Shaping Tomorrow's Nephrology: Insight-Driven Kidney Care
KSN SEOUL, KOREA 2026
The 46th Annual Meeting of the Korean Society of Nephrology
THE KOREAN SOCIETY OF NEPHROLOGY
Jun 11 (Thu) – 14 (Sun), 2026
COEX, Seoul, Korea

Abstract Type : Poster exhibition
Abstract Submission No.: A-0925
Abstract Topic : Basic Research

MIT-003 Selectively Protects Hippocampal Neurons from Uremic Toxin-Induced Ferroptosis via the NRF2/GPX4/SLC7A11 Pathway, Independent of Renal Function Recovery, in an Ischemia-Reperfusion Acute Kidney Injury Model

Janghyun Jo[1], Hyerim Park[1], Seongyeop Jeong[2], Kyungho Park[2], Eu Jin Lee[2], Young Rok Ham[2], Ki Ryang Na[2], Dae Eun Choi[1]
[1]Department of Department of Medical Science, Chungnam National University, Korea, Republic of
[2]Department of Internal Medicine-Nephrology, Chungnam National University Hospital, Korea, Republic of

Objectives : Renal failure leads to systemic accumulation of uremic toxins, notably indoxyl sulfate (IS), causing hippocampal neuronal injury and cognitive impairment. Ferroptosis—iron-dependent cell death driven by lipid peroxidation and suppression of the NRF2/GPX4/SLC7A11 antioxidant axis—has emerged as a key mechanism of uremic neurotoxicity. MIT-003, a novel synthetic compound, was investigated for its ability to protect hippocampal neurons from uremia-induced ferroptosis independently of renal function.
Methods : In vitro: HT-22 hippocampal neurons were exposed to IS (5 mM, 24 h) ± MIT-003 (0.1, 0.5 μM). Cell viability (MTT), cytotoxicity (LDH), intracellular Fe^{2+}, lipid peroxidation (MDA), antioxidant capacity (GSH), and GPX4 expression (Western blot) were assessed. In vivo: A renal failure model with sustained uremic toxin elevation was established in mice. MIT-003 was administered systemically. Serum BUN and s-Cr confirmed equivalent uremic burden between groups. Hippocampal tissue was analyzed by immunofluorescence (NeuN, Ki67, TUNEL, DHE) and Western blot (GPX4, NRF2, SLC7A11, xCT).
Results : In vitro: IS significantly reduced cell viability and elevated LDH cytotoxicity ($p < 0.001$). IS induced intracellular Fe^{2+} accumulation (~2.0-fold, $p < 0.001$), elevated MDA (~1.0 nmol/mg, $p < 0.001$), depleted GSH ($p < 0.01$), and suppressed GPX4 ($p < 0.001$)—consistent with ferroptosis. MIT-003 dose-dependently reversed all these changes ($p < 0.05$–0.001). In vivo: MIT-003 did not alter BUN, s-Cr, or renal injury scores versus uremic controls, confirming equivalent uremic burden. Nevertheless, MIT-003 significantly restored $NeuN^+$ and $Ki67^+$ cell counts ($p < 0.001$, $p < 0.05$), reduced $TUNEL^+$ cells from ~8 to ~1 cell/field ($p < 0.001$), attenuated DHE oxidative stress ($p < 0.05$), and recovered hippocampal GPX4, NRF2, SLC7A11, and xCT expression ($p < 0.05$–0.001).
Conclusions : MIT-003 selectively protects hippocampal neurons from uremia-induced ferroptosis by restoring the NRF2/GPX4/SLC7A11 axis. These findings position MIT-003 as a promising therapeutic candidate for uremic encephalopathy across the full spectrum of renal failure.