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NOVEMBER 9–14
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# ImmunoPET-Informed Sequence for Focused Ultrasound-Targeted mCD47 Blockade Controls Glioma

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# Disclosures

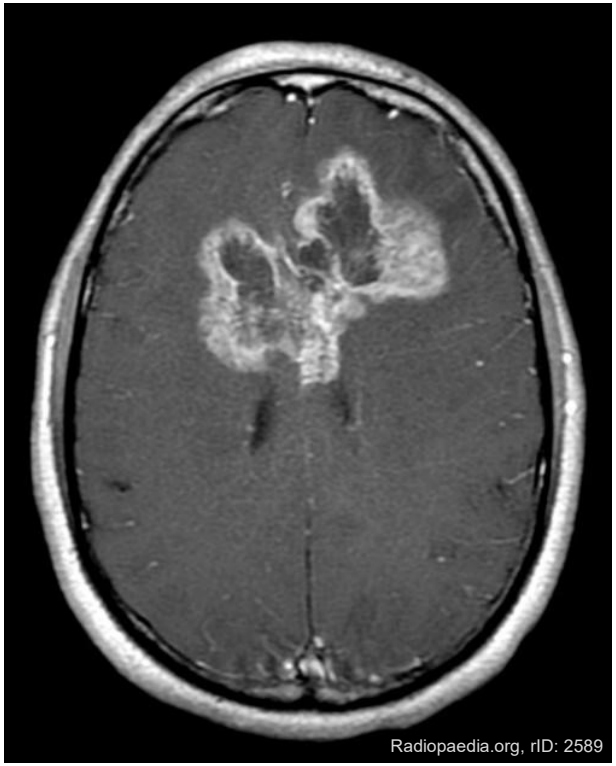
No relevant disclosures.

# Glioblastoma

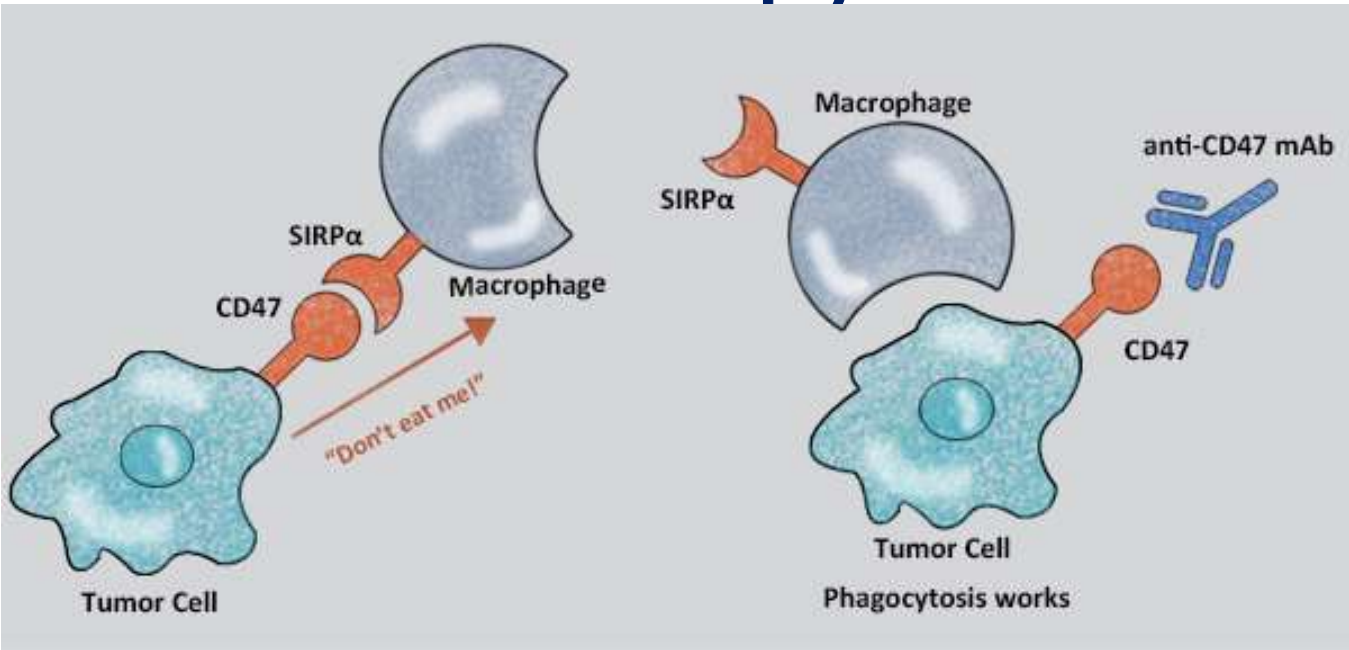
**Most common & aggressive** malignant brain tumor in adults.

