

ONCOLYTIC HSV-1 STRAINS ENGINEERED TO COUNTER THE INNATE HOST RESPONSE

Principal Investigator

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A new modality for the treatment of cancer involves the use of oncolytic viruses. Typically, these viruses are genetically engineered so that they are unable to replicate in normal tissue and cause disease, yet they still retain the ability to replicate in and destroy malignant cells. Using this strategy, oncolytic herpes simplex virus type 1 (HSV-1) strains have been generated by removing the viral $\gamma_{134.5}$ gene, a critical determinant of viral virulence. HSV-1 $\gamma_{134.5}$ mutants are radically attenuated and have been safely administered to rodents, non-human primates, and humans. The use of HSV-1 is proving to be safe as a cancer treatment in several clinical trials. However, $\gamma_{134.5}$ mutant viruses grow poorly in tumor cells, as they are unable to counteract the powerful innate host response mediated by interferon.

Description of the Project

Dr. Mohr's laboratory has discovered that a specific gene in the HSV-1 virus functions to counteract the innate host response mediated by interferon. Taking advantage of this knowledge, a method has been developed whereby the growth properties of a $\gamma_{134.5}$ mutant virus in malignant cells can be dramatically improved.

Applications

- 1) An oncolytic virus capable of counteracting the innate antiviral response of malignant cells, thereby providing a more effective oncolytic agent to treat cancer.
- 2) This HSV-1 gene product can function as an interferon resistance gene, preventing innate host defenses from inhibiting protein synthesis in infected cells.
- 3) An oncolytic virus that also has the capability to evade the host CD8⁺ response.

Patent Status

A provisional patent application has been filed in the United States.