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AN UPDATED STUDY ON MONOCLONAL ANTIBODIES

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ABSTRACT

The field of clinical and laboratory medicine has benefited greatly from the advancement of monoclonal antibody (MAb) technology. It has made it possible to mass-produce pure, homogenous antibodies against a wide range of antigens. Although MAbs have numerous applications, they are not always worth the time and money it takes to develop them. There are still situations when the more common, cheaper, and more accessible traditional anti-serum will do just fine. Despite this, murine MAbs have been used widely in the fields of cancer and other clinical studies. Human MAbs have been the focus of significant research and development because antibodies of human origin are widely considered to be better in therapeutic and in vivo diagnostic applications. However, limitations in technology hinder its broad use at the present time. Last but not least, several promising new directions are outlined that make use of genetic engineering methods.

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Introduction

Antibodies called monoclonal antibodies (mAbs) are created by repeatedly cloning the same kind of immune system cell. Every single antibody that follows in this lineage may be traced back to a single origin[1].

When it comes to binding, certain monoclonal antibodies are quite picky (the part of an antigen that is recognised by the antibody)[2]. On the other hand, polyclonal antibodies are generated by many different types of plasma cells, each of which may bind to a different epitope. One monoclonal antibody's therapeutic potential may be doubled by engineering a bispecific monoclonal antibody that recognises both of the antigen's epitopes[3].

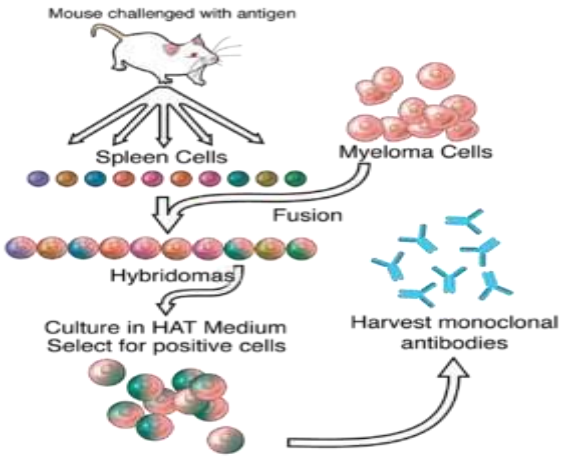

Figure 1: Monoclonal antibody production overview

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History

In the early 1900s, immunologist Paul Ehrlich devised the notion of a Zauberkugel, which literally translates to "magic bullet." This "magic bullet" would be a material that would selectively target a disease-causing bacterium and then provide a poison for that organism. This "magic bullet" would be able to eradicate disease-causing bacteria[4]. This laid the groundwork for the development of monoclonal antibodies and monoclonal drug conjugates by providing a theoretical foundation for their creation. In recognition of the theoretical groundwork that they had laid for immunology, Paul Ehrlich and Élie Metchnikoff were jointly presented with the Nobel Prize in Physiology or Medicine in the year 1908[5].

The malignancy of B-cells, known as multiple myeloma, was first identified in the 1970s, and it was shown to be caused by lymphocytes that only produce a single antibody. In the past, researchers had to rely on these aberrant antibodies, known as paraproteins, to learn more about the structure of antibodies[6]. However, it was not possible to mass generate antibodies that were directed just against a particular antigen. This was due to the complexity of the process. In 1973, Jerrold Schwaber was the first person to discover that human-mouse hybrid cells could produce monoclonal antibodies. These antibodies could then be used in research. Those that deal with hybridomas produced from humans continue to reference this study often. This allowed them to develop hybridomas that could manufacture antibodies. Due to their groundbreaking discovery, they were awarded the Nobel Prize in Physiology or Medicine in 1984, sharing the honour with Niels Kaj Jerne[7].

Humanizing monoclonal antibodies was first achieved by Gregory Winter and colleagues in 1988, removing the responses that many monoclonal antibodies provoked in certain people [8]. Cancer treatment by suppression of negative immune regulation utilising monoclonal antibodies that block inhibitory links was discovered in the 1990s, and in 2018, Awardees of the Nobel Prize in Physiology or Medicine in this category include James P. Allison and TasukuHonjo[9].

When comparing monoclonal and polyclonal antibodies, what are the key differences?

The names of the two kinds of antibodies give away their key distinction. The prefix "mono" indicates a single unit, whereas the suffix "-poly" indicates several units. The unique monoclonal antibodies we use here are clones of a single antibody that only recognise and respond to a particular antigen. Polyclonal antibodies may recognise and bind to more than one antigen, and they are generated by a wide range of immune cells[10].

Antibodies known as polyclonal antibodies (pAbs) are produced by several B cell subsets. They are a group of immunoglobulin molecules that recognise distinct epitopes on the same antigen[11].

