Rutherford County Schools

Individual Learning Modules

Course: Biology I **April 20th – April 24th**

Main Idea/Focus: Biotechnology/CRISPR	**Aligned resource (Biology, Pearson)** Pg. 532-533

Standard(s):
How does this align with your state standards?

BIO1.ETS2.1 – Obtain, evaluate, and communicate information on how molecular biotechnology may be used in a variety of fields.

BIO1.ETS2.2 – Analyze scientific and ethical arguments to support the pros and cons of applications of a specific biotechnology technique.

Resource(s):
What do you need? Text, data sets, tools, etc.

Textbook:
Tennessee Biology, Miller & Levine, Pearson
Access via Clever – check with your teacher on login credentials, if needed

Videos, Interactives:
HHMI BioInteractive (optional)
https://www.biointeractive.org/classroom-resources/crispr-cas-9-mechanism-applications

Task(s):
What will you do? What will you investigate?

Scenario 1: Jessie Gelsinger (Gene Therapy)
(Source: Tennessee Biology, Miller & Levine, Pearson, pg. 532)

It all seemed so simple. To cure a disease caused by defective gene, why not replace it with a healthy version of the same gene? In 1990, Drs. Kenneth Culver and Michael Blaese had done just that for a four-year-old girl with a genetic disorder called adenosine deaminase deficiency. Give such success, in 1999, researchers at the University of Pennsylvania thought they might be able to do something similar for eighteen-year-old Jessie Gelsinger.

Jessie suffered from ornithine transcarbamylase deficiency (OTCD), which prevents the liver from processing ammonia as it should. Although drugs had enabled Jessie to lead a fairly normal life, he volunteered to be a test subject for experimental gene therapy. His parents went along with his wishes, in hopes of helping children with potentially fatal versions of the same disease.

The treatment involved medical researchers inserting copies of the healthy gene into a virus. They expected that the virus would carry the replacement gene into Jessie's liver cells, curing him of OTCD. The virus had been carefully engineered for this purpose, and the researchers were confident it would be harmless. But shortly after they injected these viruses into the artery leading to Jessie's liver, something went terribly wrong.

Within days of the treatment, his immune system reacted against the virus so strongly that his liver and other organs underwent a complete shutdown. Five days later, this courageous volunteer was removed from life support, and died.

Scenario 2: Promise of CRISPR
(Adapted from: Doctors try 1st CRISPR editing in the body for blindness, HHMI Bionteractive, March 4, 2020: https://www.biointeractive.org/planning-tools/science-news/doctors-try-1st-crispr-editing-body-blindness)

Scientists say they have used the gene editing tool CRISPR inside someone's body for the first time, a new frontier for efforts to operate on DNA, the chemical code of life, to treat diseases.

The people in this study have Leber congenital amaurosis, caused by a gene mutation that keeps the body from making a protein needed to convert light into signals to the brain, which enables sight. They're often born with little vision and can lose even that within a few years.

Scientists can't treat it with standard gene therapy -- supplying a replacement gene -- because the one needed is too big to fit inside the disabled viruses that are used to ferry it into cells. So, they're aiming to edit, or delete the mutation by making two cuts on either side of it. The hope is that the ends of DNA will reconnect and allow the gene to work as it should.

It's done in an hour-long surgery under general anesthesia. Through a tube the width of a hair, doctors drip three drops of fluid containing the gene editing machinery just beneath the retina, the lining at the back of the eye that contains the light-sensing cells. "Once the cell is edited, it's permanent and that cell will persist hopefully for the life of the patient," because these cells don't divide, said one study leader not involved in this first case, Dr. Eric Pierce at Massachusetts Eye and Ear. Doctors think they need to fix one tenth to one third of the cells to restore vision. In animal tests, scientists were able to correct half of the cells with the treatment, Albright said.

