

p-IRS-1 (Ser 374)-R: sc-17193-R

BACKGROUND

Insulin receptor substrate-1 (IRS-1) is a substrate of the Insulin receptor that undergoes phosphorylation in response to Insulin, IGF-1 and IL-4. Tyrosine (Tyr) phosphorylation of IRS-1 mediates Insulin-stimulated responses, while Serine (Ser)/Threonine (Thr) phosphorylation of IRS-1 can either enhance or negate Insulin effects. Tyrosines 465, 612, 632, 662, 941 and 989 of IRS-1 resemble YXXM motifs that upon phosphorylation are predicted to bind SH2 domains in the p85 regulatory subunit of PI 3-K, resulting in activation of p110 catalytic subunit. SHP-2 binding to IRS-1 can occur upon phosphorylation at Tyr 1179 and Tyr 1229. GRB2 binding can occur upon phosphorylation at Tyr 896. Rodent Ser 99 and Thr 502 of IRS-1 are casein kinase II-dependent phosphorylation sites. There is an increase in Ser 636 phosphorylation of IRS-1 in primary skeletal muscle cells from patients with type 2 diabetes. IGF-1 and Anisomycin treatment converge downstream onto mTOR and PKC δ to induce IRS-1 Ser 312 phosphorylation. Insulin resistance in the aorta of hypertensive rats is associated with elevated IRS-1 phosphorylation at Ser 307 and increased SAPK/JNK activation. IRS-1 contains three putative binding sites for 14-3-3 protein at Ser 270, Ser 374 and Ser 641 that are capable of phosphorylation.

REFERENCES

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- Esposito, D.L., et al. 2001. Tyr 612 and Tyr 632 in human Insulin receptor substrate-1 are important for full activation of Insulin-stimulated phosphatidylinositol 3-kinase activity and translocation of Glut4 in adipose cells. *Endocrinology* 142: 2833-2840.
- Hers, I., et al. 2002. Reciprocal feedback regulation of Insulin receptor and Insulin receptor substrate tyrosine phosphorylation by phosphoinositide 3-kinase in primary adipocytes. *Biochem. J.* 368: 875-884.
- Ishizuka, T., et al. 2004. Protein kinase C (PKC) β modulates serine phosphorylation of Insulin receptor substrate-1 (IRS-1)—effect of overexpression of PKC β on Insulin signal transduction. *Endocr. Res.* 30: 287-299.
- Liu, Y.F., et al. 2004. Serine phosphorylation proximal to its phosphotyrosine binding domain inhibits Insulin receptor substrate-1 function and promotes Insulin resistance. *Mol. Cell. Biol.* 24: 9668-9681.
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CHROMOSOMAL LOCATION

Genetic locus: IRS1 (human) mapping to 2q36.3; Irs1 (mouse) mapping to 1 C5.

SOURCE

p-IRS-1 (Ser 374)-R is a rabbit polyclonal antibody raised against a short amino acid sequence containing Ser 374 phosphorylated IRS-1 of human origin.

PRODUCT

Each vial contains 200 μ g IgG in 1.0 ml of PBS with < 0.1% sodium azide and 0.1% gelatin.

Blocking peptide available for competition studies, sc-17193 P, (100 μ g peptide in 0.5 ml PBS containing < 0.1% sodium azide and 0.2% BSA).

APPLICATIONS

p-IRS-1 (Ser 374)-R is recommended for detection of Ser 374 phosphorylated IRS-1 of mouse, rat and human origin by Western Blotting (starting dilution 1:200, dilution range 1:100-1:1000), immunoprecipitation [1-2 μ g per 100-500 μ g of total protein (1 ml of cell lysate)], immunofluorescence (starting dilution 1:50, dilution range 1:50-1:500) and solid phase ELISA (starting dilution 1:30, dilution range 1:30-1:3000).

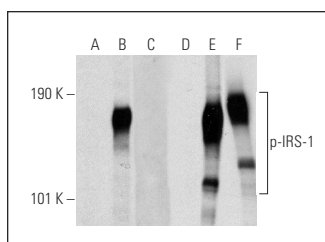
p-IRS-1 (Ser 374)-R is also recommended for detection of correspondingly phosphorylated IRS-1 in additional species, including equine, canine, bovine and porcine.

Suitable for use as control antibody for IRS-1 siRNA (h): sc-29376, IRS-1 siRNA (m): sc-29377, IRS-1 shRNA Plasmid (h): sc-29376-SH, IRS-1 shRNA Plasmid (m): sc-29377-SH, IRS-1 shRNA (h) Lentiviral Particles: sc-29376-V and IRS-1 shRNA (m) Lentiviral Particles: sc-29377-V.

Molecular Weight of p-IRS-1: 170-185 kDa.

Positive Controls: MCF7 + Insulin cell lysate: sc-24733 or IRS-1 (h): 293T Lysate: sc-116569.

DATA



Western blot analysis of IRS-1 phosphorylation in non-transfected: sc-117752 (A,D), untreated human IRS-1 transfected: sc-116569 (B,E) and lambda protein phosphatase (sc-200312A) treated human IRS-1 transfected: sc-116569 (C,F) 293T whole cell lysates. Antibodies tested include p-IRS-1 (Ser 374)-R: sc-17193-R (A,B,C) and IRS-1 (A-19): sc-560 (D,E,F).

STORAGE

Store at 4° C, **DO NOT FREEZE**. Stable for one year from the date of shipment. Non-hazardous. No MSDS required.

RESEARCH USE

For research use only, not for use in diagnostic procedures.

PROTOCOLS

See our web site at www.scbt.com or our catalog for detailed protocols and support products.