# Monoclonal Antibodies : Structure & Applications : A Review

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**ABSTRACT : In the last three decades, more than 20 therapeutic Monoclonal Antibodies targeting a range of antigens (Working through a variety of mechanisms) have been approved for treatment of serious diseases. The first to be approved were murine antibodies, followed by humanized molecules with superior efficacy, safety and tolerance. Most of Monoclonal Antibodies have been produced by different methods using the various animals and hybridoma technology. In addition to this, the in Vivo and in Vitro manufacture of Monoclonal Antibodies is carried out to ensure the finished product of pharmaceutical quality. These Monoclonal Antibodies can be used to treat the various types of diseases including the cancer.**

**KEYWORDS : Monoclonal, Superior Epicacy, Cancer.**

## INTRODUCTION :

Monoclonal Antibodies (MAbs) are:

- Antibodies of exceptional purity and specificity
- Able to recognize and bind to a specific antigen
- Components of the immune system

Antibodies (immunoglobulins) are glycoprotein molecules present in serum. They are made by foreign immunogen-stimulated B-cells and secreted into the blood to react with antigen present on soluble or cell surface immunogen. They are produced in response to antigens, which are either proteins or polysaccharide molecules that are foreign to the body. They may be a component of organism such as bacteria, virus or environmental agents that enter the organism accidentally. B-lymphocytes secreting antibodies form a plasma cells. Antibodies are produced when body comes in contact with foreign particle. Each antibody produced is specific to that particular antigen which has stimulated its production. The elicited antibody reacts with the specific antigen by binding to it. Antibodies induce different immunological effects such as neutralization of pathogens either by forming antibody-antigen complexes or by involving other immune cells. immortalized cell cultures of antibodies producing B-cells can be propagated outside of living organism to maintain infinite supply. Antibodies constructed by this method are directed against single epitopes and are known as monoclonal antibodies (MAbs).

Antibodies are the laboratory-produced substance that can locate and bind to cancer cells wherever they are in the body. Many monoclonal antibodies are used in cancer detection or therapy; each one recognizes a different protein on certain cancer cells. Monoclonal antibodies can be used alone, or they can be used to deliver drugs, toxins, or radioactive material directly to a tumour, Cancer. Monoclonal antibodies (MAb) are antibodies that are identical because they were produced by one type of immune cell and are all clones of a single parent cell. Antibodies that are derived from only one cell and recognize only one portion of a molecule. Because monoclonal antibodies are highly specific, they can be used to diagnose disease or to protect against disease-causing organisms. MAbs are genetically engineered and custom-designed to bind specifically to a particular antigen and destroy it. When used as a therapeutic agent, monoclonal antibodies generally work quickly, for a significant amount of time, with minimal side effects. These are manufactured compounds specifically designed to find targets on cancer cells for diagnostic or treatment purposes. Rituxan and Herceptin are monoclonal antibodies used in the treatment of lymphoma and breast cancer, respectively.

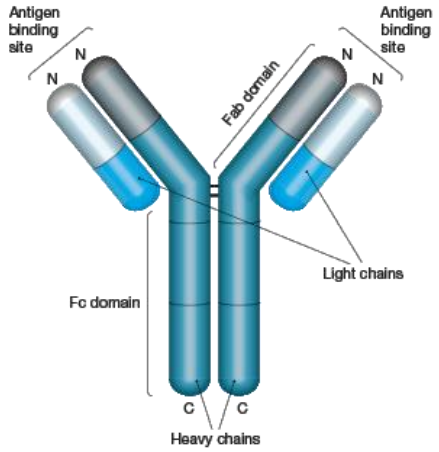
Antibodies are composed of two identical heavy and two identical light chains. Antibodies may be classified as IgA, IgG, IgM, IgE, and IgD. The antibodies produced in response to antigen are heterogeneous in nature because of multiple epitopes on the antigen that could induce proliferation and differentiation of a variety of B cell clones. Removal of antibodies with unwanted specification from a polyclonal antibody preparation is a time-consuming task involving repeated adsorption techniques. Antibodies or immunoglobulins are a crucial component of the immune system, circulating in the blood and lymphatic system, and binding to foreign antigens expressed on cells.

