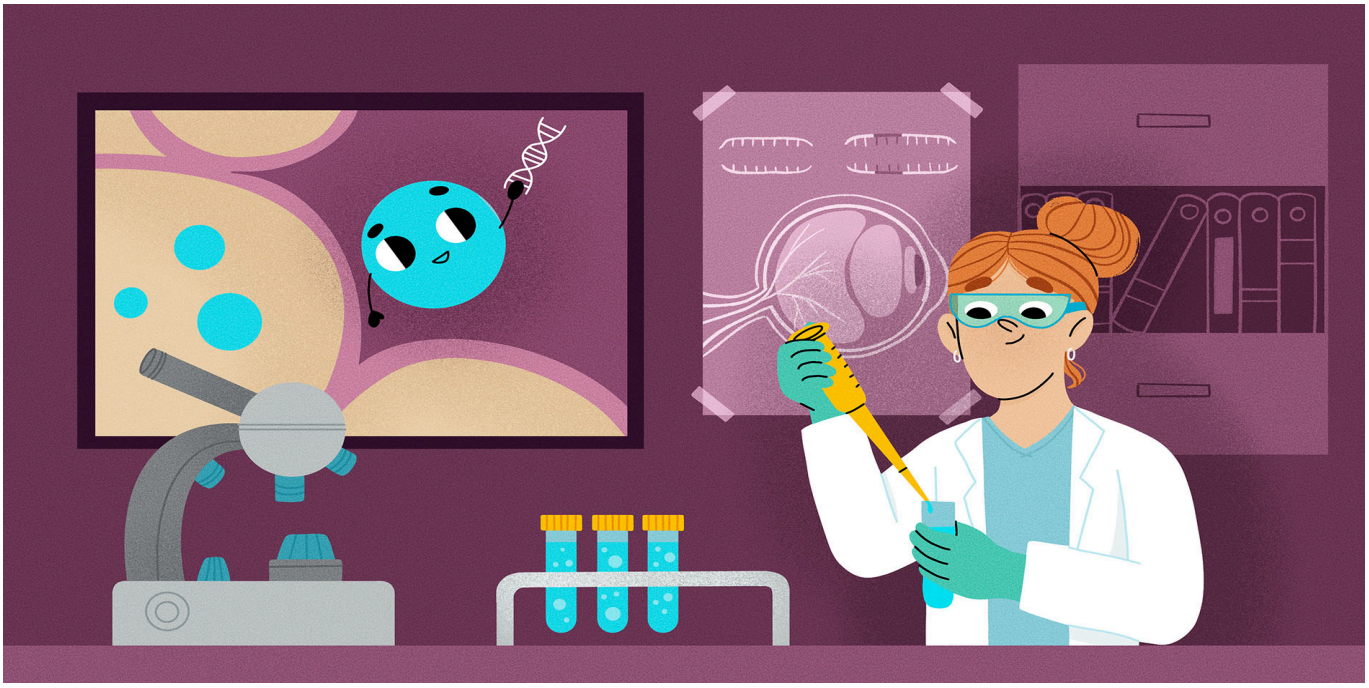
frontiers | Frontiers for Young Minds

HUMAN HEALTH
Published: 18 October 2023
doi: 10.3389/frym.2023.1021056



CAN VIRUSES BE USED TO MAKE PEOPLE HEALTHY?

Marina Levochkina[1], *Avigail Beryozkin*[1], *Hamzah Aweidah*[1], *Oliver M. Beale*[1] *and Leah C. Byrne*[1,2,3*]

[1]*Department of Ophthalmology, University of Pittsburgh, Pittsburgh, PA, United States*
[2]*Department of Neurobiology, University of Pittsburgh, Pittsburgh, PA, United States*
[3]*Department of Bioengineering, University of Pittsburgh, Pittsburgh, PA, United States*

YOUNG REVIEWERS:

CAEDMON
AGE: 13

JOHN P. FREEMAN OPTIONAL SCHOOL
AGES: 9–13

QANYA
AGE: 13

Viruses are small particles that are so tiny they cannot be seen by a regular light microscope. However, viruses can be found almost anywhere you look. Viruses specialize in carrying genetic material into all kinds of cells, including human cells. Many viruses are harmless to humans while others can cause illnesses like the cold, the flu, or COVID-19. Recently, scientists have been using viruses to deliver genes into cells to cure human diseases! This is called gene therapy. Genes are the blueprints for the proteins that make up the human body, and mistakes in a gene can cause disease. Gene therapy is a way to treat these types of diseases. To create a gene therapy, scientists cut out a virus's genes and replace them with properly working human genes. These modified viruses can then be used to deliver healthy genes and treat disease.