Despite current SOC, remains nearly **intractable** due to its **highly invasive** nature.

Patients face a dismal prognosis – **high recurrence** rate (>90%) and survival on order of **months.**



# CD47 Blockade: A Promising Strategy for Glioblastoma Therapy

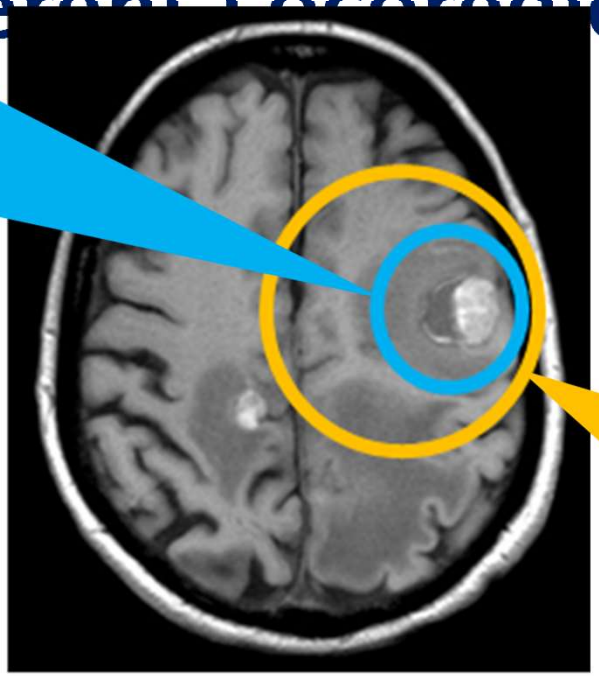



*Acrobiosystems*

