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REPORT

Centenarian Rockfish

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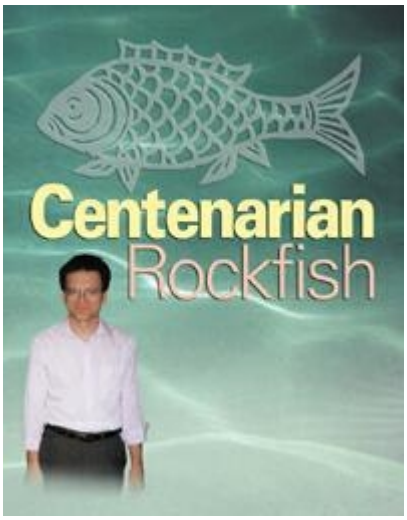

Usually we do not tend to think of our dinner contents in terms of age. But if you were told the fish you had for supper was 100 years old, what would you think? Believe it or not, people are eating rockfish that were born around the turn-of-the-century! And according to John C. Guerin, Centenarian Rockfish Project Director at Oregon State University, there is no difference in taste or texture between centenarian and younger rockfish.

Recent analysis of commercial catches of rockfish showed that 16% were more than 50 years old, and several had reached, if not surpassed, the 100-year-old mark.

But these fish are not only long-lived, they don't grow old! Instead, they manifest what is known as negligible senescence-chronological aging without increased mortality. In other words, they continue to grow and reproduce after reaching maturity but show no evidence of senescence. In fact, fecundity increases with increasing age.

How do we know these fish are that old? What mechanism(s) allow them to live so long without aging? Can humans benefit from such knowledge?

These are the questions that Guerin considered as he learned more about these fish. He had always been interested in the problems of aging but was fascinated by the idea of growing older chronologically without senescence.

The Guerin studied the phenomenon of negligible senescence, the more passionate he became because he discovered the paucity of research that had been done in this area. Determined to fill this void, he began to assemble a network of scientists who could apply the principles of gerontological research to these issues.

Currently, the principal investigators on the project are Dr. Jerry D. Hendricks, a fish pathologist, and Dr. David E. Williams, a biochemist, both of Oregon State University. Serving as informal advisor is the noted gerontologist Dr. Leonard Hayflick of the University of Southern California at San Francisco.

It was Hayflick's research that led to what is known as the "Hayflick limit": normal, human cells in culture are limited to about 50 cell divisions. This is because some of the information encoded in telomeres at the tips of chromosomes is lost each time the cell divides. Subsequently, it was learned that addition of the enzyme telomerase prevents the loss of telomere DNA, so cell division continues.

Rockfish are also known as Pacific Ocean perch and belong to the genus Sebastes, which has some 70 species. They are among a few species of vertebrates- animals with backbones- that can have lifespans exceeding 100 years. Others include sturgeon that hold the record of 154 years, turtles, whales and humans. What is interesting about turtles and rockfish is that they do not become senescent.

Guerin and coworkers found that rockfish satisfied the criteria for selecting the ideal species in which to study negligible senescence: (1) live 50 years or more; (2) are not endangered; (3) are readily available for research; (4) if fish, live near the surface; (5) manifest limited hibernation/torpor.

The species selected for the Centenarian Rockfish Project were yelloweye rockfish (S. ruberrimus) and rougheye rockfish (S. aleutianus).

One of the more important aspects of studying longevity in animals is accurate determination of age. While various methods are in use, most are not applicable to fish. Even the technique employed by fishery biologists, the analysis of length-frequency data, could not be used in Guerin's work because it cannot be used to determine the age of an individual fish. Consequently, the otolith method is being employed. It is based on the fact that fish scales and certain bones reveal annual growth rates via growth rings that are laid down in these structures. These rings are analogous to the rings visible in the cross section of a tree trunk, and are counted to determine age.

Otoliths are bony parts of the ear in all species of vertebrates, and are located on each side of a fish's head. They are made up of three bones of which one is used routinely for processing. It is removed, processed, and ground thin enough so that the annual growth rings can be seen through a microscope and counted. Using otolith method, Guerin's team determined the age distributions of three separate rockfish collections off the coast of Sitka, Alaska. The oldest specimen in each collection was 109, 107 and 93 years old.

To begin their pioneering studies of negligible senescence in these fish, Guerin formulated the following working hypothesis: "... [rockfish], which survive to old age, must have mechanisms for preventing or repairing oxidative damage." In order to test this hypothesis, Dr. Williams is examining rockfish livers for evidence of oxidized protein and DNA adducts (damaged DNA). He is also searching for "antioxidants that may prolong lifespan and function as chemoreceptive agents against diseases by inhibiting this oxidative damage." These efforts represent the first attempts to study the biochemical basis of negligible senescence.

Preliminary results of these studies have shown that lipid peroxidation in liver microsomes was significantly reduced compared to rat and monkey liver microsomes. Since biochemical markers of oxidative stress tend to increase with increasing age, it appeared that some mechanism was protecting the rockfish from oxidative reactions. Whether this mechanism results in negligible senescence remains to be seen.

Consider the possibilities for a moment. Suppose the basis of negligible senescence turns out to be genetic. In light of scientists' ability today to successfully insert genes into another species' genome, it is conceivable that a gene for negligible senescence could be inserted into the human genome. Currently, scientists worldwide are working on The Human Genome Project to map every gene on our chromosomes, and expect to complete it in the year 2005. This effort will increase our understanding of human growth, development, aging and disease.

To determine whether rockfish tissues manifest histological (microscopic study of tissues) evidence of senility, Dr. Hendricks is examining samples of rockfish liver, spleen and kidney. Preliminary results showed an increase in the number of melano-macrophage centers with age. These are repositories or deposits commonly seen in fish where macrophages accumulate after phagocytosing breakdown products of metabolism, including cellular debris and remnants of mitochondria. These substances are in the form of fatty pigments called "lipofuscins" that primarily consist of oxidized fats. While the significance of this observation is not known, their increased number did not appear to affect organ function.

Guerin is planning additional studies such as investigating anion exchange proteins in rockfish brain tissue. These proteins are known to increase with age in humans, especially in regions of the brain affected by Alzheimer's disease.

Recently, other researchers reported that rainbow trout and lobsters, which continue to grow throughout their lifespans, have high levels of telomerase in their tissues. Guerin plans to study telomerase activity in rockfish to determine any possible connection between the enzyme, continued growth and negligible senescence.

Further studies may also include coenzyme Q10 because of its antioxidant and mitochondria-stabilizing effects, and a biochemical technique called "profiling." Guerin believes profiling "could be a very effective 'shotgun' approach [to] explaining the negligible senescence of rockfish. [The technique] could test for well more than one hundred chemicals, including antioxidants, proteins, enzymes, hormones, etc." In the long run, such studies of negligible senescence may well provide clues that lead to strategies for increased longevity in humans.

References

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