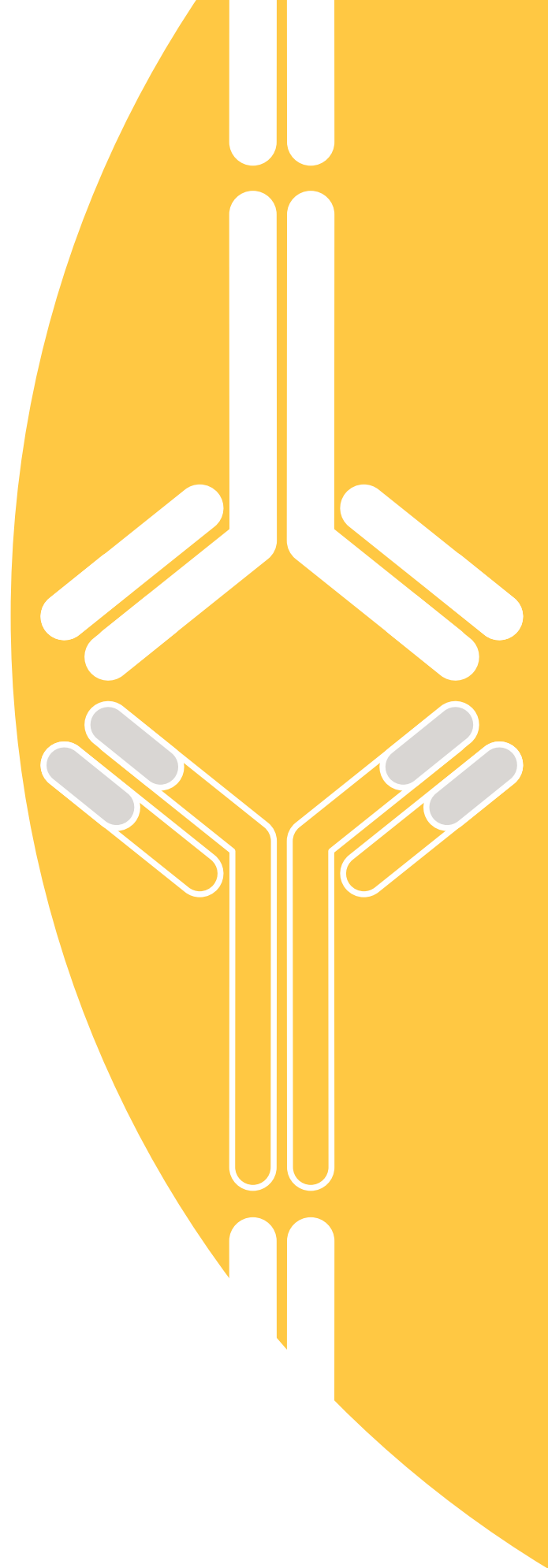


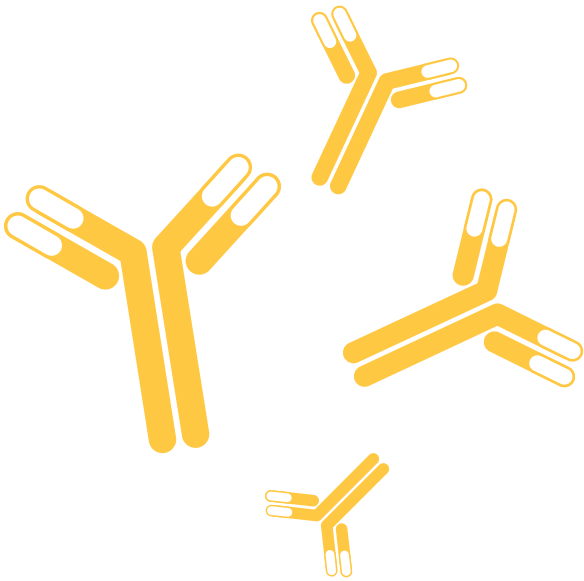
Antibody testing and gene therapy: What's the connection?

You may have heard that one of the common eligibility criteria for gene therapy in Duchenne muscular dystrophy requires measuring a specific type of antibody in the blood. What is it, and why?

Let's take a closer look.



What are antibodies?



Antibodies are an important part of the immune system. Their job is to help protect against illness, including viruses, by blocking their effect on the body. When someone has been exposed to a virus, the body's immune system creates specific antibodies that help fight the virus.

Antibodies can remain in the body for a long time, even after someone recovers from a virus. This helps the body fight off the same or similar virus if it appears again.

Why do antibodies matter in gene therapy?

