(Total: 100 pages)

SCHOOL OF MEDICINE CV FORMAT

Name: **Bhanu P. Jena**

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Place of Birth: Odisha, INDIA

Education:

1975	**B.Sc.** First Class Honors & Highest Distinction National Merit Award	Chemistry, Zoology, Botany	B.J.B. College, Utkal University
1978	**M.Sc.** Ranked First (First Class First) University Gold Medal Prashant Ku. Prize	Zoology (Hypothalamic-Pituitary Hormone Control) D. R. Naik	Utkal University
1988	**Ph.D.** Research Excellence Award	Zoology (GTP binding G-Protein Signaling) Joel Abramowitz	Iowa State University

Postdoctoral Training:

Dec. 1988-June 1990	Post Doctoral Fellow	Biochemistry (Protein Tyrosine Phosphatases & Kinases) T. S.	Iowa State University

		Ingebritsen	
June 1990-1992	Post Doctoral Fellow (Swebilius Fellow)	Cell Biology (Rab's on cell secretion) James D. Jamieson	Yale University School of Medicine
1992-1993	Associate Research Scientist	Cell Biology (Rab's on cell secretion) James D. Jamieson	Yale University School of Medicine

Faculty Academic Appointments:

1994-2000	Assistant Professor	Surgery & Bioengineering Program	Yale University School of Medicine
2000-pr	Professor	Department of Physiology	Wayne State University School of Medicine
2004-pr	Distinguished Professor	University-Wide	Wayne State University
2004-pr	George E. Palade University Professor	University-Wide	Wayne State University
2006-pr	Adjunct Professor	Department of Chemical Engineering & Materials Science	Wayne State University College of Engineering
2014-pr	Adjunct Professor	Department of Physics & Astronomy	Wayne State University College of Liberal Arts & Science

Appointments at Hospitals/Affiliated Institutions (Selected):

1998-2000	Founding Director	Drug Delivery & Discovery Center	Yale University School of Medicine
1999-2000	Full Member	Yale Cancer Center	Yale University School of Medicine
2001-pr	Founding Director	NanoBioScience Institute	Wayne State University School of Medicine
2001-pr	Full Member	Karmanos Cancer Center	Wayne State University School of Medicine
2002-2006	Co-Founding Director	Asian & Korean Institute of Nanoscience & Technology	Pusan National University
2002	Distinguished Visiting Professor	Cell Biology	Vasile Goldis University

2002-2005	Distinguished Visiting Professor	Molecular Biology	Pusan National University
2002	Distinguished Visiting Professor	Physics	Vinca Research Institute
2003	Distinguished Visiting Professor	Biology	Babes-Bolyai University
2006	Distinguished Visiting Professor	Nanoscience	Agharkar Research Institute
2014	Honorary Professor	University-Wide	Târgu Mureș University
2016	Visiting Professor	University-Wide	Aligarh Muslim University
2016	Distinguished GIAN Visiting Professor	Life Sciences	Jawaharlal Nehru University
2016-pr	Member	Advisory Board	Vedanta University (In Progress)
2016-pr	Advisor	Doctoral Program Development in Cellular Neuroscience	Ilia State University
2017-pr	Honorary Scientist	Victor Babes National Research Institute	Bucharest, Romania
2018-pr	President & Co-Founder	QPathology LLC	Boston, MA
2020-pr	President & Co-Founder	VironTherapeutics LLC	Boston, MA
2021 (Invited)	President & Director	Molecular Medicine Institute [10-yr endowment $10.45 billion]	Cambridge, MA (Pending Acceptance)

Other Professional Positions (Selected):

2002	Foreign Member	Korean Academy of Science and Technology
2006	Foreign Member	Romania Academy of Medical Sciences
2007	Member	Academy of Scholars, Wayne State

		University
2011	Fellow	AAAS
2012	Foreign Member	Georgian National Academy of Science
2018	Foreign Member	European Union Academy of Science
2019	Fellow	Society for Experimental Biology and Medicine

Major Administrative Leadership Positions (Selected):

Local

1987&1988	Student Mayor	Iowa State University, Overlooked University Police Force, Housing, and Transport
1986-1988	Executive Member	Student Body Council, Iowa State University
1998-2000	Co-Founding Director	Yale Drug Delivery & Discovery Center
2001-pr	Co-Founding Director	NanoBioScience Institute, Wayne State University
2018-pr	Founder	Institute of Molecular Medicine, Cambridge, MA
2018-pr	President & Co-Founder	QPathology LLC, Boston, MA
2020-pr	President & Co-Founder	Viron Therapeutics LLC, Boston, MA

International

2002-2006	Co-Founding Director	Asian & Korean Institute of Nanoscience & Technology
2016-pr	Advisory Board Member	Vedanta University
2016-pr	Academic Program Director	Establishment of Colleges, Departments & Institutes, for the Vedanta University, India
2017-pr	Advisory Board Member	Victor Babes National Research Institute, Bucharest, Romania
2018-pr	Advisor & Consultant	Neuroscience Research Program, Georgia National Science Foundation,

Ilia State University, Tbilisi, Georgia

Professional Societies (Selected):

1989	Sigma Xi Scientific Society	Full Member
1984-1988	Endocrine Society	Member
1991-2000	Cell Biology Society	Member
2002	Korean Academy of Science and Technology	Foreign Member
2002	America Physiological Society	Member
2006	Romania Academy of Medical Sciences	Foreign Member
2007	Academy of Scholars, WSU	Member
2011	AAAS	Fellow
2012	Georgian National Academy of Science	Foreign Member
2012	Experimental Biology & Medicine Society	Member
2014	American Chemical Society	Member
2018	European Union Academy of Science	Foreign Member
2019	Society for Experimental Biology and Medicine	Fellow

Honors and Prizes (Selected):

1976	National Merit Scholarship	Government of India	One of top 3 students in the Bachelor of Science Program
1978	University Gold Medal	Utkal University	First-Class-First in the Masters of Science Program
1978	Prasant Ku. Memorial Prize	Utkal University	Top Student & established new grade record in the Masters of Science Exam

1988	Research Excellence Award	Iowa State University	Award Winning Research & Thesis in the Doctoral Program
1988	Humanitarian Award	Iowa State University	Dedicated contribution to the general welfare of students and being the first international student to be elected to serve as Mayor
1992	Swebelius Cancer Research Award	Swebelius Foundation	Role of phosphatases in cell secretion
1993	Swebelius Cancer Research Award	Swebelius Foundation	Role of GTP-binding proteins in cell secretion
1995	OHSE Award	Yale University School of Medicine	Monomeric GTP-binding proteins on cell secretion
1996	OHSE Award	Yale University School of Medicine	Monomeric GTP-binding proteins on cell secretion
2002	Foreign Member	Korean Academy of Science & Technology, Seoul, S. Korea	“for the discovery of a new cellular structure the porosome and for dedicated service to science and education”
2002	Hallim Distinguished Award (Shared with Prof. Ahmed H. Zewail)	Korean Academy of Science & Technology, Seoul, S. Korea	“for the discovery of a new cellular structure the porosome”
2003	Wise & Hellen Burroughs Foundation Distinguished Lecture	Iowa State University	“porosome discovery”
2004	Distinguished Professor	Wayne State University	“for outstanding contribution to science and education”
2004	George E. Palade University Professor	Wayne State Univertsity	“for the discovery of a new cellular structure the ‘porosome’ and for his pioneering contributions to the understanding of cell secretion and membrane fusion”
2005	Sir Aaron Klug	Mississippi State University	“pioneering discoveries on

