CS-30. PROTEIN KINASE CK2 IS IMPORTANT FOR THE FUNCTION OF GliOBLASTOMA BRAIN Tumor INITIATING CELLS

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Casein kinase 2 (CK2) is an ubiquitously expressed serine/threonine kinase composed of two catalytic subunits (α and/or α') and two regulatory (β) subunits. The expression and kinase activity of protein kinase CK2 are elevated in many different cancers, including glioblastoma (GBM). Brain tumor initiating cells (BTICs) are a subset of cells that are tumorigenic and are considered to promote the resistance of GBM to current therapies. Previously our lab has reported that CK2 activity promotes prosurvival signaling in GBM; however, the role of CK2 in BTICs has not been examined. In this study, we found that the expression of CK2α was increased in CD133+ BTICs compared to CD133- cells from GBM xenografts. We found that GBM cells are sensitive to cell death caused by CX-4945, an ATP-competitive inhibitor of CK2. Inhibition of CK2 also reduced the frequency of CD133+ BTICs over the course of 7 days, indicating a role for CK2 in BTIC persistence and survival. Additionally, using an in vitro limiting dilution assay, we found that CX-4945 reduced neurosphere formation in bulk cells from GBM xenografts. On the other hand, inhibition of CK2 had no effect on the proliferation or neurosphere formation of normal murine neural precursor cells. We are currently investigating the mechanism of cell death and reduced neurosphere formation and have found a reduction in the constitutive activation of signal transduction pathways dysregulated in GBM including NF-kB and MAPK pathways. Due to the integration of CK2 in multiple signaling pathways important for BTIC survival, protein kinase CK2 is a promising target in GBM.