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# ProductInformation

**Z-Leu-Glu(OMe)-Thr-Asp(OMe) Fluoromethyl Ketone**

Product Number **C 8734**
Storage Temperature –20 °C

## Product Description

Molecular formula: $C_{30}H_{43}N_4O_{11}F$
Molecular Weight: 654.7

Z-Leu-Glu(OMe)-Thr-Asp(OMe) Fluoromethyl Ketone is the methylated, cell permeable derivative of the caspase inhibitor Z-Leu-Glu-Thr-Asp Fluoromethyl Ketone (Z-LETD-FMK, Z = benzyloxycarbonyl).

Z-LETD-FMK is a potent inhibitor of caspase-8. It can also bind caspase-1, -6, and -10, but with lower efficiency. Caspases are a group of cysteine aspartate-specific proteases, that play a role in apoptosis.[1,2] Caspase-8 activates all known caspases, the action of which, in turn, leads to apoptotic cell death.[3,4]

Methylation of the acidic amino acids Glu and Asp enhances the cell membrane permeability of Z-LETD-FMK. Once in the cell, endogenous esterase activity hydrolyzes the methyl groups to form the biological active form. For *in vitro* studies an esterase needs to be included in the reaction mix to generate the active form of the molecule.

FMK is a trapping group responsible for irreversible inhibition, but is non-cytotoxic. Inhibition occurs when the the FMK group covalently bonds to the –SH of an adjacent cysteine residue on the target protein.

Z-Leu-Glu(OMe)-Thr-Asp(OMe)Fluoromethyl Ketone is supplied as a yellow powder.

## Preparation Instructions

Prepare stock 20 mM solutions in dry (≥ 99.9 %) DMSO to maintain product stability. DMF has also been used as a solvent.

## Storage/Stability

Store desiccated at –20 °C. Stable for at least one year. Allow container to equilibrate to ambient temperature before opening.

## References

1. Nicholson, D.W., and Thornberry, N.A., Caspases: killer proteases. Trends. Biochem. Sci., **22**, 299 (1997).
2. Cohen, G.M., Caspases: the executioners of apoptosis. Biochem. J., **326**, 1 (1997).
3. Fernandes-Alnemri, T., et al., In vitro activation of CPP32 and Mch3 by Mch4, a novel human apoptotic cysteine protease containing two FADD-like domains. Proc. Natl. Acad. Sci. USA, **93,** 7464-7469 (1996).
4. Srinivasula, S.M., et al., Molecular ordering of the Fas-apoptotic pathway: the Fas/APO-1 protease Mch5 is a CrmA-inhibitable protease that activates multiple Ced-3/ICE-like cysteine proteases. Proc Natl Acad Sci USA, **93,** 14486-14491 (1996).

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