Sarah Kane, PhD

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PROFILE

Highly collaborative, published molecular biologist with diverse research interests, teaching experience, extramural funding record, and robust publication record. My background and training included multidisciplinary approaches to understand cell biological and microbiological processes underpinning disease. The ultimate goal of my research projects aims to elucidate mechanisms and develop preventative measures, diagnostics, or cures for various human ailments. As a PhD rotation student in the Molecular, Cellular, and Integrative Neurosciences program, I rotated in laboratories focusing on Alzheimer's, Parkinson's, and prion diseases. In Dr. James Bamburg's laboratory, I successfully constructed adenoviruses to elucidate the roles of the cellular prion protein and NAPDH oxidase (NOX) in generating actin-cofilin rods, and these findings were published in PLoS ONE. As a PhD candidate and NIH predoctoral fellow in Dr. Mark Zabel's laboratory, I studied the interplay between the Complement system and infectious prions. These projects afforded the opportunity to learn techniques spanning animal husbandry, biochemistry, neuroscience, and immunology. To date, these projects culminated in two first-author publications, although I also pioneered a new immunology and microbiology project that determined the cellular prion protein plays a role in adaptive immune signaling in response to extracellular bacterial infections. Upon receiving my PhD in December 2017, I accepted a postdoctoral position in Dr. Glenn Telling's laboratory to study the daunting and facile chronic wasting disease (CWD) in cervids, as well as other mammalian prion diseases. My postdoctoral projects include understanding the biochemical and cellular processes involved in prion conversion. To date, my postdoctoral achievements include one co-first author publication and two middle author publications, as well as an abstract selected for oral communications at the international Prion conference. All the aforementioned projects provided ample experience to train fellow scientists and harness leadership skills.

Early during the COVID-19 pandemic, I was approached by the CEO of a biotechnology startup company to develop wastewater testing methods and digital PCR assays for SARS-CoV-2 in wastewater. Through these efforts, I gained an appreciation for analyzing difficult matrices and environmental sampling nuances that will be directly transferrable to chronic wasting disease research. Upon realizing the utility of wastewater-based epidemiology for SARS-CoV-2, I led the Research and Development, as well as commercialization efforts to expand targets to include influenza, respiratory syncytial virus, poliovirus, norovirus, adenovirus, antimicrobial resistance genes, *Candida auris*, mpox, and others. Further, I helped foster and head collaborations with multiple bio-technology corporations. Collectively, employment at GT Molecular culminated in multiple opportunities for career advancement and mentorship; a funded NIH grant; a contract with the CDC; and two patent applications. At the University of Wyoming, students in the Kane laboratory will benefit from mentorship that will uniquely poise them for various career paths.

EDUCATION

INSTITUTION AND LOCATION	DEGREE	COMPLETION DATE	GPA
Texas State University – San Marcos	BS	12/2010	3.83
Texas State University – San Marcos	MS	08/2012	3.81
Colorado State University – Fort Collins	PhD	12/2017	4.00

POSITIONS AND EMPLOYMENT

2011 – 2012	Instructional Assistant for courses in Cell Physiology and Cytology & Microtechnique
2011 – 2012	Lab Manager for Dr. Shannon Weigum's Optical Biosensors and Nanomaterials
2012 – 2013	One year Molecular, Cellular, and Integrative Neurosciences (MCIN) program
2013 – 2014	Graduate Student in Dr. Mark Zabel's Prion Immunology laboratory
2014 – 2017	Fellowship Grant Trainee (NIH) under Dr. Mark Zabel
2017 – 2020	Postdoctoral Researcher under Dr. Glenn Telling
2020 – 2021	Research Scientist at GT Molecular
2021 – 2022	Scientist-II and Biosafety Officer at GT Molecular
2022 – 2025	Director of R&D and Biosafety Officer at GT Molecular
2025 – Present	Assistant Professor and Riverbend Chair – University of Wyoming