Polyclonal antibodies have an advantage over monoclonal antibodies because they can recognise antigen from several angles. Potentially helpful in situations when the use of a single epitope would prevent the detection of an analyte. On top of that, unlike monoclonal reagents, polyclonal reagents are easy and inexpensive to create in the near run. Antibody-rich serum may be recovered in considerable volumes (for instance, 60 ml from a rabbit) when bigger animals (such as horses, goats, and rabbits) are used[12].

Generally speaking, monoclonal antibodies are potent research tools for studying macromolecules and cells, and they have also shown to be very specific reagents for clinical diagnostics. Humanized versions of murine monoclonal reagents have been employed in

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clinical practise with different degrees of success in recent years[13].

Production
Outline

Combine myeloma cells with spleen cells from an immunised mouse using polyethylene glycol (PEG) (P3.653). In HAT medium, pick out the hybrid colonies (hybridomas). Expansion, freezing, and subcloning the required hybridomas to guarantee monoclonality is performed 10 to 14 days after fusing (the ELISA screening methodology should be designed before to the fusion)[14].

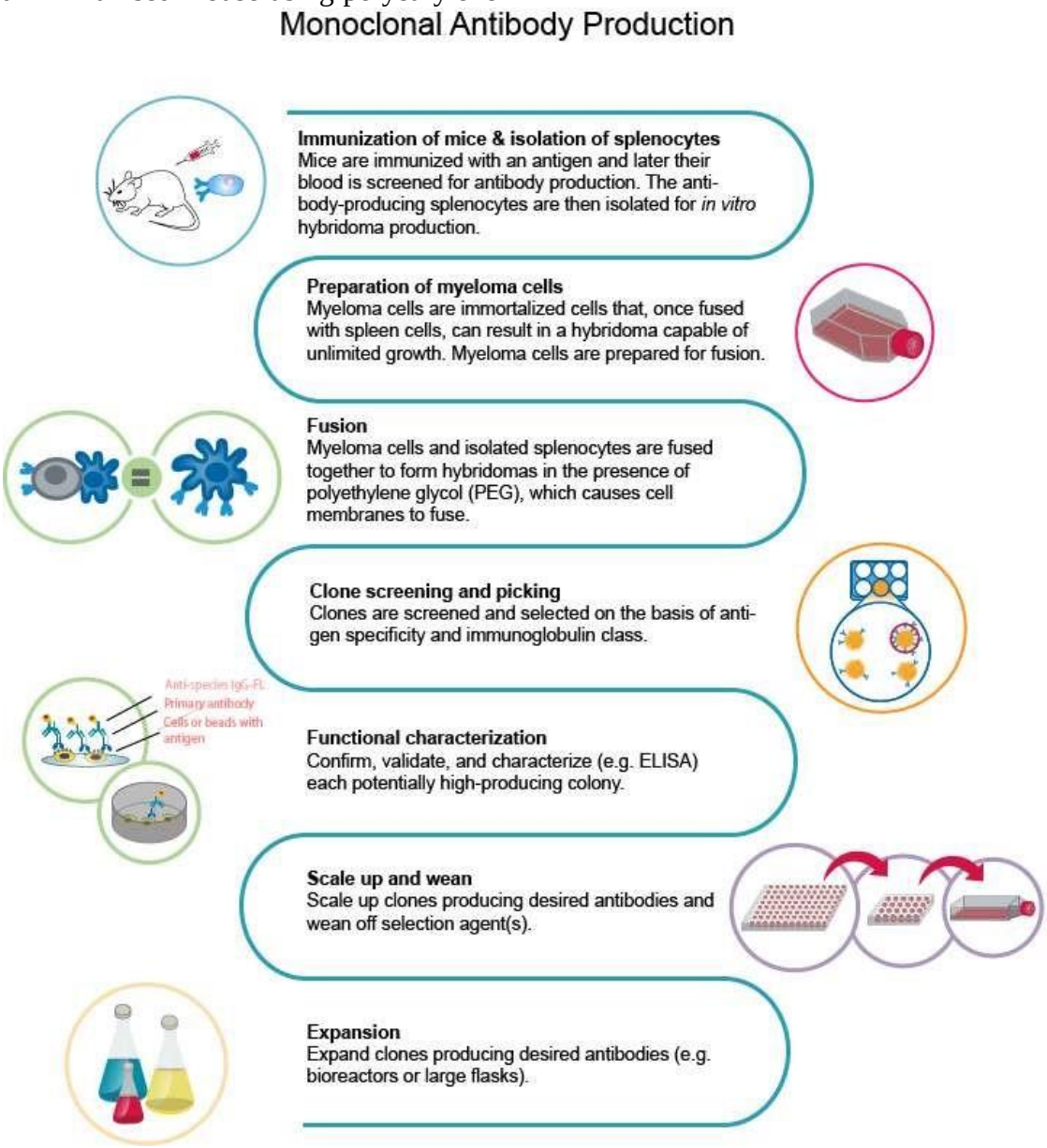

Figure 2: Steps in production of antibodies

Stage 1: Immunization

Immunogens are substances that are alien to the host and cause an immunological response. The primary vaccination of mice may be carried out using either protein (50-100 g), cells (1 107), numerous antigenic synthetic peptides, or a short peptide (6-18 amino acids) coupled to a carrier protein. Freund's adjuvants come in two primary varieties:

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Freund's Complete Adjuvant (FCA) and Freund's Incomplete Adjuvant (FIA) (FIA). The antigen is contained inside the FCA, which is a water-in-oil emulsion, for up to 6 months[15].

