Journal of Animal Sciences and Livestock Production

ISSN: 2577-0594

Open Access Review Article

Review on Diagnostic and Therapeutic Role of Monoclonal Antibodies

Isayas Asefa Kebede*

Department of Veterinary, Wolaita Sodo University, Wolaita Sodo, Ethiopia

ABSTRACT

Monoclonal antibodies are antibodies which have a single, selected specificity and which are continuously secreted by immortalized hybridoma cells. The monoclonal antibodies being directed against single epitopes are homogeneous, highly specific and can be produced in unlimited quantities. In animal disease diagnosis, they are very useful for identification and antigenic characterization of pathogens. Monoclonal antibodies are effective targeted therapeutic agents. The high specificity of the antibodies makes them ideal to reach their intended target and thus is useful to treat a variety of disease states. Being biological agents, the moAbs have their own profile of side effects like hypersensitivity, development of neutralizing antibodies, immune suppressions leading to enhanced possibilities of opportunistic infections.

Keywords: Antibodies; Diagnostic; Monoclonal antibodies; Specificity; Therapeutics

INTRODUCTION

Monoclonal antibodies (mAb or moAb) are mono specific antibodies which are made from identical immune cells that are all clones of a unique parent cell. Monoclonal antibodies have monovalent affinity, in that they bind to the same epitope.

Polyclonal antibodies mixtures contain different antibodies developed in the blood of immunized animals from different cell types. As most antigens bear multiple epitopes, they can stimulate the proliferation and differentiation of a variety of B-cell clones. Thus, a heterogeneous pool of serum antibodies can be produced with specificity for particular epitope(s) of the antigen.

Monoclonal antibody production using hybridoma technology was first discovered by Georges Kohler and Cesar Milstein. One unique advantage of hybridoma production is that mixture of antigens can be used to generate specific antibodies. This also enables screening of antibodies of choice from a mixture of antibody population generated by purified antigen where single cell clones can be isolated.

Monoclonal antibodies are important reagents used in biomedical research, microbiological research, in diagnosis of Hepatitis, AIDS, Influenza, Herpes simplex, and in treatment of such diseases as infections and cancer [1-6].

Monoclonal antibodies have been revealed to be extremely useful reagents, because of their high specificity, affinity, and robust structure. Moreover, because of their modular structure they can be easily engineered through molecular biology technologies; this is extremely useful in case of a therapeutic use in humans. One of the best examples in cancer therapy is Trastuzumab (Herceptin®: Genentech Inc.), which was approved by the FDA in 2006 for patients with invasive breast cancers over expressing the tyrosine kinase orphan receptor HER2, generally in a combined therapy with

Received:	24-January-2023	**Manuscript No:**	IPJASLP-23-15555
Editor assigned:	27-January-2023	**PreQC No:**	IPJASLP-23-15555 (PQ)
Reviewed:	08-February-2023	**QC No:**	IPJASLP-23-15555
Revised:	24-March-2023	**Manuscript No:**	IPJASLP-23-15555 (R)
Published:	31-March-2023	**DOI:**	10.36648/2577-0594.7.2.46

Corresponding author: Isayas Asefa Kebede, Department of Veterinary, Wolaita Sodo University, Wolaita Sodo, Ethiopia; E-mail: byisayas@gmail.com

Citation: Kebede IA (2023) Review on Diagnostic and Therapeutic Role of Monoclonal Antibodies. J Anim Sci Livest Prod. 7:46.

chemotherapeutics. Therefore, the objectives of this seminar paper are:

- To highlight general properties of monoclonal antibody.
- To give an overview diagnostic and therapeutic roles of monoclonal antibody.

