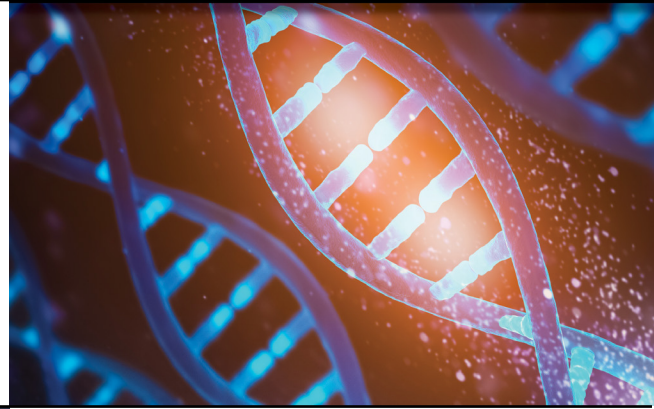


**BIOTECHNOLOGY!****Part 4:**  
**Biotechnology  
and  
Human Health****SUSTAINABLE  
DEVELOPMENT GOALS**

developed by

**Smithsonian**  
*Science Education Center*

in collaboration with

**iap** **SCIENCE  
HEALTH  
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## PART 4: BIOTECHNOLOGY AND HUMAN HEALTH

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### **Find out More!**

For additional resources and activities, please visit the *Biotechnology!* StoryMap at <https://bit.ly/3pQUDpc>.



## Planner

Activity	Description	Materials and Technology	Additional Materials	Approximate Timing	Page Number
<b>Task 1: How can we diagnose diseases using biotechnology?</b>					
<b>Discover</b>	Explore what you know about diagnosing disease and how this relates to genetic variants.			20 minutes	135
<b>Understand</b>	Determine which disease is causing a patient's symptoms and identify the genetic variant. Consider the risks of genetic diseases related to ancestry.			30 minutes	141
<b>Act</b>	Take on the role of genetic counselor and share with others ethical and personal considerations related to genetic testing.		<u>Ethical Concerns List</u> (Part 1)	20 minutes	145
<b>Task 2: How can we fix genetic diseases using biotechnology?</b>					
<b>Discover</b>	Consider what you know about disease treatment. Use an analogy to explore the stages of diagnosis, design, and delivery of gene therapy.	<ul style="list-style-type: none"> <li>• Paper or class board</li> <li>• Pens or pencils</li> </ul>		20 minutes	150
<b>Understand</b>	Model gene therapy options and investigate ongoing gene therapy clinical trials.	<ul style="list-style-type: none"> <li>• Paper</li> <li>• Pens or pencils</li> </ul>		30 minutes	154
<b>Act</b>	Develop a communication plan to share more about the diagnosis, design, and delivery of gene therapy with your community.		<u>Futures Mood Board</u> (Part 1)  <u>Ethical Concerns List</u> (Part 1)	20 minutes + action time	160



## Task 1: How can we diagnose diseases using biotechnology?

Knowing the cause of a medical problem can be an important step in figuring out how to treat or cure it. In this task, you will **discover** more about the way **biotechnology** is used to help **diagnose** or identify a disease. You will **understand** how diagnosing disease works by modeling how diseases can be detected using genetic data. Finally, you will **act** on this information and consider when genetic diseases should be diagnosed.

### *Meet Your Research Mentor*



Meet Dr. Filippo Pinto e Vairo. Filippo (pronounced FIH-lee-po) is one of the many researchers around the world trying to use biotechnology to improve human health and create a healthier future. As action researchers you are also trying to improve health in the future. Filippo will be your research mentor to help you understand more about the role biotechnology can play in diagnosing disease.

Filippo is a clinical geneticist and associate professor at the Mayo Clinic in Minnesota, United States. He has a master's degree in medical sciences and a PhD in genetics and molecular biology, and completed a postdoctoral fellowship in individualized medicine as well as a specialization in data science. However, he also has knowledge and perspectives that came from other parts of his identity. Since Filippo is now working with you, it is important to understand who he is.

To help you, Filippo filled out an identity map, just like you did in Part 1. Filippo's identity map includes the following things.

- Physician for 15 years, geneticist for 12 years
- Huge sports (of any kind) fan
- Enjoys walking, loves traveling
- Lives in Rochester, Minnesota, USA
- Born in north Brazil, but lived for 30 years in south Brazil
- 39 years old

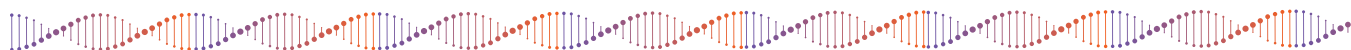


- Male and uses he/his/him pronouns
- Black hair (“When I had it!”), black eyes, average height
- Optimistic, good-tempered, curious
- Speaks Portuguese, English, a little Spanish, and French
- Interested in genomic and translational medicine
- Life goal: help diagnose individuals with undiagnosed diseases using state-of-the-art technologies
- Father of a unique, wonderful daughter
- Son of a physician and a lawyer

Before you begin this task, think quietly to yourself about Filippo’s identity map.

- Are there things you have in common with Filippo?
- Are there ways in which you are different from Filippo?
- Can you see anything about Filippo’s identity, in addition to his university degrees, that would help him understand different perspectives or ideas about human health?

Throughout this task you will notice Filippo sharing ideas and experiences with you. He may help you understand better ways to do your research, or share some of the research he has done.



### **Discover:** *What do I know about diagnosing disease?*

You may think diagnosing diseases is something only doctors do, but really many of us diagnose common diseases all the time. In this part we will be talking about two different types of diseases.

