



IRS-1 (905-1070): sc-4250 WB

BACKGROUND

The insulin receptor substrate-1 (IRS-1), a 170-185 kDa protein major substrate of the insulin receptor, is phosphorylated in response to stimulation of cells by insulin, insulin-like growth factor 1 (IGF-1) and interleukin 4 (IL-4). IRS-1 is phosphorylated on serine, threonine and tyrosine residues in a variety of tissues. An insulin-sensitive serine/threonine kinase casein kinase II mediates a portion of the insulin-stimulated serine/threonine phosphorylation of overexpressed IRS-1 *in vivo*. Thr 502 is identified as the major casein kinase II-catalyzed phosphorylation site in rat IRS-1, and Ser 99 is an additional phosphorylation site catalyzed by casein kinase II. Thus, casein kinase II-catalyzed phosphorylation of IRS-1 may be a component of the intracellular insulin signaling cascade. IRS-1 contains three putative binding sites for 14-3-3 (Ser 270, Ser 374 and Ser 641) and the motif around Ser 270 is located in the phosphotyrosine binding domain of IRS-1, which is responsible for the interaction with the insulin receptor. The association of 14-3-3 with IRS-1 increases significantly upon treatment with okadaic acid, a potent serine/threonine phosphatase inhibitor. Therefore, the association of 14-3-3 protein may play a role in the regulation of insulin sensitivity by interrupting the association between the insulin receptor and IRS-1.

REFERENCES

1. Myers, M.G. Jr., Backer, J.M., Sun, X.J., Shoelson, S.E., Hu, P., Schlessinger, J., Yoakim, M., Schaffhausen, B., and White, M.F. 1992. IRS-1 activates the phosphatidylinositol 3'-kinase by associating with the Src homology 2 domains of p85. *Proc. Natl. Acad. Sci.* 89: 10350-10354.
2. Myers, M.G. Jr., Sun, S.J., Cheatham, B., Jachna, B.R., Glasheen, E.M., Backner, J.M., and White, M.F. 1993. IRS-1 is a common element in insulin and IGF signaling to the phosphatidylinositol 3'-kinase. *Endocrinology* 132: 1421-1430.
3. Myers, M.G. Jr. and White, M.F. 1993. The new elements of insulin signaling: insulin receptor substrate-1 and proteins with SH2 domains. *Diabetes* 42: 643-650.
4. Tanasijevic, M.J., Myers, M.G. Jr., Thoma, R.S., Crimmins, D.L., White, M.F., and Sacks, D.B. 1993. Phosphorylation of the insulin receptor substrate IRS-1 by casein kinase II. *J. Biol. Chem.* 268: 18157-18166.
5. Ogihara, T., Isobe, T., Ichimura, T., Taoka, M., Funaki, M., Sakoda, H., Onishi, Y., Inukai, K., Anai, M., Fukushima, Y., Kikuchi, M., Yazaki, Y., Oka, Y., and Asano, T. 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.

SOURCE

IRS-1 (905-1070) is expressed in *E. coli* as a 45 kDa tagged fusion protein corresponding to amino acids 905-1070 mapping to an internal domain of IRS-1 of human origin.

PRODUCT

IRS-1 (905-1070) is purified from bacterial lysates (>98%) by glutathione agarose affinity chromatography; supplied as 10 µg in 0.1 ml SDS-PAGE loading buffer.

APPLICATIONS

IRS-1 (905-1070) is suitable as a Western blotting control for sc-7200 and sc-8038.

STORAGE

Store at -20° C; stable for one year from the date of shipment.

RESEARCH USE

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