ProductInformation

ANTI-STAT6
Developed in Rabbit, Whole Antiserum

Product Number **S6433**

Product Description

Anti-STAT6 is developed in rabbit using a synthetic peptide (GEDIFPPLLPPTEQDLTK) corresponding to human STAT6 (amino acids 787-804) conjugated to KLH as immunogen. This sequence is highly conserved between mouse and human. Anti-STAT6 is supplied as whole rabbit antiserum.

Anti-STAT6 reacts specifically with human STAT6 (100 kD). The antibody also reacts weakly with mouse STAT6.

Anti-STAT6 may be used for the detection of STAT6 by immunoblotting. This antiserum is not recommended for immunoprecipitation.

STATs (signal transducers and activators of transcription) are a family of transcription factors that are activated by the JAK family of kinases or by receptor tyrosine kinases. When cells encounter various extracellular ligands, such as interferons and EGF, the STATs promote rapid induction of genes.[1-3]

The STAT proteins are highly conserved at their N-terminal, but have divergent C-terminals, which are thought to be essential for their selective activity. Seven STAT proteins have been described (STAT1, STAT2, STAT3, STAT4, STAT5A, STAT5B and STAT6) and range in MW from 84-113 kD. STATs 1, 3, 4, 5A and 5B have between 750 and 795 amino acid residues, whereas STATs 2 and 6 have approximately 850 amino acid residues.[2,4] Phosphorylation on a single tyrosine located around residue 700 in each protein is required for STAT activation.[1,2]

Activation of the JAK/STAT pathway begins with ligand (such as Interferon-α) binding to receptor on the plasma membrane and activation of certain members of the JAK tyrosine kinase family. JAKs are associated with the intracellular tail of many cytokine receptors. Receptors to which JAKs are bound are often referred to as cytokine receptors. Their ligands include interferon-α, β, and λ; interleukins (IL) 2-7, 10-13, and 15; and erythropoietin, growth hormone, prolactin, thromopoietin, and other polypeptides. STAT6 is activated by IL-3 and IL-4 and recent evidence shows that STAT6 becomes activated after PDGF stimulation of NIH 3T3 fibroblasts.[5] Ligand-induced dimerization of the receptor results in the reciprocal tyrosine phosphorylation (activation) of the associated JAK. JAK then phosphorylates tyrosine residues on the cytoplasmic tail of the receptor. These phophorylated tyrosines function as docking sites for the SH2 domains of the STAT proteins. Thus, STATs are recruited to the receptor. JAK then catalyzes the tyrosine phosphorylation of the receptor-bound STAT. The phosphorylated STAT molecules then rapidly form homo- or heterodimers. Dimers or heterodimers, but not monomers are competent to bind DNA. The known DNA binding heterodimers are STAT1:2 and STAT1:3.[2] The heterodimer STAT1:2 requires a protein termed p48, a member of the interferon regulatory factor-1 (IRF-1) family of proteins,[7] to become the DNA binding protein ISGF3 (interferon-stimulated growth factor 3). STAT homodimers that bind DNA include STATs 1,3,4, 5 (STAT5A and STAT5B interact in a manner equivalent to a heterodimer), and 6.[2,3,6] STAT2:2 dimers form sparingly in the absence of STAT1 and bind DNA weakly,[8] as do STAT2:3 heterodimers.

Homo- or heterodimers of the STATs translocate to the nucleus, where they either directly interact with promoter elements (gamma-activated sequence or GAS motifs) or combine with a DNA-binding protein (interferon stimulable response element or ISRE motifs). STATs activate distinct target genes despite having similar DNA binding preferences.[2, 9-13] Selective gene activation by the various STATs may be attributed to differential STAT dimer binding to DNA. Cooperative binding to neighboring sites of two or more STAT dimers enables the STAT proteins to recognize variations of the consensus site. These sites can be specific for the different STAT proteins and may function to direct selective transcriptional activation.

SOCS (suppressor of cytokine signaling) proteins are induced in response to cytokine and suppress signal transduction in two ways. SOCS-1 appears to bind directly to JAKs and inhibit their catalytic activity, and CIS appears to bind to activated receptors and prevent docking of signaling intermediates. SHP-1 suppresses the signal by dephosphorylating either JAKs or the

activated receptor subunits, depending on the specific pathway that is activated. PIAS (protein inhibitor of activated STAT) family members inactivate STAT dimers by an unknown mechanism. Activated STAT dimers are probably also downregulated by degradation and dephosphorylation by unknown phosphatases.[14] STAT6 is distinguishable from the other STATs by its ability to bind a GAS-like element found in the Ig germ line ϵ promoter of the IL-4 responsive human Cϵ gene (Iϵ).

Reagents
The product is supplied as whole antiserum.

Storage/Stability
For continuous use, add 15 mM sodium azide as a preservative and store at 2-8°C for up to one month. For extended storage freeze in working aliquots. Repeated freezing and thawing is not recommended. Storage in "frost-free" freezers is not recommended. If slight turbidity occurs upon prolonged storage, clarify the solution by centrifugation before use.

Product Profile
Working dilution is at least 1:1,000 by immunoblotting using a human A431 cell lysate, anti-rabbit IgG conjugated to peroxidase and enhanced chemi-luminescence.

Note: In order to obtain best results and assay sensitivity in different techniques and preparations we recommend determining optimal working dilutions by titration test.

References

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lpg 3/99