Our most recent data on the regulation of cPLA$_2$ and attendant free arachidonic acid (AA) by phosphatidylinositol bisphosphate, and the putative involvement of a cluster of four lysine residues located on the catalytic domain but far from the active site will, be discussed. The current paradigm for activation of the cytosolic Group IV phospholipase A$_2$ (cPLA$_2$) by stimuli contemplates a scenario wherein both an increase in intracellular calcium and mitogen-activated protein kinase (MAPK)-mediated phosphorylation, act together to fully activate the enzyme. The calcium is needed for translocation of the cPLA$_2$ to the membrane; whereas cPLA$_2$ phosphorylation increases enzyme activity. However there are instances where the enzyme translocates to the membrane in the absence of sustained elevations of intracellular Ca$^{2+}$. Thus, increased Ca$^{2+}$ availability is a dispensable signal for cPLA$_2$ activation, which suggests the existence of alternative mechanisms for the enzyme to efficiently interact with membranes. Previous studies in intact cells suggested the importance of phosphatidylinositol 4,5-bisphosphate in the regulation of cPLA$_2$ activity [1-18]. By using advanced confocal microscopy techniques, we show that phosphatidylinositol 4,5-bisphosphate promotes translocation of cPLA$_2$ to perinuclear membranes of intact cells in a manner that is independent of rises in the intracellular Ca$^{2+}$ concentration. PIP$_2$ appears to anchor the enzyme to perinuclear membranes and allow for a proper interaction with its phospholipid substrate to release arachidonate. Preliminary results suggest the involvement of 4-Lys cluster in the enzyme response to PIP$_2$ since a mutant in the polybasic cluster Lys488/Lys541/Lys543/Lys544, that cannot bind PIP$_2$, does not translocate to membranes [19,20].

Slide List.
Slide 1 – Title.
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Slide 3 – Role of Phospholipase A$_2$ in Arachidonic Acid Release.
Slide 4 – 22 Phospholipase A$_2$s.
Slide 5 – PLA$_2$ Families.
Slide 6 – Phospholipase A$_2$ Regulation of AA Release.
Slide 7 – cPLA$_2$.
Slide 8 – LPS-induced AA Release Is Inhibited by MAFP.
Slide 9 – Phosphatidylinositol Bisphosphate.
REFERENCES


