Investigating the Molecular Basis of cPLA$_2$α Membrane Bending

Katherine E. Ward[1], James P. Ropa[1], Emmanuel Adu-Gyamfi[1] and Robert V. Stahelin[1,2]

[1]Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, IN 46656; [2]Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, South Bend, IN 46617

Signal transduction mediates disease through key molecular targets that initiate signaling networks. As protein-lipid interactions have been examined in the literature, their role in cellular signaling has become more prevalent as lipid-binding proteins have become high impact drug targets in cancer, inflammation and viral egress. One such target, termed cytosolic phospholipase A_2 α (cPLA$_2$α), has been shown to play a key role in the production of the inflammatory mediators prostaglandins and leukotrienes. A novel function of the protein was recently discovered in our lab showing cPLA$_2$α bends zwitterionic bilayers using model membranes, a process that is mediated by cPLA$_2$α's ability to deeply penetrate membranes. Others in the field have reported cPLA$_2$α to participate in Fc mediated phagocytosis, intra-Golgi trafficking and endosomal trafficking, further supporting cPLA$_2$α's ability to bend membranes in biological processes. In addition, direct evidence has been reported in the literature using siRNA showing that cPLA$_2$α C2 domain induced vesiculation in cells. These results translate into our cellular system as cells transfected with EGFP- cPLA$_2$α form cytoplasmic vesicular structures. We have preliminary evidence showing cPLA$_2$α membrane bending is mediated by curvature sensing and protein oligomerization. The origin of oligomerization is currently under further investigation using both *in vitro* and cellular techniques.

This work was supported by AHA Predoctoral Fellowship 11PRE7640028 and CBBI Training Fellowship T32GM075762.