LITERATURE REVIEW

General Properties of Monoclonal Antibody

The properties of mAb that include high specificity, purity, and ability to enhance host immune system make immunoglobulins attractive candidates for the next generation of therapeutics and the usefulness of monoclonal antibodies stems from three characteristics they are their specificity of binding, their homogeneity, and their ability to be produced in unlimited quantities. The specificity of an antibody refers to its ability to recognize a specific epitope in the presence of other epitopes. An antibody with high specificity would result in less cross reactivity. While mAb development is primarily focused on the candidates with the greatest medicinal potential, one should be cautious that the mAbs categorized as non-protective on single antibody screen, which comprise the majority of naturally-produced antibodies could be false negative results. In other words, it is possible that those antibodies are biologically active when they function in combination with other antibodies. Combination testing could reveal new properties of these so called non-protective or indifferent antibodies with the caveat that evaluating antibodies in combinations would increase considerable cost and complexity to any screen for useful mAbs.

The principal advantages of mAbs are their homogeneity and consistency. The mono specificity provided by mAbs is useful in evaluating changes in molecular conformation, protein-protein interactions, and phosphorylation states, and in identifying single members of protein families. It also allows for the potential of structural analysis (e.g., x-ray crystallography or gene sequencing) to be determined for the antibody on a molecular level. However, the mono specificity of mAbs may also limit their usefulness. Small changes in the structure of an epitope (e.g., as a consequence of genetic polymorphism, glycosylation, and denaturation) can markedly affect the function of a mAb. For that reason, mAbs should be generated to the state of the antigen to which it will eventually need to bind. In contrast, because PAbs are heterogeneous and recognize a host of antigenic epitopes, the effect of change on a single or small number of epitopes is less likely to be significant. PAbs are also more stable over a broad pH and salt concentration, whereas mAbs can be highly susceptible to small changes in both. Another key advantage of mAbs is that once the desired hybridoma has been generated, mAbs can be generated as a constant and renewable resource. In contrast, PAbs generated to the same antigen using multiple animals will differ among immunized animals, and their avidity may change as they are harvested over time. The quantity of PAbs obtained is limited by the size of the animal and its lifespan.

Monoclonal antibodies generally exhibit exquisite specificity for the target antigen. The binding site on the antigen called the epitope, can be linear or conformational, and may comprise continuous or discontinuous amino acid sequences. The epitope is the primary determinant of the antibody's modulatory functions and depending on the epitope, the antibody may exert antagonist or agonist effect, or it may be non-modulatory. The epitope may also influence the antibody's ability to induce Antibody Dependent Cell Mediated Cytotoxicity (ADCC) and Complement Dependent Cytotoxicity (CDC). MAbs exert their pharmacological effects *via* multiple mechanisms that include direct modulation of the target antigen, CDC, ADCC, and delivery of a radio nucleotide or immune toxins to target cells [7-11].

Production of Monoclonal Antibodies

The production of monoclonal antibodies was invented by Cesar Milstein and Georges JF. Kohler in 1975. They shared the Nobel prize of 1984 for medicine and physiology with Niels Kaj Jerne, who made other contributions to immunology.

The production of monoclonal antibodies allows the isolation of reagents with a unique, chosen specificity. Because all of the antibodies produced by descendants of one hybridoma cell are identical, monoclonal antibodies are powerful reagents for testing for the presence of a desired epitope. Hybridoma cell lines also provide an unlimited supply of antibodies. Even the most farsighted researchers have found that large supplies of valuable antisera eventually run out. Hybridoma overcomes these difficulties. In addition, one unique advantage of hybridoma production is that impure antigens can be used to produce specific antibodies. Because hybridoma is single cell cloned before use, monospecific antibodies can be produced after immunizations with complex mixtures of antigens.