One type is **infectious disease**, which means you catch a disease from someone or something. Viruses and bacteria are two common types of microorganisms that can cause infectious disease. For example, when someone who is infected with a virus coughs, sometimes that cough pushes small pieces of virus out of their body and into the air, and someone else can be infected by breathing in those small pieces.

Another type of disease is **genetic disease**. Genetic disease occurs when a **variation** within a person’s **genome** causes the disease. You cannot catch a genetic disease.



Sometimes you **inherit**, or are born with, the genetic variation that causes the disease. One example of an inherited genetic disease is sickle cell disease. Sometimes you **acquire**, or develop the genetic variation over time, as you grow and your cells divide. Cancer is one example of an acquired type of genetic disease.

1. Imagine you and your friends share a meal. Not long afterwards everyone who ate together begins to feel sick and starts vomiting. Would you have an idea of what might have caused the disease? If so, congratulations! You just made a possible diagnosis. It is very likely you all ate some food that had a harmful microorganism that your body wanted to get rid of, so you started vomiting. This is an example of an infectious disease.
2. Now think about another infectious disease, COVID-19. Share with your team what you know about COVID-19 **symptoms**, or signs that you might be sick. Which COVID-19 symptoms are you familiar with?
3. Many of the common symptoms of COVID-19 can also be caused by other infectious diseases. For example, many infectious diseases cause a runny nose, coughing, and fever. With your team, discuss, how you could find out for sure whether someone with these symptoms has COVID-19 or another illness.
4. After you have discussed how to diagnose someone with COVID-19 symptoms, read *Testing for COVID*.

### Testing for COVID

There are two common types of tests to diagnose someone with COVID-19.

One is called an **antigen** test. The antigen test is often taken at home. Sometimes it is called a rapid test because it can give results in around 15 minutes. The COVID-19 virus has specific antigens, or proteins, that are unique to the virus. The COVID-19 antigen test contains a substance that reacts when the antigen is present. So if enough of the virus is in your body, it reacts with the substance in the test and often signals the presence of the antigen by turning a color. Figure 4-1 shows an example.





Figure 4-1: This is a positive antigen COVID-19 test. A line at the C (control) shows the test is working. A line at the T (test) shows the test is positive and the protein antigen of COVID-19 is present.

The other common COVID-19 test is called a **PCR** test. PCR is a biotechnology technique that creates many copies of existing genetic material. The PCR technique can be used in many ways. In the case of the COVID-19 PCR test, if the COVID-19 viral genetic materials are present, the PCR creates many copies, so they are easy to detect.

#### Emotional Safety Tip

The COVID-19 pandemic has affected people's health and lives. You may have been sick yourself or have had friends or family who were sick or died from COVID-19. Thinking about this may be upsetting. If you need to pause and take a break, that is okay.

5. Have you or someone else you know ever been tested for COVID -19? If you feel comfortable doing so, share that experience with your teammates.
- Which type of test do you think was used?
  - Was it useful to have the results of the test? Why or why not?
  - Have you ever known anyone who had trouble having their disease diagnosed?





### *Filippo says . . .*



Diagnosis is so important. For example, if a newborn is very sick, it could be an infection. But it could be a genetic disease. And if you can diagnose this child, you can offer the right treatment, the right medicine, the right diet. You can save lives, and we are doing this. When you sequence the genome of a newborn that is ill in the intensive care unit, you find a genetic answer 50% to 60% of the time.

### 6. Read *Genetic Variation and Diseases*.

#### *Genetic Variation and Diseases*

As you read before, infectious diseases like COVID-19 are only one type of disease. Another type of disease is genetic. When cells grow and divide, the **DNA** in the cells is copied. During this copying process there is a chance of making errors. These errors may delete, insert, or change a portion of DNA. These errors are sometimes called **mutations**. These mutations create genetic **variants**, or **genes** with one or more differences from the original.

You inherit some genetic variants from your parents when you are born. You also continue to acquire genetic variants throughout your life as your DNA is copied when your cells divide. Other things can also cause mutations and genetic variants, like exposure to tobacco, certain chemicals, radiation, ultraviolet light, and certain viruses.

Not all mutations are harmful; many do not have any effect at all. Your body has many ways of identifying and getting rid of cells that do have harmful mutations.

However, sometimes people inherit DNA that has harmful variants. Often this matters more in some cells than in others. For example, in the genetic disease cystic fibrosis, the genetic variant is in all the person's cells, but is particularly harmful in cells in the lungs and intestines.



People also acquire harmful variants. If a cell that has harmful variants is not identified and removed by the body, it can continue to divide. This means all the cells that come from those cell divisions will almost always also have the harmful variants. This uncontrolled growth of cells with harmful variants is called cancer. Cancers usually start in one area of the body, like the liver, brain, or stomach.

 **Emotional Safety Tip**

You or someone you care about may suffer from an inherited or acquired genetic disease. This is not your or their fault. It is okay to feel sad, frustrated, or upset. If you need to pause and take a break, that is okay.

*Filippo says . . .*



There is no such thing as a normal genome. Everyone has genetic variants when compared to a so-called **reference genome**. I am different from you in part because we have genetic variants. What clinicians and researchers do is to find out if there are specific genetic variants that are causing a patient's symptoms.

