

DESCRIPTION

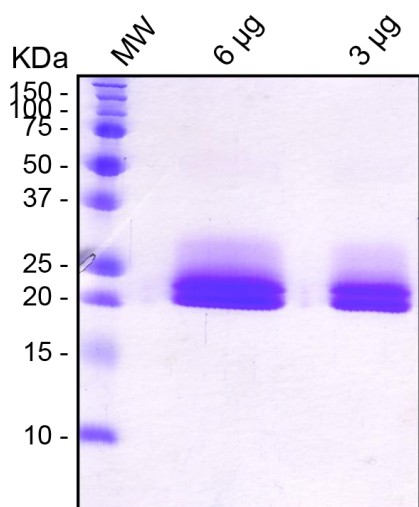
<i>Description</i>	Recombinant Human Interleukine-6 (IL-6), NCBI Accession Number: P05231
<i>Sequence</i>	Ala28-Met212
<i>Expression system</i>	HEK293 cells
<i>Tag</i>	His Tag C-Terminus
<i>Purification</i>	Affinity chromatography followed by Ion exchange chromatography
<i>Extinction coefficient</i>	10220 M ⁻¹ .cm ⁻¹ Abs 0.1% (=1 g/l) 0.470 assuming all pairs of Cys residues form cystines
<i>Predicted Molecular Weight</i>	21.7 kDa

SPECIFICATIONS

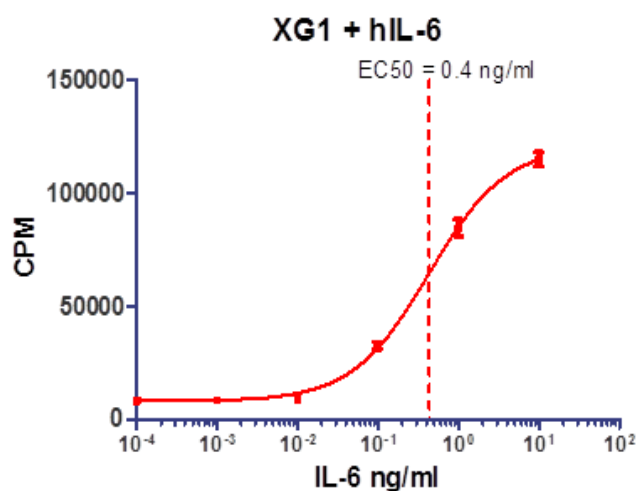
<i>SDS Page</i>	21 & 22 kDa, second band results of glycosylation (confirmed by mass spectrometry)
<i>Concentration</i>	10µg/ vial (715-H01-010-CF) or 25 µg/ vial (715-H01-025-CF)
<i>Purity</i>	>95% by SDS PAGE gel
<i>Formulation</i>	Lyophilized from PBS pH 7.4 (NaCl 155mM, Na ₂ HPO ₄ 8mM & KH ₂ PO ₄ , 1.8mM, Trehalose)
<i>Reconstitution</i>	Centrifuge the vial prior opening It is recommended to reconstitute in sterile water at 100 µg/ml
<i>Endotoxins</i>	Negative on cell based assay
<i>Activity</i>	Measured in a cell based assay on stimulated XG1 cells (EC ₅₀ = 0.4 ng/ml)
<i>Stability and Storage</i>	Store at -20°C. Avoid repeated freeze-thaw cycles Stable one week at 2 to 8°C after reconstitution under sterile conditions Stable 12 months -20°C to -80°C after reconstitution under sterile conditions

DATA

SDS-PAGE 15% under reducing conditions and visualized by Coomassie blue staining showing a band at 21 and 22 kDa (glycosylated form)



Biological Activity measured in a cell proliferation assay using XG1 cells
The EC₅₀ for this effect is 0.4 ng/ml



HUMAN IL-6

Interleukin-6 (IL-6) is a multi-functional cytokine that regulates immune responses, acute phase reactions and hematopoiesis and may play a central role in host defense mechanisms (13, 31). The gene for human IL-6 has been localized to chromosome 7p21 (1). The genomic sequence has been determined (36). IL-6 is usually not produced constitutively by normal cells, but its expression is readily induced by a variety of cytokines (28), lipopolysaccharide (25) or viral infections (3). The IL-6 gene product is a single chain protein with a molecular mass ranging from 21 to 28 kDa, depending on the cellular source. Extensive post-translational modifications like N- and O-linked glycosylation (20) as well as phosphorylation (21) seem to account for this heterogeneity. The cDNA for IL-6 predicts a precursor protein of 212 amino acids (10). IL-6 is a pleiotropic cytokine produced by a variety of cells. It acts on a wide range of tissues, exerting growth-induction, growth-inhibition, and differentiation respectively, depending on the nature of the target cells.

