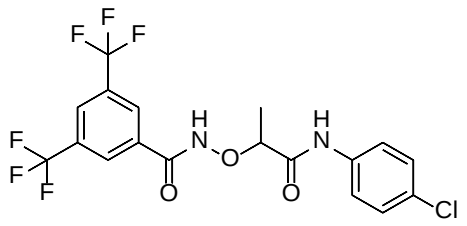
Product data sheet

MedKoo Cat#: 406613 Name: CCG1423 CAS#: 285986-88-1 Chemical Formula: $C_{18}H_{13}ClF_6N_2O_3$ Exact Mass: 454.0519 Molecular Weight: 454.75	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
CCG-1423 is a small-molecule inhibitor of RhoA transcriptional signaling. CCG-1423 displays activity in several in vitro cancer cell functional assays. CCG-1423 potently (<1 mumol/L) inhibits lysophosphatidic acid-induced DNA synthesis in PC-3 prostate cancer cells, and whereas it inhibits the growth of RhoC-overexpressing melanoma lines (A375M2 and SK-Mel-147) at nanomolar concentrations, it is less active on related lines (A375 and SK-Mel-28) that express lower levels of Rho.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMF	10.0	21.99
DMSO	42.87	94.27
DMSO:PBS (pH 7.2) (1:5)	0.15	0.33
Ethanol	2.13	4.68

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.20 mL	11.00 mL	21.99 mL
5 mM	0.44 mL	2.20 mL	4.40 mL
10 mM	0.22 mL	1.10 mL	2.20 mL
50 mM	0.04 mL	0.22 mL	0.44 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Yu L, Yang G, Zhang X, Wang P, Weng X, Yang Y, Li Z, Fang M, Xu Y, Sun A, Ge J. Megakaryocytic Leukemia 1 Bridges Epigenetic Activation of NADPH Oxidase in Macrophages to Cardiac Ischemia-Reperfusion Injury. Circulation. 2018 Dec 11;138(24):2820-2836. doi: 10.1161/CIRCULATIONAHA.118.035377. PMID: 30018168.

In vivo study

1. Zabini D, Granton E, Hu Y, Miranda MZ, Weichelt U, Breuils Bonnet S, Bonnet S, Morrell NW, Connelly KA, Provencher S, Ghanim B, Klepetko W, Olschewski A, Kapus A, Kuebler WM. Loss of SMAD3 Promotes Vascular Remodeling in Pulmonary Arterial Hypertension via MRTF Disinhibition. Am J Respir Crit Care Med. 2018 Jan 15;197(2):244-260. doi: 10.1164/rccm.201702-0386OC. Erratum in: Am J Respir Crit Care Med. 2019 Apr 1;199(7):932. PMID: 29095649.
2. Yu L, Yang G, Zhang X, Wang P, Weng X, Yang Y, Li Z, Fang M, Xu Y, Sun A, Ge J. Megakaryocytic Leukemia 1 Bridges Epigenetic Activation of NADPH Oxidase in Macrophages to Cardiac Ischemia-Reperfusion Injury. Circulation. 2018 Dec 11;138(24):2820-2836. doi: 10.1161/CIRCULATIONAHA.118.035377. PMID: 30018168.

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7. Bioactivity

Biological target: CCG-1423 is an inhibitor of RhoA/C-mediated gene transcription.

In vitro activity

Fluorescence staining showed that MLK1 inhibition by CCG-1423 (Figure 3B) significantly downregulated ROS (reactive oxygen species) production in F4/80+ macrophages after IRI (ischemia-reperfusion injury). In response to hypoxia-reoxygenation (H/R), there was augmented occupancy of MKL1 on the proximal Nox gene promoters but not on the Gapdh promoters in cultured macrophages (RAW264.7) as demonstrated by ChIP assay (Figure 3C), indicating that MKL1 might directly regulate NOX gene transactivation. Reporter assay confirmed that overexpression of MKL1 dose-dependently activated promoter activities of NOX genes (Figure IVA in the online-only Data Supplement). In contrast, depletion of endogenous MKL1 with a short-hairpin RNA plasmid downregulated NOX promoter activities (Figure IVB). CCG-1423 treatment abrogated the induction of Nox messages (Figure 3D) and proteins (Figure 3E) in a dose-dependent manner. In keeping with reduced Nox expression, there was a decrease in intracellular ROS levels in CCG-1423-treated cells as assayed by both DHE and DCFH-DA stainings (Figure 3F) and quantitative luminescence assay (Figure 3G).

Reference: Circulation. 2018 Dec 11;138(24):2820-2836.
https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.118.035377?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub++0pubmed&

In vivo activity

The effect of an MKL1 inhibitor CCG-142330 on IRI was investigated in mice. When the mice were injected peritoneally with CCG-1423 for 3 days before the IR procedure, CCG-1423 injection resulted in a significant reduction of infarct size but did not afford detectable improvements in heart function (Figure I). When the mice were injected daily with CCG-1423 for 2 consecutive weeks before the IR procedure and found that prolonged pretreatment with CCG-1423 not only alleviated myocardial infarction (Figure 1E) but mitigated the loss of heart function (Figure 1F through 1H). This discrepancy in the effectiveness of 2 CCG regimens could be partly explained by the observation that although 2 weeks of CCG injection almost completely blocked the nuclear accumulation of MKL1 in cardiac macrophages compared with the vehicle group, 3 days of injection only marginally altered MKL1 localization (Figure II). Taken together, these data suggest that MKL1 loss of function might attenuate myocardial infarction and help retrieve the loss of heart function after IRI.

Reference: Circulation. 2018 Dec 11;138(24):2820-2836.
https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.118.035377?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub++0pubmed&