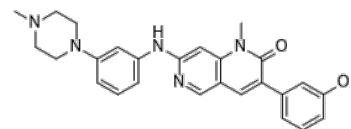


Product Name : UH15-38
Cat. No. : PC-22143
CAS No. : 2540881-21-6
Molecular Formula : C₂₆H₂₇N₅O₂
Molecular Weight : 441.54
Target : RIP kinase
Solubility : 10 mM in DMSO



CAS: 2540881-21-6

Biological Activity

UH15-38 is a potent, specific receptor interacting protein kinase 3 (**RIPK3**) inhibitor with IC₅₀ of 20 nM in NanoBRET assays, potently and selectively blocks IAV-triggered necroptosis in alveolar epithelial cells in vivo.

UH15-38 blocks TNF-induced necroptosis in primary mouse embryonic fibroblasts (MEFs) with IC₅₀ of 98 nM, 8.5-fold lower than those of GSK'843 (IC₅₀ = 843 nM) and around sixfold lower than those of GSK'872.

UH15-38 prevents phosphorylation of MLKL following necroptotic stimulation by TNF, also robustly inhibits necroptosis in a panel of human and mouse cell lines.

UH15-38 exhibits selectivity for RIPK3-driven necroptotic cell death, displays no significant activity against RIPK1 kinase-driven caspase-8-dependent cell death, also does not inhibit gasdermin D cleavage or pyroptosis upon canonical activation of the NLRP3 inflammasome by nigericin.

UH15-38 does not significantly inhibit a panel of 50 critical protein targets, as well as clean profile against a panel of 90 non-mutant human kinases (DiscoverX KinomeScan).

UH15-38 (1 μM) selectively blocks IAV-induced necroptosis in type I alveolar epithelial cells (AECs), protects type I AECs from canonical TNF-induced necroptosis with IC₅₀ of 114 nM.

UH15-38 a highly potent inhibitor of IAV-induced necroptosis in primary type I AECs (IC₅₀ = 39.5 nM) and primary MEFs (IC₅₀ = 51.9 nM), respectively.

UH15-38 (30 mg/kg) ameliorates lung inflammation and prevented mortality following infection with laboratory-adapted and pandemic strains of IAV, prevents necroptosis, inflammation, and injury in IAV-infected lungs.

UH15-38 does not alter the extent of virus replication and spread or the rate of virus clearance from infected lungs.

References

Gautam A, et al. *Nature*. 2024 Apr 10. doi: 10.1038/s41586-024-07265-8.

Caution: Product has not been fully validated for medical applications. Lab Use Only!

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