Hadassah Mendez-Vazquez

Glenn Award

Ph.D. Candidate, Neuroscience

First Year ARCS Scholar

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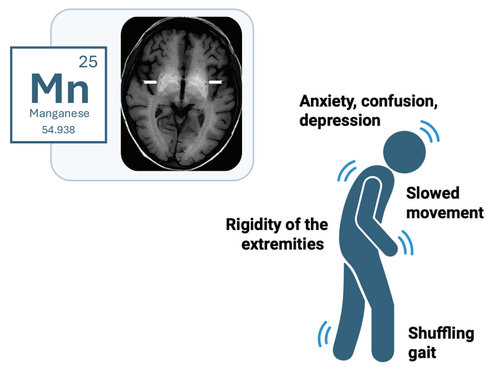
Mitochondrial transcriptional mechanisms of manganese-induced neuroinflammation

I am uncovering how manganese-induced mitochondrial RNA dysregulation contributes to neuroinflammation and neurodegeneration. Investigation of this novel mechanism linking mitochondrial dysfunction and the onset of inflammatory processes in the brain will advance the current understanding of manganese-induced neuropathology as well as aging and disease.

Framework

Manganese Toxicity

Occurs through environmental exposures or genetic defects and causes accumulation of manganese in the brain



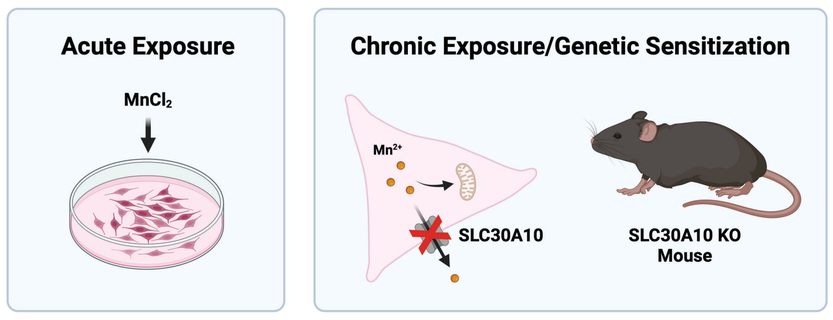
Symptoms:

- Psychiatric disturbances
- Parkinsonian motor deficits

Pathophysiological hallmarks:

- Mitochondrial dysfunction
- Neuroinflammation

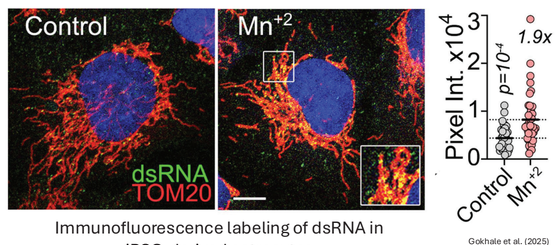
Modeling Manganese Toxicity



SLC30A10 loss results in impaired Mn extrusion from the cell

A novel mechanism of manganese-dependent mitochondrial dysfunction

Manganese exposure causes mitochondrial double-stranded RNA accumulation

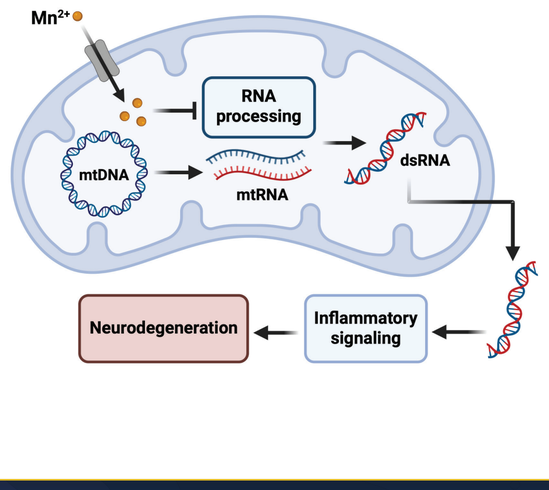


Immunofluorescence labeling of dsRNA in iPSC-derived astrocytes

Gokhale et al. (2025)

Double-stranded RNA (dsRNA) is a potent danger signal that causes the upregulation of antiviral signaling

Hypothesis:
Manganese disrupts mitochondrial RNA processing



Approach and Future Directions

Aim 1: Determine how manganese disrupts mitochondrial RNA processing to cause dsRNA accumulation

iPSC-derived astrocytes

Aim 2: Determine how manganese-induced dsRNA mediates neuroinflammation in the brain

SCL30A10 KO Mice

- **Identify cell types that are most vulnerable to dsRNA accumulation**
- **Characterize the transcripts that form dsRNA**
- **Profile inflammatory cytokines production**

Ultimate Goal:

Uncover fundamental mechanisms of mitochondrial alterations that contribute to metabolic dysfunction and inflammation in neurodegeneration

Scholar Awards Celebration

November 12, 2025

SCHOLAR AWARDS CELEBRATION ARCS FOUNDATION ATLANTA

Igniting Innovation in Georgia