Cancer — Compiling the Catalog

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 132, Episode 3
"Cancer – Compiling the Catalog" –approximately 8 minutes viewing time

Researchers and physicians at the University of Michigan Comprehensive Cancer Center are creating a tissue bank of tumor types. This is enabling them to discover specific genetic biomarkers for various tumors and types of cancer. This library of tumor types will help doctors diagnose and treat cancers on a molecular level.

Ward Television
Producer: Fran Victor
Associate Producer: Luke Cline
Featuring: Dr. Max Wicha, University of Michigan, Comprehensive Cancer Center, Founding Director Richard Perry, Dr. Mark Rubin, Pathology & Urology, University of Michigan, Dr. Arul Chinnaiyan, Pathology and Urology, University of Michigan
Lesson Author; Reviewers: Marilyn Elder; Catherine Dahl, Dick Rezba, Katherine Weyer, and Kieron Torres
Trial Testing Teachers: Reuwai Hanewald, Martin Shields

National and State Science Standards of Learning

National Science Education Standards Connection

Content Standard A: Science as Inquiry
As a result of activities in grades 9-12, all students should develop

- Understanding 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

Content Standard F: Science in Personal and Social Perspectives.
As a result of their activities in grades 9-12, all students should develop understanding of

- Personal and community health

Selected State Science Standards of Learning Connections

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

Virginia

BIO.5 The student will investigate and understand life functions of archaebacteria, monerans (eubacteria), protists, fungi, plants, and animals including humans. Key concepts include

e) human health issues, human anatomy, body systems, and life functions; and

BIO.6 The student will investigate and understand common mechanisms of inheritance and protein synthesis. Key concepts include

a) cell growth and division;
c) cell specialization;
e) genetic variation (mutation, recombination, deletions, additions to DNA);
f) the structure, function, and replication of nucleic acids (DNA and RNA);
h) use, limitations, and misuse of genetic information; and
i) exploration of the impact of DNA technologies.

Illinois

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

12.A.4a Explain how Genetic combinations produce visible effects and variations among physical features and cellular functions of organisms.
12.A.4b Describe the structures and organization of cells and tissues that underlie basic life functions including nutrition, respiration, cellular transport, biosynthesis and reproduction.
12.A.5a Explain changes within cells and organisms in response to stimuli and changing environmental conditions (e.g., homeostasis, dormancy).
12.A.5b Analyze the transmission of Genetic traits, diseases and defects.

Overview

According to the National Cancer Institute, we now know that cancer is caused by genes that have gone awry in one of the 3 critical areas of cell production. Instead of looking at all the cancers as different diseases, researchers are now focusing on the similarities of one cancer to another. Researchers are cataloguing thousands of malignant tumors and have discovered that certain cancer cells or “bio-markers” associated with those cancers have proven to be more lethal than others. So despite the fact that there are at least 100 to 200 genes that seem to be over or under expressed in any one type of cancer, it is clear that the presence of those specific “lethal” biomarkers would indicate which cancers should be treated more aggressively. This new type of diagnosis will be enormously helpful in better targeting treatment to disease, given the debilitating effects of today’s treatment of cancer that aims to kill only cancer cells but unfortunately also ends up killing healthy cells.

Prostate cancer, one of the most common cancers in men, is one type of cancer that would benefit from this new technology. The research team at the Comprehensive Cancer Center at the University of Michigan is cataloging the lethal genes for prostate cancer.

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

The Human Genome Project was begun in 1988 by scientists from 13 nations as a worldwide effort to understand the sequencing of the entire DNA in the human body. What is one potential scientific benefit of this research?

1. It will help to explain human cultural differences.
2. It will create communication between research centers.
3. It will help find the genes responsible for many diseases. *
4. It helps to classify man most accurately in the animal kingdom.