Generation of Monoclonal Antibodies using the Hybridoma Technique

Monoclonal antibodies are monovalent antibodies which bind to the same epitope and are produced from a single B-lymphocyte clone. The generation of hybridoma involves immunizing a certain species against a specific epitope on an antigen and obtaining the B-lymphocytes from the spleen of the animal. The B-lymphocytes are then fused (by chemical or virus induced methods) with an immortal myeloma cell line lacking the Hypoxanthine Guanine Phosphoribosyl Transferase (*HGPRT*) gene and not containing any other immunoglobulin producing cells. These hybridoma cells are then cultured *in vitro* in selective medium (*i.e.,* medium containing hypoxanthine-aminopterin-thymidine) where only the hybridomas (*i.e.,* the fusion between the primary B-lymphocytes and myeloma cells) survives as they have inherited immortality from the myeloma cells and selective-resistance from the primary B-lymphocytes (as the myeloma cells lack *HGPRT*, they cannot synthesize nucleotides *de novo*

as this is inhibited by aminopterin in the selective medium). The initial culture of hybridomas contains a mixture of antibodies derived from many different primary B-lymphocyte clones, each secreting its own individual specific antibody into the culture medium (*i.e.,* the antibodies are still polyclonal). Each individual clone can be separated by dilution into different culture wells. The cell culture medium can then be screened from many hundreds of different wells for the specific antibody activity required and the desired B-lymphocytes grown from the positive wells and then recloned and retested for activity. The positive hybridomas and monoclonal antibodies generated can then be stored away in liquid nitrogen [12-16].

Antibody Affinity Analysis

The measure of the binding strength of an antibody for a monovalent epitope is referred to as affinity. Whereas the affinity of an antibody reflects its binding energy to a single epitope, avidity reflects the overall binding intensity between antibodies and a multivalent antigen presenting multiple epitopes. Avidity is determined by the affinity of the antibody for the epitope, the number of antibody binding sites, and the geometry of the resulting antibody-antigen complexes.

Affinity is an important feature of monoclonal antibodies and is especially important for those used for either clinical diagnostic or therapeutic purposes. The measurement of antibody affinity provides an indication as to the strength with which a monoclonal antibody specifically binds to its target molecule. Another important characteristic of a monoclonal antibody is the specific location or region on the antigen to which the antibody binds. This region is commonly referred to as an epitope, and the determination of the specific binding location on the antigen is known as epitope mapping. Investigators have endeavored to search for an ideal, more accurate approach to measure antibody affinity and to pinpoint the critical amino acids forming the specific epitope. A rapid, accurate, reproducible and fairly universal procedure, termed Biomolecular Interaction Analysis (BIA), has recently been employed for this purpose. BIA allows for the investigation of the specific interactions between two bio ligands in real time, e.g., antibody-antigen binding affinity. BIA instruments, such as BIAcore (Pharmacia Biosensor AB), use continuous flow technology based on optical phenomenon surface plasmon resonance to measure changes in the concentration of molecules in a surface layer of solution in contact with the sensor chip surface.

Diagnostic Applications of Monoclonal Antibodies in Phatogene

MAb can react with a single antigenic determinant (epitope) and this restricted reactivity allows for precise identification of organism of interest which is the major advantage of MAbs over polyclonal anti sera. In case of a pathogen occurring as sub type defined by unique antigenic differences, specific MAbs can be used. Monoclonal antibodies are not used extensively in the animal world. They are employed in the process of genetically engineering an animal vaccine and are used mainly in the production of vaccines. Viruses, such as foot and mouth disease, are composed of large and complex protiens, all of which have many antibodies binding sites.

Cancer Diagnosis

MAbs can be used in applications against cancer cell specific antigens that will induce an immunological response against the target cancer cell. The availability of MAbs that recognize immune cell antigens has resulted in improved diagnosis of particular types of leukemia and lymphoma. MAbs are also being applied in the diagnosis of solid tumors, particularly the carcinomas of the lung, breast, colon, and rectum. MAbs are also used to examine blood, sputum, or biopsy samples for cancer cells or for materials that have been released by cancer cells. Today, special MAbs are available for colorectal cancer, ovarian cancer, and lung cancers. MAb mediated immunotherapy recruits' cells that have cytotoxicity such as monocytes and macrophages through Antibody-Dependent Cell Cytotoxicity (ADCC). In cancer immunotherapy, MAbs binds complement proteins, which leads to direct cell toxicity that is Complement Dependent Cytotoxicity (CDC).

