

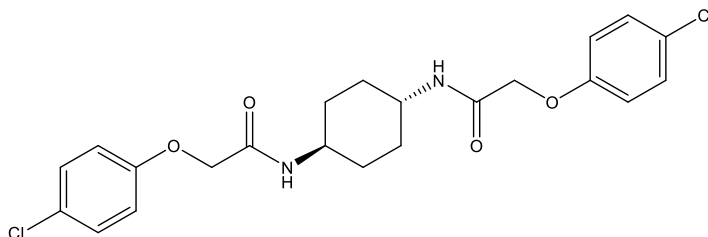
Catalog # 10-1539

ISRIB

CAS# 1597403-47-8

N,N'-trans-1,4-Cyclohexanediylbis[2-(4-chlorophenoxy)acetamide]

Lot # X106124



Integrated stress response inhibitor. Potently reverses the effects of initiation factor 2 α (eIF2 α) phosphorylation, IC₅₀=5 nM.¹ Enhances spatial and fear-associated learning in mice and enhances cognitive function.^{1,2} Mechanism of action involves activation of eIF2 β .³ Suppresses ER stress-induced inflammatory gene expression.⁴ Potently attenuates amyloid β -induced neuronal cell death (12.5-25 nM) with no effect on amyloid β production.⁵ Reverses hippocampal-dependent cognitive deficits induced by traumatic brain injury in two different injury mouse models.⁶

- 1) Sidrauski *et al.* (2013) *Pharmacological brake-release of mRNA translation enhances cognitive memory*; *Elife* **2** e00498
- 2) Sekine *et al.* (2015), *Stress responses. Mutations in a translation initiation factor identify the target of a memory-enhancing compound*; *Science* **348** 1027
- 3) Sidrauski *et al.* (2015) *Pharmacological dimerization and activation of the exchange factor eIF2B antagonizes the integrated stress response*; *Elife* **4** e07314
- 4) Guthrie *et al.* (2016) *Attenuation of PKR-like ER kinase (PERK) Signaling Selectively Controls Endoplasmic Reticulum Stress-induced Inflammation Without Compromising Immunological Responses*; *J.Biol.Chem.* **291** 15830
- 5) Hosoi *et al.* (2016) *Unique pharmacological property of ISRIB in inhibition of A β -induced neuronal cell death*; *J.Pharmacol.Sci.* **131** 292
- 6) Chou *et al.* (2017) *Inhibition of the integrated stress response reverses cognitive effects after traumatic brain injury*; *Proc.Natl.Acad.Sci.USA* **114** E6420

PHYSICAL DATA

Molecular Weight: 451.35
Molecular Formula: C₂₂H₂₄Cl₂N₂O₄
Purity: >98% by TLC
NMR: Conforms
Solubility: DMSO (5 mg/ml with warming)
Physical Description: White solid
Storage and Stability: Store as supplied at -20°C for up to 2 years from the date of purchase. Solutions in DMSO may be stored at -20°C for up to 1 month.

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