Meet the pioneering scientists transforming medicine for millions of people

Antibody science has been around since the 1790s, but it's come a long way thanks to innovators in medicine

By Deborah Abrams Kaplan for Regeneron

Antibody medicine enhances your body's natural defense mechanisms to treat serious illnesses. *Getty Images*

Everybody gets sick now and then. But if it weren't for antibodies – the weapons that help our immune systems fight viruses, bacteria or even cancer cells – some illnesses would be much more frequent and potentially lethal.[1,2]

It's no wonder medical innovators have mimicked this biological superpower in their work to treat suffering patients. Their centuries-long pursuit to produce better, faster medicine based on the principles of naturally occurring antibodies continues to improve.[3]

While antibody medicines are now standard treatments for some diseases, the science behind them is not new. In fact, antibodies were first tapped for disease prevention in 1796, when the smallpox virus was causing widespread death and disfigurement.[4] English physician Edward Jenner realized that cowpox pus could trigger a person's antibody defense system and successfully prevent against smallpox.[4] It's the first disease eradicated by a vaccine – and Jenner was the first of many "antibody architects" to come.[4,5]

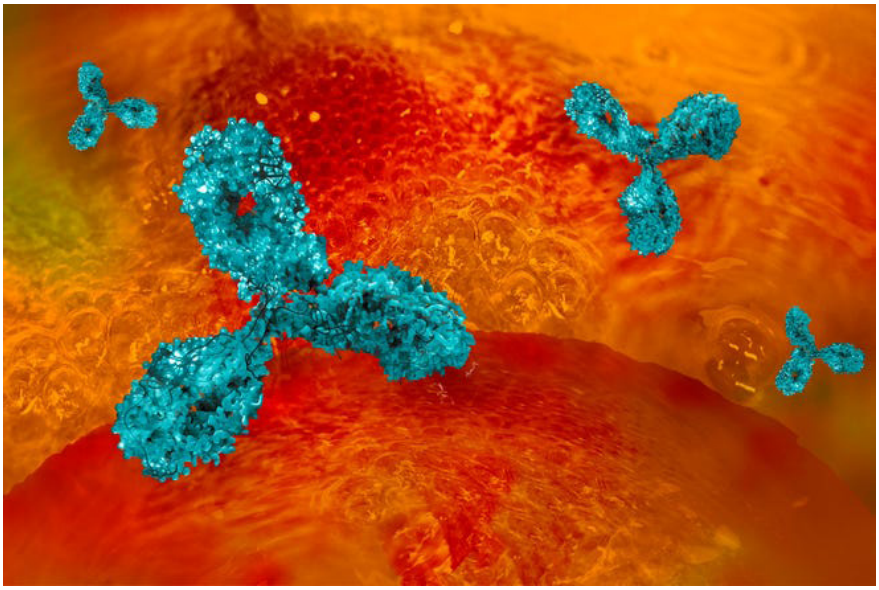
That early research was just the beginning of antibody science. During the next two centuries, scientists discovered the human body produces billions of unique antibodies, proteins in blood that neutralize antigens – harmful substances in the body like viruses, bacteria or cancer cells.[6] While antibodies were first used to prevent diseases, scientists have since discovered ways to use antibodies to treat disease.[3] These antibody architects have advanced medical science throughout history and are continuing to make waves in the medical community, with no fewer than 11 individuals earning Nobel prizes for their discoveries along the way.[3,7,8]

A quick history of modern antibody medicine

Major advances were made in the 1970s, when scientists used technology to produce large numbers of identical (monoclonal) antibodies in mice.[3] The U.S. Food and Drug Administration (FDA) approved the first monoclonal antibody medicine in 1986 to prevent kidney transplant rejection.[3] This was a feat, but early antibody medicine had some problems.[3]

James Crowe M.D., professor of microbiology and immunology at Vanderbilt University School of Medicine, recalls seeing patients reject the engineered antibody because the body did not recognize them as fully human. A new generation of antibody architects began developing techniques to make human antibodies in the 1990s, “and that’s when excitement really started to grow about using them for human therapy,” said Crowe.

Antibody architects continued refining and innovating techniques to produce these antibodies for therapeutic use, and the first human monoclonal antibody medicine was approved by the FDA in 2002. Since then, the FDA has approved more than 85 monoclonal antibody therapies to treat allergic diseases, autoimmune diseases, cancer, heart disease, high cholesterol, inflammatory diseases, multiple sclerosis, osteoporosis, psoriasis, rheumatoid arthritis, transplant rejection, and other diseases.[3,9-11]



Antibodies used in medicine are Y-shaped proteins that attach to problematic molecules and cells, to flag them for destruction or block their activity [3,10]. *Getty Images*

Antibodies used in medicine are Y-shaped proteins. The two arms work together, attaching to a problematic antigen.[3,10] These bad players could come from outside your body, like allergens or viruses, or come from inside your body, like abnormal cells or molecules that occur in cancer or autoimmune diseases. The antibody medicine blocks the antigen’s pathway, flags it to alert other cells to attack, or connects two cells to promote killing of the bad cells.[10]

Advantages of antibody medicine

“Monoclonal antibodies are made from one individual cell multiplied to target one specific antigen,” said Drew Murphy, Ph.D., Executive Vice President of Research at Regeneron Pharmaceuticals.