CONTRIBUTIONS TO SCIENCE

Prion Immunology

While infectious prions do not elicit an adaptive immune response, the Complement system promotes the initial trafficking and replication of prions in the lymphoreticular system. The central findings contributed by my predoctoral work include revealing a direct role of Complement regulatory protein Factor H and Complement Receptor CD21, but not CD35, in the initial spread and replication of prions. Specifically, we observed direct interactions between Factor H or Complement Receptors with prion amyloid, and genetic

deficiency in these Complement proteins delayed accumulation and disease onset. These findings culminated in two first author publications (below). Apart from lead authorship, heading these research projects afforded me opportunities to mentor undergraduate students. These opportunities will certainly benefit my career goals to become an independent investigator. Lastly, a collaborative study revealed soil components dictate prion binding and uptake to immunological cells. Contributions to this work led to second authorship (below). Collectively, these findings benefit the field in understanding the mechanism of prion trafficking and replication and may offer therapeutic targets to combat disease.

Kane SJ, Farley TK, Gordon EO, Estep J, Bender HR, Moreno JA, Bartz J, Telling GC, Pickering MC, Zabel MD. Complement Regulatory Protein Factor H Is a Soluble Prion Receptor That Potentiates Peripheral Prion Pathogenesis. J Immunol. 2017 Dec 1;199(11):3821-3827. doi: 10.4049/jimmunol.1701100. Epub 2017 Oct 25. PubMed PMID: 29070671; PubMed Central PMCID: PMC5698161.

Kane SJ, Swanson E, Gordon EO, Rocha S, Bender HR, Donius LR, Aguzzi A, Hannan JP, Zabel MD. Relative Impact of Complement Receptors CD21/35 (Cr2/1) on Scrapie Pathogenesis in Mice.mSphere. 2017 Nov 22;2(6). pii: e00493-17. doi: 10.1128/mSphereDirect.00493-17. eCollection 2017 Nov-Dec. PubMed PMID: 29202042; PubMed Central PMCID: PMC5700378.

Wyckoff AC, **Kane S**, Lockwood K, Seligman J, Michel B, Hill D, Ortega A, Mangalea MR, Telling GC, Miller MW, Vercauteren K, Zabel MD. Clay Components in Soil Dictate Environmental Stability and Bioavailability of Cervid Prions in Mice. Front Microbiol. 2016 Nov 23;7:1885. eCollection 2016. PubMed PMID: 27933048; PubMed Central PMCID: PMC5120086.

The role of the cellular prion protein in manifestations of Alzheimer's Disease (AD)

Several findings suggest the cellular prion protein may promote the pathogenesis of AD. For example, PrP^C may be a receptor for amyloid beta oligomers. To assess whether PrP^C plays a role in AD-related inflammation, I constructed adenoviruses to express PrP^C in $Prnp^{-/-}$ hippocampal neurons during a rotation in Dr. James Bamburg's laboratory. The central findings of this work showed that PrP^C dictates whether proinflammatory cytokines activate NADPH oxidase and cofilin-actin rod formation. These findings highlight PrP^C may promote AD pathogenesis, and ultimately the findings of this work may provide targets to combat AD.

Walsh KP, Minamide LS, **Kane SJ**, Shaw AE, Brown DR, Pulford B, Zabel MD, Lambeth JD, Kuhn TB, Bamburg JR. Amyloid-β and proinflammatory cytokines utilize a prion protein-dependent pathway to activate NADPH oxidase and induce cofilin-actin rods in hippocampal neurons. PLoS One. 2014 Apr 23;9(4):e95995. doi: 10.1371/journal.pone.0095995. eCollection 2014. PubMed PMID: 24760020; PubMed Central PMCID: PMC3997518.

