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Glenn Award

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Mitochondrial mechanisms of manganese-induced neuroinflammation

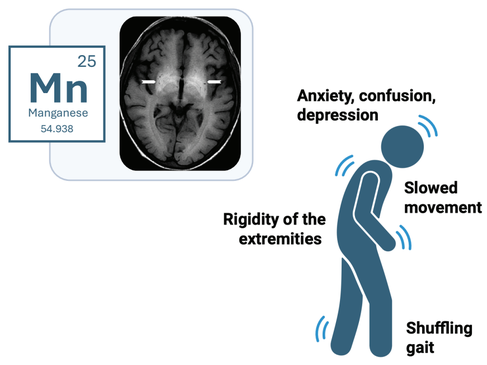
Understanding how inflammation begins in the brain is critical for uncovering the early causes of neurodegeneration. My research uses manganese toxicity as a model to study how cellular stress can trigger neuroinflammation. Through this work, we discovered that disrupted mitochondrial RNA regulation may contribute to inflammatory signaling in the brain. Investigating this novel link between mitochondrial dysfunction and inflammation will help advance our understanding of how neurodegeneration begins and may reveal new opportunities for earlier intervention.

Framework



Manganese Toxicity

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



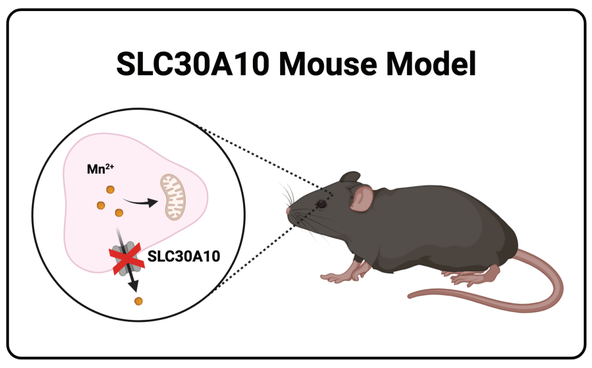
Symptoms:

- Psychiatric disturbances
- Parkinsonian motor deficits

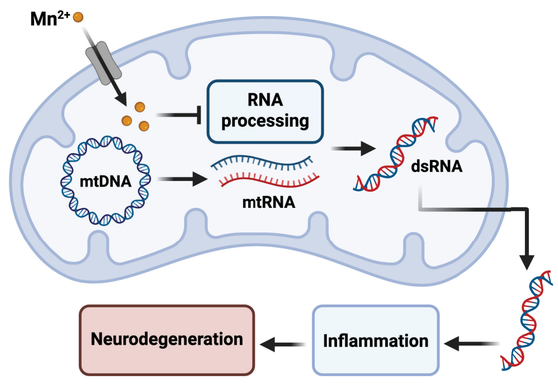
Pathophysiological hallmarks:

- Mitochondrial dysfunction
- Neuroinflammation

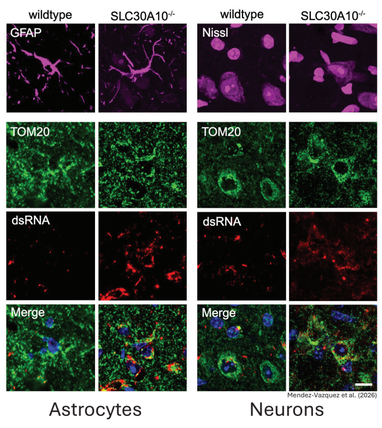
Modeling Manganese Toxicity



Hypothesis: Manganese induced-dsRNA leads to inflammation

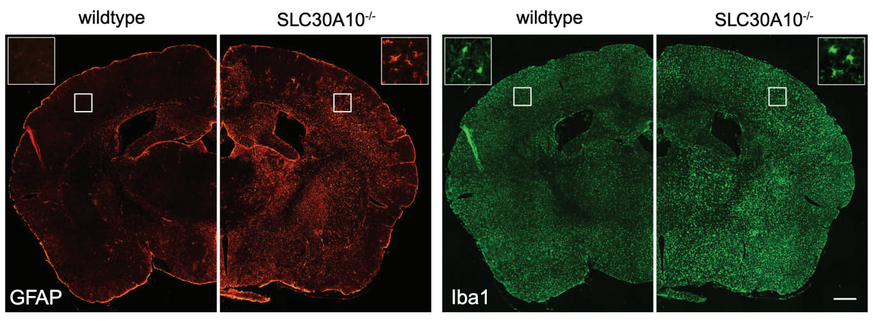


Manganese causes mitochondrial dsRNA accumulation



Double-stranded RNA (dsRNA) is a potent danger signal that causes antiviral signaling and inflammation

Manganese accumulation in the brain causes neuroinflammation



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