# The Blood Brain & Blood Tumor Barriers (BBB/BTB) Present Different Locoregional Delivery

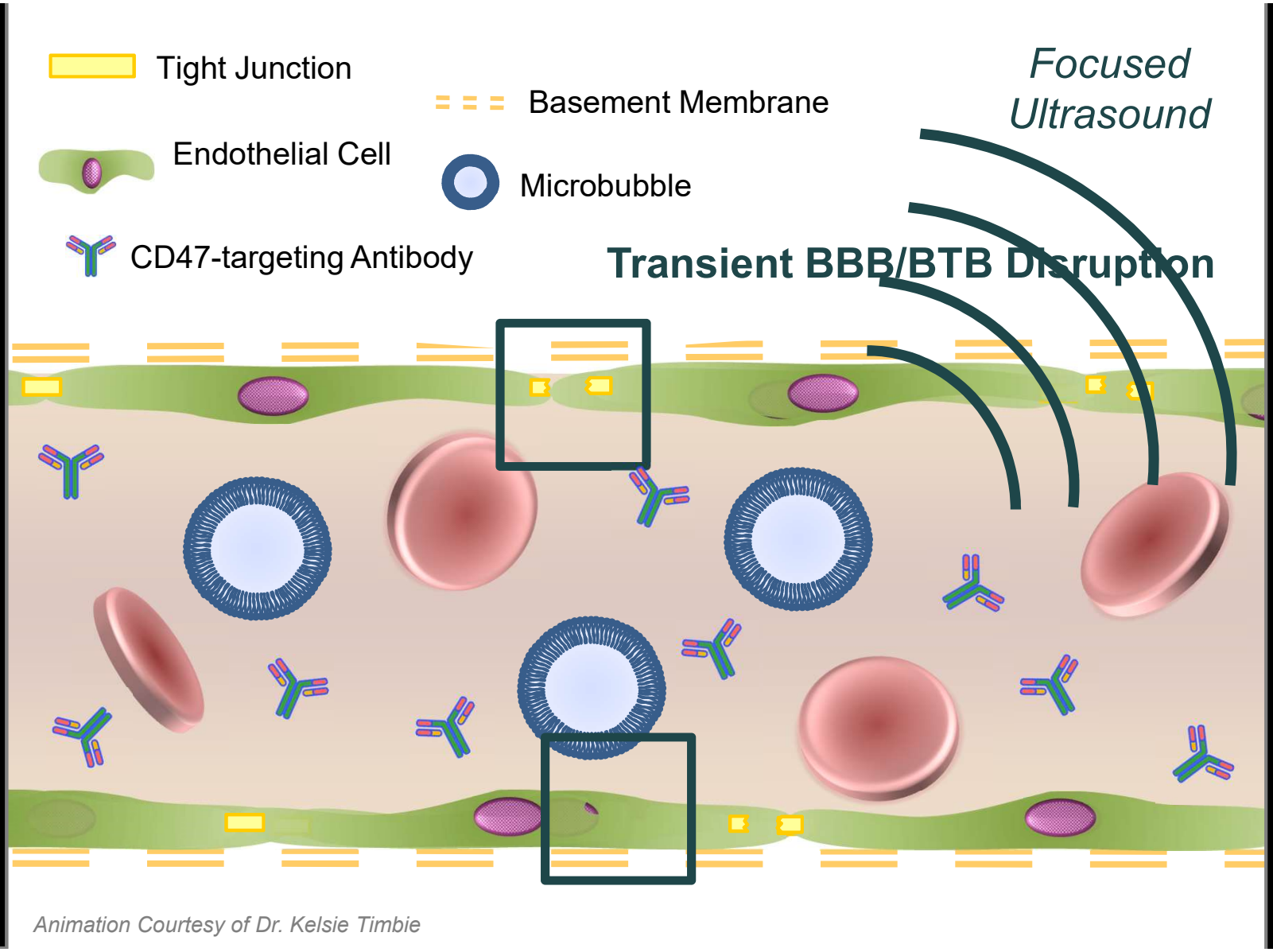
**BTB**

- Heterogeneously "leaky" microvasculature
- Presence of EPR effect
- High interstitial fluid pressure

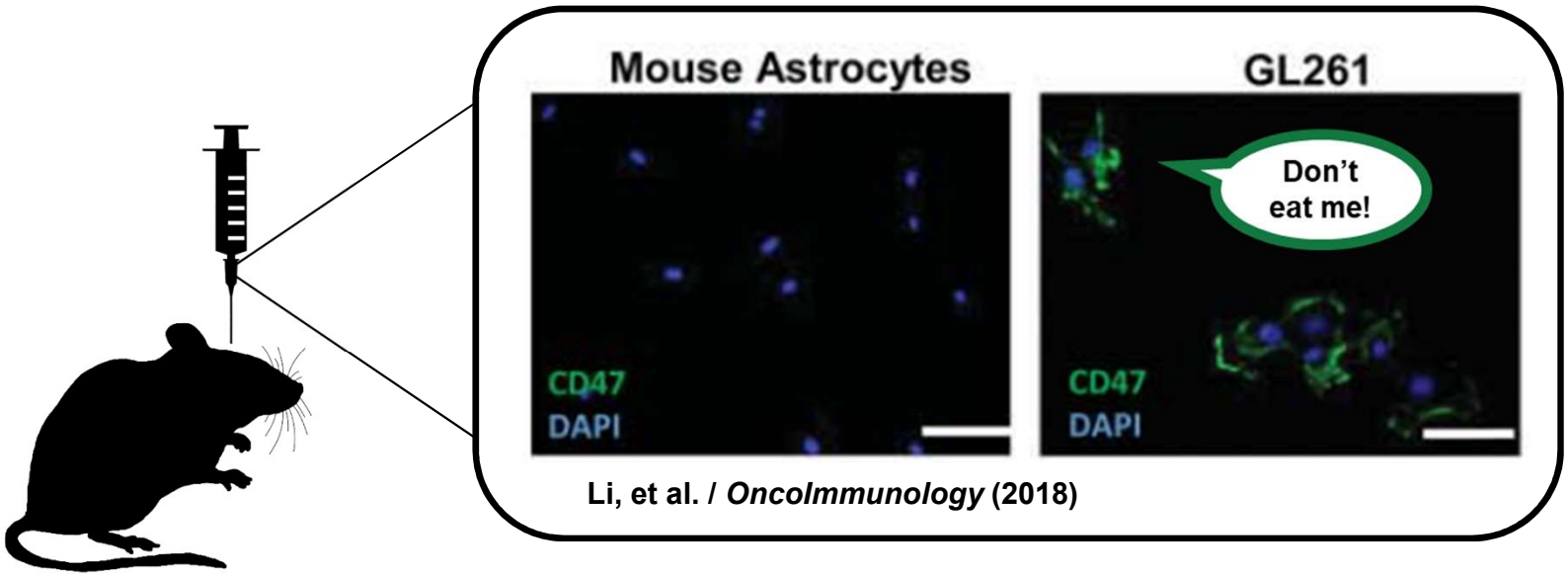


**BBB**

- Intact tight junctions restricting convective and diffusive transport
- Absence of EPR effect



