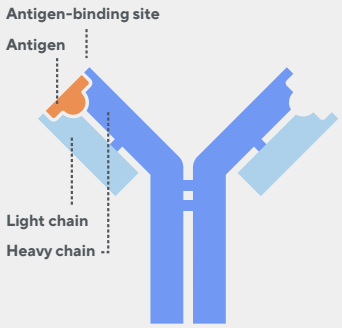
Adaptive Biotechnologies
Antibody Drug Discovery

Adaptive biotechnologies™

Adaptive Biotechnologies is pioneering a revolutionary new approach for discovering uniquely potent antibody-based therapies. Our next generation immunosequencing technology can screen antibodies at an unprecedented scale, unlocking the vast potential of the adaptive immune system to deliver groundbreaking medicines for hard-to-treat diseases.

The challenge: going beyond low-throughput, single-cell technologies

Drug discovery teams often seek to harness the potency and pinpoint the precision of antibodies in order to strike biological targets linked to disease. While more than 100 such medicines have been approved in recent decades, discovering antibody-based drugs remains a challenging and unpredictable process. Research scientists may fail to find any viable candidates to advance into clinical trials, and just 14% of antibody drugs that have entered the clinic have gained U.S. Food and Drug Administration (FDA) approval.[1]



Antibodies are large Y-shaped proteins made by our adaptive immune system's B cells in response to infections and internal threats. They have highly specific structures that spread throughout the body and bind to particular antigens, which are foreign proteins and segments of protein found on viruses and other invaders. Our immune system can't foresee the best way to attack every foreign threat that it will encounter, so B cells make antibodies against every piece of foreign protein they detect. The result is a vast array of antibodies that can vary significantly in their affinity for the target antigen (how tightly they bind) and their potency (how effectively they neutralize a threat).

The challenge arises in part from the two protein chains that form an antibody: The genes that make these chains reside on different chromosomes in the B cells that generate antibodies. To ensure that these genes are correctly paired into one full antibody, drug discovery teams typically search through individual B cells. However, this one-cell-at-a-time, low-throughput method limits the number of B cells that can be screened to a small fraction of the relevant B cells. The risk is that the best possible antibodies may not be found.

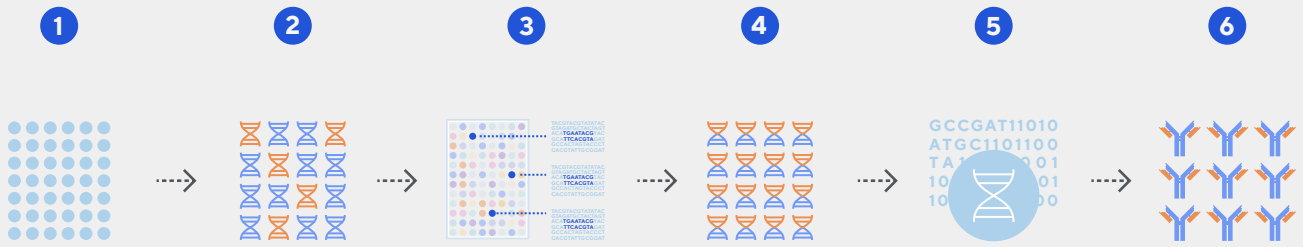
Adaptive's solution: next-generation sequencing and novel computational algorithms

Adaptive's best-in-class approach to discovery combines a suite of technologies to mount the broadest possible search for potent, high-quality antibodies that could lead to therapeutic breakthroughs. Our approach includes:

- **Large-scale B-cell receptor sequencing and accurate chain pairing.** By sequencing the full repertoire of antibody genes in large pools of B cells, Adaptive can discover antibodies at unparalleled speed (months vs. years) and scale (millions vs. thousands). Our sophisticated computational methods can accurately match pairs of light and heavy chains derived from the same B cell to provide hundreds of thousands of full antibody sequences for in-depth analysis.

- **State-of-the-art in silico screening and computational biology.** Applying sophisticated and proprietary algorithms, Adaptive analyzes vast numbers of antibody sequences, identifies the most promising ones, and produces these top-tier antibodies for lab-based testing. Using sophisticated models invented by our world-class computational biologists, we can pinpoint the antibodies with the highest therapeutic potential.

- **Speed and flexibility.** With low-throughput discovery platforms, discovery teams often require a time-consuming detour to fix potential flaws in a lead antibody candidate. Adaptive's data includes tracking of clonal lineages—essentially, the family tree and close relatives of each antibody. If an otherwise promising antibody displays a potential weakness, a closely-related antibody that lacks this liability can be advanced quickly for therapertic exploration.



Unlike single-cell methods that pinpoint the antibody genes in individual B cells and aggregate the resulting data for analysis, Adaptive's discovery method starts with **(1)** large populations of B cells, either from humans recovering from disease, or humanized mice who have been engineered to produce fully human antibodies in response to antigen exposure. **(2)** Next, Adaptive sequences all of the genes that code for antibody light chains and heavy chains. **(3)** Using proprietary algorithms, we accurately pair all matching light and heavy chain genes to generate full antibody sequences. **(4)** Sophisticated computational methods are then applied to identify antibodies with promising attributes, such as potency, high affinity, safety, stability, and manufacturability. **(5)** Adaptive then makes the top-tier antibodies and **(6)** selects the best candidate to advance into clinical trials based on lab-based assays and testing in animal models of disease.

A proven ability to make rare discoveries

Most importantly, because of Adaptive's ability to sequence and pair hundreds of thousands of antibodies, we can detect antibodies with unique therapeutic promise. In a pivotal study of 227 patients who had recovered from COVID-19, we identified hundreds of antibodies effective against all known strains of SARS-CoV-2. They included previously unknown antibodies that could also neutralize other coronaviruses.[2]

Adaptive's world-class antibody discovery engine is built on decades of immunology and computational biology experience. The antibody discovery team is applying this expertise to serious illnesses like cancers and autoimmune diseases, both through our internal discovery programs and in partnership with other biopharma companies.

To learn more about Adaptive's antibody discovery capabilities, contact drugdiscovery@adaptivebiotech.com.

1. Hay, Michael, et al. "Clinical development success rates for investigational drugs." *Nature Biotechnology* 32.1 (2014).
2. Keitany, Gladys J., et al. "Multimodal, broadly neutralizing antibodies against SARS-CoV-2 identified by high-throughput native pairing of BCRs from bulk B cells." *Cell Chemical Biology* (2023).