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IGFs, Insulin, Shh, bFGF, and TGF- β 1 Interact Synergistically to Promote Somite Myogenesis *in Vitro*

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Abstract

Studies from our group and others have shown that *in vitro* somite myogenesis is regulated by neural tube and notochord factors including Wnt, Sonic hedgehog (Shh), and basic fibroblast growth factor (bFGF) together with transforming growth factor- β 1 (TGF- β 1). In this study we report that insulin and insulin-like growth factors I and II (IGF-I and -II) also promote myogenesis in explant cultures containing single somites or somite-sized pieces of segmental plate mesoderm from 2-day (stage 10–14) chicken embryos and that the combination of insulin/IGFs with bFGF plus TGF- β 1 promotes even higher levels of myogenesis. We also found that Shh promotes myogenesis in this *in vitro* system and that Shh interacts synergistically with insulin/IGFs to promote high levels of myogenesis. RT-PCR analysis detected insulin, IGF-II, insulin receptor, and IGF receptor mRNAs in both the neural tube and the somites, whereas IGF-I transcripts were detected in entire embryos but not in the neural tube or somites. Treatment of somite–neural tube cocultures with anti-insulin, anti-IGF-II, anti-insulin receptor, or anti-IGF receptor blocking antibodies caused a significant decrease in myogenesis. These results are consistent with the hypothesis that systemic IGF-I as well as insulin and IGF-II secreted by the neural tube act as additional early myogenic signals during embryogenesis. Further studies indicate that insulin, IGFs, bFGF, and Shh also stimulate somite cell proliferation and influence apoptosis.

Keywords

somite; myogenesis; muscle; neural tube; insulin-like growth factors (IGFs); IGF receptors; Sonic hedgehog (Shh); fibroblast growth factor; TGF- β 1; apoptosis

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