Effects of Space Radiation on Hippocampal-Dependent Learning and Neuropathology in Wild-Type and Alzheimer's Disease Transgenic Mice

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The hippocampus and dentate gyrus are critically important brain regions required for long-term memory formation. Damage to these critical brain regions contributes to memory deficits in patients with Alzheimer's disease. The hippocampus and dentate gyrus are also notable as sites where brain stem cells differentiate into new neurons throughout life, a process called neurogenesis. Exposure to space radiation can result in impairments in learning and long-term reduction in hippocampal neurogenesis. It is unknown how radiation causes these impairments and whether and by what mechanism(s) radiation exposure might predispose individuals to develop Alzheimer's disease.

We utilize a well-characterized and widely used Alzheimer's disease transgenic mouse model (Tg2576) to address the following research objectives: (1) examine the long-term impact of space radiation (SR) on hippocampal-dependent spatial learning and memory, (2) evaluate the potential of SR to accelerate Alzheimer's disease pathogenesis and neuropathology, (3) evaluate a novel non-invasive laser-based eye scanner to detect and monitor molecular changes in the lens of the eye induced by radiation exposure and Alzheimer's disease pathology (Goldstein, et al., Lancet, 2003).

Our studies directly address key objectives of the NASA Human Space Flight Program, including determination of potential space-related SR dependencies related to late CNS risks such as early-onset dementia or Alzheimer's disease, assessment of SR effects on molecular, cellular and tissue environment changes in hippocampus indicative of increased risk of dementia or Alzheimer's disease, and evaluation of biological models of Alzheimer's disease or other forms of dementia that occur in humans. The existing knowledge gap is immense and presents a major obstacle to rational assessment of short- and long-term risk to the central nervous system posed by SR exposure expected during extended human space travel. Our experiments will examine the mechanisms by which SR impairs synaptic function in normal brain and assess whether SR enhances long-term risk of Alzheimer's disease.