IL-6 is involved in the:

- induction of B-cell differentiation and acute phase proteins in liver cells,
- growth promotion of myeloma/plasmacytoma/hybridoma cells,
- induction of IL-2 and IL-2 receptor expression,
- proliferation and differentiation of T cells,
- inhibition of cell growth of certain myeloid leukemic cell lines and induction of their differentiation to macrophages,
- enhancement of IL-3-induced multipotential colony cell formation in hematopoietic stem cells and induction of maturation of megakaryocytes as a thrombopoietic factor,
- induction of mesangial cell growth, neural differentiation of PC cells (12) and keratinocyte growth (14).

The abnormal production of IL-6 was first suggested to be related to polyclonal B-cell activation with autoantibody production in patients with cardiac myxoma. Since then, IL-6 has been suggested to be involved in the pathogenesis of a variety of diseases. Measurement of IL-6 levels in serum and other body fluids thus provides more detailed insights into various pathological situations. For Example:

- **Infections:** Body fluids of patients with acute local bacterial or viral infections and serum of patients with gram-negative or positive bacteremia contain elevated levels of biologically active IL-6 (7, 16).
- **Obstetric Infections:** IL-6 has emerged as a reporter cytokine for intra-amniotic infection (29).
- **Diseases associated with an altered immune system** (polyclonal B-cell abnormalities or autoimmune diseases): Elevated levels of circulating IL-6 have been detected in patients with cardiac myxoma (11), Castleman's disease (18), rheumatoid arthritis (12), IgM gammopathy and in those with acquired immunodeficiency syndrome (19, 23) as well as alcoholic liver cirrhosis (2, 32).
- **Proliferative diseases:** Elevated plasma levels of IL-6 are observed in patients with psoriasis (4, 5) and mesangial proliferative glomerulonephritis (15).
- **Neoplastic Diseases:** Increased systemic levels of IL-6 have been detected in patients with multiple myeloma (22), other B-cell dyscrasias (27), Lennert's T lymphoma, Castleman's disease, renal cell carcinoma (33) and various other solid tumors (17, 30).
- **Inflammatory responses:** IL-6 is involved in the induction of acute phase proteins and induction of fever (8). Elevated serum levels of IL-6 are also found in patients with severe burns (24, 34), in serum and plasma as a marker for predicting postoperative complications (26), in serum and urine of recipients of kidney transplants before rejection (35), in the serum of septic shock patients (6) and in patients with inflammatory arthritis and traumatic arthritis.

