BIOMEDICAL & VETERINARY SCIENCES GRADUATE PROGRAM

ANNOUNCES

The Doctor of Philosophy Seminar and Examination of

Yukitaka Kani

"Maximizing Local Access to Therapeutic Deliveries in Glioblastoma: Evaluating the utility and mechanisms of potential adverse events for minimally invasive diagnostic of two novel therapeutic techniques for brain tumors"

Monday, September 19th, 2022
9:00AM
Graduate Life Center, Meeting Room C
Zoom link information:
https://virginiatech.zoom.us/j/89185227981

Bio

Yukitaka as known as “Yuki”, had an interest in veterinary medicine from an early age. The close relationship he always had with his pets as an important family members motivated him to pursue a veterinary career to take care of their health. Completed his DVM program in the Austral University of Chile in 2013, the graduation research work was performed in collaboration with Virginia Tech thanks to the student exchange program between these universities.

Yuki’s interest in academia starts as a teaching assistant in veterinary anatomy during the DVM program, and continued afterward as an assistant professor in the same area. Master degree was obtained in Austral University of Chile in 2016, performing research of the anatomy of hyoid apparatus of dogs using CT to compare between different cephalic conformations.

Motivated to continue developing in the academic career, applied to the Biomedical and Veterinary Sciences in Virginia-Maryland College of Veterinary Medicine. Yuki joined the Rossmeisl’s lab in fall 2018 as a PhD student to participate in an interesting project about novel brain tumor treatments. The idea is to bring back all the knowledge to Chile to improve significantly the procedure of diagnosis and treatment of neuro-oncology patients.

Funded by

National Institutes of Health (NIH)/National Cancer Institute (NCI): P30CA012197, P01CA207206, R01CA139099 and R01CA213423
VMCVM Office of Research and Graduate Studies

Lay Language Abstract

Glioblastoma (GBM) is the most common adult malignant brain tumor, and the average survival of persons with GBM is about 2 years, even with aggressive treatments. Dogs and humans share common characteristics of the presentation of brain tumors, and the available treatment options are similar to those used in humans, such as surgical, radiotherapeutic, and chemotherapeutic regimens. The efficacy of these therapies in dogs with malignant brain tumors is also poor, with survival times ranging from 3-8 months, which closely mirrors the prognosis associated with human GBM. Thus, treatment of malignant gliomas represents a current and critically unmet need in both human and veterinary medicine.

This work describes how minimally invasive surgical procedures that involve placement of small diameter needles, electrodes, or catheters into the brain tissue for the purposes of obtaining a piece of tumor for diagnosis or delivering energy or drugs to kill tumor cells can be used effectively for the management of patients with brain cancer, and evaluates the types and possible causes of complications associated with of these procedures. We first demonstrate that stereotactic brain biopsy, a procedure that has been previously rarely described in dogs, is a safe and accurate method for the diagnosis of brain tumors in this species. Next, we demonstrate that a specialized type of catheter, termed the convection-enhanced thermotherapy catheter system (CETCS) that is used in our lab for use for direct drug delivery into brain tumors, can be implanted into the brain of rats for long periods of time without causing serious clinical complications or damage to the brain tissue, findings which support its use for repeated treatments of brain cancer. The final chapters investigate how an innovative treatment for brain cancer called high-frequency irreversible electroporation (H-FIRE) that uses electrical energy to kill cells may cause alterations in the brain microenvironment characterized by an excess of the neurotransmitter glutamate that could predispose patients to developing undesirable complications of treatment such as brain tissue death outside of the intended treatment area, damage to the blood-brain barrier, or seizures. While we did demonstrate that H-FIRE treatment does transiently increase the glutamate concentrations in the brain of rats and dogs with brain tumors, we also showed that the brain's natural systems for deactivating and recycling glutamate were activated following treatment, which may mitigate the clinical appearance of any glutamate-associated side effects.

The knowledge that generated in this work has contributed to defining the clinical utility and safety profiles of these novel techniques, which will facilitate their more widespread use to treat dogs with brain cancer and supports the further development and commercialization of CETCS and H-FIRE for future use in humans with GBM.

