Membrane electrical activity elicits inositol 1,4,5-trisphosphate-dependent slow Ca2+ signals through a G??/phosphatidylinositol 3-kinase ? pathway in skeletal myotubes

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Tetanic electrical stimulation of myotubes evokes a ryanodine receptor-related fast calcium signal, during the stimulation, followed by a phospholipase C/inositol 1,4,5-trisphosphate-dependent slow calcium signal few seconds after stimulus end. L-type calcium channels (Cav 1.1, dihydropyridine receptors) acting as voltage sensors activate an unknown signaling pathway involved in phospholipase C activation. We demonstrated that both G protein and phosphatidylinositol 3-kinase were activated by electrical stimulation, and both the inositol 1,4,5-trisphosphate rise and slow calcium signal induced by electrical stimulation were blocked by pertussis toxin, by a G?? scavenger peptide, and by phosphatidylinositol 3-kinase inhibitors. Immunofluorescence using anti-phosphatidylinositol 3-kinase ? antibodies showed a clear location in striations within the cytoplasm, consistent with a position near the I band region of the sarcomere. The time course of phosphatidylinositol 3-kinase activation, m