On day 0, before the first injection, the mice are bled and their sera are tested for antigen reactivity in the background. Antigen is emulsified in Freund's adjuvant or combined with 1/10 proportion of alum and vortexed before being injected into the mice. Antigen is administered as three separate intraperitoneal injections at the following times:[16]

Table 1: Antigen is administered as three intraperitoneal injections at the following times:

Day	Amount of antigen	Adjuvant
0	50 µg	Alum or complete Freund's adjuvant
14	25 µg	Alum or incomplete Freund's adjuvant
28	25 µg	Alum or D-PBSA

On day 35, another bleed is taken from the mice, and the ELISA test is used to determine the antibody titer in the serum. After diluting the serum by a factor of 1:30, it is further diluted by a factor of 1:4 all the way up to a factor of 1:1,720. A last boost of 10 g of antigen is administered intravenously (i.v.) or intraperitoneally (i.p.) to the chosen mice 3 days before to fusion.

Stage 2: Preparation of Myeloma Cells

Myeloma cell line P3.653 is grown in minimum essential medium supplemented with 10% foetal calf serum and 8azaguanine. On days one through three before fusion, the P3.653 cells are diluted to 3.5 105 cells/mL daily[17].

Stage 3: Removal of Spleen

Aseptic removal of the spleens is followed by placement in a Petri dish with 5 mL of sterile D-PBSA. Two 23G needles attached to 1 mL syringes are used to tease or burst the spleens. The number of fibroblasts in the spleens of animals that have been teased harshly is quite high[18].

After removing the aggregates, the cells are placed in a 15-mL conical tube. After a 1:100 dilution in an Unopette, clump-free spleen cells are transferred to a 50 mL conical tube and counted using a haemocytometer. For 8 minutes, the cells are spun at 200 g[19].

Following a 15-minute incubation at 4 degrees Celsius, the resulting pellet is resuspended in 0.84 percent NH4Cl (10 mL/spleen) to lyse the red blood cells. After underlapping 14 mL of horse serum with the cell suspension, you spin the mixture at 450 g for 8 minutes. The pellet is then resuspended in 50 mL of TCD buffer and spun at 200 g for 8 minutes to remove any remaining TCD buffer[20].

Stage 4: T-Cell Depletion

After centrifugation, the cell pellet is resuspended with anti-Thy 1.2 at a final concentration of 1 107 cells/mL to accomplish T-cell depletion. The suspension should be incubated at 4 C for 45 minutes before being centrifuged at 200 g for 8 minutes. Following this, the pellet is resuspended in a watered-down rabbit supplement. The suspension should be incubated at 37 degrees Celsius for 45 minutes before being centrifuged at 200 g for 8 minutes[21].

Hemocytometer counts the cells by excluding the staining effect of Trypan Blue. Between 30% and 50% of B-cells should return after treatment[22].

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Stage 5: Fusion

In a 50 mL centrifuge tube, the myeloma and B cells are combined. The largest number of spleen cells that may be fused at once is 1.2 108. There can be no more than 3 107 P3.653 cells in a fusion, since the spleen cells are combined with the myelomas at a ratio of 4:1. After mixing, the suspension is centrifuged at 200 g for 8 minutes. Using a tapping motion, crush the resulting pellet, then slowly inject 1 mL of PEG into the tube over the course of 15 seconds. For 75 seconds, gently jiggle the tube to combine the suspension. To a clean test tube, slowly pour in 1 mL of SFM over 15 seconds, and then gently shake it for 45 seconds. Slowly inject 2 mL of SFM into the tube and agitate it for 90 seconds. Slowly pour in 4 mL of HAT medium and agitate the tube for 90 seconds. After that, slowly pour in 8 mL of HAT medium over 30 seconds, and give the tube a good shake for 90 seconds[23].
Fill a sterile Nalgene bottle with the determined quantity of HAT medium plus this capacity (16 mL) (125 mL if the maximum cell concentration has been used). There are 1.5 x 108 cells in 16 mL, and 125 mL of HAT media in the container. Total volume after the subsequent wash is 150 mL, yielding a final concentration of 1 106 cells/mL. Add 9 mL of HAT medium to the bottle after using it to wash out a 50-mL conical tube[24].

Gently shake the vial, and then pour the cells into the clean reservoir. The cells should be plated onto a sterile 96-well plate at a concentration of 200 L/well using a 12-channel multipipettor[25].
This yields a final cell density of 2 105 cells/well.

