

Web link for more details: <https://www.thesgc.org/chemical-probes/MSC1186>

Overview

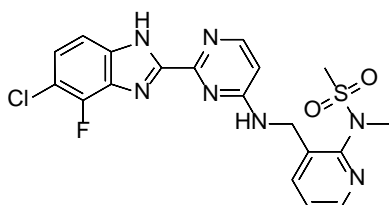
Serine-arginine protein kinases (SRPKs) are a subfamily of serine-threonine kinases, regulating pre-mRNA splicing in response to extracellular stimuli by phosphorylating serine/arginine (SR)-rich splicing factors. The human genome encodes three SRPK genes, SRPK1, SRPK2 and SRPK3. Alteration of SRPK expression has been found to induce a large number of aberrant alternative splicing events, leading to tumorigenesis.

Summary

Chemical Probe Name	MSC1186
Negative control compound	MSC5360
Target(s) (synonyms)	SRPK1 / SRPK2 / SRPK3; Serine/Arginine-Rich Protein-Specific Kinase 1 / 2 / 3; SRSF Protein Kinase 1 / 2 / 3
Recommended cell assay concentration	Use at concentration of 1 μ M; use with negative control MSC5360 for best interpretation of data.
Suitability for <i>in vivo</i> use and recommended dose	MSC1186 was not tested <i>in vivo</i> .
Publications	https://doi.org/10.1021/acs.jmedchem.2c01705
Orthogonal chemical probes	
<i>In vitro</i> assay(s) used to characterise	ITC, biochemical activity assay (Reaction Biology)
Cellular assay(s) for target-engagement	NanoBRET™

Chemical Probe & Negative Control Structures and Use

MSC1186 Chemical Probe



SMILES:

CN(C1=NC=CC=C1CNC1=NC(=NC=C1)C1=NC2=C(N1)C=CC(Cl)=C2F)S(C)(=O)=O

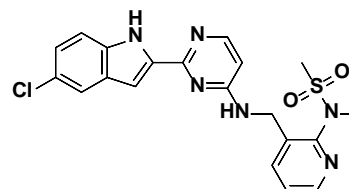
InChiKey: WBFJDKLBAAHKIL-UHFFFAOYSA-N

Molecular weight: 461.90

Storage: Stable as solid in the dark at -20°C. NB making aliquots rather than freeze-thawing is recommended

Dissolution: Soluble in DMSO up to 10 mM; use only 1 freeze/thaw cycle per aliquot

MSC5360 Negative Control



SMILES:

CN(C1=NC=CC=C1CNC1=NC(=NC=C1)C1=CC2=C(N1)C=CC(Cl)=C2)S(C)(=O)=O

InChiKey: MXAVRMOXZMBKGE-UHFFFAOYSA-N

Molecular weight: 442.92

Storage: Stable as solid in the dark at -20°C. NB making aliquots rather than freeze-thawing is recommended

Dissolution: Soluble in DMSO up to 10 mM; use only 1 freeze/thaw cycle per aliquot

Chemical Probe Profile

In vitro Potency & Selectivity:

MSC1186 had an IC₅₀ of 2.7 nM, 81 nM, and 0.59 nM to SRPK1, SRPK2 and SRPK3, respectively in the biochemical biochemical activity assay performed at Reaction Biology and exhibited a K_d of 145 nM on SRPK2 in ITC.

Potency in Cells and Cellular Target Engagement:

MSC1186 displayed an IC₅₀ of 98 nM on SRPK1 and 40 nM on SRPK3 in intact cells and 44 nM on SRPK1, 149 nM on SRPK2 and 40nM on SRPK3 in lysed cells in NanoBRET assay.

The cytotoxicity of MSC1186 was assessed in a high content screen using a confocal microscope (CQ1, Yokogawa) measured in two different cell lines (HEK293T, U2OS and MRC-9 fibroblasts). After 48 hours of 1 μ M of compound exposure to U2OS cells and HEK293T cells, there was no detectable effect on cell viability compared to 0.1 % DMSO.