Antibodies have different mechanisms to fight antigens, including blocking their activity or flagging them for destruction by the immune system.[6] “Discoveries are being made every day that can be applied to the classical blocking mechanism,” said Murphy, and there’s no limit to the number of targets.

Unlike pills, which are made from synthetic materials or chemicals, antibody medicines are natural protein molecules.[3,10] “In that way, they’re very desirable,” Crowe said. “Your body already uses the strategy to protect or heal itself.”

Antibody medicines, given by injection or infusion, have other advantages. They’re large molecules, which are typically long-lasting, working for weeks to months in the body.[3,10] Another advantage is that antibodies are specific, and most recognize and bind to only one antigen.[3]

“They’re designed to only lock onto a specific target,” Murphy said, which may reduce negative ‘off-target’ impacts that may cause side effects.[3]

This is not to say that antibody medicines are free from side effects. Like with all medicines, side effects can occur and rare but serious complications can occur with antibody medicine and should be detected and treated quickly.[3]

Bispecific antibodies

Blocking and clearing antigens is good, but with some diseases, "you want to use different mechanisms," Murphy said. Bispecific antibodies are a newer form of treatment pioneered by modern antibody architects, where each of the two Y-shaped arms has a different target.[6] The arms can each bind to separate molecules, like an immune cell and a cancer cell, activating one cell to kill the other.[6,12] The two arms can also bind to two molecules on the same cell to do a variety of other beneficial things.[12]

Antibody architects are working to identify, test and produce new medicines. *Getty Images*

"Costimulatory bispecific antibodies are another new antibody type and hold particular promise in cancer," Murphy said. The antibodies don't direct the white blood cells to kill specific tumor cells, but rather teach them to recognize the tumor cells as dangerous, so the cancer will continue being killed going forward.[13] White blood cells need two activated signals: for recognition and danger.[14]

"Your body naturally produces the danger signal when you get a virus," Murphy said. "We use the bispecific antibody to supply that danger signal for the cancer cells," so the antibody recognizes them as foreign, killing them.[13]

The goal is for white blood cells to gain immunological memory, "so if the same tumor ever comes back, it will get killed," Murphy said, since residual tumor cells often lurk in the body after treatment. With costimulatory bispecific antibodies, the hope is that these white blood cells will continue killing the tumor cells long-term, "the same way that you would have long-term immunity after getting chickenpox."[13]

The future of antibody medicines

Producing antibody medicines isn't an easy task, something antibody architects like Crowe know firsthand.

"A typical drug you take in pill or powder form is a small molecule. It's basically a chemical, which you can make on an industrial scale," Crowe said. Antibodies are larger and more complex.[3] "Your body knows how to make them, but in a factory it's much more complicated." Certain companies have developed specialized capabilities for producing these medicines in a reliable, consistent and safe manner.[15]

Antibody architects continue to discover and fine-tune their technologies to produce new medicines for people who need them.[15] That's important, as antibody medicines hold great promise treating a range of other diseases. This even includes pandemics caused by Ebola, flu, and other viruses.16 Murphy said that one benefit of using antibody medicines in this field is that treatments can be discovered quickly, even if the virus strain has never been seen before.

Whether an infectious disease, cancer or a myriad of other conditions, today's antibody architects are enhancing the body's natural processes to create better treatments.

"Your body has a remarkable capacity to heal itself," Murphy said, and the body does that with antibodies. "The better we can mimic nature's ability for the body to treat itself, the better off we'll be."

Visit regeneron.com/antibody for more information on antibody architects' quest to accelerate drug development and improve patient health.

References

1. Cancer Terms – Antibody. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/antibody
2. CRI Staff. How does the immune system work? Cancer Research Institute. https://www.cancerresearch.org/blog/april-2019/how-does-the-immune-system-work-cancer.
3. Foltz IN, et al. Circulation. 2013 Jun;127:2222-2230.
4. Centers for Disease Control and Prevention. History of smallpox. https://www.cdc.gov/smallpox/history/history.html.
5. Roth GA, et al. Am J Public Health. 2011;101:1217.
6. National Institutes of Health. Decoding the variety of human antibodies – United States, February 2019. https://www.nih.gov/news-events/nih-research-matters/decoding-variety-human-antibodies.
7. NobelPrize.org. All Nobel Prizes in Physiology or Medicine. https://www.nobelprize.org/prizes/lists/all-nobel-laureates-in-physiology-or-medicine/.
8. NobelPrize.org. The Nobel Prize in Chemistry 2018. https://www.nobelprize.org/prizes/chemistry/2018/summary/.
9. The Antibody Society. Antibody therapeutics approved or in regulatory review in the EU or US. https://www.antibodysociety.org/resources/approved-antibodies/
10. Chames P, et al. Br J Pharmacol. 2009;157:220-233.
11. Sedykh SE, et al. Drug Des Devel Ther. 2018;12:195–208.
12. Fan G, et al. J Hematol Oncol. 2015;8:130.
13. Regeneron Data on File, 2019.
14. Sharma A, et al. Chapter 77: Immunotherapy of Cancer. In: Clinical Immunology (5th ed). Elsevier Limited; 2019:1033-1048.
15. Regeneron Technology. https://www.regeneron.com/technology.
16. U.S. Department of Health and Human Services news release. October 13, 2017. https://www.phe.gov/Preparedness/news/Pages/regeneron.aspx.

This content was prepared by GET Creative, a division of USA TODAY

REGENERON®