Background: CAD is essential for the de novo synthesis of pyrimidine nucleotides and possesses the following enzymatic activities: glutamine amidotransferase, carbamoyl-phosphate synthetase, aspartate transcarbamoylase, and dihydroorotase. Thus, the enzyme converts glutamine to uridine monophosphate, a common precursor of all pyrimidine bases, and it is necessary for nucleic acid synthesis (1). In resting cells, CAD is localized mainly in the cytoplasm where it carries out pyrimidine synthesis. As proliferating cells enter S phase, MAP Kinase (Erk1/2) phosphorlyates CAD at Thr456, resulting in CAD translocation to the nucleus. As cells exit S phase, CAD is dephosphorylated at Thr456 and phosphorylated at Ser1406 by PKA, returning the pathway to basal activity (2). Various research studies have shown increased expression of CAD in several types of cancer, prompting the development of pharmacological inhibitors such as PALA. Further studies have identified CAD as a potential predictive early marker of prostate cancer relapse (3).

mTORC1 is a protein kinase that works to regulate the growth and proliferation of cells by sensing and integrating various growth signals. S6 kinase 1 (S6K1) is a downstream ribosomal protein target of mTORC1 and directly phosphorlyates Ser1859 on CAD. This phosphorylation stimulates the first three steps of the de novo primidine synthesis and thus helps to advance the cells overall progression through S phase of the cell cycle (4,5).

Specificity/Sensitivity: Phospho-CAD (Ser1859) Antibody recognizes endogenous levels of CAD protein only when phosphorylated at Ser1859.

Source/Purification: Polyclonal antibodies are produced by immunizing animals with a synthetic phosphopeptide corresponding to residues surrounding Ser1859 of human CAD protein. Antibodies are purified by protein A and peptide affinity chromatography.

Background References:

IMPORTANT: For western blots, incubate membrane with diluted antibody in 5% w/v nonfat dry milk, 1X TBS, 0.1% Tween® 20 at 4°C with gentle shaking, overnight.

Storage: Supplied in 10 mM sodium HEPES (pH 7.5), 150 mM NaCl, 100 µg/ml BSA and 50% glycerol. Store at –20°C. Do not aliquot the antibody.

*Species cross-reactivity is determined by western blot.

**Anti-rabbit secondary antibodies must be used to detect this antibody.

Recommended Antibody Dilutions:
Western blotting 1:1000

For product specific protocols please see the web page for this product at www.cellsignal.com.

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