SANTA CRUZ BIOTECHNOLOGY, INC.

p-IRS-1 (Ser 307): sc-101709

BACKGROUND

Insulin receptor substrate-1 (IRS-1) is a substrate of the insulin receptor that undergoes phosphorylation in response to insulin, IGF-I 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-I and Anisomycin treatment converge downstream onto FRAP 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

1. 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.
2. 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.
3. 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.
4. 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.
5. 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.
6. 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.
7. Kim, J.A., et al. 2005. Phosphorylation of Ser 24 in the Pleckstrin homology domain of insulin receptor substrate-1 by mouse Pelle-like kinase/interleukin-1 receptor-associated kinase: cross-talk between inflammatory signaling and insulin signaling that may contribute to insulin resistance. J. Biol. Chem. 280: 23173-23183.

STORAGE

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

CHROMOSOMAL LOCATION

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

SOURCE

p-IRS-1 (Ser 307) is a rabbit polyclonal antibody raised against a short amino acid sequence containing phosphorylated Ser 307 of IRS-1 of human origin.

PRODUCT

Each vial contains 100 µg IgG in 1.0 ml of PBS with < 0.1% sodium azide and 0.1% gelatin.

APPLICATIONS

p-IRS-1 (Ser 307) is recommended for detection of Ser 307 phosphorylated IRS-1 of human origin and correspondingly phosphorylated Ser 302 of mouse and rat origin by immunofluorescence and immunohistochemistry (including paraffin-embedded sections) (starting dilution 1:50, dilution range 1:50-1:500).

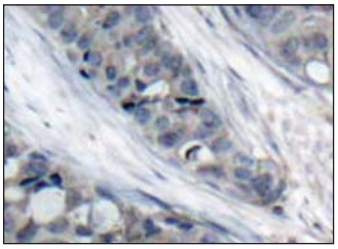
Suitable for use as control antibody for IRS-1 siRNA (h): sc-29376 and IRS-1 siRNA (m): sc-29377.

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

RECOMMENDED SECONDARY REAGENTS

To ensure optimal results, the following support (secondary) reagents are recommended: 1) Immunofluorescence: use goat anti-rabbit IgG-FITC: sc-2012 (dilution range: 1:100-1:400) or goat anti-rabbit IgG-TR: sc-2780 (dilution range: 1:100-1:400) with UltraCruz™ Mounting Medium: sc-24941. 2) Immunohistochemistry: use ImmunoCruz™: sc-2051 or ABC: sc-2018 rabbit IgG Staining Systems.

DATA



p-IRS-1 (Ser 307): sc-101709. Immunoperoxidase staining of formalin-fixed, paraffin-embedded human breast carcinoma tissue showing cytoplasmic localization.

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.