Source: Virginia end-of-course biology test, 2003

Before Viewing

1. Ask: "What percentage of people do you think will get some form of cancer during their lifetime?" "Is the percentage the same for both men and women?" *See next step.*

2. The video states that 1 in 2 men and 1 in 3 women will have cancer in their lifetime. What can you do if you know you are at a higher risk for cancer because of your family history?
   Have regular check-ups and modify your lifestyle to minimize those factors known to be linked to the disease. (Students may be motivated to research lifestyle habits linked to specific types of cancer.)

3. "What are the current treatments for cancer? What approach do all these treatments have in common? What is the most obvious side effect of these treatments? Do you think that in the next 10 years it is likely that cancer treatment will change?"
   Chemotherapy, radiation, surgery – Surgery attempts to remove the cancerous tissue. Chemotherapy and radiation aims to kill cells that are in the process of dividing. The most obvious side effect is that these treatments also kill off healthy cells. In ten years scientists may be able to target and treat cancers on a molecular level instead of a cellular level.

During Viewing

1. START the video.

2. PAUSE the video (2:33 minutes into the video) after the scientist says. "…one of those three critical areas gone wrong." ..

   List and discuss the 3 ways in which the DNA directs the cells.
   - Directs the cell to make copies of itself to grow and divide
   - Directs the cell to differentiate by expressing different genes
   - Orders the cell to die if something goes wrong in order to rid the body of unhealthy cells.

3. RESUME the video.

4. PAUSE the video (5:20 minutes into the video) after the scientist says,"…decision of waiting is a good one for them"
   Ask: "Why would a prostate cancer patient wait before receiving treatment?"

Many prostate cancer tumors are very slow growing. Most men who are diagnosed are older, causing cancer doctors to recommend watching and waiting before receiving invasive treatment.

Note: If students are unclear about the meaning of a genetic biomarker, re-play the video from 3.19 minutes.

5. RESUME the video and play to the end.

After Viewing

1. Ask: What are the 3 abnormalities found in the "lethal" genes that cause cancer?"
    - *Too much signal for the cell to grow*
    - *Too little signal for the cell to differentiate*
    - *A block in the signal that normally causes unhealthy cells to die*

2. Contrast the current methods of treating cancer (as discussed before viewing the video) with future treatments that researchers believe may soon be available.

    The new form of cancer treatment is called molecular targeting versus cellular targeting that is currently used. By looking into the nucleus of a diseased cell and into the DNA, researchers can determine what specific gene makes that cell abnormal, which will in turn allow them to create specific gene blockers. For those patients with a high risk for cancer, researchers will be able to target any possible genetic defects before cancer occurs.

3. Discuss how the Cancer Catalog is being created and what its use will be for researchers. Ask: "What is the specific example given in the video that shows how the treatment of a cancer can be affected by knowing the kind of cancer cell involved?"

    Cataloging thousands of diseased cells from malignant tumors is making it easier for scientists to immediately recognize the similarities of cancer cells among different types of cancer. They will soon be able to recognize those cells that appear to be the most lethal regardless of the type of cancer. This will help determine whether patients who have been diagnosed with a cancer, or those with a high predisposition for it, actually possess the "lethal gene".

    Knowing which genes are present would affect the type of treatment recommended. For example, in patients with prostate cancer, the side effects of surgically removing the prostate often influence a patient to "wait and watch" because the cancer could be a slow growing variety. However, if the "lethal gene" were present, the patient would know he has the aggressive variety and surgery would be advisable.

Teacher Notes for the Student Activity:
Apoptosis – Programmed Cell Death and Tadpole Tails

For every cell there is a time to live, a time to reproduce, and a time to die. Most students learn about mitosis and the cell cycle. They understand that cells perform a function; they know that cells have a job to do. However, rarely in science classes is cell death mentioned. There are two different kinds of cell death: necrosis, from toxins or mechanical injury, and apoptosis, which is inherent in the genetic makeup of the cell. Apoptosis (pronounced either *APE oh TOE sis*; or *uh POP tuh sis)* is programmed cell death. This student activity will look at how apoptosis occurs in the cell, why it happens, and why it is good for the organism.