7. Now, with a partner, think about genetic disease. Often these diseases are caused by just one small variation in the base pair DNA sequence of a gene. For example, if an A base changes to a C base, this variation can create problems building the protein for which the gene usually codes. How could you diagnose this disease? Consider the biotechnology tools you have learned about here and in Part 1 (they are listed below). Pick the tool or tools you think might be useful to diagnose an inherited genetic disease. Explain to your partner how you think that might work.
- Genome sequencing**, a tool that allows you to find out the order of all the DNA **bases** in the cell
  - CRISPR**, a tool that allows you to change specific parts of a DNA sequence in a cell



- c. Antigen test, a tool that reacts to specific proteins
- d. PCR test, a tool that makes lots of copies of a specific part of DNA

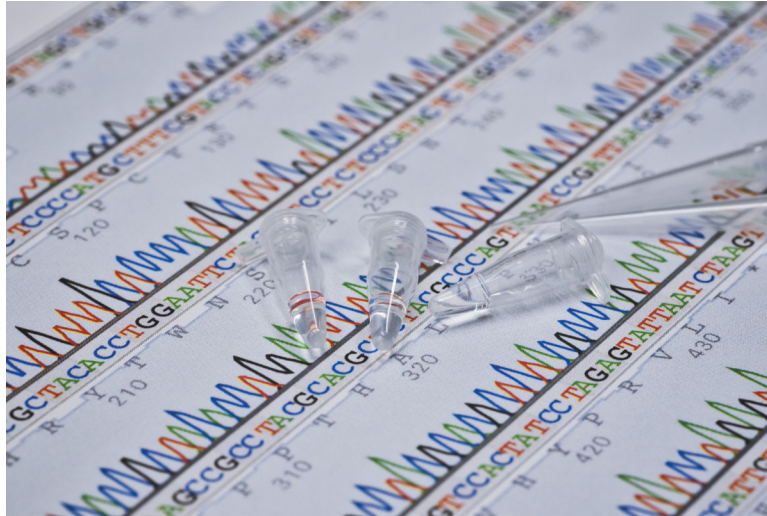


Figure 4-2: A genome sequencing result.

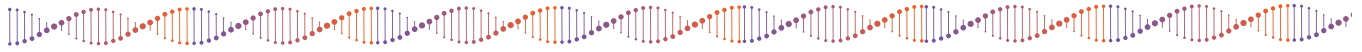
8. One common way genetic diseases are diagnosed is through genome sequencing. There are certain genetic variations that are known to be linked to genetic disease. If you have one of these variations and you have the symptoms of the disease, it is likely the genetic variation is causing the disease. As you learned in Part 1, genome sequencing is getting more inexpensive all the time. Discuss with your teammates:
- a. What are the advantages to having affordable and available genome sequencing?
  - b. Are there any disadvantages?

### Filippo says ...



Many patients have been searching for a diagnosis for a long time. Even when you give them news that is not good, it can be helpful. They can get some closure. They can start to find other similar patients and think about their options. When you are in the dark [without a diagnosis] it is just difficult to do anything.





## ***Understand:*** How can biotechnology determine the specific causes of disease?

Genome sequencing can help medical researchers find out more about whether a genetic disease is causing specific symptoms. Though everyone is born with dozens to hundreds of new variants, many of these variants do not create problems. But some specific variants of human genes have already been identified as often leading to disease. The difficulty is in determining which variants may be causing the symptoms of a genetic disease.

1. Clinicians and medical researchers are like disease detectives. They are trying to work backwards from the symptoms to the cause of a disease. Sometimes they can do this by looking at things people with specific symptoms have in common. One of the things people may have in common is the same genetic variant.
2. Read and follow the *Disease Detective Instructions* to become a disease detective yourself.

### ***Disease Detective Instructions***

These are the steps clinicians and medical researchers use when they are trying to find the cause of a disease.

- a. **Examine the symptoms:** When searching for a genetic cause of a disease, the first thing researchers usually examine is a person's symptoms. If others have similar symptoms and a genetic cause is known, that genetic cause might be the first place to investigate.
- b. **Decide which part of the genome to sequence:** If a specific genetic variation is suspected to be the cause of the disease, sometimes only one gene is sequenced. However, as genetic sequencing is becoming more affordable, researchers often will sequence a person's whole genome.
- c. **Analyze the genome:** Researchers have created something called a reference genome using the most common DNA sequences they collected. They use computers to compare the DNA sequences of the patient with sequences from the reference genome. They analyze large amounts of data to identify variants. Variants can be due to several causes.



- Deletion: A variant can have one or more base pairs deleted. For example, if the reference sequence was ACTAGAG but the patient had the sequence AAGAG, the base pairs CT were deleted.
  - Insertion: A variant can have one or more base pairs **inserted**, or added. For example, if the reference sequence was ACTAGAG and the patient had the sequence ATCTAGAG, the base pair T was inserted right after the first A.
  - Substitution: A variant can have one or more base pairs substituted. For example, if the reference sequence was ACTAGAG and the patient had the sequence CCTAGAG, the base pair C was substituted for the first base pair A.
- d. **Match the variant to the disease:** If other people in the population have the same variant and the same symptoms, that is a good clue that the variant may be causing the disease.

3. Now you can try to be a disease detective yourself, using the same steps.

 **Emotional Safety Tip**

There has been a lot of progress in diagnosing and treating genetic diseases, but still, if you know someone with one of these diseases you may be worried about them. Even if you don't know someone personally, learning about diseases can feel hard and scary. It is okay to pause and take a break if you need to.

4. Examine the symptoms: Use the clues in the following steps to help identify the cause of the patient's symptoms.
- a. Patient A symptoms: persistent coughing, frequent respiratory infections, wheezing, salty-tasting skin
5. Decide which part of the genome to sequence: Figure 4-3 shows four common genetic diseases and the genes that have been linked to those diseases. Which gene do you think you should sequence for Patient A?



<p style="text-align: center;"><b>Tay-Sachs Disease</b></p> <p><b>Symptoms:</b> weakness, difficulty swallowing, loss of hearing or vision</p> <p><b>Linked gene:</b> <i>HEXA</i> (hexosaminidase A)</p>	<p style="text-align: center;"><b>Sickle Cell Disease</b></p> <p><b>Symptoms:</b> anemia (lack of red blood cells), periods of pain, swelling of hands and feet, delayed growth</p> <p><b>Linked gene:</b> <i>HBB</i> (hemoglobin-beta-locus)</p>
<p style="text-align: center;"><b>Cystic Fibrosis</b></p> <p><b>Symptoms:</b> frequent coughing and lung infections, shortness of breath and wheezing, poor growth, salty skin</p> <p><b>Linked gene:</b> <i>CFTR</i> (cystic fibrosis transmembrane conductance regulator)</p>	<p style="text-align: center;"><b>Hemochromatosis</b></p> <p><b>Symptoms:</b> feeling tired, pain in joints, darkening of skin</p> <p><b>Linked gene:</b> <i>HFE</i> (homeostatic iron regulator)</p>

Figure 4-3: Symptoms and linked genes of four genetic diseases.

6. Analyze the genome: Let's assume you decided to sequence the *CFTR* gene that is linked with cystic fibrosis. The *CFTR* gene has almost 200,000 base pairs. A computer gives you another clue and identifies one place in the *CFTR* gene in Patient A that is variant, meaning it is different than the reference sequence.

- a. Can you find the variant in patient A? Remember, the variant could be a deletion of one or more base pairs, an insertion of one or more base pairs, or a substitution of one or more base pairs.

Reference *CFTR* partial sequence:      AAAATATCATCTTTGGTGTTT

Patient A *CFTR* partial sequence:      AAAATATCATTGGTGTTT

7. Match the variant to the disease: The *CFTR* gene codes for the *CFTR* protein, which is usually part of the cell membrane. The *CFTR* protein helps maintain the balance between salt and water within and outside of cells. There are many variants that can cause a problem with the *CFTR* protein, and those variants can cause cystic fibrosis. Figure 4-4 shows three common *CFTR* variants.

- a. Which variant do you think Patient A has?
- b. Would you diagnose Patient A with cystic fibrosis?



CFTR Variant Name	CFTR Variant Description
P.Phe508del	This variant is the deletion of three base pairs (CTT), which results in a protein missing one amino acid. This protein does not get properly folded and so is not usable.
P.Gly542*	This variant is caused by a substitution of a G for a T. This substitution stops the protein from adding the remaining amino acids and the protein is not usable.
p.Asn1303Lys	This variant is caused by the substitution of a C for a G. This changes the amino acid asparagine to the amino acid lysine. The stops the protein from functioning correctly.

Figure 4-4: Three common CFTR variants and their effects in the body.<sup>1</sup>

8. Read *Patient A Diagnosis* to find out if you diagnosed Patient A correctly.

### *Patient A Diagnosis*

If you thought the symptoms of patient A matched the symptoms of cystic fibrosis and so you should test the CFTR gene, you are right.

The reference sequence had three base pairs (shown in bold) that were deleted in Patient A's CFTR gene: AAAATATCAT**CTT**TGGTGT**TTG**G.

The scientific name of this variant is P.Phe508del and it is the most common cause of cystic fibrosis globally. Once the variant is identified, scientists can start thinking about how to fix the genetic problem. You will learn more about this in Task 2.

Because cystic fibrosis is an inherited disease, certain variants can be more or less common among different populations. For example, in many parts of Europe more than 70% of cystic fibrosis patients have the P.Phe 508del variant. However, in Turkey only around 20% of cystic fibrosis patients have this variant. Your genetic **inheritance** from your biological parents, grandparents, and so on is called your **ancestry**. Your ancestry is important when thinking about genetic diseases.

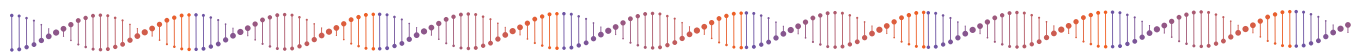


9. Most reference sequences were built by gathering DNA from people with European ancestry and finding their most common base pair sequences. Discuss with your team:
- Why might that be a problem for identifying whether a variant is causing a disease if the patient does not have European ancestry?
  - How could gathering reference sequences from people with other ancestries help scientists better diagnose disease?
10. Not all genetic diseases are caused by a problem with just one gene. Read what Filippo has to say. How might having multiple genes that cause a disease change what you need to do to diagnose it?

### *Filippo says . . .*



With some diseases it is a single gene causing a single disease. This is straightforward. But this is not always the case. For example, with epilepsy there are multiple genes involved. Every single day we are discovering new genes that cause epilepsy. The sequencing technology has developed a lot. With next-generation sequencing we can sequence the entire genome more quickly and affordably. Then we can search for variants in thousands of genes at a time—even ones we didn't know caused epilepsy, for example.



### **Act:** *How can we use this information ethically and wisely?*

Not everyone wants to know everything about their health. It is the nature of genetics that when a person finds out things about their health, they sometimes find out information they did not want to know. They may also find out about potential health problems of their relatives. Often before a genetic test is done, a **genetic counselor** will help people think through what it will mean to have this knowledge. In this activity you will think about the questions you might raise if you were a genetic counselor.





1. Imagine you are a genetic counselor. What are some of the things you think might be very important to think about before being tested for a genetic variant?
2. Write down questions you might like to ask or topics to raise with someone making this choice. What should they think about?
3. Examine your *Ethical Concerns List* from Part 1. If anything on the list reminds you of any questions you might like to ask or ideas you would want the patient to think about, write down those ideas now.

### *Filippo says . . .*



We are now using genetic testing in all sorts of different ways. We are testing people who are healthy who want to know if they are likely to develop a genetic disease or if they might pass a genetic disease on to their children. So we are now using genome testing not just for diagnosis, but also to help people plan and make decisions.

