Phospho-IRS-1 Sampler Kit

E051036

Kits Includes	Cat.	Quantity	Application	Reactivity	Source
IRS-1 (Phospho-Ser636) Antibody	E011230-2	50μg/50μl	IHC, WB	Human, Mouse, Rat	Rabbit
IRS-1 (Phospho-Ser639) Antibody	E011231-2	50μg/50μl	IHC	Human, Mouse, Rat	Rabbit
IRS-1 (Phospho-Ser307) Antibody	E011235-2	50μg/50μl	IHC	Human, Mouse, Rat	Rabbit
IRS-1 (Ab-636) Antibody	E021223-2	50μg/50μl	IHC, WB	Human, Mouse, Rat	Rabbit
IRS-1 (Ab-307) Antibody	E021228-2	50μg/50μl	IHC	Human, Mouse, Rat	Rabbit

Tyrosine kinase receptors, including the insulin receptor, mediate their activity by causing the addition of a phosphate group to particular tyrosines on certain proteins within a cell. The "substrate" proteins which are phosphorylated by the Insulin Receptor include a protein called "IRS-1" for "insulin receptor substrate 1". IRS-1 binding and phosphorylation eventually leads to an increase in the high affinity glucose transporter (Glut4) molecules on the outer membrane of insulin-responsive tissues, including muscle cells and adipose tissue, and therefore to an increase in the uptake of glucose from blood into these tissues. Briefly, the glucose transporter (Glut4), is transported from cellular vesicles to the cell surface, where it then can mediate the transport of glucose into the cell.

Insulin receptor substrate 1 (IRS-1) plays a key role in transmitting signals from the insulin and insulin-like growth factor-1 (IGF-1) receptors to intracellular pathways PI3K / Akt and Erk MAP kinase pathways.

Tyrosine phosphorylation of the insulin or IGF-1 receptors, upon extracellular ligand binding, induces the cytoplasmic binding of IRS-1 to these receptors, through its SH2 homology domains. Multiple tryosine residues of IRS-1 itself are then phosphorylated by these receptors. This enables IRS-1 to activate several signalling pathways, including the PI3K pathway and the MAP kinase pathway.

The activated IRS-1 acts as a secondary messenger within the cell to stimulate the transcription of insulin-regulated genes. First, the protein Grb2 binds the P-Tyr residue of IRS-1 in its SH2 domain. Grb2

is then able to bind SOS, which in turn catalyzes the replacement of bound GDP with GTP on Ras, a G protein. This protein then begins a phosphorylation cascade, culminating in the activation of mitogen-activated protein kinase (MAPK), which enters the nucleus and phosphorylates various nuclear transcription factors (such as Elk1).

Glycogen synthesis is also stimulated by the insulin receptor via IRS-1. In this case, it is the SH2 domain of PI-3 kinase (PI-3K) that binds the P-Tyr of IRS-1. Now activated, PI-3K can convert the membrane lipid phosphatidylinositol 4,5-bisphosphate (PIP2) to phosphatidylinositol 3,4,5-triphosphate (PIP3). This indirectly activates a protein kinase, PKB, via phosphorylation. PKB then phosphorylates several target proteins, including glycogen synthase kinase 3 (GSK-3). GSK-3 is responsible for phosphorylating (and thus deactivating) glycogen synthase. When GSK-3 is phosphorylated, it is deactivated, and prevented from deactivating glycogen synthase. In this roundabout manner, insulin increases glycogen synthesis.

IRS-1 plays important biological function for both metabolic and mitogenic (growth promoting) pathways: mice deficent of IRS1 have only a mild diabetic phenotype, but a pronounced growth impairment, i.e. IRS-1 knockout mice only reach 50% of the weight of normal mice. IRS-1 may also play a role in cancer, as it has been shown that transgenic mice overexpressing IRS-1 develop breast cancer.

The cellular protein levels of IRS-1 are regulated by the Cullin7 E3 ubiquin ligase, which targets IRS-1 for ubiquitin mediated degradation by the proteasome.