Background: Apoptosis:

Apoptosis was first described in 1972 by John Kerr, Andrew Wyllie, and Alastair Currie, three researchers at the University of Aberdeen. The researchers also coined the term, which comes from the Greek word that describes the falling of leaves from a tree or petals from a flower. In contrast to the messy process of necrosis, apoptosis is quick and neat. Instead of swelling, a cell undergoing apoptosis shrivels and separates from its neighbors. The DNA and organelles condense. The cell then divides or 'blebs' into several small vesicles, which are consumed by neighboring cells. Apoptosis can occur in as little as 20 minutes and leaves no trace behind, which may explain why biologists failed for so long to see it. "Apoptosis is a normal developmental and safety process," says Dr. Michael Shelanski, Delafield Professor and Chairman of Pathology. "It gets sick cells out of the way and makes sure we develop properly."

Apoptosis is of interest to the immunologist because of its role in cell deletion in the immune system and in the deregulation of the process seen in a number of autoimmune diseases and AIDS. To the cancer biologist, apoptosis not only appears to contribute to the development of some cancers, but also hinders their treatment when cells become resistant to apoptosis and are not killed following drug treatment. Developmental biologists also have a keen interest in the process because of the programmed loss of cells that occurs by apoptosis during tissue sculpting and embryonic development.

The hand of a developing fetus begins as a flat paddle. Apoptosis sculpts it into individual fingers through the programmed death of selected cells. A developing brain makes more than twice the neurons it will eventually use; neurons that fail to make the right connections are eliminated by apoptosis. When genetic damage occurs, internal sentries, such as p53, halt cell division until repairs can be made. If the damage is beyond repair, apoptosis is invoked.

Cells in the gut, skin, and elsewhere undergo apoptosis or programmed cell death every day as part of the normal maintenance of tissue. But when the death machinery goes awry, disease can result. In neurodegenerative disorders, autoimmune disorders, and stroke, cells die prematurely. *In cancer, cells fail to die when they should.*

Apoptosis has brought a certain balance to biology. Scientists are now learning as much about the end of a cell's life as they already know about its beginning. And in its complexity, they see opportunities for therapy. They realize that a better understanding of death may one day save lives.

Apoptosis: Programmed Cell Death and Tadpole Tails

Part I

Review Mitosis with students.

Arrange to have students watch http://www.cellsalive.com/Mitosis.htm. Have them answer the questions on the Student Handout. Discuss the different phases in mitosis. Emphasize that where there was just one cell, as a result of mitosis, now there are two. Have students fill in Table 1. Discuss the uncontrolled, rapid mitosis of some cancer cells. Discuss how a tumor is formed.

1. How many cells were there at the beginning of the animation?
   one

2. How many cells were there at the end of the animation?
   two

3. Suppose that this cell divides once every 20 minutes. From that one cell, how many cells could there be after 1 hour? 2 hours? 3 hours? 4 hours? Fill in Table 1.

Table 1. Mitosis *(with answers)*

Time	0m	20m	40m	1 hour	1h 20m	1h 40m	2 hours	2h 20m	2h 40m	3 hours	3h 20m	3h 40m	4 hours
# of Cells	*1*	*2*	*4*	*8*	*16*	*32*	*64*	*128*	*256*	*512*	*1024*	*2048*	*4096*

4. If the cell in Question 3 was inside an organ, how would this change the appearance of the organ? Eventually *there would be a bulging of the cell mass, a tumor.*

The Cell at Work. Then watch http://www.cellsalive.com/cell_cycle.htm. Have students answer the questions on the Student Handout. Discuss how much time is spent in each phase. Emphasize the G1 and G2 phases are a time for the cell to do its job. During this time the cell will make RNA and synthesize protein.
Ask: "What if cellular division or "doing its job" is no longer needed? What happens to the cell?"

