Association between PI3K/Akt/TOR pathway and stretch-induced hypertrophy in primary cultured chick myotubes

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Skeletal muscle cells are hypertrophied by mechanical stresses, but the underlying molecular mechanisms are not fully understood. Two signaling pathways, phosphatidylinositol 3-kinase (PI3K)/Akt to target of rapamycin (TOR) and extracellular signal-regulated kinase kinase (MEK) to extracellular signal-regulated kinase (ERK), have been proposed to be involved in muscle hypertrophy. In this study we examined the involvement of these pathways in primary cultures of chick skeletal myotubes subjected to passive cyclic stretching for 72 hours, a time that was sufficient to induce significant hypertrophy in our preparations. Hypertrophy was largely suppressed by wortmannin or rapamycin, inhibitors of PI3K or mTOR, respectively. Furthermore, phosphorylation of Akt was enhanced by stretching and suppressed by wortmannin. The MEK inhibitor, U0126, exerted a minimal influence on stretch-induced hypertrophy. We found that cyclic stretching of myotubes activates the PI3K/Akt/TOR pathway, resulting in muscle hypertrophy. The MEK/ERK pathway may contribute negatively to spontaneous hypertrophy.