BIOGRAPHICAL SKETCH

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NAME: Carsten Mim

eRA COMMONS USER NAME (credential, e.g., agency login):N/A

POSITION TITLE: Associate 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
Johan Wolfgang Goethe Universität	Diploma	05/2002	Biophysics
	PhD	11/2006	Biophysics

A. Personal Statement

I have a longstanding interest in processes at the membrane interface. I started my research as an electrophysiologist, where I became familiar with mechanisms of transporter processes. Later I transitioned into electron microscopy of membrane complexes to gain insight into structures at this important biological interface. My PostDoctoral supervisor solved the first sub-nm structure of a gap junction. During my tenure in this laboratory I learned about the isolation and reconstitution of transmembrane proteins. Since I started my own group, I work on structures of ion channels and their scaffolding proteins. Recent developments in electron microscopy, positions it as the method of choice for structures at the membrane interface which comprise the majority of drug targets. My group is also interested in the molecular mechanisms that govern the assembly of membrane associated scaffolds. Currently, my laboratory is working on two different channels and trafficking proteins that are important in neurological disorders, inflammation and cancer.

B. Positions and Honors

2007-2010	PostDoctoral Fellow	(Yale university)
20010-2014	PostDoctoral Fellow	(Northwestern University)
2015-2018	Assistant Professor	(Kungliga Tekniska Högskolan)
Since 2019	(tenured) Associate Professor	(Kungliga Tekniska Högskolan)

C. Contributions to Science

1. Functional diversity of Glutamate transporters in the nervous system

The only mechanism to terminate glutamatergic transmission is the removal of glutamate from the synaptic cleft. In humans there are four different (plasma membrane) glutamate transporters to achieve this task. All transporters are dependent on the Na^+/K^+ Gradient and have an anion conductance. Also, glutamate transporters fall into two categories either low affinity-high turnover or high affinity-low turnover. This lead to two questions in the field: 1. Why are there so many transporters for one task? 2. What is the significance of the two categories of glutamate transporters?

To answer this question I characterized the transport cycle of a high affinity-low turnover transporter (EAAT4), to complement previous findings from my supervisor's laboratory. We found that the kinetics of

EAAT4 differs significantly from glutamate transporters investigated earlier. We discovered a voltage sensitive step in EAAT4 that slows the turnover rate at a hyperpolarized membrane potential and increases EAAT4's apparent affinity. Taken together, we think that EAAT4 acts as a glutamate sink in the periphery of the synapse.
Characterisation of a high-affinity glutamate transporter: Mim *et al J Gen Physiol*. 2005 Dec;126(6):571-89.

2. Thermodynamic and kinetic dissemination of the glutamate transport cycle

Electrophysiological experiments in cells are usually performed at one temperature. As a consequence the forces that drive the binding of the substrates are not well characterized. Further, rate limiting steps in the transport cycle are seldom identified. This information is only obtainable in temperature dependent experiments. We developed and build an electrophysiological set-up to record transient and steady state data from mammalian cells that heterologously express a glutamate transporter (EAAT3). Our results showed that the binding of glutamate is enthalpy-driven, surprisingly this is not the case for the binding of Na^+. The temperature experiments revealed two distinct, kinetic states in the translocation step, which are characterized by high activation energy. We interpreted these events as the closing of the external gate and opening of the internal gate, respectively. Taken together our data indicate that glutamate transporters are fast enough to transport glutamate out of the cleft within the time scale of synaptic transmission. This contradicted the prevalent assumption that glutamate diffusion terminates the signal.
Temperature dependent states in the glutamate transport cycle Mim *et al* Biochemistry. 2007 Aug 7;46(31):9007-18

3. The structural basis of membrane bending

Eukaryotic cells have a plethora of membranous structures that need to be created and maintained to sustain life. All these structures are formed by dedicated proteins. While many bits and pieces have been identified, mechanisms of membrane bending remained elusive. Electron microscopy has been the method of choice to visualize membrane:protein complexes, since other techniques fail to visualize membrane associated proteins in the context of the membrane. My work on the Bin/Amphyphysin/Rvs domain (BAR) protein endophilin in complex with the bilayer resulted in the unexpected discovery that the stability and dynamics of endophilin scaffolds entirely depend on non-specific interactions between amphipathic helices in the bilayer. My findings also provided a first structurally motivated hypothesis how BAR-scaffolds selectively recruit downstream interaction partners through steric selection mechanisms.
CryoEM structure of endophilin scaffolds bound to the membrane Mim *et al Cell.* 2012 Mar 30;149(1):137-45.
The role of amphipathic helices in membrane remodeling Cui *et al* Biophys J. 2013 Jan 22;104(2):404-11

