

Case Teaching Notes for “But I’m Too Young! A Case Study of Ovarian Cancer”

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Introduction / Background

This case study is a “clicker case.” It combines the use of student personal response systems (clickers) with case teaching methods and formats. The case is presented in class using a series of PowerPoint slides in parts, or stages. After each stage, students are asked to respond to questions (called “clicker questions”) posed by the instructor. Students work their way through the material to understand, and solve, the problem presented in the case. Specifically designed for use in large introductory science classes, the method integrates lecture material, case scenario material, student discussion, (clicker) questions, clarification of the answers to those questions, more lecture, and data.

This case introduces students to the basic cellular and genetic mechanisms that are responsible for cancer formation. In the case, students follow the story of a college student, Abby, through the onset of symptoms, diagnosis, and eventual treatment of ovarian cancer. While ovarian cancer is used as a specific example of cancer in this case, students gain a general understanding of how cells become cancerous through genetic mutations, how cancers can spread throughout the body by metastasizing, and how modern medicine is currently treating patients diagnosed with cancer through surgery, radiation, and chemotherapy. Often at the end of the case, students will ask the instructor whether this is a true story. The story, as presented here, is fictitious; however, it is similar to many real cases.

Students should be familiar with cells and the cell division/cell cycle prior to this case; a working knowledge of mitosis is not necessary.

Objectives

- Define cancer and differentiate between benign and malignant tumors.
- Explain that cancers result from mutations in genes that control the cell cycle.
- Understand how cancerous cells move around the body.
- Know the difference between tumor suppressor genes and oncogenes, and understand how these genes contribute to cancer formation.

Misconceptions

- All tumors are cancerous.
- Cancer can be inherited.
- Cancer is simply a result of poor lifestyle choices.

Classroom Management / Blocks of Analysis

This case was written for a large section of an introductory biology course for both science majors and non-majors that uses personal response systems or “clickers.”

Pre-Class Student Preparation

Students should receive and read the case handout before class; instructors can either pass the handout out one class period prior to the case or alternatively post it to a class website.

In-Class Case Presentation

In class, the instructor presents the case using a series of PowerPoint presentation slides punctuated by multiple choice questions which the students answer using their clickers.

Slide 1 introduces the case.

Slide 2 summarizes what the students know about Abby’s medical situation up to this point from the case handout they have read before class.

Slide 3 and Slide 4 prompt the students to develop general questions about cancer in an open discussion, followed by a clicker question (*Do you know someone personally that has had cancer?*) that helps them to become personally involved in the case.

Slide 5 and Slide 6 provide demographic information regarding overall cancer trends and those of ovarian cancer in particular.

Overall, cancer is increasingly becoming a treatable disease and mortality rates have sharply declined in recent times. However, this is not true for all types of cancer. Ovarian cancer, for example, has maintained constant mortality rates (Slide 6). In women aged 35 to 74, ovarian cancer is the fifth leading cause of cancer-related deaths and 4% of all cancers in women. An estimated one woman in 58 will develop ovarian cancer during her lifetime. In 2006, the American Cancer Society estimates that there will be 20,180 new cases of ovarian cancer diagnosed and 15,310 women will die of the disease. If diagnosed and treated early, when the cancer is confined to the ovary, the 5-year survival rate is over 90%. Unfortunately, due to ovarian cancer’s nonspecific symptoms, only 19% of all cases are found at this early stage. If caught in stage III or higher, the survival rate can be as low as 29%. A good side question for your students is to explore why different ethnic groups have different mortality rates.

Slide 7, which poses the second clicker question (*What is the difference between cancer and tumor?*), addresses the first misconception that many people have, i.e., that all tumors are cancers. The next slide, Slide 8, provides a definition for cancer and explains the differences between a benign tumor (non-cancerous) and a malignant tumor (cancerous).

Basically, cancer begins in cells, the building blocks that make up tissues. Tissues make up the organs of the body. Normally, cells grow and divide to form new cells as the body needs them. When cells grow old, they die, and new cells take their place. Sometimes, this orderly process goes wrong. New cells form when the body does not need them, and old cells do not die when they should. These extra cells can form a mass of tissue called a growth or tumor. Tumors can be benign or malignant. Benign tumors are not cancer, are rarely life-threatening, in general can be removed, and do not invade the tissues around them, i.e., cells from benign tumors do not spread to other parts of the body. Malignant tumors are cancerous. Malignant tumors

are generally more serious than benign tumors and may be life-threatening. Malignant tumors often can be removed, but sometimes they grow back. Malignant tumors can invade and damage nearby tissues and organs.

