



Verdin Lab

The Verdin Lab investigates how diet, exercise, metabolism, and chronic inflammation influence the aging process and contribute to diseases such as diabetes, cardiovascular disease, and Alzheimer's. Our research seeks to define the molecular and metabolic pathways that regulate aging and to uncover novel targets that promote healthy longevity.

Mitochondrial dysfunction is a hallmark of aging and neurodegeneration, leading to the accumulation of reactive metabolites that chemically modify essential cellular molecules, including proteins, lipids, and nucleic acids, thereby compromising cellular integrity and function. A central focus of the lab is on metabolites such as acetyl-CoA and NAD (nicotinamide adenine dinucleotide), both of which change significantly with age and disrupt cellular resilience. When NAD levels fall, the activity of sirtuins declines. These enzymes are critical for maintaining stress resistance, genomic stability, and metabolic flexibility. At the same time, increased activity of NAD-consuming enzymes such as CD38 and PARPs further depletes NAD and intensifies metabolic stress. Together, these changes weaken tissue stability and promote inflammation and neurodegeneration.

We also study the links between cellular senescence, innate immune activation, and chronic inflammation in aging. As cells accumulate damage, they enter a senescent state and secrete inflammatory factors that activate nearby immune cells such as macrophages. These immune cells express enzymes like CD38 that consume NAD, creating a cycle that connects senescence to NAD loss and inflammation. This process is particularly harmful in the brain, where aging increases the permeability of the blood-brain barrier and allows immune cells to infiltrate neural tissue. Our findings suggest that senescent cells contribute directly to inflammation and neuronal injury, forming a molecular bridge between aging, immune activation, and neurodegeneration.

By combining studies in genetically modified mouse models, human immune cells, and metabolomics platforms, we aim to understand how metabolic signals, immune aging, and senescence intersect to drive organismal aging. We view chronic inflammation as a central mechanism underlying many diseases of aging, including neurodegeneration, cancer, type 2 diabetes, and atherosclerosis, and believe that uncovering its metabolic basis will lead to new strategies that extend healthspan and reduce the burden of age-related disease.

Verdin lab projects:

The Verdin Lab investigates how metabolic pathways shape the aging immune system through a series of interconnected research areas. Using genetically modified mouse models and human or murine cell systems lacking key enzymes in NAD metabolism (CD38) or mitochondrial regulators (Sirt5, Mff), the lab examines how altered NAD and mitochondrial pathways affect cellular function and organismal health. Complementary *in vivo* studies employ low-grade inflammation models and pharmacological interventions, such as NAD precursors (NMN, NR) and brain-penetrant NADase inhibitors (78c) to restore NAD levels and assess impacts on tissue integrity and cognition. Current work focuses on the choroid plexus, a critical regulator of cerebrospinal fluid production and brain homeostasis, to uncover the molecular mechanisms by which CD38 drives senescence, neuroinflammation, neurodegeneration, blood-brain barrier maintenance, and hippocampal synaptic plasticity.

In parallel, the lab is developing human immune organoid systems as high-throughput platforms to identify metabolic and immunological biomarkers that reflect biological rather than chronological aging. By integrating immune profiling, metabolomics, and proteomics across human cohorts, these efforts aim to define molecular signatures of immune aging and translate them into strategies that enhance metabolic resilience and healthspan.

Additionally, the lab has established a comprehensive metabolomics core, implementing both targeted and untargeted LC-MS protocols to profile metabolic transitions from youth and health to aging and disease, with a focus on the NAD metabolome, central carbon metabolism, and amino acid pathways.

Together, these projects converge on a unifying goal: to identify and mechanistically validate metabolic biomarkers that both drive and reflect biological aging, paving the way for translational interventions that promote longevity and functional health.

Desired Skills and experience:

We are seeking a highly motivated and curious individual who thrives in a collaborative and multidisciplinary environment. The ideal candidate will bring strong technical expertise, attention to detail, and the ability to adapt to evolving research directions.

A solid foundation in molecular and cellular biology techniques: DNA, RNA, and protein extraction; PCR/qPCR; and immunoassays, is essential. Experience with cell culture systems, particularly human primary immune cells or established cell lines, is highly desirable. Familiarity with analytical approaches such as metabolomics, proteomics, or epigenetic assays is an advantage. Experience with *in vivo* mouse models, including husbandry, genotyping, or experimental support, is desirable but not strictly required.

Equally important are strong data analysis and documentation skills, with the ability to manage large experimental datasets, ensure reproducibility, and contribute to collaborative, multi-team projects. Effective communication, scientific curiosity, and adaptability are key to success within the dynamic culture of the Verdin Lab.