4. Fusogenic properties of N-BAR proteins

Membrane bending is only one aspect by which cells generate membranous structures in cells. Several structures are comprised of interconnected membrane structures/tubules some of which have BAR domain proteins are the constituting element. Before my work, models describing the mechanism were scarce. My data together with molecular dynamics showed that membrane perforation and fusion is a function of the local concentration of N-BAR proteins. My work provided more evidence that endophilin is fusogenic. The controlled nature of this phenomenon is an alternative avenue how cells can generate membrane structures. Further, the simulations showed that endophilin can act as a diffusion barrier for lipids and sort lipids in the nascent vesicles or membrane structures.
N-BAR domain induced membrane structures Ayton *et al* Biophys J. 2009 Sep 16;97(6)
Formation of membrane tubular network by N-BAR proteins Simunivic *et al* Biophys J. 2013 Aug 6;105(3):711-9

5. Structural biology of ex vivo clathrin coated vesicles

Previous high resolution structural studies of clathrin coats have been conducted on samples that have been assembled in vitro. We presented structures of clathrin coated vesicles isolated from animal tissues. Our reconstruction allows us to propose a sterical hindrance of the vesicular ATPase by the coat, which prevents the acidification (and maturation) of the synaptic vesicles before the clathrin coat is shed.
Clathrin Coat prevents acidification in vesicles Farsi *et al* Elife 2018 Apr 13;7

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

Funding

Co-Investigator, Human Frontier Science Program; Young Investigator Grant (11/2016-10/2019)
$115,000 per year
Co-Investigator, Swedish Research Council (01/2017-12/2020) ~$20000 per year

Invited talks
1st CryoNET symposium, Copenhagen (2018)
'Inter-organelle communication and neurodegeneration' Symposium Mediterranean Life Science Institute Split, 2018
HFSP Awardees Symposium (2018)
9th International Conference on Structural Biology
Zurich, 2017
Global Research Laboratory Symposium
Daejon, Jeju Island (2015,2017)
CECAM workshop
'International Workshop on Biomembranes: The consequences of complexity'
Helsinki, (2016)
Biophysical Symposium, Northwestern University
Evanston (2011, 2012)
Publications

Original research papers

'Clathrin coat controls vesicle acidification by blocking vacuolar ATPase activity' (2018)
Z Farsi, S Gowrisankaran, M Krunic, B Rammner , A Woehler , E M Lafer, C Mim, R Jahn, I Milosevic, Elife Apr 13;7.

'Protein-mediated transformation of lipid vesicles into tubular networks' (2013)
M Simunovic, C Mim, TC Marlovits, G Resch, VM Unger, GA Voth
Biophysical journal 105 (3), 711-719

'Understanding the role of amphipathic helices in N-BAR domain driven membrane remodeling' (2013)
H Cui, C Mim, FX Vázquez, E Lyman, VM Unger, GA Voth
Biophysical journal 104 (2), 404-411

'Structural basis of membrane bending by the N-BAR protein endophilin' (2012)
C Mim, H Cui, JA Gawronski-Salerno, A Frost, E Lyman, GA Voth, VM Unger
Cell 149 (1), 137-145

'New insights into BAR domain-induced membrane remodeling' (2009)
GS Ayton, E Lyman, V Krishna, RD Swenson, C Mim, VM Unger, GA Voth
Biophysical journal 97 (6), 1616-1625

'Two conformational changes are associated with glutamate translocation by the glutamate transporter EAAC1' (2007)
C Mim, Z Tao, C Grewer
Biochemistry 46 (31), 9007-9018

'The glutamate transporter subtypes EAAT4 and EAATs 1-3 transport glutamate with dramatically different kinetics and voltage dependence but share a common uptake mechanism' (2005)
C Mim, P Balani, T Rauen, C Grewer
The Journal of general physiology 126 (6), 571-589

Research Reviews

'Regulated protein turnover: snapshots of the proteasome in action' (2014)
S Bhattacharyya, H Yu, C Mim, A Matouschek

