



## Verdin Lab

The Verdin Lab investigates how metabolic and epigenetic pathways contribute to aging, chronic inflammation, and age-related disease, with a particular focus on mechanisms that regulate NAD metabolism, vascular integrity, mitochondrial function, and neurodegeneration. A major area of interest is CD38-mediated NAD<sup>+</sup> depletion and its impact on the aging brain. One project examines how elevated CD38 expression in brain pericytes may drive NAD<sup>+</sup> loss, cellular dysfunction, and increased vulnerability to Alzheimer's disease, particularly in the context of the APOE4 genotype. Using human iPSC-derived pericytes and choroid plexus organoid models, the lab aims to define how CD38 alters cellular metabolism, mitochondrial function, senescence, and disease-associated pathways, and to test whether pharmacological inhibition of CD38 can restore NAD<sup>+</sup> homeostasis and improve cellular resilience.

A complementary project focuses on CD38 in endothelial aging and blood-brain barrier dysfunction. This work investigates how CD38 contributes to age- and senescence-associated endothelial dysfunction by altering barrier integrity, calcium signaling, and endothelial-to-mesenchymal transition (EndMT)-like programs, including cadherin switching and loss of endothelial identity. The project seeks to define how CD38-dependent NAD<sup>+</sup> metabolism and signaling influence endothelial cell-cell adhesion, vascular permeability, and inflammatory activation. By determining how these processes interact during aging and cellular senescence, the lab aims to understand how CD38-driven endothelial dysfunction contributes to blood-brain barrier breakdown, neuroinflammation, and impaired brain homeostasis, and whether targeting CD38 can preserve vascular integrity and resilience during aging.

The lab also studies SIRT5, a mitochondrial sirtuin that regulates lysine acyl modifications and helps maintain mitochondrial and protein homeostasis. Current work examines how SIRT5 protects myelin integrity by limiting the accumulation of damaging metabolic protein modifications that arise during mitochondrial stress. Loss of SIRT5 activity may promote myelin instability, neuroinflammation, and neurodegenerative pathology.

Together, these projects define a broader research program centered on how NAD metabolism, CD38 activity, pericyte and endothelial function, mitochondrial stress, and sirtuin signaling interact to drive brain aging and age-related disease. The long-term goal is to identify metabolic interventions that preserve vascular and neural function, reduce chronic inflammation, and improve resilience during aging.