Regulation of Ubiquitin Specific Peptidase 2 by Farnesoid X Receptor in Glioblastoma NCI-60 Cell Lines

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Glioblastoma multiforme is the most common primary brain tumor in adults. It is extremely aggressive and one of the least treatable types of cancers. Although treatment options include surgery, chemotherapy, and radiotherapy, the median survival is 14-15 months after diagnosis. With no obvious cause and little progress in development of new therapies, there is a clear need to identify new potential targets. Farnesoid X Receptor (FXR) is a nuclear receptor predominantly expressed in the liver and intestine, where it is has been reported to be critical in maintaining bile acid homeostasis and suppress hepatocellular carcinoma through anti-inflammatory activity and repair of liver injury. Our laboratory has previously found FXR expressed in the brain. Specifically, in mouse and human astrocytes FXR regulates the inflammatory response to pro-inflammatory cytokines. Additionally, we evaluated the expression of FXR in six NCI-60 glioblastoma cell lines, one immortalized glioblastoma cell line (ATCC U118), and primary human astrocytes. Basal levels of FXR were measured by qPCR and immunofluorescent staining, indicating the presence of this gene product and protein in glioblastoma and human astrocyte cells. When these cells were treated with an FXR agonist (10µM WAY 362450), significant induction of the validated downstream target gene small heterodimer partner (SHP) occurred. Further, Ubiquitin Specific Peptidase 2 (USP2), a deubiquitinating enzyme with a complex role in tumorigenesis, was increased following FXR agonist treatment in the glioblastoma and primary human astrocyte cell lines. qPCR and immunofluorescent staining revealed a significant increase in USP2 mRNA (≥1.5-2.1 fold) and protein (≥1.2-2.0). These data further solidify the presence of functional FXR in human astrocytes and glioblastoma, identifying it as a desirable target for further research.