Wnt pathway in atypical teratoid rhabdoid tumors.

Abstract

BACKGROUND: Atypical teratoid rhabdoid tumor (ATRT) is an aggressive pediatric brain tumor with limited therapeutic options. The hypothesis for this study was that the Wnt pathway triggered by the Wnt5B ligand plays an important role in ATRT biology. To address this hypothesis, the role of WNT5B and other Wnt pathway genes was analyzed in ATRT tissues and ATRT primary cell lines.

METHODS: Transcriptome-sequencing analyses were performed using nanoString platforms, immunohistochemistry, Western blotting, quantitative reverse transcriptase PCR, immunoprecipitation, short interference RNA studies, cell viability studies, and drug dose response (DDR) assays.

RESULTS: Our transcriptome-sequencing results of Wnt pathway genes from ATRT tissues and cell lines indicated that the WNT5B gene is significantly upregulated in ATRT samples compared with nontumor brain samples. These results also indicated a differential expression of both canonical and noncanonical Wnt genes. Immunoprecipitation studies indicated that Wnt5B binds to Frizzled1 and Ryk receptors. Inhibition of WNT5B by short interference RNA decreased the expression of FRIZZLED1 and RYK. Cell viability studies indicated a significant decrease in cell viability by inhibiting Frizzled1 receptor. DDR assays showed promising results with some inhibitors.

CONCLUSIONS: These promising therapeutic options will be studied further before starting a translational clinical trial. The success of these options will improve care for these patients.

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KEYWORDS: ATRT; Frizzled 1; Ryk; Wnt pathway; Wnt5B

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