

BIOGRAPHICAL SKETCH

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NAME: Nadine Ahmed Kerr, PhD

eRA COMMONS USER NAME (credential, e.g., agency login): NADINEKERR

POSITION TITLE: Research Assistant Professor

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
The George Washington University	BA	08/2001	05/2005	French, International Studies
University of Miami	Post-Bacc	08/2010	12/2011	Pre-med
Rutgers University	PhD candidate	08/2013	08/2014	Neuroscience
University of Miami	PhD	08/2014	12/2018	Neuroscience
University of Miami	Postdoc	01/2019	12/2022	Neurotrauma

A. Personal Statement

I have significant research experience in Central Nervous System (CNS) Injury and neurodegenerative disease. My expertise is in studying the inflammasome-mediated pyroptosis in systemic organ damage after CNS injury and in neurodegenerative disease, particularly in Traumatic Brain Injury (TBI), stroke, and Alzheimer's Disease (AD). This involves the development of a comprehensive understanding of extracellular vesicles and neuroinflammatory pathways in neurotrauma and how this affects multiple organ systems. My ongoing research focuses on the role of the inflammasome in neurological and systemic inflammatory changes in a triple transgenic mouse model of AD using a TBI model as well as stroke model. Using these models of CNS injury, my main goal is to understand disruption of peripheral organ systems, such as the lungs, and how this contributes to the progression Alzheimer's Disease and neuroinflammation.

My academic training and research experience have provided me with an excellent background on translational neuroscience, trauma and multi-organ damage, inflammation, extracellular vesicles and neuroinflammation. As a PhD student I examined a novel neural respiratory inflammasome axis, contributing to pyroptotic cell death, in Traumatic Brain Injury-Induced Acute Lung Injury. As a postdoctoral associate, I was involved in creating a novel photothrombotic stroke (PTS) model in order to create a reproducible closed head cortical infarct that causes systemic inflammation in mice and published an important study on the role of the gut-brain axis in stroke in wild type mice. Recently, as an independent faculty member at the University of Miami's Miami Project to Cure Paralysis, I am studying the role of pyroptotic cell death in the progression of AD and aging in the preclinical models of TBI and stroke. In addition, I have several years of experience in the novel field of extracellular vesicle research, both technically and conceptually, and their role in the pathogenesis of both neurological and systemic organ dysfunction. My goal as an independent faculty member is to continue to grow the area of systemic organ dysfunction and bring my expertise in this field to create important collaborations with other scientists.

Relevant Citations that I'd like to highlight:

- a. **Kerr NA**, de Rivero Vaccari JP, Abbassi S, Kaur H, Zambrano R, Wu S, Dietrich WD, Keane RW. Traumatic Brain Injury-Induced Acute Lung Injury: Evidence for Activation and Inhibition of a Neural-Respiratory-Inflammasome Axis. *J Neurotrauma* 35: 2067-2076. PMID: 29648974.
- b. **Kerr NA**, Bramlett HM, Sanchez-Molano J, Higuera AF, Walters W, de Rivero Vaccari JP, Keane RW, Dietrich WD. Stool-derived extracellular vesicles increase inflammasome signaling and regulate the gut-brain axis after stroke in Alzheimer's disease transgenic mice
- c. Johnson NH, **Kerr NA**, de Rivero Vaccari JP, Bramlett HM, Keane RW, Dietrich WD. Genetic predisposition to Alzheimer's disease alters inflammasome activity after traumatic brain injury. *Transl Res.* 2023 Jul; 257:66-77. doi: 10.1016/j.trsl.2023.02.001PubMed PMID: 36758791; PMCID: PMC10192027.
- d. **Kerr N**, García-Contreras M, Abbassi S, Mejias NH, Desousa BR, Ricordi C, Dietrich WD, Keane RW, de Rivero Vaccari JP (2018) Inflammasome proteins in serum and serum-derived extracellular vesicles as biomarkers of stroke. *Front Mol Neurosci.* 4; 11:309. PMID: 30233311 PMCID: PMC6131639
- e. **Kerr NA**, de Rivero Vaccari JP, Umland O, Bullock MR, Conner GE, Dietrich WD, Keane RW (2019) Human lung cell pyroptosis following traumatic brain injury. *Cells.* 18;8(1). PMID: 30669285 PMCID: PMC6356886

Ongoing and recently completed projects that I would like to highlight include:

U.S. Army Contracting Command Rajguru (PI) Kerr (Co-I)
11/15/2024 – 11/14/2026

Department of Veteran's Affairs
Raval (PI), Role: Co-Investigator
10/01/2021 – 09/30/2025
Therapeutic interventions for post-stroke rehabilitation

