Glioblastoma and the Senescent Brain Microenvironment

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ABSTRACT

The long-term goal of these pilot studies is to determine whether the senescent brain promotes brain tumor pathogenesis, and whether we can enhance length and quality of life in older patients with brain tumors. Glioblastoma (GBM) is the most common and aggressive brain tumor. Despite surgery, radiation, and temozolomide chemotherapy, most GBMs recur within six months.

GBM is a disease of aging., and its incidence increases dramatically after age 60. However, very little research has focused on the age-dependent microenvironmental factors that promote their growth and recurrence. Our central hypothesis is that senescence – either from the aging brain or treatments themselves – promotes tumorigenesis and recurrence. Using genetically modified mice, and repurposing therapies known to be safe in humans and that have senolytic properties, we will test the causal effects of the senescent brain microenvironment on tumor pathogenesis. Pertinent to the mission of the Longer Life Foundation, we will chart a path to clinical translation and deeper mechanistic studies, so that this work will improve the longevity and quality of life of patients at risk for, or who have, brain tumors.

LAY SUMMARY

Brain tumors increase in frequency with age. To date, all approved therapies target the tumor cells themselves. We are taking a different approach, that is, treating the aging brain. We hypothesize that the aging brain environment helps cause these tumors to grow. We will test whether senescent cells play a causative role in the development of brain tumors. We will also test whether therapies that target senescent cells in the brain can help prolong survival of animal models of disease. If successful, this work can be brought rapidly to the clinic, and will change the way we treat and prevent cancer.