

Muscle Power

By Stephen Fraser

Gene therapy builds up muscles to fight AIDS virus.

Muscles defy gravity. They resist the planet's downward pull, enabling us to stand upright and move. Now a team of California researchers has endowed muscles with a new kind of strength: the power to combat disease.

The researchers injected muscle tissue with tiny pieces of genetic material. That material transformed the muscles into factories of proteins that attack viruses.

Although the technique has been tested only in laboratory animals, it defends them against one of the deadliest of all infections: acquired immune deficiency syndrome (AIDS). Human trials could begin in 2013.

Pseudo Infection

Since AIDS was first identified in 1981, it has killed more than 25 million people around the world(Nearly 30 million according to http://www.unaids.org/documents/20101123_FS_Global_em_en.pdf). AIDS disarms the immune system, leaving the body without protection against disease. Medical researchers have devised several drugs that keep people from getting sick after they've been infected with the human immunodeficiency virus (HIV), which causes AIDS. But no one has yet come up with an effective HIV *vaccine*—a drug that guards people against becoming infected in the first place. Some HIV vaccines exist, but even the best one shields only three out of 10 people from infection.

A vaccine is a safe germ—a normally harmful virus or bacterium that has been disabled or killed in the laboratory. Though the germ can no longer cause disease, when injected into the body it still prompts the immune system to create specially designed proteins called *antibodies* that destroy it. The immune system remembers that response and will mount it again if the body ever comes in contact with the harmful germ. Effective vaccines have been designed to prevent many infections—among them, mumps, measles, hepatitis, polio, various flus, and whooping cough. HIV vaccines do not work well, it appears, because HIV targets the very defense mechanism—the immune system—that protects us from disease.

A lucky few individuals are naturally resistant to HIV. Their immune systems manufacture powerful antibodies that destroy HIV. Those antibodies are called broadly neutralizing antibodies (bNAbs). They are a key to a new treatment devised by scientists at the California Institute of Technology (Caltech). David Baltimore, a Nobel Prize–winning medical researcher, oversees the lab where the work is being done.



(label Baltimore),
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Scientists have known about the anti-HIV bNAbs for some time. They've also located the *genes* responsible for the bNAbs. A gene is a segment of DNA that instructs the body to make certain proteins.

Mighty Mice

The Caltech scientists have used the bNAb genes on a group of specially bred mice. Most mice don't develop AIDS; HIV has no effect on them. But the Caltech mice are vulnerable to HIV; they react to it the way people do.

The first step in the Caltech experiment involved endowing the mice with the bNAb genes. That was done by inserting the genes into a harmless virus, then injecting that virus into the leg muscles of each mouse. The virus then slipped the genes into the mouse's muscle tissue. The mouse's muscles, not its immune system, started making the antibodies.

Step two involved infecting the mice with HIV and then monitoring their condition. Would they get sick, or would the antibodies produced by the bNAb genes protect them? The researchers began with a tiny dose of HIV. The mice showed no signs of sickness. The dose was increased. Still no symptoms. Even when megadoses of HIV were given to the mice, the animals remained in the pink of health. "We expected that at some dose, the

antibodies would fail to protect the mice," says Alejandro Balazs, a member of the Caltech team.

"But there was no infection even when we gave mice 100 times more HIV than would be needed to infect seven out of eight mice."

Baltimore is very encouraged by the results. "We're not promising that we've actually solved the human problem," he says. "But the evidence for prevention in these mice is very clear."



(again,label)
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The logical next step, says Balazs, is an experiment with human volunteers. "We are currently in discussions to start a clinical trial of this approach in people and are at the early stages of identifying exactly how this will happen," he says. "It will take at least a year or more until we could start."