WHAT ARE VIRUSES?

Viruses are found everywhere—they exist on your skin, in your gut, and on surfaces all around you. There are about 100 times more viruses in your body than human cells [1]. Of the many different kinds of viruses that exist, most are harmless and exist peacefully within living organisms. There are over 140,000 different kinds of viruses found in the healthy human gut alone [2]. Most of the viruses that you have heard of, however, cause illnesses like the flu or COVID-19. Even the common cold is often caused by a family of viruses called rhinoviruses.

GENETIC MATERIAL

The "blueprints" cells (and viruses) use for making proteins. DNA and RNA are the genetic materials in human cells and in viruses.

GENES

The instructions for making proteins.

A virus is a tiny particle made of a protein shell, containing its own **genetic material** (Figure 1A). A virus's main purpose is to make more copies of itself, and it does this by hijacking a cell, delivering its genetic material into the cell, and forcing the cell to create virus copies (Figure 1B). DNA is the genetic material that contains the instructions, like a set of blueprints, for how to make all the proteins in the body. Proteins are complex molecules, and different proteins have different purposes and functions, including making up the shell of a virus or carrying out important work inside a cell. Sections of the DNA that contain the instructions for how to make individual proteins are called **genes**.

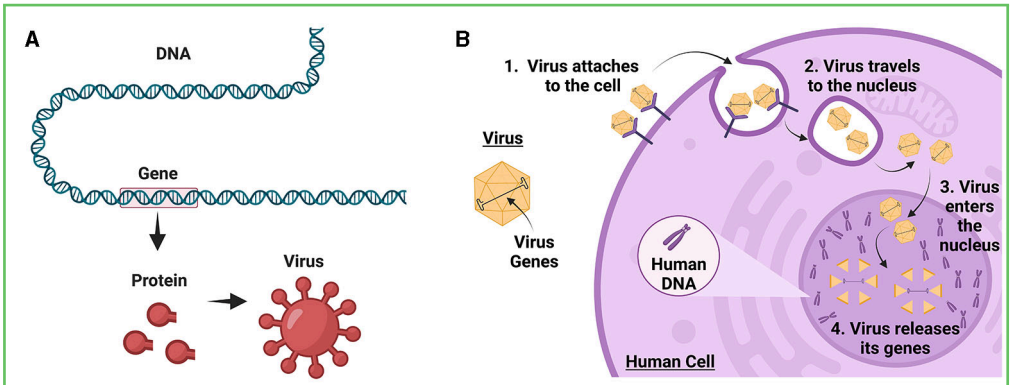


Figure 1

Figure 1

(A) Genes are sections of DNA that contain the instructions for specific proteins. Proteins carry out essential jobs inside a cell, and they also make up the shells of viruses. **(B)** To reproduce, viruses hijack a cell, using that cell's machinery to make more copies of themselves. A virus attaches to the surface of the cell, is absorbed by the cell, and then travels to the cell's nucleus where it releases its genes. The human cell has a hard time telling the difference between its own genes and the virus's genes, so it makes more viruses. Figure created with BioRender.com.

Although a virus has its own genetic material, it does not have the proper machinery for reading genes and creating its own proteins. This is why viruses must infect cells—they rely on the protein factories inside the cells they infect. The human cell has a hard time telling its own genes apart from a virus's genes, so the cell mistakenly reads the virus's genes and produces viral proteins along with human proteins. That is why viruses are not considered living organisms—they cannot multiply on their own, without infecting a cell.

After a virus multiplies inside a cell, newly made viruses are released from the cell and can infect neighboring cells. As we mentioned, this process can lead to contagious diseases like COVID-19 but, in the past few decades, scientists have been harnessing the gene-delivery power of viruses to *treat and cure* diseases.