Stage 6: Selection of Hybridomas

Aspirate most of the culture media from the wells of the fusion plates 5 days after fusion, and replace it with new HAT medium at a rate of 150–200 L/well. Every other day, fill the plates. To pick the best hybridomas from the clones, ELISA testing is performed about two weeks following fusing. Retest the positive clones after a further 48 hours[26].

The most fruitful hybridomas may be multiplied by cultivating them in two separate wells of a 96-well plate with medium containing 10% FBS and HT. Screen 2 mL of culture supernatant after retesting the clones, expanding the positive hybridomas to a 24-well plate, and weaning them off HT medium. At this point, enough material is collected to conduct several selection tests, which are used to verify that the antibody recognises just the target antigen. Cryopreserve the hybridomas by expanding them to fill only four wells in a 24-well plate. Repeat cryopreservation after you've grown the hybridoma to a 75-cm2 flask[27].

Stage 7: Screening

You must take care in designing the screening approach in order to find a monoclonal antibody with the desired properties. The supernatants of hybridoma cultures should be analysed as soon as possible to identify reactive patterns of interest. The expanded culture supernatant must be evaluated in the proper setting after the first selection by ELISA for reactivity to the immunogen (Western blot, competitive immunoassay, flow cytometry, etc)[28].

Most of the wells will either lack the required antibodies or contain non-functional hybridomas. The goal of this screening process is to identify the wells that contain hybridomas that produce the required specificity of antibody. Under an inverted microscope, when most of the wells are between 10 and 25 percent confluent, or when some of the denser wells become yellow within 2 days after feeding, it is time to do a preliminary screening[29].

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This may happen anywhere between 10 and 14 days after a mouse-mouse fusion, 14 to 21 days after a rat-mouse fusion, or even sooner in a hamster-mouse fusion. It is possible to screen the densest wells first and the less dense wells as they get denser, but this is inefficient and unnecessary. So, the wells are fed, and then two days later, the screening assay is run on aliquots of the supernatants to look for the target antibody[30].

Stage 8: Establishment of Hybridoma Lines

Following the selection of potential hybridomas (described in the preceding supplementary procedure), these cells are cultured and nourished until they reach the desired size, after which they are frozen and cloned by limiting dilution. As unfortunate as it may be, this must be done for each prospective line before the specificity of the monoclonal antibody can be determined. This extra effort guarantees that functional antibody-producing hybridomas will be accessible after the first screening. Pick the top 20 potential wells to drill in order to cut down on time and effort. Once the supernatants have been verified, all twenty vials should be frozen and limiting-dilution plates put up[31].

