SR-302: A Chemical Probe for DDR1/2, MAPK11/14

Version 1.0 (24th March 2021)

Web link for more details: https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/SR-302

Overview

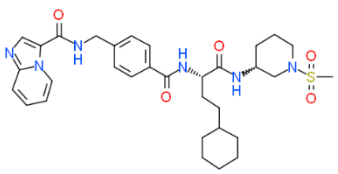
The receptor tyrosine kinases DDR1 and DDR2 are involved in the regulation of proliferation, differentiation, adhesion and survival. Dysregulation is related to a number of human diseases, including fibrotic disorders, atherosclerosis, and cancer and matrix remodelling.

Summary

Chemical Probe Name	SR-302
Negative control compound	SR-301
Target(s) (synonyms)	DDR1/2 (discoidin domain receptor tyrosine kinase 1/2; DDR1: NTRK4, PTK3A, NEP, CAK, EDDR1; DDR2: TYRO10, NTRKR3)
Recommended cell assay concentration	Use at concentration of 100 nM for SR-302 and SR-301; use with control and orthogonal probe for best interpretation of data
Suitability for *in* vivo use and recommended dose	SR-302 was not tested in vivo.
Publications	None at time of writing
Orthogonal chemical probes	BAY-826, SR-318, Skepinone-L, FS-694
In vitro assay(s) used to characterise	Enzyme kinetic assay
Cellular assay(s) for target-engagement	NanoBRET

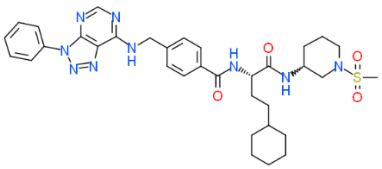
Chemical Probe & Negative Control Structures and Use

SR-302 Chemical Probe



SMILES: CS(N1CCCC(C1)NC([C@H](CCC1CCCCC1)NC(c1ccc(CNC(c2cnc3ccccn23)=O)cc1)=O)=O)(=O)=O
InChiKey: WGMNFJAFXXXRLZ-GEVKEYJPSA-N
Molecular weight: 622.3
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

SR-301 Negative Control



SMILES: CS(N1CCCC(C1)NC([C@H](CCC1CCCCC1)NC(c1ccc(CNc2c3c(ncn2)n(c2ccccc2)nn3)cc1)=O)=O)(=O)=O
InChiKey: JINDDPNTLQVRRX-ACEFPKFPSA-N
Molecular weight: 673.3
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:

SR-302 shows potent activity on DDR1/2 and MAPK11/14. Closest off-targets found in KinomeScan are ABL1, RIPK2, RPS6KA5, CHEK2, STK38L, but for all the IC_{50} > 25 µM (> 125 fold selective) in NanoBRET assay.

	DDR1	DDR2	MAPK11	MAPK14
Enzyme kinetic assay ("Reaction Biology") IC_{50} (nM) ([ATP](µM))	53.3 (100)	0.75 (5)	45.1 (50)	6.2 (2.5)
NanoBRET assay (HEK293T, full-length) IC_{50} (nM) for SR-302	23 ± 2	18 ± 2	196 ± 8	125 ± 11
NanoBRET assay IC_{50} (µM) for SR-301	21.9 ± 5.44	15.5 ± 5.08	1.83	5.39 ± 3.1

Potency in Cells and Cellular Target Engagement:

SR-302 shows destabilizing effect on E-cadherin.