Bacterial Infection Diagnosis

A major advantage for direct isolation of bacteria from patient material is the analysis of antibiotic sensitivity of the particular strain. However, this is not always feasible, since some species do not grow rapidly enough or do not grow at all in the laboratory. Rapid identification is advantageous to allow early treatment with appropriate antibiotics. Monoclonal antibodies are used to confirm identification of bacterial pathogens, and in situations where identification by other means is complex and time consuming. An example is in the diagnosis of *Neisseria gonorrhea* and its differentiation from other *Neisseria* species, which would otherwise require complex biochemical testing. Monoclonal antibodies are also used in rapid agglutination tests and in the detection of bacterial products such as toxins. Assay formats include antibody coated latex beads for rapid agglutination tests, enzyme linked immunoassays and detection of bacteria in tissue or culture using fluorochrome labelled antibody coupled with either fluorescence microscopy or flowcytometry.

Parasitic Infection Diagnosis

Since the introduction of hybridoma technology, it is becoming possible to accurately diagnose different protozoal and helminth parasitic helminth infections of animals with the help of monoclonal antibodies that is specifically bind to specific epitope of the parasite antigen. Thus, it was studied that monoclonal antibodies are able to accurately characterize and localize the parasitic antigen to the species level with the help of ELISA, PCR, radioimmune assay and fluorescent immunoassay. Certain protozoal (coccidiosis, babesiosis, theileriosis, toxoplasmosis and cryptosporidiosis) and helminth (fasciolosis, dirofilariasis, trichinosis, and cystic echinococcosis) diseases of animals can be diagnosed

accurately and treated with the help of monoclonal antibodies.

Viruses Infection Diagnosis

Viruses are detected usually in enzyme immunoassay format or by immunofluorescence using antibody against viral antigens, often after infecting cells in culture using tissue isolates thought to contain the virus. The most appropriate test format depends on the biology of infection. For example, Cytomegalovirus (CMV) produces along lasting infection, with latent virus inhabiting cells of the immune system. The virus can be grown in human fibroblasts in the laboratory, but it may take several weeks before the cells show cytopathic changes. However, CMV early antigens may be detected in the cells by immunofluorescence within hours, or may be detected directly in patient blood cells.

Recently, antibodies have been used to distinguish different strains of virus for some time, and MAbs have been used for characterizing individual antigenic sites on individual components of the viruses. Additionally, antigenic variants of Influenza virus have been isolated artificially by inactivating a batch of virus with MAbs and the residual variant virus 'clones' were grown separately.

Identification of Cell Surface Markers

Cluster Differentiation (CD) and Human Leukocyte Antigen (HLA) are expressed as cell surface molecules/ antigens on various immune cells. Through flow cytometry, the CD markers or HLA molecules are identified using MAbs directed against a specific cell surface antigen. In flow cytometry, if the numbers of CD markers are under-represented, immunodeficiency disease is suspected, while if the numbers of CD markers are over produced, cancer is indicated. Thus, calculating the expression of CD markers can be used for disease diagnosis. The MAbs have also helped to define the functions of immune cells. MAbs directed to CD4 markers on TH cells indicate the functions of T-cells. If the number of CD4 is decreased, a patient may have Acquired Immunodeficiency Syndrome (AIDS), which may also indicate the stage of the disease. Thus, MAbs may be able to be used for understanding, diagnosing, and managing immune system related diseases.

Therapeutic Applications of Monoclonal Antibodies

Monoclonal antibodies can function through various mechanisms of action, such as through receptor blockade or agonist activity (e.g., Vascular Endothelial Growth Factor (VEGF) and EGFR), induction of apoptosis, or delivery of a drug or cytotoxic agent, and immune mediated cell killing mechanisms, e.g., CDC, ADCC and regulation of T cell function. Because the mechanisms involved in one disease may differ from those involved in another, extensive consideration should be given to the setting in which clinical comparability is to be tested, especially where it is known that extrapolation to other indications and uses will be sought.

