

#49: Poliovirus 3C protein is a phosphatidylinositol-phosphate-binding protein  
Djoshkun Shengjuler, Simou Sun, Yan Mei Chan, Joseph M. Moran, Akira Uchida, Ibrahim M. Moustafa, Jamie J. Arnold, Paul S. Cremer, David D. Boehr, and Craig E. Cameron

One of the most exciting advances in virology over the past few years has been the realization that phosphatidylinositol 4-phosphate (PI4P) is an essential lipid component of positive-strand RNA virus replication organelles. In the cell, phosphoinositides are used as markers of specific membranes that proteins and enzymes use to ensure appropriate localization and/or activation. Cellular proteins recognize phosphoinositides using one of a few structural scaffolds, the most famous of which is the Pleckstrin homology (PH) domain. We observed that poliovirus 3C protein binds to several phosphoinositides, including PI4P. Hints of the location of the binding site were obtained by molecular docking experiments and confirmed by using nuclear magnetic resonance spectroscopy. To measure the affinity, we used supported lipid bilayer binding experiments in the context of a microfluidic platform. This is a label-free, fluorescence method, which allowed us to test the interaction in a physiologically relevant manner. Together, these data reveal a new structural scaffold competent for phosphoinositide binding that may represent a tractable target for the design of antiviral agents.