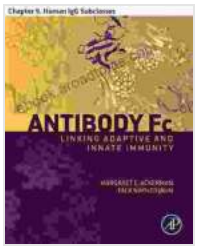
Antibody Fc Chapter: A Comprehensive Guide to Human IgG Subclasses

Antibodies, the cornerstone of adaptive immunity, are Y-shaped proteins produced by B cells that specifically recognize and neutralize foreign invaders. They play a crucial role in defending the body against infections and diseases.

One significant aspect of antibody research focuses on the Fc region, the tailpiece of the antibody responsible for mediating interactions with immune effector cells and triggering various immune responses.

Immunoglobulin G (IgG) is the most abundant antibody subclass in humans, accounting for approximately 75% of total immunoglobulins. IgG subclasses, namely IgG1, IgG2, IgG3, and IgG4, exhibit unique structural and functional characteristics.



Antibody Fc: Chapter 9. Human IgG Subclasses

★★★★★ 5 out of 5

Language	: English
File size	: 720 KB
Text-to-Speech	: Enabled
Enhanced typesetting	: Enabled
Print length	: 49 pages
Screen Reader	: Supported

IgG1: The All-Rounder

IgG1 is the most prevalent IgG subclass, constituting about 60% of total IgG. It boasts a balanced profile of effector functions and plays a versatile role in both humoral and cellular immunity.

- **Antibody-dependent cell-mediated cytotoxicity (ADCC)**: IgG1 effectively engages with Fc receptors on immune cells, triggering the destruction of target cells through ADCC.
- **Complement-dependent cytotoxicity (CDC)**: IgG1 binds to complement proteins, initiating a cascade of events that ultimately results in target cell lysis.
- **Opsonization**: IgG1 helps tag pathogens for recognition and engulfment by phagocytic cells.

IgG2: The Subclass with Enhanced ADCC Potency

IgG2 accounts for about 25% of total IgG. It stands out with its particularly robust ADCC activity, which is essential for controlling viral infections and tumor cell killing.

- **ADCC**: IgG2 is highly effective in promoting ADCC, efficiently triggering the destruction of target cells by natural killer (NK) cells and other immune effector cells.
- **Neutralization**: IgG2 contributes to neutralizing pathogens and toxins, preventing them from binding to receptors on host cells.
- **Cytokine modulation**: IgG2 has been shown to modulate cytokine production, influencing the overall immune response.

IgG3: The Inflammation Mediator

IgG3 constitutes approximately 5% of total IgG. It is known for its potent complement activation capability, making it crucial for combating specific pathogens and immune disFree Downloads.

- **CDC**: IgG3 is highly efficient in activating the complement cascade, leading to target cell lysis.
- **Antibody-dependent cellular phagocytosis (ADCP)**: IgG3 facilitates the phagocytosis of target cells by macrophages through ADCP.
- **Inflammation**: IgG3 has pro-inflammatory properties, contributing to the recruitment of immune cells and promoting tissue inflammation.

IgG4: The Subclass with Regulatory Functions

IgG4 represents a minor subclass, accounting for about 5% of total IgG. It surprisingly exhibits anti-inflammatory and immunomodulatory properties.

- **Antibody blockade**: IgG4 can block the binding of other antibodies to antigens, inhibiting antibody-mediated effector functions.
- **Immune tolerance**: IgG4 has been associated with immune tolerance, preventing excessive or inappropriate immune responses.
- **Allergic diseases**: IgG4 is often reduced in allergic diseases, suggesting a role in regulating allergic reactions.

In-depth understanding of IgG subclasses has opened avenues for therapeutic applications. Engineered antibodies tailored to specific IgG subclasses can enhance their functionality for treating various diseases.

- **IgG1**: Antibodies engineered with an IgG1 Fc region are commonly used in cancer immunotherapy, due to their potent ADCC and CDC

activities.

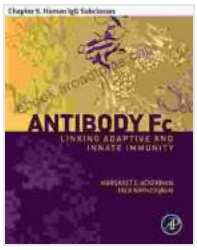
- **IgG2**: Antibodies with an IgG2 Fc region are particularly valuable in treating viral infections, leveraging their strong ADCC capability.
- **IgG3**: Engineered antibodies with an IgG3 Fc are beneficial in combating bacterial infections, utilizing their robust complement activation potential.
- **IgG4**: Antibodies modified with an IgG4 Fc region have shown promise in treating autoimmune diseases and allergic conditions, as they can modulate immune responses and prevent excessive inflammation.

In addition to IgG subclass selection, researchers have developed advanced Fc engineering techniques to further enhance antibody functionality:

- **Fc glycosylation**: Modifying the glycosylation pattern of the Fc region can impact antibody binding affinity, stability, and effector functions.
- **Fc fucosylation**: Fucnsylation of the Fc region has been shown to modulate antibody-Fc receptor interactions, potentially improving effector cell engagement.
- **Fc mutants**: Targeted mutations within the Fc region can fine-tune antibody properties, enhancing specific immune responses or reducing unwanted effects.

The Antibody Fc Chapter provides a comprehensive understanding of human IgG subclasses, their unique structural features, and functional roles in immunity. This knowledge has paved the way for the development of highly effective antibody-based therapies. By manipulating IgG

subclasses and employing advanced Fc engineering techniques, researchers can tailor antibodies to specific therapeutic needs, revolutionizing the treatment of a wide range of diseases.



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