

GENE PATENTING WEBQUEST

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Do you know who owns your DNA? The race is on between Biotech Companies to research human genes because one new finding could lead to pharmaceutical advances worth millions. Courts have ruled that ownership of this type of information is legal. In this activity, you will be directed to a series of Internet sites to help you answer questions regarding the ethics of gene patenting.

A. The Cases:

I. John Moore

http://biotech.law.lsu.edu/cases/consent/Moore_v_Regents.htm

Go to sections [14] – [33].

1. Who is being sued by John Moore?
2. John Moore is suing on what grounds?
3. What illness did John Moore suffer from?
4. Which organ was removed from Mr. Moore's body? What was the reason given?
5. For nearly seven years following the operation, Mr. Moore was asked to return to the clinic for follow up testing. What was being done with the tissue samples?
6. What type of cells were patented in this case? Whose names are on the patent as "the inventors of the cell line?"
7. How much money did Genetics Institute agree to pay out for "exclusive access to the materials and research performed?"

II. Erich Fuchs and Steve Crohn

<http://online.sfsu.edu/~rone/GEessays/WhoOwnsYourGenes.html>

- 8. To what disease is Erich Fuchs seemingly immune?**
- 9. What research facility finally agreed to take a closer look at Mr. Fuchs' case?**
- 10. How does Mr. Fuchs' immunity occur?**
- 11. The scientists filed for a gene patent specifically for what?**
- 12. According to Mr. Fuchs and Steve Crohn, what were their contributions to the research effort?**

Now check out this website to see the cellular reasons behind HIV immunity:

http://www.pbs.org/wnet/secrets/case_plague/interview.html

- 13. What is the name of the mutation in the receptor that determines HIV susceptibility?**
- 14. CCR5 is a receptor that allows HIV to enter the cell. Why is it OK that cells don't necessarily have this receptor?**
- 15. What other disease does this mutation protect humans against?**
- 16. Which of the following groups would you predict would be most likely to be immune to HIV infection? Defend your position. African-Americans, Asian-Americans, or European-Americans.**

III. Daniel M. Greenberg and Sharon and Patrick Terry

<http://online.sfsu.edu/~rone/GEessays/WhoOwnsYourGenes.html>

Scroll down to the section: The Families I, Searching for Good From Sorrow

17. With what disease was Mr. and Mrs. Greenberg's children diagnosed? What are the symptoms? What is the average life span?
18. What contributions did Mr. Greenberg make to the research efforts?
19. Who now owns the patent on the gene? How much does a test for the gene cost?
20. What disease do the Terry's children have? What are the symptoms?
21. What contributions did Mr. and Mrs. Terry make to the research efforts?
22. How did the Terry's experiences with gene patents differ from that of the Greenberg's?

IV. Arupa Ganguly, Ph.D., University of Pennsylvania

<http://jncicancerspectrum.oupjournals.org/cgi/content/full/jnci;92/8/596>

23. BRCA 1 and BRCA 2 are genes associated with what medical conditions?
24. Who owns the commercial rights to the two genes?
25. What group is offered the test at a reduced rate? Why would Myriad Genetics do this?
26. What is the cost for each commercial (publicly used) test? What is the justification, according to Dr. Greg Critchfield, of this cost?
27. In 1998, Dr. Arupa Ganguly's research was stopped by Myriad Genetics, citing an infringement on their patent. Who loses in this situation?

B. The Law:

I. Intent of Patents

http://www.nsgc.org/newsroom/position_dna.asp

28. What group of professionals does NSGC represent?
29. What is the role of patents, according to NSGC?
30. What is the NSGC's recommendation regarding royalty rates?

II. Gene Patent Law

http://www.ornl.gov/TechResources/Human_Genome/elsi/patents.html

31. What are the four criteria for any patent application?
32. At what point does DNA become patentable?
33. How long does a patent last?
34. What problem could researchers run into after they have initially filed for a patent?
35. What are some different types of genetic material that can be patented?
36. What are the four requirements specifically for genetic patents?
37. According to the Human Genome Project Information Website, "Patenting provides a strategy for protecting inventions without secrecy." Why is this advantageous to patients? Why is this advantageous to the researchers?
38. Summarize the arguments cited for and against gene patenting.

