EVALUATION OF SOX2 EXPRESSION IN Glioblastoma stem cells DURING ZIKA Virus infection

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Problem
With standard treatment, the median survival for glioblastoma patients is about 14.6 months (ABTA 2019). New and improved treatments must be created to significantly improve patient outcomes.

Background
Glioblastoma (GBM) is a deadly form of brain cancer. Standard treatment involves surgery followed by chemotherapy and radiation. Most tumors recur within six months, fueled by a small population of glioblastoma stem cells (GSCs) that resist and survive treatment. There are no pharmacological agents currently available for specific targeting of GSCs. Zika virus (ZIKV) is a flavivirus that is linked to congenital microcephaly in addition to other neurological manifestations. It appears that ZIKV selectively targets normal neural stem cells in the developing brain. ZIKV specificity is due to receptor mediated cell entry: AXL, a tyrosine kinase receptor present on neural stem cells, specifically binds ZIKV and permits cell entry. We examined the effect of ZIKV on Sox2, a transcription factor that controls the self-renewal of stem cells.

Objective
The purpose of this study is to understand AXL signaling during ZIKV infection and the effect on Sox2 expression in GBM stem cells.

Methods
ZIKV strain MR766 was propagated in Vero cells. Viral stock was then titrated by plaque assays. Glioblastoma patient derived cell lines were infected with ZIKV and the percentage of infection was quantified by flow cytometry using a pan-flavivirus antibody. Western blotting was used to characterize protein expression in glioblastoma patient derived cell lines. Immunofluorescence microscopy was used to visualize Sox2 levels after ZIKV infection.

Results
Inverse Correlation of AXL and Sox2

Axial Knockout Increases Sox2 Expression

ZIKV Infection Decreases Sox2 Expression

Conclusions
ZIKV targets AXL for cellular entry and carries out its function through downstream pathways. Our results suggest that there is an inverse correlation between AXL and Sox2. Furthermore, ZIKV infection causes a decrease in Sox2 expression in GBM stem cells.

References