# BIOMEDICAL & VETERINARY SCIENCES GRADUATE PROGRAM



# **ANNOUNCES**

The Doctor of Philosopy Seminar and Examination of

Dr. Brittanie Partridge "Overcoming therapeutic resistance in glioblastoma using novel electroporation-based therapies"

> Monday, September 12th, 2022 11:00AM VMIA Classroom 220 Zoom link information: https://virginiatech.zoom.us/j/83455650676



## <u>Bio</u>

A native of Lisbon Falls, Maine, Dr. Partridge completed her undergraduate degree in Biology at Elmira College in upstate New York, where she was first introduced to cancer research. She received her DVM degree from Kansas State University, where her contribution to cancer research continued as part of the Veterinary Research Scholars Program. Fascinated by cancer biology and motivated to make an impact in the field of oncology, Dr. Partridge, went on to complete a small animal rotating internship at a private specialty practice in Spring, TX, followed by a one-year specialty internship in medical oncology at Virginia Tech. She remained at Virginia Tech to complete her medical oncology residency during which time she was given the incredible opportunity to join Dr. Rossmeisl's research team as a PhD student investigating novel ablation therapies as a treatment for malignant brain tumors. Dr. Partridge became board-certified in veterinary medicine oncology in August 2021 and has served as a medical oncology locum at the Animal Cancer Care and Research Center since January 2022. In her spare time, Dr. Partridge enjoys spending time outside with her husband (Kurt), daughter (Lily) and two rescue dogs, Buddy and Kumar. She is also passionate about ice hockey and has been a member of the Roanoke Grizzlies team since 2018!

#### Funded by

#### National Institutes of Health (NIH)/National Cancer Institute (NCI): P30CA012197, P01CA207206, R01CA139099 and R01CA213423 Virginia Tech's Internal Research Competition Grant VMCVM Office of Research and Graduate Studies VoltMed, Inc.

#### Awards and Academic Achievements

#### Outstanding PhD Poster Presentation – 2019

#### Lay Language Abstract

Glioblastoma (GBM) is the most common and deadliest form of primary brain cancer in humans, with only 6.8% of people surviving 5 years after their diagnosis. GBM is characterized by a number of unique features that make it resistant to standard treatments, such as surgery, radiation and chemotherapy. Examples include: (1) extensive invasion of tumor cells into the brain, making complete removal via surgery very difficult; (2) tumor cells are protected by a structure called the blood-brain barrier (BBB), which restricts the entry of most drugs (i.e. chemotherapy) and many immune cells into the brain, thereby preventing them from reaching the tumor; (3) tumor cells produce substances that block the immune system from being able to detect the tumor itself, which allows it to continue to grow undetected.

High-frequency irreversible electroporation (H-FIRE) represents a new approach for the treatment of GBM. H-FIRE uses electric pulses to temporarily or permanently injure cell membranes without the use of heat, which allows for very precise treatment. The following work explores the ways in which H-FIRE can interfere with specific GBM features that drive its resistance to treatment. Here, we demonstrate that H-FIRE is capable of temporarily disrupting the BBB and characterize the mechanisms by which this occurs. This allows for drugs and immune cells within the blood to enter the brain and access the tumor cells, particularly those extending beyond the visible tumor mass and invading the brain. We also illustrate the potential for H-FIRE treatment within the brain to stimulate local and systemic immune responses by causing the release of proteins from injured cells. Similar to a vaccine, we predict these proteins are recognized by the immune system, which becomes primed to help fight off cancer cells within the body. The end result is an anti-tumor immune response. Collectively, this work supports the use of H-FIRE as an alternative treatment approach to standard therapy for GBM given its potential to overcome certain causes of treatment resistance.

## **Publications**

**Partridge BR,** Eardley A, Morales BE, Campelo SN, Lorenzo MF, Mehta JN, Kani Y, Campbell E, Arena CB, Platt S, Mintz A, Shinn RL, Rylander CG, Debinski W, Davalos RV, Rossmeisl JH. Advancements in drug delivery methods for the treatment of brain disease. *Frontiers*. Submitted August 2022.

**Partridge BR**, Kani Y, Lorenzo MF, Campelo SN, Allen IC, Hinckley J, Hsu F-C, Verbridge SS, Robertson JL, Davalos RV, Rossmeisl JH. High-frequency irreversible electroporation (H-FIRE) induced blood-brain barrier disruption is mediated by cytoskeletal remodeling and changes in tight junction protein regulation. *Biomedicines* 2022; 10(6): 1384. PMID: 35740406

**Partridge BR**, Lorenzo MF, Dervisis NG, Davalos RV, Rossmeisl JH. Irreversible electroporation applications. In: *Electroporation in Veterinary Oncology Practice: Electrochemotherapy and Gene Electrotransfer for Immunotherapy*. Impellizeri JA, ed. Springer Nature: Switzerland, 2021: pp. 165-204; ISBN 978-3-030-80668-2

