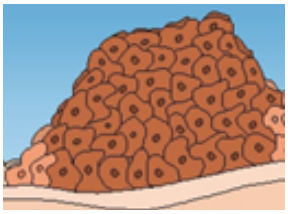

Activity 2

Cancer and the Cell Cycle

At a Glance

Focus: Students use five CD-ROM-based animations to help them construct an explanation for how cancer develops, then use their new understanding to explain several historical observations about agents that cause cancer.

Major Concepts: The growth and differentiation of cells in the body normally are precisely regulated; this regulation is fundamental to the orderly process of development that we observe across the life spans of multicellular organisms. Cancer develops due to the loss of growth control in cells. Loss of control occurs as a result of mutations in genes that are involved in cell cycle control.

Objectives: After completing this activity, students will

- understand that many different agents can cause cancer,
- understand that cancer represents a breakdown of the processes that regulate the growth of normal cells and tissues,
- recognize that cancer develops as a result of genetic damage that occurs to cells across time,
- be able to explain that cancer is associated with the occurrence of damage to par ticular classes of genes involved in the normal regulation of the cell cycle, and
- understand that studying the processes involved in the development of can cer has led to a significantly increased understanding of the normal cell cycle as well as to new strategies for treating cancer.

Prerequisite Knowledge: Students should be familiar with mitosis, the cell cycle, and terms such as “gene” and “mutation.”

Basic Science-Public Health Connection: This activity focuses students’ atten tion on how understanding the basic biology of cancer can help us make sense of the many observations people have made about risk factors related to cancer.

Introduction

Cancer has been described as a single disease and a hundred diseases. The description of cancer as a single disease arises from the observation that all cancers display uncontrolled growth, the ability to expand without limit. The description of cancer as a hundred diseases arises from the observation that cancer can appear as a result of different causes, in a variety of sites within the body, and that each type of cancer displays its own growth rate, prognosis, and treatability.

The discovery that all cancer involves a fundamental disruption in the growth of cells and tissues suggests that to understand cancer, we need to understand the events and processes that occur as both normal and abnormal cells grow and divide. In fact, much cancer research across the past two decades has focused on this challenge. This research has revealed a complex picture of how two classes of

genes, called proto-oncogenes and tumor suppressor genes, normally regulate the intricate sequence of cell cycle events. And it also has revealed how the accumu lation of mutations in these genes can contribute to the development of an altered cell, a cell that has lost the normal controls on cell division.

In this activity, students gain a flavor of the initial confusion that existed among scientists about the causes of cancer by viewing several early accounts of possible relationships between the development of cancer and various internal and exter nal factors. Students then use five CD-ROM-based animations to learn about evi dence that helped scientists understand that (1) cancer involves the uncontrolled division of body cells; (2) cell division normally is precisely regulated; (3) cell cycle regulation is accomplished by two major types of genes; (4) cancer-causing agents often damage genes; and (5) when damage occurs to genes that regulate the cell cycle, the balance between signals that stimulate cell division and signals that inhibit cell division can change, leading the cell to divide more often than it normally would. As the activity closes, students use their new understanding of cancer to explain the relationships they learned about in Step 1.

Materials and Preparation

You will need to prepare the following materials before conducting this activity:

- Master 2.1, *Understanding Cancer* (make 1 copy per student)
- *Cell Biology and Cancer* CD-ROM (1 per team)

Follow the instructions on pages 28–29 to load the CD-ROMs on the computers students will use.

Note to teachers: If you do not have enough computers equipped with CD-ROM drives to conduct this activity, you can use the print-based alternative. To view and print the instructions and masters for this alternate activity, load the CD onto a computer and click the Print button on the main menu screen. The computer will display a screen showing the resources available for printing from the CD; click on the button labeled Non-CD Lesson Plan from the choices available for Activity 2, *Cancer and the Cell Cycle*. This will reveal the lesson plan and the masters for the alternate, non-CD-based activity. Click Print again to print these resources.

Procedure

1. **Introduce the activity by noting that people have wondered about the cause of cancer for thousands of years. Throughout this time, many correlations have been noted between the development of cancer and various internal and external factors. As examples of this, ask students to organize into their teams and view each of the *News Alert* videos on the CD-ROM. Distribute one copy of Master 2.1, *Understanding Cancer,* to each student and ask students to complete Section 1, Factors Reported to Be Associated with Cancer, by identifying**
   - **what each video suggests about the cause of cancer and**
   - **what evidence the video provides to support the claim.**

Divide the class into teams for this activity. The number of teams you will have depends on the number of computers equipped with CD-ROM drives you have available. We recommend that you ask students to organize into the same teams in which they worked in Activity 1, and place three of the students from one team at one computer and the other three students at a neighboring computer. This arrangement has the advantage that students who worked together in Activity 1 will work together or near one another in this activity as well.

