MONOCLONAL ANTIBODIES: IMPACT OF ANTIBOITIES

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INTRODUCTION

Humans have the capacity to make antibodies. It will provide the basis need of protection against the disease organisms. It also helps to target various kinds of molecules present in body such as receptors or the other proteins which present on the normal cells surface and the molecules which presents uniquely on the surface of cancer cells. These are remarkable in human therapy because they only make the antibody that will only blinds these cells of cancer in patient, for destroying these cells antibody is coupling with cytotoxic agent.

In the human body the immune manufacture system creates antibodies of a high range of different structures which are used in both their binding regions and as well as their effecting region. Because of the limited potential growth of normal somatic cells, even if we isolate a single secreting cell and place it in a culture, it will die in few generations. Now it needs a make "monoclonal antibodies" – antibodies of single specificity, they are built alike as they are manufactured by a single clone of plasma cells and that can be grown indefinitely.

B-cell secreting antibody can be cancerous like any cell. This type of proliferation unchecked cell is known to be myeloma. By the research, Milstein and Kohler have discovered a process to link the great potential of myeloma cells with the prearranged antibody particularity of immune spleen cells. They had done this by intersecting the cells of myeloma with the secreting antibody cells from an immunized mouse. The technique is called somatic cell hybridization. The result is a hybridoma.

PROCEDURE

Mix the cells of spleen from an immunized mouse with the cells of myeloma. We need to use a man power simplify the fusion of adjoining plasma membranes. Use cells of myeloma which have lost their ability synthesize hypoxanthine guanine phosphoribosyltransferase (HGPR) to lose their ability of their own antibody synthesize molecule.

1. Transfer the fusion mixture of cell to a culture medium called HAT medium as it contains hypoxanthine, aminopterin and thymidine. Due to the lack of HGPRT the unfused myeloma cells cannot grow. Due to the limited life span the unfused normal spleen cells can't grow. By the successful interactions of Hybridoma cells can grow frequently due to the spleen cell partner supplies HGPRT and the myeloma partner is immortal.
2. We want to test the supernatants for each culture to know that they are producing the right antibody.
3. More than one hybridoma cell they start their own original culture. Now the cells from their antibody-positive culture must be isolated and subculture them.
4. We need check or test the every supernatant for their desired

antibodies. There for each positive subculture has been started from a single cell and then it represents a clone and its antibodies are monoclonal. Cultures of each antibody molecule directed after selecting against an antigen.

5. Increase the size of the cultures of the successful clones. It can be maintained in vitro and in vivo. The yield runs from 10-60 micro-g/ml in vitro and 1-60 mg/ml in vivo.

USES

1. To suppress the immune system

- Muromonab-CD3 and two humanized anti-CD3 monoclonals – It will bind the T-cells of a CD3 molecule on the surface. It will restrict the actual rejection of organ transplant. The humanized version inhibit the destruction of autoimmune of beta cells in Type I diabetes mellitus.
- Infliximab and Adalimumab – It will binds the tumor necrosis factor-alpha and act against inflammatory diseases of rheumatoid arthritis by blunting the activity of Th I cells.
- Omalizumab – It binds IgE thus preventing IgE from binding to mast cells. It is used against allergic asthma.
- Daclizumab– It binds the part of the IL-2 receptor which has exposed at the surface of an activated T cells. It is also used to act against T- cell lymphoma.

2. To kill or inhibit malignant cells.

- Rituximab – It binds the CD20 molecule which is found on most B-cells and is used to treat B – cell lymphomas.
- Ibritumonab – It will act against the CD20 molecule on B-cells conjugated to either radioisotope indium-111 or yitriym-90.
- Tositumomab- It will act against the CD20 molecule on B-cells conjugated to radioisotope iodine-131.
- Cetuximab – It blocks HER2, a receptor of a growth factor which is found on several types of tumor cells.
- Trastuzumab – It blocks HER2, a receptor of a growth factor which is over-expressed in breast cancers of genotype ERBB2.
- Adcetris - It is an associate of the monoclonal antibody that binds CD30, it is a cell surface molecule expressed by some lymphomas cells.
- Vedotin – By preventing the polymerization of tubulin it blocks mitosis.
- LymhoCide – It binds to CD22 which is found on some B-cell leukemias.
- Alemtuzumab – It binds to C52 of a molecule which is found on depletes and lymphocytes both cells of B and T. It has produced complete remission of chronic lymphocytic leukemia and it also prevents rejection of kidney transplants.
- Lymphoma cells can be expressed at greater levels due to the encoded histo-compatibility antigen of Lym-1 which binds HLA.
- Ipilimumab – It has power to resist from tumors.

3. Angiogenesis Inhibitors

- Vitaxin – It is used to bind the vascular integrin (alpha-v/beta-3) which is found on the blood vessels of tumors.

- Bevacizumab – It will bind the growth factor of vascular endothelial which will prevent from binding its receptor.

4. Others

- Abciximab – By blinding the receptors on surface, it will inhibit the clumping of platelets which are normally linked by fibrinogen. It is useful in preventing the reclogging of arteries of coronary in patients who have been undergone angioplasty.

PROBLEMS WITH MONOCLONAL THERAPY

Antibodies of mouse can be seen by the immune system of human as foreign and the patient mounts on an immune response against them by producing antibodies. It also causes harm to a kidneys immune complex and also causes therapeutic antibodies which is need to be eliminated quickly from host.

IN FUTURE

Transgenic mice – will be inserted in gene loci of human antibody using stem cell method of embryonic and also to have their own gene for making antibodies, knocked out.

The result is a mouse which can be immunized by the desired antigen, produces human antibodies against the antigen and that can be yield cells which are fused with cells of myeloma to manufacture all human monoclonal antibodies.