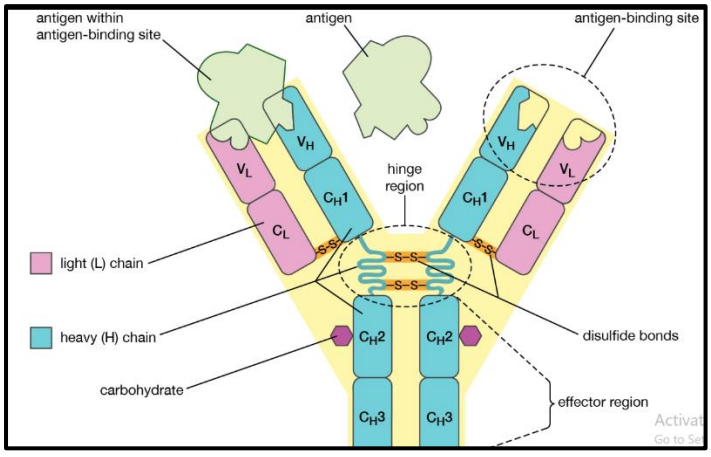
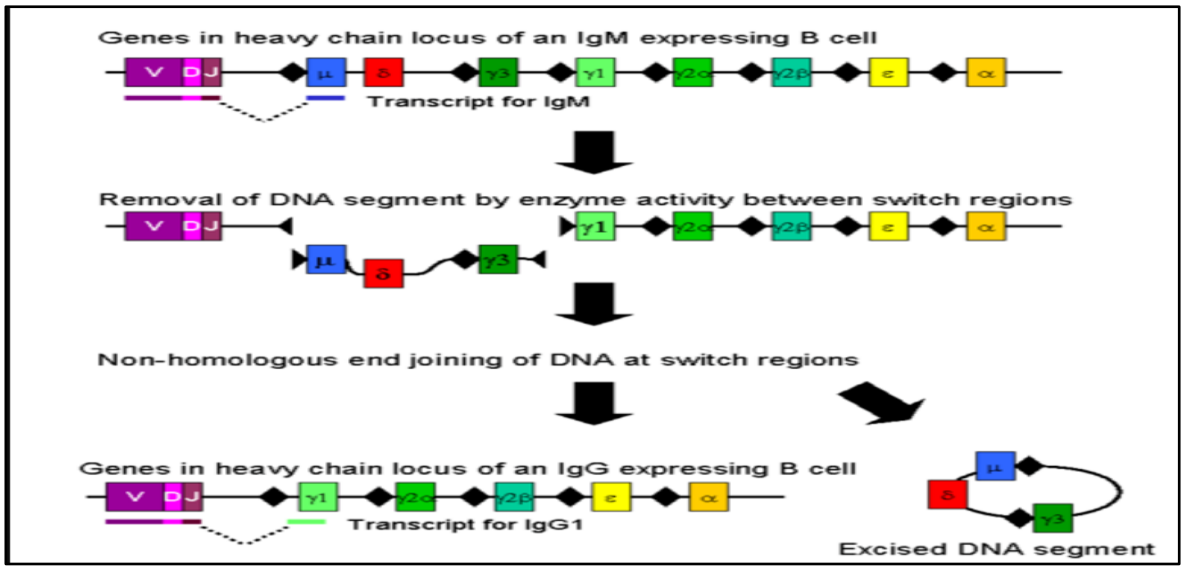
Antibodies

