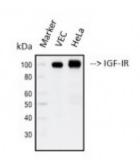


Anti-IGF-IR antibody



Western Blot (WB) analysis of VEC and HeLa cell lysates using IGF-IR Antibody (STI93647).



Description IGF-IR is a protein encoded by the IGF1R gene which is approximately

154,7 kDa. IGF-IR is localised to the cell membrane. It is involved in apoptotic pathways, the GPCR pathway and ERK signalling. It is a receptor tyrosine kinase which mediates actions of insulin-like growth factor 1. The activated protein is involved in cell growth and survival control and is also crucial for tumour transformation and survival of malignant cells. It is formed from two subunits, each of which is comprised of an extracellular alpha-subunit and a transmembrane beta-subunit with intracellular tyrosine kinase activity. IGF-IR is expressed in the nervous system, skin, pancreas, lung and muscle. Mutations in the IGF1R gene may result in insulin-like growth factor 1 resistance. STJ93647 was affinity-purified from rabbit antiserum by affinity-chromatography using epitope-specific immunogen. This polyclonal antibody detects endogenous levels of IGF-IR protein.

Model STJ93647

Host Rabbit

Reactivity Human, Mouse, Rat

Applications ELISA, IHC, WB

Immunogen Synthesized peptide derived from human IGF-IR around the non-

phosphorylation site of Y1161.

Immunogen Region 1100-1180 aa

Gene ID 3480

Gene Symbol <u>IGF1R</u>

Dilution range WB 1:500-1:2000IHC 1:100-1:300ELISA 1:10000

Specificity IGF-IR Polyclonal Antibody detects endogenous levels of IGF-IR protein.

Tissue Specificity Found as a hybrid receptor with INSR in muscle, heart, kidney, adipose tissue,

skeletal muscle, hepatoma, fibroblasts, spleen and placenta (at protein level).

Expressed in a variety of tissues. Overexpressed in tumors, including melanomas, cancers of the colon, pancreas prostate and kidney.

Purification The antibody was affinity-purified from rabbit antiserum by affinity-

chromatography using epitope-specific immunogen.

Note For Research Use Only (RUO).

Protein Name Insulin-like growth factor I receptor Insulin-like growth factor I receptor IGF-

I receptor CD antigen CD221 Insulin-like growth factor 1 receptor alpha chain

Insulin-like growth factor 1 receptor beta chain

Molecular Weight 150 kDa

Clonality Polyclonal

Conjugation Unconjugated

Isotype IgG

Formulation Liquid in PBS containing 50% glycerol, 0.5% BSA and 0.02% sodium azide.

Concentration 1 mg/ml

Storage Instruction Store at -20°C, and avoid repeat freeze-thaw cycles.

Database Links <u>HGNC:5465OMIM:147370</u>

Alternative Names Insulin-like growth factor I receptor Insulin-like growth factor I receptor IGF-

I receptor CD antigen CD221 Insulin-like growth factor 1 receptor alpha chain

Insulin-like growth factor 1 receptor beta chain

Function Receptor tyrosine kinase which mediates actions of insulin-like growth factor

1 (IGF1). Binds IGF1 with high affinity and IGF2 and insulin (INS) with a lower affinity. The activated IGF1R is involved in cell growth and survival control. IGF1R is crucial for tumor transformation and survival of malignant cell. Ligand binding activates the receptor kinase, leading to receptor autophosphorylation, and tyrosines phosphorylation of multiple substrates, that function as signaling adapter proteins including, the insulin-receptor substrates (IRS1/2), Shc and 14-3-3 proteins. Phosphorylation of IRSs proteins lead to the activation of two main signaling pathways: the PI3K-AKT/PKB pathway and the Ras-MAPK pathway. The result of activating the MAPK pathway is increased cellular proliferation, whereas activating the PI3K pathway inhibits apoptosis and stimulates protein synthesis.

Phosphorylated IRS1 can activate the 85 kDa regulatory subunit of PI3K (PIK3R1), leading to activation of several downstream substrates, including protein AKT/PKB. AKT phosphorylation, in turn, enhances protein synthesis through mTOR activation and triggers the antiapoptotic effects of IGFIR through phosphorylation and inactivation of BAD. In parallel to PI3K-driven signaling, recruitment of Grb2/SOS by phosphorylated IRS1 or Shc leads to recruitment of Ras and activation of the ras-MAPK pathway. In addition to these two main signaling pathways IGF1R signals also through the Janus kinase/signal transducer and activator of transcription pathway (JAK/STAT). Phosphorylation of JAK proteins can lead to phosphorylation/activation of signal transducers and activators of transcription (STAT) proteins. In

particular activation of STAT3, may be essential for the transforming activity of IGF1R. The JAK/STAT pathway activates gene transcription and may be responsible for the transforming activity. JNK kinases can also be activated by the IGF1R. IGF1 exerts inhibiting activities on JNK activation via phosphorylation and inhibition of MAP3K5/ASK1, which is able to directly associate with the IGF1R.; When present in a hybrid receptor with INSR, binds IGF1. PubMed:12138094 shows that hybrid receptors composed of IGF1R and INSR isoform Long are activated with a high affinity by IGF1, with low affinity by IGF2 and not significantly activated by insulin, and that hybrid receptors composed of IGF1R and INSR isoform Short are activated by IGF1, IGF2 and insulin. In contrast, PubMed:16831875 shows that hybrid receptors composed of IGF1R and INSR isoform Long and hybrid receptors composed of IGF1R and INSR isoform Long and hybrid receptors composed of IGF1R and INSR isoform Short have similar binding characteristics, both bind IGF1 and have a low affinity for insulin.

Cellular Localization

Post-translational Modifications

Cell membrane

Autophosphorylated on tyrosine residues in response to ligand binding. Autophosphorylation occurs in trans, i.e. one subunit of the dimeric receptor phosphorylates tyrosine residues on the other subunit. Autophosphorylation occurs in a sequential manner; Tyr-1165 is predominantly phosphorylated first, followed by phosphorylation of Tyr-1161 and Tyr-1166. While every single phosphorylation increases kinase activity, all three tyrosine residues in the kinase activation loop (Tyr-1165, Tyr-1161 and Tyr-1166) have to be phosphorylated for optimal activity. Can be autophosphorylated at additional tyrosine residues (in vitro). Autophosphorylated is followed by phosphorylation of juxtamembrane tyrosines and C-terminal serines. Phosphorylation of Tyr-980 is required for IRS1- and SHC1-binding. Phosphorylation of Ser-1278 by GSK-3beta restrains kinase activity and promotes cell surface expression, it requires a priming phosphorylation at Ser-1282. Dephosphorylated by PTPN1. Polyubiquitinated at Lys-1168 and Lys-1171 through both 'Lys-48' and 'Lys-29' linkages, promoting receptor endocytosis and subsequent degradation by the proteasome. Ubiquitination is facilitated by pre-existing phosphorylation. Sumoylated with SUMO1. Controlled by regulated intramembrane proteolysis (RIP). Undergoes metalloprotease-dependent constitutive ectodomain shedding to produce a membrane-anchored 52 kDa C-Terminal fragment which is further processed by presenilin gamma-secretase to yield an intracellular 50 kDa fragment.

St John's Laboratory Ltd

F +44 (0)207 681 2580

T +44 (0)208 223 3081

W http://www.stjohnslabs.com/ E info@stjohnslabs.com