**Introduction**

You are members of an elite medical investigation team, called into action because of a high number of mysterious infant deaths in a remote community in New Mexico. It is unclear whether the deaths are a result of an infectious disease or an inherited gene. As part of your investigation, your tasks are to determine the cause of these deaths and what can be done to save the lives of other children in this community.

The preliminary investigation revealed that all of the afflicted infants had two copies of a specific DNA sequence. In addition, the parents of the infants all mentioned that the children had sweat that seemed to be saltier than normal. It is your task to discover the significance of this DNA sequence, determine how it relates to those with the disease, and describe its symptoms and possible treatments. You will then prepare a report to inform public officials of the outcome of your investigation.

For this project you will break into groups of four. Each team will use the Koshland Science Museum website and other online sources to investigate DNA technology and perform an analysis of the DNA sequence that was found in the sick infants.

**Initial Group Activity**

Begin by working as a group to determine the significance of the DNA sequence shared by the afflicted infants.

1. **What kind of biological samples could have been used to collect the DNA from the sick infants?**  
   How similar is human DNA to that of other species?  
   [https://new.koshlandscience.org/sites/all/exhibits/exhibitdna/intro01.jsp](https://new.koshlandscience.org/sites/all/exhibits/exhibitdna/intro01.jsp)  
   [https://new.koshlandscience.org/sites/all/exhibits/exhibitdna/crim04.jsp](https://new.koshlandscience.org/sites/all/exhibits/exhibitdna/crim04.jsp)

2. **One way to investigate DNA is to “probe the sequence” for specific strings of nucleotides.**  
   What is the relationship between the size of a probe and the number of times it might occur in any given sequence of DNA?  
   [https://new.koshlandscience.org/sites/all/exhibits/exhibitdna/seq01.jsp](https://new.koshlandscience.org/sites/all/exhibits/exhibitdna/seq01.jsp) (go through the *Probe the Sequence* activity)

3. **In *Probe the Sequence*, you searched a fairly small stretch of DNA (about 1500 bases) for three or six base combinations. This is called a **BLAST (Basic Local Alignment Search Tool) search.****  
   Now you are going to blast the DNA sequence from the sick infants against the entire human genome, which contains 3 billion base pairs -- just as scientists must when they investigate.
The blast search compares the DNA sequence from the sick children to all known DNA sequences in the human genome.

DNA sequence:
TGATTATGGAGAACTGGAGCCCTTCAGAGGGTAAAATTAAGCACAGTGGGAAGAATTTCATTCTGTTCTCAG
TTTCTCCTGGATTTATGCTTGGCACCATAAAGAAAATACATTGTGAATATGATATAGATACAGAA
GCGTCATCAAAGCATGCCAACCTAGAAGAGGACATCCTCTCAAGTTGTCAGAGAAAGACAATATAGTTCTTGGA
GAAGGTGGAAATCACACTGAGTGGGAAGGTGGAATCACACTGAGTGGAGGTCAACGAGCAAGAATTCTTTTCTTAGCAAGAGCGATATA

Go to the DNA blast search at the National Center for Biotechnology Information website:

Copy and paste the DNA sequence for the sick children into the box titled: “Enter accession number(s), gi(s), or FASTA sequence(s):” and then press the “BLAST” button at the bottom of the page.

After a few seconds, you will get several “hits.” Scroll down to the first result, “Sequence ID: ref|NC_018918.2|” and look at the comparison of the two DNA sequences. Your sequence is on the top row (Query) and the Blast result sequence (Subject) is underneath your sequence.

***Print out the BLAST search results and turn in with group report***

a. How does your sequence compare to the known sequence? A vertical line between the two sequences indicates that they are identically matched. If no vertical line appears, it indicates that the sequence you entered has a mutation. What is missing from your sequence that is in the known sequence?

Copy the blue text that follows “Features:” This is the name of the gene. Go to http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM, paste the gene name into the white box, and press the “Search” button.

***Print out ONLY THE FIRST PAGE and turn in with group report***

Click on the first link (*602421) to find out more about the gene and what disease it causes.

b. How does the DNA sequence relate to the disease?
http://www.ygyh.org/cf/cause.htm

4. Learn more about inherited diseases. Give an example of an inherited disease and what kind of mutation causes it.
https://new.koshlandscience.org/sites/all/exhibits/exhibitdna/inh01.jsp
Individual Activity

Now that you have matched the DNA sequence to a specific disease, your medical investigation team will need to do more research. Each member of your group now takes on a different role and works individually to investigate the cause of the illness. Reference the appropriate worksheet to complete this activity.

