Neuroprotection targeting protein misfolding on chronic cerebral hypoperfusion in the context of metabolic syndrome



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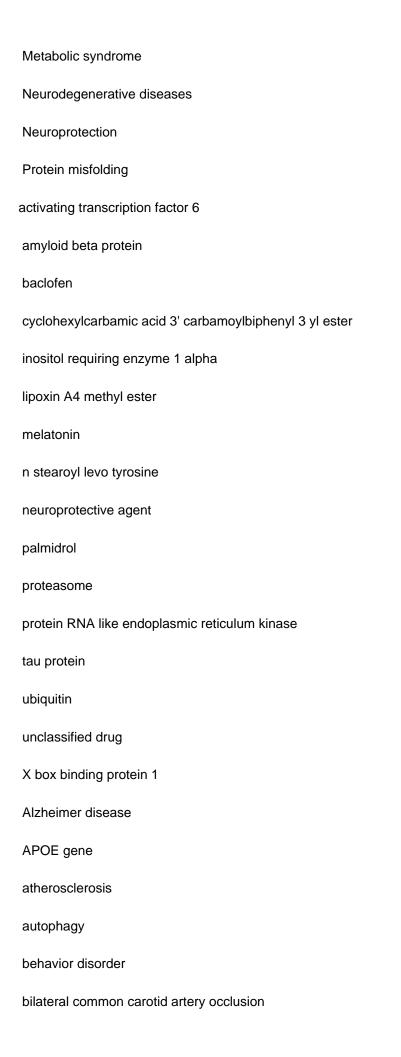
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Metabolic syndrome (MetS) is a cluster of risk factors that lead to microvascular dysfunction and chronic cerebral hypoperfusion (CCH). Long-standing reduction in oxygen and energy supply leads to brain hypoxia and protein misfolding, thereby linking CCH to Alzheimer's disease. Protein misfolding results in neurodegeneration as revealed by studying different experimental models of CCH. Regulating proteostasis network through pathways like the unfolded protein response (UPR), the ubiquitin-proteasome system (UPS), chaperone-mediated autophagy (CMA), and macroautophagy emerges as a novel target for neuroprotection. Lipoxin A4 methyl ester, baclofen, URB597, N-stearoyl-L-tyrosine, and melatonin may pose potential neuroprotective agents for rebalancing the proteostasis network under CCH. Autophagy is one of the most studied pathways of proteostatic cell response against the decrease in blood supply to the brain though the role of the UPR-specific chaperones and the UPS system in CCH deserves further research. Pharmacotherapy targeting misfolded proteins at different stages in the proteostatic pathway might be promising in treating cognitive impairment following CCH. © 2018 Herrera, Udovin, Toro-Urrego, Kusnier, Luaces, Otero-Losada and Capani.

Chaperones

Chronic cerebral hypoperfusion

Endoplasmic reticulum stress



brain atrophy
brain blood flow
brain disease
brain perfusion
carotid artery obstruction
chaperone-mediated autophagy
chronic cerebral hypoperfusion
cognitive defect
disease association
endoplasmic reticulum stress
genetic risk
hippocampal atrophy
human
hyperglycemia
hyperglycemia
hypertension
hypertension hypertriglyceridemia
hypertension hypertriglyceridemia hypoxia
hypertension hypertriglyceridemia hypoxia insulin resistance
hypertension hypertriglyceridemia hypoxia insulin resistance lipid diet
hypertension hypertriglyceridemia hypoxia insulin resistance lipid diet macroautophagy
hypertension hypertriglyceridemia hypoxia insulin resistance lipid diet macroautophagy metabolic syndrome X
hypertension hypertriglyceridemia hypoxia insulin resistance lipid diet macroautophagy metabolic syndrome X nerve degeneration
hypertension hypertriglyceridemia hypoxia insulin resistance lipid diet macroautophagy metabolic syndrome X nerve degeneration neuroprotection

oxidative stress
oxygen glucose deprivation
pathogenesis
protein deficiency
protein function
protein homeostasis
protein misfolding
protein misfolding disorder
protein phosphorylation
risk factor
Short Survey
signal transduction
unfolded protein response
vascular disease