	Distinguished Award		the molecular machinery and mechanism of cell secretion”
2005	George E. Palade Distinguished Award	Wayne State University	“for his pioneering discovery of the porosome, the universal secretory machinery in cells”
2006	Award & Felicitation (Chader Presented)	Maharashtra Association for the Cultivation of Science, Pune, India	“for contribution to science, education, and society”
2006	Foreign Member	Romania Academy of Medical Sciences	“for pioneering contribution to science and education”
2006	George E. Palade Distinction Gold Medal	Carol Davila University	Excellence in Medicine
2007	Academy of Scholars Member	Wayne State University	“for pioneering contribution to science and education”
2007	Basic Biological Science Award	American Society of Animal Science	“for the monumental and pioneering discovery of a new cellular structure called the porosome, the universal secretory machinery in cells, and elucidation of its structure, chemistry, and function.”
2009	Ranbaxy Basic Research in Medical Sciences Award	Ranbaxy Science Foundation	“for his pioneering discovery of a new cellular structure -the “porosome”, the universal secretory machinery in cells, and for the general molecular mechanism underlying cell secretion”
2011	Fellow	AAAS	“You are being honored for your pioneering discovery of the ‘porosome’ –the universal secretory machinery in cells”
2012	Foreign Member	Georgian National Academy of Science, Tbilisi, Georgia	“Pioneering contribution to science and education”
2014	Honorary Professor	Târgu Mureș University	“Pioneering contribution to

			science”
2015	Distinguished Scientist Award	Society for Experimental Biology and Medicine	Contribution to science
2017-	Honorary Professor	University of Delhi	“remarkable achievements in the area of basic and applied biology”
2017	Teaching Excellence Award	Wayne State University School of Medicine	“excellence in teaching”
2017	“Research Warrior”	Wayne State University Undergraduate Student Organization	Support and involvement in Undergraduate Research
2017	Honorary Scientist Award	Victor Babes National Research Institute	“for creativity and inventiveness invested in the discovery of the porosome, the universal portal for cell secretion”
2018	Foreign Member	European Union Academy of Science	“pioneering contributions to Science”
2019	Fellow	Society for Experimental Biology and Medicine	

HONORARY DOCTORATE DEGREES

2002 Honorary Doctor of Philosophy, Vasile Goldis University, Romania

2002 Honorary Doctor of Philosophy, Pusan National University, Korea.

2003 Honorary Doctor of Philosophy, “Iuliu Hatieganu” University of Medicine & Pharmacy, Romania.

2003 Honorary Doctor of Medicine, 'Babes-Bolyai' University, Romania, May 26, 2003, jointly with Professors George E. Palade, and Günter Blobel.

2003 Honorary Doctorate in Philosophy, Institute of Physiology, Georgian Academy of Sciences, Georgia

2005 Honorary Doctorate in Medicine, ‘Carol Davila' University, Bucharest, Romania

SERVICE (Summary followed by Selected Details)

Wayne State University
2001-pr Founding Director, NanoBioScience Institute, Wayne State University (200h)

•Advisory Board Member in a number of committees, Wayne State University (50h)

•Presented a number of scientific lectures within campus (20h)

2008-pr Co-Chair, Ahmed H. Zewail Award & Distinguished Lecture (20h)

2006-pr Member Selection Committee, George E. Palade Award (20h)

2007-pr Member, Review Committee, Academy of Scholars Research Award (20h/year)

2013 Committee Member Selected by the Provost Office to review the Academic Program of the Department of Chemical Engineering & Materials Science WSU, 2013 (100h)

2014 Committee Member Selected by the Provost Office to review the Academic Program of the Department of Bioengineering, WSU

School of Medicine (Summary)

2015-pr Member, MD-Ph.D. Advisory & Review Committee (**50h/year**)

[Interviewed 15 MD-Ph.D. candidates in 2019 & 5 MD-Ph.D. candidates in 2020]

2015 Chair, CVRI Review Committee [**50h**]

2001-pr Director, NanoBioScience Institute. Programs: Coordinate and teach a nanobioscience course, undertake, facilitate, and coordinate research collaborations across campus and within the school in nanobioscience, participate in joint research publications, and coordinate the writing and submission of both intramural and extramural research grants. (**250h/year**).

Professional (e.g., medical or scientific organizations and societies)

• Member, American Association for the Advancement of Science
• Full Member of Sigma Xi Scientific Society
• Member of the American Society for Cell Biology
• Member of the American Physiological Society
• Member of the Society for Experimental Biology and Medicine
• Member of the American Chemical Society
• Foreign Member, Korean Academy of Science and Technology.

• Foreign Member National Academy of Medical Sciences, Romania
• Fellow, American Association for the Advancement of Science
• Foreign Member of the Georgian National Academy of Science
• Honorary Scientist, Victor Babes National Research Institute
• Foreign Member of the European Union Academy of Science

Scholarly Service:

Grant Review Committees

2018-pr • Medical Research Council, UK, Scientific Review Panel
2015 • NSF IDBR Study Panel Member
2015 • NIH Neuroscience Study Section Mail Review
2003-2009 • NSF Site Visit Team Member, Cornell University, Nano Science Institute.
2003-pr • European Research Commission.
2007-pr • Israel Science Foundation.
2003-pr • Wellcome Trust.
2008-pr • American Air Force.
2000-pr • Human Frontier Science Program.
2004-pr • Netherlands Organization for Scientific Research.
2008-pr • Ministry of Education & Science, Russian Federation.
2006-pr • Austrian Science Fund.
2012-pr • US Naval Research.
2005-pr • Henry Ford Health System Internal Research Grants.
2008 • University of Wisconsin, Internal Research Grant review
2004-pr • Lawrence Berkeley National Laboratory Review Panel

National/International

• Founding Director, Asian Institute of Nanoscience & Technology, Pusan National University, S. Korea.
• Founding Director, NanoCellBiology Institute, University of Medicine & Pharmacy, Tg. Mures, Romania.
• Associate Secretary General, International Federation of Cell Biology
• Distinguished Visiting Professor, Vasile Goldis University, Romania.
• Distinguished Visiting Professor, Pusan National University, Korea.

