Spry Worms — Aging Genes

Secrets of the Sequence Video Series on the Life Sciences • Grades 9 – 12

Teaching materials developed by VCU Life Sciences.

Virginia Commonwealth University

Classroom Tested Lesson

Video Description

"Secrets of the Sequence," Show 126, Episode 3

"Spry Worms" – approximately 9.30 minutes viewing time.

Cynthia Kenyon's roundworms at the University of California, San Francisco have defied the grim reaper. They're living twice as long as they should. Why? It's in the genes.

Ward Television
Producer: Elizabeth Pearson
Associate Producer: Kelly Phipps
Featuring: Cynthia Kenyon, Biochemistry, University of California – San Francisco
Lesson Author; Reviewers: Catherine Dahl; Dick Rezba
Trial Testing Teachers: Shelley Mitchell, Martin Shields

National and State Science Standards of Learning

National Science Education Standards Connection

Content Standard A: Science as Inquiry

As a result of their activities in grades 9-12, all students should develop:

- Abilities necessary to do scientific inquiry
- Understandings about scientific inquiry

Content Standard C: Life Science

As a result of their activities in grades 9-12, all students should develop understanding of

- The cell
- Molecular basis of heredity
- Behavior of organisms
- Biological Evolution

Selected State Science Standards Connections

Use http://www.eduhound.com (click on "Standards by State") or a search engine to access additional state science standards.

Virginia

BIO.1 The student will plan and conduct investigations in which

a) Observations of living organisms are recorded in the lab and in the field;

b) Hypotheses are formulated based on direct observations and information from scientific literature;
e) Conclusions are formed based on recorded quantitative and qualitative data;
g) Validity of data is determined;

BIO.6 The student will investigate and understand common mechanisms of inheritance and protein synthesis. Key concepts include:
e) Genetic variation (mutation, recombination, deletions, additions to DNA);
h) Use, limitations, and misuse of genetic information; and
i) Exploration of the impact of DNA technologies.

Illinois

STATE GOAL 11: Understand the processes of scientific inquiry and technological design to investigate questions, conduct experiments and solve problems.

- 11.A.5a Formulate hypotheses referencing prior research and knowledge.
- 11.A.5b Design procedures to test the selected hypotheses.
- 11.A.5c Conduct systematic controlled experiments to test the selected hypotheses.

STATE GOAL 12: Understand the fundamental concepts, principles and interconnections of the life, physical and earth/space sciences

- 12.A.5b Analyze the transmission of genetic traits, diseases and defects.

Overview

This video outlines a 10 year scientific project that looks at the genetic sequence of the roundworm. This project has enabled scientists to manipulate some of the genes in that sequence in order to slow down the aging process of the worm. Scientists at the University of California – San Francisco have determined two genes that seem to be specifically associated with this aging process. One is DAF 16 that keeps us looking and acting young, and one is DaF 2 that appears to regulate DaF 16. By manipulating these genes, they have successfully altered the aging in worms. The idea that this could be extended to humans with the manipulation of a "fountain of youth" gene is enormously interesting and, of course, controversial. In addition, it is not clear whether or not the aging process may occur differently in humans and in roundworms, or whether it is just a matter of scale. It also must be remembered that the manipulating of genes is extremely complicated.

Telomeres, repeating sequences of DNA located on the ends of chromosomes, are an example of another gene that was initially associated with aging and thought maybe to be a "wonder gene". Scientists determined that telomere function was to facilitate cell division. However, although active in the early stages of human growth, the telomeres found on the end of chromosomes get shorter with successive cell divisions and chromosome matching. Therefore if telomeres were activated in older cells to create "immortal cells", scientists would be doing a great disservice to the patient. These "immortal cells" are merely another word for "cancer cells" (cells whose division is uncontrolled) and the disease would instead curtail the longevity of the patient dramatically. So far, no such concerns have arisen in the study of these roundworms so further exploration into DAF 16 and DAF 16 continues.

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Testing: A sample related multiple choice item from State Standardized Exams

Chromosomes are most easily seen during cell division because the chromosomes:

a) double in number

b) shorten and thicken *
c) move and expand
d) match up with other chromosomes

Source: Mississippi Subject Area Testing Program: Biology Test - 1

Video Preparation

Preview the video and make note of the locations at which you will later pause the video for discussion.

Before Viewing

1. Conduct a discussion to introduce the topic of aging using some of the following questions. Students will return to these questions after they have watched the video to note any changes in their responses.
   - What is today's average lifespan of a human being?
   - What was the average lifespan of a human 100 years ago, 1000 years ago?
   - How old do you consider old?
   - What is the meaning of life expectancy?

