

Stem cells and (healthy) aging

- “disposable soma” theory ^(see 1):
 - resources are allocated either to survival or reproduction
 - essential for the propagation of the species in the wild
- “protected aging” when species are protected from extrinsic causes of mortality
 - emergence of phenotypes of
 - aging
 - age-related diseases that would rarely manifest in the wild
 - Organismal aging is the failure of an integrated system that balances genetic programs for
 - survival
 - Reproduction
- The ability of an organism to ensure healthy function during adult life depends on homeostatic mechanisms.
 - in organs of mature vertebrates resident stem cells participate
 - in tissue maintenance
 - regeneration after injury,
 - tissue dependent variations of the stem cell role in homeostasis/ injury recovery ^(see e.g. 3)
 - **ongoing generation** but play a limited role in damage repair
 - minimal role in maintenance but vigorously engage in **regeneration after injury**
 - contributing to **ongoing production** of differentiated cells and **repairing tissue** after injury.
- during “protected aging” the extent to which stem cells maintain their cognate tissues depends on their own health ^(see 2) is influenced by
 - genetic mutations ^(see e.g. 4,5)
 - epigenetic changes ^(see e.g. 6,7)
 - extrinsic environmental milieu ^(see e.g.,8,9)

- (1) T. B. Kirkwood, Understanding the odd science of aging. *Cell* 120, 437–447 (2005).
- (2) L. Liu, T. A. Rando, Manifestations and mechanisms of stem cell aging. *J. Cell Biol.* 193, 257–266 (2011)
- (3) J.S. Welch et.al., The origin and evolution of mutations in acute myeloid leukemia. *Cell* 150, 264–278 (2012)
- (4) T Krieger et al., Dynamic stem cell heterogeneity. *Development.* 142, 1396-1406 (2015)
- (5) I. Martincorena et al., High burden and pervasive positive selection of somatic mutations in normal human skin. *Science* 348, 880–886 (2015)
- (6) D. Sun et al., Epigenomic profiling of young and aged HSCs reveals concerted changes during aging that reinforce self-renewal. *Cell Stem Cell* 14, 673–688 (2014) (6) L. Liu et al., Chromatin modifications as determinants of muscle stem cell quiescence and chronological aging. *Cell Rep.* 4, 189–204 (2013)
- (7) I. M. Conboy et al., Heterochronic parabiosis for the study of the effects of aging on stem cells and their niches. *Cell Cycle* 11, 2260–2267 (2012)
- (8) J.C. Fischer et al., Bone-marrow derived progenitor cells are associated with psychosocial determinants of health after controlling for classical biological and behavioral cardiovascular risk factors. *Brain Behav Immun.* 23, 419-426 (2009)