A gutsy way to extend longevity

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A commentary on

Modulation of longevity and tissue homeostasis by the Drosophila PGC-1 homolog dPGC-1 has recently emerged as an important determinant of fly life span (Biteau et al., 2010). The Drosophila midgut is maintained by multipotent ISC activity. ISCs undergo asymmetric division, giving rise to an identical daughter ISC and an immature enteroblast (EB) with differentiation potential (Michelli and Perrimon, 2006; Oehlstein and Spradling, 2006). In old flies, ISCs hyper-proliferate, but ISC daughter cells do not differentiate, which results in the accumulation of misdifferentiated ISC daughter cells, a phenotype thought to contribute to gut aging. For instance, genetic or environmental manipulations that prevent tissue maintenance have been associated with accumulation of ISCs, irregular ISC proliferation and differentiation patterns, and shorter lifespan (Biteau et al., 2010).

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The studies conducted by Rera et al. successfully demonstrate a new role for dPGC-1 and mitochondrial biogenesis in ISC homeostasis and longevity. How does it all work? dPGC-1 overexpression increases levels of anti-oxidative enzymes to decrease oxidative damage and conserve ISC homeostasis. Preserved ISC homeostasis is required for gut maintenance, which is necessary for normal energy supply and/or prevention of microbial or toxin overload. All of these factors may contribute to delaying the onset of age related phenotypes. As Zhou et al. (2011) suggested, it is also possible that an unknown factor/s released by ISC overexpression in ISCs/EBs regulates longevity directly or through affecting other longevity pathways. This work highlights the complex influence of dPGC-1 on aging at the cellular level as well as at the organismal level. Overall the data presented by Rera et al. (2011) links two major components of aging and has uncovered an attractive target for the modulation of aging.

CONCLUDING THOUGHTS

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