BIOGRAPHICAL SKETCH

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NAME: Gouaux, James Eric

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

POSITION TITLE: Senior Scientist

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
Harvard College, Cambridge MA	AB	1984	Chemistry
Harvard University, Cambridge MA	PhD	1989	Physical chemistry
Harvard University, Cambridge MA	Postdoc	1989-90	Crystallography
Massachusetts Institute of Technology, Cambridge MA	Postdoc	1990-92	Membrane proteins

A. Personal Statement

My research focuses on the molecular mechanisms underpinning signal transduction at chemical synapses. To do this, I have primarily employed x-ray crystallographic methods to elucidate atomic resolution structures of crucial neurotransmitter receptors and transporters, yet I have also enthusiastically engaged and learned complimentary biochemical and biophysical methods with the ultimate aim of using all possible approaches to elaborate structure-based mechanisms. Thus, I have extensive experience in the expression, characterization and crystallization of complex neurotransmitter receptors and transporters, as well as in x-ray crystallography and electrophysiology. In addition, I have now established single particle cryo EM in my laboratory as a central method by which to elucidate neurotransmitter receptor structures. As evidence of my progress in this area, I have published multiple papers in which we have used single particle cryo-EM as the primary tool to elucidate molecular structure and, together with biochemical, electrophysiological and computational approaches have gone on to define structure-based mechanisms for important receptors and transporters. I also participate in leadership of the PNCC, an NIH-funded, national cryo-EM center.

Projects to highlight include:

NIH 2 R01 NS038631-25
Gouaux, James Eric (PI)
03/19/1999-02/28/2025
Structure and Function of Neurotransmitter Transporters

NIH 5 R01 MH070039-20
Gouaux, James Eric (PI)
07/01/2004-02/29/2024
Structure and Function of Neurotransmitter Transporters

HHMI (no number)
Gouaux, James Eric (PI)
09/01/2010-08/31/2027
Molecular Studies of Synapses

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2015-Present	Jennifer and Bernard Lacroute Term Chair in Neuroscience Research, Portland OR
2005-Present	Senior scientist, Vollum Institute, Oregon Health and Science Univ., Portland OR
2000- Present	Investigator, Howard Hughes Medical Institute
2001-2005	Professor, Dept. Biochem. Mol. Biophys., Columbia Univ., New York NY
2000-2001	Associate professor, Dept. Biochem. Mol. Biophys., Columbia Univ., New York, NY
1996-2000	Assistant professor, Dept. Biochem. Mol. Biophys., Columbia Univ., New York NY
1993-1996	Assistant professor, Dept. Biochem. Mol. Biol., Univ. Chicago, Chicago IL

Honors

2025	Biophysical Society Lecturer
2020	National Academy of Medicine Member
2016	Anatrace Membrane Protein Award, Biophysical Society
2014	Honorary Doctorate, University of Copenhagen
2014	W. Alden Spencer Award, Columbia University
2014	Alexander M. Cruickshank Lecture, Gordon Research Conferences
2013	Physiological Society Annual Review Prize Lecture
2010	Distinguished Faculty Awards Winner for Outstanding Research
2010	National Academy of Sciences Member
2009	Medical Research Foundation Discovery Award, Oregon Health & Science University
2009	NIHMH MERIT Award
2008	NINDS Javits Investigator Award
2007	American Association for the Advancement of Science Fellow
2003	P&S Dean's Distinguished Award in the Basic Sciences, Columbia University
2000	P&S Doctor Harold & Golden Lamport Award for Excellence in Basic Science Research, Columbia University
1998	Klingenstein Research Fellow
1997	Alfred P. Sloan Research Fellow
1995	National Science Foundation Young Investigator
1994	Searle Scholar

C. Contributions to Science

My major contributions have been to provide a molecular basis for understanding the function of neurotransmitter receptor and transporters, fundamental molecular machines that mediate signal transduction at the chemical synapses of the central nervous system. We have focused on ionotropic glutamate receptors, acid sensing ion channels, ATP-gated P2X receptors and pentameric Cys-loop receptors, as well as on the transporters for glutamate and the biogenic amines. My work has not only provided insights into the three-dimensional structures of these crucial receptors and transporters, but because all of our results are deposited in the publicly accessible protein data bank, the results of my work are available to everyone throughout the world. Thus, our studies will not only inform society on the fundamental building blocks of the brain, but they will also provide a foundation for those who are devoted to developing new therapeutic agents.

