SANTA CRUZ BIOTECHNOLOGY, INC.

p-IRS-1/2 (Tyr 612)-R: sc-17195-R

SANTA CRUZ BIOTECHNOLOGY

The Power to Question

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 PI3K, 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 phsophorylation 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 PKCd 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.

CHROMOSOMAL LOCATION

Genetic locus: IRS1 (human) mapping to 2q36.3, IRS2 (human) mapping to 13q34; Irs1 (mouse) mapping to 1 C5, Irs2 (mouse) mapping to 8 A1.1.

SOURCE

p-IRS-1/2 (Tyr 612)-R is a rabbit polyclonal antibody raised against a short amino acid sequence containing Tyr 612 phosphorylated 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.

Blocking peptide available for competition studies, sc-17195 P, (100 µg peptide in 0.5 ml PBS containing < 0.1% sodium azide and 0.2% BSA).

STORAGE

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

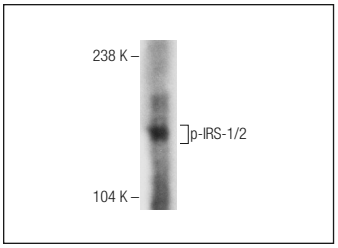
APPLICATIONS

p-IRS-1/2 (Tyr 612)-R is recommended for detection of Tyr 612 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 µg per 100-500 µg 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-1/2 (Tyr 612) is also recommended for detection of correspondingly phosphorylated IRS-1 and IRS-2 in additional species, including equine.

Molecular Weight of p-IRS-1/2: 170-185/165-185 kDa.

Positive Controls: MCF7 whole cell lysate: sc-2206 or NIH/3T3 whole cell lysate: sc-2210.

DATA



p-IRS-1/2 (Tyr 612)-R: sc-17195-R. Western blot analysis of IRS-1/2 phosphorylation in MCF7 whole cell lysate.

SELECT PRODUCT CITATIONS

1. 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.
2. Ku, H.C., et al. 2009. Green tea-epigallocatechin gallate inhibits Insulin stimulation of 3T3-L1 preadipocyte mitogenesis via the 67-kDa laminin receptor pathway. Am. J. Physiol., Cell Physiol. 297: C121-C132.
3. Shi, J., et al. 2009. Insulin receptor substrate-1 suppresses transforming growth factor-β1-mediated epithelial-mesenchymal transition. Cancer Res. 69: 7180-7187.
4. Piro, S., et al. 2010. Palmitate affects Insulin receptor phosphorylation and intracellular Insulin signal in a pancreatic α-cell line. Endocrinology 151: 4197-4206.
5. Viscarra, J.A., et al. 2011. Glut4 is upregulated despite decreased Insulin signaling during prolonged fasting in northern elephant seal pups. Am. J. Physiol. Regul. Integr. Comp. Physiol. 300: R150-R154.
6. Bonhomme, S., et al. 2011. Gastric bypass up-regulates Insulin signaling pathway. Nutrition 27: 73-80.
7. Folli, F., et al. 2011. Altered Insulin receptor signalling and β-cell cycle dynamics in type 2 diabetes mellitus. PLoS ONE 6: e28050.

RESEARCH USE

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