References:

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Dearth RK, Cui X, Kim HJ, *et al.* (2007). "Oncogenic transformation by the signaling adaptor proteins insulin receptor substrate (IRS)-1 and IRS-2.". *Cell Cycle* 6 (6): 705–13.

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Sasaoka T, Kobayashi M (2000). "The functional significance of Shc in insulin signaling as a substrate of the insulin receptor". *Endocr. J.* 47 (4): 373–81.

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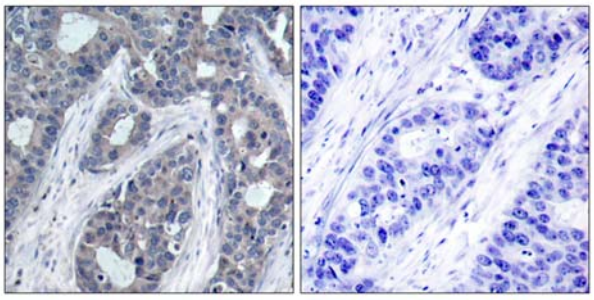
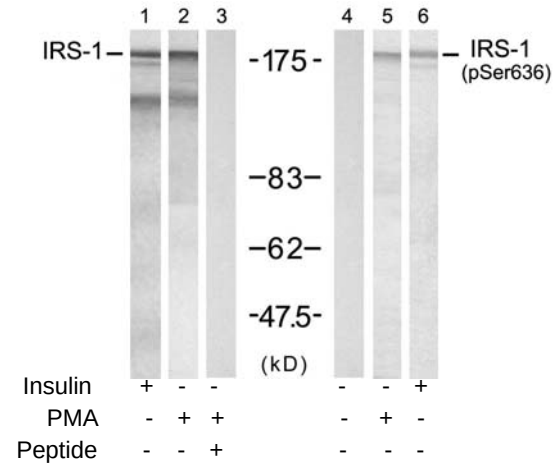
IRS-1 (Phospho-Ser636) Antibody

E011230

Catalog Number: E011230-1, E011230-2
Amount: 50μg/50μl, 100μg/100μl
Swiss-Prot No. : P35568
Form of Antibody: Rabbit IgG in phosphate buffered saline (without Mg^{2+} and Ca^{2+}), pH 7.4, 150mM NaCl, 0.02% sodium azide and 50% glycerol.
Storage/Stability: Store at -20℃/1 year
Immunogen: The antiserum was produced against synthesized phosphopeptide derived from human IRS-1 around the phosphorylation site of serine 636 (P-M-S^{P}-P-K).
Purification: The antibody was affinity-purified from rabbit antiserum by affinity-chromatography using epitope-specific phosphopeptide. The antibody against non-phosphopeptide was removed by chromatogramphy using non-phosphopeptide corresponding to the phosphorylation site.
Specificity/Sensitivity: IRS-1 (phospho-Ser636) antibody detects endogenous levels of IRS-1 only when phosphorylated at serine 636.
Reactivity: Human, Mouse, Rat
Applications: WB: 1:500~1:1000 IHC: 1:50-1:100
References: Ozes ON, et al. (2001) Proc Natl Acad Sci U S A; 98(8): 4640-4645
Tzatsos A, et al. (2006) Mol Cell Biol; 26(1): 63-76
Kadowaki T, et al. (2000) J Clin Invest; 106(4): 459-465
Ozes ON, et al. (2001) Proc Natl Acad Sci U S A; 98(8): 4640-4645
Szanto I, et al. (2000) Proc Natl Acad Sci U S A; 97(5): 2355-2360



Immunohistochemical analysis of paraffin-embedded human breast carcinoma tissue, using IRS-1 (phospho-Ser636) antibody (E011230).