The role of the cellular prion protein in adaptive immunity

While the role of the cellular prion protein (PrP^C) in establishing prion disease is well defined, the physiological role of PrP^C remains elusive. During my predoctoral work, I pioneered a project that revealed PrP^C plays a role in eliciting adaptive immunity. Specifically, $Prnp^{-/-}$ mice exhibit impaired humoral immunity when challenged with heat-killed Escherichia coli. Further, we showed upon immunological stimuli, wild type PrP undergoes a conformational change reminiscent of infectious prions. These paradigm-changing findings show that PrP^C plays a key role in adaptive immunity and may also shed light on sporadic cases of prion disease. For example, perhaps chronic inflammatory insults lead to PrP aggregation that, without

proper resolution, could lead to accumulation of misfolded PrP that ultimately reaches the brain and causes disease.

Chronic wasting disease strains, assay development, and tissue tropism

Chronic wasting disease of cervids is a highly contagious and invariably fatal prion disease that affects wildlife. The following selected publications highlight the diverse collaborations and techniques obtained through my postdoctoral work. Please note co-first authorship for Kang, Bian, and Kane et al. (2020).

Bian J, Kim S, **Kane SJ**, Crowell J, Sun JL, Christiansen J, Saijo E, Moreno JA, DiLisio J, Burnett E, Pritzkow S, Gorski D, Soto C, Kreeger TJ, Balachandran A, Mitchell G, Miller MW, Nonno R, Vikøren T, Våge J, Madslien K, Tran L, Vuong TT, Benestad SL, Telling GC. Adaptive selection of a prion strain conformer corresponding to established North American CWD during propagation of novel emergent Norwegian strains in mice expressing elk or deer prion protein. PLoS Pathog. 2021 Jul 26;17(7):e1009748. doi: 10.1371/journal.ppat.1009748. PMID: 34310663; PMCID: PMC8341702.

Bian J, Christiansen JR, Moreno JA, **Kane SJ**, Khaychuk V, Gallegos J, Kim S, Telling GC. Primary structural differences at residue 226 of deer and elk PrP dictate selection of distinct CWD prion strains in genetargeted mice. Proc Natl Acad Sci U S A. 2019 Jun 18;116(25):12478-12487. doi: 10.1073/pnas.1903947116. Epub 2019 May 30. PubMed PMID: 31147460; PubMed Central PMCID: PMC6589652.

Kang HE, Bian J, **Kane SJ**, Kim S, Selwyn V, Crowell J, Bartz JC, Telling GC. Incomplete glycosylation during prion infection unmasks a prion protein epitope that facilitates prion detection and strain discrimination. J Biol Chem. 2020 Jul 24;295(30):10420-10433. doi: 10.1074/jbc.RA120.012796. Epub 2020 Jun 8. PMID: 32513872; PMCID: PMC7383396.

Wastewater-based epidemiology

At GT Molecular, I played a pivotal role in the design, development, validation, commercialization, and launch of a nationwide COVID-19 wastewater monitoring service and assay kits. This program serves over 100 communities in 19 different states. This work culminated in co-authorship in a joint publication with Dr. De Long and Dr. Wilusz from Colorado State University. In 2021, I was responsible for designing and validating a COVID-19 variant monitoring program for our wastewater testing service. Our team also validated and commercialized these assay solutions and controls to aid in other wastewater-based epidemiologists variant tracking pursuits. These solutions provide molecular reagents for detection and quantification of SARS-CoV-2 variant-associated mutations corresponding to the α, β, γ, δ, ο, and ο subvariants. These assay kits have been sold for use in both wastewater and clinical specimens, and these kits are show-cased in multiple peer-reviewed publications.