Give the teams approximately 5 minutes to complete this task.

Notice that the videos describe reports of relationships between cancer and various causative agents that span more than 200 years. You may wish to draw students' attention to the length of time people have sys tematically studied the cause of cancer and also to the diversity of rela tionships that scientists studying the disease have identified and explained.

2. **Ask the students what each video suggests about the cause of cancer and what evidence was provided to support the claim.**

   To increase the level of student participation, ask one team to describe what a particular video suggests about the cause of cancer and a differ ent team to describe the evidence on which this claim was based.

   At the close of the reporting, you may wish to ask students whether the evidence presented in these videos is convincing and why. This is a good point in the activity to remind students of the difference between correlation and causation and ask what type of evidence would demonstrate causation.

3. **Explain that each news item describes what has proven to be a real relationship between the development of cancer and the factor described. Ask students what general question all four videos raise when they are considered collectively.**

   Students may suggest several questions that could be asked about the videos. Help students see that the fundamental challenge facing scien tists interested in understanding cancer was to explain how so many diverse factors can cause it. Students may phrase this question as "How can so many different factors all cause cancer?" or "What does each of these factors do to cause cancer?"

   Tip from the field test. Students may ask questions that relate more to the medical aspects of cancer than to its underlying cause. If students are having difficulty recognizing the question that these four videos raise about cancer's cause, you may wish to rephrase the question as "What do you think may have confused researchers trying to understand what goes wrong in cancer cells?" or "The number of different agents that can cause cancer was one of the most confusing aspects of cancer

to early researchers. Why was this confusing?" or "What do you think all these agents had in common and why was it important to discover that?"

4. **Explain that research across the past 30 years has helped scientists understand how so many different factors can cause cancer. Explain that next students will view five CD-ROM-based animations that will help them construct an explanation of the cause of cancer. They then will use their understanding of cancer's cause to explain the relationships described in the *News Alert* videos.**

5. **Direct the students to view the animations on the CD-ROM. Then ask them to complete Section 2, Building an Explanation for the Cause of Cancer (on *Understanding Cancer*) by writing a one-sentence statement that summarizes what they learned from each animation.**

Students may be surprised to learn about the cell cycle in an activity that focuses on risk factors for cancer. Point out that understanding disease typically requires scientists to examine basic cellular processes, and that understanding those processes can, in turn, help health care workers develop better prevention and treatment strategies.

- *Animation 1* (the animation of abnormal cell growth) should lead students to conclude that **cancer involves the uncontrolled division of body cells**.
- *Animation 2* (the introduction to the cell cycle) should lead students to conclude that **cell division normally is precisely regulated**.
- *Animation 3* (the information on proto-oncogenes and tumor suppressor genes) should lead students to conclude that **cell cycle regulation is accomplished by two major types of genes**.
- *Animation 4* (the information on the mutagenicity of carcinogens) should lead students to conclude that **cancer-causing agents often damage genes**.
- *Animation 5* (the information on the effect of damaging cell cycle genes) should lead students to conclude that **when damage occurs to genes that regulate the cell cycle, the balance between signals that stimulate cell division and signals that inhibit cell division can change, leading the cell to divide more often than it normally would**.

6. **After the students have completed Section 2 on *Understanding Cancer,* point out that their five statements constitute a basic explanation of what goes wrong when a cell becomes cancerous. Ask one or more teams to read their statements to the class, then invite clarifying comments and questions from the rest of the students.**

Steps 6–8 represent the closure steps for this activity. Step 6, in particular, focuses students' attention on the activity's major concepts.

7. **Ask the teams to complete Section 3, Explaining Factors Associated with Cancer, on *Understanding Cancer* by reviewing the information in Section 1 and writing four one-sentence explanations for how the relationship each video describes can be understood in the light of what scientists know today about the cause of cancer.**

   Give students approximately 5 minutes for this task, then ask a spokesperson from each team to explain one of the videos.

   Students may have difficulty with this step, primarily because they lack sufficient background in biology to make the connections required to

explain "causative" agents of cancer. For this reason, we suggest that you ask your students to provide only the most basic explanations, such as those provided in bold type below. After they have done so, you can explain as much of the detail as you think is appropriate and will be interesting to the class.