Monoclonal antibodies that bind to hair like binding sites of the antigen of certain strains of intestinal bacteria, such as *Escherichia coli* (*E. coli*) are fed to new born calves or pigs. Then the bacteria will become to bind to the gut wall and then this will reduce the severity of the disease. Monoclonal antibodies specific for some tumor antigen or viral antigen can selectively kill or neutralize when they are administered to an ailing animal.

Cancer Treatment

The mechanism by which monoclonal antibodies work can be either direct or indirect. The direct therapeutic effect is carried out by producing programmed cell death or apoptosis. They have the ability to stop the proliferation of tumor cells by blocking the growth factor receptors. Effects of antibody therapy are attained indirectly either by direct cell toxicity, binding complement, or by using macrophages and monocytes to destroy the target cell. This is also called antibody-mediated cell toxicity. The monoclonal antibody can also be conjugated to radioisotope, toxin or cytotoxic agent, which then binds to the antigen and causes cell death.

MAbs combined with antineoplastic drugs are specifically targeted to tumor cell receptors, thus avoiding damage to the healthy cells. MAbs also generate biological responses in the immune system; as a result, and in addition to direct cytotoxic action, they can induce antitumor responses *via* indirect mechanisms.

The treatment for cancer involves monoclonal antibodies that bind only to cancer cell-specific antigens and induce immunological responses against the target cancer cells. Such mAb 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 antigens and to a conjugate or effector cells. In fact, every intact antibody can bind to cell receptors or other proteins with its Fc region [17-20].

Autoimmune Diseases Treatment

Use of mAbs specific for B-lymphocyte surface proteins could theoretically lead to reduced production of autoantibodies. This approach could be useful in immune mediated hemolytic anemias/thrombopenia, myasthenia gravis, and autoimmune blistering diseases such as pemphigus, among other conditions.

MAbs used for autoimmune diseases include infliximab and adalimumab, which are effective in rheumatoid arthritis, Crohn's disease, and ulcerative colitis due to their ability to bind to and inhibit Tumor Necrosis Factor (TNF), TNF-α. Basiliximab and daclizumab inhibit IL-2 on activated T-cells and thereby help prevent acute rejection of kidney transplants. Daclizumab is also a promising drug against T-cell lymphoma. Omalizumab inhibits human IgE and is useful in moderate to severe allergic asthma. Several immune diseases are caused

by an apparent attack of the immune system on the tissues of the body. Investigators are attempting to determine whether MAbs that are directed against immune cell components involved in triggering the abnormal immune responses could be used to treat such autoimmune conditions. To suppress the immune system, muromonab-CD3 (OKT3), infliximab, adalimumab, omalizumab and daclizumab are the most widely used drugs. A human MAb against *Escherichia coli* endotoxin has been produced which protects mice from bacteremia. It is also being tested in humans. An anti-T-cell MAb is available that has been used to remove T-cells from the donor marrow prior to transplantation, leading to reduction in graft versus host disease.

Allergic Diseases

Allergic diseases produced as a result of type I hypersensitivity reactions and resistant to habitual treatment can be treated with humanized MAbs selectively targeted to the mediators of the allergic reaction: IgE, IL-5, IL-4, TNF-alfa, and others. At present, humanized MAbs (5% murine, 95% human) targeted to IgE (omalizumab) are used in clinical practice with special indications and in patients over 12 years of age. The anti-IgE MAb rhu MAb-E25, known as omalizumab (Xolair), selectively binds to the C3 epsilon domain of free IgE, blocking binding to the high affinity receptor. As a result, IgE does not bind to mast cells and basophils, and these cells therefore do not release their mediators. The MAb only binds to circulating IgE, not to other immunoglobulins, forming immune complexes that neither precipitate nor cause disease. The drug can be administered intravenously or *via* the subcutaneous route at variable doses according to the levels of IgE in serum and the weight of the patient. The dosage ranges according to different authors between 0.016 mg/kg-0.50 mg/kg ever 2-4 weeks. These MAbs have been used in asthma and allergic rhinitis, producing a rapid decrease in serum IgE levels, in correlation with improvement of the clinical manifestations and patient quality of life.

