Washington University in St. Louis
Office of Technology Management

ENGINEERED ONCOLYTIC ZIKA VIRUS THERAPY FOR GLIOBLASTOMA

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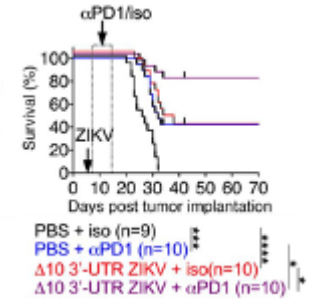
T-017429 Engineered Oncolytic Zika Virus Therapy for Glioblastoma

Technology Description

Researchers in the laboratories of Michael Diamond and Milan Chheda at Washington University have developed prospective treatments for glioblastoma (GBM) through the application of an engineered Zika virus (ZIKV) that is safe and non-transmissible by mosquitos. ZIKV has specific lytic activity against treatment-resistant GBM stem cells & extends survival in multiple murine models. A recent study demonstrated GBM regression and enduring tumor non-occurrence in a human patient due to incidental infection during a Zika outbreak.[1]



Stage of Research

Potent anti-tumor effects and significantly greater survival shown in multiple murine models, with improved safety via selectively engineered sensitivity to the host innate immune response. The virus has been tested in the brains of Rhesus macaques with no observed toxicity and or recoverable infectious virus.

While ZIKV treatment alone had significant efficacy, greater efficacy was shown in combination with anti-PD1 immunotherapy (left). Efficacy of ZIKV is due to a combination of GBM stem cell targeting and its ability to induce strong anti-tumor immune responses that facilitate $CD8^+$ T cell–dependent clearance of tumor components not directly killed by ZIKV.

Publications

Nair, S., Mazzoccoli, L., Jash, A., Govero, J., Bais, S.S., Hu, T., Fontes-Garfias, C.R., Shan, C., Okada, H., Shresta, S., et al. (2021). Zika virus oncolytic activity requires CD8+ T cells and is boosted by immune checkpoint blockade. JCI Insight *6*, e144619. 10.1172/jci.insight.144619.

Zhu, Z., Gorman, M.J., McKenzie, L.D., Chai, J.N., Hubert, C.G., Prager, B.C., Fernandez, E., Richner, J.M., Zhang, R., Shan, C., et al. (2017). Zika virus has oncolytic activity against glioblastoma stem cells. Journal of Experimental Medicine *214*, 2843–2857. 10.1084/jem.20171093.

Applications

- Glioblastoma and potentially other tumors such as grade 4 astrocytoma.

Key Advantages

- **Complementary to other therapeutic strategies. (e.g. Nair et al. 2021 – anti-PD-1 antibody therapy; Zhu et al. 2017 – temozolomide)**
- **Relative to other oncolytic viruses, ZIKV specifically targets GBM stem cells.**

Patents

- Patent Pending (US20210145907A1)

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[1] Garcez et al. (2023). Case report: Regression of Glioblastoma after flavivirus infection. Front. Med. 10, 1192070. 10.3389/fmed.2023.1192070.