BIBLIOGRAPHY

1. Bowcock A. M., J. R. Kidd, M. Lathrop, L. Danshvar, L. May, A. Ray, P. B. Sehgal, K. K. Kidd, and L. L. Cavallisforza. (1988). The human "beta-2 interferon/hepatocyte stimulating factor interleukin-6" gene: DNA polymorphism studies and localization to chromosome 7p21. *Genomics* 3, 8-16.
2. Byl B. I. Roucloux, A. Crusiaux, E. Dupont, and J. Deviere. (1993). Tumor Necrosis Factor-alpha and Interleukin-6 plasma levels in infected cirrhotic patients. *Gastroenterology* 104, 1492-1497.
3. Cayphas S. J. Van Damme, A. Vink, R. J. Simpson, A. Billiau, and J. Van Snick. (1987). Identification of an interleukin HPI - like plasmacytoma growth factor produced by L cells in response to viral infection. *J. Immunol.* 139, 2965-2969.
4. Elder J. T., C. I. Sartor, D. K. Boman, S. Benrazavi, G. J. Fisher, and M. R. Pittelkow. (1992). Interleukin-6 in psoriasis-expression and mitogenicity studies. *Arch. Derm. Res.* 284, 324-332.
5. Grossman R. M., J. Krueger, D. Yourish, A. Granelli-Piperno, D. P. Murphy, L. T. May, T. S. Kupper, P. B. Sehgal, and A. B. Gottlieb. (1989). Interleukin 6 is expressed in high levels in psoriatic skin and stimulates proliferation of cultured human keratinocytes. *Proc. Natl. Acad. Sci. USA* 86, 6367.
6. Hack C. E., E. R. De Groot, R. J. F. Felt-Bersma, J. H. Nuijens, R. J. M. Strack van Schijndel, A. J. M. Eerenberg-Belmer, L. G. Thjojs, and L. A. Aarden. (1989). Increased plasma levels of interleukin 6 in sepsis. *Blood* 74, 1704.
7. Helfgott D. C., S. B. Tatter, U. Santhanam, R. H. Clarick, N. Bhardwaj, L. T. May, and P. B. Sehgal. (1989). Multiple forms of IFN- β /IL-6 in serum and body fluids during acute bacterial infection. *J. Immunol.* 142, 948.
8. Helle M. J. P., J. Brakenhoff, E. R. De Groot, and L. A. Aarden. (1988). Interleukin 6 is involved in interleukin-1-induced activities. *Eur. J. Immunol.* 18, 957.
9. Hirano T., T. Taga, N. Nakano, K. Yasukawa, S. Kashiwamura, K. Shimizu, K. Nakajima, K. H. Pyun, and T. Kishimoto. (1985). Purification to homogeneity and characterization of human B-cell differentiation factor (BCDF or BSFp-2). *PNAS* 82, 5490-5494.
10. Hirano T., K. Yasukawa, H. Hirata, H. Shiki, Y. Fujii, K. Dohi, and H. Ishikawa. (1993). Role of interleukin-6 in the progression of mesangial proliferative glomerulonephritis. *Kidney Intern.* 43, 71-75.
11. Hirano T., T. Taga, K. Yasukawa, K. Nakajima, N. Nakano, F. Takatsuki, M. Shimizu, A. Murashima, S. Tsunasawa, F. Sakiyama, and T. Kishimoto. (1987). Human B-cell differentiation factor defined by an anti-peptide antibody and its possible role in autoantibody production. *PNAS* 84, 228-231.
12. Hirano T., T. Matsuda, M. Turner, N. Miyasaka, G. Buchan, B. Tang, K. Sato, M. Shimizu, R. Maini, M. Feldmann, and T. Kishimoto. (1988). Excessive production of interleukin 6/B cell stimulatory factor-2 in rheumatoid arthritis. *Eur. J. Immunol.* 18, 1797-1801.
13. Hirano T., and T. Kishimoto. (1990). Interleukin-6. In: *Handbook of Experimental Pharmacology. Peptide Growth Factors and Their Receptors*, edited by M. B. Sporn, A. B. Roberts. Berlin, Springer-Verlag, pp 633-665.
14. Hirano T., A. Shizuo, T. Taga, and T. Kishimoto. (1990). Biological and clinical aspects of interleukin 6. *Immunology Today* 11, 443-449.
15. Horii Y., M. Iwano, E. Hirata, H. Shiki, Y. Fujii, K. Dohi, and H. Ishikawa. (1993). Role of interleukin-6 in the progression of mesangial proliferative glomerulonephritis. *Kidney Intern.* 43, 71-75.
16. Houssiau F. A., K. Bukasa, C. J. M. Sindic, J. Van Damme, and J. Van Snick. (1988). Elevated levels of the 26k human hybridoma growth factor (interleukin 6) in cerebrospinal fluid of patients with acute infection of the central nervous system. *Clin. Exp. Immunol.* 71, 320ff.
17. Kishimoto T. (1989). The biology of interleukin-6. *Blood* 74, 1-10.
18. Kishimoto T., and T. Hirano. (1988). Molecular regulation of B lymphocyte response. *Ann. Rev. Immunol.* 6, 485-512.