Slide 9 illustrates how malignant cells can lead to metastasis, i.e., the invasion of other tissues.

A tumor is a clump of cells with no function. Tumors may remain benign, or they can be malignant. Malignant tumor cells may move, or metastasize, to other locations in the body. Malignant and metastatic tumors are cancerous. Cancer of the ovaries is considered very dangerous because small cancers don't produce symptoms, the ovaries are in close proximity to many other abdominal organs, and the risk of cancer cells traveling to other body areas (metastasis) is high.

Slide 10 asks students to evaluate the results of the CA-125 blood tests that Dr. Allen ordered for Abby (see case story handout).

CA-125, cancer antigen-125, is a protein that is found in most ovarian cancer cells at levels that are elevated compared to normal cells. CA-125 is produced on the surface of cells and is released in the blood stream. The CA-125 test assesses the concentration of CA-125 in the blood. The test requires a sample of the patient's blood to be drawn. While almost all healthy people have CA-125 levels below 35 U/ml of serum, cancer patients may have elevated CA-125 levels that can even reach 10,000 U/ml when they are diagnosed. The level of CA-125 has become a key measurement of the effectiveness of tumor treatment. It should be noted that CA-125 tests can give false positives, and levels can be elevated due to a variety of other physiological factors.

Slide 11 continues the story. Dr. Allen informs Abby of her test results and indicates it would be best to remove both ovaries now instead of only one. Dr. Allen shows three histological images (Slide 12) of ovarian tissues from a brochure. When stained and viewed under a microscope, (a) normal cells have a different appearance than (b) benign and (c) malignant tumors.

Slide 13 is a conversation between Abby and Dr. Allen. This slide also introduces students to the two genes that have been linked to susceptibility in ovarian and breast cancer, BRCA1 and BRCA2. It is important that students understand Dr. Allen's last quote in which he explains that BRCA1 and BRCA2 require that both gene alleles are mutated in order to result in cancer, i.e., are tumor suppressor genes. Students will learn in subsequent slides about tumor suppressor genes, but the information on this slide will allow them to answer Clicker Question 6 (Slide 20). We also like to point out here to students that, while Abby has done a lot of research herself on the Internet to learn more about ovarian cancer, consultation with certified health care providers is always necessary since information on the Internet is not always accurate.

Slide 14 is a clicker question (*Why does cancer primarily affect older people rather than young people?*) assessing what students already know and sets the stage for understanding the role of genetic mutations in cancer formation. Slide 15 explains the role of mutations in cancer formation and addresses the misconception that cancer can be inherited. Slide 16 reviews the cell cycle, since mutations in genes that regulate the cell cycle are quite often mutated in cancer.

The cell cycle checkpoint is reviewed in Slide 17. Additionally, the role of p53 as a key mediator of the cell cycle is introduced.

p53 is mutated in approximately 80% of all cancers. p53 is a transcription factor that is activated in response to DNA damage and other cellular stresses. It is responsible for activating transcription of CKIs (cyclin kinase inhibitors), which stop the cell cycle. If p53 is mutated or not functional, the cell cycle will not be stopped, and cells that have been damaged in some way will continue to proliferate thus leading eventually

to cancer.

Slide 18 asks students to evaluate what would happen in cells with mutated p53. Slide 19 connects to a URL of the National Institute of Health (see Supporting Materials under References, below) to learn more about tumor suppressors and oncogenes through an animation. (It is possible that the NIH website could become obsolete or removed from the Internet. Therefore, we encourage instructors wishing to teach this case to feel free to adopt similar animations from other reputable websites if necessary.)

Basically, an oncogene is a gene that when mutated gains a function or is expressed at abnormally high levels and as a result contributes to converting a normal cell into a cancer cell. A tumor suppressor gene encodes for a protein that is involved in suppressing cell division. When mutated, it is no longer functional.

Slide 20 asks students to evaluate their knowledge of tumor suppressor genes and oncogenes in light of what Dr. Allen has told Abby and draw some conclusions with regard to BRCA1 and BRCA2. At this point, the instructor can point out that BRCA1 and BRCA2 are tumor suppressor genes that are involved in repairing damaged DNA. When rendered non-functional due to mutations, an accumulation of damaged DNA in cells occurs, eventually causing cells to divide out of control (i.e., cancer).

