A Study on the Applications of Hybridoma Technology

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Abstract— Hybridoma technology is the technology which is used to form the hybrid cell. In fact, the hybrid cells are generated by fusing the B-lymphocyte with the B cell cancer called tumour cell or myeloma cells. Monoclonal antibodies are generated with specialized cells by using the technique called hybridoma technology. The monoclonal antibodies are the one which being used to track the cancer antingens and also connected to anti-cancer agents in order to attack the cancer metastases. Apart from these, various applications are using hybridoma technology in order to obtain several benefits. This research discusses about the hybridoma technology and also about the applications of hybridoma technology.

Index Terms— Hybridoma technology, monoclonal antibodies, applications, and hybridoma cells

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INTRODUCTION TO HYBRIDOMA TECHNOLOGY

Hybridomas are the type of cells which have been engineered in order to generate large amounts of desired antibody to generate monoclonal antibodies (Bretton, Melamed and Cote, 1994). Monoclonal antibodies can be generated through the specialized cells by using the technique which is known as the hybridoma technology. In 1975, two scientists namely, Cesar Milstein and Georges Kohler discovered hybridoma technology jointly with Niels Jerne. Hybridoma technology is a technology which helps to form hybrid cell lines (known as Hybridoma) by fusing a particular antibody in order to generate B cell with a B cell cancer (myeloma cell) which is selected for its ability in order to freeze, grow in tissue culture and also for the absence of the antibody chain synthesis.

Apart from these, the antibodies which are generated by hybridoma may have single specificity and so it is called as monoclonal antibodies. Using the antibodies for immunization against infectious diseases provides such as tumors and injured tissue are the potential benefits to the antibodies. The heterogeneity of immune will have capacity to response to the technical and ethical problems that involved in producing the human antibodies which has natural products of human humoral immune system (Kohler and Milstein 1975).

The following figure illustrates the history of monoclonal antibodies.

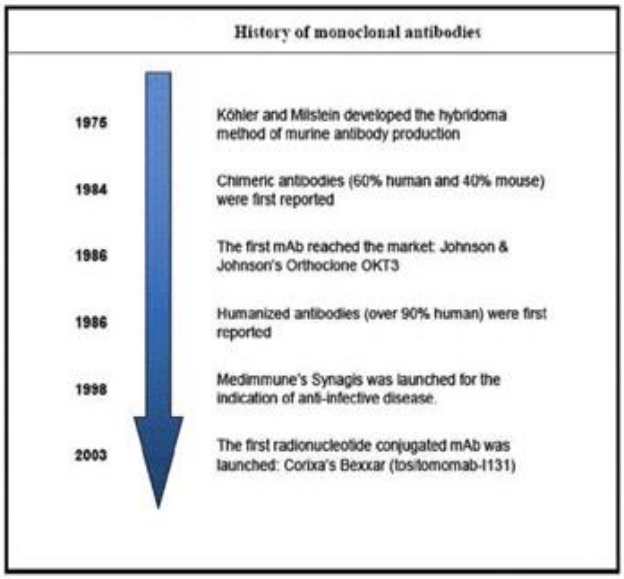

Figure: History of Monoclonal Antibodies

Source: Pharma Express (2009): mAbs, retrieved on 2nd April 2013 from http://pharma.financialexpress.com/20091115/expressbiotech10.shtml

The hybridoma technology makes possible to immortalize the cells that formed from antibodies from immunized host by the fusion with the myeloma cell and also to produce the

clones which have capacity to generate single, homogeneous antibody (Morrison, 1989). Apart from these, hybridoma cells can be frozen and it can be grown in mass culture or otherwise injected into the animal in order to form tumors which have capacity to generate antibodies in large amounts. The ability to freeze the cells makes possible to store the cells for long term. The hybridoma technology is the one which makes to produce monospecific antibodies to the antigens that are impure and also poorly characterized (Bankert, 1980). In addition to these, availability of monoclonal antibodies let the antibodies selection with specific functional characteristics and affinities. Hybridoma technology has several scientific benefits and it provides several opportunities for the examination of clinical and fundamental questions that with the monoclonal antibodies.

MAbs (Monoclonal Antibodies) are the antibody proteins which have a target antigen (molecule) at antigenic site (one specific site) (Kohler and Milstein, 1975). Monoclonal antibodies are acting as a key in order to develop new kinds of vaccines. The following figure illustrates the hybridoma technology in order to generate monoclonal antibodies.