• Distinguished Visiting Professor, “Iuliu Hatieganu” University of Medicine & Pharmacy, Romania, March.
• Distinguished Visiting Professor, “Babes-Bolyai” University, Romania
• Distinguished Visiting Professor, Agharkar Research Institute, Govt. of India, Pune, India
• Honorary Professor, University of Medicine & Pharmacy, Tirgu Mures, Romania
• Honorary Scientist, Victor Babes National Research Institute, Bucharest, Romania
• Member, Advisory Board, Vedanta University, Odisha, India

Regional/Local

•Co-Director, Institute of NanoBioScience, Wayne State University
•Co-Chair, Ahmed H. Zewail Award & Distinguished Lecture (20h)
•Member Selection Committee, George E. Palade Award (20h)
•Member, Review Committee, Academy of Scholars Research Award (20h/year)
•Committee Member Selected by the Provost Office to review the Academic Program of the Department of Chemical Engineering & Materials Science WSU, 2013 (100h)
• Committee Member Selected by the Provost Office to review the Academic Program of the Department of Bioengineering, WSU, 2018

Committee Service (Selected):

Local

2002-2007	Presidents Committee on International Collaboration & Affiliations	Member, Wayne State University
2007-	George E. Palade Award Selection Committee	Member, Wayne State University
2007-	Academy of Scholars Research Award Review Committee	Member
2008-	Ahmed H. Zewail Award Selection Committee	Co-Chair, Wayne State University
2013	Provost’s Committee on Department Performance Review: Chemical Engineering & Material Sciences	Member, Wayne State University
2014	University Academic Program Review	Member
2015	Dean’s Committee, Cardiovascular	Chair, Wayne State University School

	Research Institute Review	of Medicine
2015-	MD-Ph.D. Program	Member Selection Committee & Advisory Board Member, Wayne State University School of Medicine
2000-	Various Departmental Committees: Salary Committee, P&T Committee; Faculty Recruitment Committee; Junior Faculty Mentoring	Member, Physiology, Wayne State University School of Medicine

International

2002	Organizing Chair, *'International Nanoscience Symposium'*	Wayne State University School of Medicine
2002	Co-Chair, International Nanoscience Symposium	Asian Institute of Nanoscience & Technology, Foundation Ceremony, Pusan, S. Korea
2005	Chair, Conference on *'Nanoscience in the Understanding of Nature'*	World Expo, Aichi, Japan
2008-	Co-Chair, Selection Committee, Ahmed H. Zewail Award	Wayne State University
2016-	Doctoral Neuroscience Program Foreign Advisor	Ilia State University, Tbilisi, Georgia
2017-	Advisory Board Member	Vedanta University, Odisha, India
2017-	Member Advisory Board	Victor Babes National Research Institute, Bucharest, Romania

Service for Peer-Reviewed Journals

Editorship (SIX BOOKS)

1. **Jena, B. P.** (2020) Cellular Nanomachines: *Natures Engineered Marvels*. *Springer Nature Publishing.* ISBN 978-3-030-44495-2 ***[Cover: Porosome Complex].***

2. **Jena, B. P.,** Taatjes, D.J. (2013) NanoCellBiology: Multimodal Imaging in Biology & Medicine *Pan Sanford Publishing Pte. Ltd.* ISBN: 9789814411790 ***[Cover: Neuronal Porosome Complex].***

3. **Jena, B.P.** (2012) NanoCellBiology of Secretion: Imaging its Cellular and Molecular Underpinnings. *Springer Briefs in Biological Imaging* 1:1-70.

4. **Jena, B. P.** (2008) Methods in nano cell biology. *Methods in Cell Biology*, *Academic Press* 90:1-505. ***(Cover: Porosome Complex).***

5. **Jena, B. P.,** Hoerber, J.K.H. (2006). Force microscopy: application in biology and medicine. *Wiley & Sons, Inc.* 1-300. ***[Cover: Porosome Complex].***

6. **Jena, B. P.,** Horber, J.K.H. (2002) Atomic force microscopy in cell biology. *Methods in Cell Biology*, *Academic Press* 68:1-409. ***[Cover: Porosome Complex].***

Editorial Board Membership

- Guest Editor: *'Seminars in Cell and Developmental Biology'*.
- Member, Editorial Board: *'Journal of Cellular & Molecular Medicine'*.
- Member, Editorial Board: *'Micron'*.
- Assistant Editor: *'Cell Biology International'*.
- Senior Editor: *'Discoveries Journal'*.
- Senior Editor: *'Discoveries Reports'*.
- Member, Editorial Board: *'Biomedical Reviews'*.
- Member, Editorial Board: *'Journal of Proteomics, Bioinformatics & Genomics'*.
- Member, Editorial Board: *'The Scientific World Journal: Physiology'*.
- Member, Editorial Board: Austin, *'Proteomics'*.

Review of Manuscripts

• Peer Review: Nature Reports
• Peer Review: JMIC MICRON

• Peer Review: Neurotoxicity Research
• Peer Review: Cell Biology International
• Peer Review: Journal of Physics D
• Peer Review: J. Physiobiol. Rev.
• Peer Review: Nature Protocols
• Peer Review: Biochemistry
• Peer Review: Microscopy
• Peer Review: Journal of Royal Society Interface
• Peer Review: Neuroscience Lett.
• Peer Review: Experimental Biology & Medicine
• Peer Review: Theranostics
• Peer Review: F1000
• Peer Review: JoVE
• Peer Review: Journal of Histochemistry and Cell Biology
• Peer Review: Int. J. Dev. Neurosci.

Grant Review Activities (Recent):

2003-2009	NSF Nano Biotechnology Center Site Visit Team	Member
2008	Israel Science Foundation Grants	Expert Reviewer
2008-pr	Henry Ford Research Grants	Reviewer
2009	Human Frontier Science Program	Reviewer
2009	Wellcome Trust Proposals	Reviewer
2010	Air Force Office of Scientific Research Grant	Reviewer
2011	Israel Science Foundation Grants	Expert Reviewer
2013	Netherlands Organization for Scientific Research Grants	Expert Reviewer
2013, 2014	Russian Research Foundation Proposals	Expert Examiner
2013	Australian Scientific Fund Grants	Reviewer
2015	University of Wisconsin Internally Funded Research Proposals	Reviewer
2015	NSF IDBR Panel	Member

2015	NIH Grants	Reviewer
2016-2017	German-Israeli Foundation for Scientific Research and Development Grants	Expert Reviewer
2018-	MRC UK	Expert Reviewer

Editorial Activities (Recent):

Ad hoc Reviewer (Selected)

Reviewer for a number of international scientific journals including, *Nature; Science; PNAS; JACS; JBC; CBI; Langmuir; J. Royal Society; Biochemistry; Journal of Cell Research; J. of Theoretical Biology; Microscopy; Mol. Cell. Biol.; Exp. Biol. And Med.; Physiological Reviews; Exp. Cell Res.; J. Animal Reprod.; J. Proteom Res.; Mol. Cell Biol.; Micron, J. Phys. D.; JCMM; among others.*

Other Editorial Roles (Selected)

2000-2010	Editorial Board Member	Cell Biology International
2005-pr	Editorial Board Member	Journal of Cellular & Molecular Medicine
2010-2014	Editorial Board Member	Cell Biology International Reports
2014-pr	Senior Editor	Discoveries Journal
2014-pr	Senior Editor	Discoveries Report
2010-2016	Assistant Editor	Cell Biology International
2010-pr	Editorial Board Member	Biomedical Reviews
2014-pr	Editorial Board Member	Journal of Proteomics, Bioinformatics, and Genomics
2014-pr	Editorial Board Member	Scientific World Journal: Physiology
2014-pr	Editorial Board Member	Austin, Proteomics
2015-pr	Editorial Board Member	Micron
2017-pr	Advisor	Cell Biology International
2019-pr	Guest Editor	Seminars in Cell & Development Biology

Report of Local Teaching and Training (Recent)

Teaching of Students in Courses:

2006-pr	General Endocrinology Graduate/Undergraduate Seniors PSL5680; 3 Credit	Course Director (50 students) Wayne State University School of Medicine **[2019 Student Evaluation:4.7/5]**
2006-pr	NanoBioScience (Interdisciplinary) Graduate PSL7215; 3 Credit	Course Director (25-30 students) Course Developer Wayne State University School of Medicine
2016-pr	Graduate Physiology PSL7010/PSL7011; 4 Credit	Course Director [2016-2019] Three Lectures (100-110 students) Wayne State University School of Medicine **[2019 Student Evaluation:4.7/5]**
2014-pr	Medical Physiology (Pituitary, Hypothalamus, Thyroid) MD1 Students	Three 1h Lectures (300 students) Wayne State University School of Medicine
2014-pr	Biotechnology Graduate PSL6300; 2 Credit PSL6010; 1 Credit	One 2h Lecture Wayne State University School of Medicine Laboratory Mentoring **[2019 Student Evaluation:4.8/5]**
2006-pr	Physiology Lab. Graduate PSL7020; 2 Credit	One 5h Hands-on Laboratory Exercise Wayne State University School of Medicine **[2019 Student Evaluation:4.3/5]**
2004-pr	Advanced Neurophysiology Graduate PSL7660; 3 Credit	One 3h Lecture on Molecular Mechanism of Neurotransmitter Release Wayne State University School of Medicine
2020-pr	Cellular & Molecular Physiology Graduate PSL7640; 3 Credit	Two 3h Contact hour didactic course Cell & Mol. Physiol. Wayne State University School of Medicine

2020-pr	Advanced Endocrinology Graduate PSL7680; 4 Credit	One 2h Lecture on Thyroid Wayne State University School of Medicine
2016-pr	Membrane Physiology Graduate PSL7825; 2 Credit	ne 2h Lecture on Membrane Fusion Wayne State University School of Medicine
2015-16	Current Literature Graduate PSL7060; 1 Credit	Co-Director Wayne State University School of Medicine
2015-pr	Research Methods in Biomedical Physics Graduate PHY6780; 3 Credit	One 3h Lecture Department of Physics Wayne State University
2018-19	Medical Neuroscience (Presynaptic and Postsynaptic Transmission) MD1 Students	Two 1.5h Lectures (300 Students) Wayne State University School of Medicine
2019-pr	M1 Endocrine-Reproductive System	1h Lecture (300 Students) Wayne State University School of Medicine
2019-pr	M2 Research Elective	10h Preparation, Research Paper Discussion & Critical Review (20 Students)
2019-pr	Mi Research Elective	10h Preparation, Research Paper Discussion & Critical Review (20 Students)

Formal Teaching of Residents, Clinical Fellows and Research Fellows:

1995-2000	Mentor Surgical Residents Research Fellows	Yale University School of Medicine

2000-pr	Mentor Residents Research MD Students Research MD. Ph.D. Research Research Fellows	Wayne State University School of Medicine

Curriculum Development and Administration

2000-pr Founding-Director NanoBioScience Institute, Wayne State University School of Medicine. [Selected as one of the top 4 Nano Institutes in the USA by Reid Academic Publishing].

2006-pr Developed the PSL7215 NanoBioScience Course, serving as Director of this multidisciplinary course taught by faculty from all four colleges Participating Colleges: School of Medicine, School of Pharmacy, College of Engineering and College of Liberal Arts & Sciences), Wayne State University School of Medicine.

2019: Developed a Ph.D. Concentration in "Biophysics and Biomaterials Science, serving as Director and Coordinator of this multidisciplinary, multi-departmental and multi-college program (Participating Colleges: School of Medicine, School of Pharmacy, College of Engineering and College of Liberal Arts & Sciences), Wayne State University.

Laboratory and Research Supervisory and Training Responsibilities (Recent):

2000-pr	Mentor Graduate (Doctoral Students) PSL7886	Research & Thesis Advisor
2000-pr	Mentor Graduate (Masters Students) PSL7996	Research & Thesis Advisor
2000-pr	Mentor Undergraduate Student Research PSL7010	Research Advisor
2000-pr	Mentor Undergraduate Thesis PSY4991; BIO6999	-Thesis Advisor -National Conference on Undergraduate Research (NCUR) Presentations -Amgen Scholar Competition
2000-pr	Mentor High School Research	-Detroit Science Fair Competition -INTEL Science Competition -NASA Science Competition -SIEMENS Competition in Math,

[Students at every level have competed and won prizes in all categories listed above at the National and International level]

A. Successful Doctoral Thesis Mentored:

Year: 2019
Candidate: Akshata R. Naik
Citation: "Molecular Machinery for the 'Kiss and Run' Mechanism of Insulin Secretion"
Degree: Ph.D. in Physiology, School of Medicine, Wayne State University

Year: 2017
Candidate: Kenneth T. Lewis
Citation: "Understanding the Molecular Structure, Composition, and Regulation of the Neuronal Porosome Complex"
Degree: Ph.D. in Physiology, School of Medicine, Wayne State University

Year: 2016
Candidate: Maheshika P. Arachchige
Citation: "Fe_3O_4 Nanoparticles for Magnetic Hyperthermia and Drug Delivery, Synthesis, Characterization, and Cellular Studies"
Degree: Ph.D. in Physics, College of Liberal Arts & Science, Wayne State University

Year: 2015
Candidate: Suvra S. Laha
Citation: "Understanding the Physics of Magnetic Nanoparticles and their Application in the Biomedical Field"
Degree: Ph.D. in Physics, College of Liberal Arts & Science, Wayne State University

Year: 2013
Candidate: Amanda Flack
Citation: "Altered Morphology and Composition of Zymogen Granules in Acute Pancreatitis"
Degree: Ph.D. in Physiology, School of Medicine, Wayne State University

Year: 2010
Candidate: Leah J. Zhang
Citation: "Molecular Mechanism of SNARE Assembly and Expulsion of Intravesicular Contents in Cell Secretion"
Degree: Ph.D. in Physiology, School of Medicine, Wayne State University

Year: 2006
Candidate: Rania Abu-Hamdah
Citation: "Regulation of the Water Channel Aquaporin 1 and Aquaporin 6: Isolation and Reconstitution of the Regulatory Complex"
Degree: Ph.D. in Physiology, School of Medicine, Wayne State University

Ph.D. Rotation Students:

Year: 2018-2018 (One Semester)
Candidate: Monazza Shahab
Citation: “Cellular Imaging Modalities”
Degree: Ph.D. Student in Physiology, School of Medicine, Wayne State University

MD-Ph.D. Rotation Students:

Year: 2019-2020
Candidate: Sebastian P. Pernal
Citation: “Differential Expansion Microscopy”
Degree: MD. Ph.D. Student, School of Medicine, Wayne State University

Year: 2019-pr
Candidate: Rafael Ramos
Citation: “Differential Expansion Microscopy”
Degree: MD. Ph.D. Student, School of Medicine, Wayne State University

MD Student Research:

Year: 2018-2020
Candidate: Kathleen George
Citation: “Differential Expansion Microscopy”
Degree: MD Student, School of Medicine, Wayne State University

Doctoral Thesis Committee Member (Recent):