**Partridge BR**, O'Brien TJ, Lorenzo MF, Coutermarsh-Ott SL, Barry SL, Stadler K, Muro N, Meyerhoeffer M, Allen IC, Davalos RV, Dervisis NG. High-frequency irreversible electroporation for treatment of primary liver cancer: A proof of principal study in canine hepatocellular carcinoma. *J Vasc Interv Radiol* 2020; 31(3): 10.015. PMID: 31956003

**Partridge BR**, Rossmeisl JH. Companion animal models of neurological disease. *J Neurosci Methods* 2020; 331:108484. PMID: 31733285

**Partridge BR,** Rossmeisl JH, Kaloss AM, Basso EKG, Theus MH. Novel ablation methods for treatment of gliomas. *J Neurosci Methods* 2020; 336: 108630. PMID: 32068011

## **Presentations**

#### **Oral Abstracts:**

**Partridge BR,** Loveday M, Kani Y, Lorenzo MF, Campelo SN, Allen IC, Garcia J, Hinckley J, Alinezhadbalalami N, Saunier S, Hsu F-C, Verbridge SS, Robertson JL, Davalos RV, Rossmeisl JH. Characterization of local and systemic immune responses induced by intracranial delivery of high-frequency irreversible electroporation (H-FIRE) in rat and canine glioma models. Oral and Poster. *Neuro-Oncology Symposium*, Minneapolis, MN, May 2022.

**Partridge BR,** Kani Y, Thomas SC, Lorenzo MF, Allen IC, Hinkley J, Verbridge S, Robertson JL, Davalos RV, Rossmeisl JH. Temporal characterization of blood brain barrier disruption by high-frequency irreversible electroporation (H-FIRE) treatment. *Biomedical and Veterinary Sciences Annual Research Symposium*, Blacksburg, VA, March 2021.

**Partridge BR,** Thomas SC, Kani Y, Lorenzo MF, Allen IC, Hinkley J, Verbridge S, Robertson JL, Davalos RV, Rossmeisl JH. Temporal characterization of blood brain barrier disruption and immunologic responses to H-FIRE in the brain. *Veterinary Cancer Society Annual Conference,* Houston, TX, October 2019.

#### Poster Abstracts:

**Partridge BR,** Kani Y, Thomas SC, Lorenzo MF, Allen IC, Hinckley J, Verbridge S, Robertson JL, Davalos RV, Rossmeisl JH. Temporal characterization of blood-brain barrier disruption by high-frequency irreversible electroporation (H-FIRE) treatment. *Virginia Tech Cancer Research Alliance Inaugural Retreat,* Roanoke, VA, March 2022.

**Partridge BR**, Kani Y, Thomas SC, Lorenzo MF, Allen IC, Hinkley J, Verbridge S, Robertson JL, Davalos RV,Rossmeisl JH. Temporal characterization of blood brain barrier disruption by high-frequency irreversible electroporation (H-FIRE) treatment. *Veterinary Cancer Society Annual Conference*, Virtual, October 2021.

**Partridge BR**. Thomas SC, Kani Y, Lorenzo MF, Allen IC, Hinkley J, Verbridge S, Robertson JL, Davalos RV, Rossmeisl JH. Temporal characterization of blood brain barrier disruption and immunologic responses to H-FIRE in the brain. *Biomedical and Veterinary Sciences Annual Research Symposium,* Blacksburg, VA, November 2019.

**Partridge BR**, O'Brien TJ, Lorenzo MF, Coutermarsh-Ott SL, Barry SL, Allen IC, Davalos RV, Dervisis NG. High-frequency irreversible electroporation for treatment of primary liver cancer – a pilot study. *Veterinary Cancer Society Annual Conference*, Louisville, KY, October 2018.

## **Examination Graduate Committee**

### Major Advisor/Chair:

John H. Rossmeisl, Jr., DVM, MS, DACVIM (Internal Medicine and Neurology) Associate Department Head of Small Animal Clinical Sciences Dr. and Mrs. Dorsey Taylor Mahin Professor of Neurology and Neurosurgery Department of Small Animal Clinical Sciences

### **Graduate Advising Committee Members:**

Nick Dervisis, DVM, PhD, DACVIM (Oncology) Associate Professor, Medical Oncology Animal Cancer Care and Research Center Department of Small Animal Clinical Sciences

Shawna Klahn, DVM, DACVIM (Oncology) Associate Professor, Medical Oncology integrated Translational Health Research Institute of Virginia (iTHRIVE) Scholar Animal Cancer Care and Research Center Department of Small Animal Clinical Sciences

Rafael Davalos, PhD L. Preston Wade Professor Department of Biomedical Engineering and Mechanics

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