

CASE TEACHING NOTES

for

“A Right to Her Genes”

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INTRODUCTION

Case Synopsis

In this true story, a woman is grappling with a potential family predisposition to breast and ovarian cancer. She is trying to get some information to confirm this predisposition from a reluctant aunt so that she can better decide whether to remove her breasts and/or ovaries prophylactically. The aunt is illiterate and poor and had previously been estranged from the rest of the family. A genetic counselor is involved to help educate the aunt and hopefully obtain consent to get a DNA sample from her. Interestingly, the DNA sequence mutation actually found in the two family members is not in the coding region for the gene. Michelle must decide for herself what course of action she should take.

Use of This Case

This case was designed for an advanced undergraduate molecular biology course where many of the techniques discussed are being used to show their application, but the scientific information needed can be modified to make this amenable for use in an introductory biology, genetics, or ethics classes. The case was first presented for a molecular biology laboratory class by a local genetic counselor. Background information on the events and situation described was collected and verified, and the story was then personalized, with the names changed and the conversations fictionalized. I used the case for the first time at a Case Studies in Science Workshop held in June 1999 at the State University of New York at Buffalo to 13 hired undergraduates with little or no previous science course work. Coincidentally, the case presented just prior to this one at the workshop was about DNA identification and so the students did have some advanced preparation on the meaning of DNA and genes.

Since the first presentation of this case in the Fall of 1997, the aunt (named Anne in this case) has died.

Case Objectives

- Become aware of the ability to detect mutations associated with cancer.
- Become aware of the ethical concerns about DNA testing—getting DNA, who might also want to use this information, how to interpret information.
- Understand the scientific techniques useful for analyzing DNA mutations in people.
- Develop questions from unknowns in given reading material and learn to know where to go for the answers.
- Become aware of the scientific limitations of our understanding of DNA sequence changes in human genes.
- Become aware of alternative career paths, including working as a genetic counselor, doing laboratory research on cancer genes, designing drugs at pharmaceutical companies.

CLASSROOM MANAGEMENT

Variation 1

This case can be done in a single 1-hour class period and I have used this approach several times in presenting the case. It should follow material on DNA, genes, and mutations in a course. This variation works well with introductory biology students, as the focus is not on the scientific content but the ethics of the science. Start class with introductory questions on cancer, then construct a list of causes of cancer following a short 2- to 3-person group discussion (1 minute). Then, one can break these down into two groups—causes we can control [like smoking, sunbathing, eating processed fatty foods] and ones that are beyond our control [like mutations from our families, family history or predisposition]. Then give the students the case to read (takes 5 to 7 minutes). The case can then be run in several different ways (which are not necessarily mutually exclusive):

- A. Run a directed question/answer discussion focusing on the problems faced by Michelle, Anne, and Laura and then the ethics of collection of DNA information.
- B. Have the students role-play the different people at the coffee diner—Laura, Anne, Anne's daughter [might want to edit out some of the conversation that is written in the case], then bring in Michelle and follow that with a discussion of the options Michelle has.
- C. Small groups gather to create an informed consent document for Anne to sign. Share, compare, and discuss.

End with a listing of Michelle's options and personal vote.

I used the first approach (A) when I taught the case as part of a practice teaching session during a faculty development workshop held in Buffalo, NY, in the summer of 1999 and again at a later date when I presented the case at my laboratory meeting, but it was not ideal, as I became the center of attention and controlled the discussion. I tried the second approach (B) near the end of an upper level course on molecular biology with a good deal of success. I initiated the role-play conversation and suggested bringing in Michelle at one point, but the students really led the discussion themselves and were very lively. At one point, students from one group (acting as Anne's daughter) verbally coached Michelle to help that group argue their case for Anne. It flowed very well without much intervention on my part and all the end-of-session comments I received from the students were positive.

Variation 2

This variation would work best with an advanced class that knows how to analyze sequence information and search out information on the Internet. It would take a class and a half in time.

1st class period—1/2 hour

Review cancer caused by DNA mutations, then give the students the case to read. Next summarize the main characters and dilemma for each, more or less like the first variation above. End with saying consent is given by Anne to collect a DNA sample. Then assign all students to be in one of the 7 role-playing groups described below (4-5 people for each group—not all of the roles listed below need to be represented or others could be envisaged). Have the students search out answers to the questions provided or have the students develop and answer their own questions. The groups should return the following class period ready for discussion.

