

BACKGROUND

c-Abl is a non-receptor protein-tyrosine kinase related to the Src family. The N-terminal region of c-Abl is structurally similar to Src and includes Src homology regions 3 and 2 (SH3 and SH2) and the catalytic domain; however, Abl differs from all Src family members by the presence of a large (90 kDa) C-terminal domain. Several functional motifs have been defined in the Abl C-terminus, including a nuclear localization signal (NLS), DNA binding domain, actin binding domain, sites for phosphorylation by protein kinase C and cdc-2 kinase, and binding sites for the adapter proteins Crk, Grb-2 and Nck.¹ c-Abl has been implicated in many cellular processes including differentiation, division, adhesion, death, and stress response. c-Abl becomes activated in response to numerous extra- and intra-cellular stimuli.² c-Abl is localized in the nucleus and the cytoplasm, where it plays distinct roles. The effects of c-Abl are mediated by multiple protein-protein and protein-DNA interactions and its tyrosine kinase domain.³ Its oncogenic counterpart, the Bcr-Abl fusion protein, causes particular human leukaemias. Use of targeted therapy that inhibits BCR-ABL kinase activity by Gleevec leads to hematologic and cytogenetic responses in affected individuals.⁴

Mutation of a tyrosine (Tyr-245) in the linker region between the Src homology 2 and catalytic domains that is conserved among the Abl family inhibited the autophosphorylation-induced activation of wild-type c-Abl by 50%, whereas the c-Abl Y245F/Y412F double mutant was minimally activated by autophosphorylation. These results support a model where c-Abl is inhibited in part through an intramolecular Src homology 3-linker interaction and stimulated to full catalytic activity by sequential phosphorylation at Tyr-412 and Tyr-245.⁵ In addition, it was shown that TTK/Mps1 phosphorylates c-Abl at Thr735 and that this phosphorylation is of importance to the cytoplasmic sequestration of c-Abl.⁶

References:

1. Hantschel, O. & Superti-Furga, G.: Nat Rev Mol Cell Biol. 5:33-44, 2004.
2. Sirvent, A. et al: Biol Cell 100:617-631, 2008.
3. Wang, J.Y.: Nat Cell Biol. 6:3-7, 2004.
4. Curran, M. P. et al: Biodrugs, 18:207-210, 2004.
5. Brasher, B. B. & Van Etten, R. A.: J. Biol. Chem., 275:35631-7, 2000.
6. Nihira, K. et al.: Oncogene, 27:7285-95, 2008.

TECHNICAL INFORMATION

Source:

Phospho-c-Abl (Thr735) Antibody is a rabbit polyclonal antibody raised against the epitope surrounding and including Thr735 of human c-Abl.

Specificity and Sensitivity:

This affinity purified antibody detects endogenous Phospho-c-Abl in cell lysates.

Storage Buffer: PBS and 30% glycerol

Storage:

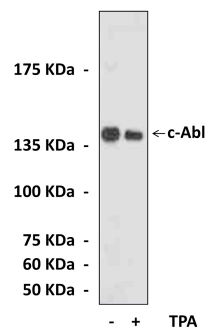
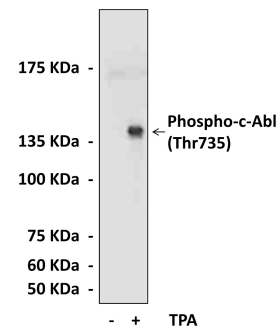
Store at -20°C for at least one year. Store at 4°C for frequent use. Avoid repeated freeze-thaw cycles.

APPLICATIONS

| Application: | *Dilution: |
|----------------|------------|
| WB | 1:1000 |
| IP | n/d |
| IHC (Paraffin) | n/d |
| ICC | n/d |
| FACS | n/d |

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

QUALITY CONTROL DATA



HeLa cells were treated with TPA and subjected to Western Blot analysis using Phospho-c-Abl (Thr735) Antibody (**top**), or c-Abl Antibody (**bottom**).

