Internship Proposal

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Project Title:
Rejuvenating interventions in models of natural and accelerated ageing

Level:

Master Student

Project Summary:

Launched in 2017, the group headed by E. Logarinho has been studying mechanistic links between ageing and aneuploidy, two conditions that exhibit common hallmarks. Initial contributions arose from the group's expertise in combining high-resolution live-cell imaging with advanced molecular/cellular biology techniques to characterize phenotypes of unique cellular models, human trisomic amniocytes [Elife 2015, Sci Rep 2016] and elderly dermal fibroblasts [Nat Commun 2018, EMBO Rep 2020]. These studies unveiled chromosomal instability (CIN) as a hallmark in both aneuploid and aged cells. Moreover, we disclosed genetic and pharmacological modulations of ageing-associated CIN as able to delay the senescence pro-inflammatory response. These findings paved the way to our current and future research goals, aiming to deepen the understanding of ageing mechanisms [BioRxiv 2023] and to test new schemes of healthspan extension in animal models [Nat Aging 2022].

Work to be developed by the student:

Several projects within two major lines of research in the lab are available to be developed by master students:

1. FOXM1 as an age reversal factor

Fundamental research will link FOXM1 master role in DNA repair to chromatin epigenetic remodeling and partial cellular reprogramming of aged cells. Translational research using animal models will explore the FOXM1 rejuvenating effect in the immune system and the efficacy of an innovative FOXM1-T cell immunotherapy against age-related dysfunction.

2. Validate FOXM1 and KIF2C as rejuvenation factors in immune cells of progeroid models

We will explore the therapeutic value of FOXM1 gene induction and KIF2C agonist treatment in models of accelerated immune ageing, namely Down syndrome.

References:

Macedo JC, Vaz S, Bakker B, Ribeiro R, Bakker PL, Escandell JM, Ferreira MG, Medema R, Foijer F, Logarinho E. FoxM1 repression during human aging leads to mitotic decline and aneuploidy-driven full senescence. Nat Commun. 2018 Jul 19;9(1):2834. doi: 10.1038/s41467-018-05258-6.

Barroso-Vilares M, Macedo JC, Reis M, Warren JD, Compton D, Logarinho E. Small-molecule inhibition of aging-associated chromosomal instability delays cellular senescence. EMBO Rep 2020. doi: 10.15252/embr.201949248. highlighted in: Tovini L and McClelland SE. EMBO Rep 2020. doi: 10.15252/embr.202050322.

Ribeiro R, Macedo JC, Costa M, Ustiyan V, Shindyapina AV, Tyshkovskiy A, Gomes RN, Castro JP, Kalin TV, Vasques-Nóvoa F, Nascimento DS, Dmitriev SE, Gladyshev VN, Kalinichenko VV, Logarinho E. In vivo cyclic induction of the FOXM1 transcription factor delays natural and progeroid aging phenotypes and extends healthspan Nat Aging 2022. doi: 10.1038/s43587-022-00209-9. highlighted in: Ouchi Y., Sahu S. K. and Belmonte J. C. I (2022). Nat Aging vol 2, pages 373-374 (News & Views).

Ferreira FJ, Galhardo M, Teixeira J, Logarinho E*, Bessa J*. FOXM1 expression reverts aging chromatin profiles through repression of the senescence-associated pioneer factor AP-1. BioRxiv https://doi.org/10.1101/2023.05.04.539315 (under revision in Nat Commun).
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