The Roles

1. *Laura, the genetic counselor*—Create Michelle’s family tree diagram, then consult a genetic counselor, if possible. Is there a strong enough case to suggest an inherited predisposition to cancer? If so, in what other family member(s) would you expect to also see the mutation? Who else would you test if Anne, the aunt, says no or the DNA sample is no good?
2. *The OB-GYN doctor*—Find information on the successfulness of prophylactic oophorectomy (ovary removal) and mastectomy (breast removal) to remove tissue and prevent cancer appearance.
3. *Michelle, the patient*—Consult with women who have been diagnosed with breast cancer or clinics that do breast cancer diagnosis or mammograms. Find out what’s involved in mammograms and surgery. How long is the recovery from oophorectomy and mastectomy?
4. *Lab chief of group analyzing DNA sample*—This group should be given the actual BRCA1 sequence in Anne’s DNA sample (see [attached document](#)). They should be told to compare this sequence to the normal BRCA1 gene in the BLAST program database (available via the National Center for Biotechnology Information web site at <http://www.ncbi.nlm.nih.gov/BLAST/>). (Note: I don’t recommend that the students be given the sequence as a handout, since they would then have to type it in to do the BLAST search and that could lead to errors. Instead you might give them the URL from this web site for the sequence and ask them to copy and paste it into their search or you could copy and paste the sequence yourself into an email message to the students for them to copy and paste in turn into the database.) Where is the mutation and is it likely to alter the protein coding? Compare this information to other previously known BRCA1 mutations. Come back with information for Laura to give to Michelle (see below, in the questions, what the expected position of the mutation is in Anne’s BRCA1 gene).
5. *Lab technical assistant*—What sample did they use to get the DNA and how did they get the DNA out of the sample? What did they use to get the sequence, what techniques, and how accurate the information is likely to be?
6. *Insurance company representative*—Get information about the proportion of cancers that are genetically linked to the total number of cancer cases recorded (generally only 10% of cancers are known to be inherited). What’s the likelihood of detecting tumors in ovaries or breasts? What is the average cost of surgery (oophorectomy or mastectomy) versus breast cancer chemotherapy at a local hospital or clinic? Consult your health insurance company and find out if they pay for mammograms, DNA testing, and/or prophylactic surgery. Are these good (i.e., cost effective) expenses for the insurance company?
7. *Michelle’s husband*—What alternative treatments are there for reducing the risk of breast or ovarian cancer? These might be hormonal or nutritional changes that have been linked to a reduced risk of developing the disease. Consult with husbands of women who have been diagnosed with breast cancer or who have gone through surgery to prevent or control the disease.

Second class period—1 hour

Have each group present the information they have gathered. Run a facilitated discussion of the most important information. Then end by asking for Michelle’s options. The whole class votes their personal preference—what they would do if they were Michelle.

Subvariation on Variation 2

The case could be run using the Problem Based Learning jigsaw format in one and a half class periods. In the 1st class period, the class is divided into “home” groups, 5-7 people in each and the same number of groups. Each student is given the case and they read it in their groups. Each student in the home group is then assigned one of the 7 roles above and the group decides what they want to know. For example, what is the BRCA1 gene? How is genetic testing performed? Time: 15-20 minutes. Then the students are reformed into “role” groups all representing the same person (i.e., all those students role-playing Michelle get together) and they discuss again what their particular person wants to know. Time: 10 minutes.

In the second class period, the role groups reform and share the information they have gathered with each other. Time: 15 minutes. Then the “home” groups reform and the students share the information they have gathered on all of the different aspects. Time: approximately 20 minutes. The group then makes some decision on what they would do if they were Michelle. Finally, the groups share with the entire class for discussion and voting, for the remaining 15 minutes.

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.

Questions for Facilitating the Discussion

For the class, before giving them the case:

- Who has ever heard of cancer? How many of you know someone with cancer? What is cancer? [At this point, you could discuss benign vs. malignant; primary tumor vs. metastasis]
- What causes cancer? [You can then discuss which of these we choose to do or have control over and which we have little or no control over]
- What is central to all causes of cancer? What happens at the level of the cell? [Ultimate answer here is DNA mutation, but it might progress via changes in the cell division or other properties that change in cancer cells]
- What is DNA and mutation?

To facilitate in-class discussion, after reading the case:

- What problems do you foresee with this situation for Michelle? Why are these problems? How would you solve these problems?
- How do you think Anne feels about this situation? Why do you think Anne has never heard of genes and DNA? If you had cancer, how would you find out more about the disease? Do you think those are ways that Anne is likely to find out about her cancer?

- What problems do you foresee Laura, the genetic counselor, having in getting the aunt to give her blood sample? What is informed consent? Why is it a requirement of giving a sample? How informed is informed? How would you get informed consent from the aunt to give her blood sample? What would you do if the aunt refused to give her blood sample?
- This can lead into the main ethical dilemma for the case: Who has the right to a DNA sample? Michelle's mother has died and not given consent to have her DNA tested. Does Michelle have the right to get that information anyway? Under what circumstances would someone not have the right or would they always have the right to the DNA sample? Consider this from the point of view of insurance companies, employers, family members, identical twins, and doctors.
- Some states (New York, for instance) take DNA sample from all jailed persons. Why do you think they do that? What is the cost-benefit to the state? What limitations, if any, should be placed on the use of that DNA sample by the state?
- Who should pay for the test? If Michelle's insurance company pays for the test, don't they have a right to the results? How would you feel if you were the husband of Michelle and didn't want the insurance company to find out that she has a cancer gene, which might increase the insurance rates? How might that affect Michelle's relationship with her husband and the insurance company?
- In reality, as noted above in the synopsis, the mutation was not in the coding region of the gene, but was a 5 base pair deletion (CAGTC) at position 29 of intron 11. This change has not been seen in any normal controls nor in other known breast cancer patients. What's the significance of the change? As this mutation does not apparently affect the coding for the gene, not clearly altering the BRCA1 protein, what would you do as Michelle? As Laura? As the daughter of Anne?

