ProPak™ GMP Recombinant Human IL-7

Catalog Number: PPK-007-GMP

DESCRIPTION

Source	*E. coli*-derived human IL-7 protein Asp26-His177, with an N-terminal Met Accession # P13232.1 Produced using non-animal reagents in an animal-free laboratory. Manufactured and tested under cGMP guidelines.
N-terminal Sequence Analysis	Met-Asp26-(Cys)-Asp-Ile-Glu-Gly-Lys-Asp-Gly
Predicted Molecular Mass	17 kDa

SPECIFICATIONS

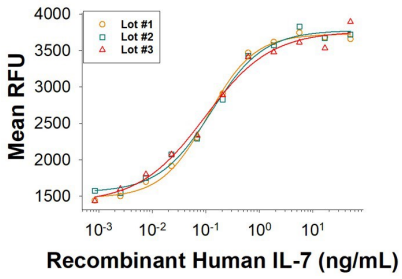
SDS-PAGE	17 kDa, under reducing conditions.
Activity	Measured in a cell proliferation assay using PHA-activated human peripheral blood lymphocytes (PBL). Yokota, T. *et al.* (1986) Proc. Natl. Acad. Sci. USA **83**:5894. The ED_{50} for this effect is 0.100-0.500 ng/mL. The specific activity of Recombinant Human IL-7 is >1.00 x 10^8 units/mg, which is calibrated against the human IL-7 reference standard (NIBSC code: 90/530).
Endotoxin Level	<5.0 EU/mL by the LAL method.
Purity	>97%, by SDS-PAGE with quantitative densitometry by Coomassie® Blue Staining.
Mass Spectrometry	The molecular weight by mass spectrometry is 17507 Da ± 50 Da.
Host Cell Protein	<0.5 ng per µg of protein when tested by ELISA.
Mycoplasma	Negative when tested in a ribosomal RNA hybridization assay.
Host Cell DNA	<0.0015 ng per µg of protein when tested by PCR.
Formulation	Supplied as a 0.2 µm filtered solution in PBS, recombinant HSA, and Trehalose. See Certificate of Analysis for details.

PREPARATION AND STORAGE

Shipping	The product is shipped on dry ice. Upon receipt, store it immediately at the temperature recommended below.
Stability & Storage	**Use a manual defrost freezer and avoid repeated freeze-thaw cycles.** A minimum of 6 months when stored between -14 °C and -40 °C. Can be stored up to 2 weeks at 2-8 °C. Refer to lot specific COA for the Use by Date.

DATA

Bioactivity



Lot to Lot Consistency ProPak GMP-grade Recombinant Human IL-7 (Catalog # PPK-007-GMP) stimulates proliferation of PHA-activated human peripheral blood lymphocytes. The ED_{50} for this effect is 0.100-0.500 ng/mL. Three independent lots were tested for activity and plotted on the same graph to show lot-to-lot consistency of ProPak GMP IL-7.

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BACKGROUND

IL-7 (interleukin-7) is a 25 kDa cytokine of the hemopoietin family that plays important roles in lymphocyte differentiation, proliferation, and survival (1-4). Human IL-7 cDNA encodes 177 amino acids (aa) that include a 25 aa signal peptide (3). Human IL-7 shares approximately 60-63% aa sequence identity with mouse, rat, canine and feline IL-7, and 72-76% with equine, bovine, ovine, and porcine IL-7. Human and mouse IL-7 exhibit cross-species activity (2, 3).

IL-7 is produced by a wide variety of cells in primary and secondary lymphoid tissues, including stromal epithelial cells of the thymus, bone marrow, and intestines (1, 2, 5). Circulating IL-7 is limiting in healthy animals, but increases during lymphopenia (1, 6). IL-7 signals through a complex of the IL-7 Receptor alpha subunit (IL-7 Rα, also known as CD127) with the common γ chain (γc) (1). The γc is also a subunit of the receptors for IL-2, -4, -9, -15, and -21 (1).

IL-7 Rα is expressed on double negative (CD4-CD8-) and single positive (CD4+ or CD8+) naïve and memory T cells, but undergoes IL-7-mediated down-regulation and shedding during antigen-driven T cell proliferation, and is absent on regulatory T cells (1, 2, 6-11). IL-7 contributes to the maintenance of all naïve and memory T cells, mainly by promoting expression of the anti-apoptotic protein Bcl-2 (9-11). It is required for optimal T cell-dendritic cell interaction (6). IL-7 is expressed early in B cell development prior to the appearance of surface IgM (1, 5, 9). In mouse, IL-7 activation of IL-7 Rα is critical for both T cell and B cell lineage development, while in humans, it is required for T cell but not for B cell development (4, 9, 12, 13). However, IL-7 functions in both mouse and human pro-B cells to suppress premature Ig light chain recombination during proliferative growth (14, 15).

Like other common gamma-chain cytokines like IL-2 and IL-15, IL-7 and its receptor, IL-7R, has been used in a variety of immunotherapy applications, often in fluid tumors and in some instances of solid tumor models (16). Sometimes use of recombinant IL-7 is preferential as current studies and early clinical trials of cancer have found less severe toxicity or side effects upon treatment with IL-7 in comparison to IL-15 or IL-2 (16).

In CAR-T cell therapies, enhanced expression and secretion of human IL-7 and CCL19 have enhanced the ability of T cells to expand and migrate in vitro (17). Engineered CAR T cells expressing IL-7 or a constitutively active IL-7R results in increased efficacy of CAR T anti-tumor effects (16, 18). IL-7 is also frequently used in combination with IL-15 as a supplement in cell culture of CAR T cells to support their expansion (19). Additionally, IL-7/IL-15 in the presence of cord blood-derived T cells helps to maintain their early differentiation state (20). Monoclonal antibodies against IL-7R or small molecule inhibitors against the IL-7R signaling pathway are commonly used in circumstances of autoimmune diseases to delay disease progression (16). Also due to its ability to stimulate both adaptive and innate immune cells, treatment with IL-7 has shown improved survival in patients with sepsis who are at risk of deadly secondary infections (21), providing evidence for IL-7 applications beyond cancer immunotherapy.

References:

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- Finished product testing includes bioassay (compliance with an established range), endotoxin level (as determined by LAL assay), and microbial testing according to USP <71>

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