Viral Disease

Palivizumab, the only mAb currently on the market for the treatment of infectious diseases, was developed as a prophylactic treatment against the viral disease RSV. Although mAbs have been shown to be able to neutralize many viral pathogens *in vitro*, the utility of mAbs therapy in viral diseases is still a matter of contention as it is unclear to what extent viral clearance depends on antibody mediated immunity. The clearance of a viral infection is usually associated with T cell-mediated adaptive immunity. $CD8^+$ T cells act by killing virus infected cells, thus preventing viral replication and reducing the viral load. However, in acute infections, neutralizing therapeutic antibodies may still be able to help by suppressing viral replication and viraemia, giving the host immune system time to develop an effective response for viral clearance. In addition, antibodies can promote the killing of infected cells expressing viral proteins on their surface through the activation of Natural Killer (NK) cells that mediate ADCC, in addition to their viral neutralization properties.

There are several mAbs for HIV in development, designed to inhibit viral entry, reduce viral load in HIV patients, and potentially to prevent infection in certain cases. Viral entry inhibitor mAbs target the cellular receptors, CCR5 and CD4, or the cognate viral protein gp120. Efforts to develop neutralizing mAbs with broader strain specificity have found success targeting the V3 loop of gp120. As is true with all mAbs designed for infectious disease, the development of a successful vaccine would reduce their need. However, given the slow progress on the front of HIV vaccine development, mAb research in the HIV field is a promising alternative. Although there are numerous antiretroviral drugs available for the treatment of HIV, the availability of effective mAb therapy could complement chemotherapy by slowing the onset of resistance and possibly enhancing therapeutic efficacy.

DISCUSSION

Side Effects and Limitations of MAbs

MAbs given intravenously have usually mild side effects as compared with chemotherapy. A mild allergic reaction (rash) may be occurring with first administration of the drug. Common side effects include fever, headache, weakness, chills, nausea with vomiting and diarrhea, and low blood pressure. Other side effects of MAbs are related to the targeted antigens. Bevacizumab (used against tumor blood vessel growth) can have side effects such as kidney damage, high blood pressure, bleeding with poor wound healing, and blood clots. Inhalational anthrax (potent biological terrorism) is caused by breathing the bacterial spores of Bacillus anthracis. The FDA approved drug raxibacumab (MAb) injection is used to treat infectious inhalational anthrax when alternative therapies have failed. Common side effects include rash with itching, extreme pain, and drowsiness.

MAb therapies are still a long way from application in most of the diseases due to technical shortcomings and still poorly understood biology of the normal and mutated antigens. Other important issues are costs, development of resistance, etc. Although novel therapies are now a reality in oncology, MAbs like rituximab, trastuzumab, cetuximab and bevacizumab, etc. are efficacious alone or in combination with chemotherapy, they are exorbitantly priced. This has led to inequalities in delivery of optimum care, particularly in developing countries. Certain factors limit the therapeutic efficacy of MAbs toxicity, serum blocking factors, antigenic modulations, immune response to xenogeneic proteins, specificity, and perhaps most significantly, inefficiency of natural immune effect or mechanism. Some of the relative lack of commercial success of monoclonal antibodies may be attributed to the high costs of its administration. For example, in leukemia treatment, it costs approximately £37,000 for a year's supply of alemtuzumab.

Therapeutic mAbs are generally considered well tolerated in humans, but with none yet available in veterinary medicine, a complete safety assessment in dogs and cats cannot yet be made accurately.

CONCLUSION

Monoclonal antibodies are specific antibodies produced by the clones derived from a single parent cell, by fusing the antibody-producing cell (B cell) with a laboratory cultured myeloma cell through the process of somatic cell hybridization. Since their discovery, monoclonal antibodies have revolutionized the diagnosis and treatment of numerous diseases. Monoclonal antibodies present an attractive option for the development of new therapies and molecular drug targets against a wide variety of common diseases due to their specificity and flexibility. Based on the above conclusion, the following recommendations are forwarded.