4. With a partner, read *Situation One*.

### **Situation One**

People with certain genetic variants in the *BRCA1* gene have a higher risk of developing breast cancer. This is true for men and women. Just because you have a *BRCA1* variant does not mean you will develop breast cancer; it is just more likely.

Others in your family have had breast cancer. You are considering testing for *BRCA1* variants. However, your sister does not want to know whether she has a *BRCA1* variant. Although her genetic results could be different, if you tested positive, it would mean she could have as much as a 50% chance of testing positive as well. Do you want to have a *BRCA1* genetic test?



5. Assign one partner to be a genetic counselor and the other to be a patient in Situation One.
  - a. As the genetic counselor, use the questions you wrote down and any others you can think of to encourage the patient to think about the potential consequences of their decision. Your role is not to judge them or make them decide a certain way; it is to help them consider all the different parts and consequences of their decision. For example, you might ask, "Why are you considering getting the *BRCA1* genetic test?"
  - b. As the patient, think about how you might feel if you were in Situation One. Try to answer the genetic counselor's questions. If the information is not provided, for example if there are questions about why your sister does not want to know, you can just use your imagination to make up realistic information. For example, you could say, "I am thinking about getting the test because I just had a friend who was diagnosed late with breast cancer and it has been hard to treat" or, "I am thinking about getting the test because I believe it is better to know than not know," or another reason that you decide.
6. Now switch. The partner who was the genetic counselor becomes the patient. The partner who was the patient becomes the genetic counselor. Use the information in Situation Two to role play another discussion, the same way you did in step 5.

### Situation Two

Your parent had a genetic disease that affects the brain called Huntington's disease. A person is born with the variant that causes the disease, but the symptoms do not develop until middle age. People with symptoms usually have problems with thinking, behavior, and movement that get worse over a period of 10 to 25 years.

There is currently no cure for this disease. If your parent had it, you have a 50% chance of inheriting this disease. Do you want to have a genetic test to find out whether you inherited Huntington's disease?



 **Emotional Safety Tip**

Having conversations about whether you would or would not test for a disease can feel emotional, especially if you know someone with a genetic disease. There are no right or wrong answers, and every person and situation is unique. If you need to pause and take a break, that is okay.

7. Discuss with your team:
  - a. Why might it be important to have conversations like those you modeled with the genetic counselor before testing?
  - b. As testing becomes more common, are there things you think people need to be talking about more frequently?
  - c. Some people are able to access genetic testing. Others may not be in a location that offers genetic testing or genetic testing may be too expensive for them. How do you feel about that?
8. Write or draw the important things you want to remember and share about diagnosing genetic disease. Be sure to include:
  - a. How it works
  - b. The types of diseases can be diagnosed
  - c. What is useful about testing to diagnose genetic diseases
  - d. What are the potential concerns
  - e. Why this might be important to your community
9. Share this information with a classmate, friend, or family member. Discuss with them why it might be important to know this information.



## Task 2: How can we fix genetic diseases using biotechnology?

In Task 1, you explored how to diagnose genetic diseases. **Gene therapy** is one type of treatment to fix genetic problems. Using gene therapy, genes can be added or changed to treat genetic diseases. Today the dream of gene therapy is rapidly becoming a reality. In this task you will **discover** the need for targeted treatments to fix genetic problems. Then you will investigate to **understand** how biotechnology is helping to deliver personalized treatments. Finally, you will **act** by integrating what you now know into community dialogues about treating disease.

### *Meet Your Research Mentor*



Meet Dr. Nicole Paulk. Nicole (pronounced nih-COLE) is one of the many researchers around the world trying to use biotechnology to improve human health and create a healthier future. As action researchers you are also trying to improve health in the future. Nicole will be your research mentor to help you understand more about the role biotechnology can play in treating disease.

Nicole is a professor of biochemistry and biophysics at the University of California, San Francisco, in the United States. She has a PhD in viral gene therapy and completed a postdoctoral fellowship in human gene therapy. However, she also has knowledge and perspectives that came from other parts of her identity. Since Nicole is now working with you, it is important to understand who she is.

To help you, Nicole filled out an identity map, just like you did in Part 1. Nicole's identity map includes the following things.

- Lives in San Francisco, California
- 38 years old
- White/Caucasian female
- Interested in viruses, gene therapy, and genome engineering
- Likes to snowboard, cycle, go on adventure vacations, and go white-water rafting

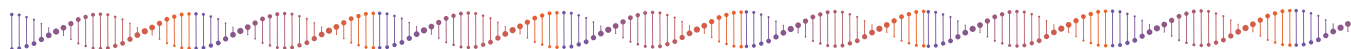


- “Tall, hazel eyes, long straight brown hair that won’t curl no matter WHAT I do to it, huge smile”
- Loud voice, goofy, detail-oriented
- Daughter of a lumberjack and a secretary, sister to an electrician
- Life goal: help discover treatments for diseases that have no therapies, particularly for diseases in kids

Before you begin this task, think quietly to yourself about Nicole’s identity map.

- Are there things you have in common with Nicole?
- Are there ways in which you are different from Nicole?
- Can you see anything about Nicole’s identity, in addition to her university degrees, that would help her understand different perspectives or ideas about human health?

Throughout this task you will notice Nicole sharing ideas and experiences with you. She may help you understand better ways to do your research or share some of the research she has done.



### **Discover:** How can we treat genetic diseases?

DNA is like an instruction manual for your cells. When there are errors with the instructions, there can be problems with your cells and your body. In Task 1 you learned about how researchers are diagnosing these errors. In this activity you will start thinking about treatments to fix these errors.