19. O. Martinezmaza. (1992). IL-6 and AIDS. Res. Immunol. 143. 764-769.
20. May L. T. J. Grayeb. U. Santhanam. S. B. Tatter. Z. Sthoeger. D. C. Helfgott. N. Chiorazzi. G. Grieneringer. and P. B. Sehgal. (1988). Synthesis and secretion of multiple forms of b2-interferon/B-cell differentiation factor 2 hepatocyte-stimulating factor by human fibroblasts and monocytes. J. Biol. Chem. 263. 7760-7766.
21. May L. T. U. Santhana. S. B. Tatter. D. C. Helfgott. A. Ray. J. Ghayeb. and P. B. Sehgal. (1988). Phosphorylation of secreted forms of human b2-interferon/hepatocyte-stimulating factor interleukin-6. Biochem. Biophys. Res. Comm. 152. 1144-1150.
22. Merico F. L. Bergui. M. G. Gregorettil. P. Ghia. G. Aimo. I. J. D. Lindley. and F. Caligariscappio. (1993). Cytokines involved in the progression of multiple myeloma. Clin. Exp. Immunol. 92. 27-31.
23. Nakajima K. O. Martinez-Maza. T. Hirano. E. C. Breen. P. G. Nishanian. J. F. Salazar-Gonzalez. J. L. Fahey. and T. Kishimoto. (1989). Induction of IL-6 (B cell stimulatory factor-2/IFN-HIV. J. Immunol. 142. 531.
24. Nijsten M. W. N. E. R. De Groot. H. J. Ten Duis. H. J. Klases. C. E. Hack. and L. A. Aarden (1987). Serum levels of interleukin-6 and acute phase responses. Lancet II. 921.
25. Nordan R.. and M. Potter. (1986). A macrophage-derived factor required by plasmacytomas for survival and proliferation in vitro. Science 233. 566-569.
26. Oka Y. A. Murata. J. Nishijima. T. Yasuda. N. Hiraoka. Y. Ohmachi. K. Kitagawa. T. Yasuda. H. Toda. N. Tanaka. and T. Mori. (1992). Circulating interleukin 6 as a useful marker for predicting postoperative complications. Cytokine 4. 298-304.
27. Pettersson T. K. Metsärinne. A. M. Teppo. and F. Fyhrquist. (1992). Immunoreactive interleukin-6 in serum of patients with B-lymphoproliferative diseases. J. Int. Med. 232. 439-442.
28. Ray A. S. B. Tatter. U. Santhanam. D. C. Helfgott. L. T. May. and P. B. Sehgal. (1989). Regulation of expression of interleukin-6: Molecular and clinical studies. Ann. NY Acad. Sci. 557. 353-362.
29. Sant hanam U. C. Avila. R. Romero. H. Viguet. N. Ida. S. Sakurai. and P. B. Sehgal. (1991). Cytokines in normal and abnormal parturition: Elevated amniotic fluid interleukin-6 levels in women with premature rupture of membranes associated with intrauterine infection. Cytokine 3. 155-163.
30. Seguchi T. K. Yokokawa. H. Sugao. E. Nakano. T. Sonoda. and A. Okuyama. (1992). Interleukin-6 activity in urine and serum in patients with bladder carcinoma. J. Urol. 148. 791-794.
31. Sehgal P. B. G. Greininger. and G. Tosato. (1989). Regulation of the acute phase and immune responses: Interleukin-6. Ann. NY Acad. Sci. 557. 1-583.
32. Sheron N. G. Bird. J. Goka. G. Alexander. and R. Williams. (1991). Elevated plasma interleukin-6 and increased severity and mortality in alcoholic hepatitis. Clin. Exp. Immunol. 84. 449-453.
33. Tsukamoto T. Y. Kumamoto. N. Miyao. N. Masumori. A. Takahashi. and M. Yanase. (1992). Interleukin-6 in renal cell carcinoma. J. Urol. 148. 1778-1781.
34. Ueyama M. I. Maruyama. M. Osame. and Y. Sawada. (1992). Marked increase in plasma interleukin-6 in burn patients. J. Lab. Clin. Med. 120. 693-698.

RELATED PRODUCTS

Code	Products	Quantity
715-H01-XXX-BSA	Recombinant Human Interleukin-6 (IL-6)-BSA	10/25 µg
857.730.000	Anti-Human IL-6 Azide Free (Clone B-E4)	200 µg/200 µl
857.730.005	Anti-Human IL-6 Azide Free (Clone B-E4)	500 µg/500 µl
855.050.000	Anti-Human IL-6 Azide Free (Clone B-E8)	200 µg/200 µl
855.050.005	Anti-Human IL-6 Azide Free (Clone B-E8)	500 µg/500 µl
855.060.000	Anti-Human IL-6 Azide Free (Clone B-F6)	200 µg/200 µl
855.060.005	Anti-Human IL-6 Azide Free (Clone B-F6)	500 µg/500 µl
879.030.002	Anti-Human IL-6 Detection Antibody (Clone B-E4)	100 µg/1 ml
879.030.001	Anti-Human IL-6 Capture Antibody (Clone B-E8)	1.0 mg/1 ml
950.030.048	Human IL-6 ELISA Kit	48 tests
950.030.096	Human IL-6 ELISA Kit	96 tests
950.030.192	Human IL-6 ELISA Kit	2 x 96 tests
851.520.XXX	Human IL-6 ELISA Set	96 to 20 x 96 tests
856.021.001PC	Human IL-6 ELISpot Kit	96 tests
856.021.002PC	Human IL-6 ELISpot Kit	2 x 96 tests
856.021.005PC	Human IL-6 ELISpot Kit	5 x 96 tests
856.021.XXX	Human IL-6 ELISpot Set	96 to 20 x 96 tests
869.020.010	Human IL-6 ELISpot Pair	10 x 96 tests

Products Manufactured and Distributed by:

Diaclone SAS

6 Rue Dr Jean-François-Xavier Girod

BP 1985, 25020 Besançon Cedex

France

Tel +33 (0)3 81 41 38 38 Fax +33 (0)3 81 41 36 36

Email: info@diaclone.com www.diaclone.com