BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Gibbs, Eric

eRA COMMONS USER NAME (credential, e.g., agency login): EGIBBS2

POSITION TITLE: Postdoctoral Scholar

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)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Brigham Young University, Provo UT	B.S.	08/2007	08/2013	Physics
Duke University, Durham NC	PhD.	08/2013	12/2018	Biomedical Engineering
Case Western Reserve University, Cleveland OH	Postdoctoral	01/2019	Present	Biophysics

A. Personal Statement

My career vision is to combine a deep curiosity of fundamental processes with outcomes relevant to human health. This has led me to develop the broad skillset and character necessary to succeed in research. I did my doctoral research under Dr. Chunlei Liu, whose interests include studying molecular structure by MRI and protein engineering. I developed a passion for ion channel research and did my dissertation research on the *in vitro* properties of purportedly radiofrequency-sensitive ion channels. My doctoral research resulted in a broad skillset in MRI, image processing, radiofrequency engineering, molecular biology, cell culture and calcium imaging. Aside from my technical skills, I faced significant challenges when Dr. Liu changed institutions in the middle of my PhD. Through this process I learned to become an independent and intrinsically motivated researcher.

These skills have translated in unexpected ways to my postdoctoral research with Dr. Sudha Chakrapani on the structure and function of ligand gated ion channels. Basic understanding of magnetic resonance has helped me set up pulsed-EPR capabilities in our lab. My knowledge of image processing has helped quickly learn the basics of cryo-EM. My skills in molecular biology and cell culture have helped me optimize difficult protein expression and purification. My expertise in calcium imaging expands the scope of our lab into drug discovery. My motivation and independence have helped me approach new challenges with confidence. The underlying constant has been my passion for medically-relevant ion channel research.

Going forward, I will continue to gain expertise in cryo-EM with training from experienced lab members and the facility manager at our cyro-EM facility. Additional training from Dr. Chakrapani and others in EPR and electrophysiology will allow me to study protein structure and function not visible by cryo-EM. The work done during this proposal will lay the foundation for a successful career as an independent researcher.

1. Basak, S., Kumar, A., Ramsey, S., **Gibbs E.**, Kapoor, A., Filizola M., and Chakrapani, S., High-resolution Structures of multiple 5-HT3AR-setron complexes reveal a novel mechanism of competitive inhibition bioRxiv [Preprint] 2020.03.30 .016154; doi: https://doi.org/10/1101/2020.03.30.015154
2. **Gibbs, E.** and Chakrapani, S. Structure, Function and Physiology of 5-Hydroxytryptamine Receptors Subtype 3 in Subcellular Biochemistry: Macromolecular Protein Complexes III. Editors: Dr. J. Robin Harris and Dr. Jon Marles-Wright
3. Hutson, M. R., Keyte, A. L., Hernández-Morales, M., **Gibbs, E.**, Kupchinsky, Z. A., Argyridis, I., Erwin, K.N., Pegram, K., Kneifel, M. Rosenburg, P.B., Matak, P., Xie, L., Grandl, J., Davis, E.E., Katsanis, N.,

Liu, C., Benner, E.J. (2017). Temperature-activated ion channels in neural crest cells confer maternal fever–associated birth defects. *Science signaling*, *10* (500)

4. **Gibbs, E.**, & Liu, C. (2015). Feasibility of imaging tissue electrical conductivity by switching field gradients with MRI. *Tomography*, *1*(2), 125.

B. Positions and Honors

Positions and Employment

2017 Summer internship program at Genentech, S. San Francisco, CA

Other Experience and Professional Membership

2019-present Member, Biophysical Society

Honors

2013 *magna cum laude,* Department of Physics, Brigham Young University, Provo UT
2013 Chancellor's scholar at Duke University
2013 Appointment to the Structural Biology and Biophysics training program at Duke University
2015 Appointment to the Medical Imaging Training Program at Duke University

