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ANTIBODIES THROUGH THE MAGNIFYING GLASS

THEIR PAST, PRESENT AND FUTURE

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ANTIBODIES THROUGH THE MAGNIFYING GLASS

THEIR PAST, PRESENT AND FUTURE

One hundred billion dollars - that's the estimated worth of antibodies, or immunoglobulins today[1]. Compared to ten years ago, when global sales of antibodies reached $39 billion, this is a great leap[2]. Today's global market value of antibodies mirrors their popularity among researchers and drug developers alike. After all, antibodies have a lot to offer the life sciences, and access to innovative antibody therapies will play a major role in drug discovery in the coming years. Read on to learn more about antibodies' past, present and future as well as their structure, function, and application.

PAST

A BRIEF HISTORY OF ANTIBODY DISCOVERY

Determining the exact year in which antibodies were discovered is nearly impossible. Upon closer inspection, however, a few famous names come into focus. Amongst them are Emil von Behring, Paul Ehrlich, Gerald Edelman and Rodney Porter. Over the course of history, all of these individuals had something to do with antibodies.

1890

Emil von Behring
Diphteria Immunity

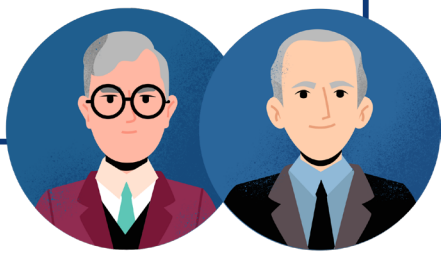
1901

Paul Ehrlich
Side Chain Theory

1947

Astrid Fagraeus
Plasma Cells Produce ABS

1957



Frank Burnet & David Talmage
Clonal Selection Theory

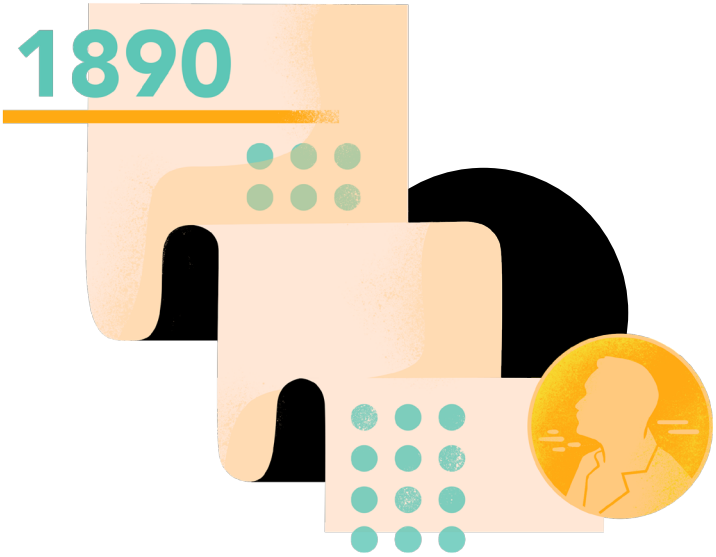
1959

Gerald Edelman & Rodney Porter
Molecular Structure of Antibodies

1975

Cesar Milstein & Georges Koehler
Hybridoma Technology

DIPHTHERIA PROVIDES FIRST CLUES



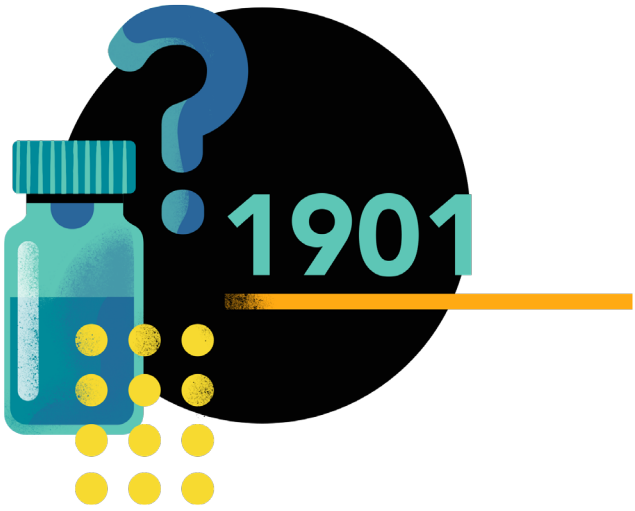
Although immunization studies were performed as early as the 1700s, it wasn't until the year 1890 that the earliest reference towards the discovery of antibodies emerged in a publication[3]. Together, Emil von Behring and Shibasabura Kitasato showed that animals infected with diphtheria could be cured with the serum of animals immunized against it as well as protect animals from later infection with the disease[3,4].

At the time, the paper stirred up the scientific community, causing great excitement due to the potential application in humans. It also resulted in Behring receiving the Nobel Prize in Physiology or Medicine in 1901[5].

