BIOGRAPHICAL SKETCH

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NAME: Kim, Elizabeth Dione

eRA COMMONS USER NAME (credential, e.g., agency login): EKIM12

POSITION TITLE: Research Associate

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)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Michigan School of Engineering, Ann Arbor, MI	BSE	05/2008	Biomedical Engineering
Louisiana State University School of Medicine, New Orleans, LA	PhD	12/2018	Biochemistry and Molecular Biology
Weill Medical College of Cornell University, New York, NY	Postdoctoral Fellow	10/2024	Physiology and Biophysics

A. Personal Statement

I am a Research Associate in the Department of Anesthesiology at Weill Cornell Medical College. I have a broad research background in bioengineering and biochemistry, with training and expertise in bioinformatics coevolution methods, enzymology, ion channel electrophysiology, and structural biology. I am particularly interested in understanding the design of proteins and how modifications to a common protein scaffold can lead to the evolution of subfamilies with distinct functional properties. These findings can uncover key structure-function relationships that tune protein function and, consequently, ion channel type-specific or isoform-specific drug discrimination. My postdoctoral work combines elements from my graduate training (computational bioinformatics) and postdoctoral training (structural biology and electrophysiology) to understand allostery of ion channels and how these allosteric networks can be co-opted by small molecules for the treatment of neurological disorders, such as early-onset epilepsy. These efforts have laid the groundwork for the proposed research.

a. **Kim E***, Wu X*, Lee S, Tibbs G, Cunningham K, Di Zanni E, Perez M, Goldstein P, Accardi A, Larsson H, and Nimigean C (2024) Propofol rescues voltage-dependent gating in HCN channel epilepsy mutants. *Nature,* 632, 451 [PMCID: PMC11634041] *co-first authors
b. Lansky S, Betancourt J, Zhang J, Jiang Y, **Kim E**, Paknejad N, Nimigean C, Yuan P, and Scheuring S (2023) A pentameric TRPV3 channel with a dilated pore. *Nature* 621, 206 (2023) [PMCID: PMC10584365]
c. Ronchi V*, **Kim E***, Summa C, Klein J, and Haas A (2017) In silico modeling of the cryptic E2~ubiquitin binding site of E6-associated protein (E6AP)/UBE3A reveals the mechanism of polyubiquitin chain assembly. *J Biol Chem*, 292,18006 [PMCID: PMC5672028] *co-first authors ***(cover image)***
d. Richard J, **Kim E**, Nguyen H, Kim C, and Kim S (2016) Allostery wiring map for kinesin energy transduction and its evolution. *J Biol Chem,* 291, 20932 [PMCID: PMC27507814]

Recently completed projects:

Source:	National Institutes of Health
Title:	Identification of potential drug binding sites within allosteric networks in cyclic nucleotide modulated channels
Grant number:	F32GM145091
Role:	Principal Investigator (Crina M. Nimigean, sponsor)
Dates:	08/24/2022 – 08/23/2024

Primary goal was to link the action of a small molecule modulator, propofol, with functional allosteric networks to drive ion channel drug discovery

Source:	The Hartwell Foundation
Title:	Allosteric drug response of HCN1 mutations associated with pediatric epilepsy
Grant number:	Postdoctoral Fellowship
Role:	Principal Investigator (Crina M. Nimigean, sponsor)
Dates:	09/06/2022 – 08/31/2024

Aims were to quantitatively assess channel rescue of epilepsy-associated mutations by an allosteric drug, propofol, using electrophysiology assays and cryoEM

B. Positions, Scientific Appointments, and Honors

Positions

2024 – present	*Research Associate*, Weill Cornell Medical College, New York, NY
2019 – 2024	*Postdoctoral Fellow*, Weill Cornell Medical College, New York, NY
2013 – 2018	*Graduate Research Assistant*, Louisiana State Univ. School of Medicine, New Orleans, LA
2012	*Research Assistant*, Tulane University School of Medicine, New Orleans, LA
2009 – 2011	*Research Assistant*, Louisiana State Univ. School of Medicine, New Orleans, LA
2005 – 2007	*Undergraduate Research Assistant*, University of Michigan, Ann Arbor, MI

Scientific Appointments

2021 – present	*Scientific Reviewer or Co-reviewer* for the Journal of General Physiology, Epilepsia, Cell, Scientific Reports, and Plos Computational Biology
2020 – present	*Member*, Society of General Physiologists
2019 – present	*Member*, The New York Academy of Sciences
2017 – present	*Member*, Biophysical Society
2016 – present	*Member*, American Society for Biochemistry and Molecular Biology
2016 – 2019	*Member*, Institute of Electrical and Electronics Engineers
2016 – 2018	*Member*, Association for Women in Science

