Cholinergic Neurons Regulate and Utilize GDNF Secreted by C2C12 Skeletal Muscle Cells in Culture

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GDNF secreted by skeletal muscle cells in culture

**Abstract**

Glia and cell line–derived neurotrophic factor (GDNF) is a potent survival factor for subpopulations of neurons in both central and peripheral systems (Liu and Weis, 1996). The presence of GDNF in skeletal muscle at the neuromuscular junction (NMJ) suggests a target for neuromuscular diseases. This study examines the role of GDNF in regulating the production of GDNF by C2C12 skeletal muscle cells in culture. The results suggest that cholinergic neural cells regulate GDNF production by muscle cells possibly through acetylcholine receptors.

**Aims**

a. Examine GDNF production by skeletal muscle cells in culture.

b. Localize GDNF in skeletal muscle and at the nerve-muscle contact.

c. Examine the role that neural cells play in regulating GDNF production by skeletal muscle.

d. Examine if cholinergic neural cells induce their effect through acetylcholine receptors.

**Introduction**

GDNF is a member of the TGF-β superfamily of growth factors involved in the development and differentiation of neural tissues. It is expressed in multiple cell types, including neurons, glia, and immune cells. GDNF interacts with two receptor tyrosine kinases, RET and GFRα1, which are associated with different signaling pathways.

**Results**

**Neural cells reduce GDNF content by skeletal muscle cells in culture**

**Neural cells reduce GDNF content in muscle cells**

**Blocking AChRs reversed the action of neural cells on GDNF secretion**

**Blocking AChRs did not reverse the action of neural cells on GDNF production in muscle cells**

**Discussion**

These results suggest that cholinergic neural cells regulate GDNF production by skeletal muscle cells through the activation of acetylcholine receptors. The findings provide insight into the potential mechanisms by which neural cells modulate GDNF production and may have implications for the treatment of neuromuscular diseases.

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**References**


**Summary**

- C2C12 skeletal muscle cells produce and secrete GDNF in culture medium. However, more GDNF is retained in cells than secreted into culture medium.

- NG108-15 neural cells regulate the production of GDNF by C2C12 skeletal muscle by reducing the amount of GDNF secreted in culture medium and modulating the release of GDNF from muscles.

- Blockade of acetylcholine receptors blocks effects of neurons on GDNF secretion by skeletal muscle cells but does not block the effect of neurons on GDNF content within muscle cells.

- Neural cells grown alone in cell culture do not contain or secrete GDNF; however, neural cells grown in co-culture contain GDNF protein.

**Conclusions**

Results from this study suggest that neural cells regulate their own supply of GDNF produced by skeletal muscle, in part, via acetylcholine receptor activation.