CRISPR Knockout of Hif1a in Glioblastoma Cancer: In vitro and in vivo Evaluation

Bawden, Neve (School: Bountiful High School)

Hypoxia is common in solid tumors, and Hypoxia-Inducible Factor 1 Alpha (HIF-1a) plays a key role in adaptation to low-oxygen environments. This year's research focused primarily on the intracranial xenograft model to evaluate the effects of Hif1a knockout in glioblastoma. Previously, CRISPR/Cas9 was used to inactivate Hif1a in several glioblastoma cell lines, with genome editing confirmed through DNA sequencing. In the current study, Hif1a knockout clones (U87CR9) and control lines (U87mgLN) were injected into the brains of 10 mice. The intracranial xenograft trials demonstrated that Hif1a knockout significantly impaired tumor growth compared to controls, mirroring but strengthening results observed in earlier subcutaneous xenograft experiments. These findings suggest that, although previous research indicated possible cellular adaptation to Hif1a loss through alternative pathways, such as GLUT1 and PDK1 regulation, the intracranial model exhibits more pronounced growth inhibition in a clinically relevant setting. Protein assays, including ELISA-HIF1 and VEGF, supported reduced tumorigenicity of Hif1a-deficient cells in vivo. The present data provide robust evidence that CRISPR-mediated Hif1a knockout directly impedes glioblastoma progression within the brain, underscoring the therapeutic potential of Hif1a targeting. Ongoing and future studies will expand intracranial trial sample sizes and further dissect post-knockout adaptive mechanisms in this model.

Awards Won: