Exercise In A Pill: Compounds That Reproduce The Effects Of Exercise On Muscle Metabolism And Growth

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SUMMARY
UCLA researchers in the Department of Neurology have identified and synthesized small molecule analogs that activate skeletal muscle growth, mediated by calcium calmodulin kinase II signaling.

BACKGROUND
Skeletal muscle has a remarkable ability to alter its metabolic and contractile phenotype in response to changes in functional demands. Increased load bearing and extended duration of activation leads to muscle adaptation by triggering target genes to induce muscle hypertrophy, fiber type transitions, or mitochondrial biogenesis. Similarly, decreased mechanical loading due to inactivity or injury activates signaling pathways that induce muscle atrophy. In skeletal muscle, calcium-mediated signaling plays an essential role in the muscle contraction relaxation cycle, as well as contractile activity-dependent and fiber type-specific gene expression. Calcium calmodulin-dependent kinases (CaMKs) have been shown to promote mitochondrial biogenesis, and expression of fiber type-specific myofibrillar proteins for fiber type transition, as well as to sense altered functional demands and activate adaptation responses.

INNOVATION
Researchers at UCLA have identified a small molecule activator of calcium calmodulin kinase II (CaMKII). Activation of CaMKII increases muscle size, mitochondrial bioenergetics, and improves the performance of mouse with limb girdle muscular dystrophy. Small molecule activator analogs are synthesized with increased solubility and reduced toxicity to develop therapeutics for individuals suffering from a variety of muscle conditions.

APPLICATIONS
- Reverse muscle wasting and metabolic deficiencies in limb girdle muscular dystrophy, sarcopenia (from aging or extended bed rest), cachexia, and triadopathies.

ADVANTAGES
- Identified mechanism of action
- Validated in animal disease models

STATE OF DEVELOPMENT
The benefit effect has been demonstrated in limb girdle muscular dystrophy type 2A (LGMD2A) mouse model.

PATENT STATUS
Patent Pending

RELATED MATERIALS

CATEGORIZED AS
- Medical
  - Disease: Musculoskeletal Disorders
  - New Chemical Entities, Drug Leads
  - Therapeutics

RELATED CASES
2019-355-0

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS
- New 3D-Exoquant Method For The Analysis Of Surface Molecules And Quantification Of Tissue-Specific Exosomes In Biological Fluids
- Pathway-Dependent Inhibition Of Proteopathic Seed Transmission
- Allosteric BACE Inhibitors For Treatment Of Alzheimer’s Disease
- Identification And Development Of Dual nSMase2-AChE Inhibitors For Neurodegenerative Disorders