Rituximab: A Breakthrough in Hematological Cancer Treatments

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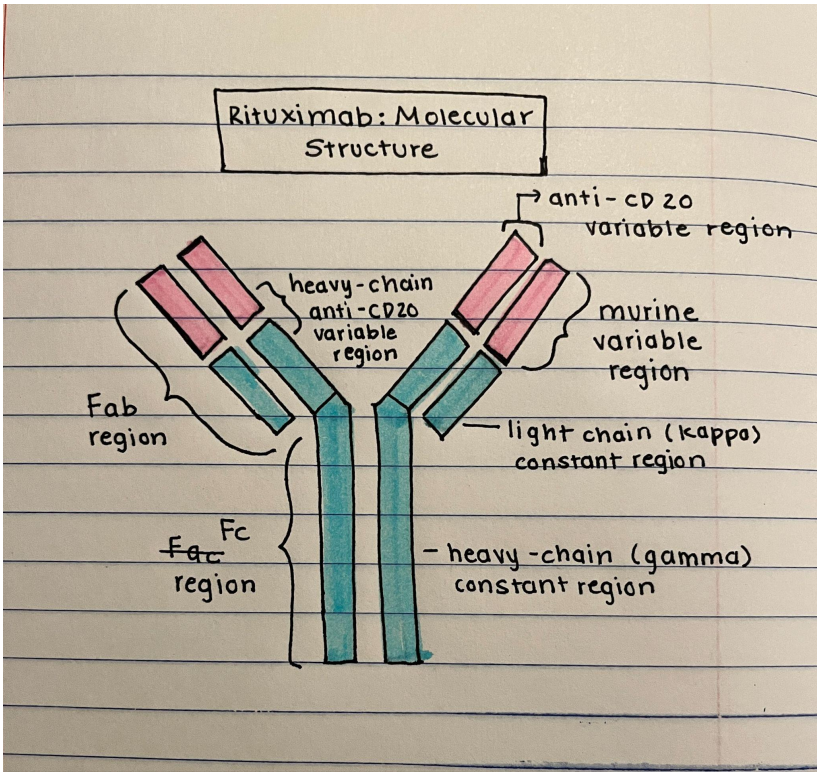
One prominent monoclonal antibody currently used in medicine is Rituximab. Rituximab is an anti-CD20 mAB primarily used to treat B-cell non-Hodgkin's lymphoma (NHL) and B-cell chronic lymphocytic leukemia (CLL) (1). Approved by the FDA for cancer treatments in 1997, the use of rituximab rather than solely relying on chemotherapy revolutionized hematological cancer treatments during the turn of the 21st century (2). The primary condition that rituximab was initially designed to target is B-cell non-Hodgkin's lymphoma, a cancer characterized by the malignant growth of lymphoid tissues from mature B-cells. Accounting for 30 - 40% of all diagnosed lymphomas, B-cell non-Hodgkin's lymphoma is prominent in populations over the age of 65 and the incidence of B-cell NHL cases has increased by over 80% since the 1970s (3). There are various risk factors associated with NHL including the Epstein-Barr virus, Hepatitis-C virus (HCV), insecticides, and autoimmune deficiencies including Hashimoto's and Sjörgen syndrome. The most common symptoms of B-cell NHL include night sweats, fever, fatigue, weight loss, and swollen lymph nodes (4). The prognosis of B-cell NHL depends on the severity and progression of the disease and can be classified as either indolent or aggresive. In addition, rituximab also treats chronic B-cell lymphocytic leukemia. Similar to B-cell NHL, chronic B-cell lymphocytic leukemia primarily affects older populations with the median diagnosis age of 67 years (3). B-cell lymphocytic leukemia is the malignant growth of white blood cells or lymphocytes found in bone marrow, and symptoms include fatigue, night sweats, frequent bleeding, and bruising (3).

Rituximab is an IgG class antibody, which is the most common class of antibodies (3). Below is a sketch of rituximab developed from Sinha et al. in 2021 in their study concerning pediatric nephrology (5).



As an anti-CD20 mAB, rituximab attacks malignant B cells by binding onto the CD20 transmembrane protein of mature, malignant B-cells (5). It is important to note that during B-cell development, CD20 proteins (which are thought to be calcium channels) are present on the cell membrane. However, CD20 proteins are downregulated once normal B-cells completely mature. Therefore, if mature B-cells still contain high levels of CD20 surface proteins, it is a sign of malignancy, and multiple studies have shown that over 90% of mature cancerous B-cells contain high levels of CD20 (4). When rituximab, the antibody, binds onto the CD20 surface proteins of malignant B-cells, the antigen, this triggers cell deactivation through apoptosis or cell-mediated cytotoxicity (6). By eliminating malignant B-cells, the majority of patients suffering from NHL or B-cell lymphocytic leukemia achieve remission and significant tumor shrinkage, especially for elderly patients who are not as physically able to undergo chemotherapy (1). In addition, one key benefit of using anti-CD20 mAB treatments is that pre-B hematopoietic stem cells do not contain

CD20 on their cell surfaces. Consequently, once the majority of malignant B cells are killed by rituximab treatments, healthy and new B cells can be regenerated (4). Furthermore, researchers have discovered that CD20 undergoes minimal post-translational modifications, which means that their binding sites are relatively common (4). Along with the absence of a natural ligand, CD20 receptors are highly favorable target for rituximab, and the FDA has even recently approved the use of rituximab in several clinical trials for autoimmune disorders including multiple sclerosis, lupus, and rheumatoid arthritis (7). Because of its safety and efficacy, rituximab is a revolutionary treatment for hematological cancers and autoimmune conditions.

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