1. Use a class board or a piece of paper to list diseases you know about. These can be diseases you or others you know have had or just diseases you have heard about. If you have time, you can ask others you know, like your family or friends, for additional ideas.
2. Now list any treatments you know next to each disease. Treatments might include pills, injections, surgery, or other methods.



3. With your team, discuss:
  - a. Do these treatments fix the cause of the problem or just make someone feel better for a while? It is okay if you do not know the answer to this question. Just do your best.
  - b. Are these treatments targeted to one specific place in the body or do they go all over the body?
  - c. How do the treatments reach the part of the body they are trying to treat?
4. Examine your list of diseases and treatments. Circle the diseases you think might be caused by problems with your genes. Next you will be thinking about the way gene therapy tries to treat genetic problems.
5. Read this **analogy**, then answer the questions with your team.
6. You know that a cell uses the instructions in DNA to build proteins. Let's imagine you are like a cell and are trying to build something. In this analogy you are trying to build a chair just like the one in Figure 4-5. What would you need?



*Figure 4-5: The chair you are trying to build in the analogy.*

7. You might think you need materials to build the chair and instructions on how to build it. This is true for a cell as well when it is building a protein. It needs materials to build the protein, and it also needs instructions. Where does the cell get its instructions?
8. The cell gets its instructions from DNA, just like you might get your instructions from an instruction manual. Imagine the instructions have an error. Maybe a sentence or a whole page is missing. Or perhaps the instructions were printed



wrong and tell you to attach a piece backwards. Or maybe there are extra steps printed that should not be there.

- a. With your team, think about how an error in your instruction manual might be an analogy for an error with the DNA instructions in a cell.
- b. Are there different types of errors possible in DNA, just as there were with your instruction manual?
- c. What do you think might happen when building a protein if there was an error in the DNA that codes for it?

9. Read *DNA Instructions and disease*.

### *DNA Instructions and Disease*

Without all the correct instructions, you might not be able to build the chair so that it is usable. And without all the correct base pairs in a gene, a cell might not be able to build a usable protein. When a cell cannot build a usable protein, this can cause a disease. Diagnosing the problem means finding the place in the instructions that is creating the problem. You learned about this in Task 1. Now you will think about how to fix this problem.

10. Continue thinking about the chair analogy. If there was an error with the instruction manual, how could it be fixed? For example, if you had a whole new instruction book that was correct, you would know how to build the chair. Or if you had a correct copy of just the missing step, you would know how to build the chair.
- a. How could fixing the chair instructions be an analogy for designing a gene therapy?
  - b. With your team, think about what you know about different biotechnology techniques. Are there any techniques you can think of that might be used to fix problems with a gene? Read *Gene Therapy Types* to learn more.



## Gene Therapy Types

There are different approaches to treating genetic diseases.

Sometimes, a whole new copy of an existing gene is added to a cell and then usable proteins can be made, along with the unusable ones from the existing variant gene. This would be like having a whole new set of instructions delivered so you could build the chair. This is called **gene replacement therapy**.

Genes can also be directly edited within the genome, using a tool like CRISPR. This would be like someone arriving at your home and using a pen to fix the error in your instruction manual. This is called **gene editing therapy**.

Sometimes, a gene that is supposed to be switched off and not make proteins gets switched on by a variant. This would be like if you had an additional step in your instruction manual. Someone could come to your home and use a marker to cross out the extra step. In the case of gene therapy, a gene that blocks that variant gene from building proteins might be introduced. This is called **gene inhibition therapy**.

### *Nicole says . . .*



A genetic medicine can either be something that's permanent or something that's temporary. It can be something where we edit your genome. For example, if you were born with a mutation in one of your really important genes, we could actually go in and fix that mutation in place so you wouldn't have that mutation anymore. Or we could give you a whole functional copy of a gene.

11. Delivering the gene therapy is another challenge. Think again about the analogy. Even though the correct instructions for the chair may exist, that doesn't help you unless you have them at your home. Imagine you need a physical copy of the correct instruction manual to build the chair. Someone reading it to you over the phone or sending you an electronic copy will not do. The company that produces





the guide is far away, but they do have correct copies. How could you get a copy of the missing step at your home?

- a. When something is delivered to your home, what kind of information do you think is necessary so the delivery person can get it to you—not to your neighbor, a person across the country, or a person across the world?
- b. Why do you think it might be important to target the delivery of a gene therapy to a specific cell (or cells)?

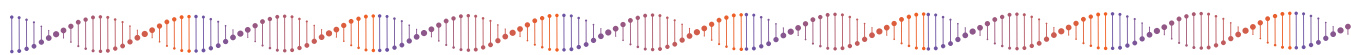
*Nicole says . . .*



The delivery of the gene therapy needs to be specific, just like a delivery truck delivers to a specific place, not just go to your country or your state. The delivery has to go to your street, to your building, right to your door.

12. Examine your list of circled genetic diseases and treatments from steps 1 and 2. Discuss with your team:

- a. Which disease would you be most excited to have a gene therapy to treat?
- b. Gene therapy targets the specific genetic problem within specific cells. How is that the same or different from the treatments you listed in step 2?



**Understand:** *How can biotechnology help provide targeted treatments?*

The goal of gene therapy is to target the specific problem with the gene in the specific cells where it is a problem. This can be challenging, but scientists have made tremendous progress.

1. Think about ways you could deliver gene therapy to specific cells and share your ideas with your team. You need to:
  - a. Protect the genetic material you are trying to deliver
  - b. Deliver genetic material to the cell



- c. Make sure the genetic material enters the cell you want, also known as the **target cell**
2. Now, with your team, read *Special Delivery*. What natural systems already target and deliver genetic material to cells?

