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MEDICAL AFFAIRS

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Efgartigimod alfa Proposed Mechanism of Action

IgG autoantibodies contribute to the pathogenesis of IgG-mediated autoimmune diseases.[1] The neonatal Fc receptor (FcRn) is a key regulator of IgG recycling and half-life of IgG[2-4]

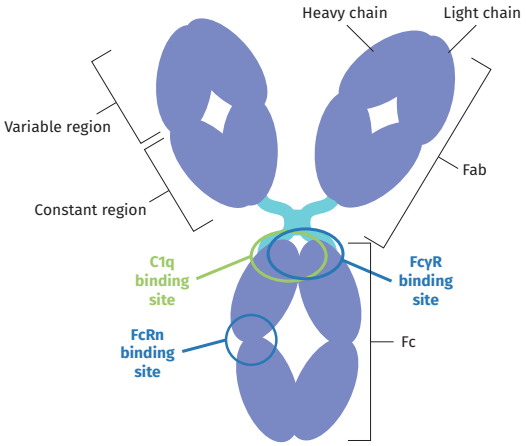
Structure and Function of IgG

Major functions[4,5]

- Neutralizing microbes and toxins
- Opsonizing antigens for phagocytosis
- Activating complement system
- Protecting the newborn

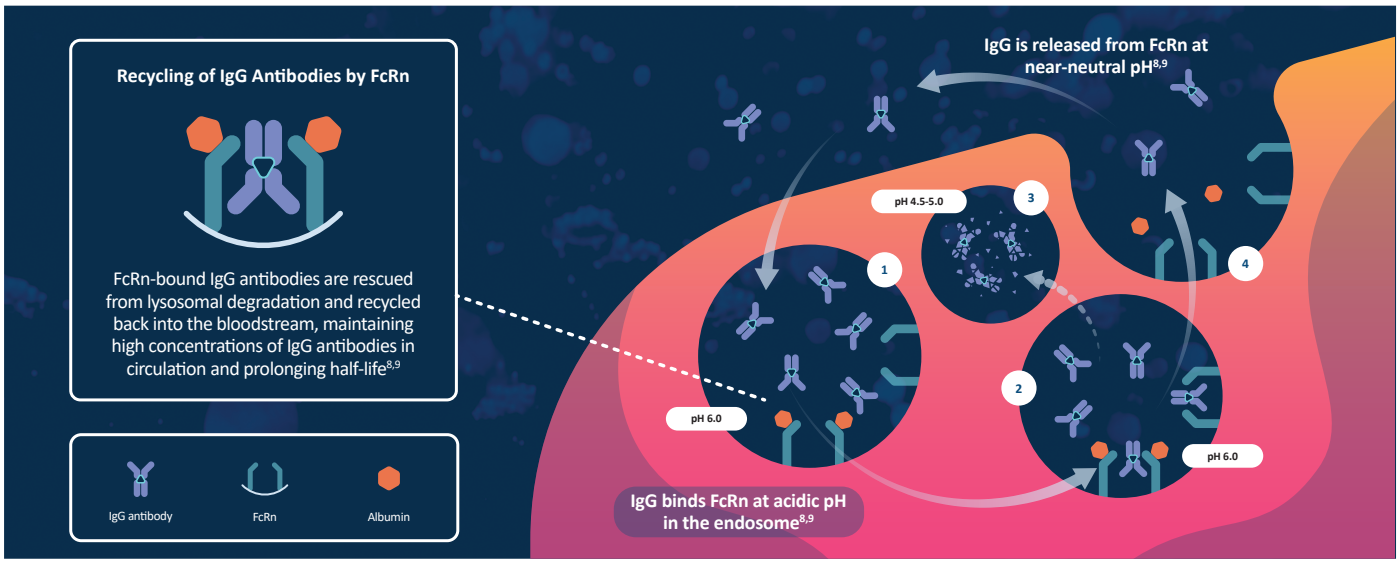
Key facts

- Primary immunoglobulin in serum with the longest half-life[4-6]
- Only immunoglobulin that crosses placenta[5]
- Numerous applications as diagnostic tool or therapeutic agent[7]
- In various autoimmune conditions, self-reactive IgGs are causal to disease symptoms[1]



IgG Autoantibodies and FcRn-mediated Recycling

IgGs are recycled by FcRn, extending the half-life of IgG and IgG autoantibodies[8,9]



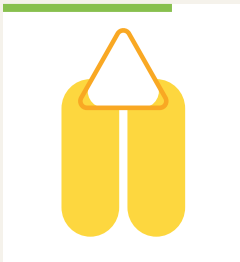
FcRn serves diverse functions in IgG endocytosis, transcytosis, and recycling across multiple tissues and cells, including skin, eyes, brain, liver, kidney, placenta, blood vessels, and the respiratory, intestinal, and genital tracts[10]

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Design of Efgartigimod alfa

Efgartigimod alfa is a human IgG1 antibody Fc fragment engineered for increased affinity to FcRn[8,11]



In a Phase 1 study in healthy volunteers:

- Observed reduction of levels of all IgG subtypes[8]
- Observed dose-dependent reduction in pathogenic IgG autoantibodies[8]

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Abbreviations: C1q, complement component 1q; Fab, fragment antigen binding; FcγR, Fc gamma receptor; Fc, fragment crystallizable region; FcRn, neonatal Fc receptor; Ig, immunoglobulin.

References

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