C. What is actually owned??

I. An Introduction to Bioinformatics

<http://www.ncbi.nlm.nih.gov/About/primer/bioinformatics.html>

39. What is a biological database?
40. What are two major requirements for databases to be useful?
41. What is bioinformatics?
42. Is this bioinformatics database complete?
43. How can this website be used to support the theory of evolution?
44. What are some questions that can be answered by using Map Viewer?

II. Looking at the CCR5 Mutant for HIV Resistance

So, now that we have a general overview of the science of Bioinformatics, let's try out this database by finding the nucleotide sequence for the CCR5, the HIV receptor. We are going to use an activity adapted from David Form from Minuteman Regional High School.

Go to: <http://www.ncbi.nlm.nih.gov/>

Step 1: In the upper left corner, Search "Entrez" is chosen for you. Change "Entrez" to "Gene."

Step 2: To the right of "Gene", you see "for" and then a box. Type "CCR5" in the box.

Step 3: Press enter.

Step 4: Click on the first entry: CCR5.

Your new screen shows you a ton of information, but some of it can be useful to us here. For example, CCR5 is found on chromosome 3. The summary tells us that the protein is found on T cells and macrophages and is an important receptor for HIV.

Step 5: Scroll down to PubMed links under the Bibliography. This is a list of research papers written about CCR5.

Step 6: Continue scrolling down to “NCBI Reference Sequences (RefSeq).” Click on the hyperlink “NM_000579” for the mRNA sequence.

Step 7: At the top of this page, they’ll tell you how many base pairs there are in CCR5: there are 3,655 bp’s. Following this, you’ll see a LONG series of papers discussing CCR5. You can scroll through all this for our purposes.

Step 8. Scroll down to the “CDS” section. Click on that hyperlink to change the CCR5 nucleotide sequence to just the coding sequence. (The beginning and the end of this strand of DNA is important for the structure of the protein, but not the function of the receptor, so we’re just going to look at the useful piece). The number of base pairs should change to 1,059 bp.

Step 9: Scroll to the “ORIGIN” section. These are all the nucleotide bases that make up the CCR5 gene. They are organized in groups of 10 base pairs and list all 1,059 bp.

****This is the “recipe” for making the protein that is found on some immune cells that allows the entry of HIV.**

Steve Crohn and Erich Fuchs have a mutation inherited from both their parents in this gene. It is called “CCR5 delta 32.” The reason behind the name is that the mutation has a deletion that is 32 base pairs. So the gene is no longer 1,059 bp. Predict the difference before actually completing this portion of the exercise.

Step 10: Go to

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8751444

Step 11: Change display “abstract” at the top to display “nucleotide links.” Click on “display.” Select the X99393 hyperlink.

At the top, middle of the page, above “Definition,” you can see how many base pairs there are in the coding region of CCR5 delta 32. Is it what you expected?

III. The Patents Themselves

We are now going to take a look at two gene patents discussed in this webquest. You’ll notice a couple of things immediately. First, they are INCREDIBLY LONG!! Don’t get intimidated by how much information is available. After all, you don’t have to decide whether to give them the patent or not. We’re just going to look at a couple of items. You’ll also notice that the companies do indeed have to know more about the gene than just the DNA sequence.