C. Contributions to Science

1. **Postdoctoral Research**: 5-Hydroxytryptamine Type III Receptors (5-HT_3R) are pentameric ligand-gated ion channels that play an important role in nausea and vomiting. Setrons are potent 5-HT_3R antagonists that are used as anti-emetics during cancer treatment. In a project led by Sandip Basak, we investigated the mechanisms of setron inhibition by obtaining several cryo-EM structures bound to various setrons. I contributed to this project by creating quantitative visual representations of differences between setron-bound structures. I also contributed by writing a book chapter on 5-HT_3R structure function and physiology. This book chapter has been a useful tool in training graduate students who have recently joined our lab.
   -Basak, S., Kumar, A., Ramsey, S., **Gibbs E.**, Kapoor, A., Filizola M., and Chakrapani, S., High-resolution Structures of multiple 5-HT3AR-setron complexes reveal a novel mechanism of competitive inhibition bioRxiv [Preprint] 2020.03.30 .016154; doi: https://doi.org/10/1101/2020.03.30.015154
   -**Gibbs, E.** and Chakrapani, S. Structure, Function and Physiology of 5-Hydroxytryptamine Receptors Subtype 3 in Subcellular Biochemistry: Macromolecular Protein Complexes III. Editors: Dr. J. Robin Harris and Dr. Jon Marles-Wright
2. **PhD. Dissertation Research**: Ferritin-based magnetogenetic ion channels have been proposed as tools for non-invasive manipulation of ion channel activity. Initial positive reports of their use *in vivo* and *in vitro* has sparked significant controversy in the field because predicted interactions are negligible between ferritin and a static or alternating magnetic field. My dissertation research directly addresses this controversy for reported magnetogenetic channels $TRPV1^{FeRIC}$ and $TRPV4^{FeRIC}$ by re-examining original *in vitro* experiments, addressing possible conflicting factors and conducting more definitive Fura-2 calcium imaging experiments. Careful analysis of thousands of cells demonstrated, contrary to initial reports, that an alternating magnetic field does not differentially affect HEK 293 cells expressing $TRPV1^{FeRIC}$ or $TRPV4^{FeRIC}$. This does not necessarily conflict with *in vivo* results but suggests that additional factors are required for the reported *in vivo* effects. This work was done at Duke University under the guidance of my PhD. advisor, Chunlei Liu and in close collaboration with Dr. Eric Benner and Dr. Mary Hutson also at Duke.
   -Hutson, M. R., Keyte, A. L., Hernández-Morales, M., **Gibbs, E.**, Kupchinsky, Z. A., Argyridis, I., Erwin, K.N., Pegram, K., Kneifel, M. Rosenburg, P.B., Matak, P., Xie, L., Grandl, J., Davis, E.E., Katsanis, N., Liu, C., Benner, E.J. (2017). Temperature-activated ion channels in neural crest cells confer maternal fever–associated birth defects. *Science signaling*, *10*(500)
3. **Additional PhD. Research:** Low-frequency tissue conductivity is a potential biomarker of disease and an important safety consideration in certain medical procedures. However, tissue conductivity is not easily measured in living patients. It was proposed that under certain conditions, there is a portion of the MRI signal that could be used to non-invasively measure low-frequency tissue conductivity. I

explored sequences and post-acquisition processing to maximize this signal. I demonstrated by simulation and MRI experiments that the noise inherent to MRI is much greater than the conductivity dependent signal. This work was done at Duke University under the guidance of my PhD. advisor, Chunlei Liu.

-**Gibbs, E.**, & Liu, C. (2015). Feasibility of imaging tissue electrical conductivity by switching field gradients with MRI. *Tomography*, *1*(2), 125.

4. **Undergraduate Research:** Neutron diffraction data can be used to determine the magnetic properties of novel materials. My research focused on methodology for determining the magnetic properties of complex magnetic materials. Dr. Branton Campbell developed a sparse representation of magnetic crystal properties known as magnetic symmetry mode analysis. To test this method, I prepared a sample of anti-ferromagnetic $LaMnO_3$ and collected neutron diffraction data at Oak Ridge National Laboratory. With this data, I applied magnetic symmetry mode analysis and global search techniques to determine the magnetic structure $LaMnO_3$. This work was done under the guidance of Dr. Branton Campbell at Brigham Young University.

