

Oncolytic Viral Therapy for ALT Dependent Cancers

INVENTION: Salk investigators have engineered a herpes simplex virus 1 (HSV-1) oncolytic virus that selectively replicates in cancer cells, specifically those cells that maintain their immortality by maintaining the length of their telomeres using a mechanism termed alternative lengthening of telomeres (ALT).

This variant of HSV-1 functions by initiating apoptosis in the ALT-positive cells via an immediate early gene. The engineered HSV-1 molecule would be useful for the treatment of ALT-positive cancers. This potential therapeutic would have the combined effect of directly killing infected cells as well as priming the immune system to seek and destroy cancers that may have metastasized to distant locations.

APPLICATIONS:

- Development of targeted oncolytic therapies.
- The HSV-1 variant could be used synergistically with telomerase inhibitors.
- Targeted ALT cancer vaccines.
- The HSV-1 variant could be combined with immune stimulatory factors for cancer immunotherapy.

ADVANTAGES:

- The HSV-1 variant specifically infects ALT-positive cancerous cells and leaves normal healthy cells untouched.
- HSV-1 backbone allows the engineered variant to infect a broad range of cell types.
- The virus remains as an episome within the cancerous cell during latency.
- Ability to manipulate the 152kb viral genome for multiple therapeutic transgenes or payloads.

STAGE OF DEVELOPMENT: Discovery; early pre-clinical in vitro data in cell lines

BACKGROUND: Cancer cells are known for their limitless replicative potential by the elongation and maintenance of telomeres, the protein-DNA complex at the end of chromosomes. In healthy cells, telomeres will undergo progressive shortening with each round of replication until the cell permanently stops dividing and undergoes programmed cell death. Cancer cells are able to counteract telomere shortening by a telomere maintenance mechanism. The infected cells are able to do this by synthesizing new telomeric DNA via a DNA template using a mechanism called alternative lengthening of telomeres (ALT). ALT occurs predominantly in certain cancers such as, glioblastoma, astrocytomas, osteosarcomas, leiomyosarcomas, and undifferentiated pleomorphic sarcomas. Currently, there are no rational targets or therapies to treat ALT dependent tumors. In addition, the current treatments for many cancers do not always remove malignant cells and leave patients with side effect detrimental to their quality of life.



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PATENT STATUS: Patent applications are pending.

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