5. In which phase does the cell spend most of its time? *interphase*

6. What does the cell do in the G_1 phase? *Cells increase in size, produce RNA and synthesize protein. An important cell cycle control mechanism activated during this period ensures that everything is ready for DNA synthesis.*

   There are times when a cell will leave the cycle and quit dividing. This may be a temporary resting period or more permanent. An example of the latter is a cell that has reached an end stage of development and will no longer divide (e.g. neuron).

7. What does the cell do in the S phase? *To produce two similar daughter cells, the complete DNA instructions in the cell must be duplicated. DNA replication occurs during this S (synthesis) phase.*

8. What does the cell do in the G_2 phase? *During the gap between DNA synthesis and mitosis, the cell will continue to grow and produce new proteins. At the end of this gap is another control checkpoint) to determine if the cell can now proceed to enter M (mitosis) and divide.*

Introduce Apoptosis using these Websites http://www.cellsalive.com/apop.htm (click on "john W. Kimball's Apoptosis Page", 2nd line from the bottom of the screen) and http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/A/Apoptosis.html and the references at the end of this lesson. Have students answer the Pre-Activity Background Review and Information questions on the Student Handout.

There are two ways a cell can die.

9. The first is necrosis. Necrosis can happen by mechanical means or a toxin. What is an example of a toxin that may kill cells? *PCB's, nicotine, asbestos, DDT, etc.*

10. The second way a cell can die is by apoptosis. This is programmed cell death (PCD). This method benefits the organism. How many cells were present after 4 hours in Question 3? *4096*

11. How would your answer to Question 4 be changed if, after the organ system reached full maturity at 2 hours, apoptosis occurred to half of the cellular population of that organ system? *The organ system would not develop a mass of cells and a tumor would not be formed.*

Part II Demonstrating Cell Necrosis and Modeling Cell Apoptosis

Materials (For each group of 2)

- 1 small round balloon
- 1 standard 8 inch straw
- Scissors
- Colored pencils or markers

The Student Activity following the pre-activity could be done as a teacher demonstration or in groups of no more than two or as partly demonstration and partly group work.

Note: You may want to control the balloon-popping (cell necrosis) segment of the activity by at least making this part a one-time teacher demonstration. Blow up a balloon and tie the balloon around the middle of the straw. Use scissors or other sharp object to pop the balloon.

Demonstration of Cell Necrosis

Demonstrate cell necrosis by popping a balloon model of a cell. This represents a type of cell death from mechanical injury or a toxin.

Modeling Cell Apoptosis

Questions on student handout:

a) How many mitotic divisions did the cell go through before it was no longer able to divide successfully? *Approximately 4*

b) How many TTAGGG base sequences did your cell have? *Approximately 8*

c) What do you think may have happened to the cellular contents in the demonstration of necrosis? *The cellular contents are scattered.*

d) What do you think may happen to the cellular contents during apoptosis? *The cell shrinks and "blebs". The cellular contents are disassembled, absorbed and reused as cellular growth components for other cells.*

e) Contrast the two types of cell death.
Necrosis is not planned. It is a more violent, abrupt end to the life of the cell. The cellular contents are scattered.
Apoptosis is planned or programmed to naturally end the life of the cell. During apoptosis the cellular contents are naturally dispersed for the benefit of the surrounding cells.

Part III: Tadpole Tails

Frogs are very interesting organisms and their growth illustrates the need for apoptosis-- programmed cell death. Consider the statement made in the following websites: "A tadpole actually eats its tail! The tail is absorbed as the frog grows." This can take from hours … to days."

http://www.atozteacherstuff.com/go/jump2.cgi?ID=1196 (click on "tadpoles" link)

1. What do you think is happening to the frog's tail?
As the tadpole grows into a frog and adapts to living on a land environment, the tadpole's tail becomes less useful. Apoptosis or programmed cell death allows the tail cells to be absorbed into the adult frog's body, using the tail cellular contents as "spare parts" in building the powerful hind legs and other features of the adult frog.

2. Do you think mitotic division in the tadpole's tail is occurring rapidly, constantly, slowly, or not at all as it develops into an adult frog?
Either slowly or not at all.

