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A BIOGERONTOLOGICAL APPROACH TO ANALYSING THE RELATIONSHIP BETWEEN MICROGRAVITY-ASSOCIATED PHYSIOLOGICAL ALTERATIONS & CELLULAR SENESCENCE

Abstract

The aim of this research is to develop a novel and up-to-date approach on analyzing the relationship between microgravity related physiological alterations and cellular senescence. This is achieved through two primary objectives. Firstly, to create an analytical framework in order to critically assess existing evidence that suggests microgravity-associated physiological alterations share a common basis with and are an accelerated form of similar changes that take place in senescence. Secondly, to outline the case for a series of definitive experiments to discern whether such changes are in fact characteristic of senescence at the cellular level or merely resemble these changes in functional outcome as the reversibility of microgravity-related changes seems to imply.

The research is carried out through a fundamental realignment of perspective from a systems and metabolism orientated gerontological approach to a damage orientated 'biogerontological' approach in line with recent theories of cellular senescence. These theories focus upon the identification of terminal sources of damage resultant from metabolic deviations (intracellular and extracellular aggregation, cell loss, nuclear and mitochondrial mutations, protein cross-linkage, death-resistant cells), all of which are correlated and in certain cases directly linked to the age-related systems level changes that have been recorded (e.g.. increased basal cortisol and insulin levels, attenuated circadian rhythms, decreased muscle, neuronal and bone mass).

Proposed tests for future research are based upon animal models that have been extensively used in both (bio)gerontology and space-based research including Caenorhabditis elegans and Drosophila melanogaster and examine the effects of microgravity upon damage formation and known damage-inducing factors.

The results demonstrate that although there are some similarities between microgravity-related physiological alterations and cellular senescence, these lie in specific cellular systems such as muscular-skeletal systems. On the other hand, post-mitotic cells, which are found in large concentrations within other systems such as the nervous system, undergo markedly different changes.

This investigation clarifies the relationship between cellular senescence and microgravity-related changes in cellular physiology and so influences space biomedical research, by either helping avoid unnecessary conflation of two highly complex fields of research or unveiling the relationship between each. In so doing it also highlights damage accumulation as a potentially tractable bioengineering problem and thus introduces the concept of Strategically Engineered Negligible Senescence to the Space community. The outcomes of this research not only advance current understanding of fundamental gravitational biology but also have important applications for future research in this area and in age-related diseases on Earth.