Intraoperative and Laboratory Studies of Human Skeletal Muscle Contractures

December 6

Tuesday, 12:30pm

Hybrid: Rosedale Room and Zoom

For Researchers

Speaker:

Richard L. Lieber, Ph.D.

Professor and Chief Scientific Officer
Shirley Ryan AbilityLab and
Departments of Physical Medicine, Rehabilitation and Biomedical Engineering
Northwestern University, Chicago, IL

Hosts: Kathleen M. Friel, Ph.D. and Rajiv R. Ratan, M.D., Ph.D.

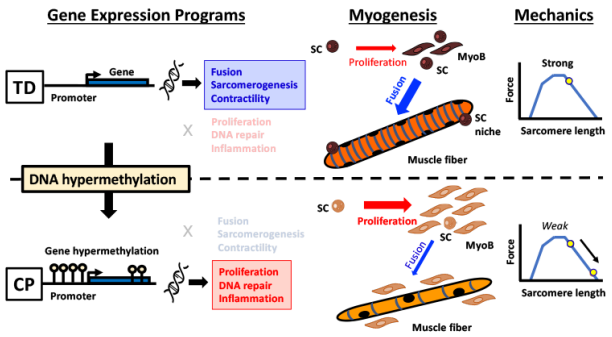
For more information contact

Darlene White

daw9085@med.cornell.edu

Abstract

Skeletal muscle is a highly plastic tissue, responding both to level of use and amount of neural input. After cerebral palsy (CP) altered neural input can result in muscle weakness and even contractures. We have studied the mechanics and biology of muscle from children with wrist flexion contractures secondary to CP. Dramatic architectural changes are observed in these children whereby sarcomere lengths are dramatically altered relative to patients without upper motor neuron lesions. This suggests dramatic alterations in the regulation of muscle growth in these children. Biomechanical studies of isolated single muscle cells reveal an increased passive modulus and decreased resting sarcomere length suggesting alterations in the cellular cytoskeleton. Gene expression profiling reveals a number of "conflicting" biological pathways in spastic muscle. Specifically, this muscle adapts by altering processes related to extracellular matrix production, fiber type determination, fiber hypertrophy and myogenesis. These transcriptional adaptations are not characteristic of muscle adaptations observed in Duchenne muscular dystrophy or limb immobilization. Superimposed upon the dramatic biological and structural adaptations is a loss in the number of satellite cells that are located throughout the muscle. Even the remaining satellite cells have epigenetic changes that can dramatically influence our ability to rehabilitate these muscles. Recently, we have shown that several anti-cancer drugs are able to reverse these epigenetic changes, thus "rescuing" the satellite cells and promoting myogenesis. Taken together, these results support the notion that, while contracture formation is multifactorial and neural in origin, significant structural alterations in muscle also occur. An understanding of the specific changes that occur in the muscle and extracellular matrix may facilitate the development of new conservative or surgical therapies for this condition.



Sibley *et al.* (2022). *FASEB J.* (PMID: 34559924)

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2. Sibley LA, Broda N, Gross W, Swaroop VT, Chambers HG, Dayanidhi S, Lieber RL, Domenighetti AA. (2021). **Different DNA methylation and transcriptional profiles mediate an accelerated expansion of muscle progenitor cells from human muscle contractures during postnatal development.** FASEB J. doi: 10.1096/fj.202100649R. PMID: 34559924.

3. Lieber RL, Fridén J. (2019). **Muscle contracture and passive mechanics in cerebral palsy.** J. Appl. Physiol. 126:1492-1501. PMID: 30571285.

Burke Neurological Institute
Academic Affiliate of Weill Cornell Medicine
785 Mamaroneck Avenue, White Plains, NY 10605
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