 12341 *Quantification of nano-scale intermembrane contact areas using fluorescence resonance energy transfer*. P. M. Bendix, M. S. Pedersen and D. Stamou.