3. Why does the young frog not need a tail anymore?
As tadpoles metamorphose into adult frogs, they go through many changes. The changes begin when the hind legs sprout. Soon after, lungs develop and the front legs appear. Meanwhile, the tail gradually shrinks. Just before becoming a frog, the tadpole's gills disappear. The tiny frog emerges from the water with just a stump of a tail, which soon disappears. The adult frog has adapted to both land and water (terrestrial and aquatic) environments.

Student Handout: Apoptosis: Programmed Cell Death and Tadpole Tails

This activity has three parts. In Part I you will watch 3 computer animations of cell activity and answer a series of questions. In Part II you will model cell apoptosis with balloons and straws. In Part III you will research what happens to a tadpole's tail.

Part I: Pre-activity Background review and information

Mitosis

Watch http://www.cellsalive.com/Mitosis.htm. Answer the following questions.

1. How many cells were there at the beginning of the animation?

2. How many cells were there at the end of the animation?

3. Suppose that this cell divides once every 20 minutes. From that one cell, how many cells could there be after 1 hour? 2 hours? 3 hours? 4 hours? Fill in Table 1.

Table 1 Mitosis

Time	0m	20m	40m	1 hour	1h 20m	1h 40m	2 hours	2h 20m	2h 40m	3 hours	3h 20m	3h 40m	4 hours
# of Cells	*1*	*2*	*4*										

4. If the cell in Question 3 was inside an organ, how would this change the appearance of the organ?

The Cell at work

Watch http://www.cellsalive.com/cell_cycle.htm. Answer the following questions.

5. In which phase does the cell spend most of its time?

6. What does the cell do in the G_1 phase?

7. What does the cell do in the S phase?

8. What does the cell do in the G_2 phase?

Apoptosis

Read http://www.cellsalive.com/apop.htm Also, click on the link for John W. Kimball's Apoptosis Page and use it as an information source.

There are two ways a cell can die.

9. The first is necrosis. Necrosis can happen by mechanical means or a toxin. What is an example of a toxin that may kill cells?

10. The second way a cell can die is by apoptosis. This is programmed cell death (PCD). This method benefits the organism. How many cells were present after 4 hours in Question 3?

11. How would your answer to Question 4 be changed if, after the organ system reached full maturity at 2 hours, apoptosis occurred to half of the cellular population of that organ system?

Part II: Activity— Modeling Apoptosis

Materials (For each group of 2)

- 1 small round balloon
- 1 standard 8 inch straw
- Scissors
- Colored pencils or markers

Background

The balloons represent the cellular membrane of an animal cell. The straws represent a chromosome in that cell. On the ends of each chromosome are telomeres that act as protective caps.
Telomeres consist of DNA and associated proteins that are essential for chromosome integrity and stability. The DNA in telomeres are base repeat sequences (TTAGGG) which may shorten or fall off each time the cell divides. There are thousands of copies of these base repeats in human cells, as well as other eukaryotic cells. However, cells that lose their telomeres also lose the ability to reproduce or undergo mitosis, and become apoptic.

Demonstration of Cell Necrosis

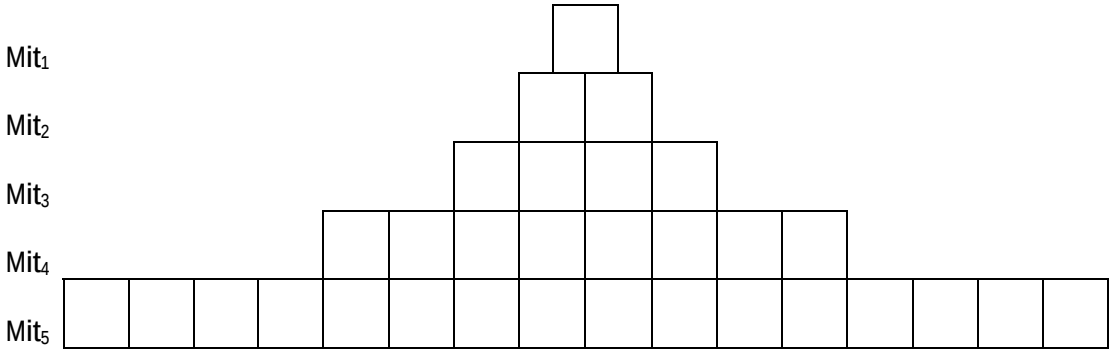
Your teacher will demonstrate cell necrosis by popping a balloon model of a cell. This represents a type of cell death from mechanical injury or a toxin.