Nature Reviews Molecular Cell Biology 15 (2), 122-133

‘Membrane curvature and its generation by BAR proteins’ (2012)
C Mim, VM Unger
Trends in biochemical sciences 37 (12), 526-533

Manuscripts under review or in preparation

‘Bin1 K35N and D151N mutants reduce membrane binding and bending by different mechanisms’
S Gowrisankaran, DG Morgan, I Milosevic and C Mim
Journal of Molecular Biology, submitted

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
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NAME: Perkins, Guy

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

POSITION TITLE: Director of Tomography, Project 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
University of Utah, Salt Lake City, UT	B.A. Honors	06/1986	Physics
University of Utah, Salt Lake City, UT	B.S.	06/1986	Mathematics
University of California, Berkeley, CA	Ph.D.	05/1992	Biophysics
Lawrence Berkeley Laboratory, Berkeley, CA	Postdoctoral	11/1992	Structural Biology
Rijksuniversiteit Groningen, The Netherlands	Postdoctoral	11/1994	Structural Biology
Brandeis University, Waltham, MA	Postdoctoral	07/1995	Structural Biology
San Diego State University and University of California-San Diego, San Diego, CA	Postdoctoral	06/1996	Structural Biology

A. Personal Statement

I am a principal investigator at the National Center for Microscopy and Imaging Research (NCMIR). My early career interests in the 1990s were in the structure and function of membrane proteins using the tools of electron crystallography, cryo-electron microscopy and single-particle analysis. I was mentored first by Prof. Robert Glaeser (UC-Berkeley) with bacteriorhodopsin and later by Prof. Gina Sosinsky in the structural studies of gap junctions, including cryo-EM. We authored four structural papers together on the connexons that form gap junctions. Upon Prof. Sosinsky's passing, I was appointed the PI on her two gap junction R01 grants, both ending in 2016. I currently lead the pannexin structural effort on an NIH grant with Prof. Dahl, who is the PI on this grant. ***Dahl and his collaborators are the only ones to have published findings on the structural biology of Panx1 and Panx2 channels.*** I am the director for the 3DEM website and discussion forum for investigators in molecular and cellular 3D structure (>3600 subscribers world-wide, highlighted by Richard Henderson in his 2017 Nobel Lecture.

I have also provided leadership at the National Center for Microscopy and Imaging Research (NCMIR) in the capacity of Director of Tomography since 2003. In this role, I have applied advanced, new instrumentation and computer algorithms to studies of biological structures in situ. After joining NCMIR in 1995, Mark Ellisman and I developed the methods of electron microscope tomography (EMT) to visualize the 3D architecture of mitochondria in cells and tissues. Applying my training in mathematics, physics and biophysics, I have been a driving force in the quantitative analysis of mitochondrial architecture and nanoscale structural landmarks. As a result, I am the world's most published researcher on the structure of mitochondria. The structure I named in a 1997 paper and characterized by my colleagues and I since, the *crista junction*, has been featured in well-respected scientific journals, including journal covers, in news articles, in molecular cell biology textbooks and was recognized by the *Royal Society of Chemistry*. Of my 134 peer-reviewed publications, 81 have focused on mitochondrial structure and function in healthy and disease states. One of my mitochondrial movies was shown in the U.S. Congress (Mootha, V., Perkins, G., Ellisman, M.H. Mitochondria 101 - How Something So Small is So Important to Human Life. *Congressional Mitochondrial Disease Caucus*, Washington D.C., Sept. 20, 2012). Another movie highlighting 3D aspects of mitochondria was used in the BBC series *Life*; my electron

microscopy of human mitochondria was in the 'Why Are We Here?' episode of *Human Universe* (BBC2 and the Discovery Channel).