1. Our studies on the ionotropic glutamate receptors have provided deep insight into their mechanism of action, showing how antagonists, agonists and allosteric modulators act on these fundamental receptors.

a. Zhao Y, Chen S, Swensen AC, Qian WJ, Gouaux E. Architecture and subunit arrangement of native AMPA receptors illuminated by cryo-EM. Science 364, 355-362 (2019). PMCID: PMC6701862
b. Zhu S. Stein RA, Yoshioka C, Lee CH, Goehring A, Mchaourab HS, Gouaux E. Mechanism of NMDA receptor inhibition and activation. Cell 165: 704-14 (2016). PMCID: PMC4914038
c. Chen S, Zhao Y, Wang Y, Shekhar M, Tajkhorshid E, Gouaux E. Activation and desensitization mechanism of AMPA receptor-TARP complex by cryo-EM. Cell 170:1234-1246 (2017). PMCID: PMC5621841

2. We have also elaborated the molecular structure of the two major classes of neurotransmitter transporters, showing how these remarkably machines carry neurotransmitter from one side of the membrane to the other.

a. Coleman JA, Yang, D, Zhao, Z, Wen, PC, Yoshioka, C, Tajkhorshid, E, Gouaux, E. Serotonin transporter ibogaine complexes illuminate mechanisms of inhibition and transport. Nature 569, 141-145 (2019). PMCID: PMC6750207
b. Coleman JA, Green EM, Gouaux E. X-ray structures and mechanism of the human serotonin transporter. Nature 532: 334-39 (2016). PMCID: PMC4898786
c. Wang KH, Penmatsa A, Gouaux E. Neurotransmitter and psychostimulant recognition by the dopamine transporter. Nature 521:322-27 (2015). PMCID: PMC4469479

3. In addition, we have elaborated the structures of other neurotransmitter receptors and ligand gated ion channels of the brain, from acid sensing ion channels and ATP-gated P2X receptors to pentameric Cys-loop receptors, thus providing the neuroscience field with molecular blueprints upon which to ground studies of mechanism and drug development.

a. Du J, Lü W, Wu S, Cheng Y, Gouaux E. Glycine receptor mechanism illuminated by electron cryo-microscopy. Nature 526:224-29 (2015). PMCID: PMC4659708
b. Baconguis I, Bohlen, CJ, Goehring A, Julius D, Gouaux E. X-ray structure of acid-sensing ion channel 1–snake toxin complex reveals open state of a sodium-selective channel. Cell 156:717-29 (2014). PMCID: PMC4190031
c. Mansoor SE, Lü W, Oosterheert W, Shekhar M, Tajkhorshid E, Gouaux E. X-ray structures define human P2X3 receptor gating cycle and antagonist action. Nature 538: 66-71 (2016). PMCID: PMC5161641.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/james.gouaux.1/bibliography/40629156/public/?sort=date&direction=ascending

BIOGRAPHICAL SKETCH

NAME: Jumi Park

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

POSITION TITLE: Postdoctoral fellowship

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Ulsan National Institute of Science and Technology, Ulsan, Republic of Korea	B.S.	03/2012	02/2016	Biological Science
Ulsan National Institute of Science and Technology, Ulsan, Republic of Korea	Ph.D.	03/2016	02/2021	Biological Science
Oregon Health & Science University	Postdoctoral	04/2021	Present	Neuroscience