Procedure for Modeling Cell Apoptosis

Follow the directions below to demonstrate how a cell reaches apoptosis. Use Table 2 to illustrate several Mitotic divisions ($Mit_{1\text{-}5}$) in eukaryotic cells. Draw in circles to represent the increasing number of cells.

1. Now you will make a balloon model of a cell. Blow up a balloon and tie the balloon in a knot around the middle of the straw.
2. Use a different color to represent one Mitotic division—Mit_2 Cut 2 cm (about 3/4 in.) off both ends of the straw.(This represents the loss of telomeres as the cell divides.)
3. Repeat Step 2 for as many times as you can cut pieces off each end of the straw.
4. When you no longer have any telomeres (straw) left, untie the balloon and slowly release the air in your balloon. Your cell is undergoing apoptosis or programmed cell death. The cell has completed its life span.

Table 2 Five Mitotic Divisions in Eukaryotic Cells.



Answer the following questions.

a) How many mitotic divisions did the cell go through before it was no longer able to divide successfully?

b) How many TTAGGG base sequences did your cell have?

c) What do you think may have happened to the cellular contents during necrosis?

d) What do you think may happen to the cellular contents during apoptosis?

e) Contrast the two types of cell death.

Part III: Tadpole Tails

Frogs are very interesting organisms and their growth illustrates the need for apoptosis - programmed cell death. Consider the following statement made in the following website: "A tadpole actually eats its tail! The tail is absorbed as the frog grows. This can take periods from hours … to days." Go to the http://www.atozteacherstuff.com/go/jump2.cgi?ID=1196 and click on the "tadpoles" link and, if time allows, explore some of the other frog links. Answer the questions below.

1. What do you think is happening to the frog's tail?

2. Do you think mitotic division in the tadpole's tail is occurring rapidly, constantly, slowly, or not at all as it develops into an adult frog? Explain.

3. Why does the young frog not need a tail anymore?

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.

Cells.

Anatomy of the cell. Interactive site explains functions of various sub cellular units.
http://www.johnkyrk.com/DNAanatomy.html

Apoptosis.

Website by award-winning Professor Tom Cotter explains the importance of studying apoptosis.
http://www.irishscientist.ie/2000/contents.asp?contentxml=178s.xml&contentxsl=insight3.xsl

Apoptosis for "Dummies". Part of Dr. John A. Kimball's online biology textbook.
http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/A/Apoptosis.html

More technical information on the mechanism of apoptosis and research in programmed cell death.
http://cpmcnet.columbia.edu/news/journal/journal-o/fall-1999/death.html

Tadpoles and Frogs

For more amazing facts about frog adaptations visit the San Francisco Exploratorium website.
The Tadpole. http://www.atozteacherstuff.com/go/jump2.cgi?ID=1195

Cancer

http://www.cancer.org/docroot/home/index.asp?level=0 (excellent reference site about the different types of cancer, and has a search option to make finding information easier)

http://cancer.about.com/ (excellent reference website, especially about diseases)

http://www.mamashealth.com/breastcancer.asp (includes many links about other disorders.)

http://www.healingwell.com/library/prostatecancer/info4.asp (Includes explanation and prevention)

http://www.yourhealthbase.com/prostate_cancer.html (summarizes research and prevention)

http://www.prostate-cancer.org.uk/learn/prostateCancer/prevention/diet.asp
(includes role of diet)

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