

**SL-3****Regulation of Phosphoinositide-specific Phospholipase C- $\gamma$  Isozyme**

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Although the activation mechanism of PLC- $\gamma$  isozyme by protein tyrosine kinase (PTK) is well established, several lines of evidence indicate that PLC- $\gamma$  isozymes can be activated directly by several lipid-derived second messengers in the absence of tyrosine phosphorylation. Herin we report that PLC- $\gamma$  isozymes are also stimulated by arachidonic acid (AA) in the presence of the microtubule-associated protein tau (in neuronal cells) or taulike proteins (in nonneuronal cells). The effect of tau and AA was specific to PLC- $\gamma$  isozymes and was markedly inhibited by phosphatidylcholine (PC). These observations suggest that the activation of PLC- $\gamma$ 1 by tau or taulike proteins might be facilitated by a concomitant decrease in PC concentration and increase in AA concentration, both of which occur in cells upon activation of an 85-kDa cytosolic phospholipase A2 (cPLA2). This enzyme is coupled to various receptors and preferentially hydrolyzes PC containing AA. Therefore, activation of PLC- $\gamma$  isozymes may occur secondarily to receptor-mediated activation of cPLA2.