Animal-Free™ Recombinant Human IL-15

Catalog Number: BT-015-AFL/LQ

DESCRIPTION

Source	*E. coli*-derived human IL-15 protein Asn49-Ser162 Accession # P40933.1 Produced using non-animal reagents in an animal-free laboratory.
N-terminal Sequence Analysis	Asn49
Predicted Molecular Mass	13 kDa

SPECIFICATIONS

SDS-PAGE	9 kDa, under reducing conditions.
Activity	Measured in a cell proliferation assay using MO7e human megakaryocytic leukemic cells. The ED_{50} for this effect is 0.300-2.60 ng/mL. The specific activity of recombinant human IL-15 is >2.00 x 10^8 units/mg, which is calibrated against the human IL-15 reference standard (NIBSC code: 95/554).
Endotoxin Level	<0.10 EU per 1 µg of the protein by the LAL method.
Purity	>97%, by SDS-PAGE with quantitative densitometry by Coomassie® Blue Staining.
Formulation	Supplied as a 0.2 µm filtered solution in PBS. See Certificate of Analysis for details.

PREPARATION AND STORAGE

Shipping	The product is shipped with dry ice or equivalent. Upon receipt, store it immediately at the temperature recommended below.
Stability & Storage	**Use a manual defrost freezer and avoid repeated freeze-thaw cycles.** • 6 months from date of receipt, ≤ -65 °C as supplied. • 1 month, 2 to 8 °C under sterile conditions after opening. • 3 months, -20 to -70 °C under sterile conditions after opening.

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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.

References:

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MANUFACTURING SPECIFICATIONS

Animal-Free Manufacturing Conditions
Our dedicated controlled-access animal-free laboratories ensure that at no point in production are the products exposed to potential contamination by animal components or byproducts. Every stage of manufacturing is conducted in compliance with R&D Systems' stringent Standard Operating Procedures (SOPs). Production and purification procedures use equipment and media that are confirmed animal-free.

Production

- All molecular biology procedures use animal-free media and dedicated labware.
- Dedicated fermentors are utilized in committed animal-free areas.

Purification

- Protein purification columns are animal-free.
- Bulk proteins are filtered using animal-free filters.
- Purified proteins are stored in animal-free containers in a dedicated cold storage room.

Quality Assurance

- Low Endotoxin Level.
- No impairment of biological activity.
- High quality product obtained under stringent conditions.
- For *ex vivo* research or bioproduction, **additional documentation** can be provided.

Please read our complete Animal-Free Statement

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