Antibodies have two very useful characteristics. First, they are extremely specific; that is, each antibody binds to and attacks one particular antigen. Second, some antibodies, once activated by the occurrence of a disease, continue to confer resistance against that disease; classic examples are the antibodies to the childhood diseases chickenpox and measles. The second characteristic of antibodies makes it possible to develop vaccines. A vaccine is a preparation of killed or weakened bacteria or viruses that, when introduced into the body, stimulates the production of antibodies against the antigens it contains. It is the first trait of antibodies, their specificity that makes monoclonal antibody technology so valuable. Not only can antibodies be used therapeutically, to protect against disease; they can also help to diagnose a wide variety of illnesses, and can detect the presence of drugs, viral and bacterial products, and other unusual or abnormal substances in the blood.

Given such a diversity of uses for these disease-fighting substances, their production in pure quantities has long been the focus of scientific investigation. The conventional method was to inject a laboratory animal with an antigen and then, after antibodies had been formed, collect those antibodies from the blood serum (antibody-containing blood serum is called antiserum). There are two problems with this method: It yields antiserum that contains undesired substances, and it provides a very small amount of usable antibody. Monoclonal antibody technology allows us to produce large amounts of pure antibodies in the following way: We

can obtain cells that produce antibodies naturally; we also have available a class of cells that can grow continually in cell culture. If we form a hybrid that combines the characteristic of "immortality" with the ability to produce the desired substance, we would have, in effect, a factory to produce antibodies that worked around the clock. In monoclonal antibody technology, tumour cells that can replicate endlessly are fused with mammalian cells that produce an antibody. The result of this cell fusion is a "hybridoma," which will continually produce from only one type of cell, the hybridoma cell; antibodies produced by conventional methods, on the other hand, are derived from preparations antibodies. These antibodies are called monoclonal because they come \ containing many kinds of cells, and hence are called polyclonal antibodies. Because selected hybrid cells produce only one specific antibody, they are more pure than the polyclonal antibodies produced by conventional techniques. They are potentially more effective than conventional drugs in fighting disease, since drugs attack not only the foreign substance but the body's own cells as well, sometimes producing undesirable side effects such as nausea and allergic reactions. Monoclonal antibodies attack the target molecule and only the target molecule, with no or greatly diminished side effects.

## STRUCTURE OF ANTIBODY




Antibodies are immune system-related proteins called immunoglobulins. Each antibody consists of four polypeptides two heavy chains and two light chains joined to form a "Y" shaped molecule.

The amino acid sequence in the tips of the "Y" varies greatly among different antibodies. This variable region, composed of 110-130 amino acids, give the antibody its specificity for binding antigen. The variable region includes the ends of the light and heavy chains. Treating the antibody with a protease can cleave this region, producing Fab or fragment antigen binding that include the variable ends of an antibody. Material used for the studies shown below originated from Fab.

The constant region determines the mechanism used to destroy antigen. Antibodies are divided into five major classes, IgM, IgG, IgA, IgD, and IgE, based on their constant region structure and immune function.

The variable region is further subdivided into hypervariable (HV) and framework (FR) regions. Hypervariable regions have a high ratio of different amino acids in a given position, relative to the most common amino acid in that position. Within light and heavy chains, three hypervariable regions exist - HV 1, 2 and 3. Four FR regions, which have more stable amino acids sequences, separate the HV regions.

The HV regions directly contact a portion of the antigen's surface. For this reason, HV regions are also sometimes referred to as complementarity determining regions, or CDRs. The FR regions form a beta-sheet structure, which serves as a scaffold to hold the HV regions in position to contact antigen.°

The Fc fragment is composed of the carboxyterminal portion of the H chain. It doesnot possess antigen combining activity but determines the biological properties of the immunoglobulin molecule such as complement fixation, placental transfer, skin fixation and secretion into body fluids. Each heavy or light chain has variable (V) region at the aminoterminal end and a constant (C) region at the carboxyl terminal end. The area of heavy chain between CH1 and CH2 is the hinge region. The polypeptide chains are held by disulfide bonds. The folding produces compact globular regions known as domains. The light chains have only two domains, one variable (VL) and one constant (CL). There are four domains in each heavy chain of IgG, IgA and IgD, one in variable regions (VH) and three in constant region (CH1, CH2, CH3). IgM and IgE have fourth constant region (CH4).

