Vesicular stomatitis virus

Vesicular stomatitis Indiana virus (VSIV; often still referred to as VSV) is a virus in the family Rhabdoviridae; the well-known rabies virus belongs to the same family. VSIV can infect insects, cattle, horses and pigs. It has particular importance to farmers in certain regions of the world where it can infect cattle. This is because its clinical presentation is identical to the very important foot and mouth disease virus.

The virus is zoonotic and leads to a flu-like illness in infected humans.

It is also a common laboratory virus used to study the properties of viruses in the family Rhabdoviridae, as well as to study viral evolution.

Vesicular stomatitis virus (VSV) shows potential for targeting and killing cancer cells, but can be dangerous in the brain due to its neurotropic glycoprotein.

Zhang et al., from the Department of Neurosurgery, Yale University School of Medicine, New Haven, United States tested a chimeric virus in which the VSV glycoprotein is replaced with the Chikungunya polyprotein E3-E2-6K-E1 (VSVΔG-CHIKV). Control mice with brain tumors survived a mean of 40 days after tumor implant. VSVΔG-CHIKV selectively infected and eliminated the tumor, and extended survival substantially in all tumor-bearing mice to over 100 days. VSVΔG-CHIKV also targeted intracranial primary patient derived melanoma xenografts. Virus injected into one melanoma spread to other melanomas within the same brain with little detectable infection of normal cells. Intravenous VSVΔG-CHIKV infected tumor cells but not normal tissue. In immunocompetent mice, VSVΔG-CHIKV selectively infected mouse melanoma cells within the brain. These data suggest VSVΔG-CHIKV can target and destroy brain tumors in multiple animal models without the neurotropism associated with the wild type VSV glycoprotein [1)].

Kimpel et al., described VSV-GP, a modified version of the vesicular stomatitis virus, as a non-neurotoxic oncolytic virus that is effective for the treatment of malignant glioblastoma and ovarian cancer.

They evaluated the therapeutic efficacy of VSV-GP for malignant melanoma. All of the human, mouse, and canine melanoma cell lines that were tested, alongside most primary human melanoma cultures, were infected by VSV-GP and efficiently killed. Additionally, they found that VSV-GP prolonged the survival of mice in both a xenograft and a syngeneic mouse model. However, only a few mice survived with long-term tumor remission. When they analyzed the factors that might limit VSV-GP's efficacy, they found that vector-neutralizing antibodies did not play a role in this context, as even after eight subsequent immunizations and an observation time of 42 weeks, no vector-neutralizing antibodies were induced in VSV-GP immunized mice. In contrast, the type I IFN response might have contributed to the reduced efficacy of the therapy, as both of the cell lines that were used for the mouse models were able to mount a protective IFN response. Nevertheless, early treatment with VSV-GP also reduced the number and size of lung metastases in a syngeneic B16 mouse model. In summary, VSV-GP is a potent candidate for the treatment of malignant melanoma; however, factors

limiting the efficacy of the virus need to be further explored [2].

Interferon gamma (IFNγ) is a dimerized soluble cytokine that is the only member of the type II class of interferons.

The existence of this interferon, which early in its history was known as immune interferon, was described by E. F. Wheelock as a product of human leukocytes stimulated with phytohemagglutinin, and by others as a product of antigen-stimulated lymphocytes or tuberculin-sensitized mouse peritoneal lymphocytes challenged with PPD; the resulting supernatants were shown to inhibit growth of vesicular stomatitis virus. Those reports also contained the basic observation underlying the now widely employed interferon gamma release assay used to test for tuberculosis. In humans, the IFNγ protein is encoded by the IFNG gene.

1)
Zhang X, Mao G, van den Pol AN. Chikungunya-vesicular stomatitis chimeric virus targets and eliminates brain tumors. Virology. 2018 Jul 25;522:244-259. doi: 10.1016/j.virol.2018.06.018. [Epub ahead of print] PubMed PMID: 30055515.
2)
Kimpel J, Urbiola C, Koske I, Tober R, Banki Z, Wollmann G, von Laer D. The Oncolytic Virus VSV-GP Is Effective against Malignant Melanoma. Viruses. 2018 Mar 2;10(3). pii: E108. doi: 10.3390/v10030108. PubMed PMID: 29498639; PubMed Central PMCID: PMC5869501.