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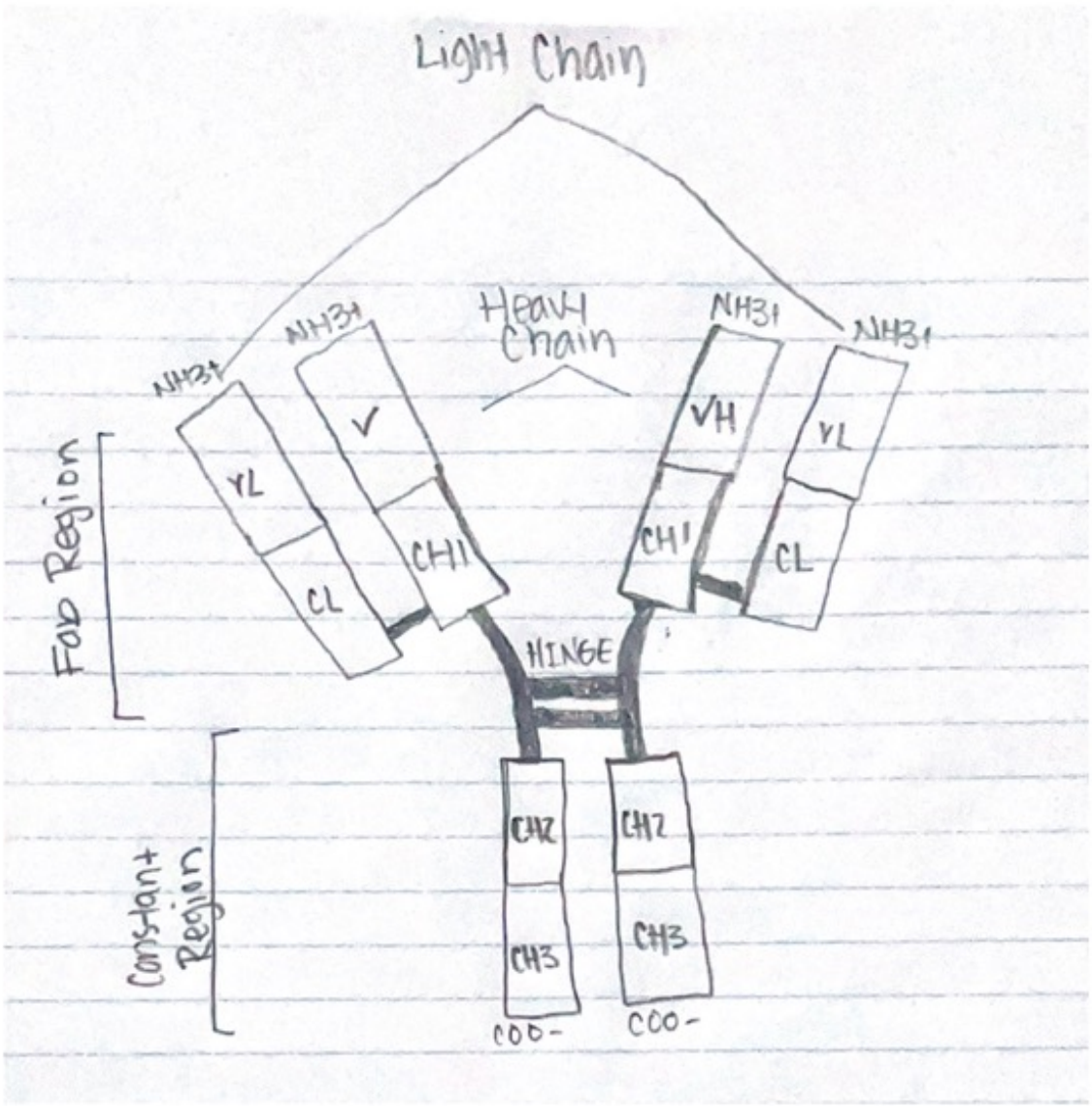
Anifrolumab

Anifrolumab is an Anti-Interferon-alpha receptor monoclonal antibody. This antibody drug is used in moderate and severe Systemic Lupus Erythematosus (SLE), which is a multisystem autoimmune disease that leads to significant morbidity and shortened lifespan. (Peng, L; etc., 2015) SLE is a chronic disease that causes inflammation in connective tissues. Symptoms of SLE are varied, but some examples of organ and system involvement can be seen in the skin, joints, kidneys, lungs, central nervous system, and the blood-forming system. SLE can begin with symptoms of fatigue, malaise, fever, loss of appetite, and also weight loss. Patients that are affected the most by SLE may also feel joint pain or muscle pain and weakness. SLE can also lead to developed kidney disease known as nephritis or also heart problems. These heart problems can include inflammation of the sac-like membrane around the heart known as pericarditis and also abnormalities of the heart valves. Patients with SLE are more likely to have heart disease caused by fatty buildup in blood vessels. Inflammation caused by SLE can also damage the nervous system, which can result in peripheral neuropathy, such as strokes, seizures, and cognitive impairment. Other symptoms that can be caused by SLE are anxiety and depression. SLE can be caused by polymorphisms in many genes in which multiple genetic factors are involved. There are rare cases where mutations in a single gene can cause SLE, but most of the time it is associated with the immune system function that controls proper targeting and control of the immune response. (Pisetsky, D; 2019)

Anifrolumab is a fully human IgG1k monoclonal antibody that binds to the type I IFN-alpha/beta/omega receptor (IFNAR), in order to prevent signaling by all type I IFNs. Anifrolumab was developed in order to treat autoimmune diseases. There are multiple epitope mapping approaches to determine how anifrolumab interacts with interferon alpha receptor 1 (IFNAR1). To identify the epitope, enzymatic fragmentation is used with phage-peptide library panning and mutagenesis approaches. Anifrolumab recognizes the SD3 subdomain of IFNAR1 with the critical residue R279. Anifrolumab sterically inhibits the binding of IFN ligands to IFNAR1, which caused the blocking of the formation of ternary IFN/IFNAR1/IFNAR2 signaling complex. The constant domain of anifrolumab contains a triple mutation L234F/L235E/P331S in order to reduce antibody Fc-mediated effector functions. Due to anifrolumab binding to a function-blocking epitope on the IFNAR1 that is different from that of IFNAR1, then neutralizes the antibodies, and provides a molecular basis for the antagonistic properties of anifrolumab. (U.S. National Library of Medicine, 2022)


Light Chain
Heavy Chain
NH3+
NH3+
NH3+
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VL
V
VH
VL
CH1
CL
CH1
CL
HINGE
Fab Region
Constant Region
CH2
CH2
CH3
CH3
COO-
COO-

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