THE SIDE-CHAIN THEORY

Famous for proposing the side-chain model, German bacteriologist Paul Ehrlich was determined to get to the bottom of immunization processes within the body. His theory stated that cells had so-called side-chains, which he later defined 'receptors', that could bind to pathogens or microbial toxins. Once bound, cells would produce more side-chains and release them into the bloodstream. There, they would act as 'antitoxins' that could subsequently protect the body against the same infection[6,7].

Today, we know that Ehrlich's side-chain theory was incorrect. However, he did bring us closer to discovering what antibodies are, how they are produced, and how vaccinations and other immunotherapies generally work.



MAGIC BULLETS BEFORE ANTIBODIES

Later, Ehrlich developed the idea of the 'magic bullet', which is often cited as the birth of antibodies. The 'magic bullet' theory proposed that attacking pathogens were specifically targeted and disarmed by the host body without causing any harm[6].

In 1908, together with Ilya Ilyich Mechnikov, Ehrlich was also awarded the Nobel Prize in Physiology or Medicine for his work in immunology[8].

DISCOVERING ANTIBODY PRODUCTION

Forty years after Paul Ehrlich received his Nobel Prize, Swedish immunologist Astrid Fagraens discovered - during her doctoral studies - that antibodies are produced by plasma cells[9,10]. Then, in 1957, Australian virologist Frank Burnet and American immunologist David Talmage proposed the clonal selection theory[11,12].

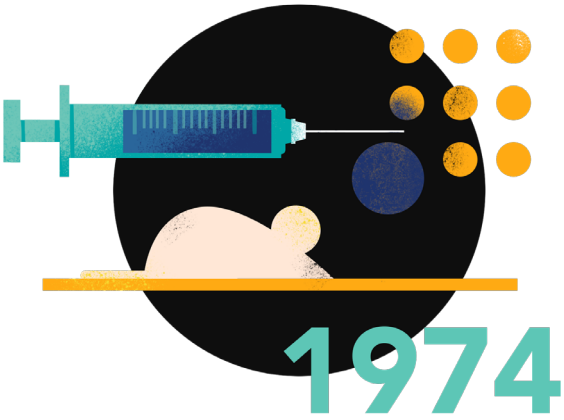
The clonal selection theory stated that lymphocytes were diverse and that an antigen would only activate its specific lymphocyte counterpart. This later led to the "one cell - one antibody" discovery, which would pave the way to the production of monoclonal antibodies, and subsequently, the massive growth in immunotherapy research and treatments we see today.

DEDUCTING THE STRUCTURE OF ANTIBODIES

In 1959, Gerald Edelman and Rodney Porter independently published their research on the molecular structure of antibodies that would later earn them the Nobel Prize[13,14,15,16]. At the time of their discovery, modern technologies such as X-ray crystallography or electron microscopy did not exist. Consequently, Edelman and Porter had to come up with an alternative to deduct the molecular structure of antibodies.

Thus, by breaking antibodies into small fragments and using chemicals and enzymes, they identified the characteristic light and heavy chains as well as the antigen-binding site of antibodies. Their findings would soon be validated with the use of the above-mentioned techniques, and finally, in 1977, the first three-dimensional structure of an antibody was published[13].

THE BIRTH OF MONOCLONAL ANTIBODIES



In 1975, antibodies with a predefined specificity could be produced in large amounts after César Milstein and Georges Köhler published their hybridoma method, paving the way for the commercialization of the monoclonal antibody technology[17].

At the time Milstein began his studies into the generation of antibody diversity, the field of antibody research was restricted by the fact that single specific antibodies could not be isolated and purified from the billions of antibodies in the body. It was an issue that Milstein and his colleagues would tackle in the years to come.

In 1974, a young German doctoral student, Georges Köhler, joined Milstein's lab and together they came up with the idea of the hybridoma technology[17]. They fused mouse spleen cells - taken from a mouse that had previously been immunized with sheep red blood cells and now secreted anti-sheep red blood cell antibodies - with mouse myeloma cells. The researchers' basic idea was to combine the longevity of myeloma cells - immortal cancer cells - with the antibody-production of B cells[18,19].

Milstein and Köhler's research led to the discovery of an unlimited source of chemically identical antibodies that targeted one specific antigen. It also won them the Nobel Prize in 1984[20].

MONOCLONAL ANTIBODIES - THE HITCH

Soon, monoclonal antibodies were being tested for treatment in humans, and in 1986, the first monoclonal antibody, Muromonab-CD3 (trade name Orthoclone OKT3) was approved to help prevent kidney transplant rejection[19].

But there was a hitch: Muromonab-CD3 is a monoclonal mouse antibody. Its use in humans is associated with severe side effects, or so-called human anti-mouse antibody (HAMA) responses[19]. HAMA responses like this occurred repeatedly in treatments with other murine antibodies.

