

# INSIG-1 (G-12): sc-51102

## 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

- Peng, Y., Schwarz, E.J., Lazar, M.A., Genin, A., Spinner, N.B. and Taub, R. 1997. Cloning, human chromosomal assignment, and adipose and hepatic expression of the CL-6/INSIG1 gene. *Genomics* 43: 278-284.
- 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.
- Yabe, D., Brown, M.S. and Goldstein, J.L. 2002. Insig-2, 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.
- Yang, T., Espenshade, P.J., Wright, M.E., Yabe, D., Gong, Y., Aebersold, R., Goldstein, J.L. and Brown, M.S. 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.
- Yabe, D., Xia, Z.P., Adams, C.M. and Rawson, R.B. 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 (G-12) is an affinity purified goat polyclonal antibody raised against a peptide mapping near 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.

Blocking peptide available for competition studies, sc-51102 P, (100 µg peptide in 0.5 ml PBS containing < 0.1% sodium azide and 0.2% BSA).

## APPLICATIONS

INSIG-1 (G-12) is recommended for detection of INSIG-1 of mouse origin by Western Blotting (starting dilution 1:200, dilution range 1:100-1:1000), 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.

## RECOMMENDED SECONDARY REAGENTS

To ensure optimal results, the following support (secondary) reagents are recommended: 1) Western Blotting: use donkey anti-goat IgG-HRP: sc-2020 (dilution range: 1:2000-1:100,000) or Cruz Marker™ compatible donkey anti-goat IgG-HRP: sc-2033 (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) Immunofluorescence: use donkey anti-goat IgG-FITC: sc-2024 (dilution range: 1:100-1:400) or donkey anti-goat IgG-TR: sc-2783 (dilution range: 1:100-1:400) with UltraCruz™ Mounting Medium: sc-24941.

## SELECT PRODUCT CITATIONS

- Chen, K., et al. 2011. Overexpression of Insig-1 protects β cell against glucolipotoxicity via SREBP-1c. *J. Biomed. Sci.* 18: 57.

## STORAGE

Store at 4° 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.

## PROTOCOLS

See our web site at [www.scbt.com](http://www.scbt.com) or our catalog for detailed protocols and support products.