Alzheimer's Association
Kerr (PI)
09/01/23 – 09/01/26
Pyroptosis-induced gut-brain axis disruption after stroke in Alzheimer's Disease

State of Florida
Dietrich (PI) Role: Co-Investigator
07/01/2025– 06/30/2026
Discovery Platform for Therapeutic and Diagnostic Innovations in the Care of Patients with Alzheimer's Disease

State of Florida- COPAC FY24
Kerr (PI)
07/01/23- 06/30/24
The role of extracellular vesicle-mediated inflammasome signaling in disruption of the gut-brain axis after traumatic brain injury

State of Florida
Bramlett (PI), Role: Co-Investigator
03/01/2021 – 02/28/2024
Post-stroke combination of therapeutic hypothermia (TH) and whole-body vibration (WBV) improves cognition in nicotine- exposed rats

B. Positions, Scientific Appointments and Honors

2013-2014	Graduate Student, Neuroscience, (Dr. Steve Levison) Rutgers University, Newark, NJ
2014-2018	Graduate Student, Neuroscience, (Dr. W. Dalton Dietrich and Dr. Robert Keane) Univ of Miami School of Medicine, Miami, FL
2019-2022	Postdoctoral Fellow, Dept of Neurological Surgery (Dr. Helen Bramlett), Univ of Miami Miller School of Medicine

2022-Present Research Assistant Professor, Dept of Neurological Surgery, Univ of Miami Miller School of Medicine

Honors

2020 University of Miami Medical Faculty Association Research Award
2019 Society for Neuroscience Trainee Professional Development Award
2019-Present American Heart Association
2019-Present Society for Neuroscience,
2019- Present National Postdoctoral Association
2018- Present Board Member for University of Miami Women in Biomedical Science Association
2017-2019 NIH F31 Fellow
2016-2017 Lois Pope Development Award

C. Contributions to Science

1. The gut-brain axis in the pathogenesis of stroke and brain injury has become an important area of research in order to understand mechanisms of systemic organ damage after injury. Here, we review the inflammasome and pyroptotic cell death in gut brain axis disruption after stroke. We examined the time course of inflammasome protein expression in brain and intestinal lysate using western blot analysis at 1-, 3-, and 7-days post-injury for caspase-1, interleukin-1 β , nod-like receptor protein 3 (NLRP3), and apoptosis speck-like protein containing a caspase-recruiting domain (ASC) and gasdermin-D (GSDMD) cleavage. We also examined intestinal tissue for morphological changes and pyroptosis of macrophages and performed behavioral tests and assessed gut permeability changes to confirm functional changes after stroke. Our study provides novel information regarding possible mechanisms underlying gut complications after stroke and the identification of new therapeutic targets for reducing the widespread consequences of ischemic brain injury.
 - a. Kerr NA, Bramlett HM, Sanchez-Molano J, Higuera AF, Walters W, de Rivero Vaccari JP, Keane RW, Dietrich WD. Stool-derived extracellular vesicles increase inflammasome signaling and regulate the gut-brain axis after stroke in Alzheimer's disease transgenic mice
 - b. Kerr NA, Sanchez J, Watson B, Bramlett HM, Dietrich WD (2022). Inflammasome-regulated pyroptotic cell death in disruption of the gut-brain axis after stroke. *Translational Stroke Res.* 13 (6) 898-912; PMID: 35306629
2. Biomarkers have become an important area of research in stroke and can serve as important guiding tools for more effective personalized therapy (Kim et al., 2013). In this study, we used a Simple Plex Assay (Protein Simple), a novel multi-analyte automated microfluidic immunoassay platform, to analyze serum and serum-derived EV samples from stroke patients and control subjects for inflammasome protein levels of caspase-1, apoptosis-associated speck-like protein containing a caspase-recruitment domain, Interleukins (IL)-1 β , and (IL)-18. Receiver operator characteristic (ROC) curves with associated confidence intervals obtained from the analysis of serum samples revealed that that ASC is a potential biomarker of stroke and highlight the role of the EVs and the inflammasome in the inflammatory response after brain ischemia.
 - a. **Kerr NA**, García-Contreras M, Abbassi S, Mejias NH, Desousa BR, Ricordi C, Dietrich WD, Keane RW, de Rivero Vaccari JP (2018) Inflammasome proteins in serum and serum-derived extracellular vesicles as biomarkers of stroke. *Front Mol Neurosci.* 4; 11:309. PMID: 30233311 PMCID: PMC6131639
3. Gender differences in the pathogenesis of stroke and brain injury has become an important area of research in order to target gender-specific treatments (Reeves et al., 2008). In this study we examined the effect of Whole-Body Vibration on inflammation and cognition in male and female middle-aged rats. We demonstrated that post-tMCAO WBV significantly lessened cognitive deficits in rats of both sexes. Post-tMCAO WBV also decreased circulating pro-inflammatory cytokines and increased serum levels of irisin, a muscle-derived hormone that may play a role in brain metabolism and inflammation regulation, which suggests putative beneficial mechanisms of WBV. We also discuss the dimorphism that exists between males and females in microglial-induced inflammation and energy metabolism after CNS injury. Finally, we describe how all of the current research and literature regarding sex differences in