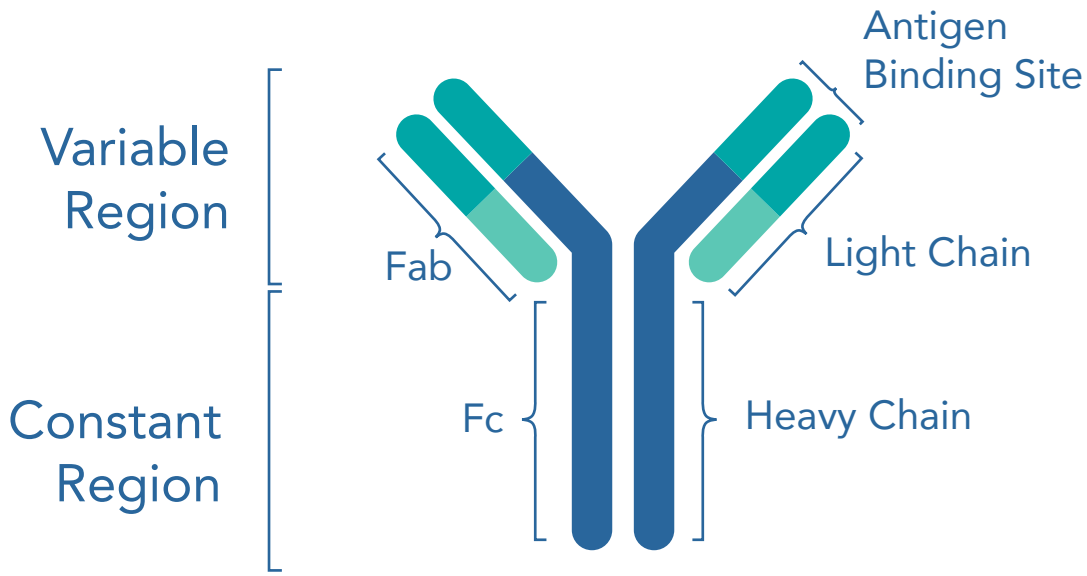
Researchers soon overcame the issue of HAMA responses by replacing the murine sequences in antibodies with their human counterpart. This lead to the development of chimeric, humanized and human therapeutic antibodies.

PRESENT

AN OVERVIEW OF ANTIBODIES

Today, antibodies can be engineered with highly selective properties, ranging from molecular size to binding affinity, stability, selectivity and catalytic activity. They are widely used in medicine, biotechnology and biomedical applications as research material and for therapies in oncology, autoimmune, infectious and cardiovascular diseases as well as in transplants.

STRUCTURE OF AN ANTIBODY



With its characteristic Y-shape, the antibody is probably the most recognizable protein configuration in biology and medicine[21]. The basic structure consists of two heavy and two light chains, which form two arms that bind antigens. They are therefore each called Fab - antigen binding fragment.

The two Fab arms are connected to a vertical structure known as the crystallizable fragment (Fc) that gives the antibody its distinguishable Y-shape. The Fc interacts with different components of the immune system, such as monocytes, macrophages and dendritic cells[22].

Each Fab arm consists of two variable and two constant domains. Whereas the constant domains form the structural framework, the variable domains are responsible for the antibody's antigen specificity. Within each variable domain, there are three hypervariable loops called the complementary determining regions (CDRs). These form the specific antigen recognition site.

ANTIBODY ISOTYPES

Mammalian antibodies have five different antibody subtypes, or isotypes: IgG, IgM, IgA, IgD and IgE. These isotypes are classified by their heavy chains and each has distinct roles and characteristics[23,24,25].