Publications

Partridge BR, **Kani Y**, Lorenzo MF, Campelo SN, Allen IC, Hinckley J, Hsu FC, 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 Jun 11;10(6):1384. doi: 10.3390/biomedicines10061384. PMID: 35740406; PMCID: PMC9220673.

Kani Y, Hinckley J, Robertson JL, Mehta JM, Rylander CG, Rossmeisl JH. Biocompatibility of the fiberoptic microneedle device chronically implanted in the rat brain. Res Vet Sci. 2021 Dec 31;143:74-80. doi: 10.1016/j.rvsc.2021.12.018. Epub ahead of print. PMID: 34995824.

Shinn RL, **Kani Y**, Hsu FC, Rossmeisl JH. Risk factors for adverse events occurring after recovery from stereotactic brain biopsy in dogs with primary intracranial neoplasia. J Vet Intern Med. 2020 Sep;34(5):2021-2028. doi: 10.1111/jvim.15885. Epub 2020 Sep 14. PMID: 32924201; PMCID: PMC7517515.

Giannasi S, **Kani Y**, Hsu FC, Rossmeisl JH. Comparison of direct measurement of intracranial pressures and presumptive clinical and magnetic resonance imaging indicators of intracranial hypertension in dogs with brain tumors [published online ahead of print, 2020 May 16]. J Vet Intern Med. 2020;10.1111/jvim.15802. doi:10.1111/jvim.15802.

Lorenzo MF, Thomas SC, **Kani Y**, Hinckley J, Lee M, Adler J, Verbridge SS, Hsu FC, Robertson JL, Davalos RV, Rossmeisl JH Jr. Temporal Characterization of Blood-Brain Barrier Disruption with High-Frequency Electroporation. Cancers (Basel). 2019 Nov 23;11(12):1850. doi: 10.3390/cancers11121850. PMID: 31771214; PMCID: PMC6966593.

Kani Y, Cecere TE, Lahmers K, LeRoith T, Zimmerman KL, Isom S, Hsu FC, Debinksi W, Robertson JL, Rossmeisl JH. Diagnostic accuracy of stereotactic brain biopsy for intracranial neoplasia in dogs: Comparison of biopsy, surgical resection, and necropsy specimens. J Vet Intern Med. 2019 May;33(3):1384-1391. doi: 10.1111/jvim.15500. Epub 2019 Apr 16. PMID: 30990928; PMCID: PMC6524398.

Presentations

Poster presentation:
“2022 Neuro-oncology Symposium”. Poster presentation: High-Frequency Irreversible Electroporation treatment of intracranial tumors induces a transient increase in brain glutamate concentration. Minneapolis, Minnesota. (May 2022)

“31th Annual Research Symposium” Virginia-Maryland College of Veterinary Medicine, Virginia Polytechnic Institute and State University. Characterization of the luciferase expressing orthotopic F98 glioma in rats using In vivo Bioluminecence Imaging. Blacksburg, Virginia. (March 2021)

Oral presentation:
“30th Annual Research Symposium” Virginia-Maryland College of Veterinary Medicine, Virginia Polytechnic Institute and State University. Comparison of direct measurement of intracranial pressures and presumptive clinical and magnetic resonance imaging indicators of intracranial hypertension in dogs with brain tumors. Blacksburg, Virginia. (November 2019)

“Southeast Veterinary Neurology Group Meeting”. Comparison of direct measurement of intracranial pressures and presumptive clinical and magnetic resonance imaging indicators of intracranial hypertension in dogs with brain tumors. Organized by Southeast Veterinary Neurology Group. Gainesville, Florida. USA (October 2019)

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:

John Robertson, V.M.D., PhD
Research Professor
Department of Biomedical Engineering and Mechanics

Thomas E. Cecere, DVM, PhD, DACVP–Anatomic Pathology
Associate Professor Anatomic Pathology
Department of Biomedical Sciences and Pathobiology
VA-MD College of Veterinary Medicine

Scott Verbridge, PhD
Associate Professor
Department of Biomedical Engineering and Mechanics

VIRGINIA TECH™