

Product datasheet

Recombinant human Insulin Receptor protein ab70687

2 Images

Overview

Product name	Recombinant human Insulin Receptor protein
Protein length	Protein fragment

Description

Nature	Recombinant
Source	Baculovirus infected Sf9 cells

Amino Acid Sequence

Species	Human
Amino acids	1011 to 1382
Tags	GST tag N-Terminus

Specifications

Our [Abpromise guarantee](#) covers the use of **ab70687** in the following tested applications.

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

Biological activity	The Specific activity of ab70687 was determined to be 2683nmol/min/mg.
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Applications	Functional Studies SDS-PAGE
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Form	Liquid
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Additional notes	ab204853 (IRS1 peptide) can be utilized as a substrate for assessing kinase activity
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Preparation and Storage

Stability and Storage	Shipped on dry ice. Upon delivery aliquot and store at -80°C. Avoid freeze / thaw cycles. Preservative: None Constituents: 25% Glycerol, 50mM Tris HCl, 150mM Sodium chloride, 0.25mM DTT, 0.1mM EGTA, 0.1mM EDTA, 0.1mM PMSF, pH 7.5 This product is an active protein and may elicit a biological response in vivo, handle with caution.
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General Info

Function

Receptor tyrosine kinase which mediates the pleiotropic actions of insulin. Binding of insulin leads to phosphorylation of several intracellular substrates, including, insulin receptor substrates (IRS1, 2, 3, 4), SHC, GAB1, CBL and other signaling intermediates. Each of these phosphorylated proteins serve as docking proteins for other signaling proteins that contain Src-homology-2 domains (SH2 domain) that specifically recognize different phosphotyrosines residues, including the p85 regulatory subunit of PI3K and SHP2. Phosphorylation of IRSs proteins lead to the activation of two main signaling pathways: the PI3K-AKT/PKB pathway, which is responsible for most of the metabolic actions of insulin, and the Ras-MAPK pathway, which regulates expression of some genes and cooperates with the PI3K pathway to control cell growth and differentiation. Binding of the SH2 domains of PI3K to phosphotyrosines on IRS1 leads to the activation of PI3K and the generation of phosphatidylinositol-(3, 4, 5)-triphosphate (PIP3), a lipid second messenger, which activates several PIP3-dependent serine/threonine kinases, such as PDK1 and subsequently AKT/PKB. The net effect of this pathway is to produce a translocation of the glucose transporter SLC2A4/GLUT4 from cytoplasmic vesicles to the cell membrane to facilitate glucose transport. Moreover, upon insulin stimulation, activated AKT/PKB is responsible for: anti-apoptotic effect of insulin by inducing phosphorylation of BAD; regulates the expression of gluconeogenic and lipogenic enzymes by controlling the activity of the winged helix or forkhead (FOX) class of transcription factors. Another pathway regulated by PI3K-AKT/PKB activation is mTORC1 signaling pathway which regulates cell growth and metabolism and integrates signals from insulin. AKT mediates insulin-stimulated protein synthesis by phosphorylating TSC2 thereby activating mTORC1 pathway. The Ras/RAF/MAP2K/MAPK pathway is mainly involved in mediating cell growth, survival and cellular differentiation of insulin. Phosphorylated IRS1 recruits GRB2/SOS complex, which triggers the activation of the Ras/RAF/MAP2K/MAPK pathway. In addition to binding insulin, the insulin receptor can bind insulin-like growth factors (IGF1 and IGFII). Isoform Short has a higher affinity for IGFII binding. When present in a hybrid receptor with IGF1R, 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

Isoform Long and isoform Short are predominantly expressed in tissue targets of insulin metabolic effects: liver, adipose tissue and skeletal muscle but are also expressed in the peripheral nerve, kidney, pulmonary alveoli, pancreatic acini, placenta vascular endothelium, fibroblasts, monocytes, granulocytes, erythrocytes and skin. Isoform Short is preferentially expressed in fetal cells such as fetal fibroblasts, muscle, liver and kidney. Found as a hybrid receptor with IGF1R in muscle, heart, kidney, adipose tissue, skeletal muscle, hepatoma, fibroblasts, spleen and placenta (at protein level). Overexpressed in several tumors, including breast, colon, lung, ovary, and thyroid carcinomas.

Involvement in disease

Rabson-Mendenhall syndrome
Leprechaunism
Diabetes mellitus, non-insulin-dependent
Familial hyperinsulinemic hypoglycemia 5
Insulin-resistant diabetes mellitus with acanthosis nigricans type A

Sequence similarities

Belongs to the protein kinase superfamily. Tyr protein kinase family. Insulin receptor subfamily. Contains 3 fibronectin type-III domains. Contains 1 protein kinase domain.

Domain

The tetrameric insulin receptor binds insulin via non-identical regions from two alpha chains, primarily via the C-terminal region of the first INSR alpha chain. Residues from the leucine-rich N-terminus of the other INSR alpha chain also contribute to this insulin binding site. A secondary insulin-binding site is formed by residues at the junction of fibronectin type-III domain 1 and 2.

Post-translational modifications

After being transported from the endoplasmic reticulum to the Golgi apparatus, the single glycosylated precursor is further glycosylated and then cleaved, followed by its transport to the plasma membrane.

Autophosphorylated on tyrosine residues in response to insulin. Phosphorylation of Tyr-999 is required for binding to IRS1, SHC1 and STAT5B. Dephosphorylated by PTPRE at Tyr-999, Tyr-1185, Tyr-1189 and Tyr-1190. Dephosphorylated by PTPRF and PTPN1. Dephosphorylated by PTPN2; down-regulates insulin-induced signaling.

Cellular localization

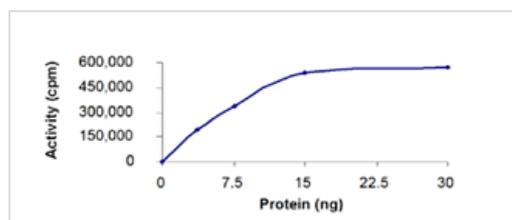
Cell membrane.

Images



SDS-PAGE showing ab70687 at approximately 70kDa.

SDS-PAGE - Insulin Receptor protein (Active)
(ab70687)



Kinase Assay showing the specific activity of ab70687

Functional Studies - Insulin Receptor protein (Active)
(ab70687)

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