Honors

2025	*Featured Cover Image* for the Cold Spring Harbor Asia Conference program on Membrane proteins: from physiology to pharmacology
2024	*Joseph F. Artusio Jr. Trainee Award* for Basic Science Research, Weill Cornell Medical College
2022	*Postdoctoral Fellowship*, Hartwell Foundation
2022	*Ruth L. Kirschstein National Research Service Award*, National Institutes of Health
2018	*Travel Award* for the Innovation Louisiana annual conference sponsored by Chosen Diagnostics
2018	*Graduate/Postdoctoral Travel Award* for the American Society for Biochemistry and Molecular Biology annual meeting
2017	*Featured Cover Image* for the Journal of Biological Chemistry (Ronchi V* and **Kim E*** *et al.* In silico modeling of the cryptic E2~ubiquitin binding site of E6-associated protein (E6AP)/UBE3A reveals the mechanism of polyubiquitin chain assembly, *J. Biol. Chem.*, *co-first authors)
2016	*First Prize Poster* at the 6th International Conference on Structural Biology (Richard J, **Kim E**, *et al*. Motor domain beta-sheet motifs contribute to diversification of kinesin-microtubule interactions)
2016	*Grand Prize Winner* of Metrics Mania, Annual competition held by the Intellectual Property & Science division of Thompson Reuters to generate a predictive analysis of research performance of nearly 70 North American institutions
2015	*Top 10 Finalist* of Metrics Mania, Annual competition held by the Intellectual Property & Science division of Thompson Reuters to generate a predictive analysis of research performance of nearly 70 North American institutions

2012 *Travel Award* for the Frontiers in Phylogenetics Spring Symposium and Workshop, sponsored by the National Science Foundation

C. Contributions to Science

1. **Defining allosteric mechanisms of cyclic nucleotide modulated ion channels.** Cyclic nucleotide binding domain (CNBD) ion channels employ allostery to respond to ligand binding or changes in voltage across cellular membranes. Many small molecule modulators used to treat disorders associated with ion channel defects are unspecific and possess affinity for multiple receptors, channels, and transporters. Consequently, these treatments have varying degree of side effects. To remove low specificity and off-target effects, there has been growing interest in the development of allosteric drugs. We use an informatics-based genomics method to identify two main classes of allosteric modulation in CNBD channel protomers. The bioinformatics results support the substantial role of protomer-protomer interactions and that these networks can potentially be co-opted by drug design. My specific contributions include expression and purification of proteins, the bioinformatics implementation and analysis, resolving structures by cryoEM, and performing the electrophysiological recordings of ion channels.
    a. **Kim E***, Wu X*, Lee S, Tibbs G, Cunningham K, Di Zanni E, Perez M, Goldstein P, Accardi A, Larsson H, and Nimigean C (2024) Propofol rescues voltage-dependent gating in HCN channel epilepsy mutants. *Nature,* 632, 451 [PMCID: PMC11634041] *co-first authors
    b. Agarwal S, **Kim E**, Lee S, Simon A, Accardi A, and Nimigean C (2025) Ball-and-chain inactivation of a human large conductance calcium-activated potassium channel. *Nat Commun,* 19, 1769 [PMCID: PMC11840039]
    c. Lansky S, Betancourt J, Zhang J, Jiang Y, **Kim E**, Paknejad N, Nimigean C, Yuan P, and Scheuring S (2023) A pentameric TRPV3 channel with a dilated pore. *Nature* 621, 206 (2023) [PMCID: PMC10584365]
    d. **Kim E**, Kim C, Chaney J, and Kim S (2021) Allostery in proteins: canonical models and new insights. *Encyclopedia of Biological Chemistry*, 3rd Edition, Vol. 3, pp. 27-43 Oxford: Elsevier [DOI:10.1016/B978-0-12-819460-7.00259-0]

2. **Uncovering the mechanism of ubiquitin chain assembly by HECT ligases.** Homologous to the E6AP Carboxyl Terminus (HECT) ligases interact with multiple proteins within a cascade of reactions to post-translationally modify its substrate proteins with ubiquitin. Because of the remarkably pleiotropic consequences of ubiquitin signaling, defects in the HECT ligases are associated with a spectrum of diseases, including neurological disorders and cancers. However, many aspects of how these ligases assemble chains of ubiquitin molecules that act in signaling are unknown and, therefore, attempts at therapeutic targeting of these proteins have been unsuccessful. Unprecedented for the ubiquitin ligases, we use Statistical Coupling Analysis (SCA) to pinpoint specific amino acid residues that integrate genomic, structural, and functional significance within the catalytic domain through identification of co-evolving positions within a multiple sequence alignment. The SCA results provide an evolutionarily based blueprint in understanding how HECT ligases function and provides support for a novel mechanism for polyubiquitin chain assembly. My specific contributions included expression and purification of proteins, performing kinetic assays, and bioinformatics implementation and analyses.
    a. Ronchi V*, **Kim E***, Summa C, Klein J, and Haas A (2017) In silico modeling of the cryptic E2~ubiquitin binding site of E6-associated protein (E6AP)/UBE3A reveals the mechanism of polyubiquitin chain assembly. *J Biol Chem*, 292,18006 [PMCID: PMC5672028] *co-first authors *(**cover image**)*
    b. **Kim E**, Klein J, Ronchi V, Summa C, and Haas A (2017) Evolutionary sequence data mining of ubiquitin homologous to the E6AP carboxyl terminus (HECT) ligases. *5th Annual Louisiana Conference on Computational Biology and Bioinformatics*, New Orleans, LA
    c. Richard J, **Kim E**, Nguyen H, Kim C, and Kim S (2016) Allostery wiring map for kinesin energy transduction and its evolution. *J Biol Chem*, 291, 20932 [PMCID: PMC27507814]
    d. Ronchi VP, **Kim E**, Todaro D, Klein JM, Summa CM, and Haas AL (2016) Evolution of the HECT and HECT-like ubiquitin ligases. *Evolutionary Biology Meeting*, Marseilles, France