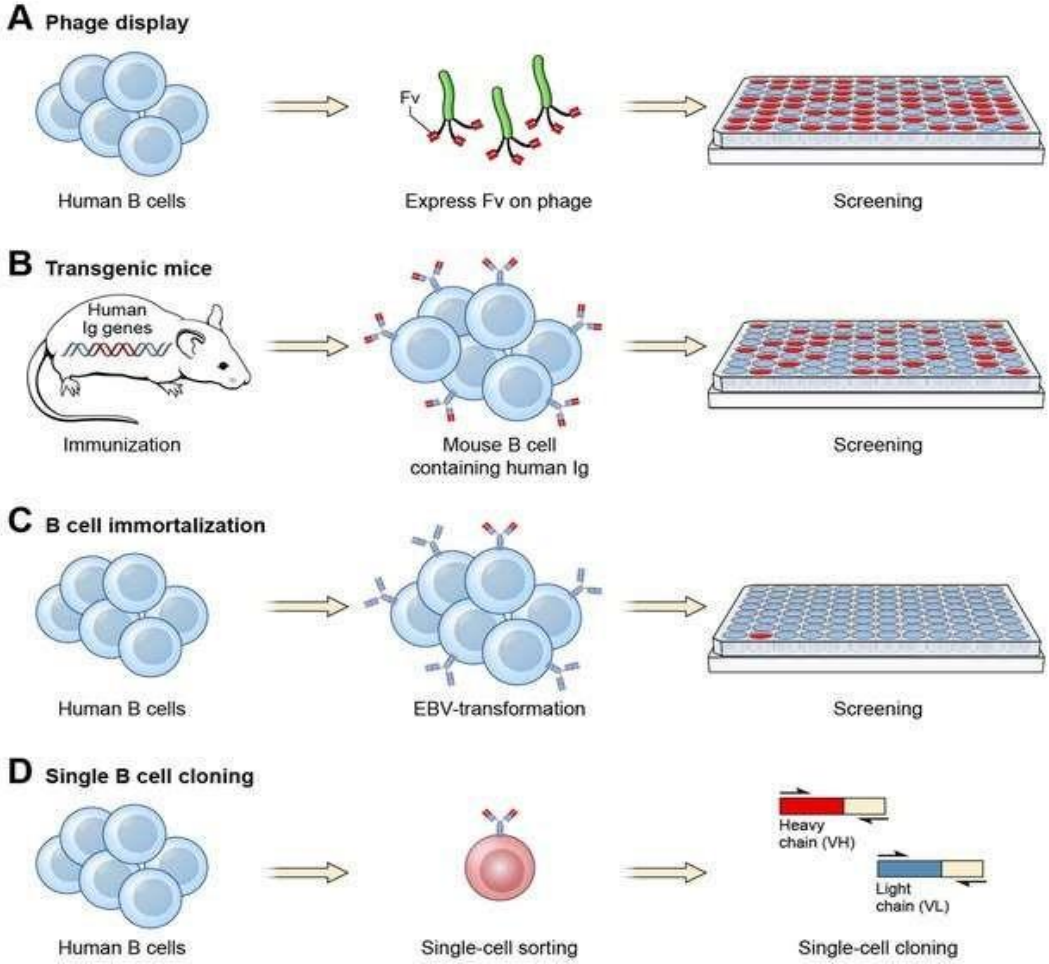

Figure 3: Isolation of human monoclonal antibodies

Types

Chimeric antibodies

Although there are structural similarities between mouse and human antibodies, injecting murine monoclonal antibodies into humans triggered an immune response that led

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to the rapid clearance of the antibodies from the blood, systemic inflammatory effects, and the development of human anti-mouse antibodies (HAMA)[32].

Human antibodies

Scientists have been working toward the development of entirely human goods since the discovery of monoclonal antibodies in an effort to lessen the negative consequences of humanised or chimeric antibodies. Transgenic mice, phage display, and the cloning of individual B cells are only a few of the proven methods.Scientists have been working toward the development of entirely human goods since the discovery of monoclonal antibodies in an effort to lessen the negative consequences of humanised or chimeric antibodies. Transgenic mice, phage display, and the cloning of individual B cells are only a few of the proven methods[33].

Cost

The production cost of monoclonal antibodies is substantially higher than that of smaller molecules because of their vast size and the complexity of the methods necessary to create them. This is in addition to the significant expenditures involved with identifying and developing a novel chemical entity and getting it to patients[34].

By the 10thof November 2014, 47 monoclonal antibody medicines had been authorised for use in the United States or Europe to treat a broad variety of disorders; several of these treatments had also been approved for use in other regions of the globe[35]. Since the introduction of the first therapeutic monoclonal antibody product to the market in 1986, this category of biopharmaceuticals has expanded greatly. If the current rate of approval of new drugs each year continues, there would be seventy monoclonal antibody products accessible on the market by 2020, with worldwide sales of roughly 10 lakh crores[36].

Applications
Diagnostic tests

Monoclonal antibodies may be employed for detection after they have been developed for a specific chemical. Two methods for detecting proteins are the Western blot and the dot blot. It is possible to identify antigens in fixed tissue sections using monoclonal antibodies in immunohistochemistry, and in frozen tissue slices or living cells using immunofluorescence[37].

Analytic and chemical uses

Immunoprecipitation is a technique that use antibodies to isolate their target substances from complex mixtures[38].

Cancer treatment

Monoclonal antibodies are a promising cancer therapeutic option because they may stimulate an immune response against cancer cells by binding solely to antigens expressed on those cells. These mAbs may be modified to deliver a poison, radioisotope, cytokine, or other active conjugation, or to generate bispecific antibodies that bind target antigen and a conjugate or effector cell through their Fab sections. Any whole antibody has an Fc region that might potentially bind to a cell receptor or another protein[39].

Different types of monoclonal antibodies are created for specific purposes. There might be a number of different ways in which a given medicine works. Antibodies are required by certain immune system cells in order to identify and attack their intended target. Coating cancer cells with monoclonal antibodies might make them easier to identify and eradicate. Certain monoclonal antibodies have been shown to cause an immune response capable of destroying the membrane

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around cancer cells. Tumor growth and survival depend on communication between cancer cells and proteins that promote cell division[40].

A malignant tumour requires a blood supply for its continued growth and survival. A number of monoclonal antibody medications inhibit protein-cell interactions vital to vascular growth[41].

Your body avoids an overactive immune system by producing proteins that control the activity of immune system cells. By blocking this pathway, monoclonal antibodies free your immune system cells to get to work killing off cancerous tissue. It's possible that certain monoclonal antibodies go straight for the cell nucleus. Some of these antibodies, when binding to a cell, may set off a cascade of events inside the cell that ultimately leads to the cell's own destruction[42].

Since monoclonal antibodies may connect to cancer cells, they can be engineered to deliver additional treatments. Radiation therapy may be more effectively delivered to cancer cells when a monoclonal antibody is paired with a tiny radioactive particle[43].

In a similar vein, some monoclonal antibodies are paired with a chemotherapeutic medicine to preferentially target cancer cells for therapy. Some pharmaceuticals use a pair of monoclonal antibodies, each of which targets a different component of the immune system. The immune system's ability to target cancer cells may be boosted as a result of this link[44].

