BIOGRAPHICAL SKETCH

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NAME: Kindig, Kayla Jeanne

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POSITION TITLE: Ph.D Candidate

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
Case Western Reserve University, Cleveland OH	BA	05/2016	Biology
Case Western Reserve University, Cleveland OH	MS	05/2019	Biology
Case Western Reserve University, Cleveland OH	PhD	05/2024 (Expected)	Physiology and Biophysics

A. Personal Statement

While I have always had an interest in science, my interest in research began in earnest when I was an undergraduate student. As a senior, I had to pick a topic for a final, in-depth research project. Since I was a child, I had suffered from chronic pain in the form of daily headaches, which range in severity from mild to debilitating and do not respond well to any medication. This is the topic that I chose for my capstone research review, and I would consider that my first foray into the world of neuroscience. I applied for a Master's program with the express intent of doing neurobiological research, as well as taking and teaching classes on neuroscience. I used electrophysiology to probe the function of cells responsible for converting auditory or vestibular stimuli into neural impulses, and this established my deep interest in electrophysiology and ion channels, along with the neurobiology lab I was teaching in which we run simulated electrophysiological experiments to illustrate concepts such as synaptic plasticity and cable theory. I became interested in structural biology when trying to find information on the structure of proteins we studied functionally in my Master's research and realizing there was surprisingly little information. I chose a PhD lab that was doing both structural and electrophysiological work, so that I could learn something new while also maintaining a connection with one of my passions. I am currently trying to solve the structure of a ligand-gated ion channel that acts under physiological conditions to inhibit nociceptive neurons and reduce the sensation of pain. Through a greater understanding of this protein, we can potentially design better analgesic drugs and help chronic pain sufferers such as myself without using medications that cause severe side effects due to nonspecific interactions with proteins that function elsewhere in the body.

B. Positions, Scientific Appointments, and Honors

2021-Present	PhD Candidate, Department of Physiology and Biophysics, CWRU, Cleveland, OH
2020	Recknagel Academic Honors Award, CWRU, Cleveland, OH
2020	Recknagel Best Presentation Award, CWRU, Cleveland, OH
2017-2018	Teaching Assistant for Neurobiology Laboratory, CWRU, Cleveland, OH
2017-2018	Mentor in Cleveland Neuroscience Innovators Program, Cleveland, OH
2016-2018	Teaching Assistant for Intro Development and Physiology Lab, CWRU, Cleveland, OH

2018 Michelson Morley Competition Judge
2016 Member of Phi Beta Kappa

C. Contributions to Science

1. **MS Research:** During my Master's degree, my research was centered on understanding the function of vestibular and auditory hair cells both under physiological and pathophysiological conditions. One project that I worked on was focused on a particular family of mechanically-gated ion channels called TMCs (transmembrane channel-like proteins), which had previously been implicated in cases of hereditary deafness. Our lab generated mutations in the genes encoding different TMC proteins, and I did *in vivo* electrophysiological recordings to assess the ability of the mutant hair cells to transmit mechanical signals into electrical impulses. We conducted these studies both in hair cells of the zebrafish lateral line that detect water flow and hair cells of the ear that detect auditory stimuli. We discovered a differential requirement for TMC proteins depending on hair cell type, providing us with information as to what proteins may be best suited to particular types of mechanical stimuli, which allows us to better understand the process of hearing and how it has evolved. A second project I developed and worked on was the investigation of protein composition and electrophysiological function between two different subpopulations of hair cells in the lateral line of zebrafish. A manuscript describing the findings of this research is currently in review, but in brief we found that two distinct types of hair cell that are polarized to optimally detect mechanical stimuli from two different directions actually have different intrinsic sensitivity to stimuli; this starts at the level of the mechanically gated channels, as shown by electrophysiological data and mutation of a candidate channel gene, and is conferred to the afferent neuron, which is shown by calcium imaging. These findings could be potentially translated into the study of human vestibular function in the maculae of the inner ear, where orthologous proteins are utilized to a similar effect.

a) Chou S., Chen Z., Zhu S., Davis R.W., Hu J., Liu L., **Kindig K.**, Brown W., Fernando C.A., Stepanyan R., and McDermott B.M. Jr. (2017) A molecular basis for water motion detection by the mechanosensory lateral line. *Nature Communications* 8(2234).
b) Chen Z.*, Zhu S.*, **Kindig K.***, Wang S., Chou S-W., Davis R.W., Dercoli M.R., Weaver H., Stepanyan R., and McDermott B.M. Jr. (2020) Tmc proteins are essential for zebrafish hearing where Tmc1 is not obligatory. *Human Molecular Genetics*, 29(12): 2004–2021. *Authors contributed equally

2. **PhD Research:** My current research involves determination of the structure and function of glycine receptors, inhibitory ionotropic neurotransmitter receptors whose role is primarily in the spinal cord. I have worked on two different forms of homomeric glycine receptors, one involved in motor control and the other involved in perception of pain. I am using cryo electron microscopy (cryoEM) to determine the structure of these channels, in order to better understand the motions they go through during activation and to potentially help design better therapeutic drugs, with more receptor-specific binding properties and thus fewer off-target effects. I am also using electrophysiological techniques to connect the function of these receptors with the structure and examine the effect of mutations. Currently, we have a manuscript in review in which I performed all of the electrophysiology and generated all of the mutants used for experiments testing positive allosteric modulation. We used insights gained by the cryoEM structure to determine which residues to target for mutagenesis, and the resulting functional data provides us with a better understanding of the role of these residues in modulator binding. This protein is known to be mutated and have reduced functionality or expression in cases of hyperekplexia, a motor disease characterized by an excessive startle response and muscle rigidity. Positive allosteric modulators of this protein can be used to ameliorate the effects of this disease, and structural insight is crucial to design drugs that are highly specific and potent.