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Stem Cell Mitochondria during Aging

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Abstract

Mitochondria are the central hubs of cellular metabolism, equipped with their own mitochondrial DNA (mtDNA) blueprints to direct part of the programming of mitochondrial oxidative metabolism and thus reactive oxygen species (ROS) levels. In stem cells, many stem cell factors governing the intricate balance between self-renewal and differentiation have been found to directly regulate mitochondrial processes to control stem cell behaviors during tissue regeneration and aging. Moreover, numerous nutrient-sensitive signaling pathways controlling organismal longevity in an evolutionarily conserved fashion also influence stem cell-mediated tissue homeostasis during aging via regulation of stem cell mitochondria. At the genomic level, it has been demonstrated that heritable mtDNA mutations and variants affect mammalian stem cell homeostasis and influence the risk for human degenerative diseases during aging. Because such a multitude of stem cell factors and signaling pathways ultimately converge on the mitochondria as the primary mechanism to modulate cellular and organismal longevity, it would be most efficacious to develop technologies to therapeutically target and direct mitochondrial repair in stem cells, as a unified strategy to combat aging-related degenerative diseases in the future.

Keywords: Stem cells, Mitochondria, mtDNA, Regeneration, Degeneration, Aging

Introduction

Mitochondria are subcellular organelles which function as power generators within each cell. More than 2 billion years ago, the bacterial ancestors of mitochondria began a symbiotic relationship with eukaryotic ancestor cells in response to an increase in atmospheric oxygen on Earth. As these symbionts co-evolved with eukaryotes, most of the mitochondrial DNA (mtDNA) was transferred to and consolidated within the DNA of the eukaryotic nucleus. A remainder of 37 genes in the mitochondrial DNA of humans resisted this transfer during evolution. Of these 37 genes, 13 genes encode metabolic enzymes in the electron transport chain, 22 genes encode transfer RNAs and 2 genes encode ribosomal RNAs involved in mitochondrial protein translation. However, most mitochondrial proteins are encoded by the nuclear genome, dependent on the elaborate mechanisms that have evolved to allow each cell nucleus to control its mitochondria [1].