Go to: <http://dnapatents.georgetown.edu/ostext/5679635.htm>

45. What disease is associated with the information patented in this document?

46. Who is the “assignee” for this patent?

47. Who is noticeably absent from the list of inventors?

Now go to: <http://dnapatents.georgetown.edu/ostext/5753441.htm>

48. What diseases are associated with the information patented in this document?

49. Who is the “assignee” for this patent?

50. When will this patent expire?

Teacher Resources: Gene Patenting **WebQuest**

Bioethics is a topic that needs to be covered in every biology class, especially in terms of genetics. Even those students who do not go into the biological sciences as a profession will find this information necessary in their adult lives. Our students will be voting for politicians who will influence stem cell research, genetic engineering (genetically modified food), and tissue and cell ownership. Not only does this unit provide necessary scientific background for informed adults, it stimulates debate and therefore interest in the subject material. My students (all levels) this past year became passionately engaged when they discovered that biotech companies could potentially “own” DNA sequences in their bodies. Some contacted lawyers to find answers to their questions, others did extensive research on the Internet to further understand the issues. I was very excited to see this outpouring of self-motivated learning. I decided to make a more formal lesson plan to guide them in this process and to “hook” those students who might otherwise not be so self-motivated.

This lesson could be used in its entirety or piecemeal, depending on the time allowed. The bioinformatics portion is a very interesting tool, crucial for researchers, but difficult and daunting to navigate unless specific routes are laid out for the beginner. The Cases and The Law portions of this WebQuest are probably easily done in a single class period, leaving time for discussion or debate.

If time allows, there is another activity that would be a wonderful compliment to this WebQuest. It can be found at:

http://www.ornl.gov/TechResources/Human_Genome/elsi/patents.html

Scroll down to the Educator Resources at the end. “To Own or Not to Own DNA”.

Answer Key:

A. The Cases:

I. John Moore

1. Who is being sued by John Moore?
His physician, Dr. Golde, and others who used his cells.
2. John Moore is suing on what grounds?
These defendants used "his cells in potentially lucrative medical research without his permission." The physician did not tell Mr. Moore the motivation for obtaining his cells.
3. What illness did John Moore suffer from?
hairy-cell leukemia
4. Which organ was removed from Mr. Moore's body? What was the reason given?
His spleen was removed to "slow down the progress of his disease" and to save his life.
5. For nearly seven years following the operation, Mr. Moore was asked to return to the clinic for follow up testing. What was being done with the tissue samples?
Dr. Golde was conducting research on the cells.
6. What type of cells were patented in this case? Whose names are on the patent as "the inventors of the cell line?"
T-lymphocytes / inventors: David Golde and Shirley Quan
7. How much money did Genetics Institute agree to pay out for "exclusive access to the materials and research performed?"
\$330,000 over three years, but was increased by \$110,000 later.

II. Erich Fuchs and Steve Crohn

8. To what disease is Erich Fuchs seemingly immune?
HIV
9. What research facility finally agreed to take a closer look at Mr. Fuchs' case?
Aaron Diamond AIDS Research Center in New York.
10. How does Mr. Fuchs' immunity occur?
He "inherited a gene that results in a blocked porthole into white blood cells, preventing the virus from slipping in."
11. The scientists filed for a gene patent specifically for what?
They developed a test to identify who has the gene for HIV resistance.
12. According to Mr. Fuchs and Steve Crohn, what were their contributions to the research effort?
"They offered blood, they participated in the research project, they helped the research center garner publicity for its discovery."

13. What is the name of the mutation in the receptor that determines HIV susceptibility?

delta 32

14. CCR5 is a receptor that allows HIV to enter the cell. Why is it OK that cells don't necessarily have this receptor?

There are "several other genes [that] can perform the same function."

15. What other disease does this mutation protect humans against?

The Bubonic Plague

16. Which of the following groups would you predict would be most likely to be immune to HIV infection? Defend your position. African-Americans, Asian-Americans, or European-Americans.

European-Americans: Those individuals who survived the plague were more likely to have inherited the delta32 mutation and were therefore more likely to pass on the mutation to the next generation. That mutation would therefore be found at a higher frequency in their descendants today.

III. Daniel M. Greenberg and Sharon and Patrick Terry

17. With what disease was Mr. and Mrs. Greenberg's children diagnosed? What are the symptoms? What is the average life span?