Autoimmune diseases

The autoimmune disorders rheumatoid arthritis, Crohn's disease, ulcerative colitis, and ankylosing spondylitis are treated with the monoclonal antibodies infliximab and adalimumab, which bind to and neutralise the effects of tumour necrosis factor-. Acute rejection of kidney transplants may be prevented with the use of basiliximab or daclizumab, two drugs that block the production of IL-2 by activated T cells. Human immunoglobulin E (IgE) inhibition by omalizumab makes it a promising therapy for treating severe cases of allergic asthma[45].

Side effects

Side effects from monoclonal antibodies like bevacizumab and cetuximab might vary. There are two types of adverse effects: mild and severe[46].

This is a list of some common adverse effects:

- Dizziness
- Headaches
- Allergies
- Diarrhoea
- Cough
- Fever
- Itching
- Insomnia

It's conceivable that you might get some really severe adverse effects, including:[47]

- Anaphylaxis
- Bleeding
- Blood clots in the arteries and veins
- Disease of the thyroid caused by the immune system
- Hepatitis
- Cancer
- Having fewer immune system cells
- Stomatitis
- Enterocolitis
- Perforation of the GI Tract
- Mucositis

CONCLUSION

Research, diagnosis, and treatment all benefit greatly from the use of monoclonal antibodies. It was not until the introduction of hybridoma technology by Kohler and Milstein in 1975 that monoclonal antibodies began to displace polyclonal antibodies in a variety of settings. Once created, monoclonal antibodies may be

used in several fields, from research to diagnostics to medicine.

Some of the money needed for future studies might come from the commercial exploitation of monoclonal antibodies, and there are also chances for collaboration. By combining molecular modelling with epitope mapping of monoclonal antibodies, it is possible to better visualise and localise key antigenic regions of a protein. Possible medicinal applications include a better understanding of the structure-function connections of proteins, polysaccharides, and other substances. A major focus of monoclonal antibody researchers is, of course, expanding the use of antibodies in the clinic. These reagents have found extensive usage for the detection and identification of serum analytes, cell markers, and pathogenic agents because to their high level of specificity. Monoclonal antibodies provide antigenic profiling and visualisation of macromolecular surfaces when used in conjunction with other methods, such as epitope mapping and molecular modelling.

In terms of production, cost, and general uses, polyclonal and monoclonal antibodies each have their own set of benefits and drawbacks. Finally, monoclonal antibodies are only made when absolutely essential due to the fact that their creation is time intensive, difficult, but ultimately very gratifying. When a monoclonal antibody may help with clinical diagnosis or therapy, or when it can be employed successfully in a standard pathology laboratory, these benefits become readily apparent.
The article details the reasons for and methods of creating monoclonal antibodies. Multiple potential uses have also been proposed.

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REFERENCES:

[1]. Chen RE, Zhang X, Case JB, Winkler ES, Liu Y, VanBlargan LA, Liu J, Errico JM, Xie X, Suryadevara N, Gilchuk P. Resistance of SARS-CoV-2 variants to neutralization by monoclonal and serum-derived polyclonal antibodies. Nature medicine. 2021 Apr;27(4):717-26.

[2]. Liu WL, Zou MZ, Qin SY, Cheng YJ, Ma YH, Sun YX, Zhang XZ. Recent advances of cell membrane-coated nanomaterials for biomedical applications. Advanced Functional Materials. 2020 Sep;30(39):2003559.

[3]. Crowley AR, Ackerman ME. Mind the gap: how interspecies variability in IgG and its receptors may complicate comparisons of human and non-human primate effector function. Frontiers in immunology. 2019 Apr 8;10:697.

[4]. Butterfield LH, Kaufman HL, Marincola FM, editors. Cancer immunotherapy principles and practice. Springer Publishing Company; 2021 Aug 25.

[5]. Adhikari A, Shen B, Rader C. Challenges and opportunities to develop enediyne natural products as payloads for antibody-drug conjugates. Antibody therapeutics. 2021 Jan;4(1):1-5.

[6]. Cooper MD. The early history of B cells. Nature Reviews Immunology. 2015 Mar;15(3):191-7.

[7]. Cruse JM, Lewis RE. Atlas of immunology. Springer Science & Business Media; 2013 Mar 14.

[8]. Lu RM, Hwang YC, Liu IJ, Lee CC, Tsai HZ, Li HJ, Wu HC. Development of therapeutic antibodies for the treatment of diseases. Journal of biomedical science. 2020 Dec;27(1):1-30.

[9]. Sung PS, Jang JW. Natural killer cell dysfunction in hepatocellular carcinoma: pathogenesis and clinical implications. International journal of molecular sciences. 2018 Nov 19;19(11):3648.