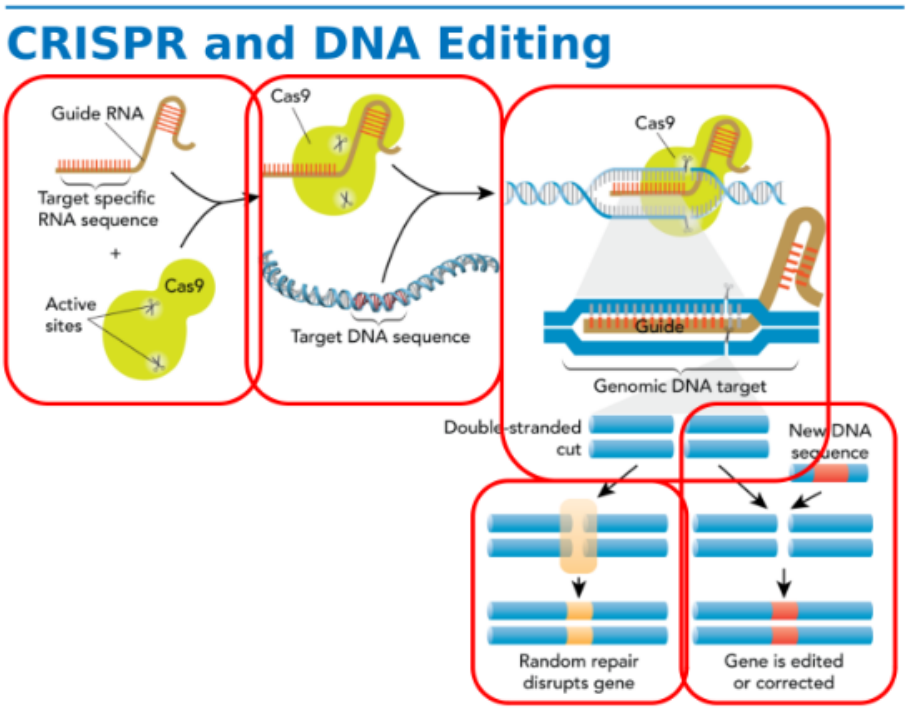
The eye surgery itself poses little risk, doctors say. Infections and bleeding are relatively rare complications.

One of the biggest potential risks from gene editing is that CRISPR could make unintended changes in other genes, but the companies have done a lot to minimize that and to ensure that the treatment cuts only where it's intended to, Pierce said. He has consulted for Editas and helped test a gene therapy, Luxturna, that's sold for a different type of inherited blindness.

Although the new study is the first to use CRISPR to edit a gene inside the body, another company, Sangamo Therapeutics, has been testing zinc finger gene editing to treat metabolic diseases. Other scientists are using CRISPR to edit cells outside the body to try to treat cancer, sickle cell and some other diseases.

All of these studies have been done in the open, with government regulators' approval, unlike a Chinese scientist's work that brought international scorn in 2018. He Jiankui used CRISPR to edit embryos at the time of conception to try to make them resistant to infection with the AIDS virus. Changes to embryos' DNA can pass to future generations, unlike the work being done now in adults to treat diseases.

(Additional information on CRISPR mechanism may be found in your textbook on pages 512-513)



Final Product(s):
What will you answer? What will you create? What will you communicate?

1. Define the Problem – Jessie was the first reported patient to die during a gene therapy trial, and his death had an impact on the direction of the technology.
    a. Research the gene therapy treatment that was given to Jessie Gelsinger. Prepare a description of the treatment and an explanation of what may have gone wrong.
    b. Why did it seem as though gene therapy would be a promising treatment for people with disorders caused by a single gene?
2. Evaluate a Solution – How might CRISPR revolutionize medicine, among other genetic applications?
    a. How might CRISPR technology offer hope for the future of gene therapy?
    b. What problems might be solved by delivering replacement genes via CRISPR rather using other types of vectors?
3. Develop and Use a Model – Develop a model for how CRISPR works. Use the model to explain CRISPR to a family member, friend, or teacher.
4. Ask Questions – What ethical questions should be considered, related to genetic engineering and biotechnology applications of CRISPR? How is the scientific community addressing ethical implications? How are governments responding to ethical concerns?