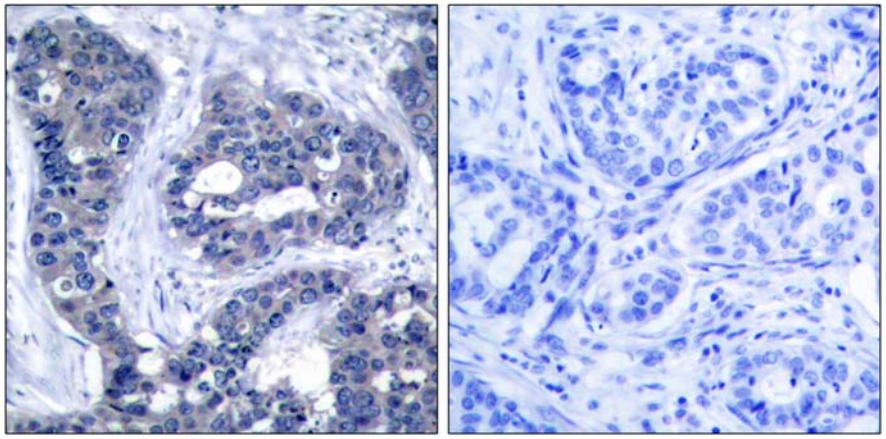


Western blot analysis of extracts from 293 cells treated with insulin(100nM, 30min) or PMA (0.2μM, 15min) using IRS-1 (Ab-636) antibody (E021223, Lane 1, 2 and 3) and IRS-1 (phospho-Ser636) antibody (E011230, Lane 4, 5 and 6).

IRS-1 (Phospho-Ser639) Antibody

E011231

Catalog Number: E011231-1, E011231-2
Amount: 50μg/50μl, 100μg/100μl
Swiss-Prot No. : P35568
Form of Antibody: Rabbit IgG in phosphate buffered saline (without Mg^{2+} and Ca^{2+}), pH 7.4, 150mM NaCl, 0.02% sodium azide and 50% glycerol.
Storage/Stability: Store at -20℃/1 year
Immunogen: The antiserum was produced against synthesized phosphopeptide derived from human IRS-1 around the phosphorylation site of serine 639 (P-K-S^{P}-V-S).
Purification: The antibody was affinity-purified from rabbit antiserum by affinity-chromatography using epitope-specific phosphopeptide. The antibody against non-phosphopeptide was removed by chromatogramphy using non-phosphopeptide corresponding to the phosphorylation site.
Specificity/Sensitivity: IRS-1 (phospho-Ser639) antibody detects endogenous levels of IRS-1 only when phosphorylated at serine 639.
Reactivity: Human, Mouse, Rat
Applications: IHC: 1:50~1:100
References:
Ozes ON, et al. (2001) Proc Natl Acad Sci U S A; 98(8): 4640-4645
Tzatsos A, et al. (2006) Mol Cell Biol; 26(1): 63-76
Steppan CM, et al. (2005) Mol Cell Biol; 25(4): 1569-1575
Batty IH, et al. (2004) Biochem J; 379(Pt 3): 641-651



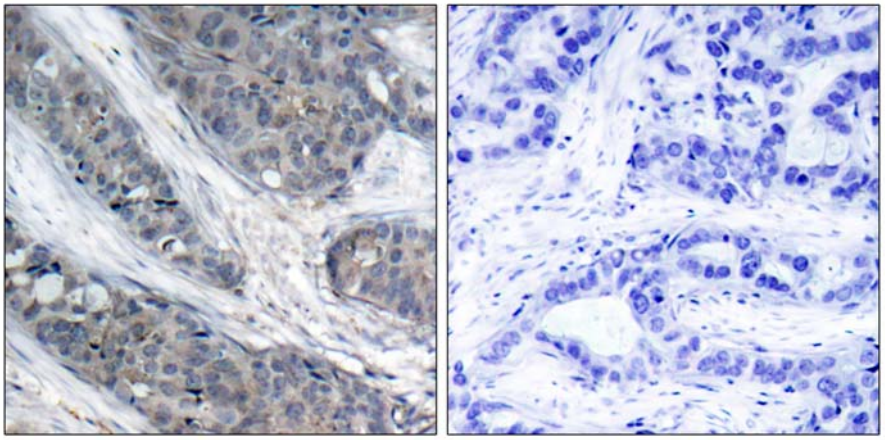
P-Peptide - +

Immunohistochemical analysis of paraffin-embedded human breast carcinoma tissue, using IRS-1 (phospho-Ser639) antibody (E011231).