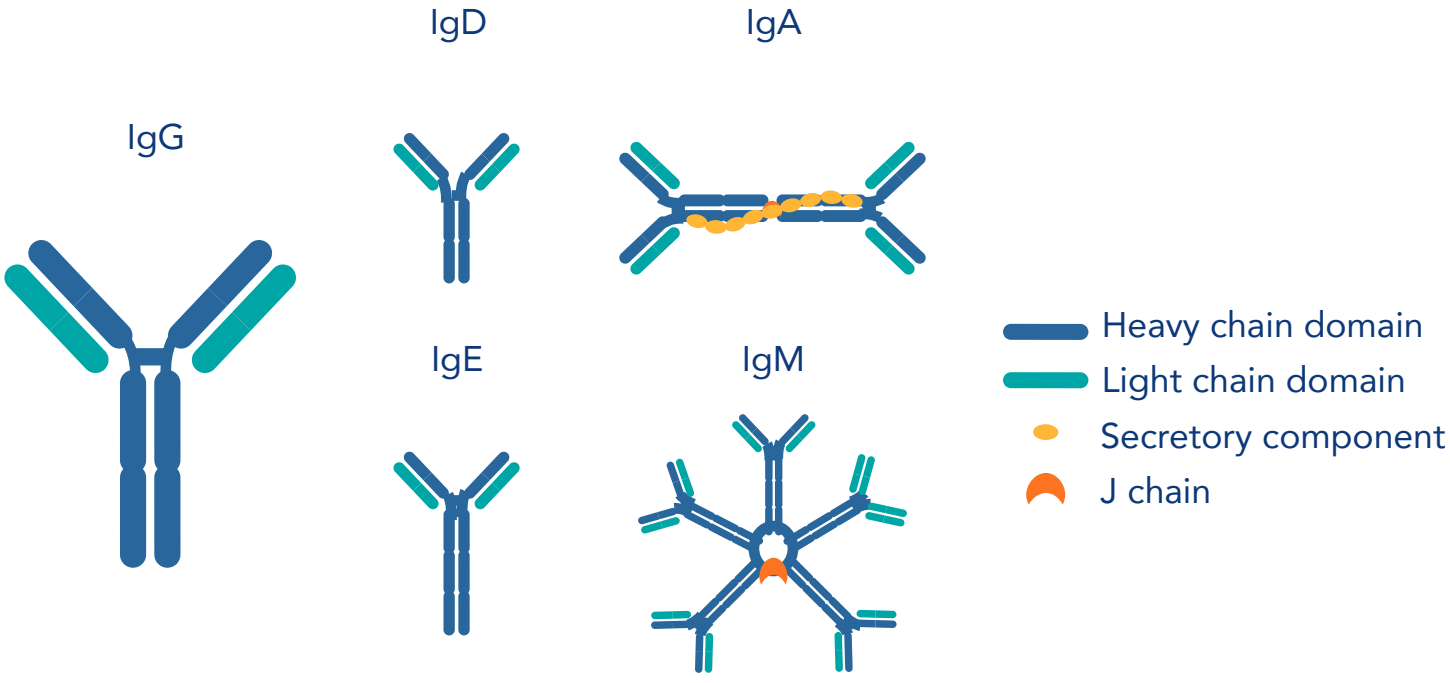
Immunoglobulin G, or IgG, is the most common antibody isotype in the human body, making up about 75 percent of all antibodies. It can be found in the blood plasma and is responsible for recognizing and marking pathogens, which are then eliminated by phagocytes. There are four subclasses of IgG: IgG1, IgG2, IgG3 and IgG4.

Accounting for approximately five to 10 percent of antibodies, IgM circulates in the blood and is produced by B cells as the primary immune response to infection by pathogens. Because of its pentameric structure — it is made up of five Y-shaped molecules — it has a high affinity to antigens. It can also activate cell signaling pathways by binding to a cell's surface receptors.

The antibody isotype IgA is mostly found in mucous secretions - saliva, nasal mucus, intestinal fluids or tears - and makes up about five to 15 percent of antibodies in the human body. After secretion, it can form dimers. The gastrointestinal tract of neonates is protected by IgA, which can also be found in breast milk.

IgD is present in less than one percent of all plasma antibodies but is widely found on B cell membranes[23.] Although this isotype looks very similar to IgG antibodies, its function is still unknown.

Lastly, the antibody isotype IgE is very scarce; it can only be found in the blood and extracellular fluid. This isotype is thought to be involved in allergies, such as peanut or pollen. Bound to mast cells, it can cause the cells to release strong chemicals, which can induce extreme reactions, including sneezing, coughing or vomiting[23,25].



TYPES OF ANTIBODIES & THEIR PRODUCTION

HUMANIZED MONOCLONAL ANTIBODIES

Humanized antibodies are a combination of human antibody with a small part of a rodent antibody[26]. Whereas the human part of the antibody is less likely to be attacked by the body's immune system, the portion made up of the rat, or mouse antibody, can bind to the target antigen. Humanized antibodies have the advantage of lowering the risk for HAMA responses in the patient; consequently, humanized antibodies are seen as a safer treatment option compared to murine antibodies.

The first humanized monoclonal antibodies emerged after George P. Smith described the phage display technique in 1985. It was a method that used bacteriophages - viruses that can only infect bacteria - to connect proteins with their encoding genetic information.

The phage display technique allowed for the direct comparison between a genotype and phenotype. It can be used to compare proteins with proteins, proteins with peptides and proteins with DNA. Smith's discovery gave rise to the antibody phage display technique, which used human genes coding for antibodies integrated within transgenic mice or rabbits[27,28].

POLYCLONAL ANTIBODIES

Unlike monoclonal antibodies, which are produced by a single cell line, polyclonal antibodies are secreted by different B cells after they have reacted to a specific antigen[29]. Polyclonal antibodies can be seen as a double-edged sword: On the one hand, their characteristic of binding to several different antigen epitopes potentially increases nonspecific reactions. On the other hand, this characteristic also increases specificity and provides a higher chance of binding to the desired antigen.

Polyclonal antibodies are extremely versatile. They can be used as therapies in areas, such as oncology, infectious diseases or sepsis and septic shock, as well as in transplantations[30,31,32]. Immunized rabbits, mice or goats are commonly used for the production and harvest of polyclonal antibodies.

Large animals, such as goats are frequently used in antibody production, as they provide greater quantities of antiserum. Rabbits and mice, on the other hand, are often used in laboratory settings. They are cheaper to maintain and yield more particular sera. The fact that genetic mouse strains and their immune responses are clearly documented is also a great advantage for researchers.

