

**DESCRIPTION**

<b>Source</b>	Chinese Hamster Ovary cell line, CHO-derived human LAG-3 protein Leu23-Leu450, with a C-terminal 6-His tag Accession # P18627
<b>N-terminal Sequence Analysis</b>	Leu23
<b>Predicted Molecular Mass</b>	47 kDa

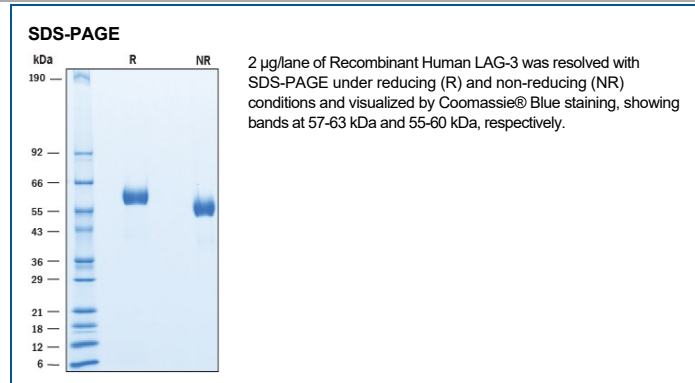
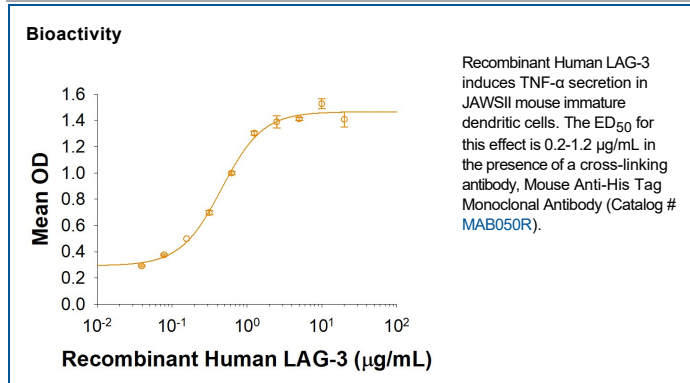
**SPECIFICATIONS**

<b>SDS-PAGE</b>	57-63 kDa, reducing conditions
<b>Activity</b>	Measured by its ability to induce TNF- $\alpha$ secretion by JAWSII mouse immature dendritic cells. The ED <sub>50</sub> for this effect is 0.2-1.2 $\mu$ g/mL in the presence of a cross-linking antibody, Mouse Anti-polyHistidine Monoclonal Antibody (Catalog # MAB050R).
<b>Endotoxin Level</b>	<0.10 EU per 1 $\mu$ g of the protein by the LAL method.
<b>Purity</b>	>95%, by SDS-PAGE visualized with Silver Staining and quantitative densitometry by Coomassie® Blue Staining.
<b>Formulation</b>	Lyophilized from a 0.2 $\mu$ m filtered solution in PBS. See Certificate of Analysis for details.

**PREPARATION AND STORAGE**

<b>Reconstitution</b>	Reconstitute at 500 $\mu$ g/mL in PBS.
<b>Shipping</b>	The product is shipped at ambient temperature. Upon receipt, store it immediately at the temperature recommended below.
<b>Stability &amp; Storage</b>	Use a manual defrost freezer and avoid repeated freeze-thaw cycles. <ul style="list-style-type: none"> <li>• 12 months from date of receipt, -20 to -70 °C as supplied.</li> <li>• 1 month, 2 to 8 °C under sterile conditions after reconstitution.</li> <li>• 3 months, <math>\leq</math> -20 °C under sterile conditions after reconstitution.</li> </ul>

**DATA**



**BACKGROUND**

LAG-3 (Lymphocyte activation gene-3), designated CD223, is a 70 kDa type I transmembrane protein that is a member of the immunoglobulin superfamily (IgSF) (1, 2). LAG-3 shares approximately 20% amino acid sequence homology with CD4, but has similar structure and binds to MHC class II with higher affinity, providing negative regulation of T cell receptor signaling (1, 2). Human LAG-3 cDNA encodes 525 amino acids (aa) that include a 28 aa signal sequence, a 422 aa extracellular domain (ECD) with four Ig-like domains, a transmembrane region and a highly charged cytoplasmic region. Within the ECD, human LAG-3 shares 70%, 67%, 76%, and 73% aa sequence identity with mouse, rat, porcine, and bovine LAG-3, respectively. LAG-3 is expressed on activated CD4<sup>+</sup> and CD8<sup>+</sup> T cells, NK cells, and plasmacytoid dendritic cells (pDC), but not on resting T cells (1-3). LAG-3 on activated CD4<sup>+</sup>CD25<sup>+</sup> Treg cells plays a role in their suppressive activity (4). LAG-3 limits the expansion of activated T cells and pDC in response to selected stimuli (3-5). A soluble 54 kDa form, sLAG-3, can be shed by metalloproteinases ADAM10 and TACE/ADAM17 (6, 7). While monomeric sLAG-3 itself may be inactive, shedding allows for normal T cell activation by removing negative regulation (7). Binding of a homodimerized sLAG-3/Ig fusion protein to MHC class II molecules induces maturation of immature DC, and secretion of cytokines such as IFN-gamma and TNF-alpha by type 1 cytotoxic CD8<sup>+</sup> T cells and NK cells (8, 9). sLAG-3/Ig has been used as a potential adjuvant to stimulate a cytotoxic anti-cancer immune response (9, 10). In mice, deletion of LAG-3 and another negative regulator, PD-1, facilitates anti-cancer response but also blocks self-tolerance and increases susceptibility to autoimmune diseases (11, 12). In humans, antibody-mediated down-regulation of LAG-3 and PD-1 allows more effective control of chronic malaria, while in NOD (non-obese diabetic) mice, deletion of LAG-3 alone accelerates diabetes (12-14). LAG-3 is an immune checkpoint protein that modulates T-cell activation and homeostasis and is a promising target for cancer immunotherapy (15, 16).

**References:**

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