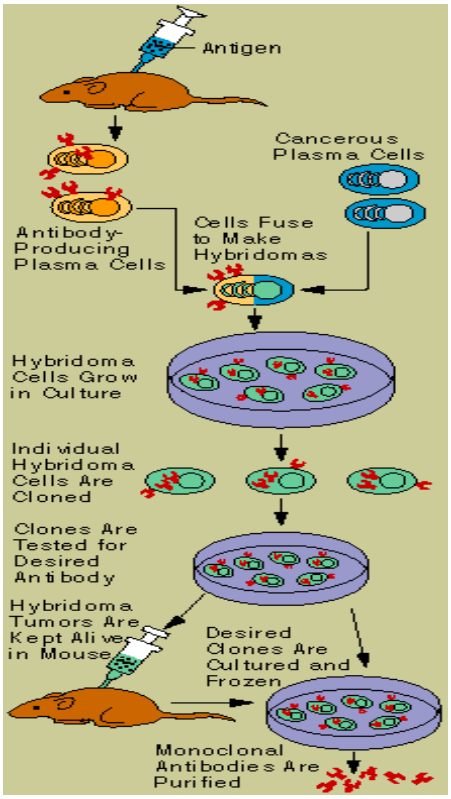

Figure: Using hybridoma technology to make monoclonal antibodies

Source: LSRHS (nd): Understanding the Immune System, retrieved on 2nd April 2013 from http://www.lsrhs.net/departments/science/faculty/Rami/Understanding.the.Immune.System/page.28.html

Today, many monoclonal antibodies are used in the clinical trials as a treatment for many diseases. Monoclonal antibodies are mainly utilized in several diagnostic procedures which include: identifying infectious agents, identifying tumour antigents and also auto-antibodies, identifying leukemia and lymphomas, measuring drug levels and proteins in serum, identifying and quantifying the hormones and typing tissue and blood, and identifying the cells that involved in the immune response.

APPLICATIONS OF HYBRIDOMA TECHNOLOGY:

Hybridoma technology is used by several applications and also applications are gaining several advantages. These applications are used to develop many new approaches in order to find various treatments for the several diseases.

The applications of hybridoma technology may include purification of protein, radioimmunoassay and Lymphocyte phenotyping. Apart from these, immuno-cytochemical is also an application that describes about lymphoma. In addition to these, there are few recent applications that derived monoclonal antibodies of hybridoma technology in order to diagnosis of parasitic disease. Here, in order to detect the antigen in body fluids and host tissues the test such as ELSIA (enzyme-linked immunosorbent assay) and RIA (radioimmunoassay) will be used. Apart from these, monoclonal antibodies are mainly used as the treatment for cancer and monoclonal antibodies can also be modificated for delivery of the cytokine and radioisotope. The following are few applications of the hybridoma technology.

DIAGNOSTIC TESTS:

Monoclonal antibodies for the specified substance have been generated then they will be used to detect the presence of that substance. The immuno dot blot tests and western blot test may have capacity to detect the presence of the protein on the membrane (Zuckier LS, Rodriguez and Scharff, 1989). Apart from these, this is also useful in immunofluorescence test which helps to identify the substance in live cells or frozen tissue section and immunohistochemistry which helps to detect the antigen in the fixed tissue sections.

The following table illustrates the types of Immuno experiments and its associated labels.

Immunossay	Labels
Western blot	Enzymes (alkaline phosphatase or HRP)
Immunofluorescence	Fluorescent dyes
ELISA	Streptavidin, Biotin and Enzymes
Flow Cytometry	Tandem dyes, Fluorescent dyes or proteins
Immunohistochemistry	Streptavidin, Biotin and Enzymes

Table: Types of Immuno Experiments and its Associated Labels

Source: Novus Biologicals (n.d): Antibody Conjugation, retrieved on 2nd April 2013 from http://www.novusbio.com/support/support-by-application/antibody-conjugation/illustrated-assay.html

MONOCLONAL ANTIBODIES FOR THE CANCER TREATMENT:

Monoclonal antibodies are one of the possible treatments for the cancer. Here, monoclonal antibodies bind only to the cancer cell antigens and then induce the response of immunological against the targeted cancer cell (Johnston et al, 1987). Monoclonal antibodies are possible to be modified for the delivery of the cytokine, toxin, radioisotope or other active conjugate. Apart from these, it is possible to design the bi-specific antibodies which can have capacity to bind with Fab regions in order to target both conjugate or effector cell and antigen (French et al, 1986).

The following table illustrates various types of monoclonal antibodies that used to treat various types of cancer.

Name of drug	Type of cancer used to treat
Alemtuzumab (Campath)	Chronic lymphocytic leukemia
Bevacizumab (Avastin)	Breast cancer Colon cancer Lung cancer
Cetuximab (Erbitux)	Colon cancer Head and neck cancers
Gemtuzumab (Mylotarg)	Acute myelogenous leukemia
Ibritumomab (Zevalin)	Non-Hodgkin's lymphoma
Panitumumab (Vectibix)	Colon cancer
Rituximab (Rituxan)	Non-Hodgkin's lymphoma
Tositumomab (Bexxar)	Non-Hodgkin's lymphoma
Trastuzumab (Herceptin)	Breast cancer

Table: Various types of monoclonal antibodies that used to treat various types of cancer.