Slide 21 has more information about benign and malignant tumors. Slide 22 is another clicker question (*How do cancer cells travel through the human body?*) to assess what students already know about metastasis of cancer. Slide 23 illustrates the lymphatic system and how cancer cells break away from the primary tumor and move through the lymph and blood vessels to secondary locations in the body. This process is referred to as metastasis and is the most dangerous and devastating part of cancer.

Slide 24 continues the story with Dr. Allen's visit to Abby after the surgery. The purpose of the doctor's visit at this time is to discuss with Abby different therapeutic strategies that are typically used in the treatment of cancer cells.

Radiation therapy is rarely used in the initial treatment of ovarian cancer, but it may be used to relieve pain and other problems caused by the disease. The treatment is given at a hospital or clinic. Each treatment takes only a few minutes. Most women have chemotherapy for ovarian cancer after surgery. Some women have chemotherapy before surgery. Usually, more than one drug is given. Drugs for ovarian cancer can be given in different ways. Chemotherapy is given in cycles. Each treatment period is followed by a rest period. The length of the rest period and the number of cycles depend on the anticancer drugs used. The side effects of chemotherapy depend mainly on which drugs are given and how much. The drugs can harm normal cells that divide rapidly such as immune and blood cells, and hair cells. Taxol is the most commonly used chemotherapy for ovarian cancer and is illustrated in Slide 25.

Slide 26 presents some early signs that may be signals of cancer development if they go unnoticed.

Slide 27 is the final clicker question about metastasis.

Slide 28 concludes the case, indicating that Abby's cancer has been in remission for several years, thus allowing her to carry on happily with her life.

Assessment

This case was developed as part of an NSF-sponsored grant (# DUE 0618570) to determine whether clicker cases such as this one produced greater learning than the traditional lecture approach. As part of that project, the clicker cases had questions that were asked of students both before and after the class in which the material was presented. The questions were also used again during the final exam.

A transfer question was also developed for the case. This is a question designed to test whether a student could apply the knowledge that was given by the instructor in class to a new situation—a test of higher level thinking, according to Benjamin Bloom’s taxonomy of cognitive domain. This question, together with the additional pre- and post-case questions, are presented in the Answer Key.

Answer Key

Answers to the questions posed in the case study are provided in a separate answer key to the case. Those answers are password-protected. To access the answers for this case, go to [the key](#). You will be prompted for a username and password. If you have not yet registered with us, you can see whether you are eligible for an account by reviewing our [password policy and then apply online](#) or write to answerkey@sciencecases.org.

References

Supporting Material

“Cell Cycle Animations,” *Cell Biology and Cancer*, National Cancer Institute, National Institutes of Health http://science.education.nih.gov/supplements/nih1/cancer/activities/activity2_animations.htm Last accessed: July 23, 2008

This is an animation that is used on Slide 19 to explain the difference between tumor suppressor genes and oncogenes (the 5th animation). It should be noted that it may take some time to load this website so it is recommended that the site be loaded prior to the start of class. Additionally, the image is fairly small, and if you do not have Quicktime Pro you will not be able to resize the image. While only animation 5 is used for the case itself, all of the animations on the site are applicable to the case and could be used by the instructor if desired.

Journal Articles

Aunoble, B., R. Sanches, E. Didier, and Y.J. Bignon. 2000. Major oncogenes and tumor suppressor genes involved in epithelial ovarian cancer. *International Journal of Oncology* 16(3):567–76.

Examines the role of various tumor suppressor genes in ovarian cancer, including the link to BRCA1 and BRCA2.

Cannistra, S.A. 2004. Cancer of the ovary. *New England Journal of Medicine* 351(24):2519–2529.

A review paper that describes the clinical features of epithelial ovarian cancer. Advances in chemotherapy have resulted in improved survival and in more effective treatment of relapsed disease. In addition, a better understanding of genetic risk factors has permitted a tailored approach to preventive strategies.

Rowell, S., B. Newman, J. Boyd, and M-C. King. 1994. Inherited predisposition to breast and ovarian cancer. *American Journal of Human Genetics* 55:861–65.

The genetic predisposition to breast and ovarian cancer is the main focus of this paper, with implications for early detection and treatment.

Smith, L.H., C.R. Morris, S. Yasmeen, A. Parikh-Patel, R.D. Cress, and P.S. Romano. 2005. Ovarian cancer: Can we make the clinical diagnosis earlier? *Cancer* 104(7):1398–1407.

This article indicates how an early diagnosis of ovarian cancer may be beneficial to both physician and patient in fighting the disease through a broader spectrum of options, while offering the best chances for a successful healing.

Venkitaraman, A.R.. 2001. Functions of BRCA1 and BRCA2 in the biological response to DNA damage.

