

## PASSIVE IMMUNIZATION ESSENTIALS

One way that vaccines work is by prompting the immune system to create antibodies against a particular pathogen. Passive immunization—on the other hand—refers to the transfer of pre-made antibodies to a person. (Some refer to this as antibody mediated prevention, or AMP.) It can occur naturally, like when maternal antibodies are transferred to the fetus through the placenta, as well as artificially, when specific antibodies are administered (e.g., through infusion) to a person.

Researchers have been studying passive immunization for HIV prevention for a number of years. These include lab and animal studies, and some early passive immunization studies in pregnant women. More recently, researchers have launched small safety and tolerability studies with a number of bNAbs (3BNC117, PG9, VRC01) in HIV-positive and -negative individuals. These trials could lead to larger studies of these bNAbs for both treatment and prevention. Key issues include evaluating safety and tolerability of different doses as well as seeing what levels are required for efficacy and, hopefully, establishing proof of concept. From there, scientists can work to enhance bNAbs' breadth and potency and seek innovative ways to use this potential development for treatment and prevention.

## GLOSSARY

### Broadly neutralizing antibody (bNAbs)

Y-shaped protein produced by B cells (immune cells) that binds to a specific part of HIV's surface, rendering it harmless; bNAbs neutralize many different types of HIV in lab tests.

### Half-life

The time required for half the amount of a substance to be eliminated from the body or to be converted to another substance.

### HIV subtypes

Families of HIV viruses that have similar genetic sequences. A way of describing the diversity of the virus. Different subtypes, also referred to as clades, are found in different parts of the world.

### Monoclonal antibody

Antibody made using identical immune cells that are all clones of the same parent cell.

### Potency

Relationship between the therapeutic effect of a drug or vaccine and the dose necessary to achieve that effect.

### Passive immunization

Transfer of antibodies to an individual (versus immunization with a vaccine that teaches the body to make the antibody itself).

## PASSIVE IMMUNIZATION RESEARCH

### *An important piece of the puzzle*

Early in the research process scientists knew that developing an HIV vaccine would be more challenging than for many other vaccines. HIV mutates rapidly allowing it to evade immune responses and targets a key set of cells a vaccine is designed to produce. It has been hard to identify how a person's immune system would naturally protect against HIV infection—an important building block to vaccine design.

In the early 2000s, researchers started testing **passive immunization** with anti-HIV antibodies in animals to better understand its potential in protecting against HIV. They found that direct infusion of certain antibodies could prevent infection with strains of the virus that matched the antibody being tested. It is understood, though, that an antibody that only protects against one **HIV subtype** would not be widely effective given HIV's broad genetic diversity.

Since 2009, scientists have identified many new **broadly neutralizing antibodies (bNAbs)** that are effective in the lab at blocking HIV infection against a wide range of **HIV subtypes**. These antibodies have been selected for testing in HIV prevention, treatment and cure studies. In animal studies antibody levels declined over time, so repeat dosing was required to maintain a protective effect. Early passive immunization clinical trials are underway in people and additional research is ongoing to try and improve the **potency** and **half-life** of existing bNAbs. The hope is that more potent candidates will require smaller and potentially less frequent dosing and still be safe and effective.

As of 2015, preliminary results from a subset of small-scale clinical trials show that passive immunization can reduce viral load in people living with HIV not on ART. Studies also show that the antibodies are safe and generally well-tolerated. Larger-scale studies to evaluate safety and efficacy of various bNAbs and dosing strategies for treatment and prevention are planned and/or underway.

If these studies provide proof of concept, (i.e., they show that bNAbs can be effective in reducing viral load and/or preventing infection), it could lead to additional research on vaccines to help the body make these protective antibodies on its own.

### Early 2000's

#### KEY QUESTION

Can passive infusion of antibodies protect against HIV infection in animals?

### 2009 - 2015

#### KEY QUESTION

What should the passive immunization clinical trials pathway look like?

#### KEY QUESTION

Which antibodies used in passive immunization could provide the most potent and long-lasting protection?

#### KEY QUESTION

How might this work contribute to the development of preventive AIDS vaccines?

### 2016 and beyond