A. Personal Statement

My research career began when I joined Dr. Changwook Lee lab at UNIST, Republic of Korea as an undergraduate research student. My project focused on elucidating the crystal structures and functions of protein complexes at the membrane contact sites between organelles, especially, the ER-Mitochondrial encounter structures (ERMES). During this period, I learned basic molecular biological and biochemical techniques such as gene cloning, protein purification, and crystallography and became interested in the structural biology. After the graduation, I joined the same lab as a graduate student and kept working on the same project including another membrane contact site in yeast, Nucleus-Vacuole Junction (NVJ). As working on these projects, I got trained in the determination of 3D structures using X-ray crystallography of macromolecular protein complex structures and biochemical analyses. With these experiences, I also focused on the structural and functional studies of novel DNA/RNA processing enzyme and achieved nucleotide related experiences.

After earning Ph.D., I wanted to step forward as an independent scientist and learn newly developed technologies. Thus, I joined Dr. Eric Gouaux's lab who is a leading pioneer in receptor and transporter biology of the central nervous system and focused on research of AMPA receptor complexes from rodent brain. For last 3 years after joining Dr. Gouaux's lab, I have built on various experiences of molecular biology, membrane protein biology, and cryo-EM. I look forward to how much I am going to develop independent experiences and solve scientific questions with various scientific approaches. In summary, I have the expertise, training, and enthusiasm necessary to successfully carry out the research project.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2014.03 – 2016.02 Undergraduate research students (Dr. Changwook Lee Lab), UNIST, Republic of Korea

Honors

2012.03 – 2016.02 National Scholarship for Science and Engineering, Korea Student Aid Foundation, Republic of Korea

2015.12 Graduation Poster Award, School of Life Sciences, UNIST, Republic of Korea

2017.02 – 2021.02	Biomedical Science Scholarship, ASAN Foundation, Republic of Korea
2017.07	Best Poster Award, Korean Society for Structural Biology, Republic of Korea
2018.05	Best Poster Award, Molecular Mechanisms of Membrane Trafficking Symposium, Center for Single Molecule System Biology, Republic of Korea
2020.09	Takara Award, Korean Society for Biochemistry and Molecular Biology
2021.02	Best Poster Award, Korean Society for Structural Biology

C. Contributions to Science

1. My major publications elucidated the molecular mechanisms of membrane contact sites between organelles. Recent studies revealed that organelles make close contact sites of ~10 nm distance, which are mediated by protein complexes from organelle membranes. These membrane contact sites play important roles in phospholipid biosynthesis and transfer, Ca^{2+} signaling, autophagic processes through direct communication between organelles. We specifically focused on ER-Mitochondrial membrane contact sites (ERMES) and Nucleus-Vacuole Junction (NVJ) in yeast. Both membrane contact sites are involved in phospholipid biosynthesis and transfer and the regulation of autophagic processes. Major protein complexes that mediate ERMES are cytosolic Mdm12, ER membrane protein Mmm1, mitochondrial membrane proteins Mdm34, and Mdm10. Through two publications, we demonstrated the mechanism of membrane contact site formation structure and lipid transport using 3D crystal structures and lipid biochemistry. These are the very first structures of proteins in membrane contact sites and provide the basic understanding for further membrane contact sites and related diseases including neurodegenerative disorders, cardiomyopathies, metabolic syndrome, cancer, obesity and aging. NVJ is the first revealed membrane contact sites and is mainly formed by the interaction between nuclear membrane protein Nvj1 and vacuole membrane protein Vac8. In addition, Vac8 forms a protein complex with autophagic protein Atg13 and mediates cytoplasm-to-vacuole targeting (Cvt) vesicle – vacuole contact sites. These contact sites are important for selective microautophagy in yeast. Two publications revealed how these membrane contact sites are formed by specific protein-protein interactions and mediate various autophagic processes and contributed to understanding the molecular regulation of autophagy. As a main researcher of these projects, I contributed to purification and crystallization of protein/protein complexes, data collection and processing, determination of structures, and performance for biochemical experiments.

