BIOMEDICAL & VETERINARY SCIENCES

GRADUATE PROGRAM

ANNOUNCES

The Doctor of Philosophy Seminar and Examination of

Alexandra M. Kaloss

"Therapeutic Targeting of Arteriogenesis Following Ischemic Stroke"

Friday, August 4th, 2023
12:00PM
Life Sciences 1, Room 101
https://virginiatech.zoom.us/j/87943266966?pwd=dG43amZuQ1NsNmRyVkZMSU9aeDRaZz09
Meeting ID: 879 4326 6966
Passcode: 159710

Bio

Alexandra “Allie” Kaloss is originally from Ijamsville, Maryland and obtained her Bachelor of Science in Animal Sciences from the University of Maryland. She joined the dual DVM/PhD program at the Virginia-Maryland College of Veterinary Medicine in 2019. Under the guidance of Dr. Michelle Theus, her PhD research has focused on vascular remodeling after ischemic stroke. Following the completion of her PhD, Allie will be joining the DVM class of 2027.

Funded by

NIH National Institute of Neurological Disorder and Stroke
Virginia Tech Graduate and Professional Student Senate
VMCVM Office of Research and Graduate Studies

Lay Language Abstract

Worldwide, strokes are a leading cause of death and long-term disability with many cases being ischemic strokes, where a blood clot blocks blood flow to the brain. Without the critical oxygen and nutrients that the blood provides, cells in the affected region of the brain begin to rapidly die, leading to neurological deficits. While current treatments focus on removing the clot, it does not guarantee the restoration of blood flow to the damaged area. In contrast, our research focuses on pre-existing blood vessels in the brain, called pial collaterals, that can ease the loss of blood flow after stroke. These vessels, although relatively inactive under normal conditions, can enlarge after a stroke to reroute blood flow to the injured tissue. Thus, pial collateral growth is a critical process in the initial hours after stroke when this blood flow can prevent brain cells from dying. Previous work has shown EphA4, a receptor known for its role in nervous system development, restricts pial collateral size by inhibiting the Tie2 signaling pathway. Loss of EphA4 in endothelial cells allows for Tie2 receptor activation, increased pial collateral size, and decreased tissue damage. To explore therapeutic enhancement of pial collaterals, we administered Vasculotide, a drug that activates the Tie2 receptor, to wildtype mice expressing EphA4 after a stroke. The mice treated with Vasculotide displayed significantly larger pial collateral vessels one day after the stroke, compared to control mice. Moreover, Vasculotide-treated mice exhibited reduced tissue damage and performed better on behavioral assessments. In addition to pharmaceutical stimulation with Vasculotide, we also investigated the effects of low-intensity focused ultrasound (LIFU) on collateral size. LIFU treatment resulted in decreased tissue damage compared to untreated controls; however, it did not impact collateral size. These findings suggest that inhibiting EphA4 or stimulating Tie2 could serve as novel therapeutic targets to promote the expansion of pial collateral blood vessels, thereby restoring critical blood flow to injured areas of the brain.

Publications

Gudenschwager-Basso, E. K., Shandra, O., Volanth, T., Patel, D. C., Kelly, C., Browning, J. L., Wei, X., Harris, E. A., Mahmutovic, D., **Kaloss, A. M.,** …& Theus, M. H. (2023). Atypical Neurogenesis, Astrogliosis, and Excessive Hilar Interneuron Loss Are Associated with the Development of Post-Traumatic Epilepsy. *Cells*, 12(9), 1248

Kaloss, A. M., Arnold, L. N., Soliman, E., Langman, M., Groot, N., Vlaisavljevich, E., & Theus, M. H. (2022). Noninvasive Low-Intensity Focused Ultrasound Mediates Tissue Protection following Ischemic Stroke. *BME Frontiers.*

Fritsch, L. E., Ju, J., Gudenschwager Basso, E. K., Soliman, E., Paul, S., Chen, J., **Kaloss, A.M.**, ... & Pickrell, A. M. (2022). Type I Interferon Response is Mediated by NLRX1-cGAS-STING Signaling in Brain Injury. *Frontiers in Molecular Neuroscience,* 53.