3. **Defining structural biomarkers for human Kinesin-5 protein that inform on drug potency.** Human Kinesin-5 is essential for mitosis and is consequently a target for >80 different classes of allosteric compounds that bind to a surface-exposed site formed by the L5 loop. However, not established are the underlying differences in efficacies of the drugs in inhibiting the motor protein. We found that structural

plasticity of the central β-sheet is key to allosteric drug response upon comparing ligand-bound states of two L5-directed inhibitors against 15 empirical Kinesin-5 mutants. Implemented to uncover broad principles at the atomic level, our multivariate analysis of vibrational spectra showed two degenerate categories of structural changes, L5-localized 3_{10}-helix and disordered content. Coupled to these changes are two types of rearrangements in β-sheet hydrogen bonding. My specific contributions included expression and purification of proteins, performing kinetic assays, collecting FTIR spectroscopic data, and performing multivariate analysis.

a. Kim C, **Kim E**, Liu L, Buckley R, Parameswaran S, Kim S, and Wojcik E (2019) Small molecule allosteric uncoupling of microtubule depolymerase activity from motility in human Kinesin-5 during mitotic spindle assembly. *Sci Rep*, 9, 19900 [PMCID: PMC6934681]
b. Richard J, **Kim E**, Nyugen H, Kim C, and Kim S (2016) Allostery wiring map for kinesin energy transduction and its evolution. *J Biol Chem*, 291, 20932 [PMCID: PMC5076506]
c. Richard J, **Kim E**, Dauphin V, Luo M, Buckley R, Parke C, Worthylake D, Wojcik E, and Kim S (2016) Motor domain beta-sheet motifs contribute to diversification of kinesin-microtubule interactions. *6th International Conference on Structural Biology*, New Orleans, LA *(**first prize poster**)*
d. **Kim E**, Buckley R, Learman S, Richard J, Parke C, Worthylake D, Wojcik E, Walker R, and Kim S (2010) Allosteric drug discrimination is coupled to mechanochemical changes in the kinesin-5 motor core. *J Biol Chem*, 285, 18650 [PMCID: PMC2881790]

4. **Development of closed-loop neural interface technology.** Neuroscience studies with electrode interfaces have typically demonstrated conditioning of neural units through a (food) reward system. I contributed towards work that culminated in the demonstration of a direct visual and motor neural interface in rat. This was a proof-of-concept study towards a closed loop system where a motor and sensory interface was combined in a single preparation. We successfully trained a rat to modulate motor cortex signals in response to intracortical microstimulation of the visual cortex. I carried out preliminary hardware fabrication, event programming to measure input and output signals, and data analysis. I also assisted in surgeries and post-experiment histology.

a. Marzullo T, **Kim E**, Lehmkuhle M, and Kipke D (2007) A direct visual and motor neural interface demonstration in a rat. *Proceedings from the 3rd International IEEE Engineering in Medicine and Biology Conference on Neural Engineering*. 9-12. [DOI:10.1109/CNE.2007.369598]
b. Yazdan-Shahmorad A, Gage G, Marzullo T, **Kim E**, and Kipke D (2007) Linear electrode depth estimation in a rat motor cortex by laminar analysis of ketamine-xylazine induced oscillations. *Proceedings from the 3rd International IEEE Engineering in Medicine and Biology Conference on Neural Engineering*. 642-645. [DOI: 10.1109/CNE.2007.369755]
c. Marzullo T, Parikh H, **Kim E**, and Kipke D (2006) Analysis of field potentials during neuroprosthetic tasks using spikes as the control signal. *National Society for Neuroscience Meeting,* Atlanta, GA.
d. Marzullo T, Hanus M, **Kim E**, Stoetzner C, Miller C, Trejo L, and Kipke D (2005) Spikes, local field potentials, and electrocorticogram characterization during motor learning in rats for brain machine interface tasks. *National Society for Neuroscience Meeting*, Washington, DC.

Complete List of Published Work and Scientific Abstracts in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1XuUak7YumwQb/bibliography/47420863/public/?sort=date&direction=descending