

## Gene Section

### Mini Review

# STAT3 (Signal Transducer and Activator of Transcription 3)

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## Identity

**Other names:** Acute Phase Response Factor, APRF

**HGNC (Hugo):** STAT3

**Location:** 17q21.2

**Local order:** STAT3 is flanked by STAT5a and PTRF.

## DNA/RNA

### Note

24 exons spanning 74444 bp.

### Transcription

There are two major transcripts, STAT3a and STAT3b. STAT3a mRNA is 4973 bp. The STAT3b arises due to an alternate splice acceptor site in exon 23 which gives rise to a protein that is essentially truncated after amino acid 715. Another variant differs by 1 amino acid.

## Protein

### Description

There are two major isoforms of STAT3. The long form is known as STAT3 (or STAT3a) and is a 770 amino acid protein (93 kDa on gels). Notable features are STAT family DNA binding domain, an SH2 domain, a major tyrosine phosphorylation site at Y705

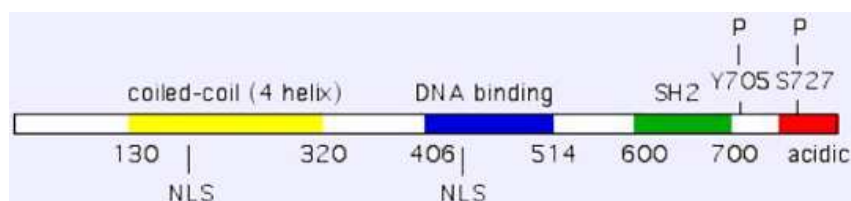
and a major serine phosphorylation site at S727. Phosphorylation leads to dimerization of STAT3 via intermolecular pTyr-SH2 interactions. STAT3 can also heterodimerize with STAT1. (Recent data suggests that STAT3 can possibly form a dimer without tyrosine phosphorylation and that phosphorylation leads to changes dimer conformation). Tyrosine of the protein activates its high affinity DNA binding activity (TTCNNGAA) and can stimulate nuclear translocation of the protein. Stimulation of STAT3 tyrosine phosphorylation occurs in response to a variety of cytokines and growth factors including LIF, OSM, IL-6, leptin, EGF, PDGF, and HGF. The C terminal domain is a transcriptional activation domain whose activity is enhanced by phosphorylation of serine 727. The STAT3 beta isoform (84 kDa) is missing this domain (1-715 + 7 unique amino acids resulting from frameshift) and is sometimes used as a dominant negative though there is also evidence that it regulates distinct genes as well.

### Expression

Near ubiquitous.

### Localisation

Cytoplasmic, but translocates to the nucleus upon tyrosine phosphorylation.



## Function

Transcription regulation.

## Homology

Shares homology with the other 6 mammalian STAT genes: STAT1, STAT2, STAT4, STAT5A, STAT5B, STAT6.

## Implicated in

### Disease

Upregulated in many cancers including glioblastoma, head and neck cancer, prostate cancer, and breast cancer. A constitutively active form of STAT3 is oncogenic, though these mutations have not been identified in human cancer as yet. STAT 3 activation is associated with Crohn's disease, and other inflammatory diseases such as pulmonary fibrosis and acute lung injury. STAT3 is critical for leptin signaling and its mutation leads to obesity in mice.

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