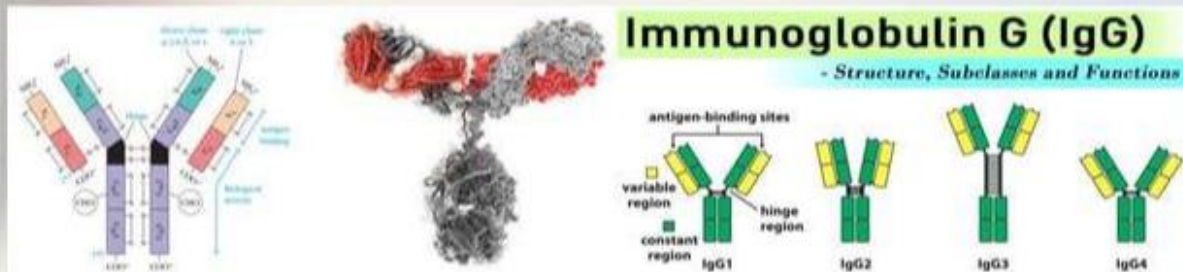


# ANTIGENIC DETERMINANTS ON IMMUNOGLOBULINS

Isotype, Allotype, Idiotype

## INTRODUCTION

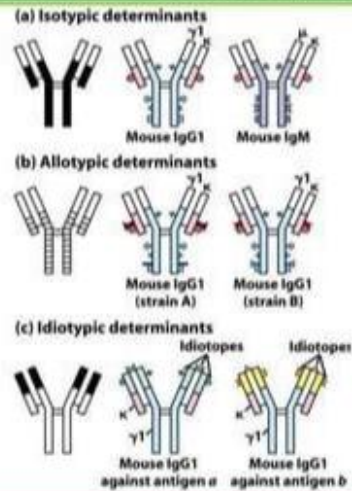
- Since antibodies are glycoproteins, they can themselves function as potent immunogens to induce an antibody response.
- Such anti-Ig antibodies are powerful tools for the study of B-cell development and humoral immune responses.



## Antigenic determinants on immunoglobulins

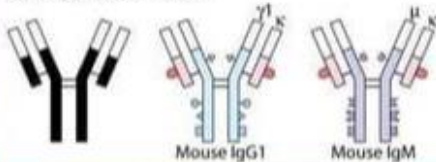
The antigenic determinants, or epitopes, on immunoglobulin molecules fall into three major categories: isotypic, allotypic, and idiotype determinants, which are located in characteristic portions of the molecule.

- Isotype
- Allotype
- Idiotype



## ISOTYPE

(a) Isotypic determinants



Isotypic determinants are constant region determinants that distinguish each Ig class and subclass within a species.

Isotype Isotypic determinants are constant-region determinants that collectively define each heavy-chain class and subclass and each light-chain type and subtype within a species.

Each isotype is encoded by a separate constant region gene, and all members of a species carry the same constant-region genes (which may include multiple alleles).

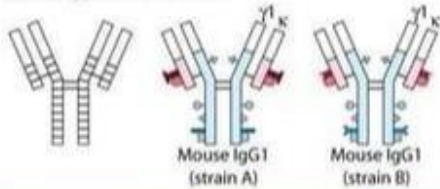
Within a species, each normal individual will express all isotypes in the serum.

Different species inherit different constant-region genes and therefore express different isotypes. Therefore, when an antibody from one species is injected into another species, the isotypic determinants will be recognized as foreign, inducing an antibody response to the isotypic determinants on the foreign antibody.

Anti-isotype antibody is routinely used for research purposes to determine the class or subclass of serum antibody produced during an immune response or to characterize the class of membrane-bound antibody present on B cells.

# ALLOTYPE

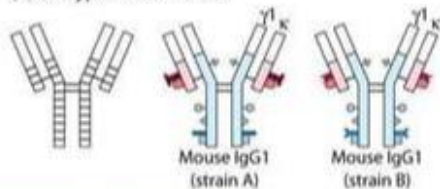
(b) Allotypic determinants



Allotypic determinants are subtle amino acid differences encoded by different alleles of isotype genes. Allotypic differences can be detected by comparing the same antibody class among different inbred strains.

- Allotype Although all members of a species inherit the same set of isotype genes, multiple alleles exist for some of the genes. These alleles encode subtle amino acid differences, called allotypic determinants, that occur in some, but not all, members of a species.
- The sum of the individual allotypic determinants displayed by an antibody determines its allotype.
- In humans, allotypes have been characterized for all four IgG subclasses, for one IgA subclass, and for the light chain.
- The  $\gamma$ -chain allotypes are referred to as Gm markers. At least 25 different Gm allotypes have been identified; they are designated by the class and subclass followed by the allele number, for example, G1m(1), G2m(23), G3m(11), G4m(4a).
- Of the two IgA subclasses, only the IgA2 subclass has allotypes, as A2m(1) and A2m(2). The light chain has three allotypes, designated m(1), m(2), and m(3).

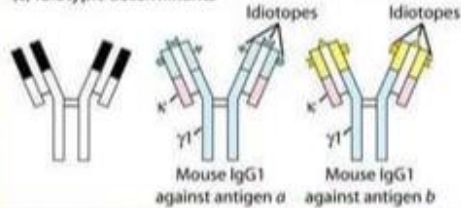
(b) Allotypic determinants



- Each of these allotypic determinants represents differences in one to four amino acids that are encoded by different alleles.
- Antibody to allotypic determinants can be produced by injecting antibodies from one member of a species into another member of the same species who carries different allotypic determinants.
- Antibody to allotypic determinants sometimes is produced by a mother during pregnancy in response to paternal allotypic determinants on the fetal immunoglobulins. Antibodies to allotypic determinants can also arise from a blood transfusion.

# IDIOTYPE

(c) Idiotypic determinants



Idiotypic determinants are generated by the conformation of the amino acid sequences of the heavy- and light-chain variable regions specific for each antigen. Each individual determinant is called an **idiotope**, and the sum of the individual idiotopes is the **idiotype**.

The unique amino acid sequence of the VH and VL domains of a given antibody can function not only as an antigen-binding site but also as a set of antigenic determinants.

The idiotypic determinants arise from the sequence of the heavy- and light-chain variable regions.

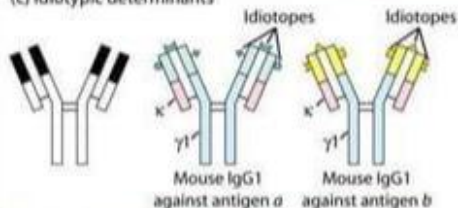
Each individual antigenic determinant of the variable region is referred to as an **idiotope**.

In some cases an idiotope may be the actual antigen-binding site, and in some cases an idiotope may comprise variable-region sequences outside of the antigen binding site.

Each antibody will present multiple idiotopes; the sum of the individual idiotopes is called the **idiotype** of the antibody.

Because the antibodies produced by individual B cells derived from the same clone have identical variable-region sequences, they all have the same idiotype.

(c) Idiotypic determinants



Anti-idiotype antibody is produced by injecting antibodies that have minimal variation in their isotypes and allotypes, so that the idiotypic difference can be recognized.

Often a homogeneous antibody such as myeloma protein or monoclonal antibody is used. Injection of such an antibody into a recipient who is genetically identical to the donor will result in the formation of anti-idiotype antibody to the idiotypic determinants.