BIOGRAPHICAL SKETCH

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NAME: Kim, Hyojin (Kelly)

eRA COMMONS USER NAME (credential, e.g., agency login): hk208kkim

POSITION TITLE: 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)*	Completion Date MM/YYYY	FIELD OF STUDY
Simon Fraser University (BC, Canada)	B.Sc.	05/2006	Molecular Biology & Biochemistry
Simon Fraser University (BC, Canada)	Ph.D.	09/2012	X-ray crystallography
Harvard Medical School (Boston, MA)	Postdoc	08/2015	Cryo-EM
The Rockefeller University (New York, NY)	Postdoc	02/2020	Cryo-EM

A. Personal Statement

A thread connecting my past, current and future work is my interest in structural biology that allows us to visualize a given protein's mechanism of function. By combining structural and biochemical approaches, the goal of my laboratory is to study how an essential class of membrane proteins, known as 'tail-anchored proteins,' are accurately sorted to the endoplasmic reticulum (ER) following their synthesis in the cytoplasm.

My previous trainings have provided me with the technical and intellectual expertise in structural determination and analysis of membrane proteins. In my PhD work with Dr. Mark Paetzel at Simon Fraser University (BC, Canada), I used X-ray crystallography, nuclear magnetic resonance (NMR) and various protein-protein interaction analysis methods to elucidate the organization of the 'ß-barrel assembly machinery' complex, a membrane protein complex that inserts ß-barrel proteins into the outer membrane of Gram-negative bacteria.

While I developed a fascination with membrane proteins and protein complexes in graduate school, I realized that they are often difficult targets for structural studies. With the goal of learning cryo-EM as an alternative approach, I began my postdoctoral work with Dr. Thomas Walz in 2013, at the time at Harvard Medical School (later relocated to The Rockefeller University). As a postdoctoral researcher, I determined negative-stain and cryo-EM structures of various cell-surface receptors and protein complexes. My PhD and postdoctoral research allowed me to hone my skills as a structural biologist and to gain competence in membrane protein expression, purification and reconstitution into lipid systems such as nanodiscs. Moreover, through many collaborative studies, I had the privilege to build valuable relationships with and learn from leading experts in various fields of membrane biology.

I began my career as an independent investigator in 2020 at Michigan State University. My vision is to leverage my background in cryo-EM and membrane protein biology to embark on a new exciting scientific journey to study how newly synthesized tail-anchored proteins are captured, transported, and inserted into the ER membrane. Specifically, my lab is currently focused on structural and functional analysis of various proteins in the TA-targeting pathway known as the GET (Gated-Entry of Tail-Anchored Proteins) pathway. The studies of the GET pathway will set a strong foundation for my future research goal of expanding the research program to investigate how tail-anchored proteins are sorted to organelles other than the ER.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2020 – Present	Assistant Professor, Biochemistry and Molecular Biology, Michigan State University, (East Lansing, MI)
2015 – 2020	Postdoctoral Fellow (continued), Rockefeller University (New York, NY)
2013 – 2015	Postdoctoral Fellow, Department of Cell Biology, Harvard Medical School (Boston, MA)
2006 – 2012	Graduate Student, Department of Molecular Biology and Biochemistry, Simon Fraser University (BC, Canada)

Honors

2017 – 2019	Helmsley Postdoctoral Fellowship
2014 – 2017	Canadian Institute of Health Research (CIHR) Postdoctoral Fellowship
2009 – 2011	Simon Fraser University Graduate Fellowship
2010	1st Place for the film 'Sequence Me', Gene Screen BC Video Competition
2007	Simon Fraser University Graduate Student Teaching Assistant Award

C. Contributions to Science

1. Understanding Structure-Function Relationships of Cell-Surface Receptors

During my postdoctoral training in Dr. Thomas Walz's laboratory, I carried out research projects to study the structure-function relationships of various cell-surface receptors that play pivotal roles in a cell's communication with its surrounding.

I studied the highly flexible human EGF (epidermal growth factor) and insulin receptors, both of which belong to the Receptor Tyrosine Kinase (RTK) family. The goal of my research was to work towards elucidating their transmembrane signaling mechanism by visualizing the full-length proteins in the context of a lipid membrane. I invested substantial efforts in mastering the nanodisc technology to provide a membrane environment for the RTKs, which I custom-designed to include regulatory lipids and to mimic raft conditions. While the very flexible nature of the full-length RTKs has so far prevented me from determining high-resolution structures, even with the latest methodologies provided by cryo-EM (this work is still ongoing), my work already provided insights into the conformational changes underlying transmembrane signaling. Using glycosylated full-length human insulin receptor reconstituted into lipid nanodiscs, I have shown by negative-stain EM that the receptor undergoes a drastic conformational change upon insulin binding. More specifically, we observed that the structural rearrangement of the insulin-binding ectodomain propagates to the transmembrane domains, which are well separated in the inactive conformation but come close together upon insulin binding, facilitating autophosphorylation of the cytoplasmic kinase domains. This collaborative work with the laboratory of Dr. Ünal Coskun (Technische Universität Dresden) provided novel structural insights that answered longstanding questions concerning the mechanism of how insulin activates the receptor, thus providing new perspectives for pharmacological intervention strategies.

**** denotes equal contribution***

a. Gutmann, T.*, **Kim, K.H.***, Grzybek, M., Walz, T., and Coskun, U. (2018). Visualization of ligand-induced transmembrane signaling in the full-length human insulin receptor. *J. Cell Biol.* 217, 1643-1649.

