

## Understanding Heterogeneity in Large Transcriptomic Datasets using a Deep Generative Model

*Vanessa Rivas (Mentors: Mathini Vaikunthan, Cody Slater, Dr. José L. McFaline-Figueroa, 2024 IICD SRP)*

Molecular and cellular composition and phenotypic heterogeneity can impact disease onset and therapeutic response across many diseases, ranging from neurodegenerative diseases such as Alzheimer's disease (AD) to brain tumors such as meningioma. This summer project will focus on implementing deep generative frameworks to identify transcriptional programs in *in vitro* models of neurons and glial cells associated with detrimental exposures associated with AD, and meningioma samples obtained after resection and treated with common chemotherapeutics.

Alzheimer's Disease (AD) is a progressive disease involving putative causes such as the accumulation of amyloid-beta plaques, and aberrant activity from non-neuronal cell types such as microglia and astrocytes. The contribution of these various factors in heterogeneous cell-type systems is still poorly understood. Thus, we employed a high-throughput single-cell characterization of Alzheimer-associated exogenous insults. To explore and categorize the transcriptional responses, we will employ deep generative models to identify programs that differ between different chemical treatments in a multicellular multi-condition model system.

Meningiomas are the most common type of primary brain tumor occurring in nearly 170,000 people each year. Meningioma typically responds well to resection, but a subset of patients recur and there is no current medical treatment, and it is unknown if specific molecular subtypes respond well to common drugs. Here, we will apply the same deep generative model to a cohort of ex-vivo-treated meningioma samples.