Immunoglobulin class switching

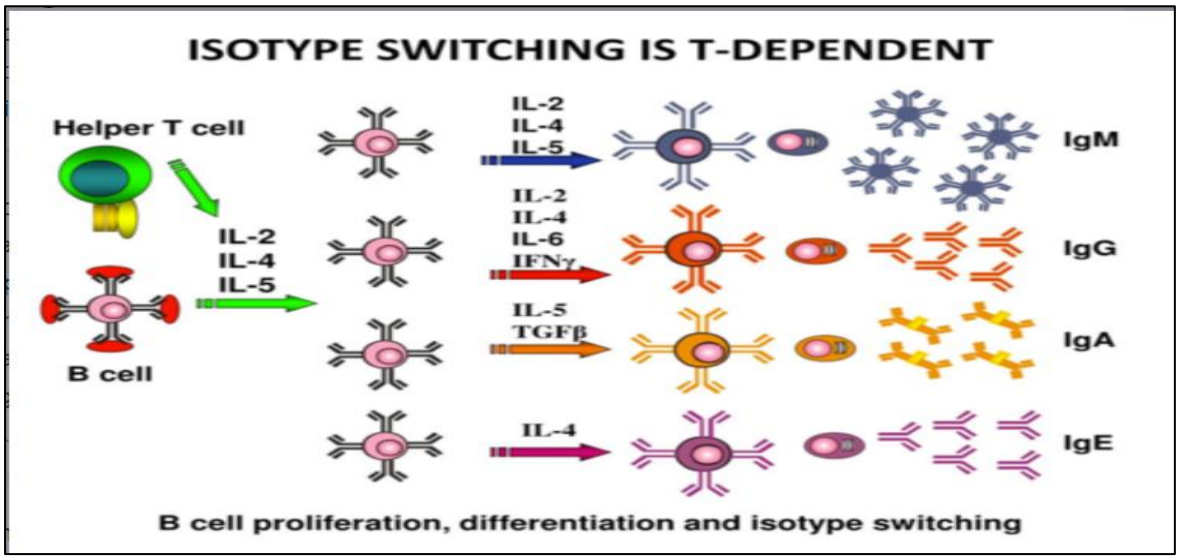
Immunoglobulin class switching, also known as **isotype switching**, isotypic commutation or class-switch recombination (CSR), is a biological mechanism that changes a B cell's production of immunoglobulin from one type to another, such as from the isotype IgM to the isotype IgG. During this process, the **constant-region portion** of the antibody **heavy chain is changed**, but the **variable region** of the **heavy chain stays the same** . Since the variable region does not change, **class switching does not affect antigen specificity**. Instead, the antibody retains affinity for the same antigens.

The antibody isotype of a B cell changes during cell development and activation. Immature B cells, which have never been exposed to an antigen, are known **as naïve B cells** and express only the IgM isotype in a cell surface bound form. B cells begin to express both IgM and IgD when they reach maturity; the co-expression of both of these immunoglobulin isotypes renders the B cell 'mature' and ready to respond to an antigen. B cell activation follows engagement of the cell-bound antibody molecule with an antigen, causing the cell to divide and differentiate into an antibody-producing cell, called a plasma cell. In this activated form, the B cell starts to produce antibody in a secreted form rather than a membrane-bound form. If these activated B cells encounter specific signaling molecules via their CD40 and cytokine receptors (both modulated by T helper cells), they undergo antibody class switching to produce IgG, IgA or IgE antibodies (from IgM or IgD) that have defined roles in the immune system.





Mechanism of class-switch recombination that allows isotype switching in activated B cells.



Monoclonal antibody

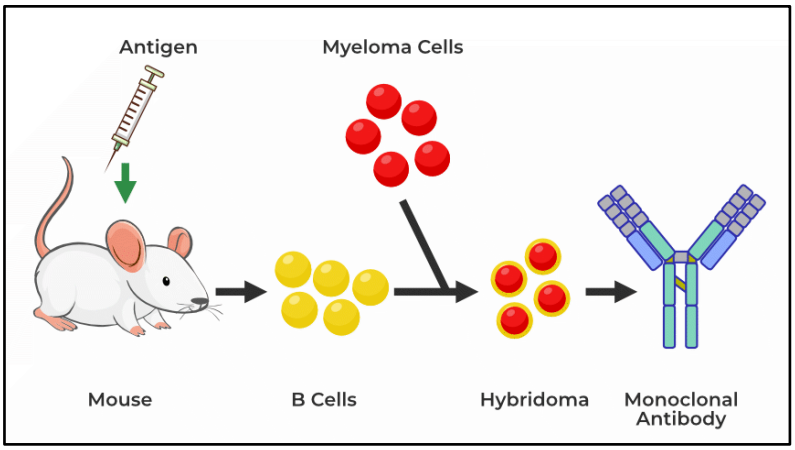
A monoclonal antibody is an antibody produced from a cell lineage made **by cloning a unique white blood cell**. All subsequent antibodies derived this way trace back to a unique parent cell.