[10]. Busby M, Xue C, Li C, Farjoun Y, Gienger E, Yofe I, Gladden A, Epstein CB, Cornett EM, Rothbart SB, Nusbaum C. Systematic comparison of monoclonal versus polyclonal antibodies for mapping histone modifications by ChIP-seq. Epigenetics & chromatin. 2016 Dec;9(1):1-6.

[11]. He W, Mullarkey CE, Duty JA, Moran TM, Palese P, Miller MS. Broadly neutralizing anti-influenza virus antibodies: enhancement of neutralizing potency in polyclonal mixtures and IgA backbones. Journal of Virology. 2015 Apr 1;89(7):3610-8.

[12]. Wang L, Shi W, Chappell JD, Joyce MG, Zhang Y, Kanekiyo M, Becker MM, van Doremalen N, Fischer R, Wang N, Corbett KS. Importance of neutralizing monoclonal antibodies targeting multiple antigenic sites on the Middle East respiratory syndrome coronavirus spike glycoprotein to avoid neutralization escape. Journal of virology. 2018 May 15;92(10):e02002-17.

[13]. Ulbrich K, Hola K, Subr V, Bakandritsos A, Tucek J, Zboril R. Targeted drug delivery with polymers and magnetic nanoparticles: covalent and noncovalent approaches, release control, and clinical studies. Chemical reviews. 2016 May 11;116(9):5338-431.

[14]. Zola H, Brooks D. Techniques for the production and characterization of monoclonal hybridoma antibodies. InMonoclonal hybridoma antibodies: techniques and applications 2018 May 4 (pp. 1-57). CRC Press.

[15]. Piccinni MZ, Guille MJ. Purifying antibodies raised against Xenopus peptides. Cold Spring Harbor Protocols. 2020 Sep 1;2020(9):pdb-rot105619.

[16]. Parveen N, Fernandez MC, Haynes AM, Zhang RL, Godornes BC, Centurion-Lara A, Giacani L. Non-pathogenic Borrelia burgdorferi expressing Treponema pallidum TprK and Tp0435 antigens as a novel approach to evaluate syphilis vaccine candidates. Vaccine. 2019 Mar 22;37(13):1807-18.

[17]. Meister S, Schubert U, Neubert K, Herrmann K, Burger R, Gramatzki M, Hahn S, Schreiber S, Wilhelm S, Herrmann M, Jäck HM. Extensive immunoglobulin production sensitizes myeloma cells for proteasome inhibition. Cancer research. 2007 Feb 15;67(4):1783-92.

[18]. Kimura W, Yano M, Sugawara S, Okazaki S, Sato T, Moriya T, Watanabe T, Fujimoto H, Tezuka K, Takeshita A, Hirai I. Spleen-preserving distal pancreatectomy with conservation of the splenic artery and vein: techniques and its significance. Journal of Hepato-Biliary-Pancreatic Sciences. 2010 Nov;17(6):813-23.

[19]. Abelseth E, Abelseth L, De la Vega L, Beyer ST, Wadsworth SJ, Willerth SM. 3D printing of neural tissues derived from human induced pluripotent stem cells using a fibrin-based bioink. ACS Biomaterials Science & Engineering. 2018 Nov 26;5(1):234-43.

[20]. Takasato M, Little MH. Making a kidney organoid using the directed differentiation of human pluripotent stem cells. InOrgan Regeneration 2017 (pp. 195-206). Humana Press, New York, NY.

[21]. Okoye AA, Picker LJ. CD 4+ T-cell depletion in HIV infection: mechanisms of immunological failure. Immunological reviews. 2013 Jul;254(1):54-64.

[22]. Zhang Y, Lazarus J, Steele NG, Yan W, Lee HJ, Nwosu ZC, Halbrook CJ, Menjivar RE, Kemp SB, Sirihorachai VR, Velez-Delgado A. Regulatory T-cell Depletion Alters the Tumor Microenvironment and Accelerates Pancreatic CarcinogenesisTreg Depletion Accelerates Pancreatic Carcinogenesis. Cancer discovery. 2020 Mar 1;10(3):422-39.

[23]. Ou SH, Zhu VW. Catalog of 5′ fusion partners in RET+ NSCLC Circa 2020. JTO Clinical and Research Reports. 2020 Jun 1;1(2):100037.

[24]. Xia S, Zhu Y, Liu M, Lan Q, Xu W, Wu Y, Ying T, Liu S, Shi Z, Jiang S, Lu L. Fusion mechanism of 2019-nCoV and fusion inhibitors targeting HR1 domain in spike protein. Cellular & molecular immunology. 2020 Jul;17(7):765-7.

[25]. Lai JW, Chang J, Ang LK, Cheong KH. Multi-level information fusion to alleviate network congestion. Information Fusion. 2020 Nov 1;63:248-55.

[26]. Listek M, Hönow A, Gossen M, Hanack K. A novel selection strategy for antibody producing hybridoma cells based on a new transgenic fusion cell line. Scientific Reports. 2020 Feb 3;10(1):1-2.

