Targeting Hif1a: Attenuating in vivo Growth and Ferroptosis in Glioblastoma Cells

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Hypoxia is common in solid tumors. Hypoxia Inducible Factor 1 Alpha (Hif1a) is upregulated and stabilized under hypoxic conditions, leading to tumor growth. This experiment targets Hif1a because normal cells do not generally require it. Ferroptosis is a natural cell death mechanism dependent on iron accumulation and lipid reactive oxygen species. CRISPR with Cas-9, has previously been used to inactivate Hif1a in the glioblastoma cell line U251. Previous research indicated CR2 and CR6 made the same amount of GLUT1 as the control while CR5 produced less. PDK1 showed no difference in any clones. This study includes an Iron Chelation Assay and in vivo testing of CR6 and CR7. CR7 was used as the control. The Assay's results were counterintuitive to the expected outcome. CR6 and CR7 were injected into 5 mice. CR6 had minimal growth. CR7 showed exponential growth. This showed the effect that Hif1a's knockout had on a solid tumor model and displays how cells can adapt to Hif1a inactivation and regulate GLUT1 and PDK1 through alternate pathways. This indicates CRISPR can be used to knock out Hif1a effectively to create cell lines for detailed study of Hif1a in glioblastoma. Solid tumor models in the brain can also be used for further experimentation.

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