

BACKGROUND

Glycogen synthase kinase 3 (GSK-3), a ubiquitously expressed and evolutionarily conserved protein serine/threonine kinase, was originally identified as an enzyme that regulates glycogen synthesis in response to insulin. GSK-3 was subsequently shown to function in cell division, proliferation, motility and survival. GSK-3 plays a role in a number of pathological conditions including cancer and diabetes and is increasingly seen as an important component of neurological diseases. GSK-3 phosphorylates tau and presenilin-1, which are involved in the development of Alzheimer's disease. Both isoforms of GSK-3 are ubiquitously expressed, although particularly high levels of GSK-3beta are found in the brain where it is involved in synaptic plasticity, possibly via regulation of NMDA receptor trafficking.¹

There are two mammalian GSK-3 isoforms encoded by distinct genes: GSK-3alpha and GSK-3beta. They are closely related in function. GSK-3alpha has a mass of 51 kDa, whereas GSK-3beta is a protein of 47 kDa. The difference in size is due to a glycine-rich extension at the N-terminus of GSK-3alpha. Although highly homologous within their kinase domains (98% identity), the two gene products share only 36% identity in the last 76 C-terminal residues. Moreover, they are not functionally identical. GSK-3 phosphorylates over 40 different substrates including signaling proteins, transcription factors and structural proteins, and is part of the signal transduction cascade of a large number of growth factors and cytokines. GSK-3 has also been implicated in the regulation of cell fate in *Dictyostelium* and is a component of the Wnt signaling pathway required for *Drosophila* and *Xenopus* development.²

The activity of GSK is regulated by phosphorylation (Akt, S6K, RSK, PKA and PKC), dephosphorylation (PP1 and PP2A), and by binding to protein complexes (with beta-catenin, axin, CK1 and the APC complex). In mammalian cells, on stimulation with insulin or other growth factors, GSK-3 is rapidly phosphorylated at serine 21 in GSK-3alpha or serine 9 in GSK-3beta, resulting in inhibition of GSK-3 kinase activity. Protein kinase B (PKB/Akt), a serine/threonine kinase located downstream of phosphatidylinositol 3-kinase (PI3K), has been demonstrated to phosphorylate both of these sites *in vitro* and *in vivo*, suggesting that growth factors down-regulate GSK-3 activity through the PI3K-PKB signaling cascade. Consistent with its position downstream of the PI3K-PKB pathway, GSK-3 activity suppresses cell proliferation and survival.³ It was also demonstrated that serine 21 in GSK-3alpha and serine 9 in GSK-3beta are also physiological substrates of cAMP-dependent protein kinase A (PKA). PKA physically associates with, phosphorylates, and inactivates both isoforms of GSK-3. Thus PKA functions as a GSK-3 kinase

that, in parallel with PKB, controls the activity of the multifunctional enzyme GSK-3.⁴

References:

1. Ali, A. et al: *Chem. Rev.* 101:2527-40, 2001
2. Doble, B.W. & Woodgett, J.R.: *J. Cell Sci.* 116:1175-86, 2003
3. Elder-Finkelman, H. et al: *Trends Mol. Med.* 8:126-32, 2002
4. Fang, X. et al: *Proc. Natl. Acad. Sci. USA* 97:11960-5, 2000

TECHNICAL INFORMATION

Source:

GSK-3 alpha antibody is a mouse monoclonal antibody raised against purified recombinant human GSK-3 alpha fragments expressed in *E. coli*.

Specificity and Sensitivity:

This antibody detects endogenous GSK-3 alpha proteins without cross-reactivity with other family members.

Storage Buffer: PBS and 30% glycerol

Storage:

Store at -20°C for at least one year. Store at 4°C for frequent use. Avoid repeated freeze-thaw cycles.

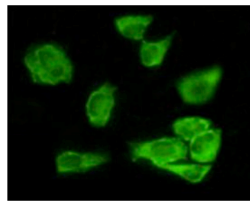
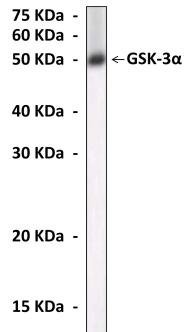
APPLICATIONS

Application:	*Dilution:
WB	1:1000
IP	n/d
IHC	n/d
ICC	n/d
FACS	n/d

**Optimal dilutions must be determined by end user.*



QUALITY CONTROL DATA



Top: Western Blot detection of GSK-3 alpha proteins in HeLa cell lysate using GSK-3 alpha Antibody.
Bottom: Immunofluorescent analysis of HeLa using GSK-3alpha Antibody.