Canavan Disease. Nervous degeneration. 11-12 years

18. What contributions did Mr. Greenberg make to the research efforts?

Mr. Greenberg raised "tens of thousands of dollars in donations and grants for the project, including several thousand dollars of his own money, and helped...obtain...blood, urine, and skin biopsy samples from children with Canavan Disease and their parents.

19. Who now owns the patent on the gene? How much does a test for the gene cost?

Miami Children's Hospital. \$12.50 per test.

20. What disease do the Terry's children have? What are the symptoms?

Pseudoxanthoma elasticum. Mineralization of elastic tissue leads to blindness.

21. What contributions did Mr. and Mrs. Terry make to the research efforts?

They established a foundation to raise money, found 2,000 people with the disease, and set up a repository to store tissue samples.

22. How did the Terry's experiences with gene patents differ from that of the Greenberg's?

Hearing about the Greenberg's difficulties with the researchers crediting their contribution to the eventual patent, the Terry's had the researchers in their case sign a contract that would name the foundation in the event that any patent be created, and profits that might arise need to be shared with the foundation.

IV. Arupa Ganguly, Ph.D., University of Pennsylvania

23. BRCA 1 and BRCA 2 are genes associated with what medical conditions?

Breast and Ovarian Cancer

24. Who owns the commercial rights to the two genes?

Myriad Genetics of Salt Lake City

25. What group is offered the test at a reduced rate? Why would Myriad Genetics do this?

The National Institute of Health (NIH). To continue collecting research data regarding the "utility of their test."

26. What is the cost for each commercial (publicly used) test? What is the justification, according to Dr. Greg Critchfield, of this cost?

\$2,580. There is a need to continue funding research in related mutations.

27. In 1998, Dr. Arupa Ganguly's research was stopped by Myriad Genetics, citing an infringement on their patent. Who loses in this situation?

The women who now have no access to genetic screening for Breast and Ovarian Cancer.

B. The Law:

I. Intent of Patents

28. What group of professionals does NSGC represent?

Genetic Counselors

29. What is the role of patents, according to NSGC?

"Encouraging [and] promoting" the "development of commercially available genetic tests and therapies."

30. What is the NSGC's recommendation regarding royalty rates?

That they should be "reasonable...such that they do not significantly increase the cost of genetic testing or therapy, and do not hinder accessibility to genetic testing or therapy."

II. Gene Patent Law

31. What are the four criteria for any patent application?

"The invention must be useful,...novel,...nonobvious,...[and] described in sufficient detail to enable someone skilled in the field to use it for the stated purpose."

32. At what point does DNA become patentable?

When they are isolated, purified, or modified to produce a unique form not found in nature.

33. How long does a patent last?

20 years from the filing date.

34. What problem could researchers run into after they have initially filed for a patent?

Since the US Patent Office has 3 years to issue a patent after it has been filed, and the information filed is kept confidential, other researchers could be working on previously patented projects without knowing it.

35. What are some different types of genetic material that can be patented?

Genes, gene fragments, SNPS, Gene Tests, Proteins, and Stem Cells

36. What are the four requirements specifically for genetic patents?

1. identify novel genetic sequences, 2. specify the sequence's product, 3. specify how the product functions in nature—ie, its use, and 4. enable one skilled in the field to use the sequence for its stated purpose.

37. According to the Human Genome Project Information Website, "Patenting provides a strategy for protecting inventions without secrecy." Why is this advantageous to patients? Why is this advantageous to the researchers?

In order to obtain a patent, the knowledge must be made public. Now, others can use the information to work on clinical applications.

38. Summarize the arguments cited for and against gene patenting.

PRO: Researchers are rewarded for their discoveries and can use monies gained from patenting to further their research.

The investment of resources is encouraged by providing a monopoly to the inventor and prohibiting competitors from making, using, or selling the invention without a license.

Wasteful duplication of effort is prevented.

Research is forced into new, unexplored areas.

Secrecy is reduced and all researchers are ensured access to the new invention.