RECOMMENDATIONS

- Further research should be carried out to produce mAbs against antigens of pathogens of medical and veterinary importance.
- There should be a study on the importance of monoclonal antibodies in the diagnosis and treatment of animal diseases both at the national and global level.

REFERENCES

1. Brodeur B, Tsang P (1986) High yield monoclonal antibody production in ascites. J Immunol Methods. 86:239-246.
2. Buss N, Henderson S, McFarlane M, Shenton J, De Haan L (2012) Monoclonal antibody therapeutics: History and future. Curr Opin Pharmacol. 12(5):615–622.
3. Cambrosio A (1992) Between fact and technique: The beginnings of hybridoma technology. J Hist Biol. 25(2): 175-230.
4. Carter P (2001) Improving the efficacy of antibody based cancer therapies. Nat Rev Cancer. 1(2):118-129.
5. Carte P, Weiner L, Davis H (2007) Antibody constructs in cancer therapy: Protein engineering strategies to improve exposure in solid tumors. Cancer. 109(2):170–179.
6. Chames P, van-Regenmortel M, Weiss E, Baty D (2009) Therapeutic antibodies: Successes, limitations and hopes for the future. Br J Pharmacol. 157(2):220-233.
7. Drew W (1988) Diagnosis of Cytomegalovirus infection. Rev Infect Dis. 3:468-476.
8. Edward A (2014) Greenfield, generating monoclonal antibodies. Br J Pharmacol. 7:1-21.
9. Fahy J, Cockcrof D, Boulet L, Wong H, Deschesnes F, et al. (1999) Effect of aerosolized anti IgE (E25) on airway responses to inhaled allergens in asthmatic subjects. Am J Resp Crit Care Med. 160:1023-1027.
10. Green M, Murray J, Hortobagyi G (2000) Monoclonal antibody therapy for solid tumors. Cancer Treat Rev. 26:269-286.
11. Hayes D, Thor A, Dressler L, Weaver D, Edgerton S (2007) HER2 and response to paclitaxel in node positive breast cancer. N Engl J Med. 357:1496-1506.
12. Heddy Z, Roberts T (2001) Monoclonal antibodies. Mol Pathol. 53(3):111-117.
13. Hessell A, Rakasz E, Poignard P, Hangartner L, Landucci G, et al. (2009) Broadly neutralizing human anti-HIV antibody 2G12 is effective in protection against mucosal SHIV challenge even at low serum neutralizing titers. PLoS Pathog. 5(5):1000433.
14. Hezareh M, Hessell A, Jensen R, van de Winkel J, Parren P (2001) Effector function activities of a panel of mutants of a broadly neutralizing antibody against Human immunodeficiency virus type 1. J Virol. 75:12161-12168.
15. Jing Y, Quing Y (2011) Therapeutic monoclonal antibodies for multiple myeloma: An update and future prospective. Am J blood Res. 1:1-12.
16. Joseph P, Laurino D, Qinwei S, Jun G (1996) Monoclonal antibodies, antigens and molecular diagnostics: A practical overview. Ann Clin Lab Sci. 29:158-166.
17. Kohler G, Milstein C (1975) Continuous cultures of fused cells secreting antibody of pre defined specificity. Nature. 256:495-497.
18. Khumar S, Gupta SK, Sharma PK (2012) Recent developments in targeted drug delivery system for crossing blood brain barrier; A review. Int J Pharm Pharmacology Science. 4(2):36-41.
19. Lonberg N, Huszar D (1995) Human antibodies from transgenic mice. Int Review Immunol. 13(1):65-93.
20. Malmqvist M (1993) Surface plasmon resonance for detection and measurement of antibody-antigen affinity and kinetics. Curr Opin Immunol. 5(2):282-286.