[27]. Lu RM, Hwang YC, Liu IJ, Lee CC, Tsai HZ, Li HJ, Wu HC. Development of therapeutic antibodies for the treatment of diseases. Journal of biomedical science. 2020 Dec;27(1):1-30.

[28]. Giron CC, Laaksonen A, da Silva FL. On the interactions of the receptor-binding domain of SARS-CoV-1 and SARS-CoV-2 spike proteins with monoclonal antibodies and the receptor ACE2. Virus research. 2020 Aug 1;285:198021.

[29]. Zahavi D, Weiner L. Monoclonal antibodies in cancer therapy. Antibodies. 2020 Jul 20;9(3):34.

[30]. Lu RM, Hwang YC, Liu IJ, Lee CC, Tsai HZ, Li HJ, Wu HC. Development of therapeutic antibodies for the treatment of diseases. Journal of biomedical science. 2020 Dec;27(1):1-30.

[31]. Akagi S, Nakajima C, Tanaka Y, Kurihara Y. Flow cytometry-based method for rapid and high-throughput screening of hybridoma cells secreting monoclonal antibody. Journal of bioscience and bioengineering. 2018 Apr 1;125(4):464-9.

[32]. Iberg CA, Hawiger D. Advancing immunomodulation by in vivo antigen delivery to DEC-205 and other cell surface molecules using recombinant chimeric antibodies. International immunopharmacology. 2019 Aug 1;73:575-80.

[33]. Briney B, Inderbitzin A, Joyce C, Burton DR. Commonality despite exceptional diversity in the baseline human antibody repertoire. Nature. 2019 Feb;566(7744):393-7.

[34]. Dammes N, Peer D. Monoclonal antibody-based molecular imaging strategies and theranostic opportunities. Theranostics. 2020;10(2):938.

[35]. Madelain V, Nguyen TH, Olivo A, De Lamballerie X, Guedj J, Taburet AM, Mentré F. Ebola virus infection: review of the pharmacokinetic and pharmacodynamic properties of drugs considered for testing in human efficacy trials. Clinical pharmacokinetics. 2016 Aug;55(8):907-23.

[36]. Behzadi MA, Leyva-Grado VH. Overview of current therapeutics and novel candidates against influenza, respiratory syncytial virus, and Middle East respiratory syndrome coronavirus infections. Frontiers in microbiology. 2019 Jun 19;10:1327.

[37]. Pimpitak U, Putong S, Komolpis K, Petsom A, Palaga T. Development of a monoclonal antibody-based enzyme-linked immunosorbent assay for detection of the furaltadone metabolite, AMOZ, in fortified shrimp samples. Food Chemistry. 2009 Oct 1;116(3):785-91.

[38]. Hage DS, Matsuda R. Affinity chromatography: a historical perspective. Affinity chromatography. 2015:1-9.

[39]. Marhelava K, Pilch Z, Bajor M, Graczyk-Jarzynka A, Zagozdzon R. Targeting negative and positive immune checkpoints with monoclonal antibodies in therapy of cancer. Cancers. 2019 Nov 8;11(11):1756.

[40]. Zahavi D, Weiner L. Monoclonal antibodies in cancer therapy. Antibodies. 2020 Jul 20;9(3):34.

[41]. Matsueda S, Graham DY. Immunotherapy in gastric cancer. World journal of gastroenterology: WJG. 2014 Feb 2;20(7):1657.

[42]. Wink DA, Hines HB, Cheng RY, Switzer CH, Flores-Santana W, Vitek MP, Ridnour LA, Colton CA. Nitric oxide and redox mechanisms in the immune response. Journal of leukocyte biology. 2011 Jun;89(6):873-91.

[43]. Weiner GJ. Building better monoclonal antibody-based therapeutics. Nature Reviews Cancer. 2015 Jun;15(6):361-70.

ISSN *(Online)*: XXXX-XXXX

[44]. Chari RV, Miller ML, Widdison WC. Antibody–drug conjugates: an emerging concept in cancer therapy. Angewandte Chemie International Edition. 2014 Apr 7;53(15):3796-827.

[45]. Willrich MA, Murray DL, Snyder MR. Tumor necrosis factor inhibitors: clinical utility in autoimmune diseases. Translational Research. 2015 Feb 1;165(2):270-82.

[46]. Cáceres MC, Guerrero-Martín J, Pérez-Civantos D, Palomo-López P, Delgado-Mingorance JI, Durán-Gómez N. The importance of early identification of infusion-related reactions to monoclonal antibodies. Therapeutics and Clinical Risk Management. 2019;15:965.

[47]. Brédart A, Bodson S, Le Tourneau C, Flahault C, Bonnetain F, Beaudeau A, Coquan E, Dolbeault S, Paoletti X. Patients' perceived tolerance of side effects in phase I cancer clinical trials: A qualitative study. European journal of cancer care. 2017 Nov;26(6):e12596.

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