

P016 PI3K and Akt/PKB promote Ca_v channels translocation to the plasma membrane.

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Voltage-dependent calcium channels (Ca_v) represent one of the major routes for Ca²⁺ entry into excitable cells. Recently, phosphoinositide 3-kinase (PI3K) has been shown to regulate Ca_v channels. To investigate the mechanism(s) involved, we expressed both PI3K and cloned Ca_v channels in COS-7 cells. The distribution of GFP-tagged Ca_v channels was studied using confocal imaging and Ca_v currents were measured using the patch-clamp technique.

We showed that PI3K overexpression increased both whole-cell currents and Ca_v channel expression at the plasma membrane when associated with one specific subunit: Ca_vβ₂. PI3K-induced translocation of Ca_v channels was prevented by co-expression of a kinase-dead mutant of protein kinase B (Akt/PKB) and reproduced by constitutively activated Akt/PKB. The Akt/PKB-induced increase of Ca_v trafficking also specifically required Ca_vβ₂ subunits and was prevented by mutation of a unique Akt/PKB consensus site. This mutation also precluded PI3K-induced phosphorylation of Ca_vβ₂ subunits. Our work thus reveals a new mechanism for the regulation of Ca_v channels, where PI3K increases Ca_v currents via Akt/PKB-induced translocation of Ca_vβ₂-associated calcium channels to the plasma membrane.