D. Additional Information: Research Support and/or Scholastic Performance

NIH Supported Training Grants

T32 Medical Imaging Training Program, Duke University. Sept. 2015 – Nov. 2017
T32 Structural Biology and Biophysics, Duke University. Sept. 2013 – Sept. 2015

YEAR	COURSE TITLE	GRADE
	DUKE UNIVSERITY	
2013	Structural Biochemistry I	A
2013	Structural Biochemistry II	A
2013	Physical Biochemistry	A
2013	Responsible Conduct in Research	CR
2014	Intro to Physiology	B
2014	Radiation Therapy Physics	A
2014	Nuclear Medicine Physics	A-
2014	Signals and Systems	B
2014	Random Signals and Noise	A-
2014	Scientific Computing	A
2015	Digital Signal Processing	A
2015	Biophysics of Neuroscience Tools	A
2015	MRI: Principles and Sequence Design	A
2015	Radiology in Practice	A-

OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Chakrapani, Sudha

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

POSITION TITLE: 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
University of Madras, Chennai, India	B.S.	06/1995	Chemistry
University of Pune, India	M.S.	06/1997	Biochemistry
Indian Institute of Technology, India	M.Tech.	02/1999	Biomedical Engineering
University at Buffalo, Buffalo, NY	Ph.D.	05/2004	Physiology & Biophysics
University of Virginia, Charlottesville, VA	Postdoctoral	01/2006	Physiology & Biophysics
University of Chicago, Chicago, IL	Postdoctoral	07/2008	Physiology & Biophysics

A. Personal Statement

My long-standing scientific interest has been in developing a molecular-level understanding of ion-transport phenomenon across cellular membranes that occurs under normal and pathophysiological conditions. My research over the last 20 years has focused on ion channels that mediate fast synaptic transmission at the neuronal and neuromuscular junction; namely, ligand- and voltage- gated ion channels. An area of emphasis of my research is in understanding the critical interaction between ion channels and membrane lipids, and in determining how this interaction is altered in the presence of allosteric modulators such as neurosteroids, alcohols, and anesthetics. My scientific approach is a combination of cutting-edge multidisciplinary tools that includes X-ray crystallography and Cryo-EM for high-resolution structure determination, EPR spectroscopy for protein dynamic measurements, and electrophysiology for functional characterization of ion channels.

We solved the first cryo-EM structure of the full-length 5-HT_{3A}R channel in its resting conformation (*Nature Communications, 2018*) and then determined the structures of 5-HT_{3A}R in serotonin-bound states that revealed the conformational changes underlying channel activation (*Nature, 2018*). Together, these structures represent the first set of gating conformational states along the ligand-driven activation pathway described for a full-length pentameric-ligand gated ion channel (pLGIC). We determined a 2.9 Å structure of 5-HT_{3A}R bound to granisetron, a clinically used drug in the treatment of nausea and vomiting in patients undergoing cancer treatments, revealing the mechanism of setron-mediated inhibition in these channels (*Nature Communications, 2019*). We recently developed a comprehensive structural scheme of glycine receptors gating by determining cryo-EM structures of the channel in the apo, open, and desensitized conformations in a lipid bilayer environment (*Nature Communications*, 2020). In summary, with the experience I have gained in diverse structural, dynamics, and functional approaches, and further equipped with the cutting-edge cryo-EM technique, we are now poised to address some of the fundamental questions in the membrane protein field that have remained elusive so far.
Specific to this proposal, Dr. Eric Gibbs has made substantial progress in establishing the heteromeric glycine receptor expression and purification system and has collected high quality preliminary cryo-EM data that sets the stage for the proposed work. I am very much committed to Eric's professional development, and will offer a stimulating research environment for his postdoctoral work and facilitate his transition to becoming in an independent scientist in academics.

