The Mechanisms of Glioblastoma Migration in a Bioengineered 3D Brain Model

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Glioblastoma Multiforme is a lethal cancer originating from the glial cells of the brain. Current treatments are unsuccessful partly due to GBM's rapid migration along white matter tracts and blood vessels, causing secondary tumors. A novel assay was created utilizing collagen-hyaluronic acid (HA) hydrogels and polycaprolactone nanofibers, representing the chemistry of the extracellular matrix and white matter topography. Previous work demonstrated that increasing concentrations of HA slowed cell migration. It was hypothesized that as HA concentration increased (1 mg/mL-10 mg/mL), the intensity of associated receptors (CD44, RHAMM) would increase, adhesion protein Vinculin would decrease, and collagen receptor beta-1 would remain constant. Increasing HA concentration represented the gradient that the cells migrated through after exiting the tumors. Immunocytochemistry was utilized to track the presence of receptors. It was found that as HA concentration increased, the presence of associated receptors increased as well; Vinculin decreased, and beta-1 remained constant. It was then proposed that as HA concentration increases, GBM slows migration due to CD44's regulation of the mesenchymal to amoeboid migration transition. A blocking antibody was used to inhibit CD44 function; afterwards, timelapse microscopy was used to track GBM migration. With the inhibition of CD44, there were no significant differences in GBM migration between levels of HA, demonstrating that CD44 plays a key role in GBM migration. Future work will examine the mechanical properties of the system. Use of a 3D brain mimetic model helps to enhance our understanding of GBM migration, leading to the development of therapeutic treatments.