2. Ask: "What kinds of things affect the "normal" process of aging?"
   - *Health habits*
   - *Country of residence*
   - *Cultural practices*
   - *Specific diseases*
   - *Natural disasters*
   - *Accidents*
   - *Genes*

3. Ask: "Do you think it is likely that scientists will be able to "control" the aging process or does that sound like science fiction?"

4. If you were to study the aging process, what would make a good test subject (plant or animal species) and why? Consider life span, gestation period, space available, care needed, etc.

During Viewing

1. **START** the video.

2. **PAUSE** the video (4:48 minutes into the video) after the scientist says, "…we have quadrupled the lifespan!" Remind students that they have just viewed a section of the video describing how researchers have found two genes called DaF 16 and DaF 2, both of which are associated with the aging process.

   Ask: "Can you explain the major difference between them?"

   DaF 16 is associated with healthy young cells (life) while DaF 2 regulates DaF 16 in such a way that it is associated with the end of the life cycle (death).

3. **RESUME** the video and play to the end**.**

After Viewing

1. Ask: "What new idea is the scientist in this video proposing that is different from the widespread view on aging?"

   The prevailing view on aging is that it is natural and passive but this scientist suggests that it is highly regulated and therefore controllable and able to be manipulated.

2. Ask: "Can you give four reasons why this scientist uses round worms in this study on aging?"
   a) *round worms are multi-celled animals with similar organs to humans but are small and easy to maintain*
   b) *round worms are relatively transparent and easy to study*
   c) *the round worm genome has been fully sequenced*
   d) *life cycle of a round worm is approximately 30-45 days. Such a study would be very difficult with species that have life spans in years, decades or centuries.*

3. Ask: "Why must scientists be careful about drawing conclusions about human aging based on animal studies?"

   Some answers may include:
   - *Animals may be susceptible to diseases that would not affect humans.*
   - *Life spans of animals used in many experiments are often quite short and therefore scientists do not know the long-term effects of the study.*
   - *Although humans and other animals share many genes there are also many differences.*
   - *Genetic influences on aging may be more complex in humans than in roundworms.*

4. Ask: "What does "spry" mean? How is the title "Spry Worms" appropriate for the research on the video?"

   Spry means "lively" or "active". It is appropriate because by manipulating the DaF 16 and DaF 2 genes, the scientists were able to make aged worms appear youthful and "active".

5. Have students do additional research on aging and telomeres to understand the consequences of "turning on" a gene associated with potential immortality.

Teacher Notes for the Student Activities

Choose between the following two short activities or, if time permits, use both. Alternatively, the second activity could be given as a homework assignment followed by an in-class discussion.

- Science of Aging (Student Handout A)
- The Paradox of Immortality (Student Handout B)

1. Depending on which activity you choose, give each student a copy of the Handout.

2. Have students read the article in that particular Handout.

3. For the students who have read the article in Handout A, divide them into small groups of 2 or 3.
   For the students who have read the article in Handout B, have them work on their own.

4. For Handout A, have students discuss and answer the questions on their handout.
   For Handout B, have each student write a paragraph in response to one of the three bullet points offered.

5. Follow each activity with a class discussion.

Student Handout A: Science of Aging

Introduction

This is an activity to help you think about what "aging" really means. You will read excerpts from an article and then answer questions relating to the article.

Part 1: Read the following excerpts from *The Science of Aging*:

With advancements in health and medicine, along with a better understanding of the aging process, life expectancy for humans keeps increasing. It is probable that the life expectancy of today's middle-school students is going to be longer than the life expectancy of current adults.

There appears to be a maximum life span for each species, including humans. Although some humans live more than a hundred years, most do not; the average length of life, including individuals who die in childhood, ranges from as low as 35 in some populations to as high as 75 in most industrialized nations. The high averages are due mostly to low death rates for infants and children but also to better sanitation, diet, and hygiene for most people, and to improved medical care for the old. Life expectancy also varies among different socioeconomic groups and by gender. The most common causes of death differ for various age, ethnic, and economic groups. In the United States, for example, fatal traffic accidents are most common among young males, heart disease causes more deaths in men than women, and infectious diseases and homicides cause more deaths among the poor than among the rich.

The aging process in humans is associated not only with changes in the hormonal system but also with disease and injury, diet, mutations arising and accumulating in the cells, wear on tissues such as weight bearing joints, psychological factors, and exposure to harmful substances. Sometimes diseases that appear late in life will affect brain function, including memory and personality. In addition, diminished physical capacity and loss of one's accustomed social role can result in anxiety or depression. On the other hand, many old people are able to get along quite well, living out independent and active lives, without prolonged periods of disability.

There have been two main traditional methods by which scientists study the effects of human aging. One is to compare the physical and mental skills of a large group of people and evaluate the group for differences across the different age groups. This type of study is called a cross-sectional study. This method is not always effective since some of the observed differences may be more of a result of the time period they lived in, (such as changes in nutrition over the years or environmental changes such as air or water pollution) rather than aging directly.

Another method examines changes in one group of people over a long period of time. This kind of study is called a longitudinal study. This method is often considered superior to the first since it measures changes over time among individuals, rather than comparing differences across age groups.

Clearly with the onset of genetic studies such as those undertaken by Dr. Cynthia Kenyon in the video you have just seen, the study of aging is taking a completely new and revolutionary turn. The concepts of control, regulation and manipulation are central to these newer scientific studies. As you answer the following questions (some of which were discussed earlier in this lesson), consider how this new field of study may change your original thoughts about aging.

Part 2: In small groups discuss the following questions: NOTE: some of these questions have no "right" or "wrong" answers.

a) Why do you think some species live longer than others? (Consider both animals and plants.)

_____

b) Name several species that you think have the longest average life span. How long are their life spans?

_____

c) Name several species that you think have the shortest average life span? How short are their life spans?

_____

d) What does "old" mean to you? Define "aging".

_____

e) What characteristics come to mind when you think of an old person? A young person?

_____

f) Do you think you will have any control over how you age? What behaviors might influence whether you show signs of aging sooner or later?

_____

g) What effect do you think your genes have on aging?

_____

h) Why would a gene exist that limits the lifespan of individuals?

_____

i) What effects do you think nutrition and your eating habits (balanced diet, eating "on the go", etc.) have on aging?

_____

j) Who is likely to live longer—single people or married/partnered people? Why?

_____

k) What effect do you think education (high school, college, and beyond) has on aging? As people age, does staying mentally active have any effect on their quality of life? How and why or why not?

_____

l) What effect do you think income has on aging?

_____

m) What effect does stress have on aging?

_____

n) What effect do you think residential area (city, rural, suburban, etc.) has on aging?

_____

o) If a pill/injection /treatment became available that could extend your life expectancy to 130 healthy, active years, would you want to have it? Explain? What would be the implications for society?

_____

p) What would it be like if some people took a treatment that extended their life expectancy but others didn't? Or, if some babies were born with genetic modifications to extend the span but others weren't?

_____

**Some questions adapted from http://www.secretsofaging.org/body/how.html and http://www.sciencenetlinks.com/lessons.cfm?BenchmarkID=6&DocID=191*

Student Handout B: The Paradox of Immortality

Introduction

This is an activity to help you understand the consequences inherent in manipulating our genetic code in order to "turn on" what we may think is a "Fountain of Youth" gene. There are also issues of "vitality" as well as "longevity". "Vitality" is a measure of the quality of life.

Part 1: Read the following excerpts from the article **"The Paradox of Immortality***"* by Morgan Lyons.

The same biology that allows cancer cells to divide indefinitely may hold the answers to human aging.

The tip of something is usually considered little more than an end point. But cell biologist and neuroscientist Drs. Jerry Shay and Woodring Wright have discovered that the tips of chromosomes may hold the beginning of hope for cancer patients and for people hoping to defy old age.

The Telomere
Telomeres reside at the end of chromosomes and shorten each time a cell divides. They are composed of specific repeated segments of deoxyribonucleic acid (DNA) -- the material containing the genetic code of a cell. Eventually, healthy telomeres shorten, and the cell stops dividing and enters senescence, or the state of being old.

Human cancer cells do not follow the same schedule. Some cells live too long, and some become what Shay and Wright call "immortal." Instead of shortening, the tumor cell produces an enzyme not found in normal cells -- telomerase, which maintains the length of the telomere, allowing it to divide indefinitely.

Shay and Wright first presented their model of cell aging nearly 10 years ago. Their ideas helped explain how cells become immortal. They also speculated that the changes brought about by an "ageless" cell may contribute to a greater understanding of how humans age. The two professors of cell biology and neuroscience generated international attention when they manipulated the length of telomeres to alter the life span of human cell hybrids. However, cell immortality is a critical step in the progression of cancer and 85 percent of all primary human tumor types exhibit telomerase activity.

Telomeres and cancer
The clinical applications of telomere biology are significant. Many investigators believe the ability to measure and perhaps alter telomere length and/or telomerase activity may one day give physicians new diagnostic and treatment tools for managing the care of patients with cancer. "There are lots of markers for cancer," Shay said. "This one, singly or together with other markers, may give us a new way of catching cancer before it becomes advanced and difficult to treat." For example, telomerase plays an important role in the development of neuroblastoma, a common and often fatal cancer of childhood. . Early diagnosis and treatment of the disease is very important, and the telomerase test could help clinicians plan more effective therapy.

Telomerase activity also has been linked with the development of lung cancer. In fact, Shay and Wright's research may help physicians determine which patients who smoke are more likely to get lung cancer.

While a clear link between the presence of telomerase and patient survival has not been established, the ability to detect telomerase activity still could give clinicians valuable additional information about the patient's prognosis and treatment options. In one study, telomerase activity was found in more than 90 percent of advanced breast cancers

and in nearly one-third of less-advanced cancers. Clinicians can use that kind of information to determine a patient's need for surgery compared with other treatment choices.

Measuring telomerase also helps determine the effectiveness of cancer therapy. By measuring telomerase in blood cells from patients with acute myelogenous leukemia, Shay and Wright found that the chemotherapy that killed the cancer cells also inhibited telomerase expression. Knowing telomerase levels before and throughout treatment could alert the physician to the need for more aggressive treatment, which might prevent a relapse.

The key to human aging

Just as the telomere explains the progression of cancer, it also presents a clearer understanding of how humans age. Shay and Wright wanted to find out if they could manipulate the length of telomeres to alter the life span of human cells. By lengthening the telomere they were able to extend the life of the new cell hybrids so that they "now know there is a causal relationship between telomere length and the proliferative capacity of cells." "Our study is strong evidence that telomere length is the clock that counts cell divisions."

Their findings on telomere length and cell aging are of great interest to cancer researchers, Shay said. "Our observations increase confidence in the hypothesis that immortal cells and reactivated telomerase are essential components of human tumors. Ultimately, we may be able to regulate tumor cells by inhibiting telomerase activity."

The potential implications for research on human aging are equally compelling. "It is still speculative, but understanding the role of telomere shortening in cell aging may give us the information we need to increase the life span of an organism," Wright said.

New directions

Beyond their work with telomere biology and its role in cancer and human aging, Shay and Wright are just beginning to examine the connections telomeres have to other human ailments. Telomerase may offer an approach to head off the deadly assault of the AIDS virus. The telomeres of immune cells in people with AIDS are shorter than those in people with the human immunodeficiency virus (HIV). Shay and Wright believe the cells responsible for protecting the body's immune system work too hard too fast and are used up, leaving a person with AIDS vulnerable to deadly, opportunistic infections. , "It may be possible to take cells that have not been infected with HIV from the patient and lengthen the telomeres. Those cells would then be given back to the patient to protect the immune system. It would not cure AIDS, but it would keep AIDS from developing." They are quick to recognize the limitations of the idea. "There's no reason, theoretically, we couldn't do it right now. The problem is that by the time people know they have AIDS their healthy cell count already is low, and their physicians may not want to take away any of the healthy cells they need."

This pair of scientists is equally enthusiastic about other clinical applications of their work such as telomerase-based treatment of rheumatoid arthritis, psoriasis and baldness. And so they continue, as the Jerry Shay and Woody Wright collaboration enters its third decade, motivated by the desire to offer hope and to test the limits of their scientific creativity.

Source: http://www.swmed.edu/home_pages/publish/magazine/immortal/paradox.html

Part 2: Summarize your understanding of this article by writing a paragraph on each of the following points:

- The difference between vitality and longevity.

- The difference between the two uses of telomerase.

- To which of those uses do you think scientists should be directing their time, energy and resources? Why?

Part 3: Progeria is a rare genetic aging disorder. Use a search engine on the Internet to become more familiar with this condition in order to answer the following questions.

- What is progeria?

- What causes progeria?

- Is progeria inherited?

- What are the symptoms of progeria?

- How long do people with progeria usually live?

- How common is progeria?

- What are the different types of progeria?

- How would studying progeria help us learn about the human aging process?

Additional Resources

Because Web sites frequently change, some of these resources may no longer be available. Use a search engine and related key words to locate new Web sites.

http://www.progeriaresearch.org/ (information on the aging disease progeria)
http://www.infoaging.org/b-tel-home.html (information on telomeres)
http://www.pbs.org/stealingtime/
http://www.worldbank.org/depweb/english/modules/social/life/
http://www.swmed.edu/home_pages/publish/magazine/immortal/paradox.html

Genomic Revolution
http://www.ornl.gov/sci/techresources/Human_Genome/education/education.shtmL
The Web site to the government-funded Human Genome Project with links about genomics, the history of the project, and more.

Secrets of the Sequence Videos and Lessons
This video and 49 others with their accompanying lessons are available *at no charge* from www.vcu.edu/lifesci/sosq