

Poliovirus Receptor (CD155) Expression in Pediatric Brain Tumors Mediates Oncolysis of Medulloblastoma and Pleomorphic Xanthoastrocytoma

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Introduction

Poliovirus oncolytic viral immunotherapy is a putatively novel approach to treat both low grade and malignant pediatric brain tumors. However, the expression of the poliovirus receptor (PVR), CD155, on a variety of pediatric brain tumors and its ability to infect, propagate, and lyse pediatric brain tumor cells is unknown.

Methods

CD155 expression in a variety of pediatric tumor specimens including pleomorphic xanthoastrocytoma (PXA), medulloblastoma, atyptical teratoid rhaboid tumor, embryonal tumor, and anaplastic ependymoma was assessed using a validated rabbit monoclonal antibody. The ability of poliovirus:rhinovirus genetic recombinant, PVSRIPO, to infect PXA (645 [BRAF V600E mutation] and 2363) and medulloblastoma (D283, D341) cell lines was determined by measurement of viral propagation and cell killing. Gene expression data from a medulloblastoma patient cohort of 763 patients was used to determine differential PVR mRNA expression and compared using analysis of variance.

Results

CD155 expression was present in 53 of 57 patient specimens analyzed in all PXA and medulloblastoma cell lines. One-step growth curves of PVSRIPO at a multiplicity of infection of 10 demonstrated productive infection and peak plaque formation units at 5-10 hours. PVSRIPO infection of all four cell lines demonstrated decreased proliferation in 2363, 645, and D341 cell lines at 48 hours (p<0.0001) and resulted in cell death. PVR expression was significantly highest in Group 3 gamma, WNT alpha, and WNT beta compared to the other medulloblastoma subtypes (p<0.001).

Conclusions

Poliovirus receptor, CD155, is widely expressed in a variety of brain tumor specimens. This proof-of-concept in vitro study demonstrated that PVSRIPO was capable of infecting, propagating, and prohibiting cell proliferation in PXA with and without BRAF V300E mutations and Group 3 medulloblastoma. In patients, CD155 has preferential expression in select subtypes known to overexpress c-Myc. Future studies will evaluate PVSRIPO to treat pediatric brain tumors.

Learning Objectives

Describe CD155 expression in pediatric brain tumors.

Describe the in vitro results of oncolytic poliovirus to treat pediatric brain tumors.

References

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