Cleveland Clinic Innovations

PRODUCT

Small recombinant protein therapeutic that inhibits brain tumor growth and therapy resistance, as well as negating cancer-associated adverse hypercoagulation state

INDICATION

Treatment for primary glioblastoma and other brain cancers

VALUE PROPOSITION

Stable and potent peptide therapeutic to treat brain cancer that works alone, or synergistically in combination with standard of care radiation treatment

DEVELOPMENT STAGE

Preclinical candidate with demonstrated in vivo efficacy

INTELLECTUAL PROPERTY

PCT/US2024/026844

RELATED PUBLICATIONS

Jeon et al, Tissue factor is a critical regulator of radiation therapy-induced glioblastoma remodeling. ***Cancer Cell***, **2023**, PMID: 37451272

CONTACT INFORMATION

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Human Factor VII Deletion Constructs for Treating Brain Cancer

Jeongwu Lee, PhD and Hye-Min Jeon, PhD

UNMET NEED

There are no curative therapeutic approaches for patients with malignant brain tumors including primary glioblastoma (GBM) and brain metastasis (BM).

Therapy-induced senescence found in tumor and its microenvironment is a main cause of therapeutic failures in cancer patients. However, there are little or no therapeutic agents to target this vulnerability.

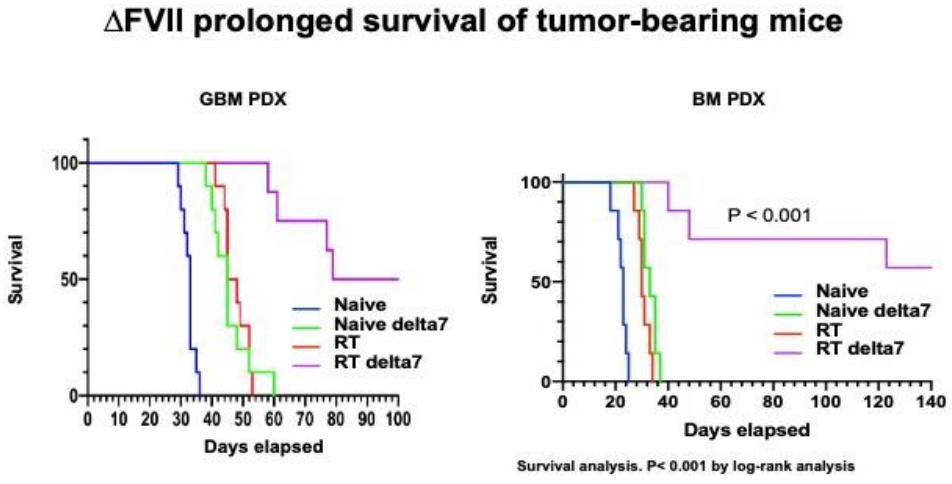
SOLUTION

Tissue factor (F3) signaling is a critical driver of radiation resistance mechanisms by promoting active clonal expansion of tumor cells and global reorganization of immune, extracellular matrix, and cytokine landscapes in the tumor microenvironment.

The inventors have developed ΔFVII, a novel F3-targeting agent, that is effectively delivered to the brain tumor region and radio-sensitizes orthotopic brain tumors in various preclinical patient-derived xenograft (PDX) models.

Compared to Tisotumab vedotin-tftv (Tivdak, FDA approved F3-directed ADC for recurrent/metastatic cervical cancer), the CCF ΔFVII-based approach provides multiple advantages:

- No noticeable systemic toxicity in animal models.
- Superior Blood-brain-barrier penetrance due to low molecular weight (14 kDa).
- Stable in vivo, and effectively delivered to brain tumor in orthotopic preclinical GBM and BM models.



ΔFVII therapy radio-sensitizes and prolongs survival of orthotopic GBM and brain metastasis (BM) PDX bearing mice. Kaplan-Meier survival curves of tumor bearing mice treated with radiation, ΔFVII, or both. p < 0.001 by log-rank analysis.