The impact of HA-CPNs on CD44 pathway activation and stem cell properties of glioma

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Glioblastoma (GBM) is the most aggressive brain tumor with a median survival of only 15 months. Despite decades of research, GBM continues to pose a great therapy challenge due to its extreme genetic and phenotypic heterogeneity. The pools of stem- like tumour initiating cells (TICs) maintain and recapitulate the heterogeneity of GBM; their ability to self-renew fuels resistance to treatment and tumour recurrence. Furthermore, successful treatment of GBM is hindered by the poor penetration of the available therapeutics through tightly regulated blood-brain barrier (BBB). Conjugated polymer nanoparticles (CPNs) are a class of nanotechnology of potential novel application for GBM treatment. CPNs can penetrate the BBB and can also be encapsulated with drugs for cargo delivery, in addition to functionalizing their surface with ligands complementary to protein receptors expressed on the glioma cell surface. In collaboration with the Rondeau-Gagné lab, my project focuses on a diketopyrrolopyrrole (DPP)-based CPNs labeled with a fluorescently tagged hyaluronic acid (HA). HA is the primary ligand of the CD44 receptor present on the surface of TICs. CD44 overexpression is implicated in GBM progression and correlates with poor patient survival. Using the human U-251MG GBM cells and patient- derived primary lines, I will investigate the effects of CPNs on CD44 signaling and stem cell properties of TICs *in vitro* as well as *in vivo,* using a Zebrafish model. Collectively, these results will not only further validate CPN system as a potential future anti-GBM therapy but also contribute to a better understanding of CD44 biology in GBM.