Case Study: Module 7 Aging (Part 1)

Methods in Neurobiology

Overview

In this assignment you are asked to write a short research proposal focused on aging research employing techniques and/or organisms models presented in modules 2 through 7.
This a 20-point assignment.

Instructions

1. The study of Aging focuses on discovery new mechanisms related to cellular or systemic senescence. Develop a short research proposal where you will describe one or more experiments (1-2 pages max, not including citations) to further improve our understanding of the aging process using models and techniques introduced in module 2-7.
2. This proposal can include a new model (see example) or a new protocol that can be used in aging research. Describe then how you would apply this method to the study of aging.
3. Include the appropriate references, following the usual format.

Example

Background
During normal metabolism, reactive oxygen species (ROS) are produced in all cells from the respiratory chain of the mitochondria. These ROS have the capacity to oxidize and damage a variety of cellular constituents including lipids, DNA, and proteins. An increase in ROS production has been shown during aging and it is thought that oxidative stress plays a pivotal role in cellular senescence[1].

Aim
Build a model that can help understand the impact of ROS on cellular senescence.

Research Plan
To understand the effect of ROS production on aging and life expectancy, I have taken a genetic approach and cross *C. Elegans* knock out (KO) worms for the *daf2* gene (*daf2 -/-*), that have an extended life expectancy of about 30-40 days when kept at 25C, with a *C. Elegans* KO line for *SOD1 (SOD1 -/-)*, a gene whose product is implicated in detoxifying ROS. Offspring was selected to develop a new line of *C. Elegans* mutants, a double KO for *Daf2-/-; SOD1 -/-*. Deletion of SOD1 should result in a massive over accumulation of ROS. If ROS accumulation contributes to aging, double mutant *daf 2 -/-; SOD 1-/-* will have a shorter life span than single mutants for *daf2*.
Double (*Daf2-/-; SOD1 -/-)*, single mutants (*Daf2-/-* or *SOD1 -/-)* and wild-type lines of C. Elegans will be then aged and observed for up to 2 months and the survival curve of all the animals will be recorded.
Thus, by comparing the life expectancy of the double mutant against the single mutants this strategy can infer on the contribution of oxidative stress to aging.
This model can be then used to test modifications such as treatments or compounds that can improve aging by targeting accumulation of ROS and to study in greater details pathways that can link ROS production to aging.

1. Ana L. Santos, Sanchari Sinha, Ariel B. Lindner, "The Good, the Bad, and the Ugly of ROS: New Insights on Aging and Aging-Related Diseases from Eukaryotic and Prokaryotic Model Organisms", *Oxidative Medicine and Cellular Longevity*, vol. 2018. https://doi.org/10.1155/2018/1941285.