Atlas of Genetics and Cytogenetics in Oncology and Haematology

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# Gene Section
## Mini Review

# LIFR (leukemia inhibitory factor receptor alpha)

**Nathalie Dagoneau, Valérie Cormier-Daire**

Department of Genetics and INSERM U781, Paris Descartes University, Tour Lavoisier, Hopital Necker Enfants Malades, 149 rue de Sevres, 75015 Paris, France (ND, VCD)

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## Identity

**Other names:** CD118; FLJ98106; FLJ99923; LIF-R; SJS2; STWS; SWS

**HGNC (Hugo):** LIFR

**Location:** 5p13.1

## DNA/RNA

### Description

At least 20 exons.

### Transcription

10258 pb mRNA; 3293 pb open reading frame.

## Protein

### Description

1097 amino acids; 190 kDa.

### Expression

Chondrocytes; osteoblasts; skin fibroblasts placenta; brain; mixed; muscle; lung; embryonic tissue; uterus; stomach; kidney; ovary; liver; prostate; vascular; thyroid; testis; eye; pancreas; adrenal gland; spleen; thymus; trachea; larynx; connective tissue; ear; ascites; ganglia; nerve; tonsil; heart; adipose tissue; intestine; mouth (not in lymphocytes).

### Localisation

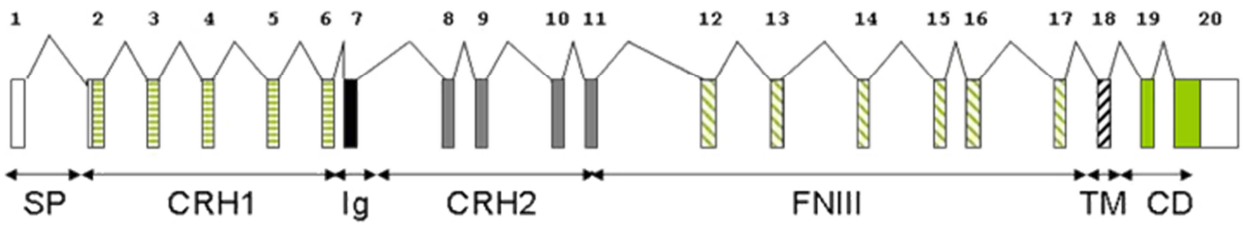
Cytoplasmic membrane.

### Function

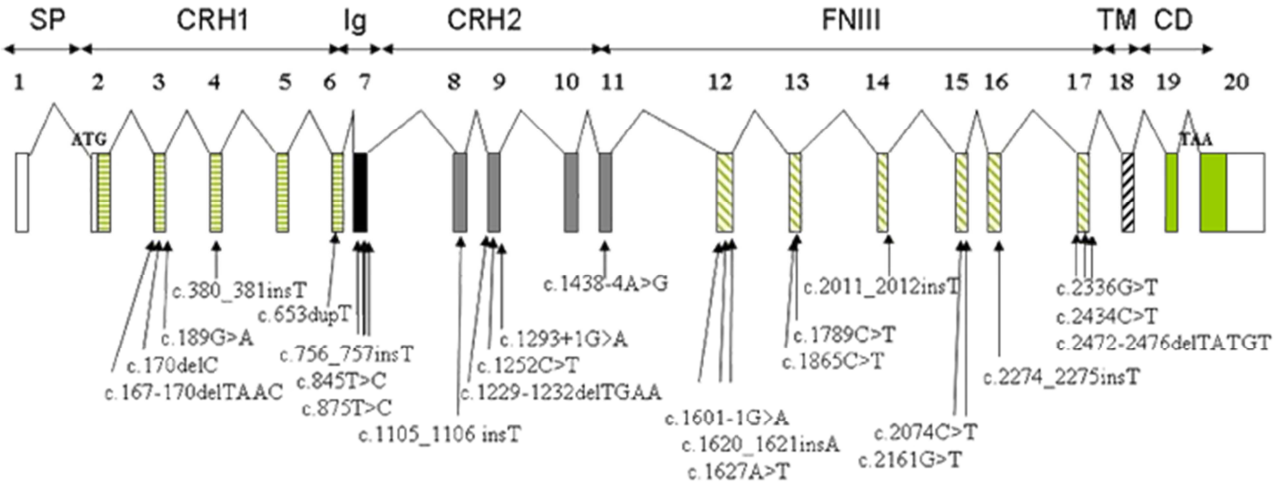
LIFR (gp190) and gp130 compose an heterodimeric receptor. The addition of ligand LIF enhances the dimer formation and signal transduction involves the activation of the JAK/STAT and MAPK cascades.

### Homology

With the IL6 cytokine family receptors.
LIFR depends of the class I cytokine receptor family. The members of this family contain a conserved domain with ~200 amino acid residues in the amino-terminal half and a WSXWS motif in the carboxy-terminal end.




SP: signal peptid, CRH1/CRH2: cytokine receptor homology domain, Ig: Ig-like domain, FNIII: type III fibronectin domain, TM: transmembrane domain, CD: cytoplasmic domain




# Mutations

**Note**

14 distinct mutations were identified in 19 families. An identical frameshift insertion (c.653_654insT) was identified in families from the United Arab Emirates, suggesting a founder effect in that region. 12/14 mutations predicted premature termination of translation (Dagoneau et al., 2004; Corona-Rivera et al., 2009).

# Implicated in

## *Stüve-Wiedemann syndrome*

**Note**

SWS / SJS2

**Disease**

Stüve-Wiedemann syndrome is a severe autosomal recessive condition characteried by bowing of the long bones, with cortical thickening, flared metaphyses with coarsened trabecular pattern, camptodactyly, respiratory distress, feeding difficulties, and hyperthermic episodes responsible for early lethality.

## *ACTH-secreting pituitary adenomas*

**Disease**

LIFR was expressed in all ACTH-secreting adenomas and non functioning adenomas. No LIFR mutations were found (Heutling et al., 2004).

## *Pancreatic carcinoma*

**Disease**

Pancreatic carcinoma cells expressed LIF, LIFR and gP130 mRNAs. LIF upregulates LIFR mRNA expression and antisense oligonucleotide of LIFR suppresses cell proliferation. The results may be of potential value in immunotherapy for pancreatic carcinoma (Kamohara et al., 2007).

## *Neuroblastoma*

**Disease**

Growth factors (EGF, FGF) cause a decrease in LIFR levels in neuroblastoma cells that correlated with the activation of extracellular signal-regulated kinase (Erk1/Erk2). The decrease in LIFR is due to an increase in the rate of protein degradation and is blocked by inhibitors of lysosomal degradation (Port et al., 2008).

## *Glioblastoma multiforme (GBM)*

**Disease**

Glioblastoma multiforme (GBM) represents an extremely chemoresistant tumour type. The authors analysed the expression of selected neural and non-neural differentiation markers including LIFR. They found that LIFR expression was associated with chemosensitivity of tumour cells to several chemotherapeutic agents. However, its role in glioma pathogenesis and response to therapy remains to be elucidated.

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