## MECHANISM OF ACTION :

Monoclonal antibodies achieve their therapeutic effect through various mechanisms. They can have direct effects in producing apoptosis or programmed cell death. They can block growth factor receptors, effectively arresting proliferation of tumor cells. In cells that express monoclonal antibodies, they can bring about anti-idiotype antibody formation. Indirect effects include recruiting cells that have cytotoxicity, such as monocytes and macrophages. This type of antibody-mediated cell kill is called antibody-dependent cell mediated cytotoxicity (ADCC). Monoclonal antibodies also bind complement, leading to direct cell toxicity, known as complement dependent cytotoxicity (CDC). Rituximab is an lgG monoclonal antibody, and has an Fc receptor. The Fc fragment of the monoclonal antibody binds the Fc receptors found on monocytes, macrophages, and
natural killer cells. These cells in turn engulf the bound tumor cell and destroy it. Natural killer cells secrete cytokines that lead to cell death, and they also recruit B cells.

## ADVANTAGES OF MONOCLONAL ANTIBODIES :

Monoclonal antibodies are of exceptionally high quality ; represents homogeneous State. Conventional antiserums possess certain disadvantages, for e.g. they consist of a mixture of antibodies and a major portion of the sample contain irrelevant immunoglobulin.The advantages of MAbs over conventional antisera are given below:

1. Pure one molecular species only.
2. Specificity for one antigenic determinant.
3. Cross reaction means shared determinants.
4. Antiserum titer values obtained are very high.
5. Antibodies with high avidity can be produced.
6. Immune immunogen can be used.
7. 1n vitro or in vivo productions are possible with high production rate
8. Maintenance of farm/animals is not required for immunization and bleeding.
9. Immortal cell lines.
10. Antiserum having identical antibody with an identical specificity and constant property can be obtained worldwide.
11. High reproducibility with respect to specificity and avidity.
12. Production of cell lines to individual components of a mixture is possible.
13. Radiolabelling and fluorescent conjugation or enzymes marking of MAbs are easy.

## Limitations of Monoclonal Antibodies:

1.Precipitate formation

In general, MAbs do not form a precipitate in a standard double-immune diffusion method. This leads to the necessity to produce a lattice framework for precipitation in test like ouchterlony assay.

2. Complement fixation

Conventional antiserum Possesses better compliment fixing capabilities than do MAbs. IgM and IgG are the classes of antibody, which fix compliment easily. Among them IgM is the best.MAbs produced via cell fusion contain mainly IgG class.Yet ,they show poor complement fixing capabilities.

3. Antibody specificity

Production of MAbs is against a single antigenic determinant principally incorporates high level of selective specificity in to the MAbs thus rendering them incapable to distinguish between a group of different molecules, cells bearing the chemical structure or determinants except one against which they are raised. A conventional antiserum contains antibodies to all the determinants on an antigen and can be precisely used as ‘fingerprint’ identification for that antigen. However, complete cross section can occur for MAbs and may pose problems in assay where one molecular species amongst several very similar molecular entities is to be detected.

4. Antibody avidity

The energy of binding to an antigen is ’precise’ in case of MAbs where it is ‘average’ in case of conventional antiserum. The high antibody avidity of a MAb has advantages as well as disadvantages. It is advantages in case of immunoassay methods and undesirable for Purification process (affinity chromatography).

## Applications of Monoclonal Antibodies:

Monoclonal antibodies with specificity and high purity have a wide range of applications, which can be broadly categorized as follows:

1. Diagnostic applications
2. Therapeutic applications
3. Clinical applications
4. Miscellaneous applications.

1. Diagnostic applications of Monoclonal Antibodies

a)Diagnostic reagents: Monoclonal antibody based reagents include products for detecting pregnancy, diagnosing infectious protozoan, bacterial and viral pathogens, detecting heart damage, detecting diabetes and detecting tumor cells.

b)Diagnostic imaging: This is also known as immunoscintography using a planar gamma Camera to detect the two dimensional distribution in the body of gammaemitting radioisotopes conjugated to MAbs.

c)Cardiovascular Disease:

Myocardial Infarction: The antimyosin Mab is specific for human myosin and binds to intracellular myosin exposed as a consequence of myocardial necrosis. Myosin is the antimyosin containing Mab product. It consists of a kit containing 0.5 mg of santimyosin Fab conjugated with the chelator DTPA (diethylene triaminepenta acetic acid). Imaging is performed after 24 to 48 h using either a planar gamma camera OF single photon emission computed topography (SPECT). The product has shown a high degree of sensitivity for detecting infarction and specificity excluding a recent ischemic event in patients with chest pain syndrome. Indium antimyosin is able to detect the location and extent of necrotic heart tissue and useful in diagnosis of heart attack and in the early risk stratification of patients demonstrated to have myocardial damage.

