

Anti-Human CD38 (Daratumumab) [Clone HuMax-CD38] — Fc Muted™

Biosimilar Recombinant Human Monoclonal Antibody

Product Information

Product No.:	LT2505
Clone:	HuMax-CD38
Isotype:	Human Human IgG1κ

Product Description

Specificity:

This non-therapeutic biosimilar antibody uses the same variable region sequence as the therapeutic antibody Daratumumab. This product is for research use only. Daratumumab activity is directed against human CD38.

Antigen Distribution:

CD38 is expressed on plasma cells, other lymphoid and myeloid cell populations, natural killer cells, B cells, activated T cells, some peripheral regulatory T cells, monocytes, lymph node germinal center lymphoblasts, intrafollicular cells, dendritic cells, erythrocytes, platelets, committed stem cells, Purkinje cells, neurofibrillary tangles in the brain, epithelial cells in the prostate, β-cells in the pancreas, retinal cells in the eye, and sarcolemma of smooth and striated muscle. CD38 can also be detected on early osteoclast progenitors but not on osteoblasts and mature osteoclasts. CD38 expression is very high and uniform on all malignant cells in multiple myeloma. While generally found on the plasma membrane, CD38 has also been detected in the cytosol or nucleus in brain, pancreatic acinar cells, smooth muscle, and osteoclasts.

Background:

CD38 is a type II transmembrane glycoprotein that functions as an adhesion molecule with ectoenzymatic activities that contribute to intracellular calcium mobilization^{1,2}. Dysregulation is associated with a number of diseases, including HIV, autoimmune, type II diabetes mellitus, osteoporosis, and hematological malignancies such as multiple myeloma (MM)¹, a neoplasm characterized by clonal expansion of malignant plasma cells². CD38 is a target of MM immunotherapy, and, in 2015, the US Food and Drug Administration approved the use of daratumumab for MM treatment³.

Daratumumab kills CD38-expressing tumor cells by inducing apoptosis directly through Fc mediated cross linking^{3,4} as well as by immune-mediated tumor cell lysis via complement dependent cytotoxicity (CDC)⁵, antibody dependent cell mediated cytotoxicity (ADCC)⁵, and antibody dependent cellular phagocytosis (ADCP)^{3,4,6}. Daratumumab also modulates CD38 enzymatic activities, blunting cyclase

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activity and enhancing hydrolase activity, resulting in decreased Ca^{2+} mobilization and reduced downstream signaling¹. Furthermore, subsets of myeloid derived suppressor cells (CD38+MDSCs), regulatory T cells (CD38+Tregs), and B cells (CD38+Bregs) are decreased by daratumumab³, and CD38 is uniformly removed from the surface of red blood cells without inducing detectable hemolysis⁷.

Daratumumab was generated by immunizing HuMAb-mice with purified HA-CD38 recombinant protein alone or alternating with CD38-transfected NIH-3T3 cells⁵. Mouse splenocytes and lymph node cells were isolated, fused with SP2/0 myeloma cells, and tested for binding to CHO-CD38 cells. The daratumumab epitope maps to two β -strands containing amino acids 233–246 and 267–280 of CD38. Binding to CD38 is completely abolished when the serine at position 274 is replaced with phenylalanine. Daratumumab does not bind to cynomolgus CD38.

Daratumumab clone AL9, a non-therapeutic biosimilar antibody for research use only was developed recombinantly and has the same variable regions as the original therapeutic.

Known Reactivity Species:
Human

Expression Host:
HEK-293 Cells

Format:
Purified No Carrier Protein

Immunogen:
Human CD38

Formulation

This biosimilar antibody is aseptically packaged and formulated in 0.01 M phosphate buffered saline (150 mM NaCl) PBS pH 7.2 - 7.4 with no carrier protein, potassium, calcium or preservatives added. Due to inherent biochemical properties of antibodies, certain products may be prone to precipitation over time. Precipitation may be removed by aseptic centrifugation and/or filtration.

Purity
 $\geq 95\%$ by SDS Page, $\geq 95\%$ monomer by analytical SEC

Endotoxin
< 1.0 EU/mg as determined by the LAL method

Storage and Stability

Functional grade preclinical antibodies may be stored sterile as received at 2-8°C for up to one month. For longer term storage, aseptically aliquot in working volumes without diluting and store at $\leq -70^\circ\text{C}$.
Avoid Repeated Freeze Thaw Cycles.

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Product Preparation

Recombinant biosimilar antibodies are manufactured in an animal free facility using only *in vitro* protein free cell culture techniques and are purified by a multi-step process including the use of protein A or G to assure extremely low levels of endotoxins, leachable protein A or aggregates.

Pathogen Testing

To protect mouse colonies from infection by pathogens and to assure that experimental preclinical data is not affected by such pathogens, all of Leinco's recombinant biosimilar antibodies are tested and guaranteed to be negative for all pathogens in the IDEXX IMPACT I Mouse Profile.

Other Applications Reported in Literature:

ELISA,
WB,
IP,
FA,
FC

Country of Origin

USA

References

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