Publications

Kaloss, A. M., & Theus, M. H. (2022). Leptomeningeal anastomoses: Mechanisms of pial collateral remodeling in ischemic stroke. *WIREs Mechanisms of Disease*, e1553.

Kowalski, E. A., Soliman, E., Kelly, C., Basso, E. K. G., Leonard, J., Pridham, K. J., Ju.J., Cash, A., Hazy, A., de Jager, C., **Kaloss, A.M.**, ... & Theus, M. H. (2022). Monocyte proinflammatory phenotypic control by ephrin type A receptor 4 mediates neural tissue damage. *JCI insight*, 7(15).

Soliman, E., Mills, J., Ju, J., **Kaloss, A. M.**, Basso, E. K. G., Groot, N., ... & Theus, M. H. (2021). Conditional Deletion of EphA4 on Cx3cr1-Expressing Microglia Fails to Influence Histopathological Outcome and Blood Brain Barrier Disruption Following Brain Injury. *Frontiers in Molecular Neuroscience*, 196.

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

Presentations

Kaloss, A.M., Li, J., Browning, J.L., Pan, Y., Watson, S., Olsen, M.L., and Theus, M.H. *Meningeal artery accumulation of vascular amyloid beta correlates with loss of cerebral blood flow in a murine model of Alzheimer's disease.* Poster presented at the Annual Neurotrauma Symposium. (June 2023).

Kaloss, A.M., Groot, N.A., Lyles, K., Zhu, J., Matson, J., and Theus, M.H. *Game of Proteins: How EphA4 and Tie2 Battle to Control Blood Vessel Growth After Stroke.* 15-Minute Oral presentation at the Virginia Tech Graduate and Professional Student Senate Research Symposium. (March 2023)

Kaloss, A.M., Groot, N.A., Lyles, K., Zhu, J., Matson, J., and Theus, M.H. *Time is Brain: Stimulating Tie2 Improves Pial Collateral Growth and Reduces Tissue Damage After Ischemic Stroke.* Flash talk at Biomedical and Veterinary Sciences Annual Research Symposium. (March 2023)

Kaloss, A.M., Groot, N.A., Lyles, K., Zhu, J., Matson, J., and Theus, M.H. *Targeting EphA4/Tie2 Signaling Improves Pial Collateral Response Following Ischemic Stroke.* Poster presented at the Virginia College of Osteopathic Medicine Research Day. (February 2023)

Kaloss, A.M., Groot, N.A., Lyles, K., Zhu, J., Matson, J., and Theus, M.H. *A tale of two proteins: How EphA4/Tie2 crosstalk fluences blood vessel growth following ischemic stroke.* Oral presentation at National Combined DVM/PhD Colloquium. (August 2022)

Presentations continued

Kaloss, A.M., Groot, N.A., Lyles, K., Zhu, J., Matson, J., and Theus, M.H. *Inhibition of Vascular Remodeling by EphA4 in the Acute Phase of Ischemic Stroke.* Poster presented at the Annual Neurotrauma Symposium. (June 2022)

Kaloss, A.M., Groot, N.A., Lyles, K., Zhu, J., Matson, J., and Theus, M.H. *Regulation of Leptomeningeal Anastomoses by EphA4/ Tie2 Signaling Following Ischemic Stroke.* Poster presented at the American Society for Neurochemistry Annual Meeting. (April 2022)

Kaloss, A.M., Groot, N.A., Lyles, K., Zhu, J., Matson, J., and Theus, M.H. *Different "strokes" for different folks: How EphA4 expression alters stroke severity."* 10-Minute Oral presentation at the Virginia Tech Graduate and Professional Student Senate Research Symposium. (March 2022)

Kaloss, A.M., Groot, N.A., Lyles, K., Zhu, J., Matson, J., and Theus, M.H. *Endothelial cell specific EphA4 Inhibits acute pial collateral response following ischemic stroke.* Poster presented at the Virginia College of Osteopathic Medicine Research Day. (February 2022)

Kaloss, A.M., and Theus, M.H. Loss of Endothelial Cell Specific EphA4 *Improves Acute Leptomeningeal Collateral Growth Following Ischemic Stroke.* Oral presentation at the International Stroke Conference. (February 2022)