Deep vein thrombosis: The approaches have been divided into use of labeled Mabs directed against platelets, which are components of actively developing thrombi, and against fibrin.""In labeled Fab-DTPA showed a sensitivity of 86 to 100 % in directing thrombi in the extremities of the patients. Certain membrane proteins are present on the tumor cells but are absent from the normal cells. Monoclonal antibodies specific for these tumors associated membrane proteins can be produced and used in tumor detection and imaging. Production of Mabs specific for these membrane proteins involves screening of large numbers of hybridomas to identify clones secreting antibody specific for the tumor associated antigens.

ABD and rare blood groups: Anti-ABD, anti (rare blood groups) and anti-HLA monoclonal antibodies Produced by immunizing mouse with human cells are practically useful in blood Grouping. Monoclonal antibodies have been produced against group A ‘erythrocytes. Monoclonal antibodies against membrane glycoproteins of the human erythrocytes (glycophorin A) at different sites as well as antibodies which bind to other erythrocyte surface molecules have been developed. Thus, it is possible to use these antibodies to detect similar determinants on other cells as well as to isolate and purify the cell surface molecules.

Cell separation Cell sub-populations belonging to the liver, lung, kidney, central nervous system, sperm cells, macrophage and monocytes can be separated using labeled antibodies and reisolating as 'pure' cells. Separation can be achieved using FITC techniques, where antibody will bind to only one cell sub-population and then separation is achieved using fluorescent-activated cell sorter (FACS).

Location of Primary or Metastatic Tumors Primary and metastatic tumors can be located in patients by using radiolabelled monoclonal antibodies specific to tumor associated membrane proteins. monoclonal antibodies specific to breast cancer cells labelled with iodine 131 when introduced into blood, detects tumor spread to regional lymph nodes. The radiolebelled monoclonal antibody detects breast cancer metastases that otherwise Stands to be undetectable by other scanning techniques. ,

2)Therapeutic applications:

Mabs when used intact however free i.e. without attachment to cytotoxic agents have therapeutic activity in certain cases. By binding to an antigen, its biological effect may be neutralized or activity of growth factor receptor may be blocked by Mab.

a)Monoclonal Antibodies in diagnosis, screening and therapy: Monoclonal antibodies or specific antibodies are now an essential tool of much biomedical research and are of great commercial and medical value. For instance, ABO blood groups could be earlier identified with the help of humansera Carrying antibodies of known specificity. These human sera in U.K. have been replaced by Monoclonal antibodies produced by hybridomas for identification ABO blood groups. Besides these, the uses of monoclonals are described.

i) Diagnosis (including ELISA test for detection of viruses and imaging)

ii) Immunopurification

iii) Therapy

In diagnosis, pregnancy can be detected by assaying of hormones with monoclonals. Immunopurification involves separation of one substance from a mixture of very similar molecules. For instance, individual interferons could be purified using Monoclonal antibodies and could be used for inactivating T lumphocytes responsible for rejection of organ transplants. Removal of tumour cells from bone marrow is another therapeutic use of Monoclonal antibodies.

For therapeutic uses, Monoclonal antibodies are so designed that they will neutralize the reaction or response by one defined antigen, but still preserve the reaction of all other antigens. Several antigen of T cell receptor complex, including CD3, CD4, and CD8 have been targets of specific antibodies for therapy. Most widely used monoclonal antibody is OKT3 for treatment of acute renal allograft rejections.

Monoclonal antibodies have also been used for treatment of patients with

1) Malignant leukemic cells,

2) B cell lymphomas, and

3) A variety of allograft rejections after transplantation.

'Monoclonal antibodies-cytotoxic agent conjugates' called immunotoxins designed as Carriers of cytotoxic substances to the target cells.

