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# APPLICATIONS OF MONOCLONAL ANTIBODY TECHNOLOGY

MANTHRI S. RAMASAMY
*Division of Life Sciences, Institute of Fundamental Studies, Kandy.*

The immunization of laboratory animals (mice, rabbits etc) with antigen is the conventional method used to raise antibodies to the immunizing antigen. The serum obtained from these animals is a polyclonal serum containing antibodies to many antigenic determinants. In 1975, Kohler and Milstein[1] demonstrated that the hybridization of somatic cells could be used to establish continuous cultures of specific or monoclonal antibody (MAB) producing cells. The somatic cell hybrids are known as hybridomas, and are produced by fusing *in vitro* B lymphocytes from the spleen of an immunized mouse with myeloma cells. The hybridoma produced acquires from its lymphocyte parent, the ability to produce a specific antibody and from the myeloma cell parent the ability to be maintained in culture indefinitely. Antibody molecules produced by a single hybridoma clone are identical and are specific for a single antigenic determinant, i.e. one of many such antigenic determinants present on the target antigen. Therefore, monoclonal antibodies are chemically defined immunological reagents.

Tissue cultures of hybridoma cells, which can be frozen and recovered later, have the ability to produce ascites i.e. fluid tumours, when injected into mice. This procedure enables the production of a large amount of MAB. The hybridoma technique assures a perpetual supply of specific antibodies. It takes approximately 4-6 months to produce a stable hybridoma, and MABs are convenient, reliable and relatively cost effective as reagents.

MABs have found applications in the fields of both human and veterinary medicine, agriculture and also in industry. In medicine, agriculture and industry MABs have been mainly been used for diagnostic purposes, in immunoassays. Although polyclonal antibodies are used with great success in some immunodiagnostics, highly specific antibodies are essential for some practical applications. MABs are useful in instances where specific antibodies are required. The most widely used immunodiagnostic assay is ELISA - enzyme linked immunosorbent assay. ELISA is a highly sensitive assay and can be carried out fast, on a large scale. ELISA is a test which has the potential for automation and kit development. It has been widely exploited as a detection system for antigens and antibodies in disease detection in humans and animals. In the field of agriculture, MAB - ELISA is useful in pest identification; eg. the simple - to - use MAB - ELISA developed by the Commonwealth Scientific and Industrial Research Organization (C.S.I.R.O.) in Australia to distinguish between two closely resembling cotton pests, and then scheduling insecticide application. MABs are ideal reagents for characterizing serological differences among viruses, e.g. plant viruses. In this process, the extremely specific antigenic properties of the protein coat of the virus plays an important role. ELISAs for detecting serological differences among viruses

could be done on an epitope by epitope basis, providing a level of precision that cannot be obtained with polyclonal sera. The use of this technique depends on the production and selection of monoclonal antibodies that are capable of differentiating epitopes on a number of virus serotypes. These antibodies can be produced in sufficient quantities to provide reference reagents for subsequent distribution. MABs can be pooled to form a synthetic serum capable of detecting a wide range of virus serotypes for diagnostic assays.

The generation of therapeutic antibodies is another application of MABs. To be suitable for human use, mouse MABs have been humanised - by genetic engineering to replace 90% of murine sequences with human antibody sequences. MABs are now used in the U.S. in tumour imaging eg: for the detection of colorectal cancer and ovarian cancer metastases. For this purpose a MAB labelled with Indium III has been marketed by Cytogen.

The company Cytogen A Hybritech has a MAB which is used for imaging to detect intra-abdominal tumours missed by CAT scans. MABs to detect colon cancer have been developed by Immunomedics and MAB imaging products from Oncotrace have been produced for detecting lung cancer. In the field of non-cancer imaging, MABs can be used to image dead cardiac muscle post heart attacks, in trials to image blood clots and also to age blood clots. MAB therapy has also been used in transplantation. For example, the MAB, OKT3, can be used to prevent rejection in kidney transplantation. MABs conjugated to immunotoxins have been used for the treatment of lymphomas and autoimmune disease and MABs have also been conjugated to drugs for therapeutic use. MAB immunoassays have wide usage in the food and beverage industry, in quality control, detecting of contamination, etc.

**Reference**

1. Kohler G. & Milstein C. (1975). Continuous cultures of fused cells secreting antibody of predefined specificity. *Nature* **256** : 495 - 497.