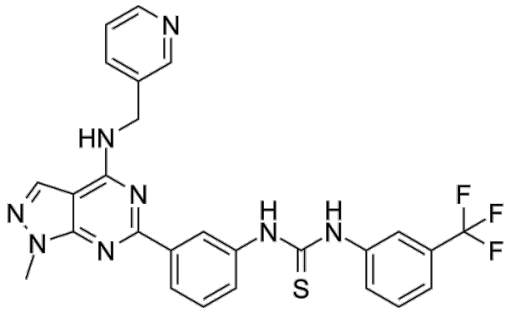
Product Data Sheet

Product Name: XMU-MP-8
Cat. No.: GC81030

Chemical Properties

Cas. No.	2271314-01-1		
Formula	$C_{26}H_{21}F_3N_8S$	M.Wt	534.56
Solubility	DMSO: 116.67 mg/mL (218.25 mM; Need ultrasonic)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure			



Background

XMU-MP-8 (SKPer1) is a potent molecular glue degrader that targets the oncoprotein SKP2. XMU-MP-8 simultaneously binds to the F-box domain of SKP2 (K d ≈ 36 μM) and the N-terminal TPR domain of the E3 ligase STUB1 (K d ≈ 2.5 μM), forming a stable SKP2-SKPer1-STUB1 ternary complex (K d ≈ 8.9 nM) that induces SKP2 ubiquitination and proteasomal degradation. XMU-MP-8 selectively eliminates SKP2-expressing cancer cells. XMU-MP-8 exhibits substantial tumour suppression with good safety profiles in vivo. XMU-MP-8 can be used for cancer research, such as

non-small cell lung adenocarcinoma (NSCLC) and prostatic adenocarcinoma [1].

In Vivo, XMU-MP-8 (15 and 30 mg/kg, i.v., daily for 14 days) demonstrates potent antitumor efficacy in A549 and PC-3 xenograft mice models, mediated through SKP2 degradation[1]. XMU-MP-8 (30 mg/kg, i.v., daily for 14 days) shows no adverse effects in BALB/c nude mice[1].

In Vitro, XMU-MP-8 (10 μM, 24 h) produces a cell survival phenotype specifically in the SKP2-F-C cell line, with no survival observed in other F-C cell lines, ruling out the possibility that it generally interferes with the activation of the F-C death protein[1]. XMU-MP-8 (1-10 μM, 0-24 h) triggers SKP2 ubiquitination and proteasomal degradation, significantly reducing its half-life and depleting endogenous SKP2 protein without affecting its mRNA levels[1]. XMU-MP-8 (72 h) inhibits proliferation of SKP2-high cell lines with IC50s of 3.7 μM (PC-3), 6.7 μM (A549), 3.7 μM (JHH-7), 6.2 μM (SW620), 4.5 μM (LoVo), 6.9 μM (RKO), 5.6 μM (Caco2) and 5.3 μM (HeLa)[1]. XMU-MP-8 (10 μM,72 h) completely blocks proliferation and induces massive cell death of SKP2-high cell lines[1]. XMU-MP-8 (10 μM, 24 h) induces the degradation of SKP2 protein and the accumulation of p27 protein in SKP2-high cell lines (JHH-7 and PC-3), with no significant changes in SKP2-low cell lines (IMR-90 and MCF-10A)[1]. XMU-MP-8 (2.5-10 μM, 0-5 days) shows no significant effect on the growth of normal mouse intestine organoids and human peripheral blood mononuclear cells[1]. XMU-MP-8 (10 μM,2.5 h) induces SKP2 degradation by recruiting the E3 ligase STUB1 to the F-box domain of SKP2, forming a ternary complex that enhances the SKP2-STUB1 interaction by 122-fold and ultimately leads to SKP2 ubiquitination and degradation[1].

References:
[1]. Chu Y, et al. A rapid imaging-based screen for induced-proximity degraders identifies a potent degrader of oncoprotein SKP2. Nat Biotechnol. 2025 Sep 10.