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# Investigating Sex Differences in the Brain Tumor Microenvironment

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TOWARD A BETTER UNDERSTANDING OF ...

## Investigating Sex Differences in the Brain Tumor Microenvironment

Cameron Hill

Mentor: Joshua Rubin

The risk of cancer increases with age, and senescent cells accrue in the body with age. Cellular senescence is an anti-cancer response that arrests cells in response to potentially oncogenic stresses, such as DNA double strand breaks, oxidative stress, or oncogene activation. Although cellular senescence protects an individual cell from propagating, it can be harmful to surrounding cells. Senescent cells exhibit the senescence-associated secretory phenotype (SASP), which can have deleterious effects, such as promoting inflammation or tumor progression, and stimulating cell proliferation. The link between the increased development of cancer with age and the accumulation of senescent cells has been documented in breast cancer; however, it has not before been considered for brain tumors. Glioblastoma (GBM) is the most frequent primary malignant brain tumor in adults. Patients with GBM have a dismal prognosis, with a median survival of about one year. Glioblastoma arises preferentially in men, with a male to female ratio of 1.6. Furthermore, increasing age is a greater risk factor for males than for females in developing GBM. Therefore, the question remains whether the senescence response and the SASP in the brain, specifically in astrocytes, differs between males and females. My aim is to characterize the threshold of the cellular senescence response in male and female mouse wild-type (WT) astrocytes in order to illuminate whether the SASP microenvironment contributes to 1) males' higher susceptibility to developing brain tumors as they age in comparison to females and/or 2) differences in growth of male and female GBM cells. Thus, I developed a protocol for inducing and characterizing senescence in mouse astrocytes by causing oxidative stress via hydrogen peroxide and staining for senescence associated ß-galactosidase, a marker of cellular senescence. My results indicate that male astrocytes undergo oxidative stress induced senescence at a higher frequency than females. Elucidating the sex differences in the senescence response and the SASP will allow for a better understanding of GBM biology and ultimately uncover novel targets for GBM treatment.