Roles:

• DNA Scientist (Ph.D. Biologist): Investigate the structure of DNA and how it codes for proteins
• Epidemiologist: Study the history of the disease, including when and how it was discovered, when the genetic basis was determined, how many people are affected and what the risk factors are.
• Disease Specialist (Pediatrician): Learn about the disease, its symptoms, and current treatment options.
• Genetic Counselor: Explore how genetic counseling works and use genetics to analyze inheritance patterns in families with disease.

Group Activity

When you are finished with your individual research, share what you have learned with your group, then prepare a report and/or presentation. It should include recommendations to local officials, detailing what you think their community policies should be regarding the prospect for future disease, treatments, counseling recommendations, and any other relevant topics. See the relevant worksheet to complete the group activity.

DNA Scientist

1. What kind of training and education do you need to become a DNA researcher? What kind of activities do you do on a day-to-day basis?  

2. What, exactly, is DNA and how is it related to a gene? What are the names of the two processes needed to code DNA into protein? How many nucleotides are in a codon?  
   http://learn.genetics.utah.edu/content/basics/  
   http://www.dnaftb.org/dnaftb/21/concept/index.html  
   http://www.dnaftb.org/dnaftb/22/concept/index.html
3. What is the name of the gene that causes the disease and where is it located in the human genome? How do changes in the gene cause the disease?
http://web.ornl.gov/sci/techresources/Human_Genome/posters/chromosome/chromo07.shtml

4. This disease is caused by a mutation in the DNA that causes a change in the amino acid sequence of the protein. Given the normal and diseased DNA sequences below, what are the mRNA sequences after transcription, and what are the resulting amino acids after translation?

Normal: AATATCATTTTGGGTGTTT
Disease: AATATCATTGGGTGTTTCC

http://www.nature.com/scitable/topicpage/translation-dna-to-mrna-to-protein-393

5. In the previous question, the third codon is different between the two sequences, but the amino acid remains the same. What is the benefit of having more than one codon for an amino acid? http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=stryer.section.685

1. What kind of training and education do you need to become a DNA researcher? What kind of activities do you do on a day-to-day basis?
2. What, exactly, is DNA and how is it related to a gene? What are the names of the two processes needed to code DNA into protein? How many nucleotides are in a codon?

3. What is the name of the gene that causes the disease and where is it located in the human genome? How do changes in the gene cause the disease?

4. This disease is caused by a mutation in the DNA that causes a change in the amino acid sequence of the protein. Given the normal and diseased DNA sequences below, what are the mRNA sequences after transcription, and what are the resulting amino acids after translation?

   Normal: AATATCATCTTTGGTGTTT
   Disease: AATATCATGTTGGTGTTTCC
5. In the previous question, the third codon is different in the normal DNA sequence and the disease sequence, but the amino acid remains the same. What is the benefit of having more than one codon for an amino acid?

1. What kind of training and education do you need to become an epidemiologist? What kind of activities do you do on a day-to-day basis?

2. Describe the history of this disease. When was it discovered? When was the biochemical cause understood? It might be useful to discuss this question with the Disease Specialist.

3. How many people in the United States are affected by this disease? Worldwide? How many babies born in the next year are expected to have this disease?

4. How does this disease affect the life of the patient? What are the physical limitations that a patient experiences? What is the typical lifespan of a person with this disease?
   http://ghr.nlm.nih.gov/condition=cysticfibrosis
   http://www.ygyh.org/cf/whatisit.htm
1. What kind of training and education do you need to become an epidemiologist? What kind of activities do you do on a day-to-day basis?

2. Describe the history of this disease. When was it discovered? When was the biochemical cause understood? *It might be useful to discuss this question with the Disease Specialist.*

3. How many people in the United States are affected by this disease? Worldwide? How many babies born in the next year are expected to have this disease?

4. How does this disease affect the life of the patient? What are the physical limitations that a patient experiences? What is the typical lifespan of a person with this disease?

