**Study the aging dynamics of the E. coli gene networks**

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1. **Introduction**

**1.1 Statement of the research problem, Goals and Objectives.**

For years people have wondered the cause of aging, when it starts, and what the aging markers are. Many have explored different theories on aging, none unraveling the true causes of it. As an attempt to understand aging, we will explore a single cell and how it relates to its different organelles. Thus, giving a better understanding of aging and its effects on the body. Mitochondrial aging is known to be a major cause of human aging and disease.

**1.2 Endosymbiotic theory, aging of mitochondria and E. coli**

The mitochondria has a proteobacterial origin based on the endosymbiotic theory. This theory states that the mitochondria is a result of years of evolution created by endocytosis of bacteria. The bacteria are not digested; it became symbiotic instead. Endocytosis requires a cell to engulf another cell without passing through the membrane, which will create a double membrane. This process results in the outer membrane trapping in the foreign material causing an intracellular vesicle to form. Ultimately creating organelles such as the mitochondria.

Mitochondrial aging is a main cause of human aging, because the aerobic respiration that occurs inside of mitochondria produce reactive oxygen species (ROS) as byproducts. ROS are highly reactive molecules with unpaired electrons that can react with intracellular macromolecules and prevent them from performing normal functions. At the center of the free radical theory of aging lies the very important role of the mitochondria.

The free radical theory of aging states that highly reactive molecules with unpaired electrons, termed as free radicals, cause oxidative damages to macromolecules within cells; thereby hindering normal biological functions. Mitochondria produce more reactive oxygen species such as superoxide radical and hydroxyl radical. These oxygen species with unpaired electrons are highly reactive and can damage the mitochondria’s DNA and proteins. The damaged mitochondria will then produce more ROS. This vicious cycle gradually leads to catastrophic consequences and is a major cause of aging.

*Escherichia coli* is a model organism in the phylum proteobacteria, and therefore is informative on mitochondrial aging. *E. coli* is a great model for mitochondria because they reproduce in the same manner. *E coli* is an organism with asymmetric division, no juvenile phase, and no identified separation between germ line and soma; making it still susceptible to aging. Ituses asymmetric division that will exhibit no distinction between the parent and offspring. This division requires an old pole from the parent cell and builds a new pole with the occurring offspring. A Juvenile phase requires a cell to go through a time of growth or differentiation from the parent cell. *E. coli* does not demonstrate this phase and allows for immediate rejuvenation of the offspring.

**1.3 Gene network model of cellular aging**

Aging is defined as the increasing chance of failure with time. Recently, Qin proposed a gene network model of cellular aging. The basic idea of this network model of cellular aging is to use the random failure of gene interactions to model the declining of cellular activities. When an essential gene loses all of its gene interactions, it is equivalent to the deletion of essential genes and thereby leads to cell death. We will apply this general framework to study the aging of *E coli* gene networks.

­­­To test our modeling work, we will compare the aging process of the E coli gene network with experimental data. We will implement this modeling work in the open source language R environment.

**1.4 Significance of Study**

By understanding how E. Coli gene networks interact within its system we will be able to model how the mitochondrial gene networks. The relationship between the mitochondria, organelle, and the overall cell will give us different insights on how aging relates to single cells and the entire body. The mitochondria plays a major role in the production of energy for the cell. If the damages in the mitochondria affect the operation of the overall cell and leads to cell deterioration, cellular aging, we are now able to explore how to strengthen single organelles to control aging. We plan to bring a clear understanding of the importance of the mitochondria and its relation to the existence of the cell. It is important to know that the mitochondria has its own nucleus and the connection between the cells nucleus and the mitochondria’s nucleus will also give a better understanding of their connecton.

**1.5 Hypothesis**

One of the major causes of human aging, mitochondrial aging, can be understood through the modeling of E. Coli gene networks.

1. **Methodology**

2.1 Materials

The gene networks of E coli is availabe at the Database of Interacting Proteins (DIP) (<http://dip.doe-mbi.ucla.edu/dip/Download.cgi?SM=7&TX=562>). There are 12263 pairwise gene interactions in this network data set.

E.Coli gene network database is also available at EcoCYC

The list of essential genes in E coli is availabe at EcoWiki ( <http://ecoliwiki.net/colipedia/index.php/Essential_genes> )

2.2

1. **Timeline**
2. **Reference**

|  |  |  |
| --- | --- | --- |
| Description | Quantity | Price |
| Travel to meetings |  | $1500 |
| PeerJ Membership for publications |  | $350 |
| Endnote software |  | $300 |
| Consultant Fee |  | $500 |
| Stipend |  | $4000 |

1. **Budget**