Insig1/2(Phospho-Ser207/151) Antibody

#58005

Number: 58005-1, 58005-2

Amount: 50μg/50μl, 100μg/100μl

Accession No. :NCBI Gene ID: 3638 (Insig1); NCBI Gene ID: 51141 (Insig2)

Form of Antibody: Rabbit IgG in phosphate buffered saline (without Mg2+ and Ca2+), pH 7.4, 150mM NaCl,0.02% sodium azide and 50% glycerol.

Storage/Stability: Store at -20℃/1 year

Immunogen: The antiserum was produced against synthesized phosphopeptide derived from Human Insig1/2 around the phosphorylation site of serine 207/151 .

Purification: The antibody was affinity-purified from rabbit antiserum by affinity-chromatography using epitope-specific phosphopeptide. The antibody against non-phosphopeptide was removed by chromatography using non-phosphopeptide corresponding to the phosphorylation site.

Specificity/Sensitivity: Insig1/2(Phospho-Ser207/151) antibody detects endogenous levels of Insig1/2 only when phosphorylated at serine207/151 .

Reactivity: Human

Applications:

Predicted MW:

Insig1 pS207: 30~40 KD

Insig2 pS151: ~25 KD

WB **:**1:500~1:1000 IHC:1:50-100

Background :

Lipid metabolism, in particular cholesterol and fatty acid synthesis, is essential for converting nutrients into metabolic intermediates for membrane biosynthesis, energy storage, and generation of signaling molecules. Tumor cells maintain high level of lipid metabolism for rapid cell proliferation[1,2,3]. Gene transcription for cholesterol and fatty acid synthesis is controlled by membrane-bound transcription factor sterol regulatory element-binding proteins (SREBPs), including SREBP-1a, SREBP-1c, and SREBP-2[4]. The function of SREBPs is mainly regulated by an escort protein, the SREBP cleavage-activating protein (SCAP), and endoplasmic reticulum (ER) anchor proteins, insulin-induced genes (Insigs), during the feedback loop of fatty acid and cholesterol synthesis (Fig.1)[5,6]. Two Insig isoforms, Insig1 and Insig2, contain six transmembrane-spanning regions and differ in their cytosolic N-termini[7, 8]. Insig proteins bind to oxysterols, which are cholesterol derivatives—including 22- , 24- , 25- , and

27-hydroxycholesterol—in the central cavities within their transmembrane domains. Insig1/2 interact with SCAP via transmembrane domains 3 and 4[5, 9-11]. The binding of 25-hydroxycholesterol to Insigs is crucial for Insigs to bind to SCAP[10, 11]. In addition to its function to hinder the ER-to-Golgi transport of the SREBP–SCAP complex, Insig promotes the degradation of 3-hydroxy-3-methylglutaryl (HMG) CoA reductase, thereby reducing lipid synthesis[12]. In a recent study, it is reported that AKT in tumor cells phosphorylates cytosolic phosphoenolpyruvate carboxykinase 1 (PCK1) at S90[13]. Phosphorylated PCK1 translocates to the ER, where PCK1 uses GTP as a phosphate donor to phosphorylate Insig1 S207 and Insig2 S151. This phosphorylation reduces the binding of sterol to Insig1/2 and disrupts Insig-SCAP interaction, leading to SCAP/SREBP1 translocation to the Golgi apparatus and subsequent SREBP1 activation and downstream gene transcription for lipogenesis, tumor cell proliferation, and tumorigenesis in mice[13].

References:

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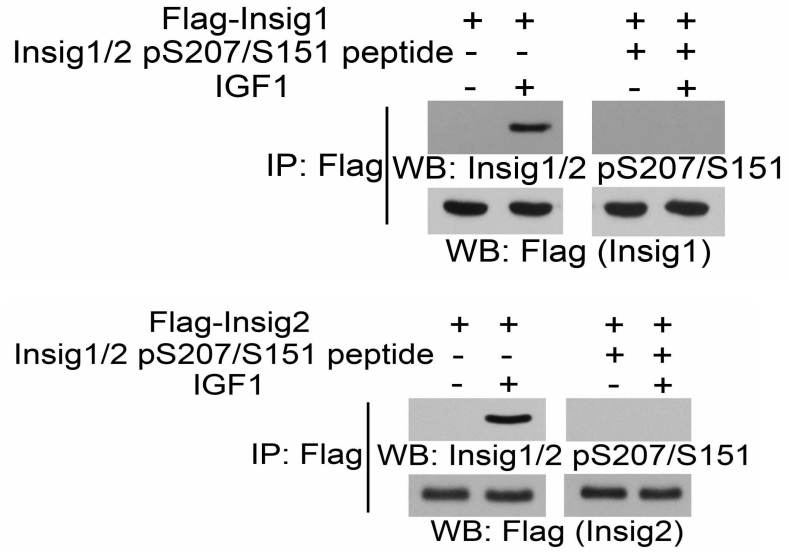
Application in this Article

IHC analyses of human HCC samples were performed with the indicated antibodies in the presence or absence of a blocking peptide for Insig1 pS207 and Insig2 pS151.



Huh7 cells expressing Flag-Insig1 (left panel) or Flag-Insig2 (right panel) were treated with or without IGF1 (100 ng/ml) for 1 h. Immunoprecipitation and immunoblotting analyses were

performed with the indicated antibodies in the presence or absence of a blocking peptide for Insig1 pS207 and Insig2 pS151.