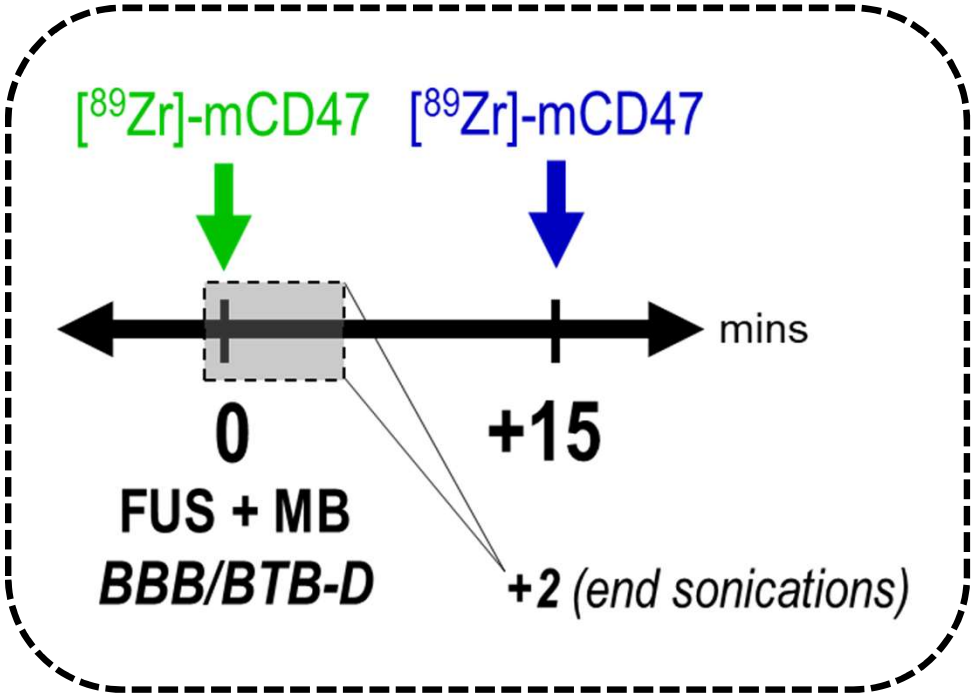

*Animation Courtesy of Dr. Kelsie Timbie*

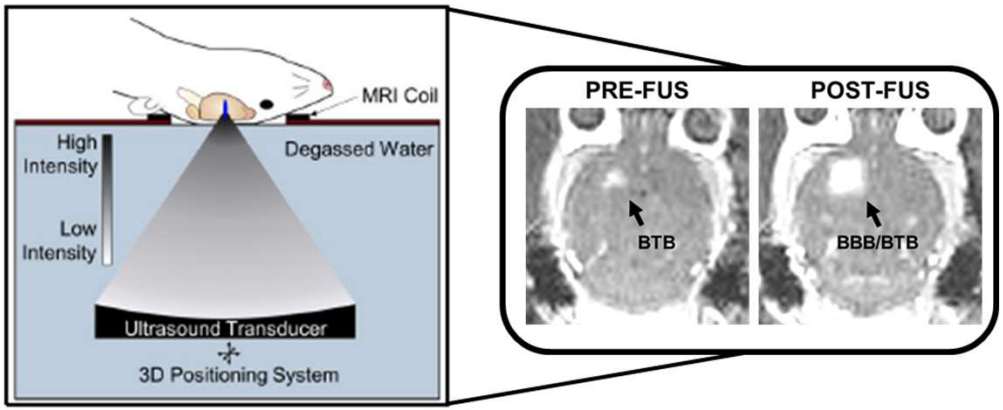



0

*Days Post-Implantation*

# Methods




**FUS:** 1.14 MHz, 2s interval, 10ms for 2 min, $10^5$ MBs/g B.W.

0 // 14

***Days Post-Implantation***

# Methods

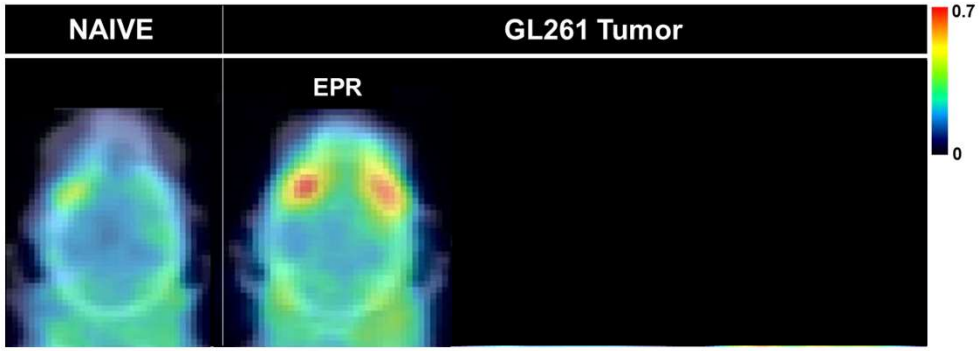
*Immuno-PET Imaging &*
*Ex Vivo Biodistribution Analysis*