Journal of Cell Science 114: 3591–98.

Venikataram, A.R.. 2002. Cancer susceptibility and the functions of BRCA1 and BRCA2. *Cell* 108: 171–182.

Websites

Kleinsmith, L.J., D. Kerrigan, and S. Spangl. *Understanding Cancer*. National Cancer Institute.

<http://newscenter.cancer.gov/sciencebehind> Last accessed: July 23, 2008

Basic information regarding cancer and treatments.

American Cancer Society

<http://www.cancer.org/docroot/home/index.asp?level=0> Last accessed: July 23, 2008

Ovarian Cancer, National Cancer Institute

<http://www.cancer.gov/cancertopics/types/ovarian> Last accessed: July 23, 2008

Website dedicated specifically to ovarian cancer.

“Questions and Answers About the CA-125 Test,” Johns Hopkins Pathology

<http://www.ovariancancer.jhmi.edu/ca125qa.cfm> Last accessed: July 23, 2008

Good website about CA125.

“Genetic Testing for BRCA1 and BRCA2: It’s Your Choice,” National Cancer Institute

<http://www.cancer.gov/cancertopics/factsheet/Risk/BRCA> Last accessed: July 23, 2008

BRCA genetic information.

Additional Recommended Resource: Editor’s Pick

CancerQuest, Emory University

<http://www.cancerquest.org> Last accessed: August 21, 2008

Cancer education website with animations and videos, including interviews with young cancer survivors.

Slide Credits

- Slide 5—Center
 - *Description:* Graph illustrating overall cancer incidence and mortality trends in the U.S. from 1980–2004.
 - *Source:* Generated using a dynamic cancer statistics website maintained by the National Cancer Institute and the Centers for Disease Prevention & Control.
 - *Link:* <http://statecancerprofiles.cancer.gov/>
 - *Permission:* Open source free access; work of U.S. Federal government under the terms of Title 17, Chapter 1, Section 105, of the U.S. Code.
- Slide 6—Center
 - *Description:* Graph illustrating ovarian cancer demographics. Unlike other cancers in which mortality rates have declined, mortality rates for ovarian cancer are relatively flat.
 - *Source:* National Cancer Institute “A Snapshot of Ovarian Cancer.” The source within this publication for incidence and mortality data: Surveillance, Epidemiology, and End Results (SEER) Program and the National Center for Health Statistics. Additional statistics and charts are available at <http://seer.cancer.gov/>.
 - *Link:* <http://planning.cancer.gov/disease/snapshots.shtml>
 - *Permission:* Open source free access; work of U.S. Federal government under the terms of Title 17, Chapter 1, Section 105, of the U.S. Code.
- Slide 9—Right

- *Description:* Schematic illustrating normal cell division versus cancer cell division.
- *Source:* Originally National Cancer Institute; also found on Wikipedia.
- *Link:* Originally published at <http://press2.nci.nih.gov/sciencebehind/cancer/cancer01.htm> (outdated link); now available from Wikimedia Commons.
- *Permission:* Open source free access; work of U.S. Federal government under the terms of Title 17, Chapter 1, Section 105, of the U.S. Code.
- Slide 12—Lower left
 - *Description:* Histopathological image of an ovarian cyst.
 - *Source:* Wikimedia Commons.
 - *Link:* http://commons.wikimedia.org/wiki/Image:Ovary_cystoadenoma_mucinous_1.jpg
 - *Permission:* Open source free access; permission is granted to copy, distribute and/or modify this document under the terms of the GNU Free Documentation license, Version 1.2, or any later version published by the Free Software Foundation.
- Slide 12—Lower right
 - *Description:* Histopathological image of serous adenocarcinoma (cancer) arising in bilateral ovaries.
 - *Source:* Wikimedia Commons.
 - *Link:* http://commons.wikimedia.org/wiki/Image:Ovarian_serous_adenocarcinoma_%283%29.jpg
 - *Permission:* Open source free access; permission is granted to copy, distribute and/or modify this document under the terms of the GNU Free Documentation license, Version 1.2 or any later version published by the Free Software Foundation.
- Slide 12—Top
 - *Description:* Histological image of the germinal epithelium that lies along the edge of a human ovary. The specimen was stained with hematoxylin and eosin dyes.
 - *Source:* John Cotter, M.D., Pathology and Anatomical Sciences, School of Medicine and Biomedical Sciences, University at Buffalo.
 - *Link:* NA
 - *Permission:* Used with permission.
- Slide 16 and Slide 17—Right
 - *Description:* Schematic of the cell cycle.
 - *Source:* Wikimedia Commons.
 - *Link:* http://upload.wikimedia.org/wikipedia/commons/c/c4/Cell_cycle.png
 - *Permission:* Open source free access.
- Slide 20—Right
 - *Description:* BRCA1 protein crystal structure.
 - *Source:* The Research Collaboratory for Structural Bioinformatics (RCSB) Protein Data Bank: PDB ID: 1JM7 Brzovic, P.S., Rajagopal, P., Hoyt, D.W., King, M.C., Klevit, R.E. (2001) Structure of a BRCA1-BARD1 heterodimeric RING-RING complex. *Nat.Struct.Biol.* 8: 833–837
 - *Link:* <http://www.rcsb.org/pdb/>
 - *Permission:* Open source free access as a result of funding from numerous government agencies. Data contained in the RCSB PDB are free of all copyright restrictions and made fully and freely available for both non-commercial and commercial use. Structures used from the PDB should be cited with the PDB ID and the JRNL reference (as given above for this structure).
- Slide 23—Top left
 - *Description:* The human lymphatic system.
 - *Source:* National Institutes of Health/ National Cancer Institute
 - *Link:* <http://www.cancer.gov/images/Documents/6b08d7cc-2a8f-4d32-9a38->