GT Molecular was awarded an SBIR Phase I to expand wastewater testing to influenza and develop next generation sequencing for wastewater-borne pathogens. The proposal was highly successful, and all aims culminated in commercial service offerings. Further, GT Molecular was also awarded a sole-source contract from the CDC to develop a panel of 30 assays for the next phase of wastewater surveillance. Targets span respiratory viruses, gastrointestinal pathogens, antimicrobial resistance genes, and controls. This work was also highly successful and culminated in >30 commercial offerings. These funded mechanisms, in which I served as PD/PI, provided ample opportunities for supervising, mentoring, and managing various research assistants and associates. See below relevant new stories, articles, and bulletins highlighting contributions to the COVID-19 pandemic:

- MIT Technology Review, The fast-spreading coronavirus variant is turning up in US sewers, Antonia Regaldo, Feb 8, 2021, https://www.technologyreview.com/2021/02/08/1017609/the-fastspreading-coronavirus-variant-is-so-prevalent-its-turning-up-in-us-sewers/

- COVID Mutations Emerge in County; Two found in Oxnard Wastewater, Feb 3, 2021, Kimberly Rivers, VC Reporter, https://vcreporter.com/2021/02/covid-mutations-ventura-county-oxnardwastewater/

- COVID-19 provides opportunities, challenges for waster utilities, Oct. 24, 2020, Lucas High, Reporter Herald, https://www.reporterherald.com/2020/10/24/covid-19-provides-opportunitieschallenges-for-water-utilities/

- Wastewater Surveillance: It Takes a Village. **Sarah Kane**, Water Environmental Technology, https://www.waterenvironmenttechnologydigital.com/waterenvironmenttechnology/february_2023/MobilePagedArticle.action?articleId=1855 160#articleId1855160

Alsarraj, M. and **Kane, S**. Proactive Community Detection of the Human Monkeypox Virus with Droplet Digital™ PCR and Wastewater-Based Epidemiology. White Paper available for download here: https://info.bio-rad.com/wastewater-based-epidemiology-ddpcr.html

Ghanbari M, Huang J, Luc A, Arabi M, Goldman JE, Byrne-Nash R, **Kane SJ**, Ferrell RV, Fielder T, De Long SK, C Wilusz. View of an Evolving Pandemic: Changes in the Relationship between Clinical Cases and Levels of SARS-CoV-2 RNA in Colorado Wastewater. ACS ES&T Water. Accepted March 2024.

Patent Applications

Kane, S. et al. GT Molecular, Inc. Multiplexed genotyping assays with a single probe using fluorescent amplitude tuning. U.S. Application Serial No. 17/693,129, filed March 11, 2022
Claiming priority to U.S. Provisional Appln. Nos. 63/160,432, filed March 12, 2021 and 63/172,839, filed April 9, 2021

Kane, S. et al. GT Molecular, Inc. Off-target blocking sequences to improve target discrimination by polymerase chain reaction. U.S. Application Serial No. 18/049,563, filed October 25, 2022

AWARDS AND ACKNOWLEDGEMENTS

Funded Extramural Grants and Contracts

NIH F31 NS087762
Kane (PI)
09/30/2014 – 09/29/2017

NIH R43 AI167462
Kane (PI)
01/02/2022 – 07/31/2022

CDC 75D301-22-Q-75423
Kane (PI)
9/1/2022 – 3/31/2024

CDC 75D30124C19209
Kane (PI)

Academic Honors

2006	Valedictorian of Bremond High School
2006 – 2010	Recipient of Roy and JoAnn Mitte academic scholarship
2006 – 2012	Dean's List every semester during time at Texas State University
2010	Summa Cum Laude (BS)
2012	Summa Cum Laude (MS)
2013	Received highest possible score after MCIN oral examination
2012 – 2017	Maintained 4.0 GPA during all graduate work at Colorado State University

Research Honors

2014-2017	PD/PI of NIH National Institute of Neurological Disorders and Stroke F31NS087762
2015	Top Scholars for University-Wide Graduate Programs award
2019	Microbiology, Immunology, and Pathology Research Teams Award
2022	PD/PI of NIH National Institute of Allergy and Infectious Diseases R43-AI167462
2022	PD/PI of CDC sole source bid (Notice 75D301-22-Q-75423)
2024	PD/PI of CDC Contract (75D30124C19209)