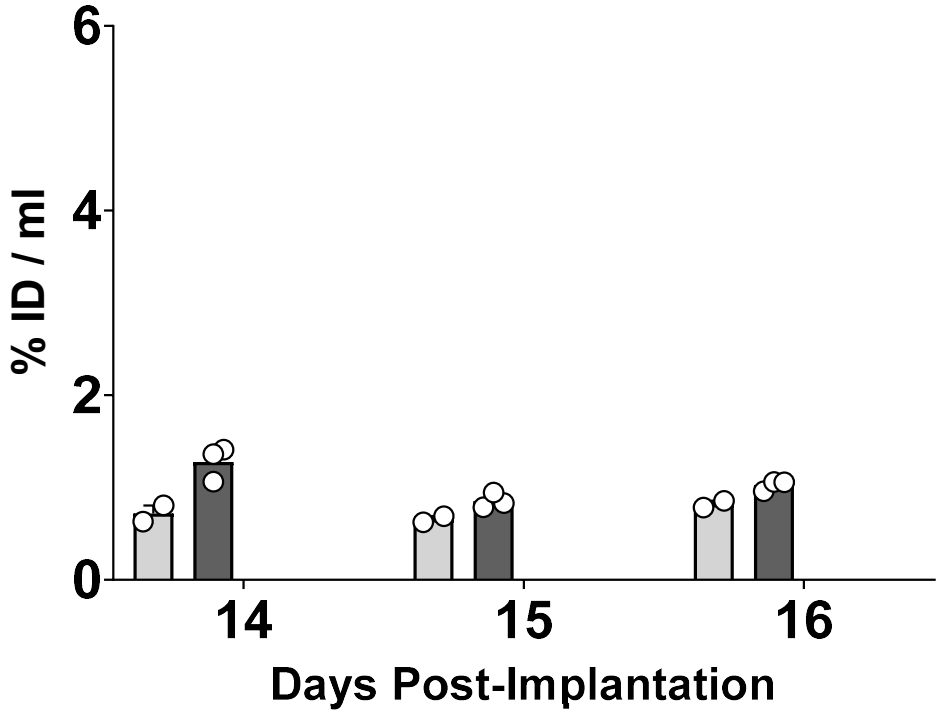
**0** **14** **15** **16** **17**

***Days Post-Implantation***

# Methods

# mCD47 Sequencing Relative to FUS BBB/BTB Disruption Markedly Impacts Penetrance into GL261 Tumors

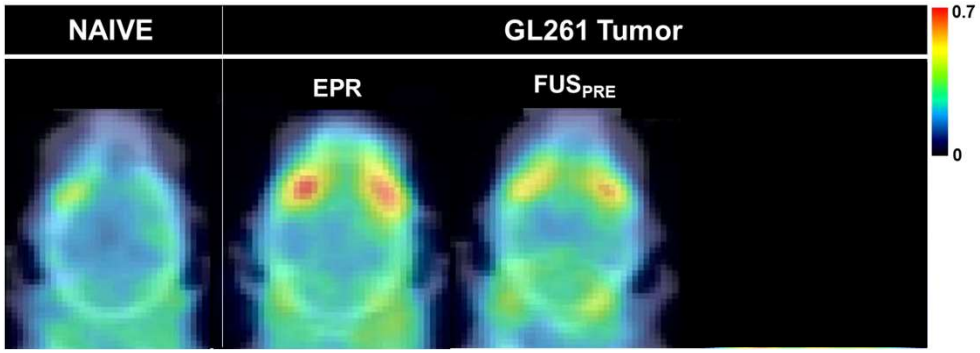



Naive
GL261 (EPR)
GL261 + $FUS_{PRE}$
GL261 + $FUS_{POST}$

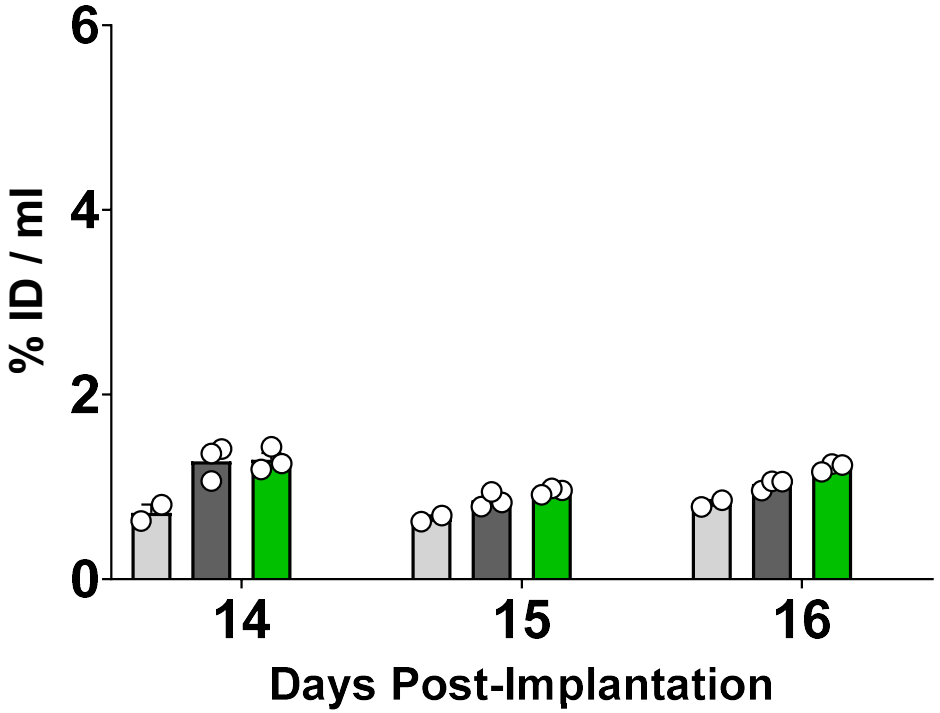