IRS-1 (Phospho-Ser307) Antibody

E011235

Catalog Number: E011235-1, E011235-2
Amount: 50μg/50μl, 100μg/100μl
Swiss-Prot No. : P35568
Form of Antibody: Rabbit IgG in phosphate buffered saline (without Mg^{2+} and Ca^{2+}), pH 7.4, 150mM NaCl, 0.02% sodium azide and 50% glycerol.
Storage/Stability: Store at -20℃/1 year
Immunogen: The antiserum was produced against synthesized phosphopeptide derived from human IRS-1 around the phosphorylation site of serine 307 (T-E-S^{P}-I-T).
Purification: The antibody was affinity-purified from rabbit antiserum by affinity-chromatography using epitope-specific phosphopeptide. The antibody against non-phosphopeptide was removed by chromatogramphy using non-phosphopeptide corresponding to the phosphorylation site.
Specificity/Sensitivity: IRS-1 (phospho-Ser307) antibody detects endogenous levels of IRS-1 only when phosphorylated at serine 307.
Reactivity: Human, Mouse, Rat
Applications: IHC: 1:50~1:100
References: Steppan CM, et al. (2005) Mol Cell Biol; 25(4): 1569-1575
Tuncman G, et al. (2006) Proc Natl Acad Sci U S A; 103(28): 10741-10746
Shoelson SE, et al. (2006) J Clin Invest; 116(7): 1793-1801

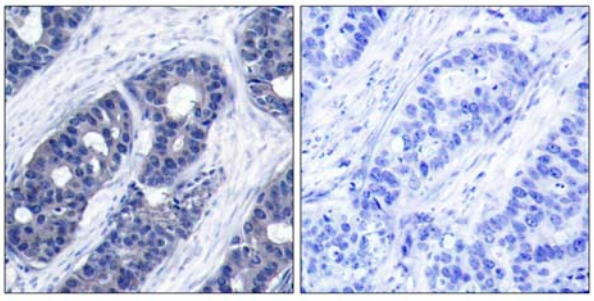


Immunohistochemical analysis of paraffin-embedded human breast carcinoma tissue, using IRS-1 (phospho-Ser307) antibody (E011235).