2. Determining the first Structure of an Insect Odorant Receptor

In other postdoctoral work that I performed in collaboration with Dr. Vanessa Ruta's group (The Rockefeller University), I helped to determine the ~3.5 Å cryo-EM structure of the parasitic fig wasp *Apocrypta bakeri* Orco, an insect odorant receptor that forms an odor-gated cation channel. As our structure was the first insect olfactory receptor structure solved, it provided several valuable structural insights into the receptor family that had previously been unknown, such as formation of the tetrameric channel architecture, identification of the ion conduction pathway and a putative odorant-binding pocket. Complemented by mutational and electrophysiological analyses from the Ruta lab, this new structural information also provided insight into how this large family can rapidly diversify, allowing insects to adapt to different chemical landscapes.

**** denotes equal contribution***

a. Butterwick, J.A., del Marmol, J.*, **Kim, K.H.***, Kahlson, M.A., Rogow, J.A., Walz, T., and Ruta, V. (2018). Cryo-EM structure of the insect olfactory receptor Orco. *Nature* 560, 447-452.

3. Understanding the Molecular Mechanism of Cdc48 and its Role in ER-Associated Protein Degradation

ER-associated protein degradation (ERAD) is a process in which misfolded proteins are extracted from the ER membrane and then degraded in the cytoplasm by the proteasome. The multifunctional ATPase Cdc48 and its cofactor Ufd1/Npl4 play a crucial role in ERAD by extracting and unfolding proteins that have been marked with ubiquitination for proteosomal degradation. However, in the absence of high-resolution structural information, the mechanism by which the Cdc48-Ufd1/Npl4 complex recognizes and unfolds its poly-ubiquitinated substrates had remained unclear.

In collaboration with the laboratory of Dr. Tom Rapoport (Harvard Medical School), during my postdoctoral training, I determined the cryo-EM structure of the Cdc48-Ufd1/Npl4 complex at ~4 Å resolution. This structural work revealed that Ufd1/Npl4 binds above the central pore of Cdc48, through which poly-ubiquitinated substrates are translocated. Based on the potential ubiquitin-binding sites identified by the cryo-EM structure, we devised a model for how poly-ubiquitinated substrates bind to and are translocated into Cdc48.

**** denotes equal contribution***

a. Bodnar, N.O.*, **Kim, K.H.***, Ji, Z., Wales, T.E., Svetlov, V., Nudler, E., Engen, J.R., Walz, T., and Rapoport, T.A. (2018). Structure of the Cdc48 ATPase with its ubiquitin-binding cofactor Ufd1-Npl4. *Nat. Struct. Mol. Biol.* 25, 616-622.
b. Twomey EC, Ji Z, Wales TE, Bodnar NO, Ficarro SB, Marto JA, Engen JR, Rapoport TA. (2019). Substrate processing by the Cdc48 ATPase complex is initiated by ubiquitin unfolding. *Science.* 365(6452), eaax1033. DOI: 10.1126/science.aax1033.

(This citation is included to demonstrate that the Rapoport group was able to build on the initial structure to elucidate how the Cdc48-Ufd1/Npl4 complex engages substrate.)

4. Dissecting the Structural Organization of the BAM Complex, a β-Barrel Membrane Protein Insertion Machinery in Gram-Negative Bacteria

As a PhD student, I investigated the structure and function of the β-barrel Assembly Machinery (BAM) complex, which is essential for folding and insertion of β-barrel proteins into the outer membranes of Gram-negative bacteria. Although the BAM complex is considered an attractive target for the development of antimicrobial agents, its most elementary functional and structural characteristics had remained unknown.

The goal of my PhD project was to investigate the functional roles of the individual components (BamA, B, C, D, and E) and how they are arranged in the BAM complex. Over the course of my PhD training, I purified and determined individual and sub-complex structures of four of the five proteins that make up the

Escherichia coli BAM complex (BamB, BamC, BamE and BamCD complex) using X-ray crystallography and NMR. The structures provided important clues about the functional roles of each protein and location of putative substrate-binding sites. In addition to structure determination and analysis, I carried out mutagenesis, pull-down and surface plasmon resonance (SPR) experiments to characterize how different components of the BAM complex interact with each other. Together, the structural and protein-protein interaction data obtained from my thesis project contributed to a better understanding of the spatial organization of proteins in the BAM complex, and provided an important framework for starting to understand the β-barrel protein folding and insertion mechanism of the BAM complex.

a. **Kim, K.H.**, Aulakh, S., and Paetzel, M. (2011). Crystal structure of the β-barrel assembly machinery BamCD complex. *J. Biol. Chem.* 286, 39116-39121.
b. **Kim, K.H.**, and Paetzel, M. (2011). Crystal structure of *Escherichia coli* BamB, a lipoprotein component of the β-barrel assembly machinery complex. *J. Mol. Biol.* 406*,* 667-678.
c. **Kim, K.H.**, Kang, H.S., Okon, M., Escobar-Cabrera, E., McIntosh, L.P., and Paetzel, M. (2011). Structural characterization of *Escherichia coli* BamE, a lipoprotein component of the β-barrel assembly machinery complex. *Biochemistry* 50*,* 1081-1090.
d. **Kim, K.H.**, Aulakh, S., and Paetzel, M. (2014). Outer membrane protein biosynthesis: transport and incorporation of proteins into the OM bilayer. *Bacterial Membranes: Structural and Molecular Biology. UK: Horizon Scientific Press.* 91-132*. (invited book chapter)*

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