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Simulating Muscle Atrophy due to Microgravity and Ionizing Radiation

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Abstract:

A primary concern for astronauts in low gravity and high radiation environments is muscle atrophy. A major cause of muscular atrophy is oxidative stress, which is amplified by increased levels of ionizing radiation during spaceflight. Due to prohibitively high costs for in vivo studies in space, a ground-based simulation is better-suited for studying potential causes of muscle atrophy. To do this, USU's Space Survivability Test Chamber was used to irradiate C2C12 mouse myoblasts with dosages mimicking those on the ISS, and both a 1 and 10-year deep space mission. Microgravity was simulated using a custom rotary cell culture system (RCCS) designed to withstand the radiation dosages of the test chamber. Cell changes due to microgravity and increased levels of radiation were characterized with fluorescent imaging for H2AX, scheduled measurements of muscle fibers, and viability staining.

***Methods*:** Skeletal muscle cells were cultured in standard tissue culture flasks, a NASA developed Synthecon 4H-RCCS, and the custom RCCS. Cells were maintained using high glucose DMEM medium with 10% FBS for the first three days of culture then 2% FBS for the remainder of the culture to promote differentiation. Differentiated monolayers were exposed to 0.5, 1.0, 2.0, and 4.0 Gy following fourteen days of culture. Cells were immediately stained for to quantify DNA damage and viability measurements.

Results and Discussion: Cell viability of irradiated monolayers decreased with increased accumulated radiation dose. Irradiated cell morphology lacked cell-to-cell contact inhibition and lost unidirectional cell growth indicating cell damage at the molecular level. Viability percentages were as follows: 0.5 Gy viability: 89.3 ± 1.4%, 1.0 Gy viability: 81.1 ± 1.1%, 2.0 Gy viability: 74.0 ± 1.4%, and 4.0 Gy viability: 68.7 ± 0.9%.

Conclusions: Monolayer cultures exposed to high dosage radiation approach the lethal dosage limit marked by approximately 50% cellular death. The RCCS designed for this study accurately models microgravity and allows simultaneous radiation exposure.

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