Exploring *Caenorhabditis elegans* in aging research: healthspan parameters and ferroptosis during lifespan

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One of the main challenges of the 21st century is the progressively aging society: life expectancy has greatly increased in the past few decades, without being accompanied by a similar increment in healthspan. In fact, considering that aging is a time-dependent progressive decline in physiological functions, an increase in frailty and a growing risk of disease are direct consequences (previously published in Yu M et al. (2021) Cells 10(3), 660).

Therefore, research is now focusing on identifying actions to promote a healthier aging, rather than just extending lifespan. A promising strategy to reduce frailty is targeting ferroptosis, a newly discovered mode of cell death that is caused by massive lipid-peroxidation mediated membrane damage, triggered by the accumulation of intracellular ROS and iron. Drugs that block lipid peroxidation or scavenge intracellular iron have already been proven to be beneficial at specific late points in *C. elegans*'s lifespan (previously published in Larrick JW et al. (2020) Rejuvenation Research 23(5), 434-438).

Here, the decline of the main healthspan parameters during lifespan has been analyzed in the N2 wild type strain. These behavioral studies allowed us to identify the days 4, 7, 14 as the time points of lifespan in which the main phenotypic changes occur. Afterwards, molecular studies were carried out on animals collected in the identified time points. In particular, fluorescent assays and real time PCR analysis were performed on worm lysates in order to follow ROS levels and gene expression changes over time. The tested genes were selected from DEG induced by pro-longevity frataxin silencing, based on their possible involvement in the ferroptotic process (previously published in Schiavi A et al. (2023) Iscience 26(4)). As expected, a progressive increase in ROS levels during lifespan could be observed and the selected genes were found to be mostly downregulated, supporting their role as inhibitors of the ferroptotic process.