1. Kumar A, Basak S, Rao S, Gicheru Y, Mayer ML, Sansom MSP, **Chakrapani S*.** (2020) Mechanisms of activation and desensitization of full length glycine receptors in lipid nanodisc. ***Nature Communications*** Jul 27;11(1):3752. doi: 10.1038/s41467-020-17364-5.PMID: 32719334
2. Basak S[a], Gicheru Y[a], Kapoor A., Mayer ML., Filizola M, and **Chakrapani S***. (2019) Molecular mechanism of setron-mediated inhibition of full-length 5-HT3A receptors. ***Nature Communications*** 10, 3225, doi:10.1038/s41467-019-11142-8. PMCID:PMC6642186
3. Basak S, Gicheru Y, Rao S, Sansom MSP, **Chakrapani S***. (2018) Cryo-EM reveals two distinct serotonin-bound conformations of full-length 5-HT3A receptor. ***Nature***.;563(7730):270-4. doi: 10.1038/s41586-018-0660-7. PubMed PMID: 30401837; PMCID:PMC6237196 (*Article Recommended by Faculty 1000)*
4. Basak, S., Gicheru, Y., Samanta, A., Molugu, S. k., Huang, W.,, de la Fuente, M., Hughes, T., Taylor, D.J., Nieman, M. T., Moiseenkova-Bell, V., and **Chakrapani, S*** (2018) Cryo-EM structure of 5-HT_{3A} receptor in its resting conformation. ***Nature Communications*** 9(1):514. doi: 10.1038/s41467-018-02997-4. PubMed PMID: 29410406; PMCID:PMC5802770
5. Basak, S. [a], Schmandt, N. [a], Gicheru, Y [a]., and **Chakrapani, S*.** (2017) Crystal structure and dynamics of a lipid-induced potential desensitized state of a pentameric ligand-gated channel ***eLIFE,*** doi: 10.7554/eLife.23886. PMCID:PMC5378477

B. Positions and Honors.

Positions and Employment

2008-2010	Research Assistant Professor, Department of Biochemistry and Molecular Biology, University of Chicago, Chicago, IL
2010-2017	Assistant Professor (Tenure-track), Department of Physiology and Biophysics, Case Western Reserve University, Cleveland, OH
2017-2020	Associate Professor (Tenured), Department of Physiology and Biophysics, Case Western Reserve University, Cleveland, OH
2018-present	Director, Cryo-Electron Microscopy Core, Case Western Reserve University, Cleveland, OH
2020-present	Professor, Department of Physiology and Biophysics, Case Western Reserve University, Cleveland, OH
2020-present	Director, Cleveland Center for Membrane and Structural Biology

Other Experience and Professional Memberships

2003-present	Member, Biophysical Society
2010-present	Member, American Heart Association
2005	Early Career Committee, Biophysical Society
2012-2013	Panelist, Early Career Development Committee, Biophysical Society
2014	Reviewer, NIGMS Program Projects Grants (P01) special emphasis panel
2015-present	Member, Society for General Physiology
2015-2017	Reviewer, American Heart Association (Basic Cell, Proteins & Crystallography1 and Proteins & Crystallography 1 and 3)
2015-2021	Committee for Professional Opportunities for Women Committee (CPOW), Biophysical Society
2015-2018	Councilor (elected to office), Society for General Physiologists.
2016	Ad hoc Reviewer, NIH BBM study Section (Feb and Sep cycles).
2018	Ad hoc Reviewer, NIH BPNS study Section (Feb cycle).
2017	Reviewer, MCMB grant proposal, Medical Research Council (MRC) UK
2018	Editorial Advisory Board, Journal of General Physiology
2018	Reviewer, United States-Israel Binational Science Foundation
2018	Reviewer, French National Research Agency (ANR), France
2018	Reviewer, MCMB grant proposal, Medical Research Council (MRC) UK
2018-2020	Reviewer, United States-Israel Binational Science Foundation
2019	Editorial Board, Biophysical Journal
2019-2023	*Permanent Member*, Biochemistry and Biophysics of Membranes, NIH Study Section.

Honors

1995-1997	National Chemical Laboratory Scholarship, Pune, India
1997	Selected for Junior Research Fellowship, Council for Scientific and Industrial Research, India
1997-1999	Biomedical Engineering Scholarship, Indian Institute of Technology, Bombay, India
1999	Selected for the Cambridge Commonwealth Trust Scholarship and Overseas Research Scholar Award.
2004	Herbert Schuel Award for outstanding research in the field of Cell and Developmental Biology, University at Buffalo, SUNY.
2004	Dean's Award for Outstanding Dissertation, First Prize. University at Buffalo, SUNY.
2004	University at Buffalo nominee for the CGS/UMI Distinguished Dissertation award.
2005-2008	Postdoctoral Fellowship, American Heart Association
2007-2008	Postdoctoral Fellowship (Competitive Renewal), American Heart Association
2012-2016	Scientist Development Grant, American Heart Association.
2018	CWRU nominee for the Mallinckrodt Scholar Program.
2019-present	Joseph T. Wearn, MD, University Professorship in Medicine