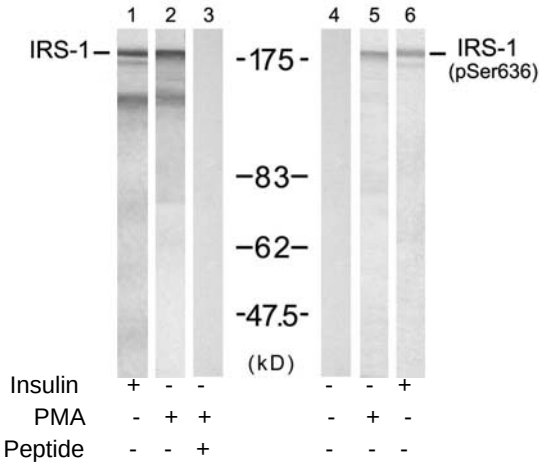
IRS-1 (Ab-636) Antibody

E021223

Catalog Number: E021223-1, E021223-2
Amount: 50μg/50μl, 100μg/100μl
Swiss-Prot No. : P35568
Form of Antibody: Rabbit IgG in phosphate buffered saline (without Mg^{2+} and Ca^{2+}), pH 7.4, 150mM NaCl, 0.02% sodium azide and 50% glycerol.
Storage/Stability: Store at -20℃/1 year
Immunogen: The antiserum was produced against synthesized non-phosphopeptide derived from human IRS-1 around the phosphorylation site of serine 636 (P-M-S^{P}-P-K).
Purification: The antibody was affinity-purified from rabbit antiserum by affinity-chromatography using epitope-specific immunogen.
Specificity/Sensitivity: IRS-1 (Ab-636) antibody detects endogenous levels of total IRS-1 protein.
Reactivity: Human, Mouse, Rat
Applications: WB: 1:500~1:1000 IHC: 1:50-1:100
References:
Ozes ON, et al. (2001) Proc Natl Acad Sci U S A; 98(8): 4640-4645
Tzatsos A, et al. (2006) Mol Cell Biol; 26(1): 63-76
Kadowaki T, et al. (2000) J Clin Invest; 106(4): 459-465
Ozes ON, et al. (2001) Proc Natl Acad Sci U S A; 98(8): 4640-4645
Szanto I, et al. (2000) Proc Natl Acad Sci U S A; 97(5): 2355-2360



Immunohistochemical analysis of paraffin-embedded human breast carcinoma tissue, using IRS-1 (Ab-636) antibody (E021223).

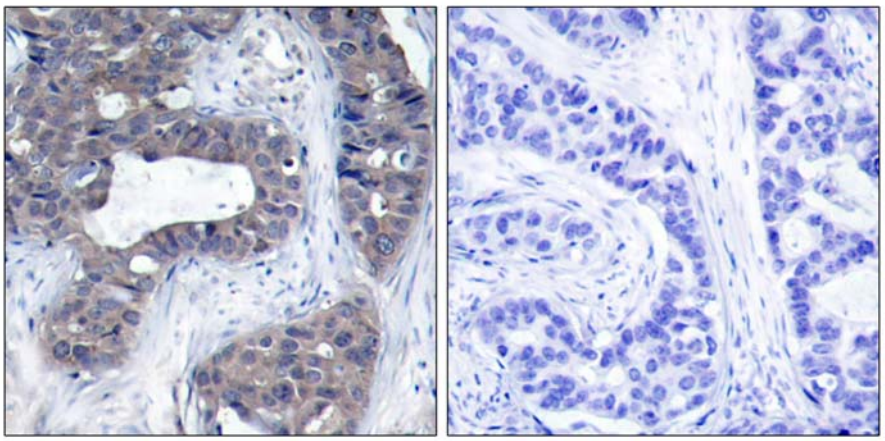


Western blot analysis of extracts from 293 cells treated with insulin(100nM, 30min) or PMA (0.2μM, 15min) using IRS-1 (Ab-636) antibody (E021223, Lane 1, 2 and 3) and IRS-1 (phospho-Ser636) antibody (E011230, Lane 4, 5 and 6).

IRS-1 (Ab-307) Antibody

E021228

Catalog Number: E021228-1, E021228-2
Amount: 50μg/50μl, 100μg/100μl
Swiss-Prot No. : P35568
Form of Antibody: Rabbit IgG in phosphate buffered saline (without Mg^{2+} and Ca^{2+}), pH 7.4, 150mM NaCl, 0.02% sodium azide and 50% glycerol.
Storage/Stability: Store at -20℃/1 year
Immunogen: The antiserum was produced against synthesized non-phosphopeptide derived from human IRS-1 around the phosphorylation site of serine 307(T-E-S^P-I-T).
Purification: The antibody was affinity-purified from rabbit antiserum by affinity-chromatography using epitope-specific immunogen.
Specificity/Sensitivity: IRS-1 (Ab-307) antibody detects endogenous levels of total IRS-1 protein.
Reactivity: Human, Mouse, Rat
Applications: IHC: 1:50~1:100
References: Steppan CM, et al. (2005) Mol Cell Biol; 25(4): 1569-1575
Tuncman G, et al. (2006) Proc Natl Acad Sci U S A; 103(28): 10741-10746
Shoelson SE, et al. (2006) J Clin Invest; 116(7): 1793-1801



Peptide - +

Immunohistochemical analysis of paraffin-embedded human breast carcinoma tissue, using IRS-1 (Ab-307) antibody (E021228).