

p-IRS-1/2 (Ser 270): sc-17192

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

- Ogihara, T., et al. 1997. 14-3-3 protein binds to insulin receptor substrate-1, one of the binding sites of which is in the phosphotyrosine binding domain. *J. Biol. Chem.* 272: 25267-25274.
- 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.
- Liberman, Z., et al. 2005. Serine 332 phosphorylation of insulin receptor substrate-1 by glycogen synthase kinase-3 attenuates insulin signaling. *J. Biol. Chem.* 280: 4422-4428.

CHROMOSOMAL LOCATION

Genetic locus: IRS1 (human) mapping to 2q36, IRS2 (human) mapping to 13q34; Irs1 (mouse) mapping to 1 C5, Irs2 (mouse) mapping to 8 A1.1.

SOURCE

p-IRS-1/2 (Ser 270) is available as either goat (sc-17192) or rabbit (sc-17192-R) polyclonal affinity purified antibody raised against a short amino acid sequence containing phosphorylated Ser 270 of 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-17192 P, (100 μ g peptide in 0.5 ml PBS containing < 0.1% sodium azide and 0.2% BSA).

APPLICATIONS

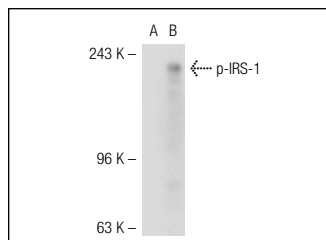
p-IRS-1/2 (Ser 270) is recommended for detection of Ser 270 phosphorylated IRS-1 and correspondingly phosphorylated IRS-2 of mouse, rat and human origin by Western Blotting (starting dilution 1:200, dilution range 1:100-1:1000), immunoprecipitation [1-2 μ g per 100-500 μ g of total protein (1 ml of cell 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).

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

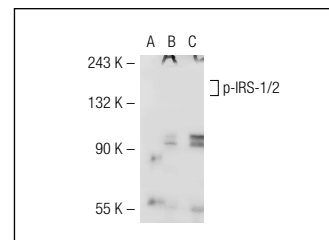
Molecular Weight of p-IRS-2: 165-185 kDa.

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

DATA



p-IRS-1/2 (Ser 270): sc-17192. Western blot analysis of IRS-1 phosphorylation in non-transfected: sc-117752 (A) and human IRS-1 transfected: sc-116569 (B) 293T whole cell lysates.



p-IRS-1/2 (Ser 270): sc-17192. Western blot analysis of IRS-1/2 phosphorylation in untreated (A), insulin treated (B) and insulin and lambda protein phosphatase (sc-200312A) treated (C) 293T whole cell lysates.

SELECT PRODUCT CITATIONS

- Gao, Z., et al. 2003. Aspirin inhibits serine phosphorylation of Insulin receptor substrate 1 in tumor necrosis factor-treated cells through targeting multiple serine kinases. *J. Biol. Chem.* 278: 24944-24950.
- Zhang, J., et al. 2008. S6K directly phosphorylates IRS-1 on Ser-270 to promote insulin resistance in response to TNF α signaling through IKK2. *J. Biol. Chem.* 283: 35375-35382.

STORAGE

Store at 4 $^{\circ}$ 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.