RECOMBINANT ANTIBODIES

Whereas monoclonal antibodies are produced using traditional hybridoma technologies, recombinant antibodies are monoclonal antibodies with a synthetic genetic makeup that are produced in vitro[33].

After the desired antibody genes are selected from source cells and manipulated accordingly, the antibody genes are amplified then cloned into a phage vector. The vector carrying the antibody genes is then introduced into a host, such as a mammalian cell line, yeast or bacteria. The host expresses the desired antibody in large amounts.

Today, novel genetic engineering techniques are allowing for the development of more disease-targeted and personalized recombinant antibodies that can be used as therapeutic treatments for cancer, autoimmune diseases and many other disorders. Advantages of recombinant antibodies include reproducibility, specificity, fast production timelines, cost effectiveness and animal-free antibody production.

ANTIGEN-BINDING FRAGMENTS

Over the past three decades, antibodies have been broken down into smaller antigen-binding fragments (Fab). As the name indicates, this is the part of the antibody that binds to antigens. Fab are composed of variable regions of both the heavy and light chains and may contain a small segment of the Fc domain. They are used to block signaling molecules or receptors and can penetrate solid tumors better than full length antibodies. Some engineered antigen-binding fragments can target antigens in multiple diseases[34,35,36].

ANTIBODY-DRUG CONJUGATES

One of the more recent approaches in the evolution of antibodies is the use of antibody-drug conjugates (ADCs)[37,38]. ADCs are monoclonal antibodies that carry a cytotoxic payload, namely a chemotherapy drug. Thus, ADCs are currently being studied and used as anti-cancer treatments.

The technique combines the specificity of the antibody with the toxicity of a chemotherapy. Unlike traditional chemotherapies, which attack cancerous as well as healthy cells, causing severe side effects, ADCs only target specific antigens on tumor cells. This way, healthy cells remain unscathed, and treatments may have a less negative impact on the patient.

BISPECIFIC ANTIBODIES

Although the idea of bispecific antibodies is about as old as monoclonal antibodies themselves, it wasn't until the development of antibody engineering and cloning techniques that bispecific antibodies were developed[36]. Bispecific antibodies are antibodies that can bind two different antigens. Bispecific antibodies are used to retarget effector cells of the immune system, such as T-cells, neutrophils or macrophages. At the same time, bispecific antibodies can stimulate these effector cells by binding to a receptor, resulting in tumor cell lysis.

NANOBODIES

Often, conventional antibodies are too large to reach tumor cells. Various domains in engineered antibodies can be hydrophobic, limiting solubility while increasing instability. These limitations can be overcome by so-called nanobodies[86].

Nanobodies, which Camelids naturally produce, are antigen-binding fragments that have their origin in Camelid heavy-chain antibodies. The production of nanobodies is therefore quite cost-effective. Advantages of nanobodies include their small size, high solubility, stability and efficient targeting of tumors. Compared to mAbs, which are usually about 150kDa in size, nanobodies are about 15kDa. Furthermore, nanobodies can be linked to other nanobodies, to Fc-domains, different toxins or peptides, as well as conjugated to drugs[86,87].

ANTIBODIES IN DISEASE AREAS

Today, antibodies are playing an exciting role in the advancement of drug discovery as they are being used as treatments in a wide variety of areas, including cancers, autoimmune diseases, infectious diseases, cardiovascular diseases, as well as in transplant rejection and diagnosis. Advancements in immunotherapies and treatment options with antibodies are being studied worldwide, pushing the global market for antibody research to an estimated value of $3 billion by 2022[39].

IMMUNE DISEASES

Possibly the best known and most commonly used antibody on the market today is AbbVie's Humira. Humira, which carries the therapeutic name adalimumab, is a human monoclonal antibody that binds specifically to TNF-α. TNF-α is prevented from binding to TNF receptors, resulting in reduced inflammation[40,41,42,43].

Approved by the FDA in 2002 for rheumatoid arthritis, adalimumab is also used for Crohn's disease, ankylosing spondylitis, psoriasis and psoriatic arthritis. It was approved by the EMA in 2003.

Humira has been predicted to be one of the world's top 10 best-selling drugs in 2018, as it raked in $14 billion in 2015, and has maintained yearly revenues of more than $10 billion. In 2018, Humira's global sales are expected to exceed $20 billion.

Similar to Humira, Johnson & Johnson's infliximab, which carries the trade name Remicade, can be used to treat Crohn's disease[44]. However, while Humira is a human monoclonal antibody, Remicade is a chimeric monoclonal antibody. Like Humira, it binds to TNF-α and neutralizes it, reducing inflammatory cascades in the process.