WHAT IS GENE THERAPY?

MUTATION

A change in DNA that can cause disease.

Genetic disorders are diseases that occur when there is a mistake called a **mutation** in a person's DNA. Because DNA contains the instructions for building proteins, mutations can lead to the loss of a protein that is important for a body function or even for survival.

GENE THERAPY

Treating disease by transferring genetic material into cells.

About 50 years ago, scientists had an interesting idea: what if we could transfer healthy genes into the cells of people who suffer from a genetic disease [3]? Treating disease by transferring genetic material into cells is called **gene therapy**. Scientists also thought that maybe we could use viruses to insert a healthy gene into cells. Maybe the viruses could "trick" cells into producing the healthy, functional protein they are missing. A few decades later, scientists achieved just that (Figure 2)! To use viruses for gene therapy, scientists replace viral genes with a corrected version of the mutated human gene. They then inject these modified viruses into the part of the body where the protein should be found. There, the modified virus enter human cells and release healthy copies of the gene. The cells can then read this corrected gene and build a functional protein. Removing the viral genes makes gene therapy viruses unable to replicate, so they can no longer spread from cell to cell.

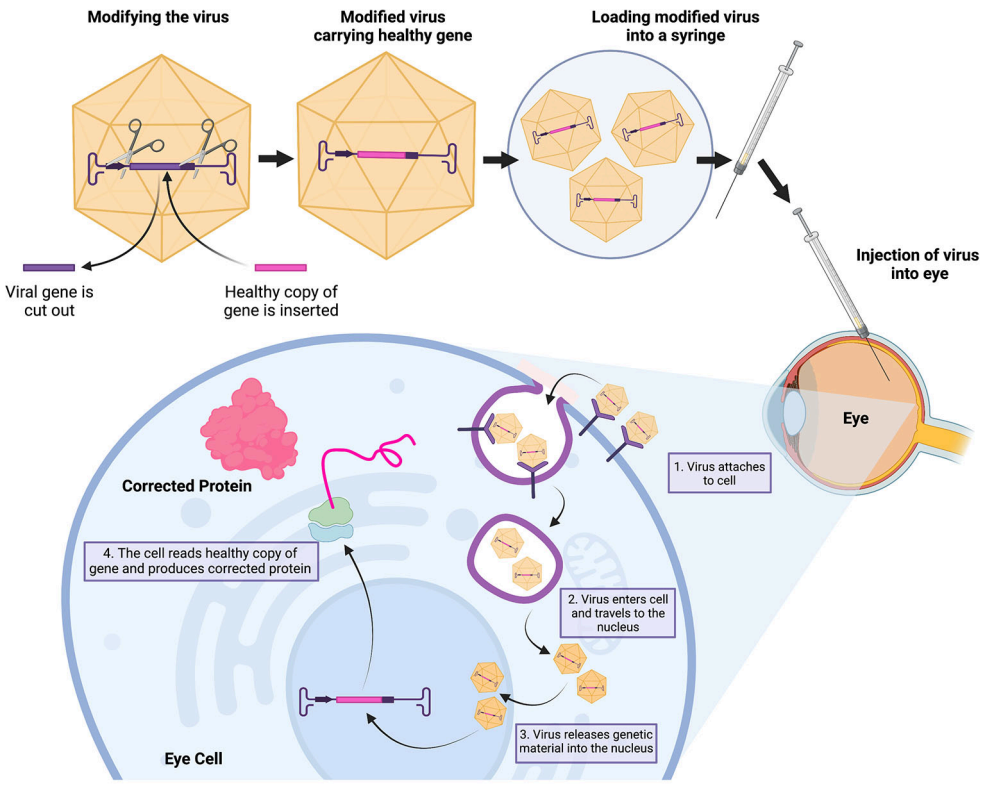


Figure 2

Figure 2

To use viruses for gene therapy, scientists cut out the viral genes and replace them with a healthy copy of a human gene. These viruses are then injected into the area of the body that needs the therapy. In the body, the modified viruses follow their natural life cycle, by attaching and entering human cells, where they release their genetic material. The healthy genes are then read by the cell and copies of the corrected protein are made. The virus cannot spread to other cells because no new copies of the virus are made. Figure created with BioRender.com.

