Ca2+ signals promote GLUT4 exocytosis and reduce its endocytosis in muscle cells

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Elevating cytosolic Ca2+ stimulates glucose uptake in skeletal muscle, but how Ca2+ affects intracellular traffic of GLUT4 is unknown. In tissue, changes in Ca2++ leading to contraction preclude analysis of the impact of individual, Ca2+-derived signals. In L6 muscle cells stably expressing GLUT4myc, the Ca2+ ionophore ionomycin raised cytosolic Ca2++ and caused a gain in cell surface GLUT4myc. Extra- and intracellular Ca2+ chelators (EGTA, BAPTA-AM) reversed this response. Ionomycin activated calcium calmodulin kinase II (CaMKII), AMPK, and PKCs, but not Akt. Silencing CaMKII? or AMPK?1/?2 partly reduced the ionomycin-induced gain in surface GLUT4myc, as did peptidic or small molecule inhibitors of CaMKII (CN21) and AMPK (Compound C). Compared with the conventional isoenzyme PKC inhibitor Gö6976, the conventional plus novel PKC inhibitor Gö6983 lowered the ionomycin-induced gain in cell surface GLUT4myc. Ionomycin stimulated GLUT4myc exocytosis and inhibited its endocytosis in live ce