Radiolabelled Monoclonal antibodies have been developed for delivery of a cytotoxic effector to target cells and for radioimaging. For therapy, radiolabelled antibodies kill cells from a distance and thus can also kill cells adjacent to antigen expressing cells. Further, the radiolabelled antibody need not be internalized to kill the tumour cells. For the purpose both B emitting and a emitting radionuclides have been used for patients with hepatoma, HTLV-1 (human T cell leukemia/lymphoma virus-1), ATL (adult T-cell leukemia), a variety of allografts, etc. Radioimmunodetection is widely used. (Fab') 2 and Fab fragments are preferred for imaging, because both targeting and blood clearance are rapid. Tumours as small as 0.5 cm, which are missed by other radiological methods, can be detected by radiolabelled antibodies or Fab fragments.

i) Monoclonal Antibodies in vaccine production

Antibodies have also been used to immunize against certain disease in humans and cattles. Monoclonal antibodies that inhibit the in vitro multiplication of plasmodium, and the antigametocyte antibodies that inactive male gametes have been developed. Monoclonal antibodies that destroy merozoite infected red blood cells have also been developed now such antibodies may prove useful as vaccines.

ii) Monoclonal Antibodies as enzymes (abzymes):

The antibodies may often bind specific ligands (haptens), but may not carry out chemical reactions. By modifying these ligands, antibodies may be generated that will catalyse specific reactions just like enzymes. Production of abzymes is based on following two principles:

1.Enzymes work by binding the transition state of a reactant better than the ground state

2) Antibodies, which bind to specific small molecules, can be produced by coupling this small molecule to a protein barrier and using this protein for immunizing experimental animals. If this small molecule is a transition state analogue, then the antibodies that were produced to bind to this molecule will function as enzyme towards the substrate of this reaction.

iv) Monoclonal Antibodies for cytogenetic analysis: The technique of ELISA (enzyme linked immunosorbant assay), utilizing Monoclonal antibodies has been used for cytogenetic analysis in wheat. Monoclonal antibodies specific to chromosomes 1B, 6A and 6D are already available and those for other chromosomes will become available in future, due to proteins coded by chromosomes of all the homoeologous groups. Nullisomic and monosomic for the chromosome 1B and the absence of 1BS in 1BL/1RS wheat-rye translocation could be ascertained using the Monoclonal antibody P24B, which is specific for 1BS gliadins.'"

3)Clinical Applications of Monoclonal Antibodies:

i) Haematologic malignancies: There are a number of antigens and corresponding monoclonal antibodies for the treatment of B cell malignancies. One of the most popular target antigens is CD20, found on B cell malignancies. The CD52 antigen is targeted by the monoclonal antibody alemtuzumab, which is indicated for treatment of chronic lymphocytic leukemia. The CD22 is targeted by a number of antibodies, and has recently demonstrated efficacy combined with toxin in chemotherapy-resistant hairy cell leukemia.

Two new monoclonal antibodies targeting CD20, tositumomab and ibritumomab, have been submitted to the Food and Drug Administration (FDA). These antibodies are conjugated with radioisotopes.

The first monoclonal antibody to receive FDA approval was rituximab. Rituximab Is a chimeric unconjugated monoclonal antibody directed at the CD20 antigen, a signature B cell antigen. CD20 is thought to act as a calcium channel as well, given the great structural homology between the CD20 protein and the calcium channels. When CD20 was introduced into cell lines by transfection, an increase in intracellular calcium was observed within the transfected cells.

Calcium chelators blocked apoptosis induced by CD20 stimulation by monoclonal antibodies.

When monoclonal antibodies attach and particularly cross-link CD20 antigen, an increase in intracellular calcium is observed. This increase appears to activate the SER family of tyrosine kinases, resulting in further phosphorylation of the CD20 inner cytoplasmic chain and also phospholipase C-gamma. At the same time there is an upregulation of C-myc and may messenger ribonucleic acid (RNA), an increase in adhesion molecule expression and an upregulation of MHC class II proteins. The ultimate result is caspase 3 activation, causing cell apoptosis.

The monoclonal antibody rituximab was designed specifically to target CD20. Rituximab is predominantly human (95%). The variable light and heavy Chain portion of rituximab is murine, but the remainder is humanized so the formation of human anti-mouse antibody is not significant. Rituximab is thought to induce cell apoptosis by inducing calcium influx, releasing caspase activity. In addition, evidence of indirect effects through ADCC and CDC has been observed. Rituximab is indicated for treatment of low-grade lymphomas 'refractory to conventional chemotherapy.

