DEEP DIVE MOLECULES THAT MATTER

SEPTEMBER 2024

Dr.Reddy's

RITUXImAb

sounds like (ruh·tuhk·suh·mab)

"monoclonal antibody

mAbs are **similar to our body's antibodies** that are designed and made in a **laboratory**, meant to **modulate our immune system.**

Rituximab is a **chimeric** monoclonal antibody (mAb) used to treat certain autoimmune diseases and types of cancer.

Used to treat | **Non-Hodgkin lymphoma** and **Rheumatoid arthritis**

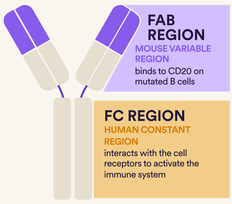
Chimeric mAbs are a type of antibody that are made in a lab by **combining a human antibody with a mouse or rat's antibody.**

The **mouse** or rat part of the antibody (murine variable) **binds to the target antigen**, while the **human** part makes it **less likely to be destroyed** by the body's immune system.

1st In the year **2007**

Dr. Reddy's was the first company to launch a Rituximab biosimilar in the world.

MOLECULAR STRUCTURE



MECHANISM OF ACTION

1 Targeting CD20 on B cells

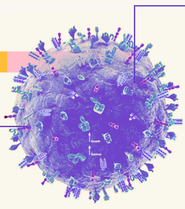
Rituximab is designed to bind specifically to the CD20 antigen

2 Depleting B cells

After binding to CD20, Rituximab initiates the process for B cell depletion

B cells

Part of the immune system, involved in producing antibodies



CD20

A protein found on the surface of most B cells

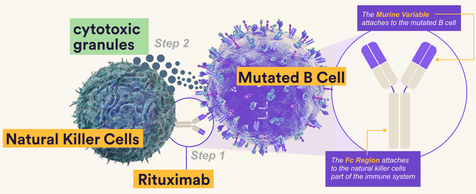
B CELL DEPLETION PROCESSES

Fun Fact! Rituximab has **multiple mechanisms of action** because the binding to the CD20 antigen can trigger **various immune responses depending on the cellular environment** resulting in different types of cell destruction.

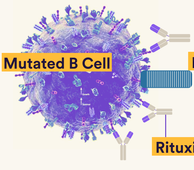
A Antibody-Dependent Cellular Cytotoxicity (ADCC):

In ADCC[1], the immune cells **recognize the mutated cells** by their attachment to Rituximab and bind to the Fc region of Rituximab.

This interaction triggers the natural killer cells to **release cytotoxic granules that induce cell death in the mutated B cell.**



B Complement-Dependent Cytotoxicity (CDC):



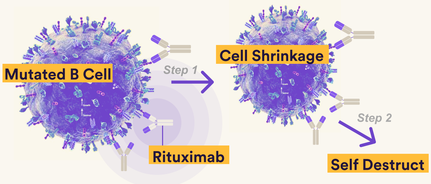
It is a cylindrical structure made up of proteins that form a pore in the cell membrane.

In CDC[2], the binding of Rituximab to the mutated B cell, activates the **complement system** (a group of proteins in the blood). This structure is known as the **membrane attack complex (MAC)**.

These complement proteins attach to the mutated B cell and **form pores, leading to the destruction of the cell.**

C Direct Apoptosis

In Direct Apoptosis, the binding of Rituximab to the mutated B cell can **send a signal directly** to it, causing it to **shrink and eventually self-destruct** through the process known as apoptosis.



CD20 is present on most B cells (both healthy and cancerous) **so...**

Does Rituximab kill the healthy cells as well?

Yes, Rituximab does target and destroy healthy B cells along with the cancerous ones.

While this can lead to a **temporary reduction** in the number of healthy B cells, the **body is capable of regenerating** these cells after the treatment is completed.

1997 Rituximab was the first mAb to be approved for the treatment of cancer.

World Health Organization Rituximab is on the WHO's **List of Essential Medicines**

Citations & Glossary

[1] ADCC - Antibody Dependent Cellular Cytotoxicity
[2] CDC - Compliment Dependent Cytotoxicity
[3] MAC - Membrane Attack Complex

Citations & Glossary:

1. Hanif, N., & Anwer, F. (2024). Rituximab. In StatPearls. StatPearls Publishing.

2. Boross, P., & Leusen, J. H. (2012). Mechanisms of action of CD20 antibodies. American journal of cancer research, 2(6), 676–690.

3. Wang, S. Y., Racila, E., Taylor, R. P., & Weiner, G. J. (2008). NK-cell activation and antibody-dependent cellular cytotoxicity induced by rituximab-coated target cells is inhibited by the C3b component of complement. Blood, 111(3), 1456–1463. https://doi.org/10.1182/blood-2007-02-074716

4. Johnson, P., & Glennie, M. (2003). The mechanisms of action of rituximab in the elimination of tumor cells. Seminars in oncology, 30(1 Suppl 2), 3–8. https://doi.org/10.1053/sonc.2003.50025

5. Golay, J., & Taylor, R. P. (2020). The Role of Complement in the Mechanism of Action of Therapeutic Anti-Cancer mAbs. Antibodies (Basel, Switzerland), 9(4), 58.

6. Cerny, T., Borisch, B., Introna, M., Johnson, P., & Rose, A. L. (2002). Mechanism of action of rituximab. Anti-cancer drugs, 13 Suppl 2, S3–S10. https://doi.org/10.1097/00001813-200211002-00002 https://doi.org/10.3390/antib9040058

7. Kurosawa, K., Lin, W., & Ohta, K. (2014). Chimeric antibodies. Methods in molecular biology (Clifton, N.J.), 1060, 139–148. https://doi.org/10.1007/978-1-62703-586-6_8