ONCOLOGY

There are numerous antibodies directed at a variety of cancers on the market today. One of the most well-known is Avastin, or bevacizumab, which was produced by Roche[42]. It is used to fight various cancers, including colon and lung cancer, as well as glioblastoma and renal-cell carcinoma. It can also be used to treat age-related macular degeneration. Sales of Avastin are estimated to generate more than $6 billion in 2018.
Bevacizumab binds to vascular endothelial growth factor (VEGF), which is needed for angiogenesis. The antibody inhibits the binding of VEGF to cell surface receptors, and results in reduced of growth of tumor blood vessels. Consequently, the blood supply to the tumor is decreased, and the tumor becomes more susceptible to chemotherapeutic agents[45].

Approved by the FDA in 1997, Roche's Rituxan, or rituximab, targets the CD20 antigen on the surface of malignant and normal B-Cells[46]. It is a chimeric mouse-human monoclonal antibody that is used for the treatment of non-Hodgkin's lymphoma and leukemias. In recent years, rituximab has also been used against autoimmune diseases like rheumatoid arthritis[47].

In 2017, more than 14 million women were diagnosed with breast cancer worldwide[48]. The numbers are staggering, and therapies are therefore being improved and developed constantly. One of the most common breast cancer therapies available today is Roche's Herceptin, carrying the therapeutic name trastuzumab.

Trastuzumab is a recombinant humanized monoclonal antibody that targets the extracellular domain of the HER-2 receptor on tumor cells[49]. The binding of the antibody to HER-2 results in tumor cell lysis. It is used for the treatment of human epidermal growth factor receptor (HER)-2+ metastatic breast cancer, localized HER-2+ breast cancer and HER-2+ metastatic adenocarcinoma.

INFECTIOUS DISEASES

When it comes to infectious diseases, antibodies can be used as treatments as well as a prophylactic measure, for instance, in order to prevent epidemics[50]. In recent years, we have seen at least two examples: 1) The 2015 Zika virus outbreak in Brazil[51] and 2) the Ebola virus epidemic in West Africa in 2013-2016.

Although there is currently no approved prophylactic vaccine against the Zika virus, some studies have shown that there is potential in creating a prophylactic antibody-based vaccine that could protect women from Zika prior to pregnancy in high-risk areas. Currently, researchers are working on getting such a vaccine into clinical trials[51].

Developing antibodies to treat rare or emerging infectious diseases, such as influenza, Ebola or the Middle East respiratory syndrome coronavirus (MERS-coV) comes with a variety of challenges: Firstly, conducting clinical trials for proof-of-concept is extremely difficult with unpredictable outbreaks, fluctuating patient numbers or staggering fatality rates, to name just a few. Other obstacles include ethical challenges and logistics - outbreaks often occur in remote, inaccessible villages[50].

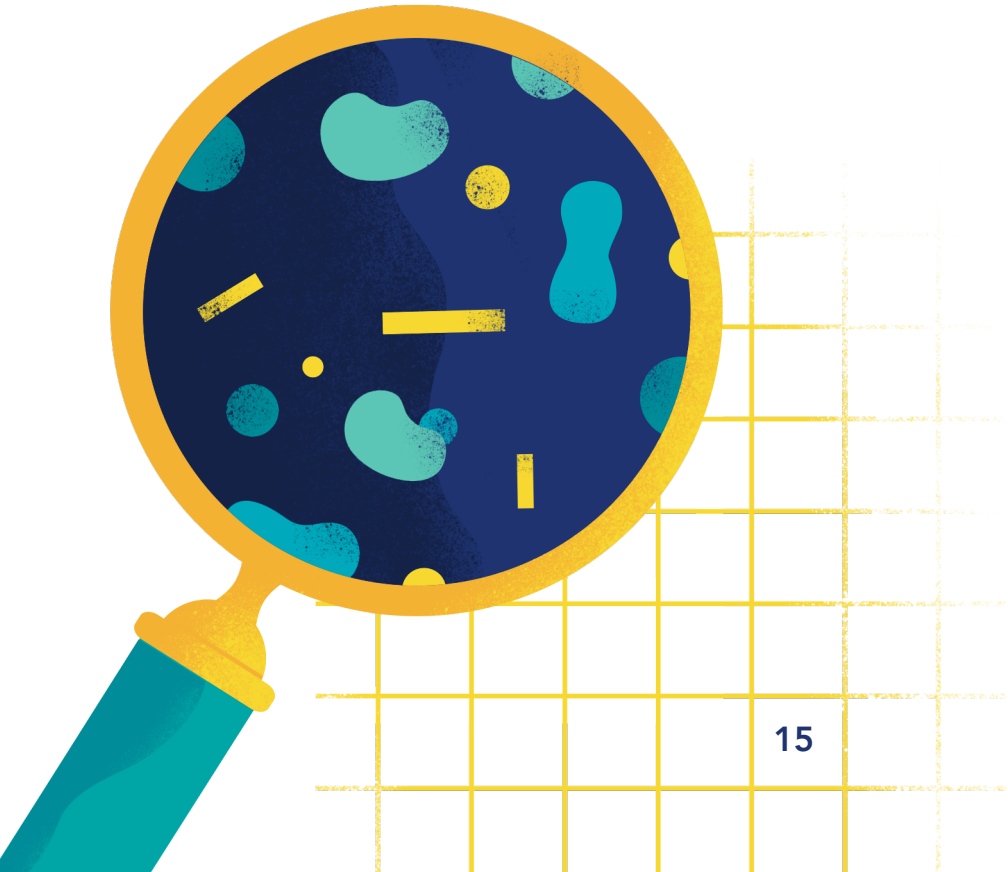
The need for more research and development in the field of antibodies became apparent with the 2013-2016 Ebola virus outbreak in West Africa that left more than 11,000 people dead[52,53]. Although research into antibody treatments for Ebola dates back to the 1990s, it wasn't until 2014 that an experimental treatment was used to treat two American health-care workers infected with Ebola.