Monoclonal antibodies can have monovalent affinity, binding only to the same epitope (the part of an antigen that is recognized by the antibody). In contrast, polyclonal antibodies bind to multiple epitopes and are usually made by several different antibody-secreting plasma cell lineages.

It is possible to produce monoclonal antibodies that specifically bind to almost any suitable substance; they can then serve to detect or purify it. This capability has become an investigative tool in biochemistry, molecular biology, and medicine. Monoclonal antibodies are being used on a clinical level for both the diagnosis and therapy of several diseases. In 2020, the administration of monoclonal antibodies was authorized by several countries for treating moderate symptoms of COVID-19.

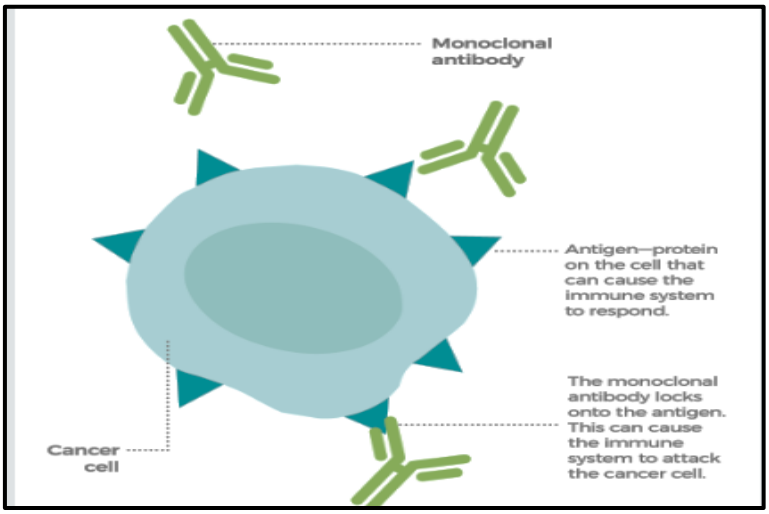
Monoclonal antibodies (MAbs) are proteins produced by **hybrid cells (hybridomas) resulting from the fusion of a B lymphocyte (BL)** capable of producing specific antibodies against a certain antigen, though in a limited manner, and a myeloma cell capable of unlimited production of nonspecific antibodies. **The fusion between a B lymphocyte (BL) and myeloma cell** results in a mixture of cells from which a selection is made of only those cells that produce specific antibodies in an almost unlimited manner. These cells are **called hybridomas**, and produce MAbs that are **all identical** and are specifically targeted to a concrete antigen.

The laboratory production of these MAbs is simple. A rodent (rat, hamster, rabbit) is immunized with an antigen, after which B lymphocytes are extracted from the spleen or a lymph node. These cells produce specific antibodies against the antigen to which the rodent was immunized. These BLs are then fused with myeloma cells, followed by the selection of those fused cells or hybridomas that form MAbs on an unlimited basis, targeted against the antigen to which the rodent was immunized. The capacity of a hybridoma to produce MAbs **persists indefinitely**, and they can be stored frozen and reconstituted at any time.



MAbs for diagnostic purposes

1-Diagnosis of neoplastic diseases : MAbs have been produced against surface antigens of tumor cells and molecules secreted by such cells, corresponding to a broad range of neoplasms. **Neoplasms** MAbs combined with antineoplastic drugs are specifically targeted to tumor cell receptors, thus avoiding damage to the healthy cells.



2-Autoimmune diseases : Autoimmune diseases are produced as a consequence of anomalous T lymphocyte (TL) activation ,use is made of MAbs targeted to T lymphocyte (TL) .

3-Treatment of graft rejection in transplant patients :In the treatment of acute rejection in transplant patients, use is made of MAbs targeted to TL surface antigens, with the purpose of inhibiting their function and thus avoiding graft rejection.

4-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.

Some commonly-used assays for antibody :

- ELISA (enzyme-linked immunosorbent assay)
- RIA (radioimmunoassay)
- Gel Precipitation
- Fluorescence-based (microscopic, cells and tissue sections)
- Flow cytometry
- Haemagglutination (e.g. influenza)
- Complement fixation (e.g. herpesviruses)
- Virus neutralization.