SM311: A Chemical Probe for LIMK1

Version 1.0 (23rd June 2025)

Web link for more details: https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/SM311

Overview

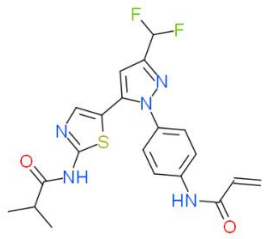
LIMK1 is a serine/threonine kinase which is activated by upstream kinases including ROCK1, PAK1 and PAK4 through phosphorylation on a threonine residue located in its activation loop. Active LIMK1 regulates actin polymerization via phosphorylation and inactivation of the actin binding factor cofilin thereby inhibiting its actin-depolymerizing activity. This relieves the levering stress on actin and allows polymerization to occur. Actin rearrangement is essential in regulating cell cycle progression, apoptosis, and migration. LIMK1 is predominantly expressed in brain tissue, embryonic tissue and skeletal muscle.

Summary

Chemical Probe Name	SM311
Negative control compound	SM311-NC
Target(s) (synonyms)	LIMK1
Recommended *in vitro* assay concentration	Use at concentration between 0.1 to 1 µM for SM311 and SM311-NC; use with negative control for best interpretation of data
Suitability for *in* vivo use and recommended dose	Not tested in vivo
Publications	None at time of writing
In vitro assay(s) used to characterise	TR-FRET assay
Cellular assay(s) for target-engagement	NanoBRET TE

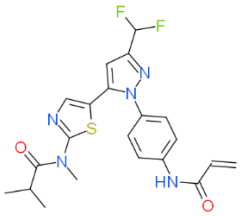
Chemical Probe & Negative Control Structures and Use

SM311 Chemical Probe



SMILES: CC(C)C(Nc1ncc(c2cc(C(F)F)nn2c2ccc(cc2)NC(C=C)=O)s1)=O
InChiKey: YOOKRVNCYQFKCT-UHFFFAOYSA-N
Molecular weight: 431.12 g/mol
Storage: As a dry powder or as DMSO stock solutions (10 mM) at -20 °C. DMSO stocks beyond 3-6 months or 2 freeze/thaw cycles should be tested for activity before use
Dissolution: Soluble in DMSO up to 10 mM; use only 1 freeze/thaw cycle per aliquot

SM311-NC Negative Control



SMILES: CC(C)C(N(C)c1ncc(c2cc(C(F)F)nn2c2ccc(cc2)NC(C=C)=O)s1)=O
InChiKey: KMKGSCXRFNDZLB-UHFFFAOYSA-N
Molecular weight: 445.14 g/mol
Storage: As a dry powder or as DMSO stock solutions (10 mM) at -20 °C. DMSO stocks beyond 3-6 months or 2 freeze/thaw cycles should be tested for activity before use
Dissolution: Soluble in DMSO up to 10 mM; use only 1 freeze/thaw cycle per aliquot

Chemical Probe Profile

In vitro Potency & Selectivity:

SM311 is a covalent inhibitor of LIMK1 with IC_{50} = 40.71 nM in the TR-FRET assay (Kinact = 0.00283 s-1, Kinact/ KI = 69516 M-1s-1). The selectivity for LIMK1 was confirmed by whole-cell proteomics. The LIMK2 NanoBRET EC_{50} is 6.74 µM. In the DSF panel were three targets with > 3 K (deltaTm [K]): LIMK1 (8.11), MAPK8 (7.36), MAPK10 (8.12 K). Closest off-targets in the NanoBRET TE panel are (EC_{50} [µM]) CDKL2 (1.5), AAK1 (10.4), MAPK8 (23), MAPK9 (14.3), MAPK10 (25.5), STK32B (31), SRC (> 50).

Potency in Cells and Cellular Target Engagement:

For LIMK1 the NanoBRET TE is EC_{50} = 45 nM.