Paper ID: 70454
student

IAF/IAA SPACE LIFE SCIENCES SYMPOSIUM (A1)
Interactive Presentations - IAF/IAA SPACE LIFE SCIENCES SYMPOSIUM (IP)

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DRUG EFFICACY TESTING IN SKELETAL MUSCLE MICROPHYSIOLOGICAL SYSTEM TO DEVELOP SPACEFLIGHT COUNTERMEASURES TO MUSCLE ATROPHY

Abstract

Sarcopenia is the process of gradual muscle loss which is associated with age. Currently, treatment for sarcopenia consists of resistance exercise, but potential pharmacological treatments are still being evaluated. For long-term spaceflight missions, drug countermeasures will be necessary to prevent muscle wasting in astronauts. Microgravity research onboard the International Space Station will enable greater understanding of these conditions due to accelerated atrophy and thus, ground-based control studies evaluating drug efficacy are crucial for future planned ISS research. To characterize mechanisms of muscle atrophy, young (20-40 years) and old (60-80 years) human myoblasts, derived from muscle biopsies from AdventHealth were used as the cell source. The young and old human muscle cells were cultured and enriched for CD56+ cell populations, and subsequently seeded into PDMS based microfluidic tissue chips. Tissue chips containing live 3D human muscle bundles were subject to an electrical stimulation regime. A twice per day regime of 3V, 2 Hz, 2 ms for 30 min was applied to approximately two-week differentiated muscle bundles for seven days. Tomatidine, a natural small molecule derived from tomato plants, was utilized in tandem with electrical stimulation to evaluate myotube contractile response and gene expression compared to non-treated bundles. Tomatidine (5 M) treated muscle bundles demonstrated a distinct contractile behavior evidenced by displacement magnitude determinations. Ongoing dose-response and gene expression profiling from RNA isolated from the myotube bundles will provide further insight into additional differences due to drug treatment. In addition, a 2D in vitro model is being investigated to provide high-throughput data from drug-treated myotube bundles. Ultimately, this will serve as a biology verification study for the SpaceX CRS-25 mission to the ISS.