B. Positions and Honors

Positions and Employment

1986-1989	**NIH Research Trainee**, University of California, Berkeley, CA
1989-1992	**Graduate Student Research Assistant**, Lawrence Berkeley Laboratory, Berkeley, CA
1996-2012	**Adjunct Faculty**, San Diego State University
1999-2006	**Assistant Project Scientist,** Univ. of CA-San Diego
2006-2012	**Associate Project Scientist,** Univ. of CA-San Diego
2003-present	**Director of Tomography**, National Center for Microscopy and Imaging Research
2007-present	**Member, Scientific Advisory Board**, NCMIR, Univ. of CA-San Diego
2012-present	**Project Scientist,** Univ. of CA-San Diego

Other Experience and Professional Memberships

2001 –	Member, Mitochondria Interest Group
2006-2008	**Faculty Mentor,** Univ. of CA-San Diego
2007-2008	**School of Medicine Recruitment and Admissions Committee**, Univ. of CA-San Diego

Honors (selected)

1980	Honors at Entrance Scholarship
1989	National Research Service Award from the N.I.H.
1993	Plenary Speaker Dutch Electron Microscopy Society, Papendaal, Netherlands, 1993
2011	Speaker: The Expanding Roles of Mitochondria Conference. HHMI
2015	Speaker: Crick-Jacobs Workshop: Function and Failure of Calcium at Synapses

Reviewer for: Journal Articles and Book Chapters:
Applied and Environmental Microbiology, Anatomical Record, Annual Review of Biophysics, Biochemistry, Biophysical Journal, Cancer Cell International, DIRASAT, Environmental Health Perspectives, FEBS Letters, Handbook of Neurochemistry and Molecular Neurobiology, IOVS, Journal of Anatomy, Journal of Comparative Neurology, Journal of Histochemistry and Cytochemistry, Journal of Neurochemistry, Journal of Nutritional Biochemistry, Journal of Structural Biology, Microscopy and Microanalysis, Mitochondrion, Molecular Biology of the Cell, Molecular Brain Research, Molecular Cancer, Neuron, Neuroscience Letters, Oxidative Medicine and Cellular Longevity, PLoS Biology, PLoS One, Protoplasma: An International Journal of Cell Biology, Science, The Plant Cell, The Tohoku Journal of Experimental Medicine, Trends in Cell Biology

C. Contributions to Science

1. In the 1990's, I developed methods to visualize membrane proteins in small crystals, including the gap junction structure. The relevant publications are:
   a. Perkins, G., Downing, K. and Glaeser, R. (1995) Crystallographic extraction and averaging of data from small image areas. *Ultramicroscopy*, **60**, 283-294.
   b. Perkins, G.A., Goodenough, D.A. and Sosinsky, G.E. (1997) Three-dimensional structure of the gap junction connexon. *Biophysical Journal*, **72**, 533-544.
   c. Perkins, G.A., Goodenough, D.A. and Sosinsky, G.E. (1998) Formation of the Gap Junction Intercellular Channel Requires a 30° Rotation For Interdigitating Two Apposing Connexons. *J. Mol. Biol.*, **277**, 171-177. **Cover Figure** for the journal issue.
   d. Sosinsky, G. and Perkins, G. (2000) Electron crystallographic methods for investigating gap junction structure. METHODS: A Companion to Methods in Enzymology, **20**, 140-155.

2. Most of my focus has been to investigate mitochondrial structure/function relationships in disease states working with collaborators. A fissioning mitochondrion in a Huntington's Disease model was awarded a prize by the French journal, *La Recherche*, as "one of the most impressive images of 2011". A few

example publications are:

a. Lee, J.H., Budanov, A.V., Park, E.J., Birse, R., Kim, T.E., Perkins, G.A., Ellisman, M.H., Bodmer, R., Bier, E., Karin, M. (2010) Sestrin is a feedback inhibitor of TOR that prevents age-related pathologies. *Science*, 327: 1223-1228. Cover Figure for the journal issue. PMCIDL PMC2866632
b. Zhang, J., Guan, Z., Murphy, A.N., Wiley, S.E., Perkins, G.A., Worby, C.A., Engel, J.L., Heacock, P., Nguyen, O.K., Wang, J.H., Raetz, C.R.H., Dowhan, W., and Dixon, J.E. (2011) Mitochondrial phosphatase PTPMT1 is essential for cardiolipin biosynthesis. *Cell Metabolism*, 13:690-700. PMCID: PMC3119201
c. Lee, J.H., Budanov, A.V., Talukdar, S., Park, E.J., Park, H., Park, H.-W., Bandyopadhyay, G., Li, N., Aghajan, M., Jang, I., Wolfe, A.M., Perkins, G.A., Ellisman, M.H., Bier, E., Scadeng, M., Viollet, B., Olefsky, J., Karin, M. (2012) Maintenance of metabolic homeostasis by Sestrin 2 and 3., *Cell Metabolism*, 16:311-321. PMCID: PMC3687365
d. Lee, Y.S., Morinaga, H., Kim, J.J., Lagakos, W., Taylor, S., Keshwani, M., Perkins, G., Dong, H., Kayali, A.G., Sweet, I.R. and Olefsky, J. (2013). The Fractalkine and CX3CR1 System Regulates Beta Cell Function: A Novel Pathway for Regulation of Insulin Secretion. *Cell*, 153:413-25. PMID: 23582329, PMCID: PMC3717389