**Sheybani, et al. / *bioRxiv* (2020) DOI: 10.1101/2020.07.27.223206**

# mCD47 Sequencing Relative to FUS BBB/BTB Disruption Markedly Impacts Penetrance into GL261 Tumors







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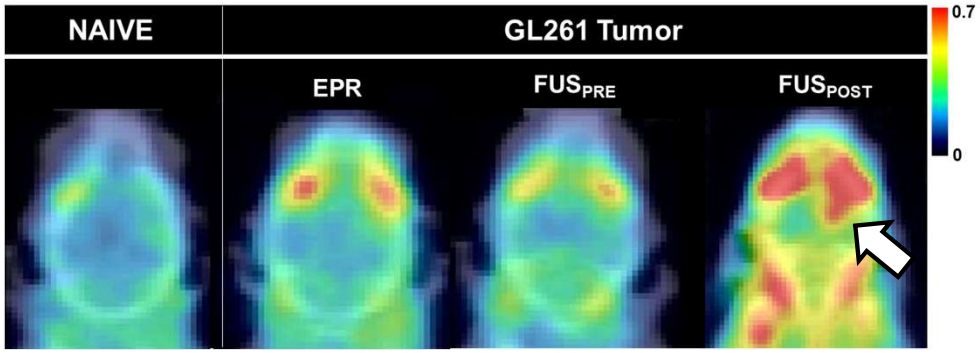
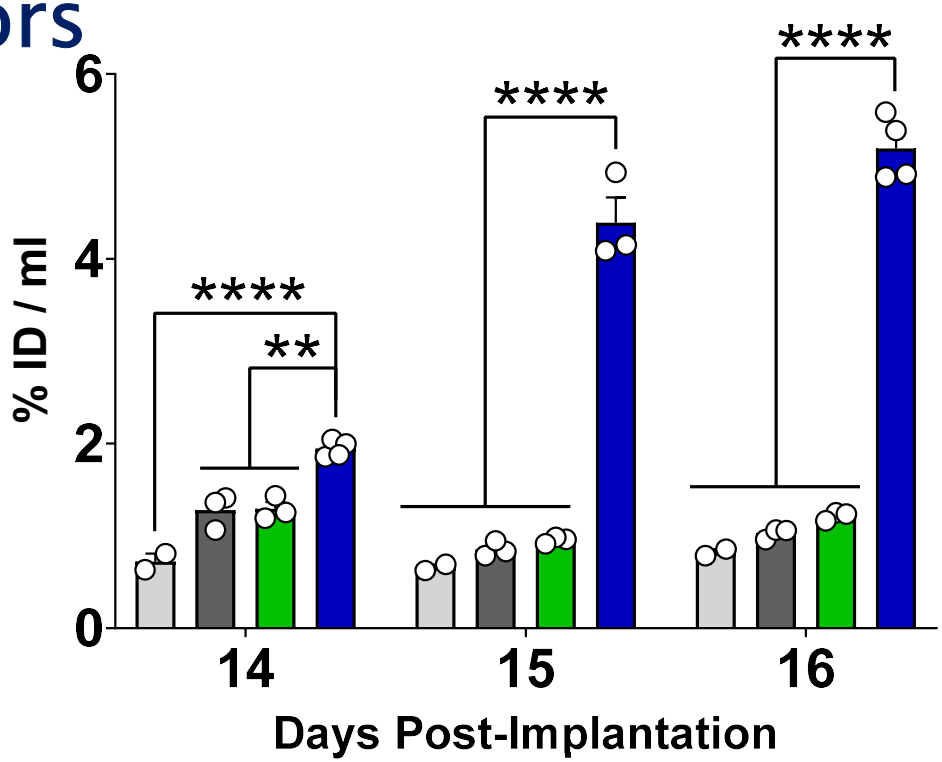
# mCD47 Sequencing Relative to FUS BBB/BTB Disruption Markedly Impacts Penetrance into GL261 Tumors