CON: Patents of partial and uncharacterized cDNA sequences will reward those who make routine discoveries but penalize those who determine biological function or application (inappropriate reward given to the easiest step in the process).

Patents could impede the development of diagnostics and therapeutics by third parties because of the costs associated with using patented research data.

Patent stacking (allowing a single genomic sequence to be patented in several ways such as an EST, a gene, and a SNP) may discourage product development because of high royalty costs owed to all patent owners of that sequence; these are costs that will likely be passed on to the consumer.

Because patent applications remain secret until granted, companies may work on developing a product only to find that new patents have been granted along the way, with unexpected licensing costs and possible infringement penalties.

Costs increase not only for paying for patent licensing but also for determining what patents apply and who has rights to downstream products.

Patent holders are being allowed to patent a part of nature -- a basic constituent of life; this allows one organism to own all or part of another organism.

Private biotechs who own certain patents can monopolize certain gene test markets.

Patent filings are replacing journal articles as places for public disclosure -- reducing the body of knowledge in the literature.

C. What is actually owned??

I. An Introduction to Bioinformatics

39. What is a biological database?

"A large, organized body of persistent data, usually associated with computerized software designed to update, query, and retrieve components of the data stored within the system."

40. What are two major requirements for databases to be useful?

Easy access to the information and a method for extracting only that information needed to answer a specific biological question.

41. What is bioinformatics?

"The field of science in which biology, computer science, and information technology merge to form a single discipline."

42. Is this bioinformatics database complete?

Definitely not! New genes and their products are constantly being discovered and imported into the database.

43. How can this website be used to support the theory of evolution?

One could use the tools at this site to compare the molecular similarity of a variety of organisms. By comparing the % similarity, one could draw inferences as to when their ancestors diverged.

44. What are some questions that can be answered by using Map Viewer?

Where does a particular gene exist within an organism's genome?

Which genes are located on a particular chromosome and in what order?

What is the corresponding sequence data for a gene that exists in a particular chromosomal region?

What is the distance between two genes?

II. Looking at the CCR5 Mutant for HIV Resistance

****This is the “recipe” for making the protein that is found on some immune cells that allows the entry of HIV.**

The sequence is as follows:

Coding Sequence (CDS) for the CCR5 Normal Allele

```
ATGGATTATCAAGTGTCAAGTCCAATCTATGACATCAATTATTATACATCGGAGCCCTGCCAAAAAATCA
ATGTGAAGCAAATCGCAGCCCGCCTCCTGCCTCCGCTCTACTCACTGGTGTTCATCTTTGGTTTTGTGGG
CAACATGCTGGTCATCCTCATCCTGATAAACTGCAAAAAGGCTGAAGAGCATGACTGACATCTACCTGCTC
AACCTGGCCATCTCTGACCTGTTTTCTTCTACTGTCCCCTTCTGGGCTCACTATGCTGCCGCCCCAGT
GGGACTTTGGAAATACAATGTGTCAACTCTTGACAGGGCTCTATTTATAGGCTTCTTCTCTGGAATCTT
CTTCATCATCCTCCTGACAATCGATAGGTACCTGGCTGTCGTCCATGCTGTGTTTGCTTTAAAAGCCAGG
ACGGTCACCTTTGGGGTGGTGACAAGTGTGATCACTTGGGTGGTGGCTGTGTTGCGTCTCTCCCAGGAA
TCATCTTTACCAGATCTCAAAAAGAAGGTCTTATTACACCTGCAGCTCTCATTTTCCATACAGTCAGTA
TCAATTCTGGAAGAATTTCCAGACATTAAGATAGTCATCTTGGGGCTGGTCTGCCGCTGCTTGTGCATG
GTCATCTGCTACTCGGGAATCCTAAAAACTCTGCTTCGGTGTGCAAAATGAGAAGAAGAGGCACAGGGCTG
TGAGGCTTATCTTACCATCATGATTGTTTATTTCTTCTTCTGGGCTCCCTACAACATTGCTTCTTCTCT
GAACACCTTCCAGGAATCTTTGGCCTGAATAATTGCAGTAGCTCTAACAGGTTGGACCAAGCTATGCAG
GTGACAGAGACTCTTGGGATGACGCACTGCTGCATCAACCCCATCATCTATGCCTTTGTCGGGGAGAAAGT
TCAGAAACTACCTCTTAGTCTTCTTCCAAAAGCACATTGCCAAACGCTTCTGCAAATGCTGTTCTATTTT
CCAGCAAGAGGCTCCCGAGCGAGCAAGCTCAGTTTACACCCGATCCACTGGGGAGCAGGAAATATCTG
TGGGCTTGTGA
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Steve Crohn and Erich Fuchs have a mutation inherited from both their parents in this gene. It is called “CCR5 delta 32.” The reason behind the name is that the mutation has a deletion that is 32 base pairs. So the gene is no longer 1,059 bp. Predict the difference before actually completing this portion of the exercise.

The gene will be 1,027 bp.

The sequence is as follows:

Coding Sequence for the CCR5 Mutant Allele

