Investigating the Inhibition of MYBL2 for Therapeutic Intervention in Group 3 Medulloblastoma

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Medulloblastoma is the most common type of pediatric brain tumor accounting for approximately 20% of all pediatric central nervous system tumors. Four distinct groups of medulloblastoma have been identified. Group 3 is considered to be the most lethal with a 39% 10-year overall survival rate. MYBL2 (MYB proto-oncogene like 2) is a transcription factor that plays a crucial role in cell cycle regulation by controlling genes necessary for cell proliferation, survival and differentiation. MYBL2 overexpression in medulloblastoma is associated with poor prognosis suggesting it is a potential therapeutic target. In this study we examined inhibition of MYBL2 with demethylzeylasteral (T-96) and fingolimod (FTY720), two therapeutics which have previously shown anti-tumor effects. We hypothesized that the use of these drugs could inhibit MYBL2 activity, disrupting the cell cycle, reducing tumor cell proliferation, and potentially enhancing the sensitivity of medulloblastoma cells to existing treatments. To test efficacy of T-96 and FTY720 we utilized cell viability assays in four group 3 medulloblastoma cell lines (HDMB-03, MB004, Med411-FHTC, and Med2112-FHTC). After identifying inhibitory concentrations of these drugs in each cell line we performed further analysis to detect MYBL2 protein levels via western blotting. Additionally, we examined cell cycle progression following drug treatment or knockdown of MYBL2 expression. Our results show that T-96 and FTY720 inhibit tumor cell growth, suggesting that they should be further investigated as potential therapeutic agents for medulloblastoma patients.