Viability reduction and Rac1 gene downregulation of heterogeneous ex-vivo glioma acute slice infected by the oncolytic Newcastle Disease Virus strain V4UPM

ABSTRACT

Oncolytic viruses have been extensively evaluated for anticancer therapy because this virus preferentially infects cancer cells without interfering with normal cells. Newcastle Disease Virus (NDV) is an avian virus and one of the intensively studied oncolytic viruses affecting many types of cancer including glioma. Nevertheless, the capability of NDV infection on heterogeneous glioma tissue in a cerebrospinal fluid atmosphere has never been reported. Recently, Rac1 is reported to be required for efficient NDV replication in human cancer cells and established a link between tumourgenesis and sensitivity to NDV. Rac1 is a member of the Rho GTPases involved in the regulation of the cell migration and cell-cycle progression. Rac1 knockdown leads to significant inhibition of viral replication. In this work, we demonstrated that NDV treatment led to significant reduction of tumour tissue viability of freshly isolated heterogeneous human brain tumour slice, known as an ex vivo glioma acute slice (EGAS). Analysis of gene expression indicated that reduced tissue viability was associated with downregulation of Rac1. However, the viability reduction was not persistent. We conclude that NDV treatment induced EGAS viability suppression, but subsequent downregulation of Rac1 gene may reduce the NDV replication and lead to regrowth of EGAS tissue.

Keyword: Oncolytic viruses; Anticancer therapy; Newcastle Disease Virus; Ex vivo glioma acute slice; EGAS.