### Special Delivery

Viruses can be very good at entering and infecting cells. Think of the virus as like the delivery vehicle from the Discover analogy. How could this be useful?

Usually, viruses contain their own genetic material that they carry into a cell when they enter it. However, imagine all the viral genetic material was removed. Only the parts needed for delivery remain. This virus delivery vehicle is called a **viral vector**. The viral vector can now deliver lots of different things. For example, you could add a gene for gene therapy to the virus and have it delivered to the cell. Viruses are not the only gene therapy delivery vehicles, but they are by far the most common. Different viruses are selected for different needs.

3. Think about a viral infection you have had (such as a cold or the flu). Did the virus tend to attack certain places in your body? Some viruses tend to infect the respiratory system, others the digestive system, others may infect other types of cells. So most viruses are already targeting specific cell types. Why might that be useful when using them as a delivery mechanism?

#### *Nicole says . . .*



People usually think of viruses as something that we treat, for example if you're sick with a virus. But in fact the vast majority of viruses on the planet don't make humans sick. They can be used as delivery tools. Different viruses tend to go different places. Viruses are already really good at getting inside of our cells, so we can use a virus to deliver the gene therapy.

We can also custom tailor viruses in all kinds of ways to make them more targeted to a particular spot in your body, or to a particular **species**, or to a particular combination of tissues or cell types.



4. Divide up into groups of three. Each member of the group will need a pencil and a piece of paper. Read *Modeling Gene Therapies Instructions*.

### **Modeling Gene Therapies Instructions**

As a group you are going to model how different types of gene therapy work once they reach the target cells.

Remember when you learned that a cell can “read” DNA to build proteins? In Part 1 we used the analogy of the sentence, “Start here: Read this sentence and then draw a box” as an analogy for how DNA gives cells instructions. In this activity you will use this analogy to model how different gene therapies work.

Choose one person to model the cell, one person to model the current gene, and one person to model the gene therapy.

#### **The cell**

If you are modeling the cell, your job is to follow the instructions you receive. Cells always need to be told to start reading a piece of DNA. So, as long as you receive an instruction begins with “Start here” you will carry out the instruction. Use a piece of paper and pencil to draw anything you are told to draw.

#### **The current gene**

If you are representing the current gene, you write instructions on the top of your piece of paper. Tear off that part of the paper and give it to the cell to carry out. If the gene therapy replaces or changes your piece of paper, you should let them do it.

#### **The gene therapy**

If you are representing the gene therapy, your goal is to make sure the cell is drawing what is needed. In this model you will have three options:

- a. **Gene Replacement:** Write down instructions on an additional piece of paper and give them to the cell to carry out. The current gene will then give your piece of paper to the cell.



- b. **Gene Editing:** Take your pencil and correct a few letters that were mutated in the current gene. Have the current gene give their corrected instructions to the cell.
- c. **Gene Inhibition:** Take your pencil and cross out what the current gene has written so it cannot be read. Have the current gene give their crossed-out instructions to the cell.

There will be four rounds. Have the current gene and the gene therapy read the details for each round. Hide the details from the cell. Can the gene therapy find a way to get the cell to meet the goal?

### Round 1

Goal: Have the cell draw a circle.

Current gene: Begin by writing the sentence, "Start here: Read this sentence and then draw a circle" on your piece of paper. Now you will model the mutation. Erase the word "circle" and substitute in the word "line." Your paper should now read, "Start here: Read this sentence and then draw a line."

Gene therapy: Use the type of therapy you think would be best to achieve your goal of getting the cell to draw a circle.

### Round 2

Goal: Have the cell draw a big triangle and then a small triangle.

Current gene: Begin by writing the sentence, "Start here: Read this sentence and then draw a big triangle and then a small triangle" on your piece of paper. Now you will model the variant. Erase the part that says, "and then a small triangle."

Gene therapy: Use the type of therapy you think would be best to achieve your goal.

### Round 3

Goal: Have the cell draw nothing.

Current gene: Begin by writing the sentence "Start here: Read this sentence" on your piece of paper. Now you will model the variant. After "sentence" add the words, "and then draw squares until the paper is filled." Your paper should



now read: "Start here: Read this sentence and then draw squares until the paper is filled."

Gene therapy: Use the type of therapy you think would be best to achieve your goal.

#### Round 4

Goal: Have the cell draw a square.

Current gene: Begin by writing the sentence, "Start here: Read this sentence and draw a square" on your piece of paper. Now you will model the variant. Erase everything between "Start" and "square." Your paper should now read: "Start square."

Gene therapy: Use the type of therapy you think would be best to achieve your goal.

5. Discuss with your group:

- a. Why were some gene therapies better than others for the different situations in the different rounds?
- b. Could you have used other ones? For example, if the gene therapy you chose was gene replacement, could you have used gene editing instead?

#### Emotional Safety Tip

Although scientists have made a lot of progress and the first gene therapies are starting to be available to the public, there is a long way to go. Many gene therapies are only in the testing phase and many more are still in development. It can be frustrating if you or someone you care about is suffering from a disease that might be cured or helped using gene therapy, but the therapy is not yet available. It is okay to feel sad or angry about that. By learning about how gene therapy works, you can help educate others and encourage the changes you want.

6. Read what Nicole says. How do you think gene therapy will change things in the future?



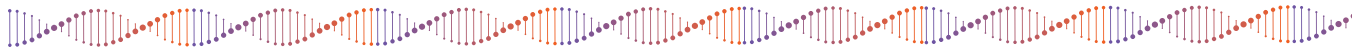
**Nicole says . . .**

A virus can now be a therapeutic drug to treat you for something. For example, there are kids who are unable to see because they are born with a specific type of blindness that is caused by a problem with one of their genes. We can give them a one-time infusion of a virus into their eye that gives them a functioning gene that they weren't born with—a gene they needed to see. Then, once they wake up from the surgery, they can see. And they can see forever. We can cure this form of blindness using gene therapy.

