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ProductInformation

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

Product Number **C 8859**
Storage Temperature –20 °C

Product Description

Molecular Formula: $C_{32}H_{45}FN_4O_{12}$
Molecular weight: 696.7

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

Z-LEED-FMK is an inhibitor of caspase 13. Caspase-13 has also been called ERICE (Evolutionarily Related Interleukin-1β Converting Enzyme) and is related to caspase-1, -4, and -5.[1] There is a question whether this enzyme occurs in human tissue.[2]

Apoptosis, or programmed cell death, plays an essential role in development, homeostasis, and defense of multicellular organisms. Among the many known effectors of apoptosis the interlukin-converting enzyme (ICE)-related, cysteine aspartic-specific proteases, or caspases, play a crucial role in apoptosis in almost every cell type.[3,4] At least 14 different caspases have been identified which differ in their substrate specificities.

Methylation of the acidic amino acids Glu and Asp enhances the cell membrane permeability of Z-LEED-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 and is also non-cytotoxic. Inhibition occurs when the the FMK group covalently bonds to the –SH of an adjacent cysteine residue on the target protein.

Z-LEED-FMK is supplied as a white lyophilized powder.

Preparation Instructions

Prepare 20 mM stock solutions in dry (≥ 99.9 %) DMSO to maintain product stability. Also soluble in DMF.

Storage/Stability

Store at –20 °C. The product is reported to be stable at room temperature for one year in a desiccator. Allow container to warm to room temperature before opening to ensure stability.

Store stock solutions at –20 °C for 6-8 months.

References

1. Humke, E. W., et al., ERICE, a novel FLICE-activatable caspase. J. Biol. Chem., **273,** 15702-15707 (1998).
2. Koenig, U., et al., Evidence that caspase-13 is not a human but a bovine gene. Biochem. Biophys. Res. Commun., **285,** 1150-1154 (2001).
3. Nicholson, D.W., and Thornberry, N.A., Caspases: killer proteases. Trends. Biochem. Sci., **22**, 299 (1997).
4. Cohen, G.M., Caspases: the executioners of apoptosis. Biochem. J., **326**, 1 (1997).

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