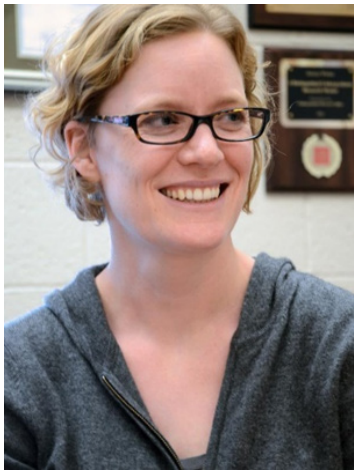
CARNEGIE MELLON UNIVERSITY
BME 2023 SPRING SEMINAR SERIES

"Mechanics in the Brain Tumor Microenvironment"



PRESENTED BY

Jessica Winter
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SCHEDULE

Hall of Arts (HOA) 160

Thursday,
January 26, 2023
(11:00AM-12:00PM)

Glioblastoma is an extremely aggressive cancer with a dismal ~ 15 month survival rate despite standard care of surgical resection followed by chemo-radiation. We are interested in the role of tumor microenvironment in glioma invasion and resistance to therapy, both of which contribute to the high mortality of this cancer. In particular, two model systems that we have developed to investigate the intersection of mechanical influences in the tumor microenvironment and glioma migration and apoptotic signaling will be discussed.

In brain cancer, tumor growth is mechanically hindered by the rigidity of the skull, which generates a compressive inward solid stress toward the tumor core. We investigated the influence of this compressive solid stress on tumor cell migration, identifying a parabolic response with highest migration at normal and high pressures. We correlated these observations to gene expression changes. Using miRNA-mRNA correlation analysis, we were able to identify key miR regulators of this behavior. These data could provide future therapeutic targets for gliomas.

In addition to compressive solid stress, the brain tumor microenvironment is affected by high interstitial fluid pressure. The leaky vasculature associated with tumors combined with compressive solid stress at the tumor core results in an inward pressure gradient and outward fluid flow. Using patient databases, we identified mechanosensory gene expression changes at the tumor core versus periphery, locations experiencing different interstitial fluid profiles. Our results highlighted apoptotic signaling as most impacted. Then, we explored the role of increasing interstitial fluid pressure on cell survival and apoptosis signaling using in vitro cultures. These data show differences in cell response at different pressures and may provide guidance on patient pressure management.

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