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Reactive oxygen species induction in oncolytic virus therapy of glioblastoma

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Reactive Oxygen Species (ROS) are signaling molecules that play versatile roles in regulating various cellular pathways in both physiological and pathological conditions such as cancer and virus infection. The effects of ROS on viral replication are context-dependent and the role of ROS in oncolytic virus therapy of cancer is poorly understood. In this study, we investigated ROS induction and its potential impacts on oncolytic herpes simplex virus (oHSV) therapy of the malignant brain tumor glioblastoma. We employed a clinically relevant glioblastoma model that is based on patient-derived glioblastoma stem cells (GSCs) that recapitulate the genotype and phenotype of primary tumors. Two oHSVs were used; G47Δthat lacks γ34.5 and α47 and has a LacZ insertion inactivating ICP6 and MG18L that contains deletion of the Us3 gene and a LacZ insertion inactivating ICP6. Measurement of intracellular ROS by H2-DCFDA and Mito SOX assays showed that both oHSVs (G47Δ and MG18L) robustly induced intracellular ROS in GSCs at 24 and 48 hours post infection, which was specifically seen in infected cells. Antioxidants reduced glutathione (GSH) and N-acetyl cystein (NAC), potently suppressed oHSVs-induced intracellular ROS. Antioxidants-mediated suppression of intracellular ROS did not affect viral replication or viral spread. However, cell viability assays (MTS and Cell Titer Glo) and dead cell staining (trypan blue or propidium iodide) demonstrated that both antioxidants protected GSCs from early cell death caused by the viruses. Thus we show that oHSV is a potent inducer of ROS upon infection of GSCs. Our results also suggest that virus-induced ROS contribute to early cell death following oHSV therapy of glioblastoma.

Biography

Fares Nigim was graduate student from Department Neurosurgery, Harvard University, USA; PhD Candidate in Neuroscience, Cambridge University; Clinical Research Fellow in Neurosurgery, Harvard Medical School, USA. He is interested in the topics Cell Culture, Neurosurgery Microscopy, Stem Cells, Immunohistochemistry, Brain Computer Interfaces, Neuroanatomy, Epilepsy and Cell Culture. He is currently working at Massachusetts General Hospital, Neurosurgery department.

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