

BACKGROUND

p130CAS (Crk-associated substrate) belongs to a family of structurally related proteins that also includes Hef and Sin. It is a major tyrosine phosphorylated protein in cells transformed by *v-crk* and *v-src* oncogenes. In nontransformed cells, p130CAS localizes to focal adhesions and undergoes tyrosine phosphorylation in response to integrin-mediated adhesion. P130CAS tyrosine phosphorylation is primarily achieved by Src family kinases. Primary structure analysis indicates that p130CAS is a "docking" protein containing multiple domains and motifs for potential interactions with other signaling proteins. P130CAS deficiency in mice results in embryonic lethality associated with growth retardation and cardiovascular abnormalities, whereas p130CAS^{-/-} mouse embryo fibroblasts exhibit disorganized actin cytoskeleton and motility defects.¹

The distinguishing feature of p130CAS is a large substrate domain characterized by 15 Tyr-X-X-Pro (YxxP) motifs. It was shown that 14 of the YxxP tyrosines including Tyr410 (all but the most amino-terminal site) are subject to phosphorylation by Src by the processive mechanism.² Recruitment of Src to p130CAS can occur by either direct binding of the Src SH3 domain to a Pro-X-X-Pro motif in the Src-binding domain of p130CAS or by indirect binding achieved by the scaffolding function of focal adhesion kinase (FAK), whereby FAK simultaneously interacts with the p130CAS SH3 domain and the Src SH2 domain. Both mechanisms seem to substantially contribute to p130CAS substrate domain tyrosine phosphorylation. The CAS SH3 domain also interacts with tyrosine phosphatases PTP1B and PTP-PEST, indicating a possible role for this domain in both positive and negative regulation of p130CAS substrate domain tyrosine phosphorylation. The phosphorylated YxxP motifs serve as docking sites for SH2-mediated binding to adaptor proteins of the Crk family and other SH2-containing downstream signaling effectors. Phosphorylation of p130CAS substrate domain YxxP sites has been linked to integrin signaling pathways controlling both cell motility and cell survival.² In both processes, p130CAS/Crk coupling is implicated as a critical step in promoting relevant downstream signaling events, including activation of the small GTPase Rac1 and JNK.³ In addition, P130CAS has also been implicated in human cancer progression. It has been revealed that p130CAS plays a major role in promoting metastasis of Src-transformed cells and that p130CAS YxxP tyrosines are critical for both *in vitro* invasiveness and *in vivo* metastasis.⁴

References:

1. Honda, H. et al: Nature Genet. 16:361-5, 1998.
2. Huang, J. et al: J. Biol. Chem. 277:27265-72, 2002
3. Dolfi, F. et al: Proc. Natl. Acad. Sci. USA 95:15394-9, 1998
4. Brabek, J. et al: Mol. Cancer Res. 3:307-15, 2005

TECHNICAL INFORMATION

Source:

Phospho-p130CAS (Tyr410) Antibody is a rabbit antibody raised against a short peptide from human p130CAS sequence surrounding and containing phospho-Tyr410.

Specificity and Sensitivity:

This antibody detects phosphorylated p130CAS (Tyr410) proteins without cross-reactivity with other family members.

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

Storage:

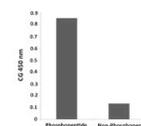
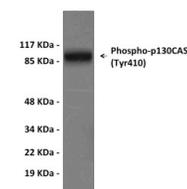
Store at -20°C for at least one year. Store at 4°C for frequent use. Avoid repeated freeze-thaw cycles.

APPLICATIONS

Application:	*Dilution:
WB	1:500-1:1,000
IP	n/d
IHC	1:50-1:100
ICC	n/d
FACS	n/d
ELISA	1:5,000

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

QUALITY CONTROL DATA



Top: Western blot analysis of extracts from NIH-3T3 cells.

Middle: Immunohistochemistry analysis of paraffin-embedded Human brain gliomas.

Bottom: ELISA for Immunogen Phosphopeptide (left) and Non-Phosphopeptide (right).