Presentations continued

Kaloss, A.M., Groot, N.A., and Theus, M.H. *Characterizing the unique pial collateral niche and the role of EphA4 in its response to ischemic stroke.* Oral Presentation at BMVS Research in Progress Seminar Series. (October 2021)

Kaloss, A.M., Groot, N.A., and Theus, M.H. *Mechanisms underlying immune cell recruitment and cellular remodeling of pial collateral arterioles following acute ischemic stroke.* Poster presented at American Society of Neural Therapy and Repair. (August 2021)

Kaloss, A.M., Groot, N.A., and Theus, M.H. *Cell specific EphA4 alters immune cell recruitment and vascular remodeling following acute ischemic stroke.* Poster presented at the National Combined DVM/PhD Colloquium (August 2021)

Kaloss, A.M., Groot, N.A., and Theus, M.H. *Effects of EC-Specific Loss of EphA4 on Leptomeningeal Anastomose Cellular Remodeling Following Acute Ischemic Stroke.* Poster presented at Vasculata. (July 2021)

Kaloss, A.M., Groot, N.A., and Theus, M.H. *EphA4 Inhibition Improves Pial Collateral Response in the First Day Following Ischemic Stroke.* Poster presented at the Central Virginia Chapter of the Society of Neuroscience. (March 2021)

Kaloss, A.M., Groot, N.A., and Theus, M.H. *A "Stroke" of Brilliance: Inhibiting EphA4 Improves Blood Flow After Stroke.* 15-Minute Oral Presentation at the Virginia Tech GSA Research Symposium. (March 2021)

Presentations continued

Kaloss, A.M., Groot, N.A., and Theus, M.H. *EphA4 Alters Immune Cell Recruitment During Leptomeningeal Vessel Remodeling Following Acute Ischemic Stroke.* Flash talk at BMVS Research Symposium. (March 2021)

Kaloss, A.M., and Theus, M.H. *Endothelial cell specific EphA4 limits vascular remodeling following ischemic stroke.* Oral Presentation at BMVS Research in Progress Seminar Series. (October 2020)

Kaloss, A.M. and Theus, M.H., *Endothelial cell specific EphA4 receptor limits pial collateral remodeling following ischemic stroke.* Poster presented at the Vascular Biology 2020 Conference. (October 2020).

Kaloss, A.M., Okyere, B., and Theus, M.H. *EphA4 limits pial collateral remodeling following ischemic stroke.* Poster presented at the National Combined DVM/PhD Colloquium. (August 2020).

Kaloss, A.M., Okyere, B., and Theus, M.H. *Improving Blood Flow Through EphA4 Inhibition as a Novel Stroke Therapy.* Poster presented at Virginia Tech Graduate Student Assembly Research Symposium (March 2020).

Awards and Adademic Achievements

Outstanding Doctoral Student – College of Veterinary Medicine (March 2023)

Virginia Tech GPSS Research Symposium, Oral Presentation: First Place (March 2023)

VCOM Research Day Poster Award: First Place Poster by Graduate Student (February 2023)

Virginia Tech GPSS Graduate Research Development Program Fellowship (September 2022)

Virginia Tech GPSS Travel Fund Program (April 2022)

Virginia Tech GPSS Research Symposium, Oral Presentation: Third Place (March 2022)

VCOM Research Day Poster Award: Second Place Poster by Graduate Student (February 2022)

Virginia Tech GPSS Graduate Research Development Program Fellowship (May 2021)

Virginia Tech GSA Research Symposium, Oral Presentation: First Place (March 2021)

Vascular Biology Conference, Poster Presentation: Outstanding Poster Award (October 2020)

Virginia Tech GSA Research Symposium, Poster Presentation: First Place (March 2020)

Examination Graduate Committee

Major Advisor/Chair:

Michelle Theus, PhD
Professor; Director of Neurotrauma Research Program
Department of Biomedical Sciences and Pathobiology

Graduate Advising Committee Members:

John Chappell, PhD
Associate Professor
Fralin Biomedical Research Institute

Paul Morton, PhD
Assistant Professor
Department of Biomedical Sciences and Pathobiology

William Huckle, MS, PhD
Associate Professor
Department of Biomedical Sciences and Pathobiology

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