Source: Pharma Express (2009): mAbs, retrieved on 2nd April 2013 from http://pharma.financialexpress.com/20091115/expressbiotech10.shtml

CHIMERIC AND HUMANIZED ANTIBODIES:

Producing the monoclonal antibodies with the standard procedure is one of the major problems in the medical applications. Murine antibodies are although very similar to the human ones (Ghosh et al, 1983). The human immune system is the one which will recognizes the mouse antibodies as foreign and then rapidly removing them from the circulation and so it may causes the systemic inflammatory effects (Kranz et al, 1980). These responses are recognized as generating Human Anti-Mouse (HAMA) antibodies or Human Anti-Chimeric (HACA) antibody antibodies.

Here, only solution to this issue is by generating the human antibodies directly from the humans. But, this process is not easy and this is because, generally it is ethical to challenge humans with the antigen to generate antibody. Apart from these, it is not easy to produce human antibodies against the human tissues.

The following table illustrates the types of monoclonal antibodies (MAbs) that used in various applications.

MAbs			
Type	Application	Mechanism	Mode
Infliximab	Rheumatoid arthritis, Crohn's disease	Inhibits TNF-α	Chimeric
Basiliximab	Acute rejection of kidney transplants	Inhibits IL-2 on activated T cells	Chimeric
Abciximab	Prevent coagulation in coronary angioplasty	Inhibits the receptor GpIIb/IIIa on platelets	Chimeric
Daclizumab	Acute rejection of kidney transplants	Inhibits IL-2 on activated T cells	Humanised
Gemtuzumab	Relapsed acute myeloid leukaemia	Targets an antigen on leukemia cells	Humanised
Alemtuzumab	B cell leukemia	Targets an antigen CD52 on T- and B-lymphocytes	Humanised
Rituximab	Non-Hodgkin's lymphoma	Targets phosphoprotein CD20 on B lymphocytes	Chimeric
Palivizumab	RSV infections in children	Inhibits an RSV protein	Humanised
Trastuzumab	Anti-cancer therapy for a specific kind of breast cancer	Targets the HER2/neu (erbB2) receptor	Humanised
Etanercept	Rheumatoid arthritis	Contains TNF receptor	Fusion protein
Adalimumab	Rheumatoid arthritis Crohn's disease	Inhibits TNF-α	Humanised
Nimotuzumab	Approved in SCCHN, Glioma Clinical trials for other indications underway	EGFR inhibitor	Humanised

Figure: Types of Monoclonal Antibodies (MAbs) that used in Various Applications.

Source: Pharma Express (2009): mAbs, retrieved on 2nd April 2013 from http://pharma.financialexpress.com/20091115/expressbiotech10.shtml

CONCLUSION

This research concludes that hybridoma technology is the one which was not changed till now from the year it was discovered. Hybridoma technology provides various benefits and advantages and also more opportunities for the fundamental and clinical questions along with the monoclonal antibodies. This research concludes that various applications are using hybridoma technology to obtain various advantages. This study concludes that diagnostic tests are utilizing monoclonal antibodies and also with ELISA (enzyme-linked immunosorbent assay) and RIA (radioimmunoassay) in order to detect antigen in body fluids and host tissues. Apart from these, this research strongly concludes hybridoma technology with monoclonal antibodies is the one which is best treatment for cancer.

REFERENCES

1. Bretton, PR, Melamed, MR, Fair, WR, Cote, RJ (1994): Detection of occult micrometastases in the bone marrow of patients with prostate carcinoma, Prostate. 25(2), 108-14

2. Kohler G, Milstein C: (1975): Continuous cultures of fused ceils secreting antibody of predefined specificity. Nature 256:495- 497, 1975

3. Zuckier LS, Rodriguez LD, Scharff MD (1989): Immunologic and pharmacologic concepts of monoctonal antibodies. Semin Nucl Med 19:166-186, 1989

3. Johnston WW, Szpak CA, Thor S, Simpson TF, Schtom J (1987): Applications of immunocytochemistry to clinical cytology. Cancer Invest 5:593-611, 1987

4. French D, Fischberg E, Buhl S, Scharff MD (1986): The production of more useful monoclonal antibodies. Immunol Today 7:344-346, 1986

5. Kranz DM, Billing PA, Herron JN, Voss EW (1980): Modified hybridoma technology: Antigen directed chemically medi- ated cell fusion. Immunol Commun 9:639-651, 1980

6. Ghosh, AK, Spriggs, Al, Taylor-papadimitriou, J and Mason, DY(1983). Immunocytochemical staining of cells in pleural and peritoneal effusions with a panel of monoclonal antibodies. J Clin Pathol, 36,1154-1164

7. Bankert R, DesSoye U, Powers L (1980): Antigen promoted cell fusion: Antigen coated myetoma cells fuse with antigen reactive spleen cells. Transplant Proc 12:443-446, 1980.

8. Morrison SL (1989): Genetically engineered (chimeric) antibodies, Hosp Pract 24:65-80, 1989