Myostatin as a potential target for treatment of muscle contractures

Marianne E Emmert, Qingnian Goh, Kritton Shay-Winkler, & Roger Cornwall.
Department of Biomedical Sciences, University of Cincinnati College of Medicine.
Division of Orthopaedic Surgery, Cincinnati Children’s Hospital Medical Center.

Overview

Neonatal Brachial Plexus Injury (NBPI) - Most common cause of upper limb paralysis in childhood, occurring in 15 of every 1,000 live births.
- Leads to the secondary formation of contractures, the hallmark symptoms of "light" injuries.
- Contractures severely impair range of motion of the involved limbs, thereby impairing activities of daily living, and ultimately resulting in restricted deformity and disabilities.
- Current treatments for contractures are ineffective in restoring muscle function and joint range of motion.
- To identify effective strategies for preventing and treating contractures, it is first needed to establish precise pathophysiologic mechanisms.

Contactopathogenesis

- Contractures following NBPI result from impaired longitudinal growth of the denervated muscle.
- Declines in longitudinal growth of denervated muscles are driven by systemic factors such as pro-inhibitors, mediators of protein degradation, and by decreased levels of synthetic proteins.
- Pro-inhibitors mediate muscle-specific receptor (Activin receptor-like 2) signaling that controls muscle growth.

Myostatin inhibition

- Inhibition of myostatin signaling dramatically enhances muscle growth in adult mice.
- In this study, dexamethasone was used at a dose of 0.01 mg/kg, daily for 10 days, to prevent muscle atrophy.

Experimental Design

Sex-Specific Response to Neonatal Myostatin Inhibition – Developmental Growth

- Neonatal myostatin inhibition decreases the loss of muscle mass, resulting in a significant increase in muscle mass in the NBPI arm.
- Inhibition of myostatin results in a significant increase in muscle mass in the NBPI arm.

Sex-Specific Response to Neonatal Myostatin Inhibition – shoulder contractures

- Neonatal myostatin inhibition decreases the loss of shoulder function, resulting in a significant increase in shoulder function in the NBPI arm.
- Inhibition of myostatin results in a significant increase in shoulder function in the NBPI arm.

Conclusion/Future Directions

- Neonatal inhibition of myostatin enhances muscle growth.
- Neonatal inhibition of myostatin enhances muscle function.
- Future studies are needed to evaluate the effectiveness of myostatin inhibition in preventing neonatal muscle contractures.

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References