Year: 2016-pr
Candidate: Stephanie Gladyck
Citation: “Understanding the role of a novel mitochondrial-nuclear regulator”
Degree: Ph.D., CMMG, School of Medicine, Wayne State University

Year: 2018-pr
Candidate: Zhenjie Liu
Citation: “The role of biomaterial in stem cell fate determination”
Degree: Ph.D., School of Medicine, Wayne State University

Year: 2017-2020
Candidate: Umit Ozer
Citation: “ROLE OF CALCIUM-BILAYER INTERACTIONS IN THE MEMBRANE FUSION: INSIGHTS FROM MOLECULAR DYNAMICS SIMULATIONS”
Degree: Ph.D., Chemical Engineering, School of Engineering, Wayne State University

Year: 2015-2019
Candidate: Carthic Rajgopalan
Citation: "MOLECULAR MECHANISMS IN CFTR-F508DEL DEGRADATION AND THE FUNCTIONAL DEFECT OF CFTR ABSENCE IN RABBITS"
Degree: Ph.D., Physiology, School of Medicine, Wayne State University

Year: 2014-2018
Candidate: Abir Kabani
Citation: "Polarized Localization Microscopy (plm) Detects Nanoscale Membrane Curvature and Induced Budding by Cholera Toxin Subunit B (ctxb)"
Degree: Ph.D. in Physics, Liberal Arts & Sciences, Wayne State University

Year: 2013-2017
Candidate: William Close
Citation: "NAVIGATING HUMAN CYTOMEGALOVIRUS (HCMV) ENVELOPMENT AND EGRESS"
Degree: Ph.D., Immunology, School of Medicine, Wayne State University

Year: 2012-2016
Candidate: Jason R. Mick
Citation: "Force Field Development with Gomc A Fast New Monte Carlo" Molecular Simulation Code"
Degree: Ph.D. in Chemical Engineering & Materials Science, College of Engineering, Wayne State University

B. Recent Master's Thesis Successfully Mentored & or In-Progress:

Year: 2018-pr
Candidate: Brent Formosa
Citation: "Differential Expansion Microscopy & its Application to Human Skeletal Muscle Pathophysiology"
Degree: MS in Physiology, School of Medicine, Wayne State University

Year: 2020-2021
Candidate: Safa Mahbuba
Citation: "Cancer Detection and Overcoming Antibiotic Resistance Using Nanothermometry"
Degree: MS in BMS, School of Medicine, Wayne State University

Year: 2020
Candidate: Yunis Dahlai

Citation: “Reconstitution of Insulin-Secreting Porosomes Complex as a Viable Alternative to Islet Transplant”
Degree: MS in BMS, School of Medicine, Wayne State University

Year: 2018-2020
Candidate: Asiri Liyanaarachchi
Citation: “Differential Expansion: Quantifying Protein Loss with Optimized Expansion”
Degree: MS in Physiology, School of Medicine, Wayne State University

Year: 2019-2020
Candidate: Samantha Silvers
Citation: “Machine Learning Application for Differential Expansion Microscopy”
Degree: MS in BMS, School of Medicine, Wayne State University

Year: 2019-2021
Candidate: Maranda Saigh
Citation: “Differential Expansion Microscopy of Drosophila Neural Network”
Degree: MS in BMS, School of Medicine, Wayne State University

Year: 2019-2021
Candidate: Christina A. Minna
Citation: “Nanothermometry of Actin-Myosin-Ion Interactions”
Degree: MS in BMS, School of Medicine, Wayne State University

Year: 2019-2020
Candidate: Ranya Aziz
Citation: “Role of HSP70 on Insulin Secretion”
Degree: MS in BMS, School of Medicine, Wayne State University

Year: 2029-2021
Candidate: Katherine Thomashow
Citation: “Differential Expansion Microscopy of Rat Liver Tissue”
Degree: MS in BMS, School of Medicine, Wayne State University

Year: 2020-2021
Candidate: Kanwar Bhullar
Citation: “The application of machine learning and artificial intelligencein diagnostic medicine: A new frontier”
Degree: MS in BMS, School of Medicine, Wayne State University

Year: 2020-2021
Candidate: Megan Crawford
Citation: “The discovery and function of the porosome”

Degree: MS in BMS, School of Medicine, Wayne State University

Year: 2020-2021
Candidate: Tasneem Gaballah
Citation: “Mycobacterium Tuberculosis: The Art of Manipulating the Macrophage”
Degree: MS in BMS, School of Medicine, Wayne State University

Year: 2019
Candidate: Sherif Hussanein
Citation: “The Insulin-Secreting Beta Cell Porosome Proteins Implicated In Diabetes”
Degree: MS in BMS, School of Medicine, Wayne State University

Year: 2018-2019
Candidate: Rishika Pulvender
Citation: “Nanoscale thermometry”
Degree: MS from CMMG, School of Medicine, Wayne State University

Year: 2019
Candidate: Kathleen Jahnke
Citation: “The Neuronal Porosome Complex and Its Associated Proteins – Implications in Health, Disease and Neurological Disorders””
Degree: MS in BMS, School of Medicine, Wayne State University

Year: 2018
Candidate: Eric R. Kuhn
Citation: “Nanoscale thermometry”
Degree: MS in Physiology, School of Medicine, Wayne State University

Year: 2018
Candidate: Keith M. Kokotovich
Citation: “Immunocytochemistry in the study of cellular structure-function”
Degree: MS in Physiology, School of Medicine, Wayne State University

Year: 2009
Candidate: Zhui H. Chen
Citation: “Involvement of beta-adrenergic receptor in synaptic vesicle swelling and implication in neurotransmitter release”
Degree: MS in Physiology, School of Medicine, Wayne State University

Recent Master’s BMS Essay Reader/Co-Advisor:

Year: 2020-2021
Candidate: Sarban Singh
Citation: “Stress Granules and their Impacts on Neurodegenerative Diseases”
Degree: MS in BMS, School of Medicine, Wayne State University

Year: 2020-2021
Candidate: Rachael Rocktoff
Citation: “The Effects of Yoga on Physiology”
Degree: MS in BMS, School of Medicine, Wayne State University

Year: 2020-2021
Candidate: Martina Cholagh
Citation: “Vaginal microbiota and susceptibility to sexually transmitted infection”
Degree: MS in BMS, School of Medicine, Wayne State University

Year: 2020
Candidate: Shauna Treib
Citation: “Thalamocortical Loops and Psychedelic Drug Experiences”
Degree: MS in BMS, School of Medicine, Wayne State University

Year: 2020-2021
Candidate: Patric Chen
Citation: “Understanding Acute Cell Injury Through Nonlinear Dynamics”
Degree: MS in BMS, School of Medicine, Wayne State University

Year: 2019
Candidate: Neena Singhal
Citation: “Peroxiome-generated oxidative stress contributes to development of Type 2 diabetes”
Degree: MS in BMS, School of Medicine, Wayne State University

Year: 2019
Candidate: Natalie Hardy
Citation: “Thalamocortical Loops and Consciousness”
Degree: MS in BMS, School of Medicine, Wayne State University

Year: 2019
Candidate: Neena Singhal
Citation: “T Peroxisome-generated oxidative stress contributes to compromised beta cell integrity and Type 2 Diabetes”
Degree: MS in BMS, School of Medicine, Wayne State University

