SANTA CRUZ BIOTECHNOLOGY, INC.

INSIG-1 (M-80): sc-98984

SANTA CRUZ BIOTECHNOLOGY

The Power to Question

BACKGROUND

INSIG-1 and INSIG-2 play distinct roles in a negative-feedback mechanism for cholesterol synthesis. INSIG-1 is highly expressed in liver and fibroblast cell lines. INSIG-1 localizes to the endoplasmic reticulum (ER) and binds the sterol-sensing domain of SREBP cleavage-activating protein (SCAP). Sterol induces INSIG-1 binding to SCAP. INSIG-2, another ER protein, binds SCAP in a sterol-regulated manner. Thus, INSIG-1 and INSIG-2 block the export of SCAP from the ER and ultimately inhibit cholesterol synthesis by preventing the proteolytic processing of SREBPs by Golgi enzymes. INSIG-1 is encoded by the Insulin-induced gene (INSIG-1). INSIG-1 gene expression is suppressed by oxysterols and restored following the introduction of the hypocholesterolemic agent LY295427. The negative feedback mechanism is absent in mutant CHO cells with a point mutation in one SCAP allele within the sterol-sensing domain. The mutant cells constitutively cleave SREBP in the presence of sterols. The critical role of INSIG-1 and INSIG-2 in cholesterol metabolism may be exploited as a therapeutic effect for hypercholesterolemia.

REFERENCES

1. Peng, Y., et al. 1997. Cloning, human chromosomal assignment, and adipose and hepatic expression of the CL-6/INSIG1 gene. Genomics 43: 278-284.
2. Janowski, B.A. 2002. The hypocholesterolemic agent LY295427 upregulates INSIG-1, identifying the INSIG-1 protein as a mediator of cholesterol homeostasis through SREBP. Proc. Natl. Acad. Sci. USA 99: 12675-12680.
3. Yabe, D., et al. 2002. INSIG, a second endoplasmic reticulum protein that binds SCAP and blocks export of sterol regulatory element-binding proteins. Proc. Natl. Acad. Sci. USA 99: 12753-12758.
4. Yang, T., et al. 2002. Crucial step in cholesterol homeostasis: sterols promote binding of SCAP to INSIG-1, a membrane protein that facilitates retention of SREBPs in ER. Cell 110: 489-500.
5. Yabe, D., et al. 2002. Three mutations in sterol-sensing domain of SCAP block interaction with INSIG and render SREBP cleavage insensitive to sterols. Proc. Natl. Acad. Sci. USA 99: 16672-16677.

CHROMOSOMAL LOCATION

Genetic locus: Insig1 (mouse) mapping to 5 B1.

SOURCE

INSIG-1 (M-80) is a rabbit polyclonal antibody raised against amino acids 1-80 mapping at the N-terminus of INSIG-1 of mouse origin.

PRODUCT

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

STORAGE

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

APPLICATIONS

INSIG-1 (M-80) is recommended for detection of INSIG-1 of mouse and rat 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).

Suitable for use as control antibody for INSIG-1 siRNA (m): sc-44433, INSIG-1 shRNA Plasmid (m): sc-44433-SH and INSIG-1 shRNA (m) Lentiviral Particles: sc-44433-V.

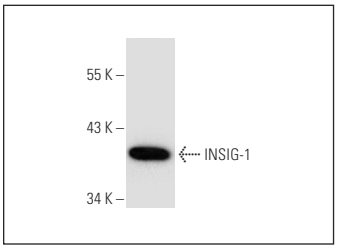
Molecular Weight of INSIG-1: 30 kDa.

Positive Controls: c4 whole cell lysate: sc-364186.

RECOMMENDED SECONDARY REAGENTS

To ensure optimal results, the following support (secondary) reagents are recommended: 1) Western Blotting: use goat anti-rabbit IgG-HRP: sc-2004 (dilution range: 1:2000-1:100,000) or Cruz Marker™ compatible goat anti-rabbit IgG-HRP: sc-2030 (dilution range: 1:2000-1:5000), Cruz Marker™ Molecular Weight Standards: sc-2035, TBS Blotto A Blocking Reagent: sc-2333 and Western Blotting Luminol Reagent: sc-2048. 2) Immunoprecipitation: use Protein A/G PLUS-Agarose: sc-2003 (0.5 ml agarose/2.0 ml). 3) 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.

DATA



INSIG-1 (M-80): sc-98984. Western blot analysis of INSIG-1 expression in c4 whole cell lysate.

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.