

Conference Abstracts

Vol. 6, Issue Supplement 2, 2026

Enhancing immunotherapy in Glioblastoma with First-in-Class Small Molecule Inhibitor Target AVIL

Yiwei Wang, PhD^{1,a}; Hui Li, PhD¹

¹ University of Virginia, 351 McCormick Rd, Charlottesville, Virginia, United States of America

Corresponding author

^a Yiwei Wang, PhD, University of Virginia, 351 McCormick Rd, Charlottesville, Virginia, United States of America

Email: dnj8qb@virginia.edu

Keywords: Novel target, immunotherapy, Glioblastoma, First-in-Class Small Molecule Inhibitor

Submission received: 2026-07-14 / Accepted: 2026-07-28 / Published: 2026-09-10

<https://doi.org/10.53876/001a.129751>

Abstract

Background

Worldwide, Glioblastoma (GBM) is characterized by limited immune infiltration and an immunosuppressive microenvironment, which makes it particularly difficult to treat with immunotherapy, including Immune checkpoint blockade (ICB). Increasing immune infiltration could be an effective strategy to enhance immunotherapy in GBM. Our group has identified the actin-binding protein advillin (AVIL) as being overexpressed, oncogenic, and necessary for tumorigenesis in GBM. We have since developed first-in-class compounds targeting AVIL (Science Translational Medicine, 2026). Here, we present a combination therapy that integrates AVIL inhibition with anti-PD-1 blockade to enhance antitumor immunotherapy via inducing immunogenic cell death (ICD).

Methods

GBM cells were treated with a first-in-class AVIL inhibitor to evaluate the induction of ICD. Classical ICD-associated markers were assessed in vitro. Additionally, a vaccinated-rechallenge assay was performed in immunocompetent mice. Briefly, mice were inoculated with AVIL inhibitor-treated GBM cells, followed by rechallenge with live tumor cells to evaluate

resistance to subsequent tumor formation. Furthermore, the AVIL inhibitor was combined with anti-PD1 therapy in an immunocompetent orthotopic GBM mouse model. Tumor progression and overall survival were monitored to evaluate treatment response. Tumor tissues and immune organs were harvested for immune profiling.

Results

AVIL inhibitor treatment induced multiple ICD features in GBM cells. In the vaccination model, AVIL inhibitor-treated GBM cells elicited protective antitumor immunity and reduced subsequent tumor formation following rechallenge with live GBM cells. In the orthotopic GBM model, combination therapy with the AVIL inhibitor and anti-PD-1 improved antitumor efficacy, as reflected by reduced tumor burden and prolonged survival. Immune profiling revealed increased immune infiltration within the tumor microenvironment, together with enhanced antigen-presenting activity in the tumor-draining lymph nodes.

Conclusion

Together, these findings identify AVIL as a promising therapeutic target in GBM and demonstrate that its first-in-class inhibitor can be effectively combined with anti-PD-1 antibody to enhance immunotherapy.

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