Decision Forcing

It is suggested that in all three variations you should have all of the students vote on what they would do as Michelle. If she can't get the DNA from Anne or if the gene change is not characteristically associated with cancer, she can still get her breasts removed or wait and see. There may also be more pro-active things she can do in the meantime.

Soliciting Student Feedback

I have asked three questions at the conclusion of the case:

- What did you learn from this case?
- What do you want to know more about this case?
- What do you think of this type of teaching method?

REFERENCES AND BIBLIOGRAPHY

Internet Sites

There are a number of web sites on cancer genes and testing mutations. These include two government-sponsored sites:

- The National Institutes of Health main web site at <http://www.nih.gov>, from which you can search for BRCA genes for information; and

- The NIH-sponsored Cancer Genome Anatomy Project web page at <http://www.ncbi.nlm.nih.gov/CGAP>.

There are also two sites sponsored by companies:

- <http://www.accessexcellence.org>, a site organized by the company Genentech for biology teaching and learning (a search for BRCA1 brought up many types of references at the Genetech site); and
- <http://www.myriad.com>, the company web site for Myriad Genetics, Inc., one of the major commercial firms doing the gene testing for BRCA.

There is also a very comprehensive web site at <http://www.pitt.edu/%7Eedugene/resource/> sponsored by the University of Pittsburgh Genetics Education and Counseling Program. There are a number of links within that site, including links to two other DNA-related case studies available through the University at Buffalo Case Studies in Science Collection.

The Centers for Disease Control and Prevention has a cancer page at <http://www.cdc.gov/health/cancer.htm>) with information on early detection programs, while the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program web page, at <http://seer.cancer.gov/>, provides national statistics on breast cancer.

Books and Other Resources

Food, Nutrition, and the Prevention of Cancer: a Global Perspective, published by the American Institute for Cancer Research for the World Cancer Research Fund. 1997. ISBN 1-899533-05-2. As the title implies, this book summarizes articles comparing world rates of cancer and relating that to food and nutrition in those different areas. There are sections on several types of cancer including breast and ovarian.

Understanding Gene Testing, published by the National Cancer Institute at the National Institutes of Health. 1995. This is a short booklet that describes in very simple language and with lots of pictures what genes are, how faulty genes trigger disease and what scientists do to develop predictive gene testing. It also has a glossary of common terms in cancer diagnosis and therapy. It is available free in multiple copies from the National Cancer Institute by phoning their Information Service 1-800-4-CANCER (1-800-422-6237). It is also available on the web at http://rex.nci.nih.gov/PATIENTS/INFO_TEACHER/bookshelf/NIH_gene_testing/gene00.html.

There is also a book entitled *Understanding Breast Cancer Risk*, written by Patricia T. Kelly, Ph.D., a specialist in breast cancer risk assessment and counseling for more than fifteen years. The book is a guide that addresses the social as well as the scientific aspects of breast cancer risk, helping health care professionals to better guide and inform their patients and helping patients to better inform themselves. It is published by Temple University Press and can be ordered on-line at <http://www.dnai.com/~ptkelly/index.html>, which is also a web site with other good information on breast cancer, which uses simplified language and diagrams.

Other resources include local breast cancer treatment or screening facilities, genetic counseling offices, or local chapters of the American Cancer Society.

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Sequence of a section of Anne's BRCA1 gene

GTAATATTGG CAAAGGCATC TCAGGAACAT CACCTTAGTG AGGAAACAAA ATGTTCTGCT
AGCTTGTTTT CTTACAGTG CAGTGAATTG GAAGACTTGA CTGCAAATAC AAACACCCAG
GATCCTTTCT TGATTGGTTC TTCCAAACAA ATGAGGCATC AGTCTGAAAG CCAGGGAGTT
GGTCTGAGTG ACAAGGAATT GGTTCAGAT GATGAAGAAA GAGGAACGGG CTTGGAAGAA
AATAATCAAG AAGAGCAAAG CATGGATTCA AACTTAGGTA TTGGAACCAG GTTTTTGTGT
TTGCCCTATT TATAGAAGTG AGCTAAATGT TTATGCTTTT GGGGAGCACA TTTTACAAAT
TTCCAAGTAT AGTTAAAGGA ACTGCTTCTT AAAGTTGAAA CATGTCCTC CTAAGGTGCT
TTTCATAGAA AAAAGTCCTT CACACAGCTA GGACGTCATC TTTGACTGA ATGAGCTTTAA
CATCCTAATT ACTGGTGGAC TTAATTCTGG TTTCATTTA TAAAAGCAAA