

Muscle Physiology

Fibroblast growth factor 21 promotes glucose uptake by a GLUT4-dependent and Akt-independent mechanism in isolated fibers of skeletal muscle

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Introduction: Fibroblast growth factor 21 (FGF21) is a pleiotropic peptide hormone that induces glucose uptake in both primary myotubes and C2C12 myoblasts. However, the cellular mechanism involved and its role in adult skeletal muscle fibers is poorly understood.

Material and Methods: Male mice were used at 6-8 weeks of age. The glucose uptake was evaluated in single living fibers from *flexor digitorum brevis* muscle. To determine glucose uptake, we used the phosphorylable, non-metabolizable fluorescent glucose analog 2-NBDG (300 μ M) that has been used to monitor glucose uptake in single living cells.

Results: FGF21 induces a dose-response effect, increasing glucose uptake in isolated skeletal muscle fibers. This effect is prevented by the use of either Cytochalasin B (5 μ M) or Indinavir (100 μ M), both antagonists of GLUT4 activity. The use of PI3K inhibitors such as Wortmannin (100 nM) and LY294002 (50 μ M) prevents the FGF21-dependent glucose uptake. In fibers electroporated with the construct encoding GLUT4^{myc}-eGFP chimera and stimulated with FGF21 (100 ng/mL) for 20 min, a strong sarcolemmal GLUT4 presence was detected. This effect, promoted by FGF21, is independent of Akt phosphorylation and is partially prevented by the inhibition of PKCs.

Conclusions: These results suggest that FGF21 regulates glucose uptake by a mechanism dependent on PI3K activity and independent of Akt phosphorylation.

Keywords: Fibroblast growth factor 21, glucose uptake, GLUT4-dependent and Akt-independent mechanism, isolated fibers, skeletal muscle

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