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Product Information

Anti-Flipα, C-Terminal

produced in rabbit, IgG fraction of antiserum

Catalog Number F6550

Synonyms: Anti-Casper, Anti-I-FLICE, Anti-FLAME-1, Anti-CASH, Anti-CLARP

Product Description

Anti-FLIP α , C-Terminal is produced in rabbit using as immunogen a synthetic peptide corresponding to amino acids 447-464 of the C-terminal of human FLICE-inhibitory protein (FLIP α /FLIP $_{\rm I}$)¹.

Anti-FLIP α detects human FLIP α (55 kDa) by immunoblotting.

Apoptosis plays an important role in tissue homeostasis and is related to many diseases. The death receptors induce apoptosis after triggering with ligand or agonistic antibodies.² The best-characterized member of the death receptor subfamily is CD95 (APO-1, Fas).

Stimulation of CD95 leads to clustering of the receptor. This enables the adapter molecule FADD/MORT1^{3, 4} and the death protease caspase-8 (FLICE, MACH, MCH5), ⁵⁻⁷ to bind to the receptor via homophilic death domain and death effector domain (DED) interactions, respectively, forming the death-inducing signaling complex (DISC). Recruitment of caspase-8 to the DISC leads to its proteolytic activation, which initiates a cascade of caspases, leading to apoptosis (⁹).

Viral FLICE-inhibitory proteins (v-FLIPs)¹⁰⁻¹² are composed of two death effector domains, a structure resembling the N-terminal half of caspase-8. Via DED-DED interaction, v-FLIPs are recruited to the CD95 DISC,¹⁰ preventing caspase-8 recruitment and processing and thereby CD95-induced apoptosis.

Human FLIP was identified by different groups and termed c-FLIP, 13 CASH, 1 Casper, 14 CLARP, 15 FLAME, 16 I-FLICE, 17 MRIT 18 and Usurpin. 19 On the mRNA level, c-FLIP seems to exist as multiple splice variants, FLIP α , β , γ and δ , respectively. 20 Only two endogenous forms of the protein have been detected, c-FLIP $_{long}$ and c-FLIP $_{short}$. c-FLIP is structurally similar to caspase-8, since it contains two death effector domains and a caspase-like domain. However, this domain lacks residues that are important for its

catalytic activity, most notably the cysteine within the active site. The short form of c-FLIP structurally resembles v-FLIP. The role of c-FLIP in apoptosis signaling may be as pro-apoptotic molecule 1,14,15,18 or as an anti-apoptotic molecule. In addition, whether c-FLIP interacts with FADD and/or caspase-8 is not clear. Some groups have reported that c-FLIP can interact with both FADD and caspase-8, 1,13,14,16,18 while others could only detect an interaction between c-FLIP and caspase-8.

Reagents

Supplied at 1 mg/ml in phosphate buffered saline containing 0.02% sodium azide.

Precautions and Disclaimer

This product is for R&D use only, not for drug, household, or other uses. Please consult the Material Safety Data Sheet for information regarding hazards and safe handling practices.

Storage/Stability

Antibody can be stored at 2-8 °C for three months and at -20 °C for one year. As with all antibodies care should be taken to avoid repeated freeze thaw cycles. Antibodies should not be exposed to prolonged high temperatures.

Product Profile

Immunoblotting: the recommended concentration is $0.5-1 \mu g/ml$ using total HeLa cell lysate.

Note: In order to obtain best results and assay sensitivities of different techniques and preparations, we recommend determining optimal working dilutions by titration test.

References

- 1. Irmler, M., et al., *Nature*, **388**, 190 (1997).
- 2. Peter, M. E., et al., in Apoptosis: Problems and Diseases (Kumar, S., ed), Springer, Heidelberg pp. 25-63, (1998).

- 3. Boldin, M. P., et al., *J. Biol. Chem.*, **270**, 7795-7798 (1995).
- 4. Chinnaiyan, A. M., et al., *Cell*, **81**, 505-512 (1995).
- 5. Muzio, M., et al., Cell, 85, 817-827 (1996).
- 6. Boldin, M. P., et al., Cell, 85, 803-815 (1996)
- 7. Srinivasula, S. M., et al., *Proc. Natl. Acad. Sci. USA*, **93**, 14486-14491(1996).
- 8. Kischkel, F. C., et al., *EMBO J.*, **14**, 5579-5588 (1995)
- 9. Medema, J. P., et al., *EMBO J.*, **16**, 2794-2804 (1997)
- 10. Thome, M., et al., *Nature*, **386**, 517-521 (1997).
- 11. Hu, S., et al., *J. Biol. Chem.*, **272**, 9621-9624 (1997).
- 12. Bertin, J., et al., *Proc. Natl. Acad. Sci. U. S. A.* **94**, 1172-1176 (1997).

- 13. Goltsev, Y. V., et al., *J. Biol. Chem.*, **272**, 19641-19644 (1997).
- 14. Shu, H. B., et al., *Immunity*, **6**, 751-763 (1997)
- 15. Inohara, N., et al., *Proc. Natl. Acad. Sci. USA*, **94**, 10717-10722 (1997).
- 16. Srinivasula, S. M., et al., *J. Biol. Chem.*, **272**, 18542-18545 (1997).
- 17. Hu, S., et al., *J. Biol. Chem.*, **272**, 17255-17257 (1997).
- 18. Han, D. K., et al., *Proc. Natl. Acad. Sci. USA*, **94**, 11333-11338 (1997).
- 19. Dita, R. M., et al., *Cell Death Differ.*, **5**, 271-288 (1998).
- 20. Wallach, D., Nature, 388, 123 (1997).

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