C. Contribution to Science

1. *Structure-function relationships in nicotinic Acetylcholine receptors.* One of the fundamental challenges in the ion channel field is to understand how spatially-separated structural motifs of the channel communicate in order to fine-tune its function. In my doctoral research, I addressed this question in nicotinic acetylcholine receptor-channels (nAChR) that belong to the neurotransmitter gated Cys-loop receptor family. These channels are responsible for mediating fast synaptic transmission in neuronal and neuronal muscular junctions. Through single-channel current measurements of over 100 mutations and extensive model-based kinetic analysis within the framework of linear free energy relationships, I found that signal transduction occurs as a sequential movement of rigid "blocks" or "micro-domain" originating at the extracellular ligand-binding domain and culminating at the gate within the transmembrane region. Such an organized and linked motion of rigid bodies may underlie fast dynamics of the allosteric conformational change in these channels. This system also proved ideal to probe the speed-limits of global protein motions in the membrane. This finding has implications on barrier-less transitions in large multimeric membrane proteins.

a. **Chakrapani, S**., T.D. Bailey, and A. Auerbach. (2003). The role of loop 5 in acetylcholine receptor channel gating. ***J Gen Physiol***. 122:521-539. PMCID:PMC2229574
b. **Chakrapani, S**., T.D. Bailey, and A. Auerbach. (2004). Gating Dynamics of the Acetylcholine Receptor Extracellular Domain. ***J Gen Physiol***. 123: 341-356. (Featured on the Cover). PMCID:PMC2217457
c. **Chakrapani, S**., and A. Auerbach. (2005). A speed limit for conformational change of an allosteric membrane protein. ***Proc Natl Acad Sci U S A***, 2005. 102(1): p. 87-92. PMCID:PMC544059

2. *C-type inactivation and modal gating behavior in K^+ channels.* Studying prokaryotic channels provides a unique advantage to draw direct information from structural, dynamics, and functional measurements. However, unlike eukaryotic channels most of the bacterial members were not well-characterized at the functional level, this was particularly the case for KcsA, a pH-activated K^+ channel. As a part of my postdoctoral training, I carried out extensive kinetic analysis both at the macroscopic and single-channel level to characterize C-type inactivation and fast gating events that underlie KcsA function. To obtain high resolution structure of KcsA in multiple conformational states, I crystallized the channel in various mutant forms and in the presence of several modulators. Equating functional states to structural snapshots from crystallography, have led to a better understanding of the structural basis for inactivation from pre-open states, interaction of ions with the channel, modal gating behavior, and transitions that lead to fast gating events.

a. **Chakrapani, S**., Cordero-Morales, J. F., and Perozo, E. (2007a). A quantitative description of KcsA gating I: macroscopic currents. ***J Gen Physiol*** *130*, 465-478. PMCID:PMC2151670
b. **Chakrapani, S**., Cordero-Morales, J. F., and Perozo, E. (2007b). A quantitative description of KcsA gating II: single-channel currents. ***J Gen Physiol*** *130*, 479-496. PMCID:PMC2151667
c. **Chakrapani, S[a].**, Cordero-Morales, J. F[a]., Jogini, V., Pan, A. C., Cortes, D. M., Roux, R., and Perozo, E. (2011) On the structural basis for modal gating in K^+ channels ***Nature Structure & Molecular Biology*** *18 (1),* PMCID:PMC3059741. *[a]equal contribution.*

d. Ostmeyer J, **Chakrapani S**, Pan AC, Perozo E, Roux B. (2013) Recovery from slow inactivation in K+ channels is controlled by water molecules. ***Nature***. 501(7465):121-4. PubMed PMID: 23892782; PMCID:PMC3799803