C. Recent Undergraduate Thesis Mentored:

Year: 2016-19
Candidate: Ranya Aziz
Citation: "The Impact of HSP70 on insulin secretion in Min6 cells"
Degree: BS Chemistry Honors, Wayne State University
Currently 1st Year BMS Student WSU SOM]

Year: 2014-19
Candidate: Nikhil Yedulla
Citation: "Valproate inhibits gluose-stimulated insulin secretion in beta cells"
Degree: BS Biology Honors, Wayne State University
Currently 1st Year MD Student WSU SOM]

Year: 2014-16
Candidate: Sanjana Kulkarni
Citation: "Porosome-mediated insulin secreting from beta cells"
Degree: BS Psychology Honors, Wayne State University
[Currently 4th Year MD Student WSU SOM]

Year: 2014-15
Candidate: Amulya Rajgopal
Citation: "Proteome of the insulin-secreting Min6 cell porosome complex: Involvement of Hsp90 in its assembly and function"
Degree: BS Biophysics Honors, Wayne State University
[Currently doing Residency at Henery Ford after MD degree from WSU SOM]

D. Recent Post-Doctoral Fellows [4 Fellows]:

1. **Meishan Li, Ph.D**. [2017, **Supported by Karolinska Visiting Scholar Fel Nino Kotaria, Ph.D**.
2. **Suvra S. Laha, Ph.D**. [2015-2016 **K99 Grant submitted;** and **1 research papers completed and published**].
3. **Nino Kotaria, Ph.D**. [2010-2011**; Supported by Georgian National Science Foundation**].
4. **Vera Okuneva, Ph.D**. [2011-2012**; Supported by Georgian National Science Foundation**].

E. Recent Graduate Students [38 students]:

1. **Akshata Naik** (Physiology Ph.D. Student, 2015-19) [**12 research papers published, once recipient of Dept. of Physiology Graduate Student Research Award**]

2. **Kenneth Lewis** (Physiology Ph.D. Student, 2013-17) [**12 research papers published; twice recipient of Dept. of Physiology Graduate Student Research Award**]

3. **Sebistian Parnel** (MD2, Ph.D. Student, 2018-pr) [**3 research papers published**]

4. **Rafael Ramos** (MD2, Ph.D. Student, 2018-pr) [**1 research papers published**]

5. **Samia Jaffar** (MD2 Student, 2018-19)

6. **Kathleen George** (MD3 Student, 2018-20) [**1 research papers published**]

7. **Rishika Pulvender** (MS, BMS Student, 2018-19) [**PSL7996 research**] [**2 research papers published**]

8. **Asiri Liyanaarachchi** (MS Physiology Student, 2018-pr) [**PSL7996 research**] [**2 research papers published**]

9. **Brent Formosa** (MS Physiology Student, 2018-pr) [**PSL7996 research**] [**3 research papers published**]

10. **Katherine Thomashow** (MS, BMS Student, 2018-19) [**PSL7996 research**]

11. **Samantha Silvers** (MS, BMS Student, 2018-2021) [**PSL7996 research**]

12. **Maranda Saigh** (MS, BMS Student, 2019-2021) [**PSL7996 research**]

13. **Christina A. Minna** (MS, BMS Student, 2019-2021) [**PSL7996 research**]

14. **Ranya Aziz** (MS, BMS Student, 2019-2020) [**PSL7996 research**]

15. **Megan Crawford** (MS, BMS Student, 2019-2021)

16. **Kathleen Jahnke** (MS, BMS Student, 2018-19) [**PSL7996 research**]

17. **Yunis Dhalai** (MS, BMS Student, 2020-2021)

18. **Safa Mahbuba** (MS, BMS Student, 2020-2021)

19. **Maheshika Perera**, Physics Ph.D. candidate (2011-2016) **[2 research papers**

published & Recipient of the Summer 2016 Dissertation Fellowship; Graduated Aug. 2016].

20. **Suvra Laha**, Physics Ph.D. candidate (2012-15) **[6 research papers published & Recipient of the Summer 2015 Dissertation Fellowship; Graduated Aug. 2015].**

21. **Sherif Hassanien** (MS Student, 2015-16) [**PSL7996 research**]

22. **Eric Kuhn** (MS Physiology Student, 2016-2018) [**PSL7996 research**] [**3 research papers published, Received Dept. of Physiology Graduate Student Research Award, Received 3rd Prize in the 2018 Wayne State University Graduate & Postdoctoral Research Symposium.**]

23. **Kathleen Kolinko** (MS Student, 2016-19) [**PSL7996 research &** BMS Essay, 2019]

24. **Keith Kokotovich** (MS Physiology Student, 2016-18) [**PSL7996 research**]

25. **Bharat Kotha** (MS Student, 2016-17) [**PSL7996 research**]

26. **Monazza Shahab** (Ph.D. Physiology Student 2nd Rotation, 2018 Winter)

27. **Dennis Smythe** (BMS Essay, 2018)

28. **Sherif Hassanein** (BMS Essay, 2018)

29. **Stephanie Gladyck** (Co-Mentoring CMMG Ph.D. Student with Prof. Lawrence Grossman, 2017-pr) **[Received Dept. of Physiology Graduate Student Research Award, Received 1st Prize in the 2018 Wayne State University Graduate & Postdoctoral Research Symposium.**]

30. **Jhenjie Liu** (Committee Member for Ph.D. Physiology Student with Prof. Zhengqing Hu, 2017-pr).

31. **Umit Ozer** (Committee Member for Ph.D. Chemical Engineering Student with Prof. Jeffrey Potoff, 2017-2020).
32. **Tasneem Gaballah** (BMS Essay, 2020-2021)
33. **Shauna Treib** (BMS Essay, 2020-2021)
34. **Safa Mahbuba** (BMS Essay, 2020-2021)
35. **Sarban Singh** (BMS Essay, 2020-2021)
36. **Rachael Rocktoff** (BMS Essay, 2020-2021)
37. **Kanwar Bhullar** (BMS Essay, 2020-2021)
38. **Martina Cholagh** (BMS Essay, 2020-2021)

F. Recent Medical Students [9 students]:

1. **Steven Mekaru** (MD3. Student, 2015-16) [**Review papers**]

2. **Amulya Rajgopal** (MD4 Student, 2015-pr) [**Ongoing Research Project since Year 1**]

3. **Leah Shin** (4th year MD. Student, 2015-16) [**Research Project**]

4. **Leah Shin** (Beaumont Hospital Resident, 2017-20) [**Ongoing Research Project**]

5. **Michel Zhao** (MD1 Student, 2017) [**Honors Prospectus**]

6. **Kathleen George** (MD1 Student, 2018-20) [**Research Project**] [**1 research papers published**]

7. **Sebistian Parnel** (MD, Ph.D. Student, 2018-pr) [**3 research papers published**]

8. **Rafael Ramos** (MD, Ph.D. Student, 2018-pr) [**1 research papers published**]

9. **Samia Jaffar** (MD Student, 2018-pr)

G. Recent Undergraduate Students [9 students]:

1. Nikhil Reddy Yedulla (Med Start Freshman) (2015-2018)
(a) Title of Research: Role of Valporate on insulin secretion in Min6 cells.
(b) Received the prestigious **2018 Amgen Scholar Award** to work with my collaborator at Harvard Medical School.
(c) Received **1st Place** in the 2018 Wayne State Undergraduate Research Fair.
(d) One **1st author** research paper published.

