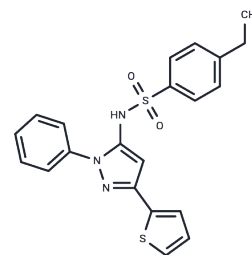


HSF1A

Chemical Properties

CAS No. :	1196723-93-9
Formula:	C ₂₁ H ₁₉ N ₃ O ₂ S ₂
Molecular Weight:	409.52
Storage:	Powder: -20°C for 3 years In solvent: -80°C for 1 year Actual storage temperature shall be subject to the COA.



Biological Description

Description	HSF1A is a cell-permeable activator of HSF1 that protects mammalian cells against stress-induced apoptosis (HSF1).
Targets(IC50)	HSP
In vitro	HSF1A is a small-molecule activator that enhances HSF1's ability to protect cells from stress-induced apoptosis by binding to and inhibiting TRiC subunits' activity, crucially without disturbing ATP hydrolysis. When the TRiC complex is genetically inactivated or depleted, HSF1 activation occurs in humans, and HSF1A is found to block the direct interaction between purified TRiC and HSF1 in vitro. Fluorescence anisotropy experiments with FITC-tagged HSF1A demonstrate its strong binding to the Tcp1 subunit of TRiC, with an affinity around 600 nM. This interaction is further supported by titration experiments with purified Tcp1, indicating qualitative validation. Moreover, a significant reduction in the number of cells displaying aggregates is observed at HSF1A concentrations as low as 2 μM, with this fraction consistently declining in a dose-dependent manner. Specifically, pretreatment with 12 μM HSF1A leads to approximately 20% of cells showing aggregates under fluorescence microscopy, highlighting HSF1A's potential in reducing cellular stress markers.
In vivo	HSF1A enhances HSF1 activity, stabilizes its expression, and mitigates Doxorubicin (DOX)-induced cardiac damage. In WKY rats treated with DOX (30 mg/kgw) and a combination of DOX and HSF1A (100 mg/kgw/day), HSF1A supplementation significantly restores cardiac function to control levels. Moreover, HSF1A promotes HSF1 nuclear translocation, increases protein chaperone expression, and reduces protein misfolding and cell death in neurodegenerative disease models. Echocardiographic data show that HSF1A also improves cardiac function in the face of DOX-induced impairments.
Kinase Assay	Protein extracts are generated from mammalian, yeast and E. coli cultures using biotin-binding buffer (20 mM HEPES, 5 mM MgCl ₂ , 1 mM EDTA, 100 mM KCl, 0.03% NP-40) supplemented with 1% Triton-X100 and protease inhibitors. Approximately 0.5 mg of protein extract is incubated with 100 μM HSF1A-Biotin for 4 h at 4°C and HSF1A-Biotin associated proteins captured by with NeutrAvidin Agarose Resin. After washing in biotin binding buffer proteins are eluted using 50 μL biotin elution buffer (100 mM Tris, 150 mM NaCl, 0.1 mM EDTA, 2 mM D-biotin), resolved on a 4-20% SDS-PAGE, and immunoblotted. For purified TRiC and Hsp70 analyses, 5 nM protein is incubated in

Kinase Assay	biotin-binding buffer+0.5% Triton X-100 with 100 µM biotin or 100 µM HSF1A-Biotin for 4 h at 4°C and captured with NeutrAvidin Resin. For NiNTA purified yeast Tcp1, different concentrations of Tcp1 0.5 µM, 1 mM, 2 mM, 3 mM and 4 mM in 25 mM Hepes pH 7.5, 150 mM NaCl are incubated with 0.5 µM Biotin or HSF1A-Biotin for 4 h at 4°C and captured with NeutrAvidin Resin.
Cell Research	PC12 cells seeded into a 96-well plate (5×10 ⁴ cells/well) are treated with increasing concentrations of HSF1A (2, 4, 8 and 12 µM) for 15 h, at which time httQ74-GFP expression is stimulated by incubation in the presence of 1 µg/mL Doxycycline for 5 d. Cell viability is assessed via the XTT viability assay.
Animal Research	RatTen-week-old Wistar Kyoto rats (WKY) are used. The rats are housed at a constant temperature (22°C) on a 12-h light/dark cycle with food and tap water. The animals are arranged into three groups: WKY rats (the control group), DOX rats and DOX rats treated with HSF1A. Each group contain five animals. The DOX group is injected with DOX (5? mg/kg) for 6 consecutive weeks intraperitoneal injection to achieve a cumulative dose of 30?mg/kg, which has been well documented to achieve cardiotoxicity. The small molecular HSF1 activator HSF1A (100?mg/kg/day) is injected intraperitoneally.

Solubility Information

Solubility	DMSO: 250 mg/mL (610.47 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (4.88 mM),Sonication is recommended. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.4419 mL	12.2094 mL	24.4188 mL
5 mM	0.4884 mL	2.4419 mL	4.8838 mL
10 mM	0.2442 mL	1.2209 mL	2.4419 mL
50 mM	0.0488 mL	0.2442 mL	0.4884 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

- Neef DW, et al. A direct regulatory interaction between chaperonin TRiC and stress-responsive transcription factor HSF1. *Cell Rep.* 2014 Nov 6;9(3):955-66.
- Neef DW, et al. Modulation of heat shock transcription factor 1 as a therapeutic target for small molecule intervention in neurodegenerative disease. *PLoS Biol.* 2010 Jan 19;8(1):e120200291.
- Huang CY, et al. Doxorubicin attenuates CHIP-guarded HSF1 nuclear translocation and protein stability to trigger IGF-IIR-dependent cardiomyocyte death. *Cell Death Dis.* 2016 Nov 3;7(11):e2455.

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