Role of LIM and SH3 protein 1 (LASP1) in the metastatic dissemination of medulloblastoma.

Abstract:
Medulloblastoma is the most common malignant pediatric brain tumor and is one of the leading causes of cancer-related mortality in children. Treatment failure mainly occurs in children harboring metastatic tumors, which typically carry an isochromosome 17 or gain of 17q, a common hallmark of intermediate and high-risk medulloblastoma. Through mRNA expression profiling, we identified LIM and SH3 protein 1 (LASP1) as one of the most upregulated genes on chromosome 17q in tumors with 17q gain. In an independent validation cohort of 101 medulloblastoma samples, the abundance of LASP1 mRNA was significantly associated with 17q gain, metastatic dissemination, and unfavorable outcome. LASP1 protein expression was analyzed by immunohistochemistry in a large cohort of patients (n = 207), and high protein expression levels were found to be strongly correlated with 17q gain, metastatic dissemination, and inferior overall and progression-free survival. In vitro experiments in medulloblastoma cell lines showed a strong reduction of cell migration, increased adhesion, and decreased proliferation upon LASP1 knockdown by small interfering RNA-mediated silencing, further indicating a functional role for LASP1 in the metastatic dissemination of medulloblastoma.
progression and metastatic dissemination of medulloblastoma.