abcam

Product datasheet

Anti-IGF1 Receptor (phospho Y1158 + Y1162 + Y1163) antibody ab5681

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Overview

Product name	Anti-IGF1 Receptor (phospho Y1158 + Y1162 + Y1163) antibody
Description	Rabbit polyclonal to IGF1 Receptor (phospho Y1158 + Y1162 + Y1163)
Host species	Rabbit
Tested applications	**Suitable for:** WB
Species reactivity	**Reacts with:** Mouse, Human **Predicted to work with:** Rat
Immunogen	Synthetic phosphopeptide derived from the region of IR/IGF1R that contains tyrosines 1158, 1162 and 1163 of the human insulin receptor. The corresponding residues in the IGF1R are 1131, 1135 and 1136.
Positive control	CHO-T cells transfected with a vector encoding the human insulin receptor and stimulated with insulin, and 3T3-L1 adipocytes +/- insulin stimulation.
General notes	The antiserum was produced against a chemically synthesized phosphopeptide derived from the region of IR/IGF1R that contains tyrosines 1158, 1162 and 1163 of the human insulin receptor (IR) as numbered according to Ebina, et al. (1146, 1150 and 1151 according to Ullrich, et al.). The corresponding residues in the IGF1R are 1131, 1135 and 1136. The sequence is conserved in human, mouse and rat for both the IR and IGF1R.The two relevant papers are:Ebina, Y., et al. (1985) The human insulin receptor cDNA: the structural basis for hormone-activated transmembrane signalling. Cell 40(4):747-758.Ullrich, A., et al. (1985) Human insulin receptor and its relationship to the tyrosine kinase family of oncogenes. Nature 313(6005):756-761. There are a long and a short isoform of this protein. This is why we are listing 1158, 1162 and 1163 in the name (where these phospho sites in the long isoform) as well as 1146, 1150 and 1151 (for the short isoform).

Properties

Form	Liquid
Storage instructions	Shipped at 4°C. Upon delivery aliquot and store at -20°C or -80°C. Avoid repeated freeze / thaw cycles.
Storage buffer	pH: 7.30 Preservative: 0.05% Sodium azide Constituents: PBS, 50% Glycerol, 0.1% BSA

Purity	Immunogen affinity purified
Purification notes	The antibody has been negatively preadsorbed using a non-phosphopeptide corresponding to the site of phosphorylation to remove antibody that is reactive with non-phosphorylated Insulin Receptor (IR). The final product is generated by affinity chromatography using an IR-derived peptide phosphorylated at tyrosines 1158, 1162 and 1163 (1131, 1135 and 1136 for IGF1R).
Clonality	Polyclonal
Isotype	IgG

Applications

Our Abpromise guarantee covers the use of **ab5681** in the following tested applications.

The application notes include recommended starting dilutions; optimal dilutions/concentrations should be determined by the end user.

Application	Abreviews	Notes
WB	★★★★☆	1/1000. Detects a band of approximately 100 kDa.

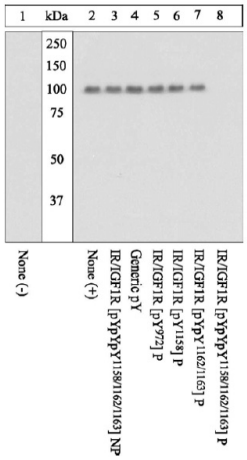
Target

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 Short have similar binding characteristics, both bind IGF1 and have a low affinity for insulin.

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.
Involvement in disease	Insulin-like growth factor 1 resistance
Sequence similarities	Belongs to the protein kinase superfamily. Tyr protein kinase family. Insulin receptor subfamily. Contains 4 fibronectin type-III domains. Contains 1 protein kinase domain.
Post-translational modifications	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.
Cellular localization	Cell membrane.

Images



Western blot - Anti-IGF1 Receptor (phospho Y1158 + Y1162 + Y1163) antibody (ab5681)

Peptide Competition: Extracts prepared from CHO-T cells transfected with an insulin receptor containing vector and left unstimulated (1) or stimulated with insulin (2-8) were resolved by SDS-PAGE on a 10% polyacrylamide gel and transferred to PVDF. Membranes were blocked with a 5% BSA TBST buffer overnight at 4°C and incubated with the ab5681 antibody for two hours at room temperature in a 3% BSA-TBST buffer, following prior incubation with: no peptide (1, 2), the non-phosphorylated peptide corresponding to the immunogen (3), a generic phosphotyrosine-containing peptide (4), the phosphopeptides corresponding to other IR/IGF1R sites (5-7) or, the phosphopeptide immunogen (8). After washing, membranes were incubated with goat F(ab' 2 anti-rabbit IgG HRP conjugate and bands were detected using the Pierce SuperSignal method. The data show that only the phosphopeptide corresponding to IR/IGF1R [pYpYpY1158/1162/1163] completely

blocks the antibody signal, thereby demonstrating the specificity of the antibody. The data also show the activation of the insulin receptor upon stimulation with insulin.

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