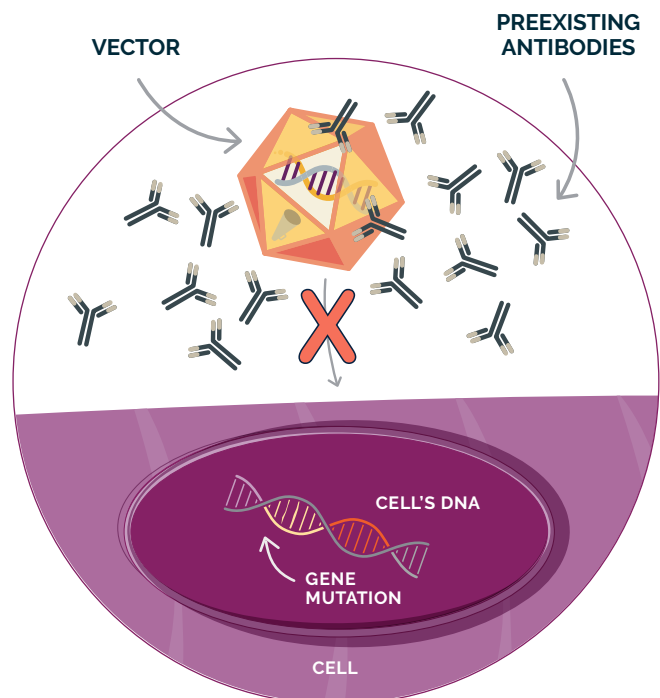
Each gene therapy has 3 key components, 1 of which is called a *vector*. The vector's job is to deliver the other 2 components (the *promoter* and the *transgene*) to cells in the body.

Vectors are similar to viruses that occur naturally. Just like viruses, they are able to selectively enter cells and deliver genetic material. Unlike viruses, they have been modified to prevent them from multiplying or causing an illness.

If someone has been exposed to a virus that is similar to a gene therapy's vector, there may already be antibodies that recognize the vector in the person's blood. These are called preexisting antibodies.

If there are too many of these specific antibodies, they may attack the vector and prevent the gene therapy from being delivered to cells. They could also cause harmful side effects.

Using a blood test to look for the specific antibodies that recognize that vector is important. If antibody levels are too high, treatment may not be possible.



Three terms you might hear in relation to antibody levels:

TITER

A measurement of the amount of antibodies in a blood sample that can recognize a specific vector

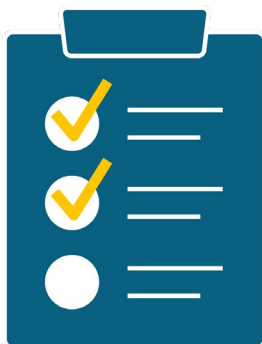
SEROPOSITIVE

Preexisting antibodies are detected at levels above the determined limit (elevated), meaning that gene therapy is not an option

SERONEGATIVE

No preexisting antibodies are detected, or they are at levels below the determined limit (not elevated)

How are those specific antibodies detected?



Since each gene therapy is different, each has its own unique test, called an *assay*, that is specific to that therapy. There is no universal test that measures antibodies across therapies. Even if 2 gene therapies use the same vector, there may be other criteria that determine whether someone is seropositive or seronegative. That's why it's so important that doctors order the therapy-specific antibody test when assessing eligibility for a particular gene therapy.

Do preexisting antibody levels change over time?

Yes. Antibody levels may rise or stay the same, but they rarely drop; if they do, it's not often by a significant amount. So, even if someone's results are seronegative, they could still potentially test seropositive in the future.

That's why it's important to test just prior to receiving the therapy. Each gene therapy has different rules about how much of the specific antibodies is acceptable. A doctor will explain those guidelines and whether or not a gene therapy may be appropriate.

What happens if the test result is seropositive?



If someone's antibody test comes back seropositive, they are not eligible for that particular gene therapy. However, that doesn't necessarily mean they won't be eligible for other gene therapies. Remember, each gene therapy is different and has its own test, so talking to a doctor about the available options is a good next step.

Patient advocacy groups can also be a great resource for learning about other treatment options and finding general support. A list of organizations can be found on [Duchenne.com](https://www.duchenne.com) in the Community Resources section.

Additionally, researchers are actively exploring if there is a way to get a vector past these preexisting antibodies without triggering an immune system alarm. While many are in the early stages of research, some of the ideas include possible treatments to break down or filter out specific antibodies in the blood, designing vectors that can sneak by antibodies undetected, and new delivery vehicles that can hide from the immune system.

Find more information on antibodies and gene therapy at [Duchenne.com/genetherapy](https://www.duchenne.com/genetherapy)



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