Verdin Lab

The Verdin lab focuses on the relationship between aging and the immune system. Aging is associated with defects in the adaptive immune system and a state of chronic activation of the innate immune system, commonly referred to as chronic inflammation. We propose that chronic inflammation is a key unifying factor underlying the development of chronic diseases associated with aging, including neurodegeneration (such as Parkinson's and Alzheimer's), cancer, type 2 diabetes, and atherosclerosis (which can lead to heart attacks and strokes).

Our research investigates how immune aging is regulated by factors such as nutrition, inflammation, and stress. We have demonstrated that the relative abundance of key cellular metabolites—such as NAD+, acetylcoenzyme A, and the ketone body beta-hydroxybutyrate—fluctuates under various nutritional conditions (including obesity, calorie restriction, fasting, time-restricted feeding, and ketogenic diets), and how these changes influence immune responses. We are particularly focused on key enzymes regulated by these metabolites, including sirtuins (which rely on NAD+), histone acetyltransferases (associated with acetylcoenzyme A), histone deacetylases (HDACs), and NAD-consuming enzymes (like Cd38). We are intrigued by potential connections between innate immune activation, chronic inflammation, and dysregulated metabolism in processes such as cellular and immune senescence, leaky gut, and alterations in the blood-brain barrier (BBB).

A deeper understanding of the mechanisms leading to metabolic dysfunction, cellular senescence, and chronic inflammation associated with aging may unveil novel therapeutic targets and potential interventions against human aging. We have several current and planned projects that have overlapping goals and experimental workflows. We are looking for a motivated student who has a keen interest in exploring metabolic dysfunction, inflammation, and senescence in the aging process.

Project 1: CD38-Mediated NAD+ Consumption, Blood Brain Barrier Function and Effects on Brain Aging
The Verdin lab has a keen interest in investigating the role of specific brain cells that support the blood-brain barrier (BBB) and cerebrospinal fluid production (CSF) and how their function is altered in neurogenerative diseases. The BBB acts as a protective filter, regulating the entry of substances into the brain. When this barrier is compromised, harmful molecules can infiltrate the brain, leading to inflammation and accelerating neurodegeneration. We will explore how targeting specific pathways within cells that make up the BBB can influence BBB integrity and potentially mitigate cognitive decline. There are two areas of focus in this project: 1) role of CD38 on NAD+ consumption, and 2) its impact on BBB integrity. To achieve our goals, we will utilize both *in vitro* and *in vivo* modeling systems and employ advanced techniques, including flow cytometry, microscopy, proteomics, metabolomics, and epigenetics, as well as neurobehavioral cognitive analyses to measure the effects of these interventions on brain health and cognitive function.

Project 2: Assessing the target of P7C3-A20 to further elucidate its neuroprotective capabilities:
In this project, we aim to identify the target of P7C3-A20 and understand its protective mechanism in neurodegenerative diseases. First, we will screen and verify candidates for the P7C3-A20 target and elucidate the molecular interactions between them. Next, we will assess the impact of P7C3-A20 on the candidate's activities and the involved pathways. Finally, we will investigate the role of the target candidate in the neuroprotective effects of P7C3-A20 using iPSC-derived neurons and mouse models. By deciphering the target of P7C3-A20, we hope to translate its benefits into clinical applications to extend human healthspan. The Verdin lab projects integrate both wet-bench and dry-bench techniques. We are employing various omics approaches, including single-nuclei sequencing, spatial transcriptomics, metabolomics, and proteomics, in conjunction with wet-bench techniques, such as immunohistochemistry (IHC), Western blot (WB), and qPCR, as well as multiple

behavior tests. Therefore, this project is multidimensional, and trainees involved will receive comprehensive training during their time in the lab.

Desired skills or experience: Coursework foundation in biology, biochemistry, chemistry preferred but not necessary. Previous research experience techniques desired, but not required: gel electrophoresis, WB, IHC, qPCR, microscopy.