3. Part of my current research is the investigation of mitochondria in neuropathies and neurodegeneration contrasted with healthy neurons. A few example publications are:
   a. Perkins, G.A., Jackson, D.R., Spirou, G.A. (2015) Resolving Presynaptic Structure by Electron Tomography. *Synapse*, 69:268-282. Cover figure for issue. PMCID4955585
   b. Spirou, G.A., Jackson, D., Perkins, G.A. (2015) Mitochondria Anchored at the Synapse *in* The Functions, Disease-Related Dysfunctions, and Therapeutic Targeting of Neuronal Mitochondria edited by Gribkoff, V.K., Jonas, E.A., and Hardwick, J.M., chapter 9:203-218 pp, ISBN: 978-1-118-70923-8, 448 pages.
   c. Yin, X., Kidd, G.J., Ohno, N., Perkins, G.A., Ellisman, M.H. Bastian, C., Brunet, S., Baltan, S. and Trapp, B.D. (2016) Myelin modulates axonal mitochondria viability via metabolic coupling. *J. Cell Biology*, 215(4):531-542. Featured in a *JCB Spotlight* by Beirowski, Babetto and Wrabetz. PMID: 5119941.
   d. Perkins, G. (2017) Three-dimensional Reconstruction of Neuronal Mitochondria by Electron Tomography In *Neuromethods* eds. Strack and Usachev, Chapter 1, pp. 1-29. ISBN 978-1-4939-6888-6

4. Part of my research has been with cardiologists studying human patients:
   a. Taub, P.R., Ramirez-Sanchez, I., Ciaraldi, T.P., Perkins, G., Murphy, A., Naviaux, R., Hogan, M., Maisel, A.S., Henry, R.R., Ceballos, G., Villarreal, F. (2012) Alterations in skeletal muscle indicators of mitochondrial structure and biogenesis in patients with type 2 diabetes and heart failure: Effects of epicatechin rich cocoa. *Clinical and Translational Science*, 5:43-47. PMID: 22376256
   b. Ramirez-Sanchez, I., Taub, P.R., Ciaraldi, T.P., Nogueira, L., Coe, T., Perkins, G., Hogan, M., Maisel, A.S., Henry, R.R., Ceballos, G., and Villarreal, F. (2013) (-)-Epicatechin rich cocoa mediated modulation of oxidative stress in skeletal muscle of heart failure and type 2 diabetes patients. *Int J Cardiol.* 168:3982-3990. PMID: 23870648
   c. Taub, P.R., Ramirez-Sanchez, I., Ciaraldi, T.P., Gonzalez-Basurto, S., Coral-Vazquez, R., Perkins, G., Hogan, M., Maisel, A.S., Henry, R.R., Ceballos, G., Villarreal, F. (2013) Perturbations in skeletal muscle sarcomere structure effects of heart failure and type 2 diabetes patients: Restorative effects of (-)-epicatechin rich cocoa. *Clinical Science*, 125:383-389. PMID: 23642227
   d. Taub, P., Ramirez-Sanchez, I., Patel, M., Higginbotham, E., Moreno Ulloa, A., Roman Pintos, L., Phillips, P., Perkins, G., Ceballos Reyes, G. and Villareal, F. (2016) Beneficial effects of dark chocolate on exercise capacity in sedentary subjects: Underlying mechanisms. A double blind, randomized, placebo controlled trial. *Food & Function* 7:3686-3693. PMID: 27491778