Rituximab has been combined with conventional chemotherapy for patients with intermediate grade or diffuse large cell non-Hodgkin lymphoma. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) is standard therapy for this type and stage of disease.

The most frequent adverse events associated with rituximab were fever and chills, primarily during the first infusion. The investigators concluded that rituximab did not appear to increase the toxicity of therapy.

ii) Solid tumors:

Compared to hematologic malignancies, solid tumors do not have as many specific targets for monoclonal antibodies that are not cross-reactive with antigens on normal tissues. Two significant monoclonal antibodies have been used in solid tumors: edrecolomab and trastuzumab.

Edrecolomab targets the 17-1A antigen seen in colon and rectal cancer, and has been approved for use in Europe for these indications. Its antitumor effects are mediated through ADCC, CDC, and the induction of an anti-idiotypic network. In an initial study of 189 patients with resected stage Il colorectal cancer, treatment with edrecolomab reduced the relative risk of mortality by 32% compared with observation alone ($P<0.01$). Edrecolomab is undergoing investigation in two large phase Ill trials in patients with stage III colon cancer, either as monotherapy or in combination with fluorouracil-based chemotherapy.

In the US, the most commonly used monoclonal antibody for the treatment of solid tumors is trastuzumab, which targets the HER-2/neu antigen. This antigen is seen on 25% to 35% of breast cancers. Trastuzumab is thought for work in a variety of ways: downregulation of HER-2 receptor expression, Inhibition of proliferation of human tumor cells that overexpress HER-2 protein, Enhancing immune recruitment and ADCC against tumor cells that overexpress NER-2 protein, and downregulation of angiogenesis factors. This last mechanism May be very important in terms of metastatic disease.

In phase | and Il trials of patients with metastatic breast cancer, treatment with a combination of trastuzumab and cisplatin resulted in prolongation of survival and higher response rates than that seen with cisplatin alone.

As first-line monotherapy, trastuzumab has demonstrated efficacy and safety in patients with metastatic breast cancer. This study included 114 women with HER-2-overexpressing metastatic breast cancer with no prior chemotherapy. Patients were randomized to receive a loading dose of trastuzumab 4 mg/kg followed by 2 mg/kg weekly, or an 8 mg/kg loading dose followed by 4 mg/kg weekly. Primary endpoint was overall response rate. Secondary endpoints were disease relapse, time to tumor progression, and overall survival. First-line monotherapy with trastuzumab appears to have better overall response. However, median time to disease progression remains disappointingly short. The incidence of cardiac toxicity cannot be minimized, particularly in patients with prior anthracycline therapy or cardiac disease. These patients had a 10% incidence of severe myocardial toxicity and one death from ventricular arrhythmia. Still, these data suggest the possibility of significant response rates, including improvement in overall survival.

While early reports on the use of monoclonal antibodies may have been overenthusiastic, the results of these studies show there is still cause for cautious Optimism as we go forward. Cure may yet elude us, but stable disease is an attainable, highly desirable goal.

4)Miscellaneous Applications:

i) Application of monoclonal antibodies to tumor diagnosis and therapy:

Monoclonal antibodies prepared by somatic cell hybridization techniques are ideal tools for the discrimination of cellular antigens and are beginning to reveal qualitative and quantitative differences in the antigenic composition of normal and malignant cells. Because these reagents are homogeneous in Nature, recognize specific antigenic determinants, and can be mass produced, monoclonal antibodies have important clinical applications in the detection and early diagnosis of cancer, in staging procedures, and in therapeutic trials. In addition, many of these reagents have the capacity to distinguish between

different types of human tumors and will be useful in the refinement of histopathologic classification schema. Monoclonal antibodies with varying degrees of specificity have already been produced against a variety of human and animal tumors. In this review, the technical aspects of monoclonal antibody production and the clinical and biologic application of these reagents are highlighted in order to demonstrate the potential of monoclonal antibodies as tools for the immunodiagnosis and therapy of malignant disease. Monoclonal antibodies can also be used in detection of tumors. Primary and metastatic tumors can be located in patients by using radiolabelled Monoclonal antibodies specific to tumor associated membrane proteins. Monoclonal antibodies specific to breast cancer cells labeled with ‘'*'l when introduced into blood, detects tumor spread to regional lymph nodes.

