The Engineering of a Three-Dimensional, Tissue-Equivalent Muscle Model from Waste Fat Tissue

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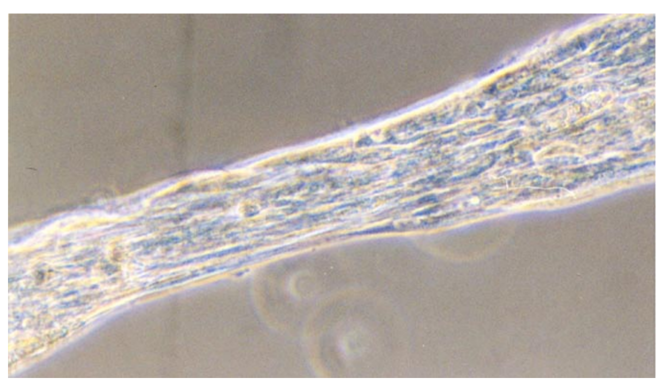
Progressive muscle atrophy is one impediment to the future of human space exploration. Muscle atrophy leads to weakness, fatigue, inability to perform efficiently assigned tasks, and compromised emergency egress operations. Currently, we know very little about cellular alterations that occur in the microgravity environment. A greater understanding of these changes will facilitate more effective countermeasure development in the future.

To study the molecular and cellular changes occurring in microgravity, it is essential to develop a suitable tissue model using human cells that can differentiate into mature human muscle cells. This will facilitate the evaluation of the effects of microgravity on the myoblast (precursor) and on mature muscle cells. Accordingly, the overall objective of these studies is to develop methods to isolate adult human progenitor cells from waste fat tissue, and to use these cells to construct human tissue-equivalent muscle models.

These were dedicated studies for generating skeletal muscle constructs to assess the effects of modeled microgravity on human muscle myoblast cells. We developed isolation methods, and the recovered adult progenitor cells were able to differentiate into multinucleated muscle myotubes and fat cells. Studies of muscle myoblasts in modeled microgravity, produced by culturing cells in the NASA-designed bioreactor (see photograph), showed the occurrence of gene expression alterations in modeled microgravity when compared to identical cells at unit gravity. These gene alterations are being used to elucidate the pathways affected by microgravity conditions so that effective cell-based countermeasures can be developed.

The overall objective of the study is to engineer a human muscle tissue-equivalent construct from progenitor (or adult) stem cells recovered from discarded human fat tissue. These muscle constructs have extensive and wide-ranging applications. For the human space program, these models will enable:

- Clarification of the mechanisms of space-induced muscle atrophy
- Development of cell-based intervention therapies and countermeasures for space-induced muscle atrophy
- Assessment of newly developed therapies and countermeasures using muscle constructs as a testbed
- Eventual replacement of damaged/lost muscle following injury or trauma using an individual's own cells.



The effects of this study will not only impact the human space program, however. Earth-based applications include developing a curative treatment of muscle diseases and burn/accident victims by generating replacement muscle tissue for transplantation, and the effective treatment of age-related and cancer-related muscle atrophy.