3. Voltage-sensing mechanism and slow-inactivation in ion channels. Voltage-gated channels play a critical role in cellular excitability and thereby form the basis for initiation and propagation of nerve impulses. The structure of the voltage-sensor and the mechanisms underlying gating-charge movement have been areas intensively studied. Both the structure and the protein motions in the sensor are critically governed by the local membrane environment. Also as a part of my postdoctoral training, I used site-directed spin labeling and electron paramagnetic resonance (EPR) spectroscopy to directly investigate the architecture of the sensor in a reconstituted system. I studied the dynamics of the isolated voltage-sensors of prokaryotic K^+ (KvAP) and Na^+ (NaChBac) channels by EPR spectroscopy. These findings provided an in-depth view of the architecture of this domain on the membrane along with insights into the open-inactivated state of the channel. More recently, my lab characterized the molecular motions underlying slow-inactivation in voltage-gated Na+ channel (NavSp1) by pulsed-EPR spectroscopy.

a. **Chakrapani, S**., Cuello, L.G., Cortes, D.M., and Perozo, E. (2008). Structural dynamics of an isolated-voltage sensor domain in lipid bilayer. ***Structure** 16, 398-409* PMCID:PMC2703488
b. **Chakrapani, S**., Sompornpisut, P., Intharathep, P., Roux, B. & Perozo, E. (2010). The activated state of a sodium channel voltage sensor in a membrane environment. ***Proc Natl Acad Sci U S A*** 107, 5435-40. PMCID:PMC2851821
c. **Chakrapani, S**. (2015) EPR studies of gating mechanisms in ion channels ***Methods in Enzymology*** 557:279-306 PMCID:PMC4503332
d. Chatterjee S, Vyas R, Chalamalasetti SV, Sahu ID, Clatot J, Wan X, Lorigan GA, Deschenes I, **Chakrapani S***. The voltage-gated sodium channel pore exhibits conformational flexibility during slow inactivation. ***J Gen Physiol***. 2018;150(9):1333-47. doi: 10.1085/jgp.201812118. PubMed PMID: 30082431; PMCID: PMC6122925.
   *This article was featured in a commentary "Progress in Understanding Slow Inactivation Speeds up" Payandeh, J ***Journal of General Physiology*** (2018)

4. Gating mechanisms in pentameric ligand-gated ion channels. Since joining the faculty at Case Western Reserve University as an Assistant professor in 2010, a major research focus of my lab has been to understand allosteric mechanisms in pentameric ligand-gated ion channels (pLGIC). Using prokaryotic homologues GLIC and ELIC as model systems, we elucidated the ligand-induced pore opening mechanism by EPR spectroscopy. Patch-clamp measurements from reconstituted channels were used to show the salient features of desensitization in GLIC that bears resemblance to the mechanism observed in the eukaryotic counterpart. These methods have allowed us to directly measure the effect of membrane lipid constituents on channel function and to determine the underlying changes in protein dynamics under these conditions. In addition, we studied long-range allosteric communications by engineering functional chimeric channels that incorporates domains from different members of the family. By using X-ray crystallography and pulse-EPR measurement, we determined the crystal structure of the chimera and measured ligand-induced structural changes which reveal conformational coupling between domains. More recently, my lab is geared towards applying these approaches in combination with cryo-EM to complex eukaryotic pLGIC. We recently determined the structures of the full-length 5-HT_{3A}R in the apo, and serotonin-bound conformations by single-particle cryo-EM. The structure reveals salient features of the resting, state and the conformational changes underlying serotonin-mediated activation. I served as the principal investigator in all these studies.

a. Basak, S.[a], Schmandt, N.[a], Gicheru, Y[a]., and **Chakrapani, S*.** (2017) Crystal structure and dynamics of a lipid-induced potential desensitized state of a pentameric ligand-gated channel (***eLIFE,*** doi: 10.7554/eLife.23886). PMCID:PMC5378477
b. Basak, S., Gicheru, Y., Samanta, A., Molugu, S. k., Huang, W.,, de la Fuente, M., Hughes, T., Taylor, D.J., Nieman, M. T., Moiseenkova-Bell, V., and **Chakrapani, S*** (2018) Cryo-EM structure of 5-HT_{3A} receptor in its resting conformation. ***Nature Communications*** 9(1):514. doi: 10.1038/s41467-018-02997-4. PubMed PMID: 29410406. PMCID:PMC5802770
c. Basak S, Gicheru Y, Rao S, Sansom MSP, **Chakrapani S***. Cryo-EM reveals two distinct serotonin-bound conformations of full-length 5-HT3A receptor. ***Nature***. 2018;563(7730):270-4. doi: 10.1038/s41586-018-0660-7. PubMed PMID: 30401837. PMCID:PMC6237196 (*Article Recommended by Faculty 1000)*