Investigations in diagnostic imaging of all major types of solid tumors including melanoma, colorectal carcinoma, ovarian carcinoma, sarcoma, lung carcinoma have been conducted the tumor markers used in diagnostic imaging using Mab.

ii) Anti-cancer-related human galactosyltransferase monoclonal antibody:

A monoclonal antibody which may be used as a diagnostic reagent of cancer is disclosed. The monoclonal antibody of the present invention Specifically reacts with a cancer-related human galactosyltransferase having a molecular weight of about 50,000 determined by SDS-polyacrylamide gel electrophoresis under reduced condition, the galactosyltransferase having a reactivity with MAb4880 (FERM BP-1758) under native conditions, a part of Which self-associates, the reactivity of the galactosyltransferase with MAb4880 and the degree of self-association of the galactosyltransferase being promoted when the galactosyltransferase is heated under reducing Conditions so that a part of the galactosyltransferase being detected in a fraction of a molecular weight of not less than 200,000 in gel permeation chromatography.

Herceptin: the first humanized monoclonal antibody approved for the treatment of breast cancer:

In 25 to30% of women with aggressive metastatic breast cancer, there is a genetic alteration in the HER2 gene that produces an increased amount of human epidermal growth factor receptor 2 proteins on the surface of thr tumour. The humanized anti-HER2 monoclonal antibody (Herceptin) contains human framework regions and mouse CDRs and is produced commercially using mammalian (CHO) cells in suspension culture as the host for the expression of the antibody. Following humanization, Herceptin binds to thr HER2 protein, indicating that the high level of specificity for the substrate has been maintained through the process of humanization.

Herceptin was most effective when administered with some of the chemicals currently in use for the treatment of breast cancer, provided that the breast cancer was at a later stage of development. It is typically administered intravenously over a period of 30 minutes. Following clinical trials, Herceptin was deemed to be an effective treatment for patients with breast cancer whose tumors overexpress the HER2 protein and who have either previously received chemotherapy or will receive chemotherapy at the same time as the monoclonal antibody.

Monoclonal antibodies for cancer treatment

One possible treatment for cancer involves monoclonal antibodies that bind only to cancer cell-specific antigens and induce an immunological response against the target cancer cell. Such MPAb could also be modified for delivery of a toxin, radioisotope, cytokine or other active conjugate; it is also possible to design bispecific antibodies that can bind with their Fab regions both to target antigen and to a conjugate or effector cell. In fact, every intact antibody can bind to cell receptors or other proteins with its Fc region. The illustration below shows all these possibilities

| TYPE | APPLICATION | MECHNISM | MODE |
|---|---|---|---|
| Infliximab | Rheumatoid arthritis | InhibitsTNF-a | Chimeric |
| Baciliximab | Acute rejection of kidney transplants | Inhibits IL-2 on activated T cells | Chimeric |
| Abciximab | Prevent coagulation in coronary angioplasty | Inhibits the receptor Gpllp/llla on plates | Chimeric |
| Daclizumab | Acute rejection of kidney transplants | Inhibits IL-2 on activated T cells | Humanized |
| Gemtuzumab | Relapsed acute myeloid leukaemi | Targets an antigen on leukemia cells | Humanized |
| Almentuzumab | B cell leukemia | Targets an antigen CD52 on T-and B-lymphocytes | Humanized |
| Rituximab | Non-Hodgkin's lymphoma | Targets phosphoprotein CD20 on B lymphocytes | Humanized |
| Palivizumab | RSV infections in children | Inhibits an RSV protein | Humanized |
| Etanercept | Rheumatoid arthritis | Contains TNF receptor | - |

CONCLUSION-: In order to play their physiological roles, antibodies are required to exhibit exquisite specificity and high affinity for foreign antigens. These properties have both fascinated and inspired chemists to better understand the unique properties of these immunological proteins. A variety of techniques have been utilized to study antibody-binding phenomena including immunoprecipitation, X-ray crystallography, and fluorescence spectroscopy. Future studies of the binding properties of antibodies will no doubt provide more clues about the complex operation of the immune system.

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