

# Hypoxia stimulates via separate pathways ERK phosphorylation and NF- $\kappa$ B activation in skeletal muscle cells in primary culture

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Mammalian cells sense oxygen levels and respond to hypoxic conditions through the regulation of multiple signaling pathways and transcription factors. Here, we investigated the effects of hypoxia on the activity of two transcriptional regulators, ERK1/2 and NF- $\kappa$ B, in skeletal muscle cells in primary culture. We found that hypoxia significantly enhanced ERK1/2 phosphorylation and that it stimulated NF- $\kappa$ B-dependent gene transcription as well as nuclear translocation of a green fluorescent protein-labeled p65 NF- $\kappa$ B isoform. Phosphorylation of ERK1/2- and NF- $\kappa$ B-dependent transcription by hypoxia required calcium entry through L-type calcium channels. Calcium release from ryanodine-sensitive stores was also necessary for ERK1/2 activation but not for NF- $\kappa$ B-dependent-transcription. N-acetylcysteine, a general scavenger of reactive oxygen species, blocked hypoxia-induced ROS generation but did not affect the stimulation of ERK1/2 phosphorylation induced by hypoxia. In contrast, NF- $\kappa$ B activati