

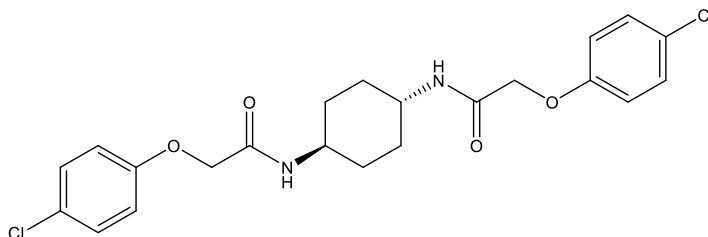
Catalog # 10-1539

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:	C ₂₂ H ₂₄ Cl ₂ N ₂ O ₄
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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