Proteostasis of aging and stem cells

https://neurodegenerationresearch.eu/survey/proteostasis-of-aging-and-stem-cells/

Principal Investigators
Institution
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Country

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Proteostasis of aging and stem cells

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Research Abstract

While it is has long been noted that genome stability is a central function required for survival of stem cells, the role of protein homeostasis (proteostasis) has not been explored. With the asymmetric divisions invoked by stem cells, the passage of damaged proteins to daughter cells can destroy the resulting lineage of cells and possibly accelerate the aging process. Furthermore, the possible retention of damaged proteins by the stem cell can result in diminished stem cell function and possibly premature aging. Therefore, a firm understanding of how stem cells maintain their proteostasis is of central importance. Because experiments with mammalian embryonic stem cells have clearly demonstrated their capacity to replicate continuously in the absence of senescence, we hypothesize that these cells could provide a novel paradigm to study the regulation of proteostasis and its demise in aging. We have recently described that human embryonic stem cells (hESCs) exhibit high proteasome activity compared to their differentiated counterparts. This enhanced proteasome activity is necessary for hESC function. Furthermore, we have uncovered that PSMD11/rpn-6, a key proteasomal subunit, is required for this activity and its mode of regulation and conservation in the aging process of the invertebrate C. elegans. Moreover, ectopic expression of rpn-6 protects from the symptoms associated to Huntington’s disease. We hypothesize that, in addition to its regulation of the

proteasome, hESCs must differentially regulate multiple subcellular stress response pathways designed to protect the hESC from disequilibrium in the synthesis, folding, and degradation of its proteome. In this work, we will: 1) define the mechanisms by which enhanced proteasome activity controls hESC function; and 2) determine how other proteostasis pathways impinges upon hESC function 3) with an eye to understand how this network can be adapted to alleviate age-related pathologies such as Huntington’s disease.

Further information available at:

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