Mapp Biopharmaceuticals' ZMapp is a cocktail made up of three different monoclonal antibodies targeting the main surface protein of the Ebola virus. While ZMapp's antiviral activity had previously only been shown in non-human primates, the urgency for treatment had become so intense that efficacy trials were soon conducted in West Africa, sparking debates about the ethicality of clinical trials in epidemics.

The trial, which was originally due to enroll 200 people, could only study the efficacy of ZMapp in 72 patients. Eight of the 36 patients who received ZMapp died. It was less than in the control group, which had only received standard care, but the trial sample size was too small to reach statistical significance[53,54]. However, Mapp Biopharmaceuticals Inc. has received further funding from the American Biomedical Advanced Research and Development Authority and support from the FDA, as well as the "go ahead" for efficacy trials if a new Ebola outbreak should occur[54].

Although various monoclonal antibody therapies against infectious diseases are currently in their development stage, only four have been licensed so far. The first one was palivizumab, also known as Synagis by MedImmune, which is a humanized monoclonal antibody against the human respiratory syncytial virus (RSV)[55,56].

In 2012 and 2016, GlaxoSmithKline and Elusys Therapeutics developed treatments against anthrax, respectively[55,57]. Whereas GlaxoSmithKline's Raxibacumab (or Abthrax) is a human monoclonal antibody, Elusys Therapeutics' Obiltoxaximab (Anthim) is a chimeric monoclonal antibody. Bezlotoxumab, also known as Zinplava, is a human monoclonal antibody against Clostridium difficile[55,58]. It was approved by the FDA in 2016 and marketed by Merck.



DIRECTION OF ANTIBODY RESEARCH

In recent years, our knowledge of antibodies has greatly expanded. Today, they are being used as treatments not only for immune diseases like cancers, but also for infectious diseases, orphan diseases and cardiovascular disorders. And with increasing research and trials, we will see many more applications of antibodies in the near future.

In 2017, the EMA and FDA approved a record number of antibody-based therapies[61]. That year, 10 antibodies passed the authorities' scrutiny, whereas eight were approved in 2015 and 2016, respectively. In 2014, seven antibodies were approved for treatment, and in 2011, 2012 and 2013, the European and American authorities approved only three antibody drugs per year[59,60,61,62].

FDA & EMA APPROVED ANTIBODIES IN 2017

DRUG NAME	ACTIVE INGREDIENT	ANTIBODY FORMAT	INDICATION	COMPANY
Siliq®, Kyntheum®[63]	Brodalumab	Recombinant human mAb	Plaque psoriasis	LEO Pharma A/S
Kevzara®[64]	Sarilumab	Human mAb	Rheumatoid arthritis	Sanofi-Aventis Groupe
Bavencio®[65]	Avelumab	Human mAb	Merkel cell carcinoma	Merck Serono Europe Limited
Dupixent®[66]	Dupilumab	Recombinant human mAb	Atopic dermatitis	Sanofi-Aventis Groupe
Ocrevus®[67]	Ocrelizumab	Humanized anti-CD20 mAb	Multiple sclerosis	Roche Registration GmbH
Imfinzi®[68]	Durvalumab	Human mAb (only FDA approved)	Metastatic urothelial carcinoma & non-small cell lung cancer	AstraZeneca
Besponsa®[69]	Inotuzumab ozogamicin	ADC: Anti-CD22 mAb with cytotoxic payload	Acute lymphoblastic leukemia	Pfizer Limited
Tremfya®[70]	Guselkumab	Human mAb	Plaque psoriasis	Janssen-Cilag International N.V.
Fasenra®[71]	Benralizumab	Humanized mAb (only FDA approved)	Asthma	AstraZeneca AB
Hemlibra®[72]	Emicizumab	Humanized mAb (EMA approved in 2018)	Hemophilia A	Roche Registration Limited

New developments in genetic engineering, gene editing techniques and genome research now allow for more personalized approaches. Also, diseases, especially orphan diseases, can be targeted more specifically, using genetic profiles and biomarker diagnostics.

Increasingly, drug discovery pipelines are moving towards the development of bispecific and recombinant antibodies. These are highly specific, as well as easy to upscale at lower costs[62,73].