AN EXAMPLE OF GENE THERAPY

RETINA

A light-sensitive, multilayer tissue, found inside the eye and responsible for vision.

RETINAL PIGMENT EPITHELIAL CELLS

Cells in the retina that are necessary for the health of the retina and normal vision.

One of the first diseases to be treated using gene therapy is called Leber congenital amaurosis (LCA). LCA causes blindness as a result of mutations in the gene coding for a protein necessary for vision. The **retina** is the part of the eye that detects light. It is located at the back of the eye and it is made up of several types of cells. In healthy eyes, cells called **retinal pigment epithelial (RPE) cells** have a gene that codes for a protein called RPE65, which allows for normal vision (Figure 3A). When there are mutations in the *RPE65* gene, the protein loses its function, which causes the retinal cells to die—leading to blindness (Figure 3B). Scientists can modify a virus by replacing virus genes with a healthy *RPE65* gene. These virus particles are then loaded into a syringe and injected into the eyes of patients with LCA. The modified virus enters RPE cells and deliver the healthy gene, so that the RPE cells can produce functioning RPE65 proteins. This allows the retinal cells to start working properly (Figure 3C). While vision is not completely restored using the currently available gene therapy, patients have experienced improvement in their ability to see [4].

CURRENT CHALLENGES

Although gene therapy has shown promising results in diseases like LCA, doctors and scientists still face several challenges to making gene therapy work perfectly. Currently available treatments are not yet fully effective. To cure inherited diseases, scientists will need to improve the delivery of gene therapy, so that *every* diseased cell receives a healthy gene—something that is not currently achievable. Scientists will also need to find ways to undo any previous damage to the tissue that happened as a result of the disease, because gene therapy cannot bring back cells that have already died—it can only prevent more damage from happening. Finally, the use of viruses to deliver therapeutic genes can sometimes cause unwanted side effects, such as an immune response in which the body tries to attack the viruses as foreign intruders.

ETHICAL

Ethical means making decisions based on what is right and just, and following principles and values that guide us to treat others with respect and fairness.

Gene therapy also raises many unique **ethical** concerns, because it involves making permanent changes to human DNA. Once a gene therapy is given, the changes cannot be undone, and they could last for a lifetime. Because gene therapies are so new, unexpected things may happen when gene therapies are given to patients. Because of the risk of unintended consequences, doctors are still only using gene therapies with great caution. Lastly, because they are so new and currently expensive, gene therapy treatments are not widely available to all patients. Creating fair and affordable access to gene therapies is an important goal. Scientists are working to make patients' lives better by developing new ways to deliver genes and produce healthy proteins.

