

Immunoglobulin G4 (IgG4)

Immunoglobulin G4 (IgG4) is one of the four subclasses of immunoglobulin G (IgG), representing less than 5% of total serum IgG in healthy individuals. It plays a unique role in immune regulation and is notably implicated in IgG4-related disease (IgG4-RD).

Basic Properties

- Molecular weight: ~150 kDa
- Serum concentration: 0.05–1.5 g/L
- Comprises <5% of total IgG
- Half-life: ~21 days
- Poorly activates complement via the classical pathway

Structural Characteristics

- Fab-arm exchange: IgG4 molecules can exchange half-molecules, leading to functionally monovalent antibodies
- Low affinity for Fc receptors and C1q → reduced pro-inflammatory activity

Functional Role

- Generally considered anti-inflammatory
- Acts as a “blocking antibody” in allergy desensitization therapy
- May downregulate immune responses by competing with other IgG subclasses

Clinical Relevance

↑ Elevated IgG4 levels observed in:

- IgG4-related disease (IgG4-RD)
- Atopic dermatitis
- Parasitic infections
- Certain cancers (e.g., pancreatic)
- Chronic inflammatory diseases (non-specific)

↓ Low IgG4 levels:

- Often not clinically significant unless associated with other immunoglobulin deficiencies

Measurement

- Serum IgG4 quantification by nephelometry or ELISA
- Used in diagnosis and monitoring of IgG4-RD, but not diagnostic alone

In IgG4-Related Disease (IgG4-RD)

- Elevated serum IgG4 in ~60–70% of cases
- Tissue infiltration with IgG4+ plasma cells is key for diagnosis
- Not all patients with elevated IgG4 have IgG4-RD, and vice versa

Differential Diagnosis for Elevated IgG4

- [Immunoglobulin G4-related disease](#)
- Allergic diseases
- Parasitic infections
- Multicentric Castleman disease
- Autoimmune pancreatitis
- Chronic sinusitis

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