a5433aaf0794/lymph.gif

- *Permission:* Open source free access; U.S. Federal government.
- Slide 23—Top right
 - *Description:* This is a schematic drawing of the stages of metastasis (1) attachment, (2) local breakdown, (3) locomotion, and (4) secondary tumor.
 - *Source:* Wikimedia Commons and National Cancer Institute Visuals Online
 - *Link:* <http://visualsonline.cancer.gov/details.cfm?imageid=2353>
 - *Permission:* Open source free access; U.S. Federal government.
- Slide 25—Right
 - *Description:* Pacific yew tree. Photo was taken in Mt. Hood National Forest.
 - *Source:* National Cancer Institute.
 - *Link:* <http://visualsonline.cancer.gov/details.cfm?imageid=2541>
 - *Permission:* Open source free access; U.S. Federal government.
- Slide 28—Center
 - *Description:* Mother and child.
 - *Source:* National Cancer Institute Visuals Online.
 - *Link:* <http://visualsonline.cancer.gov/details.cfm?imageid=2294>
 - *Permission:* Open source free access; U.S. Federal government.

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But I'm Too Young!

A Case Study of Ovarian Cancer

by

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Abby was in her Introductory Biology class that morning, listening to a speaker talk about human evolution. Although she was particularly interested in this topic because it related to the anthropology class she was currently in, she was unable to pay attention because of the pain in her abdomen. She had been experiencing it for a few weeks, but now it was becoming unbearable. She began to sweat.

“What’s the matter?” whispered her roommate Kelly, who was sitting next to her. “Are you all right?”

“My stomach hurts! I don’t think I can make it to the end of class. I really think I need to see a doctor.”

The tears running down Abby’s cheeks told Kelly that she was not joking. Kelly grabbed Abby’s book bag and helped her friend get up. They went straight to the campus health center.

“Well, the fact that you don’t have any fever and that your pain doesn’t appear to be coming from your appendix is good,” comforted the physician at the health center after checking Abby’s abdomen.

“I’m going to give you some medicine to relieve the pain for right now, but tomorrow I want you to come in to see Dr. Allen, our gynecologist. I would like her to run a few more tests in order to figure out where your pain is coming from.”

The next day Abby went to see Dr. Allen. During the examination, Dr. Allen felt a mass on Abby’s right ovary while pressing on her abdomen. Dr. Allen ordered a sonogram.

“Abby, the sonogram shows that you have a growth on your right ovary,” Dr. Allen said. “It is likely a cyst, but we’ll need to do some more testing to be sure. Many times a cyst will resolve on its own, but since this one is so large, I am going to recommend that we go ahead and have it surgically removed, along with your right ovary. This should help relieve the pain. Your remaining ovary will compensate for the one missing by ovulating every month. I would also like to run a blood test to look for signs of ovarian cancer. While rare at your age, increases in a protein called CA-125, a marker of cancer, will be able to help us determine if we are dealing with a cyst or cancer.”

Abby was scared. What did all this information mean? She felt overwhelmed, and when she returned to her dorm she broke down in tears. That night, unable to sleep, Abby and Kelly glued themselves to their laptop computers. They were searching the Internet for answers to Abby’s questions.