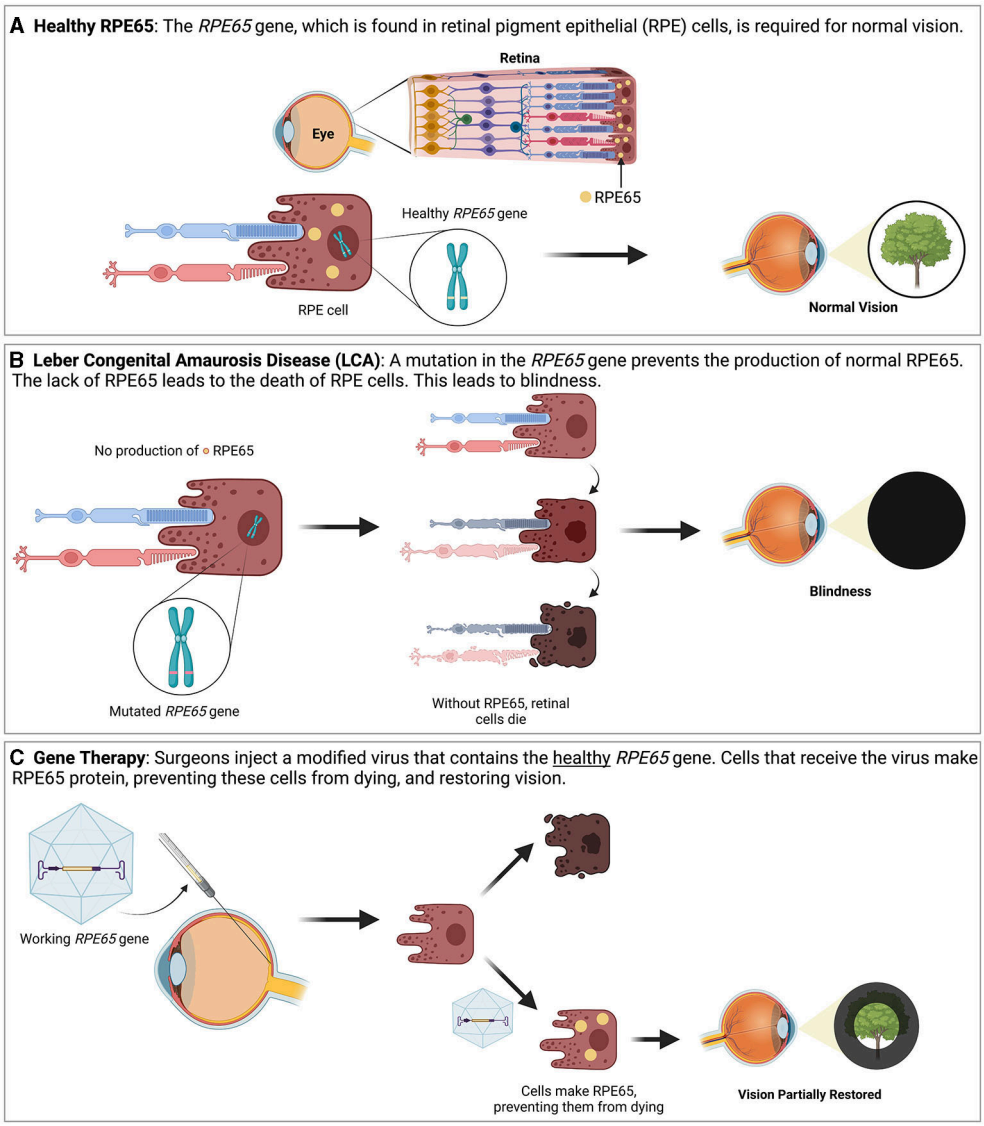


Figure 3

(A) People with normal vision have a healthy RPE65 protein, produced by the retina. **(B)** In LCA, the *RPE65* gene has a mutation that causes retinal cells to die and results in blindness. **(C)** In gene therapy for LCA, a modified virus is created that carries a healthy copy of the *RPE65* gene. These viruses are injected into the eye, where they deliver the healthy *RPE65* gene to RPE cells. The cells can then produce working RPE65 proteins, partially restoring vision. Scientists are working to improve these outcomes and achieve full recovery. Figure created with BioRender.com.

CONCLUSION

In this article, we described the basics of gene therapy for the treatment of inherited diseases. Researchers have long studied how viruses can hijack human cells by injecting their own genetic material and forcing human cells to produce viral proteins. Using this knowledge, scientists have been developing gene therapies by cutting out a virus's own genes and replacing them with healthy human genes. This way, we can use a virus's natural ability to infect cells to replace unhealthy genes in patients who suffer from genetic diseases. While the method is not perfect, scientists are working hard to improve gene therapy in the hopes of one day being able to cure devastating genetic disorders affecting the eyes, heart, blood, and much more.

REFERENCES

1. Mokili, J. L., Rohwer, F., and Dutilh, B. E. 2012. Metagenomics and future perspectives in virus discovery. *Curr. Opin. Virol*. 2:63–77. doi: 10.1016/j.coviro.2011.12.004
2. Camarillo-Guerrero, L. F., Almeida, A., Rangel-Pineros, G., Finn, R. D., and Lawley, T.D. 2021. Massive expansion of human gut bacteriophage diversity. *Cell* 184:1098–109 e9. doi: 10.1016/j.cell.2021.01.029
3. Friedmann, T., and Roblin, R. 1972. Gene therapy for human genetic disease? *Science* 175:949–55. doi: 10.1126/science.175.4025.949
4. Wang, X., Yu, C., Tzekov, R. T., Zhu, Y., and Li, W. 2020. The effect of human gene therapy for RPE65-associated Leber's congenital amaurosis on visual function: a systematic review and meta-analysis. *Orphanet. J. Rare Dis*. 15:49. doi: 10.1186/s13023-020-1304-1

SUBMITTED: 17 August 2022; **ACCEPTED:** 29 September 2023;
PUBLISHED ONLINE: 18 October 2023.