microglia contribute to the differences in poststroke responses between males and females. I contributed to the literature search/collection and writing and editing of these manuscripts.

- a. **Kerr N**, Sanchez J, Moreno, W, Furones-Alonso O, Dietrich WD, Bramlett HM, Raval AP Post-low frequency Whole-Body Vibration improves cognition in middle aged rats of both sexes. *Front Aging Neurosci* 2022. 14: 942717 PMID: 36062148 PMCID: 9428155.
 - b. **Kerr N**, Dietrich WD, Bramlett HM, Raval AP (2019). Sexually Dimorphic Microglia and Ischemic Stroke. *CNS Neuroscience & Therapeutics*. 25(12): 1308-1317 PMID: 31747126 PMCID: 6887716
4. Approximately 20-25% of TBI subjects develop acute lung injury (ALI) (Aisiku et al., 2016). Previous studies have investigated the role of the innate immune system in TBI-induced pulmonary dysfunction, particularly the HMGB1-RAGE axis (Weber et al., 2014). This study is the first to examine inflammasome activation in this phenomenon. Here we investigated whether EV-mediated inflammasome signaling contributed to the etiology of TBI-induced ALI. Mice were subjected to TBI and the brains and lungs were examined for inflammasome activation and ALI. We show that TBI releases EV containing inflammasome proteins into serum that target the lung to cause ALI, supporting activation of a neural-respiratory-inflammasome axis. This axis constitutes an important arm of the innate inflammatory response in lung pathology after TBI and targeting this axis represents a novel therapeutic treatment for TBI-induced ALI.
- a. **Kerr NA**, de Rivero Vaccari JP, Abbassi S, Kaur H, Zambrano R, Wu S, Dietrich WD, Keane RW. (2018) Traumatic Brain Injury-Induced Acute Lung Injury: Evidence for Activation and Inhibition of a Neural-Respiratory-Inflammasome Axis. *J Neurotrauma* 1;35(17) 2067-2076. PMID: 296489745 PMCID: PMC6098413
 - b. **Kerr N**, de Rivero Vaccari JP, Dietrich WD, Keane RW (2020) Neural-respiratory inflammasome axis in traumatic brain injury. *Exp Neurol*. 323:113080. PMID: 31626746 PMCID: PMC6981270
 - c. **Kerr NA**, de Rivero Vaccari JP, Umland O, Bullock MR, Conner GE, Dietrich WD, Keane RW (2019) Human lung cell pyroptosis following traumatic brain injury. *Cells*. 18;8(1). PMID: 30669285 PMCID: PMC6356886
5. Traumatic Brain Injury (TBI) is a major cause of death and disability in the US and a recognized risk factor for the development of Alzheimer's disease (AD). The relationship between these conditions is not completely understood, but the conditions may share additive or synergistic pathological hallmarks that may serve as novel therapeutic targets. Heightened inflammasome signaling plays a critical role in the pathogenesis of central nervous system injury (CNS) and the release of apoptosis-associated speck-like protein containing a caspase recruitment domain (ASC) speck from neurons and activated microglia contribute significantly to TBI and AD pathology. This study investigated whether inflammasome signaling after TBI was augmented in AD and whether this signaling pathway impacted biochemical and neuropathological outcomes and overall cognitive function.
- a. Johnson NH, **Kerr NA**, de Rivero Vaccari JP, Bramlett HM, Keane RW, Dietrich WD. Genetic predisposition to Alzheimer's disease alters inflammasome activity after traumatic brain injury. *Transl Res*. 2023 Jul; 257:66-77. doi: 10.1016/j.trsl.2023.02.001 PubMed PMID: 36758791; PMCID: PMC10192027.

Complete List of Published Work in MyBibliography:

<https://www.ncbi.nlm.nih.gov/myncbi/nadine.kerr.1/bibliography/public/>