

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

Tech ID: 30362 / UC Case 2019-355-0

### 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 $\beta$ ). Activation of CaMKII $\beta$  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

Country	Type	Number	Dated	Case
Japan	Issued Patent	7805038	01/15/2026	2019-355
United States Of America	Issued Patent	12,441,716	10/14/2025	2019-355
Japan	Issued Patent	7566775	10/04/2024	2019-355
Belgium	Issued Patent	3952849	09/18/2024	2019-355
Switzerland	Issued Patent	3952849	09/18/2024	2019-355
Germany	Issued Patent	60 2020 038 004.3	09/18/2024	2019-355
France	Issued Patent	3952849	09/18/2024	2019-355
United Kingdom	Issued Patent	3952849	09/18/2024	2019-355

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### INVENTORS

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### OTHER INFORMATION

#### KEYWORDS

musculoskeletal disease, skeletal muscle, muscle growth, muscle metabolism, muscle adaptation, limb girdle muscular dystrophy, sarcopenia, cachexia, triadopathy

#### CATEGORIZED AS

- ▶ **Medical**
  - ▶ Disease: Musculoskeletal Disorders
  - ▶ New Chemical Entities, Drug Leads
  - ▶ Therapeutics

#### RELATED CASES

2019-355-0

## RELATED MATERIALS

- ▶ Kramerova, I., Torres, J.A., Eskin, A., Nelson, S.F. and Spencer, M.J., 2018. Calpain 3 and CaMKII  $\beta$  signaling are required to induce HSP70 necessary for adaptive muscle growth after atrophy. *Human molecular genetics*, 27(9), pp.1642-1653.
- ▶ Kramerova, I., Ermolova, N., Eskin, A., Hevener, A., Quehenberger, O., Armando, A.M., Haller, R., Romain, N., Nelson, S.F. and Spencer, M.J., 2016. Failure to up-regulate transcription of genes necessary for muscle adaptation underlies limb girdle muscular dystrophy 2A (calpainopathy). *Human molecular genetics*, 25(11), pp.2194-2207.
- ▶ Kramerova, I., Kudryashova, E., Ermolova, N., Saenz, A., Jaka, O., Lopez de Munain, A. and Spencer, M.J., 2012. Impaired calcium calmodulin kinase signaling and muscle adaptation response in the absence of calpain 3. *Human molecular genetics*, 21(14), pp.3193-3204.

## ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- ▶ Identification And Development Of Dual nSMase2-AChE Inhibitors For Neurodegenerative Disorders
- ▶ New 3D-Exoquant Method For The Analysis Of Surface Molecules And Quantification Of Tissue-Specific Exosomes In Biological Fluids
- ▶ Allosteric BACE Inhibitors For Treatment Of Alzheimer's Disease

## Gateway to Innovation, Research and Entrepreneurship

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