Case Study: Module 8 Aging (Part 2)

Methods in Neurobiology

Overview

In this assignment you will be paired with another student and ask to analyze their work from Part 1 (Module 7). In this assignment, you can include techniques learned in Module 5.
This is a 20-point assignment.

Instructions

Once paired with another student, review your coworker's project illustrated in Part 1. The review will have to include:

- An initial sentence/small paragraph to summarize the project you are reviewing.
- Then answer the following questions using at least 1-2 sentences or bullet points:
    - Do you think that their research plan is scientifically sound and appropriate? Why?
    - Is there a more successful strategy or model that could be used to solve their scientific question? If yes, illustrate your plan. If no, explain why.
- Please include references. Your work should be 1 page max (not including citations).

Example

Part 1:

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.

Part 2:

Student A's research plan aims to investigate the contribution of oxidative stress and production of ROS in aging. To do that, a genetic approach that would compare the life span of *C. Elegans* mutants for SOD1, a protein implicated in detoxifying ROS in cells, and *daf2*, a longevity gene, would be employed.

Such approach is a well-structured strategy that takes advantage of *C. Elegans* short life span and easy manipulation. The use of wild-type strains as well single and double mutants in his analysis, provides a more complete view of the phenomenon by showing if SOD1 can be a good target for oxidative stress reduction in this organism.

Another strategy that could be employed, would be to treat *C. Elegans daf2 -/-* mutants chronically with peroxide (maybe choosing increased amount of concentration) and test how such treatment improves or shortens life span of those strains. This type of approach may be more straightforward that a genetic approach because it does not require the production of new genetically engineered strains of *C. Elegans* (like the SO 1 mutants) but can be conveniently tested right away. Because it is more elementary though, the result will only inform us about oxidative stress and aging, but not about cellular pathways implicated in ROS detoxification.