Revision 1

Store at -20C

#88583

# Phospho-HER2/ErbB2 (Thr686) Antibody

Cell Signaling TECHNOLOGY®

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**For Research Use Only. Not for Use in Diagnostic Procedures.**

| Applications: | Reactivity: | Sensitivity: | MW (kDa): | Source/Isotype: | UniProt ID: | Entrez-Gene Id: |
|---|---|---|---|---|---|---|
| W | H | Endogenous | 185 | Rabbit | #P04626 | 2064 |

## Product Usage Information

| Application | Dilution |
|---|---|
| Western Blotting | 1:1000 |

## 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.

## Specificity/Sensitivity

Phospho-HER2/ERBB2 (Thr686) Antibody recognizes endogenous levels of HER2/ERBB2 protein only when phosphorylated at Thr686.

## Species predicted to react based on 100% sequence homology

Mouse, Rat

## Source / Purification

Polyclonal antibodies are produced by immunizing animals with a synthetic phospho-peptide corresponding to residues surrounding Thr686 of human HER2/ERBB2 protein. Antibodies are purified by protein A and peptide affinity chromatography.

## Background

The ErbB2 (HER2) proto-oncogene encodes a 185 kDa transmembrane, receptor-like glycoprotein with intrinsic tyrosine kinase activity (1). While ErbB2 lacks an identified ligand, ErbB2 kinase activity can be activated in the absence of a ligand when overexpressed and through heteromeric associations with other ErbB family members (2). Amplification of the *ErbB2* gene and overexpression of its product are detected in almost 40% of human breast cancers (3). Binding of the c-Cbl ubiquitin ligase to ErbB2 at Tyr1112 leads to ErbB2 poly-ubiquitination and enhances degradation of this kinase (4). ErbB2 is a key therapeutic target in the treatment of breast cancer and other carcinomas and targeting the regulation of ErbB2 degradation by the c-Cbl-regulated proteolytic pathway is one potential therapeutic strategy. Phosphorylation of the kinase domain residue Tyr877 of ErbB2 (homologous to Tyr416 of pp60c-Src) may be involved in regulating ErbB2 biological activity. The major autophosphorylation sites in ErbB2 are Tyr1248 and Tyr1221/1222; phosphorylation of these sites couples ErbB2 to the Ras-Raf-MAP kinase signal transduction pathway (1,5).

Thr686 is located in the cytoplasmic juxtamembrane region of ErbB2. PKC, PKA, and PKG II kinases have been reported to phosphorylate ErbB2 at this site, but the functional consequences of phosphorylation may be context dependent. For example, one research study reported that phosphorylation of ErbB2 at Thr686 enhanced ligand-induced receptor activation (6), while a separate research study reported inhibitory effects of phosphorylation on ErbB2 activation (8).

## Background References

1. Muthuswamy, S.K. et al. (1999) *Mol Cell Biol* 19, 6845-57.
2. Qian, X. et al. (1994) *Proc Natl Acad Sci USA* 91, 1500-4.
3. Dittadi, R. and Gion, M. (2000) *J Natl Cancer Inst* 92, 1443-4.
4. Klapper, L.N. et al. (2000) *Cancer Res* 60, 3384-8.
5. Kwon, Y.K. et al. (1997) *J Neurosci* 17, 8293-9.
6. Monje, P.V. et al. (2008) *J Biol Chem* 283, 34087-100.
7. Ouyang, X. et al. (1998) *Carcinogenesis* 19, 2013-9.
8. Zhu, M. et al. (2016) *Mol Med Rep* 13, 1909-13.

## Species Reactivity

Species reactivity is determined by testing in at least one approved application (e.g., western blot).

## Western Blot Buffer

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

## Applications Key

**W:** Western Blotting

## Cross-Reactivity Key

**H:** Human

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