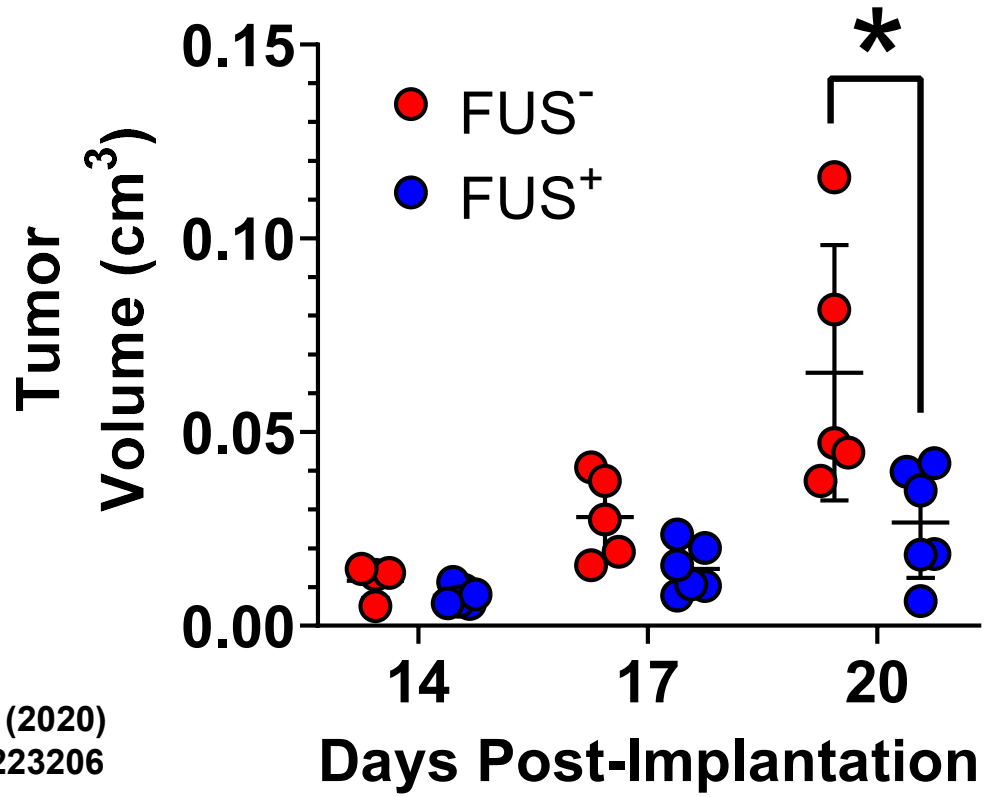



Naive
GL261 (EPR)
GL261 + $FUS_{PRE}$
GL261 + $FUS_{POST}$

**Sheybani, et al. / *bioRxiv* (2020) DOI: 10.1101/2020.07.27.223206**

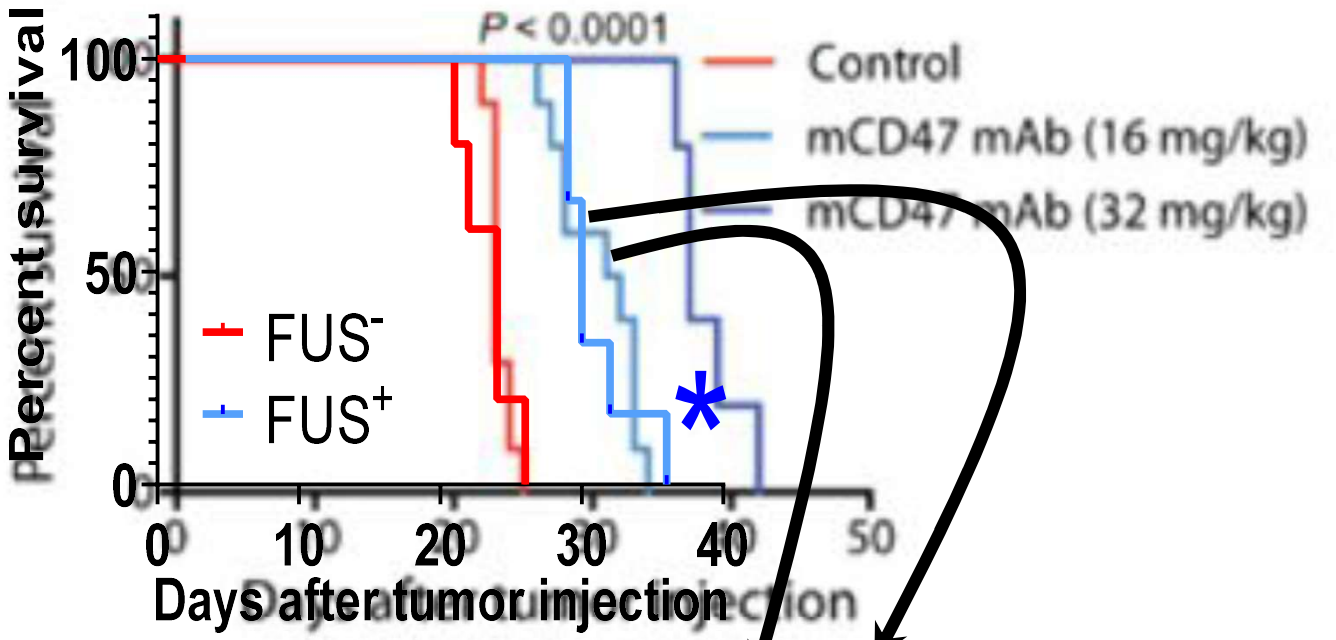
# FUS-mediated mCD47 Delivery Across the BBB/BTB Restricts GL261 Outgrowth




Sheybani, et al. / *bioRxiv* (2020)
DOI: 10.1101/2020.07.27.223206

# FUS-mediated mCD47 Delivery Across the BBB/BTB Enhances Survival of GL261-Bearing Mice

Gholamin et al. / *Sci Trans Med* (2017)




3 injections x 8 mg/kg = 24 mg/kg

~27 injections x 16 mg/kg = 432 mg/kg

(An 18-fold decrease in administered drug!)

Sheybani, et al. / *bioRxiv* (2020)
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# Take Home Messages

mCD47 **sequencing relative to FUS BBB/BTB disruption** is a critical determinant of antibody access in murine gliomas.

FUS-mediated mCD47 delivery across the BBB/BTB can **restrict tumor outgrowth and improve survival outcomes** in glioma-bearing mice.

Nuclear medicine tools hold **promise for design and monitoring** of FUS immunotherapy protocols.

# Acknowledgements

**University of Virginia**

***Faculty/Postdoc***
Tim Bullock
Aly Witter
Wilson Miller
Patrick Dillon
David Brenin
Alexander Klibanov
BJ Purow
Petr Tvrdik
James Mandell
Vic Engelhard
Mark Kester
Jenny Munson (VT)
Kiel Neumann
Stuart Berr
Bijoy Kundu

***Current Grad Students***
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Delaney Fisher
Tor Breza
Aaron Stevens (Bullock lab)
Will Garrison (Miller Lab)

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Kelsie Timbie
Brian Mead
Josh Heuslein

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***Additional Support***
Jeremy Gatesman
Jose Reyes
Soumen Paul
Katelyenn S. McCauley
Michael Welling


## Supported By

NIH National Institute of Neurological Disorders and Stroke
**R01NS111102**
**R21NS118278**

NIH National Institute of Biomedical Imaging and Bioengineering
**R01EB020147**
**R21EB024323**

National Cancer Institute
**R01CA197111**
**R21CA230088**
**F99CA234954**

Focused Ultrasound Foundation

NSF GRFP

UVA School of Medicine
UVA Robert R. Wagner Fellowship


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