ANTIBODIES TRENDING IN 2018

DRUG NAME	ACTIVE INGREDIENT	ANTIBODY FORMAT	INDICATION	COMPANY	EMA	FDA
Trogarz®[74]	Ibalizumab	Humanized mAb	HIV infection	TaiMed Biologics USA Corp.	NA	March 2018
Crysvita®[75]	Burosumab[76]	Human mAb	X-linked hypophosphatemia	Kyowa Hakko Kirin Limited	Under review	April 2018
Ilumya®	Tildrakizumab	Humanized mAb	Plaque psoriasis	Sun Pharmaceutical Industries Ltd.	Under review	March 2018
-	Caplacizumab	Humanized Nanobody	Acquired thrombotic thrombocytopenic purpura	Ablynx	Under review	Under review
Aimovig®[78]	Erenumab[77]	Human mAb	Migraine	Novartis, Amgen	Under review	May 2018
-	Fremanezumab[79]	Humanized mAb	Migraine	Teva Pharmaceuticals, USA	Under review	Under review
-	Galcanezumab[80,81]	Humanized mAb	Migraine	Eli Lilly	Under review	Under review
Evenity®	Romosozumab[82,83]	Humanized mAb	Osteoporosis	UCB, Amgen	Under review	Under review
Poteligeo®	Mogamulizumab[84,85]	Humanized mAb	Lymphoma	Kyowa Hakko Kirin Limited	Under review	Under review

The antibodies shown above are currently being reviewed by the FDA or EMA. However, there are a number of other antibodies in Phase III clinical development that are worth watching more closely. Twenty-six antibodies are currently being studied for non-cancer indications, including cardiovascular diseases, immune diseases, infectious diseases, neurological disorders and ophthalmic diseases.

A list of active ingredients and their producers follows: lanadelumab (Shire), crizanlizumab (Novartis), ravulizumab (Alexion Pharmaceuticals Inc.), eptinezumab (Alder Biopharmaceuticals), risankizumab (Boehringer Ingelheim Pharmaceuticals, AbbVie), satralizumab (Chugai Pharmaceuticals, Roche), brolucizumab (Novartis), lampalizumab (Genentech), roledumab (LFB Group), emapalumab (NovImmune SA), fasinumab (Regeneron Pharmaceuticals), tanezumab (Pfizer, Eli Lilly), etrolizumab (Genentech), gantenerumab (Hoffmann-La Roche) and anifrolumab (AstraZeneca/MedImmune LLC)[62].

Currently, there are more than 20 antibody therapies for cancer in late stage clinical development. For a few of them, marketing applications to the FDA will be completed in 2018[62]. These include sacituzumab govitecan (Immunomedics Inc.), moxetumomab pasudotox (AstraZeneca, MedImmune LLC), cemiplimab (Regeneron Pharmaceuticals) and ublituximab (TG Therapeutics). These antibodies target triple negative breast cancer, hairy cell leukemia, non-small cell lung cancer and cervical cancer as well as leukemia, lymphoma and multiple sclerosis, respectively.

In the preclinical stage, the demand for antibodies is equally impressive. According to Scientist.com, the world's largest marketplace for outsourced research services and products, requests for antibodies made by researchers has grown exponentially over the last two years. Between 2016 and 2017, antibody requests grew by 46%, and requests made in 2018 compared to 2017 are on pace to reach 68% year-over-year growth. The most popular categories of antibody services requested by various sized pharmaceutical companies include antibody production studies, antibody purification, immunohistochemistry, epitope mapping, monoclonal antibody generation/production and many highly-custom studies.

CONCLUSION

Antibodies have come a long way since their discovery by notable researchers Emil von Behring, Paul Ehrlich and Astrid Fragraens - to name just a few. More than 100 years have passed since their simple immunization studies, which paved the way for the development of monoclonal antibodies, the foundation of large-scale production techniques and their application in numerous diseases.

We have seen how genetic engineering techniques have enabled researchers to create recombinant antibodies, bispecific antibodies and antigen-binding fragments as well as how newer technologies have led to the creation of antibody-drug conjugates with greater efficacy and less side effects than traditional chemotherapies.

In addition, antibodies have become a treatment option to fight devastating epidemics. And in the hopeful not too distant future, we will see them take over the treatment and diagnosis of many more diseases and disorders. So, in the words of Paul Ehrlich it is appropriate to say: Antibodies truly are 'magic bullets' in their own distinct way.

ABOUT US

Antibodies have become an essential part of immunotherapies. The increasing need for novel antibody therapies in the fight against cancer, immune diseases and devastating epidemics means that researchers will need easy access to antibodies in order to push drug discovery forward. Founded in 2007, Scientist.com is the world's leading and fastest-growing marketplace for outsourced research services and products. The marketplace significantly accelerates the sourcing process by simplifying access to innovative tools and technologies, including custom antibodies for research. In fact, the Scientist.com marketplace features over 2,500 registered suppliers across more than 4,000 research areas, and custom antibodies remain one of the most popular service offerings. For a full list of services and providers, visit Scientist.com.

APPENDIX

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