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Basic and Translational
Investigations

The role of the membrane cytoskeleton crosslinker ezrin in medulloblastoma cells

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Abstract

Medulloblastoma is a highly malignant brain tumor that occurs predominantly in children. The molecular pathogenesis of medulloblastoma is under investigation. Previously we used cDNA microarray analysis to compare patterns of gene expression in medulloblastoma samples versus normal cerebellum. The cytoskeletal protein ezrin was found to be overexpressed in medulloblastoma when compared to normal cerebellum, an observation that was further validated by immunohistochemistry and RT-PCR analysis. To assess the role of ezrin in medulloblastoma, we studied ezrin's role in medulloblastoma migration, invasion, and adhesion. Western blotting and immunofluorescence showed high expression

of ezrin in four medulloblastoma cell lines and ezrin was primarily localized to filopodia. Ezrin-specific siRNA suppressed the formation of filopodia and in vitro migration, invasion and adhesion. We also used a stably-transfected medulloblastoma cell line to study the effect of ezrin overexpression. We showed that high expression of ezrin promotes filopodia formation and in vitro invasion. Finally, athymic mice implanted with ezrin overexpressing Daoy MB cell clones in the cerebellum showed shortened survival when compared to controls. These findings suggest that, in addition to other cytoskeletal proteins, ezrin plays an important role in medulloblastoma adhesion, migration, and invasion.

Key Words: ezrin, medulloblastoma, motility, siRNA, invasion, cytoskeleton

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