d. Basak S[a], Gicheru Y[a], Kapoor A., Mayer ML., Filizola M, and **Chakrapani S***. (2019) Molecular mechanism of setron-mediated inhibition of full-length 5-HT3A receptors. ***Nature Communications*** 10, 3225, doi:10.1038/s41467-019-11142-8. PMCID:PMC6642186
e. Kumar A, Basak S, Rao S, Gicheru Y, Mayer ML, Sansom MSP, **Chakrapani S*.** (2020) Mechanisms of activation and desensitization of full length glycine receptors in lipid nanodisc. ***Nature Communications*** Jul 27;11(1):3752. doi: 10.1038/s41467-020-17364-5.PMID: 32719334

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/sudha.chakrapani.1/bibliography/50561146/public/?sort=date&direction=ascending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support
NIH R35 GM134896 **Chakrapani (PI)** 01/01/20 – 12/31/24 7.2 cal.mo
Title: "Structure and Function of Pentameric Ligand-Gated Ion Channels"
NIGMS Direct Costs: $385, 000/year
The overall goal of this award is to determine the structural basis for gating and modulation in cationic and anionic pentameric ligand-gated ion channels.

NIH R01 GM108921 **Chakrapani (PI)** 09/1/14 – 08/31/20 3.6 cal.mo
Molecular Mechanisms of Desensitization and Drug Modulation in Ligand-Gated Ion Channels.
NIGMS Direct Costs: $190, 000/year
The goal of this award is to determine the structural basis for desensitization in ligand-gated channels and how transitions to this state are regulated by endogenous and exogenous modulators. (No Cost Extension; renewal funded as R35 MIRA Award)

NIH R01 GM131216-1S1 **Chakrapani (PI)** 07/1/19 – 08/31/20 0 cal.mo
Structure, Function, and Modulation of Serotonin (3A) receptors
NIGMS Direct Costs: $71, 615/year
Administrative Supplement for small equipment.
The goal of this supplement is to purchase GPU/CPU cluster for cryo-EM data processing in the Chakrapani lab.

NIH S10 OD025259 **Chakrapani (PI)** 09/01/18 – 08/31/2020 0 cal.mo
Title: "Pulsed-Electron Paramagnetic Resonance Spectrometer for Distance Determination in Biological Macromolecules"
OD Direct Costs: $900, 000/year
The goal of this award is to establish the first pulsed-EPR capability in the Greater Cleveland Area.

Completed Research Support
NIH R01 GM131216 **Chakrapani (PI)** 01/1/19 – 12/31/22 3.6 cal.mo
Title: "Structure, Function, and Modulation of Serotonin (3A) receptors"
NIGMS Direct Costs: $234, 943/year
The goal of this award is to elucidate the structural changes associated with gating and modulation in full-length serotonin-3A receptors. *(Terminated since the PI has accepted the R35 (MIRA) Award).*

NIH 3R01GM108921-03S1 **Chakrapani (PI)** 09/1/16 – 08/31/18
Title: "Molecular Mechanisms of Desensitization and Drug Modulation in Ligand-Gated Ion Channels"
Collaborative Supplements for Cryo-Electron Microscopy Technology Transfer (Admin Supp) to develop technical expertise in high resolution cryo-electron microscopic (cryoEM) single particle analysis in the PI's lab

NCRP Scientist Development Grant **Chakrapani (PI)** 12SDG12070069 07/01/12 – 06/30/16
American Heart Association
Title: "Structural dynamics of gating and selectivity in Voltage-gated sodium channels."
The overall goal of this award is to understand the conformational changes associated with voltage-dependent gating and selective ion permeation in voltage-gated channels.