L-744,832

Product Number L7287
Storage Temperature –20 °C

Cas #: 160141-093
Synonyms: (2S)-2-[[2S,3S]-2-[[2R]-2-Amino-3-mercaptopropyl]amino]-3-methylpentyl[oxy]-1-oxo-3-phenylpropyl]amino]-4-(methylsulfonyl)-butanoic acid 1-methylethyl ester

Product Description
Molecular Formula: C_{26}H_{45}N_{3}O_{6}S_{2} \text{COOH}
Molecular Weight: 787.8 (anhydrous)
Appearance: white solid
Purity: 98%
Melting Point: 53.5 to 57.5 °C

Farnesyltransferase (FPT) is the enzyme responsible for post-translational farnesylation (15-carbon prenylation) of a number of proteins involved in cell growth. The most notable of these is the Ras family of small GTP binding proteins. All farnesyltransferase acceptor proteins contain a unique C-terminal sequence termed the "CaaX-box".¹

L-744,832 is a CAAX analog and a potent and specific FPTase inhibitor (FTI). L-744,832 inhibits the proliferation of a number of tumor cell lines in vitro in a manner that correlates with the inhibition of the mitogen-activated protein kinase cascade. One of the PI3-kinase-dependent pathways required for mitogenic signaling involves p70^{66k}. L-744,832 inhibits in vivo p70s6k phosphorylation in mammary tumors and induces tumor regression in transgenic mice by mediating alterations in both cell cycle control and apoptosis.²

L-744,832 mimics the ability of rapamycin to induce p70^{66k} and PHAS-1 dephosphorylation, p70^{66k} inactivation, and inhibit DNA synthesis. PHAS-1 phosphorylation causes a 30-45% reduction in DNA synthesis in keratinocytes, while L-744,832 reduces DNA synthesis by 80-90%.³ These data demonstrate that p70^{66k} and PHAS-1 are novel downstream targets of FTI and suggest that the anti-tumor properties of FTI are probably due to the inhibition of multiple mitogenic pathways. L-744,832 induces apoptosis in astrocytoma cells associated with increased expression of Bax and Bak.⁴

Preparation Instructions
L-744,832 is soluble in water at 28 mg/ml.

Storage/Stability
Store at –20 °C, desiccated.

References
3. Law, B. K. et al., Inhibition of DNA synthesis by a farnesyltransferase inhibitor involves inhibition of the p70(s6k) pathway. J. Biol. Chem., 274, 4743-4748 (1999).

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