EDITOR: Ornella Cominetti, Nestlé Research Center, Switzerland

SCIENCE MENTORS: Tayyaba Zainab, Emilio Isaac Alarcon, and Hitesh Singh Sandhu

CITATION: Levochkina M, Beryozkin A, Aweidah H, Beale OM and Byrne LC (2023) Can Viruses Be Used to Make People Healthy? Front. Young Minds 11:1021056. doi: 10.3389/frym.2023.1021056

CONFLICT OF INTEREST: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

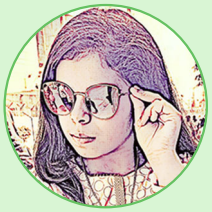
YOUNG REVIEWERS

CAEDMON, AGE: 13

My favorite school subject is Science. I love to design rockets and test them in Spaceflight Simulator. I love airplanes, and luckily I live close to a small community airport. As an Air Cadet, I have a goal of achieving my pilot license. My dream is to colonize Mars for humankind. These missions will be known as Human Exploration. I enjoy writing about aerospace, and started a book series called: Mission to Mars. Playing guitar is a favorite non-science pastime.

JOHN P. FREEMAN OPTIONAL SCHOOL, AGES: 9–13

The Future Leaders of STEM at John P. Freeman Optional School are students in grades 3–8 that meet regularly to learn from STEM professionals, compete in STEM competitions, and practice coding and robotics. They also have the chance to participate in work-based opportunities, field experiences, and STEM camps. Members are inducted into the club through a White Coat Ceremony, and they proudly wear their white coats while engaging in STEM activities.



QANYA, AGE: 13

I am young girl with a big love for science and technology especially fascination for genetics. I love to explore the mysteries of the natural world and study DNA to solve complex problems. In my free time, I enjoy reading science news, watching SCI-FI movies and YouTube videos, and keeping up with the latest research.

AUTHORS

MARINA LEVOCHKINA

Marina is a first-year medical student at the Virginia Tech Carillion School of Medicine. She holds a master's degree in infectious diseases and microbiology from the University of Pittsburgh's School of Public Health. Her primary interests are using biostatistics to explore hospital-associated infections and sepsis but when she goes home at the end of the day, she enjoys pampering her long-haired tortoiseshell cat, Lorelai.

AVIGAIL BERYOZKIN

Avigail wants to cure blindness. She has created two mouse models and tested several therapies that she developed, including gene therapy. She holds a Ph.D. in human genetics from the Hebrew University in Jerusalem and works as a post-doctoral fellow in the lab of LB. She has a family that includes one pediatrician-to-be (her husband), three children, and five cats.

HAMZAH AWEIDAH

After graduating from medical school, Hamzah completed a residency in ophthalmology followed by two fellowships at Hadassah Medical Center in Jerusalem. He completed fellowships in cataract and comprehensive ophthalmology as well as in vitreoretinal disorders. Since his residency Hamzah's research and clinical goals have been focused on understanding and finding a cure for retinal degeneration diseases. When he is not working, Hamzah enjoys spending his free time with his wife, Fatimeh, and their two kids Riyad and Lour.

OLIVER M. BEALE

Oliver is a current resident doctor at the University of Pittsburgh Medical Center. He graduated this year from the University of Pittsburgh School of Medicine. He has his sights set on a career in ophthalmology, potentially specializing in the retina. In his free time, Oliver enjoys reading, cooking, traveling, and rock climbing.

LEAH C. BYRNE

Leah studies the retina and creates gene therapies for retinal diseases. She holds a Ph.D. in neuroscience from the University of California Berkeley and works as an Assistant Professor in the Department of Ophthalmology at the University of Pittsburgh. She also spends a lot of time with her long-haired German Shepherd, and Byrne Lab "Postdogtoral" Fellow, Tilda. *lbyrne@pitt.edu