Contraction-related stimuli regulate GLUT4 traffic in C2C 12-GLUT4myc skeletal muscle cells

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Muscle contraction stimulates glucose uptake acutely to increase energy supply, but suitable cellular models that faithfully reproduce this complex phenomenon are lacking. To this end, we have developed a cellular model of contracting C2C12 myotubes overexpressing GLUT4 with an exofacial mycepitope tag (GLUT4myc) and explored stimulation of GLUT4 traffic by physiologically relevant agents. Carbachol (an acetylcholine receptor agonist) induced a gain in cell surface GLUT4myc that was mediated by nicotinic acetylcholine receptors. Carbachol also activated AMPK, and this response was sensitive to the contractile myosin ATPase inhibitor N-benzyl-p- toluenesulfonamide.

The gain in surface GLUT4myc elicited by carbachol or by the AMPK activator 5-amino-4-carboxamide-1 ?-ribose was sensitive to chemical inhibition of AMPK activity by compound C and partially reduced by siRNA-mediated knockdown of AMPK catalytic subunits or LKB1. In addition, the carbachol-induced gain in cell surface GLUT4myc