Right now a lot of the gene therapy work is on rare diseases, but work is starting on even more common ones. I think in the future there will be gene therapies for diseases like heart disease, diabetes, and cancer. If you are in middle or high school now, I feel certain that you will be eligible for a gene therapy within your lifetime. It will become a common type of treatment.

7. You have learned more about the way gene therapy works. Now choose a disease you know about in your community. You will be doing some research to investigate whether there are any ongoing **clinical trials** using gene therapy to treat that disease. A clinical trial is the final stage of developing a treatment. If a treatment appears to be working and to be safe in laboratory and other models, it usually is tested next with a small group of people. If those people have good results, it gets tested with even larger groups. If you have access to the Internet, you can go to [trialssearch.who.int](http://trialssearch.who.int) or [clinicaltrials.gov](http://clinicaltrials.gov) to search for clinical trials that are happening right now. Search for the name of the disease you are investigating and gene therapy.
  - a. How many clinical trials are underway?
  - b. How recent are the clinical trials?
8. Compare your results with your teammates.
  - a. Which disease did you find has the most gene therapy clinical trials?
  - b. Are there any gene therapy clinical trials you are really excited about?





**Act:** *How can we ethically use gene therapy to solve medical problems?*

You have learned about gene therapy and how it is used. Now you will think about how this relates to your hopes and fears for the future. Then you will consider what other people should know about gene therapy and the future.

1. Take out your Futures Mood Board from Part 1.
2. What hopes do you have for the future after learning about gene therapy? If you want, add drawings, words, or photos to help represent those hopes.
3. What concerns do you have for the future after learning about gene therapy? If you want, add drawings, words, or photos to help represent those concerns. Be sure to consider anything related to your Ethical Concerns List from Part 1.
4. Think to yourself, what is the most important thing you learned during this task?
5. Share your thoughts with your team and listen carefully when they share their ideas with you.
6. Discuss with your team:
  - a. Who are people who really need to know about the diagnosis and treatment of genetic diseases but don't know already?
7. As a team, can you come up with a way to share these important ideas with this group? For example:
  - a. Could you create a visual to present to another class?
  - b. Could you create a song, poem, or play to explain what gene therapy is and how it works?
  - c. Do you have other ideas about how to share?
8. Plan how you want to share with the audience you identified. Make sure to find a way that includes everyone on your team. Don't forget to:
  - a. List the steps you need to take.
  - b. Assign different people responsibility for different steps.
  - c. Put your plan into action!



# Congratulations!

## You have finished Part 4.

### *Find out More!*

For additional resources and activities, please visit the *Biotechnology!* StoryMap at <https://bit.ly/3pQUDpc>.





## Glossary

This glossary can help you understand words you may not know. You can add drawings, your own definitions, or anything else that will help. Add other words to the glossary if you would like.

**Acquire:** Develop over time or in response to something

**Analogy:** Comparing two things to help provide clarification

**Ancestry:** Your genetic inheritance from your biological parents, grandparents, so on

**Antigen:** A protein that is unique to a virus or specific type of cell; the immune system uses antigens to identify things to attack

**Bases:** The four types of DNA units that store information: adenine (A), cytosine (C), guanine (G), and thymine (T)

**Biotechnology:** Using living things, parts of living things, or things produced by living things to solve people's problems and meet their needs

**Clinical trial:** A test of a treatment that occurs after laboratory and other models have proven successful; the treatment is usually tested with a small group of people and if those people have good results, it gets tested with even larger groups

**CRISPR:** A biotechnology tool that cuts DNA in very specific places to add, delete, or change base pair sequences

**Diagnose:** Identify a disease

**DNA:** A molecule in all living things that transfers and stores genetic data



**Gene:** A section of the base pair sequence in DNA that codes for specific traits

**Gene editing:** Changing genes in very specific and targeted ways

**Gene editing therapy:** Changing a very specific small part of a gene in a cell to treat a disease

**Gene inhibition therapy:** Blocking a harmful variant gene from building proteins

**Gene replacement therapy:** Adding a new copy of a gene in a cell to treat a disease

**Gene therapy:** A type of treatment that uses functional genes to fix a genetic problem in the body

**Genetic counselor:** A professional who helps people think through genetic testing decisions and consider the results of that testing

**Genetic disease:** An illness caused by variation within the genome

**Genome:** The complete sequence of DNA of a living thing

**Genome sequencing:** A tool that allows you to find out the order of all the DNA bases in the cell

**Infectious disease:** An illness you catch from someone or something

**Inherit:** Born with, coming from your parents

**Inheritance:** How traits or characteristics of parents are passed on to their children



**Inserted:** Added into another thing, often into a specific place

**Mutations:** Copying errors in DNA resulting in genetic variation, now more commonly called variants

**PCR:** A biotechnology technique that creates many copies of a piece of existing genetic material

**Reference genome:** The most common gene sequences across a population

**Species:** A type of living thing, like a human or a dog or a coconut tree

**Symptoms:** Signs that you might be sick

**Target cell:** The specific cell a therapy is trying to treat

**Variants:** Genes with one or more differences

**Variation:** Differences in living things

**Viral vector:** A virus delivery vehicle for other genetic materials, such as gene therapies



## End Note

1. Cystic Fibrosis Centre at the Hospital for Sick Children in Toronto. 2022. Cystic Fibrosis Mutation Database. Retrieved from <http://www.genet.sickkids.on.ca/Home.html>.

