

Virus-Based Therapy Boosts Anti-Cancer Immune Responses to Brain Cancer

New clinical trial from the Dana-Farber Cancer Institute and Mass General Brigham may change the standard of care for glioblastoma patients.

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A team led by investigators at Dana-Farber Cancer Institute and Mass General Brigham has shown that a single injection of an oncolytic virus—a genetically modified virus that selectively infects and destroys cancer cells—can recruit immune cells to penetrate and persist deep within brain tumors. The research, which is published in *Cell*, provides details on how this therapy prolonged survival in patients with glioblastoma, the most common and malignant primary brain tumor, in a recent clinical trial.

“Patients with glioblastoma have not benefited from immunotherapies that have transformed patient care in other cancer types such as melanoma because glioblastoma is a ‘cold’ tumor with poor infiltration by cancer-fighting immune cells,” said co-senior author [Kai Wucherpfennig, MD, PhD](#), chair of the Department of Cancer Immunology and Virology at the Dana-Farber Cancer Institute. “Findings from our clinical trial and our mechanistic study show that is now feasible to bring these critical immune cells into glioblastoma.”

The oncolytic virus used in the team’s trial, which was developed by E. Antonio Chiocca, MD, PhD, Executive Director of the Center for Tumors of the Nervous System at Mass General Brigham Cancer Institute, is made from a herpes simplex virus genetically altered so it can only make copies of itself in glioblastoma cells and not normal healthy cells. The virus spreads to a glioblastoma cell, kills it, and then makes a copy of itself that spreads again to another glioblastoma cell. Infection of cells with the virus also triggers an immune response. In the phase 1 trial of 41 patients with recurrent glioblastoma, the oncolytic virus treatment extended survival compared to historically reported survival, especially among those with pre-existing viral antibodies.

In their *Cell* study, the investigators examined the extent of this immune response in clinical trial

participants. Their analysis revealed that the treatment induced long-term infiltration of immune T cells into patients' tumors. Closer proximity of cytotoxic T cells with dying brain tumor cells was associated with longer patient survival after treatment. The therapy also expanded pre-existing T cells in the brain.

"We show that increased infiltration of T cells that are attacking tumor cells translates into a therapeutic benefit for patients with glioblastoma," said Chiocca, who is also a co-senior author of the study. "Our findings could have important implications for a cancer whose standard of care hasn't changed for 20 years."

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