



Weill Cornell Medicine

FASN Inhibition Overcomes Radiation Resistance and Potentiates Anti-PD-1 Therapy in Glioblastoma

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Background & Unmet Need

- GBM incidence has risen over the past 15 years, yet median patient survival remains stagnant at 15 months
- Radiation therapy (RT) is the standard-of-care for the management of GBM and is the most widely used treatment for inoperable brain tumors
- GBM recurrence often arises within the irradiated margins, suggesting that RT can generate and/or exacerbate resistance mechanisms to support GBM progression
- Oxidative stressors, like reactive oxygen species (ROS) generated by RT, have been shown to reprogram the metabolism of an irradiated tumor which can promote the aggressivity of GBM
- **Unmet Need:** Development of novel therapeutic strategies targeting the metabolic escape pathways that drive GBM resistance to RT

Technology Overview

- **The Technology:** A combination therapy approach using radiation therapy, fatty acid synthase (FASN) inhibitors, and anti-PD-1 antibodies for treating GBM
- **The Discovery:** RT-induced fatty acid synthesis promotes GBM survival through both ER stress protection and immunosuppression via prostaglandin E2-mediated PD-1/PD-L1 upregulation.
- **PoC Data:** Triple combination therapy (RT+FASNi+anti-PD1) resulted in >100 days median survival compared to 24-45 days with single agents
- Triple combination therapy resulted in 85% long-term survival, significantly outperforming dual combination treatments which achieved only 30-40% survival rates.
- Triple combination therapy generated protective immune memory leading to long-term survival in surviving mice rechallenged with GBM

Inventors:

Claire Vanpouille-Box
Mara De Martino
Camille Daviaud
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Patents:

[US Application Filed](#)

Publications:

[De Martino et al. Cancer Lett. 2023](#)

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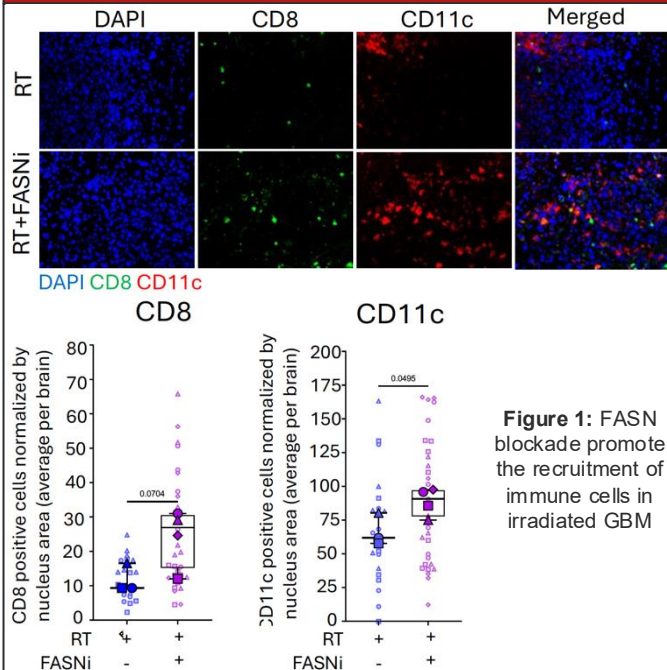
Technology Applications

- Primary treatment for newly diagnosed GBM
- Treatment for recurrent GBM
- Potential application in other cancers affected by lipid metabolism (melanoma, breast cancer, prostate cancer)

Technology Advantages

- Overcomes RT-induced resistance mechanisms
- Triggers long-lasting anti-tumor immunity
- Combines with existing standard-of-care treatments

Supporting Data / Figures



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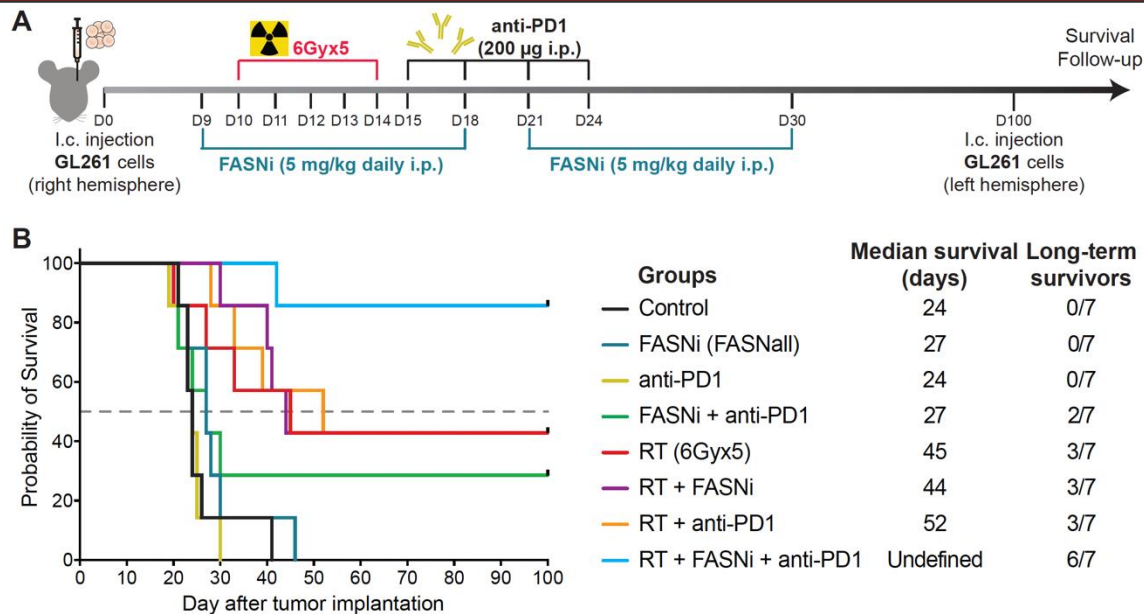


Figure 2: FASNi in combination with focal radiation therapy and anti-PD-1 prolongs survival of GBM bearing mice.

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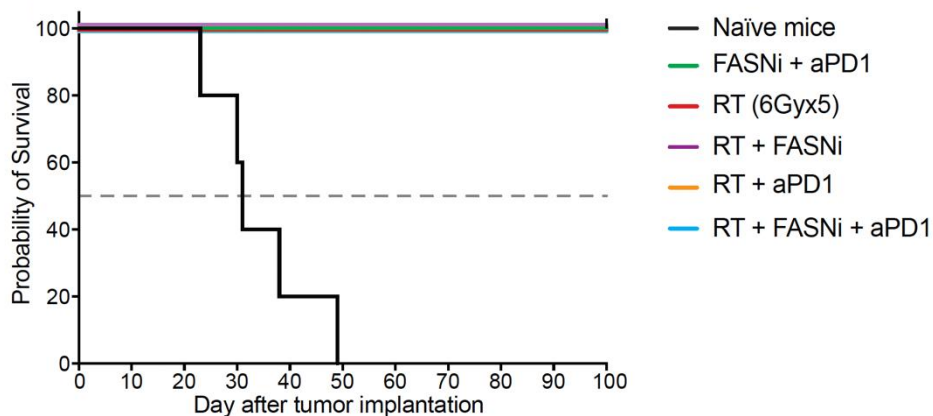


Figure 3: Mice treated with triple combination therapy (RT, FASN inhibitor, and anti-PD-1) demonstrated immune memory when rechallenged with GL261 cells after 100 days.

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