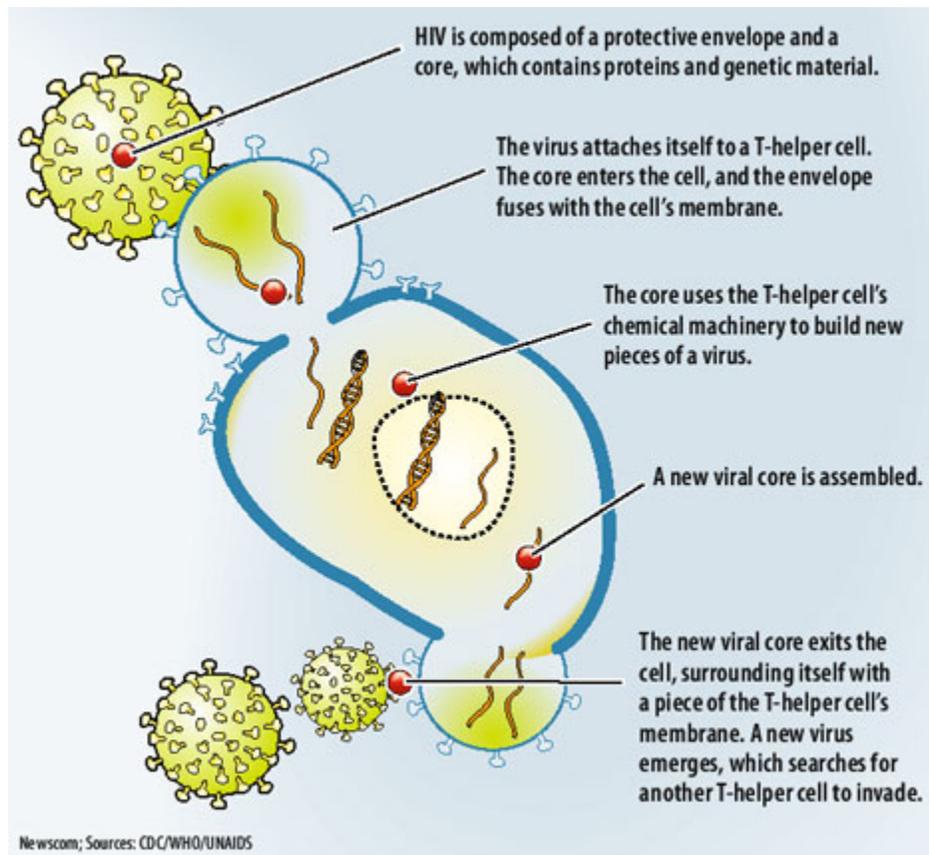
Risks And Rewards

HIV research is risky work. "We have special procedures that we follow," explains Balazs. "This includes special protective clothing like gloves and a face shield to prevent splashing. We have special rules about handling sharp objects when working with the virus. We also make sure to sterilize every surface that came into contact with it."

Still, it's work with an outcome that couldn't be more valuable. "I have always been interested in how the immune system keeps us safe from all of the diseases that are out there. I was especially interested in HIV because it is a disease that causes some of the worst suffering around the world," Balazs says. "When I heard about the idea of using other people's antibodies to prevent infection, it sounded like a really promising way to approach the problem."

HIV Infection

HIV, the virus that causes AIDS, disables the immune system. It invades immune cells called T-helper cells and reprograms them to become HIV factories. The number of healthy T-helper cells gradually dwindles, and the body becomes defenseless against diseases, such as pneumonia, tuberculosis, and lymphoma.



Inset left: Caltech/Robert J. Paz; Inset bottom: Caltech Academic Media Technologies

Name: _____ Date: _____

1. According to the passage, when was AIDS first identified?
 - A in 1975
 - B in 1981
 - C in 1992
 - D in 2001

2. The passage describes the problem of creating a vaccine for HIV. What solution did the researchers come up with to solve the problem?
 - A They inserted bNAb genes into a harmless virus and injected it into the mice.
 - B They injected bNAb genes directly into the leg muscles of each mouse.
 - C They injected the bNAb genes into a diseased virus and injected each mouse.
 - D They inserted bNAb genes into a pill and then mixed it into the mice's water.

3. Why might the author have included the HIV diagram in the passage?
 - A to explain how the gene therapy combats HIV
 - B to show how HIV disables the immune system
 - C to show how healthy cells in a mouse fight HIV
 - D to explain how to create an effective HIV vaccine

4. Read this sentence from the passage: "They are a key to a new treatment devised by scientists at the California Institute of Technology (Caltech)."

In this sentence, the word **devised** means

 - A solved
 - B destroyed
 - C invented
 - D resisted

5. The primary purpose of this passage is to describe
 - A how a team of researchers is testing a therapy to fight HIV
 - B why so many people around the world have died from AIDS
 - C why some lucky individuals are naturally resistant to HIV
 - D the risks and rewards of working as a medical researcher

6. What is the full name for AIDS?

7. Why does the author write that "HIV research is risky work"? How do you know? Please cite evidence from the text to support your answer.

8. The question below is an incomplete sentence. Choose the word that best completes the sentence.

_____ the gene therapy was successful with laboratory mice, researchers still have to conduct an experiment with human volunteers.

- A Before
- B Although
- C However
- D Otherwise

9. Answer the following questions based on the sentence below.

Nobel Prize–winning medical researcher David Baltimore oversees the lab where the HIV research is being conducted.

Who? _____

(does) What? oversees the lab

Where? _____

10. **Vocabulary Word:** segment: a part into which something is divided.

Use the vocabulary word in a sentence: _____