2. Sanjana Kulkarni (Senior; 2012-2016): Molecular mechanism of porosome-mediated insulin secretion.
a. Two research papers published.
b. Senior Thesis (Honors Directed Study in Psychology/PSY4991): "Hsp70 in the assembly and function of the Min6 cell porosome complex", implication in neurological disorders, learning and memory.
c. 2015 WSU Undergraduate Research Day, Best Poster Award.
-Selected for Poster Presentation at the 2016 NCUR North Carolina Conference: Insulin Secretion in Min6 Cells Reconstituted with the Porosome Complex.
d. PSL5010: Title of Research & Presentation: Insulin Secretion in MIN-6 Cells

Reconstituted with the Porosome Complex (2015; secured A in presentation)
e. Selected for Poster Presentation at the 2015 NCUR Kentucky Conference: Molecular mechanism of regulated insulin release from □-cells.
f. Selected for Poster Presentation at the 2014 NCUR Washington, D.C. Conference: Insulin Secretion in MIN-6 Cells Reconstituted with the Porosome Complex.
g. PSL5010: Title of Research & Presentation: Insulin Secretion in MIN-6 Cells (2014; secured A in presentation)

3. Amulya Rajgopal (Senior) (2013-2015)
a. One research papers published.
b. PSL5010: Title of Research & Presentation: The role of chaperonins in the assembly of Porosome in insulin secreting Min6 cells (secured A in presentation)
Poster Presentation: WSU Department of Physics, Undergraduate Research Conference Received the 2014 ***"George B. & Eveline R. Beard Endowed Student Prize"***
c. Selected for Poster Presentation at the NCUR Kentucky Conference : Molecular mechanism of regulated insulin release from □-cells.
d. Selected for Poster Presentation at the NCUR Washington, D.C. Conference : "Proteome of the insulin-secreting Min6 cell porosome complex: Involvement of Hsp90 in its assembly and function"
e. Senior Thesis: "Implication of Hsp90 in the assembly and function of the Min6 cell porosome complex"

4. Malek Ghandour (Senior) (2014-2016)
-PSL5010: Title of Research & Presentation: Half a century of total and transient membrane fusion: A paradigm-shift in our understanding of the process (2015; secured A in presentation)
-PSL5010: Title of Research & Presentation: Protein-Protein Interactions Within the Neuronal Porosome Complex (2014; secured A in presentation).

5. Samia Mazumdar (Junior) (2015-2016)
(a) PSL5010: Title of Research & Presentation: Role of membrane composition in membrane biogenesis.
(b) PSL5010: Title of Research & Presentation: Role of membrane curvature on lipid recruitment following membrane stretch (2015; secured A in presentation)

6. Alina Safikova (Pre-med Freshman) (2015-2018)
(a) PSL5010: Title of Research & Presentation: Effect of valproate on insulin secretion in Min6 cells.

7. Brandon Laethem (Senior) (2014-2015)
(a) Title of Research: CFTR Channel in Mucin Secretion from Human Airways Epithelial Cell Line Calu-3.
(b) Participated in the SURF Program and conducted studies on "Role of CFTR Channel in Mucin Secretion from Human Airways Epithelial Cell Line Calu-3". [**A manuscript is in preparation from this study**].

8. Palak Joshi (Med Start Freshman) (2017-2017)
(a) Title of Research: Role of heterotrimeric GTP-binding proteins on insulin secretory granules.

9. Ranya Aziz (Junior & Senior Years) (2016-2018)
PSL5010: Title of Research & Presentation: HSP70 on Insulin Secretion from Min6 Cells.

10. Heather Durfee (Freshman) (2020-pr) Title of Research: Study of platelets using expansion microscopy.

H. Recent High School Students [5 students]:

1. Naveen Karthik (Senior; 2014): CFTR Project Using Calu-3 Cells.
a. Finalist in the SIEMENS Competition in Math, Science & Technology.
b. Currently attending Medical School at Case Western University

2. Cara Skrzycki (Senior; 2014): Iron oxide nanoparticles for therapeutic applications.
a. Received admission to Yale University and University of Michigan.
b. Currently pursuing BS at the University of Michigan

3. Alina Shafikova (Senior; 2014): Iron oxide nanoparticles for therapeutic applications.
a. Wayne State University Pre-Med Student.
b. Currently working in the Jena Lab. in Physiology at WSU.

4. Priyanka G. Pulvender (Senior; 2017-18): Nano thermometry.
a. Genes in Space Award Finalist (NASA).
b. Participated in Detroit Science Fair

5. Renee Liu (Senior; 2018-19): Skeletal Muscle Physiology.
a. Participated in Detroit Science Fair
b. Admitted to John's Hopkins University

5. Arya Gowda (Sophomore, Northville High School; 2020-2021): AI & Deep Learning in Disease Detection.
a. Participated in 2020-2021 Detroit Science Fair & Won the "Green Award"

H. Recent Doctoral Program Thesis Committee Member (WSU)

1. **Jason Mick**, Ph.D. candidate Chemical Engineering & Material Sciences (2011-2016) Successfully defended.

2. **Haihui Wang**, Ph.D. candidate Physiology (2011-2014) Successfully defended.

3. **Abir Maarouf**, Ph.D. candidate Physics (2013-2018) Successfully defended.

4. **William Close**, Ph.D. candidate Immunology (2014-2017) Successfully defended.

5. **Olesya Plazyo**, Ph.D. candidate Ob Gyn (2014-2016) Successfully defended.

6. **Stephanie Gladyck** (Co-Mentoring CMMG Ph.D. Student with Prof. Lawrence Grossman, 2016-pr)

7. **Carthic Rajagopalan** (Ph.D. Thesis Committee Member, Physiology, Student with Prof. Xuequn Chen & Fei Sun, 2017-19) Successfully defended.

8. **Farhan Chaudhury** (MD Ph.D., Thesis Committee 2018-pr)

9. **Jhenjie Liu** (Ph.D. Thesis Committee Member 2018-pr)

Other Mentored Trainees and Faculty:

1995-1997 **E-H Jeong, MD**
Professor & Physician, S. Korea
Research Associate, Jena Lab., Yale University School of Medicine
Publications:
1. The native membrane fusion machinery in cells.
Jeong EH, Webster P, Khuong CQ, Abdus Sattar AK, Satchi M, Jena BP.
Cell Biol Int. 1998;22(9-10):657-70.
PMID: 10452836

2. Aquaporin 1 regulates GTP-induced rapid gating of water in secretory vesicles.
Cho SJ, Sattar AK, **Jeong EH**, Satchi M, Cho JA, Dash S, Mayes MS, Stromer MH, Jena BP.
Proc Natl Acad Sci U S A. 2002 Apr 2;99(7):4720-4.