    a. Jeong H*, **Park J***, Lee C. Crystal structure of Mdm12 reveals the architecture and dynamic organization of the ERMES complex. *EMBO reports*. 2016;17(12) 1857-1871
    b. Jeong H*, **Park J***, Kim HI*, Lee M, Ko YJ, Lee S, Jun Y, Lee C. Mechanistic insight into the nucleus-vacuole junction based on the Vac8p-Nvj1p crystal structure. *Proceedings of the National Academy of Sciences of the United States of America*. 2017;114(23) E4539-E4548
    c. Jeong H, **Park J**, Jun Y, Lee C. Crystal structures of Mmm1 and Mdm12–Mmm1 reveal mechanistic insight into phospholipid trafficking at ER-mitochondria contact sites. *Proceedings of the National Academy of Sciences of the United States of America*. 2017;114(45) E9502-E9511
    d. **Park J***, Kim H-I*, Jeong H, Lee M, Jang SH, Yoon SY, Kim H, Park Z-Y, Jun Y, Lee C. Quaternary structures of Vac8 differentially regulate the Cvt and PMN pathways. Autophagy. 2020;16(6) 991-1006

2. Another publication I focused on is a novel DNA/RNA processing enzyme. Exonuclease domain containing protein 2 (EXD2) is recently discovered protein but remains unclear for its cellular localization and functions. It was firstly identified as a component of nuclear double-strand break repair by processing DNA 3' overhang. But following papers suggested mitochondrial localization and RNA processing activity. To reveal its ambiguous localization and functions, we solved the localization and structure of EXD2 with electron microscope imaging analysis, proximity labeling, and X-ray crystallography and found its mitochondrial outer membrane localization and novel dimeric formation. In addition, using metal and substrate soaking structures, we discovered how EXD2 can cleave both DNA and RNA unlike other enzymes in the same family. This provides a new approach to DNA/RNA engineering. I contributed to this project as a main researcher and did from X-ray crystallography to DNA/RNA cleavage assays.

a. **Park J***, Lee SY*, Jeong H, Kang MG, Haute LV, Minczuk M, Seo JK, Jun Y, Myung K, Rhee HW, Lee C. The structure of human EXD2 reveals a chimeric 3′ to 5′ exonuclease domain that discriminates substrates via metal coordination. *Nucleic Acids Research*. 2019;47(13) 7076-7093

3. I also participated in the collaboration with other researches including the development of new fluorescence proteins as valuable tools for anticancer drug screening, applications in molecular and synthetic biology, and high-performance super-resolution imaging. These publications provide modified fluorescent protein labeling techniques using NqrC/RnfG – ApbE and UnaG. For the development and activity analysis of new labeling techniques, I contributed to with high-purity protein purification and structural analysis.

   a. Kang MG, **Park J**, Balboni G, Lim MH, Lee C, Rhee HW. Genetically Encodable Bacterial Flavin Transferase for Fluorogenic Protein Modification in Mammalian Cells. *ACS Synthetic Biology*. 2017;6(4) 667-677
   b. Kwon J*, Park JS*, Kang M, Choi S, **Park J**, Kim GT, Lee C, Cha S, Rhee HW, Shim SH. Bright ligand-activatable fluorescent protein for high-quality multicolor live-cell super-resolution microscopy. *Nature Communications*. 2020;11(1) 273

D. Scholastic Performance

YEAR	COURSE TITLE	GRADE
	Graduate School – Combined M.S. – Ph.D. course	
2016-1	Advanced Biochemistry	A0
2016-1	Special Lectures in Biological Sciences (Cellular signaling and differentiation)	A+
2016-2	Advanced Molecular Biology	A0
2016-2	Advanced Structural Biology	A+
2017-1	Signal Transductions in Cells	A+
2017-1	Special Lectures in Biological Sciences	A0
2017-2	Protein Crystallography	A+
2017-2	Mitochondria Biology	A+
2018-1	Special Lectures in Biological Sciences (Diabetes and Metabolic disorders)	A0
2018-2	Special Lectures in Biological Sciences (Ca2+ signaling and Autophagy)	A+