Investigating Metastatic Characteristics of Candidate Dissemination Genes on a Medulloblastoma Cell Line

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Leptomeningeal dissemination (LMD) is the metastatic spread of tumor cells from the brain to spinal chord. LMD is a characteristic of and the most fatal step in the pediatric brain tumor medulloblastoma. The purpose of this experiment is to further understand why and how this cancer spreads and to better target therapies for patients. A previous genetic screen study identified a lengthy list of genes that possibly conferred a growth and metastatic advantage to medulloblastoma tumor cells, genes that upon further study and evaluation could be targeted in treating this disease. In the human medulloblastoma cell line (DAOY), the two candidate genes that were used were aryl hydrocarbon receptor nuclear translocator (ARNT) and a protein-coding gene related to signaling protein activity (Smad5). In DAOY cells, the overexpression of ARNT and Smad5 was used to assess the canonical oncogenic traits of migration, invasiveness, and growth. By using the in vitro scratch assay, it was determined that when these cancer cells overexpress ARNT and Smad5 they have a higher average rate of cell migration than control cancer cells. In the matrigel chemoinvasion assay, overexpression of the two genes made cells more invasive compared to the control. In the soft agar colony forming assay, it was apparent that overexpressing ARNT and Smad5 created more colonies. The results indicate that overexpression of ARNT and Smad5 increase rate of cell migration, make cells more invasive, and allow cells to grow without an attachment. All attributes that make these cells more tumorigenic suggest that these proteins will be excellent future therapeutic targets.

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