

**Natureza do trabalho:** Resumo

TITLE

ZIKA VIRUS AS A THERAPY FOR GLIOBLASTOMAS

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ABSTRACT

**Introduction:** Glioblastomas (GB) are the most common malignant Central Nervous System (CNS) tumors, as well as the most lethal<sup>1</sup>. They have a diverse morphological organization and high mitotic activity, resulting in a fast growth. Despite the chemotherapy, radiotherapy and surgical treatments available, these tumors generally have a grim prognosis<sup>1</sup>. Recently, though, a new discovery unveiled an oncolytic property in the Zika Virus (ZIKV), opening a new possibility for more efficient therapy against GB. **Objectives:** This work aims to discuss some recent findings that point to the Zika virus as a therapeutic potential against glioblastomas. **Methods:** A literature review was conducted during the month of September 2017 in the databases of PubMed and Lilacs, with the following keywords: *glioblastoma* and *zika*. **Discussion:** ZIKV is a flavivirus, from the *Flaviviridae* family, transmitted by mosquitoes of the genus *Aedes*<sup>2</sup>. It is known to be a trigger of Guillain-Barret Syndrome and there is evidence of causality between ZIKV and congenital neurological and ophthalmological abnormalities<sup>2</sup>. However, the full spectrum of neurological complications and the long-term sequelae of ZIKV infection remain to be determined<sup>2</sup>. More than that, the neurotropism of ZIKV could be a possible therapeutic for CNS cancers. Researchers hypothesized that, since the ZIKV infect neuroprogenitor stem cells in developing brain, leading to loss of proliferation and cell death, it could be used against GB<sup>3</sup>. First, they infected differentiated glioma cells (DGCs) and glioblastoma stem cells (GSCs) with ZIKV *in vitro*<sup>3</sup>. The virus had as its preferred target the GSC, decreasing their formation and increasing apoptosis; otherwise the DGC were almost unaffected<sup>3</sup>. Then, to test the oncolytic activities of ZIKV *in vivo*, researchers inoculated a mouse-adapted ZIKV-Dakar strain on gliomas induced in mice<sup>3</sup>. The virus led to regression of the tumor, prolonged survival of the animals and it had marginal effects on their CNS cells<sup>3</sup>. Comparing to other viruses that have been studied in the last decades as potential antineoplastic agents, such as West Nile virus, also a flavivirus transmitted by *Aedes*, the ZIKV has been proved to be more efficient against the tumor tissue and safer, as it is less toxic to normal brain cells<sup>3,4</sup>. **Conclusion:** The Zika virus has attracted worldwide attention in last years as an emerging health threat<sup>2</sup>. However, these new studies have pointed to neurotropic properties of the virus that could be used in a beneficial way against the unfavorable prognosis gliomas. There are still many safety measures to be taken, such as making a genetically stable virus with attenuated replication in differentiated neural cells, but ongoing research is already having good results<sup>3</sup>.

**References**

<sup>1</sup>Castañeda C.A., et al. Glioblastoma: Análisis Molecular Y Sus Implicancias Clínicas. Rev Peru Med Exp Salud Publica. 2015; 32(2):316-25.

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<sup>2</sup>Sais J.C., et al. Zika Virus: What Have We Learnt Since the Start of the Recent Epidemic? *Front Microbiol.* 2017; 8: 1554. doi: 10.3389/fmicb.2017.01554.

<sup>3</sup>Zhu Z., et al. Zika virus has oncolytic activity against glioblastoma stem cells. *J. Exp. Med.* 2017. <http://dx.doi.org/10.1084/jem.20171093>.

<sup>4</sup>Southam C.M., Moore A.E. Clinical studies of viruses as antineoplastic agents with particular reference to Egypt 101 virus. *Cancer.* 5:1025–1034. 1952. [http://dx.doi.org/10.1002/1097-0142\(195209\)5:5<1025::AID-CNCR2820050518>3.0.CO;2-Q](http://dx.doi.org/10.1002/1097-0142(195209)5:5<1025::AID-CNCR2820050518>3.0.CO;2-Q)