5. As the Director of tomography at NCMIR, I have developed new tools for electron tomography
   a. Mumcuoglu, E.U., Hassanpour, R., Tasel, S.F., Perkins, G., Martone, M. and Gurcan, M.N. (2012) Computerized Detection and Segmentation of Mitochondria on Electron Microscope Images, *J. Microscopy*, 246:248-65. PMID: 22506967

b. Perkins, G. (2014) The use of miniSOG in the localization of mitochondrial proteins, In Anne N. Murphy, David C. Chan, editors: Mitochondrial Function, Vol 547, *Methods in Enzymology*, UK: Academic Press, pp. 165-179.
c. Tasel, S.F., Mumcuoglu, E.U., Reza Z. Hassanpour, R.Z. and Perkins, G. (2016) A validated active contour method driven by parabolic arc model for detection and segmentation of mitochondria. *J. Struct. Biol*., 194:253-271. PMID: 26956730
d. Sastri, M., Darshi, M., Mackey, M., Ramachandra, R., Ju, S., Phan, S., Adams, S., Stein, K., R. Douglas, C.R., Kim, J.J., Ellisman, M.H., Taylor, S.S., Perkins, G.A. (2017) Sub-Mitochondrial Localization of Genetic-Tagged MIB Interacting Partners: Mic19, Mic60 and Sam50. *J. Cell Science*, 30:3248-3260. Featured in "In This Issue".

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

Ongoing Research Support

5 P01 AG051443-03 Yamoah (PI) 09/01/16 - 05/31/21
NIH/NIA
Determinants of Age-Induced Hearing Loss and Reversal Strategies
To study structural aspects of hair cell mitochondria and characterize volume, membrane surface area, and density on cochlear hair cells in relation to damage like deafness or vertigo.
Role: Consortium PI

1 R01 DK116624-01 Strack (PI) 06/01/18 – 05/31/22
NIH / NIDDK
"Targeting Mitochondrial Fission for Neuroprotection in Dibetic Neuropathy"
This grant proposal is a collaboration between Dr. Guy Perkins at the National Center for Microscopy and Imaging Research (NCMIR) and Dr. Stafan Strack, University of Iowa. Dr. Perkins will use the electron microscopes and computer resources of the NCMIR to investigate the ultrastructure of mitochondria in sensory neurons of Bb2 KO mice challenged with type 1 and type 2 Diabetes.
Role: Consortium PI

1 R56 HL136291-01A1 Dahl (PI) 09/15/18 – 08/31/19
NIH / NHLBI
"Functional and Structural Analysis of the Closed and Two Open States of the Panx1 Channel"
This project is focused on evaluating how K+ activates the Panx1 channel. Determining the pore conformation of two distinct channel configurations induced by different stimuli. Performing a complementary EM structural analysis to determine the effect of Panx1 inhibitors on channel structure and/or stability.
Role: Consortium PI

Completed Research Support

5 P41 GM103412-30 Ellisman (PI) 04/01/14 – 03/31/19
NIH / NIGMS
"IVEM and Image Analysis Resource [National Center for Microscopy and Imaging Research (NCMIR)]"
The National Center for Microscopy and Imaging Research (NCMIR) is a Center supported by the NIH NIGMS which houses specially designed intermediate high voltage electron microscopes, and other 3D EM tools capable of computer-assisted operations, as well as custom advanced light microscopes and a large array of advanced image processing and computer graphics tools.
Role: Key Investigator

3 R01 EY018658-09 Ju (PI) 09/01/09 - 08/31/18
NIH/NEI
Mitochondrial dysfunction in glaucomatous optic neuropathy
The major goals of this project are to determine whether *in vitro* elevated hydrostatic pressure or *in vivo* elevated IOP triggers breakdown of mitochondrial network, loss of mitochondrial DNA and ultrastructural

changes of cristae in RGC somas and the ONH axons, and to determine how *in vitro* elevated hydrostatic pressure or *in vivo* elevated IOP alters mitochondrial fusion/fission mediators that degrade mitochondrial bioenergetics and induce RGC death, and to determine whether reduced Drp1 or increased OPA1 expression will block RGC loss and axon degeneration following *in vitro* elevated hydrostatic pressure or *in vivo* elevated IOP.
Role: Co-Investigator

2P01 DK054441-14A1 Taylor (PI) 04/01/14 - 03/31/18
NIH / NIDDK
PKA and PKC Targeting Mechanisms
The major goals of this project are to understand (1) the biochemical and structural basis for targeting of cAMP-dependent protein kinase (PKA) and protein kinase C (PKC) and (2) to understand the physiological importance of subcellular targeting of PKA and PKC.
Role: Co-Investigator