

## 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<sub>50</sub> for this effect is 0.300-2.60 ng/mL. The specific activity of recombinant human IL-15 is >2.00 x 10<sup>8</sup> 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** Lyophilized from a 0.2 µm filtered solution in PBS with Trehalose. See Certificate of Analysis for details.

## PREPARATION AND STORAGE

**Reconstitution** Reconstitute at 100-500 µg/mL in PBS.

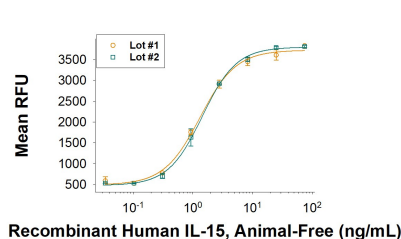
**Shipping** The product is shipped at ambient temperature. Upon receipt, store it immediately at the temperature recommended below.

**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.

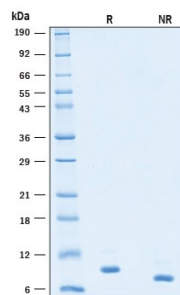
## DATA

### Bioactivity



**Recombinant Human IL-15 Protein, Animal-Free, Bioactivity.** Animal-Free™ Recombinant Human IL-15 (Catalog # BT-015-AFL) stimulates cell proliferation in the MO7e human megakaryocytic leukemic cell line. The ED<sub>50</sub> for this effect is 0.300-2.60 ng/mL. Two independent lots were tested for activity and plotted on the same graph to show lot-to-lot consistency of Animal-Free IL-15.

### SDS-PAGE



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

## 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 R $\alpha$  (4). It binds with lower affinity to a complex of IL-2 R $\beta$  and the common gamma chain ( $\gamma$ c) which are also subunits of the IL-2 receptor complex (5). IL-15 associates with IL-15 R $\alpha$  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 R $\alpha$  are coordinately expressed on the surface of one cell and interact with complexes of IL-2 R $\beta$ / $\gamma$ c on adjacent cells (7). This enables cells to respond to IL-15 even if they do not express IL-15 R $\alpha$  (6).

In human and mouse, soluble IL-15-binding forms of IL-15 R $\alpha$  can be generated by proteolytic shedding and bind up nearly all the IL-15 in circulation (8-10). Soluble IL-15 R $\alpha$  functions as an inhibitor that limits IL-15 action (4, 9). Ligation of membrane-associated IL-15/IL-15 R $\alpha$  complexes also induces reverse signaling that promotes activation of the IL-15/IL-15 R $\alpha$  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](#)