- *News Alert! Cancer and Chemical Poisons.* Students should be able to suggest that **a chemical in the coal dust caused damage to genes that regulate the cell cycle.**

  Pott was probably the first person to associate a specific type of cancer (scrotal cancer) with a specific occupation (chimney sweeping). Pott believed the problem was the coal soot that caught in the skin folds of the scrotum. In 1918, coal tar was shown to cause skin cancer in rabbits, and in 1924 the causative agent was identified as polycyclic aromatic hydrocarbons, especially benzo (a) pyrene.

- *News Alert! Cancer and Your Family History*. Students should be able to suggest that **children with inherited retinoblastoma have inherited an error (mutation) in a gene that regulates the cell cycle.**

  Retinoblastoma, a relatively rare cancer, is a highly malignant tumor of the eye. If left untreated, the malignancy moves from the eye along the optic nerve to the brain, from where it metastasizes to other tissues. Slightly more than one-third of retinoblastoma cases are inherited. The remaining cases are sporadic (not inherited). The age of onset of the inherited type is approximately 10 months, on average 8 months earlier than the sporadic type. Tumors of both eyes occur only with the inherited type.

  A mutation or deletion in the long arm of chromosome 13 is associated with the development of retinoblastoma. Both alleles of the gene involved, the *RB* gene, are either missing or altered in nearly every case of retinoblastoma (whether inherited or sporadic). The gene's normal product has an inhibitory effect on cell division.

  Children who inherit an altered allele of the *RB* gene are heterozygous for the chromosome 13 abnormality. They are at high risk for developing retinoblastoma because only a single mutation or deletion of the normal *RB* gene will result in a cell initiating uncontrolled cell division. The mutation rate for this gene is high enough that there is significant risk of experiencing the mutation in the cells of both eyes (thus, the risk of developing retinoblastoma in both eyes in the inherited type).

  In sporadic (nonhereditary) retinoblastoma, both alleles of the *RB* gene are normal, and each one must be mutated in the same cell for the tumor to arise. In contrast with hereditary retinoblastoma, the likelihood of this occurring in both eyes is so low that for all practical purposes, it does not occur.

- *News Alert! Cancer and Radiation Exposure.* Students should be able to suggest that **exposure to X-rays damages genes that regulate the cell cycle.**

Ionizing radiation is a well-known human carcinogen. The first reports of association between X-rays and cancer appear in the literature in the early 1900s. Subsequent reports include the association between radium exposure and leukemia (for example, Marie Curie died of leukemia); radium exposure and osteosarcomas (for example, cancer developed among painters of luminescent dials in watch factories in the 1930s); and radiation from nuclear tests and cancer (for example, children in the Marshall Islands exposed to radioactive iodine released from a nuclear test displayed a significant increase in thyroid cancer).

Carcinogenesis from ionizing radiation is believed to occur through the formation of mutagenic oxygen free radicals. Ionizing radiation is clearly carcinogenic when presented at unusually high doses, but it has been dif ficult to quantify its effect when presented at low doses. Because the assumption is that any amount of exposure has some effect, federal regu lations mandate that exposure to radiation be kept "as low as reasonably achievable."

Steps 6 and 7 provide excellent opportunities to assess students' understanding of the activity's major concepts. In Step 6, students should be able to express five key ideas about the regulation of cell division, and in Step 7, they should be able to apply this understanding to explain how certain risk factors increase a person's chance of devel oping cancer.

- *News Alert! Cancer and UV Light.* Students should be able to suggest that **exposure to UV light damages genes that regulate the cell cycle.**

  The relationship between sun exposure and skin cancer has been clarified greatly across the past century. In the late 1800s, observers noticed that sailors exposed to the sun developed a variety of abnormal lesions called "sailor's skin," and in the early 1900s, an increased risk of skin cancer was observed among farmers. By 1928, researchers had demonstrated the carcinogenic effect of UV radiation on the skin of laboratory animals. Today, scientists recognize excessive exposure to UV radiation (whether from the sun or other sources) as a key risk factor for skin cancer.

8. **Close the activity by asking students what the activity reveals about science's ability to bring order to even the most bewildering set of observations.**

   Students should recognize that science helps us explain and relate observations that we make about the natural world. You may wish to ask students if they can think of other examples of observations that have been organized and made comprehensible through the work of science. Students may propose the atomic theory, the cell theory, and the germ theory of disease as important organizing explanations in sci ence. If they do not mention evolution, point out that evolution is the most important organizing explanation in biology.