

## gp130 (Glycoprotein 130)

**Analyte:** Glycoprotein 130

**Specimen Type:** Serum, Inquire for additional option(s)

**Optimum Volume:** 0.5 mL

**Stability:**

2-8 Degrees C	-20 Degrees C	-70 Degrees C
7 days	1 month	3 years

**Reporting Units:** ng/mL

**Method:** ELISA

**Biological or Clinical Significance:**

Interleukin 6 (IL-6) is a multifunctional protein that plays important roles in host defense, acute phase reactions, immune responses, and hematopoiesis. IL-6 exerts its activity through binding to a high affinity receptor complex consisting of two membrane glycoproteins: an 80 kDa IL-6-binding receptor protein (IL-6R) and a 130kDa signal-transducing protein (gp130). Human gp130 consists of a 597 amino acid residue ectodomain, a 22 residue transmembrane domain and a 277 amino acid residue cytoplasmic domain. The ectodomain of gp130 consists of a cytokine receptor superfamily domain as well as an immunoglobulin-like domain and three fibronectin type III-like domains. The cytoplasmic domains of neither IL-6R nor gp130 have homology with known tyrosine kinases or other catalytic domains. IL-6 has been shown to bind to IL-6R with low-affinity. In the absence of IL-6R, IL-6 does not appear to bind to gp130. However, the presence of IL-6R together with gp130 will result in high-affinity IL-6 binding and subsequent signal transduction. In addition to serving as the signal transducing and high-affinity-converting subunit for the IL-6 receptor complex, gp130 has now been shown to be a signal transducer for several other cytokines with overlapping biological functions, including IL-11, LIF (leukemia inhibitory factor), OSM (oncostatin M), CNTF (ciliary neurotrophic factor), and Cardiotrophin-1 (CT-1). With the exception of OSM and LIF, which bind gp130 with low-affinity, the other cytokines do not appear to bind gp130 in the absence of additional receptor subunits. Gp130 has been shown to be expressed in nearly all human and mouse cell lines examined. A current model for IL-6 signal transduction assumes that one IL-6 molecule binds an IL-6R molecule forming an IL-6/IL-6R complex. The formation of this complex induces high-affinity binding to and dimerization of gp130 (involving disulfide links between two gp130 molecules). Dimerization of gp130 initiates signal transduction via the JAK/STAT (Janus kinases/Signal Transducers and Activators of Transcription) pathway. IL-6 stimulation has also been shown to activate RAS and mitogen-activated protein kinases (MAPK) that are essential for NF-IL-6 (a nuclear factor essential for IL-6 expression) activation. Based on results of size-exclusion and analytical ultracentrifugation analysis of the interaction of IL-6, soluble IL-6R and soluble gp130, it has been proposed that the high-affinity IL-6 receptor complex is a hexameric complex consisting of two molecules each of IL-6, IL-6R and gp130. A naturally occurring soluble form of the IL-6R, which binds IL-6 and which mediates IL-6 signaling through interaction with gp130, has been detected in the urine of healthy adult humans, in human and mouse serum, and in the conditioned medium of various cells, including human peripheral blood mononuclear cells, and several T cell or granulocyte/macrophage cell lines. A naturally occurring soluble form of gp130 has also been found in human serum and in the

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ascites fluid of tumor-bearing mice. Soluble gp130 has been shown to be capable of inhibiting gp130-mediated cytokine activities in vitro. Both the soluble IL-6R and the soluble gp130 are present in nanogram quantities in the serum of normal individuals. These observations suggest that a complex regulatory system is involved in the modulation of the biological activities of IL-6 under normal and pathological conditions.

Bioassays for soluble human gp130 are based on measurement of its ability to inhibit the biological activities of IL-6 and the other cytokines that have gp130 as the signal transducing component of their receptor complexes or on the ability of gp130 to inhibit the IL-6 sR-dependent enhancement of IL-6 activity. These assays are time-consuming and not completely specific for gp130.

### Principle of Test Method:

The gp 130 immunoassay is a solid-phase ELISA designed to measure human gp 130 in cell culture supernates, serum and plasma. This assay employs the quantitative sandwich enzyme immunoassay technique.

### References:

1. Oelzner P, Franke S, Lehmann G, Eidner T, Muller A, Wolf G, Hein G. Soluble receptor activator of NFkappa B-ligand and osteoprotegerin in rheumatoid arthritis – relationship with bone mineral density, disease activity and bone turnover. Clin Rheumatol. 2007; 26:2127-2135.