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Research Award Brief

The microRNA system in neurocognitive aging (2015 – 2017)

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Research Question: What are the molecular changes that promote preservation of learning and memory during aging?

Interdisciplinary Approach: Our strategy combines molecular and behavioral approaches to identify changes in the microRNA system that impact learning and memory.

Potential Implications of Research: Identification of microRNA pathways that promote successful cognitive aging may lead to therapeutic interventions to combat cognitive decline in aging, as well as other learning disorders.

A hallmark of human existence is the ability to learn and store memories of our lives. Remembering past events and experiences not only brings people great joy but is also vital to daily functions such as eating, reading and navigating. People are living longer, and thus a major challenge facing our society is the need to understand how to preserve memory functions across aging. The most pervasive aspect of age-related memory impairments is the inability to form *new* memories. This memory impairment not only creates challenges for daily life, but also can presage the development of Alzheimer's dementia, a devastating neurodegenerative condition. Accordingly, a top priority of research in this field is to identify, understand and ultimately prevent age-related changes in the brain that compromise the formation of new memories.

The neural foundations of our ability to learn and form new memories lie in microscopic structures, called synapses, which allow information to flow between neurons in the brain. The ability of synaptic connections to strengthen or weaken over time, known as synaptic plasticity, is critical to supporting learning and preserving cognitive function with age. Recent work in our laboratories suggests that the *microRNA system* provides a novel mechanism for storing new memories in the brain. MicroRNAs are tiny RNA molecules that can turn on and off the synthesis of proteins needed by synapses to store new memories. Accordingly, defects in the microRNA system may compromise the ability of the brain to form and keep new memories.

The goal of this proposal is to determine the role of the microRNA system in memory impairments associated with aging. To this end, we will measure the amount of microRNAs present in the rat hippocampus, a region of the brain known to be critical for learning and memory in both rats and humans. We will use a well-characterized rat model of aging to identify two groups of rats: those that retain normal cognitive function comparable to that displayed by young rats, and those that display impaired cognitive function, similar to that found in elderly humans diagnosed with memory impairment. We will examine whether there are any systematic differences in the amount of microRNAs present in the hippocampus of these two cognitively distinct groups of rats.

By understanding if there are differences in microRNA populations between aged rats that manifest normal and impaired memory functions, we can begin to understand the neural foundations of the memory impairments seen in aging, dementia and Alzheimer's. Understanding the neural mechanisms that allow or prevent the formation of new memories will support the development of therapies to prevent memory decline with age.