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Disease Specialist (Pediatrician)

1. What kind of training and education do you need to become a pediatrician? What kind of activities do you do on a day-to-day basis?

2. This disease is caused by a mutation in the DNA that causes a change in the amino acid sequence of the protein. How do the amino acid changes in the protein affect the function of the protein and how does this cause disease?

http://www.ygyh.org/cf/cause.htm
http://learn.genetics.utah.edu/content/disorders/singlegene/

3. What physical symptoms might infants afflicted with this disease have? What are current and future treatment options? Be sure to discuss gene therapy.

http://www.yourgenesyourhealth.org/cf/whatisit.htm
http://www.cff.org/home/

1. What kind of training and education do you need to become a pediatrician? What kind of activities do you do on a day-to-day basis?

Disease Specialist (Pediatrician)
Fact Finding Sheet

2. This disease is caused by a mutation in the DNA that causes a change in the amino acid sequence of the protein. How do the amino acid changes in the protein affect the function of the protein and how does this cause disease?
3. What physical symptoms might infants afflicted with this disease have? What are current and future treatment options? Be sure to discuss gene therapy.

1. What kind of training and education do you need to become a genetic counselor? What kind of activities do you do on a day-to-day basis?
   [Link](http://nihlifeworks.org/Alphabetical%2bList/Counselor%2c%2bGenetic.html)

2. Analyze the family pedigree of one of the individuals that has the disease. How is this disease inherited? Is the disease dominant or recessive? Explain.
   [Link](https://www.ndsu.edu/pubweb/~mcclean/plsc431/mendel/mendel9.htm)
   [Link](http://www.ygyh.org/cf/inherited.htm)

3. A Punnet Square is a way of determining probabilities for a trait to be passed down from parents to children. Learn how to use a Punnet Square, then construct one for each of the following scenarios and calculate the percentage chance that a child will have the disease if it is a recessive trait.
a. One parent has the disease and one parent does not have the gene that causes the disease.
b. One parent has the disease and one parent has the gene, but does not have the disease.
c. Both parents have the disease.
d. Both parents have the gene, but do not have the disease.

4. Will every child with this disease have parents with the disease? Explain why or why not.

1. What kind of training and education do you need to become a genetic counselor? What kind of activities do you do on a day-to-day basis?

2. Analyze the family pedigree of one of the individuals that has the disease. How is this disease inherited? Is the disease dominant or recessive? Explain.
3. A Punnet Square is a way of determining probabilities for a trait to be passed down from parents to children. Learn how to use a Punnet Square, then construct one for each of the following scenarios and calculate the percentage chance that a child will have the disease if it is a recessive trait.

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b. One parent has the disease and one parent has the gene, but does not have the disease.
c. Both parents have the disease.
d. Both parents have the gene, but do not have the disease.

4. Will every child with this disease have parents with the disease? Explain why or why not.

**Group Activity**

Once you have individually completed the questions for your roles, gather together as a group and discuss the questions below.

1. What is the cause of this disease?
2. What is known about this disease and its impact on the community?
3. What are treatment options for this disease?
4. Gene therapy is a possibility for future treatment. What are the pros and cons of gene therapy?
5. What are the pros and cons of genetic testing for this disease? Who should be tested? Who should be able to access the results of a genetic test (patients, doctors, insurance companies, employers)?
6. Make recommendations for local officials detailing what you think their community policies should be regarding the prospect for future disease, treatments, counseling recommendations, etc.
These questions might require further research into the issues. In addition to the references you used individually, you can use the references in the Resources section on the next page.

Prepare a report and/or a presentation. It should include recommendations to local officials, detailing what you think their community policies should be regarding the prospect for future disease, treatments, counseling recommendations, and any other relevant topics. Answers to the following questions should be answered.

Conclusion
Congratulations! You have figured out the cause of infant deaths in this remote community. Now on to your next medical challenge.....

Resources

HEALTH AND DISEASE

DNA/GENOME SEQUENCING
http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml
http://www.genome.gov/10001772

GENETICS
https://learn.genetics.utah.edu/
http://www.kumc.edu/gec/
http://www.estrellamountain.edu/faculty/farabee/biobk/biobooktoc.html
http://www.pbs.org/wgbh/aso/tryit/dna/

GENETIC COUNSELING
http://www.genome.gov/19016905