```
ATGGATTATCAAGTGTCAAGTCCAATCTATGACATCAATTATTATACATCGGAGCCCTGCCAAAAAATCA
ATGTGAAGCAAATCGCAGCCCGCCTCCTGCCTCCGCTCTACTCACTGGTGTTCATCTTTGGTTTTGTGGG
CAACATGCTGGTCATCCTCATCCTGATAAACTGCAAAAAGGCTGAAGAGCATGACTGACATCTACCTGCTC
AACCTGGCCATCTCTGACCTGTTTTCTTCTACTGTCCCCTTCTGGGCTCACTATGCTGCCGCCCCAGT
GGGACTTTGGAAATACAATGTGTCAACTCTTGACAGGGCTCTATTTATAGGCTTCTTCTCTGGAATCTT
CTTCATCATCCTCCTGACAATCGATAGGTACCTGGCTGTCGTCCATGCTGTGTTTGCTTTAAAAGCCAGG
ACGGTCACCTTTGGGGTGGTGACAAGTGTGATCACTTGGGTGGTGGCTGTGTTGCGTCTCTCCCAGGAA
TCATCTTTACCAGATCTCAAAAAGAAGGTCTTATTACACCTGCAGCTCTCATTTTCCATACATTAAGA
TAGTCATCTTGGGGCTGGTCTGCCGCTGCTTGTGCATGGTCATCTGCTACTCGGGAATCCTAAAAACTCT
GCTTCGGTGTGCAAAATGAGAAGAAGAGGCACAGGGCTGTGAGGCTTATCTTACCATCATGATTGTTTAT
TTTCTTCTGGGCTCCCTACAACATTGCTTCTCCTGAACACCTTCCAGGAATCTTTGGCCTGAATA
ATTGCAGTAGCTCTAACAGGTTGGACCAAGCTATGCAGGTGACAGAGACTCTGGGATGACGCACTGCTG
CATCAACCCCATCATCTATGCCTTTGTCGGGGAGAAAGTTCAGAAACTACCTCTTAGTCTTCTTCCAAAAG
CACATTGCCAAACGCTTCTGCAAATGCTGTTCTATTTTCCAGCAAGAGGCTCCCGAGCGAGCAAGCTCAG
TTACACCCGATCCACTGGGGAGCAGGAAATATCTGTGGGCTTGTGA
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III. The Patents Themselves

45. What disease is associated with the information patented in this document?

Canavan Disease

46. Who is the “assignee” for this patent?

Miami Children’s Hospital Research Institute, Inc.

47. Who is noticeably absent from the list of inventors?

Daniel Greenberg

48. What diseases are associated with the information patented in this document?

Breast and Ovarian Cancer

49. Who is the “assignee” for this patent?

Myriad Genetics, Inc.

50. When will this patent expire?

20 years from January 5, 1996: January 5, 2016.