Recombinant Human IL-15 Hyperactive

Catalog Number: BT-015H

DESCRIPTION

Source	*E. coli*-derived human IL-15 protein Proprietary, engineered based on P40933
Predicted Molecular Mass	

SPECIFICATIONS

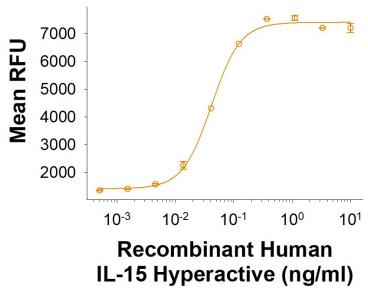
SDS-PAGE	9-11 kDa, under reducing conditions.
Activity	Measured in a cell proliferation assay using NK-92 human natural killer lymphoma cells. The ED_{50} for this effect is 0.0300-0.300 ng/mL.
Endotoxin Level	<0.10 EU per 1 µg of the protein by the LAL method.
Purity	>95%, by SDS-PAGE visualized with Silver Staining and quantitative densitometry by Coomassie® Blue Staining.
Formulation	Lyophilized from a 0.2 µm filtered solution in PBS with Trehalose. See Certificate of Analysis for details.

PREPARATION AND STORAGE

Reconstitution	Reconstitute at 100 µg/mL in water.
Shipping	The product is shipped at ambient temperature. Upon receipt, store it immediately at the temperature recommended below.
Stability & Storage	**Use a manual defrost freezer and avoid repeated freeze-thaw cycles.** • 12 months from date of receipt, -20 to -70 °C as supplied. • 1 month, 2 to 8 °C under sterile conditions after reconstitution. • 3 months, -20 to -70 °C under sterile conditions after reconstitution.

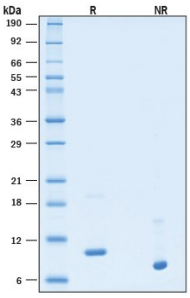
DATA

Bioactivity



Recombinant Human IL-15 Hyperactive Protein Bioactivity. The Recombinant Human IL-15 Hyperactive Protein (Catalog # BT-015H) induces proliferation of NK-92 human natural killer lymphoma cells.

SDS-Page



Recombinant Human IL-15 Hyperactive Protein SDS-PAGE. 2 µg/lane of Recombinant Human IL-15 Hyperactive Protein (Catalog # BT-015H) was resolved with SDS-PAGE under reducing (R) and non-reducing (NR) conditions and visualized by Coomassie® Blue staining, showing bands at 9-11 kDa, under reducing conditions.

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BACKGROUND

Interleukin 15 (IL-15) is a widely expressed 14 kDa cytokine that is structurally and functionally related to IL-2 and plays an important role in many immunological diseases (1, 2). Mature human IL-15 shares 70% amino acid sequence identity with mouse and rat IL-15. Alternative splicing generates isoforms of IL-15 with either a long or short signal peptide (LSP or SSP), and the SSP isoform is retained intracellularly (3). IL-15 binds with high affinity to IL-15 Rα (4). It binds with lower affinity to a complex of IL-2 Rβ and the common gamma chain (γc) which are also subunits of the IL-2 receptor complex (5). IL-15 associates with IL-15 Rα in the endoplasmic reticulum, and this complex is expressed on the cell surface (6). The dominant mechanism of IL-15 action is known as transpresentation in which IL-15 and IL-15 Rα are coordinately expressed on the surface of one cell and interact with complexes of IL-2 Rβ/γc on adjacent cells (7). This enables cells to respond to IL-15 even if they do not express IL-15 Rα (6). In human and mouse, soluble IL-15-binding forms of IL-15 Rα can be generated by proteolytic shedding and bind up nearly all the IL-15 in circulation (8-10). Soluble IL-15 Rα functions as an inhibitor that limits IL-15 action (4, 9). Ligation of membrane-associated IL-15/IL-15 Rα complexes also induces reverse signaling that promotes activation of the IL-15/IL-15 Rα expressing cells (11). IL-15 induces or enhances the differentiation, maintenance, or activation of multiple T cell subsets including NK, NKT, Th17, Treg, and CD8+ memory cells (12 - 16). An important component of these functions is the ability of IL-15 to induce dendritic cell differentiation and inflammatory activation (11, 14). IL-15 exhibits anti-tumor activity independent of its actions on NK cells or CD8+ T cells (17). It also inhibits the deposition of lipid in adipocytes, and its circulating levels are decreased in obesity (18). Immunotherapy treatment with recombinant IL-15 has the advantage of not stimulating Treg cells like IL-2 does but has the drawback of associated toxicity at higher doses. This has led to increased investigation on mitigating IL-15 toxicity and combination immunotherapy approaches using immune checkpoint inhibitors (19, 20). Preclinical and early clinical studies have shown the potential of also using IL-15 in combination with cancer vaccines to improve their anti-tumor response (20). IL-15 can also be used for the preconditioning of CAR T cells or for engineering cells to express IL-15 in vivo. Adoptive cell transfer of NK cells engineered to express CD19 and IL-15 were well tolerated in patients with CD19-positive cancers (20). IL-15 can be used in combination with other cytokines like IL-21 to increase the efficiency of NK cell expansion and maturation in stem cell culture protocols (21). The combination of IL-15 with IL-7 also promotes expansion of early-differentiated CD8+ T cells in culture with the added benefit of decreasing Treg cell generation, unlike IL-2, for adoptive cell transfer in cancer immunotherapy (22). GMP IL-7 and GMP IL-15 are commonly used in combination for ex vivo expansion of T cells for cellular therapies.rhIL-15 Hyperactive is engineered for increased affinity to IL-15Rβ and IL-15Rα, making it a more potent cytokine ideal for expanding challenging cells like TILs and NK cells that require extended ex vivo culture.

References:

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