Mechanism of inhibition of clathrin-dependent endocytosis by phospholipase A_2 in the model organism *Saccharomyces cerevisiae*

Biological membranes and the role of membrane homeostasis in several cellular processes have long been in the shadow of the overwhelmingly better studied proteins. With more research being devoted to membranes, it is becoming clear that their role stretches beyond compartmentalizing the cell, since they provide an environment for many proteins involved in cellular signalling and trafficking, and moreover they actively participate in these processes through biological activity of their lipid building blocks and through the shape and composition of the membrane itself. In humans, abnormal regulation of membrane homeostasis often leads to the development of several lipid-associated disorders. Phospholipases A_2 (PLA_2s) are key enzymes that through their enzymatic activity affect membrane composition and shape and moreover generate bioactive lipid mediators, such as arachidonic acid. Using a high-throughput whole-genome based approach, we first analyzed the impact of PLA_2 on yeast cells and on the basis of the identified genetic interactions of the PLA_2 gene with the yeast genome, and the results of *in vitro* studies, generated a hypothesis for the mechanism of inhibition of clathrin-dependent endocytosis with PLA_2 in yeast. With the use of real-time fluorescence microscopy we then analyzed the spatiotemporal dynamics of several endocytic proteins after the perturbation of the plasma membrane with PLA_2 and confirmed our hypothesis on the role of amphiphysins, proteins that sense membrane curvature and are involved in vesicle scission from the plasma membrane, in the PLA_2 mediated inhibition of clathrin-dependent endocytosis.