Recombinant Mouse LAG-3 Fc Chimera

Catalog Number: 3328-L3

DESCRIPTION

Source

Mouse myeloma cell line, NS0-derived mouse LAG-3 protein

N-terminal Sequence Analysis	Gly24
Structure / Form	Disulfide-linked homodimer
Predicted Molecular Mass	72.4 kDa (monomer)

SPECIFICATIONS

SDS-PAGE	85-100 kDa, reducing conditions
Activity	Measured by its ability to induce TNF-α secretion by JAWSII mouse immature dendritic cells. The ED_{50} for this effect is 0.4-2.4 µg/mL.
Endotoxin Level	<0.10 EU per 1 µg of the protein by the LAL method.
Purity	>95%, by SDS-PAGE visualized with Silver Staining and quantitative densitometry by Coomassie® Blue Staining.
Formulation	Lyophilized from a 0.2 µm filtered solution in PBS. See Certificate of Analysis for details.

PREPARATION AND STORAGE

Reconstitution	Reconstitute at 250 µg/mL in PBS. **Reconstitute 30 minutes prior to use with minimal agitation.**
Shipping	The product is shipped at ambient temperature. Upon receipt, store it immediately at the temperature recommended below.
Stability & Storage	• 12 months from date of receipt, ≤ -20 °C as supplied. • 1 month, 2 to 8 °C under sterile conditions after reconstitution. • 3 months, ≤ -20 °C under sterile conditions after reconstitution.

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). Mouse LAG-3 cDNA encodes 521 amino acids (aa) that include a 22 aa signal sequence, a 420 aa extracellular domain (ECD) with four Ig-like domains, a transmembrane region and a highly charged cytoplasmic region. Within the ECD, mouse LAG-3 shares 86% aa sequence identity with rat LAG-3, and 65-69% with human, porcine, and bovine LAG-3. LAG-3 is expressed on activated $CD4^+$ and $CD8^+$ T cells, NK cells, and plasmacytoid dendritic cells (pDC), but not on resting T cells (1-3). LAG-3 on activated $CD4^+CD25^+$ T_{reg} 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-γ and TNF-α by type 1 cytotoxic $CD8^+$ 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).

References:

1. Triebel, F. *et al.* (1990) J. Exp. Med. **171**:1393.
2. Baixeras, E. *et al.* (1992) J. Exp. Med **176**:327.
3. Workman, C.J. *et al.* (2004) J. Immunol. **172**:5450.
4. Huang, C.T. *et al.* (2004) Immunity **21**:503.
5. Workman, C.J. *et al.* (2009) J. Immunol. **182**:1885.
6. Li, N. *et al.* (2004) J. Immunol. **173**:6806.
7. Li, N. *et al.* (2007) EMBO J. **26**:494.
8. Andreae, S. *et al.* (2003) Blood **102**:2130.
9. Brignone, C. *et al.* (2007) J. Immunol. **179**:4202.
10. Brignone, C. *et al.* (2010) J. Transl. Med. **8**:71.
11. Woo, S.R. *et al.* (2011) Cancer Res. **72**:917.
12. Okazaki, T. *et al.* (2011) J. Exp. Med. **208**:395.
13. Bettini, M. *et al.* (2011) J. Immunol. **187**:3493.
14. Butler, N.S. *et al.* (2012) Nat. Immunol. **13**:188.

bio-techne®
Global bio-techne.com info@bio-techne.com techsupport@bio-techne.com TEL +1 612 379 2956
USA TEL 800 343 7475 Canada TEL 855 668 8722 China TEL +86 (21) 52380373
Europe | Middle East | Africa TEL +44 (0)1235 529449