

Abstract

Muscle spindles are an essential part of the neuro-muscular system because they act as sensory receptors of muscle and limb position that communicate with the nervous system and sense movement. It has been established that the neuregulin1(NRG1) - ErbB signaling pathway plays a key role in the formation of muscle spindles. Our research aims to further characterize this pathway and more specifically the role of the transcription factor serum response factor (SRF), which previous evidence suggests may be a downstream effector during NRG1 signaling. To address how SRF is targeted during neuregulin signaling, we have generated muscle cells that inactivate endogenous SRF and express a truncated mutant form of SRF, using retroviral transduction and CRISPR/Cas9. These cells were then stimulated with NRG1 and qRT-PCR was used to measure expression of Early growth response 3 (Egr3), which is a key target gene activated by SRF in the NRG1-ErbB pathway. In these cells, transcription of Egr3 is induced by NRG1 consistent with wild-type cells. These results suggest that transcriptional induction of Egr3 by NRG1 occurs independently of the N- and C-terminal domains of SRF and the MADS box is sufficient for induction. Future experiments will further investigate the MADS box and its interactions with known co factors in the development of muscle spindles.

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