Erratum in: Proc Natl Acad Sci U S A 2002 Oct 1;99(20):13357.
PMID: 11917120

1995-1997 **S. W. Schneider, MD.**
Professor & Physician, University of Hamburg, Germany
Research Associate, Jena & Geibel Lab., Yale University School of Medicine
Publications:
1. Surface dynamics in living acinar cells imaged by atomic force microscopy: identification of plasma membrane structures involved in exocytosis. **Schneider SW**, Sritharan KC, Geibel JP, Oberleithner H, Jena BP. Proc Natl Acad Sci U S A. 1997 Jan 7;94(1):316-21.
PMID: 8990206

2. Gi regulation of secretory vesicle swelling examined by atomic force microscopy.
Jena BP, **Schneider SW**, Geibel JP, Webster P, Oberleithner H, Sritharan KC.
Proc Natl Acad Sci U S A. 1997 Nov 25;94(24):13317-22.
PMID: 9371843

3. Rapid aldosterone-induced cell volume increase of endothelial cells measured by the atomic force microscope.
Schneider SW, Yano Y, Sumpio BE, Jena BP, Geibel JP, Gekle M, Oberleithner H.
Cell Biol Int. 1997 Nov;21(11):759-68.
PMID: 9768474

4. Continuous detection of extracellular ATP on living cells by using atomic force microscopy.
Schneider SW, Egan ME, Jena BP, Guggino WB, Oberleithner H, Geibel JP.
Proc Natl Acad Sci U S A. 1999 Oct 12;96(21):12180-5.
PMID: 10518596

1996-1997 **G. Aspelund, MD.**
Assistant Professor & Physician, Surgery, Columbia University
Research Associate, Jena & Andersen Lab., Yale University School of Medicine
Publications:
1. Impaired hepatocyte glucose transport protein (GLUT2) internalization in chronic pancreatitis. Nathan JD, Zdankiewicz PD, Wang J, Spector SA, **Aspelund G**, Jena BP, Seymour NE, Geibel JP, Andersen DK. Pancreas. 2001 Mar;22(2):172-8. PMID: 11249072

1996-1998 **M. R. Satchi, MD.**
Physician, NY

Research Associate, Jena Lab., Yale University School of Medicine
Publications:
1. The native membrane fusion machinery in cells.
Jeong EH, Webster P, Khuong CQ, Abdus Sattar AK, **Satchi M**, Jena BP.
Cell Biol Int. 1998;22(9-10):657-70.
PMID: 10452836

2. Aquaporin 1 regulates GTP-induced rapid gating of water in secretory vesicles.
Cho SJ, Sattar AK, Jeong EH, **Satchi M**, Cho JA, Dash S, Mayes MS, Stromer MH, Jena BP.
Proc Natl Acad Sci U S A. 2002 Apr 2;99(7):4720-4.
Erratum in: Proc Natl Acad Sci U S A 2002 Oct 1;99(20):13357.
PMID: 11917120

1998-2000 **A.V. Maker, MD.**
Associate Professor & Physician, Surgery, UIC
Research Associate, Jena & Andersen Lab., Yale University School of Medicine
Publications:
1. Insulin receptor (IR) and glucose transporter 2 (GLUT2) proteins form a complex on the rat hepatocyte membrane.
Eisenberg ML, **Maker AV**, Slezak LA, Nathan JD, Sritharan KC, Jena BP, Geibel JP, Andersen DK.
Cell Physiol Biochem. 2005;15(1-4):51-8.
PMID: 15665515

1997-1999
J.D. Nathan, MD.
Physician, Surgery, Cincinnati Children Hospital, OH
Research Assistant, Jena & Andersen Lab., Yale University School of Medicine
Publications:
1. Impaired hepatocyte glucose transport protein (GLUT2) internalization in chronic pancreatitis. **Nathan JD**, Zdankiewicz PD, Wang J, Spector SA, Aspelund G, Jena BP, Seymour NE, Geibel JP, Andersen DK. Pancreas. 2001 Mar;22(2):172-8. PMID: 11249072

2. Insulin receptor (IR) and glucose transporter 2 (GLUT2) proteins form a complex on the rat hepatocyte membrane.
Eisenberg ML, Maker AV, Slezak LA, **Nathan JD**, Sritharan KC, Jena BP, Geibel JP, Andersen DK.
Cell Physiol Biochem. 2005;15(1-4):51-8.
PMID: 15665515

1998-2000
L.A. Slezak, MD.
Physician, Surgery, Tampa, FL
Research Associate, Jena & Andersen Lab., Yale University School of Medicine

Publications:
1. Insulin receptor (IR) and glucose transporter 2 (GLUT2) proteins form a complex on the rat hepatocyte membrane.
Eisenberg ML, Maker AV, **Slezak LA**, Nathan JD, Sritharan KC, Jena BP, Geibel JP, Andersen DK.
Cell Physiol Biochem. 2005;15(1-4):51-8.
PMID: 15665515

2001-2002

R. Bonipally, Ph.D.
Senior Scientist, Forest Research Institute, NJ
Research Associate, Jena Lab., Wayne State University School of Medicine
Publications:
1. G(alpha)(i3) in pancreatic zymogen granules participates in vesicular fusion.
Sattar AA, **Boinpally R**, Stromer MH, Jena BP.
J Biochem. 2002 Jun;131(6):815-20.
PMID: 12038977

1998-2002

A.K.M Sattar, Ph.D.
Assistant Professor, Wayne State University
Research Associate/Research Assistant Professor, Jena Lab., Yale University & Wayne State University School of Medicine
Publications:
1. The native membrane fusion machinery in cells.
Jeong EH, Webster P, Khuong CQ, **Abdus Sattar AK**, Satchi M, Jena BP.
Cell Biol Int. 1998;22(9-10):657-70.
PMID: 10452836

2. Aquaporin 1 regulates GTP-induced rapid gating of water in secretory vesicles.
Cho SJ, **Sattar AK**, Jeong EH, Satchi M, Cho JA, Dash S, Mayes MS, Stromer MH, Jena BP.
Proc Natl Acad Sci U S A. 2002 Apr 2;99(7):4720-4.
Erratum in: Proc Natl Acad Sci U S A 2002 Oct 1;99(20):13357.
PMID: 11917120

3. G(alpha)(i3) in pancreatic zymogen granules participates in vesicular fusion.
Sattar AA, Boinpally R, Stromer MH, Jena BP.
J Biochem. 2002 Jun;131(6):815-20.
PMID: 12038977

2000-2004

S.J. Cho, Ph.D.
Chief Scientist, Park Systems Corporation, S. Korea

Postdoctoral Fellow, Jena Lab., Wayne State University School of Medicine
Publications:

1. Aquaporin 1 regulates GTP-induced rapid gating of water in secretory vesicles.
Cho SJ, Sattar AK, Jeong EH, Satchi M, Cho JA, Dash S, Mayes MS, Stromer MH, Jena BP.
Proc Natl Acad Sci U S A. 2002 Apr 2;99(7):4720-4.
Erratum in: Proc Natl Acad Sci U S A 2002 Oct 1;99(20):13357.
PMID: 11917120

2. Structure and dynamics of the fusion pores in live GH-secreting cells revealed using atomic force microscopy.
Cho SJ, Jeftinija K, Glavaski A, Jeftinija S, Jena BP, Anderson LL.
Endocrinology. 2002 Mar;143(3):1144-8.
PMID: 11861542

3. Structure and dynamics of the fusion pore in live cells.
Cho SJ, Quinn AS, Stromer MH, Dash S, Cho J, Taatjes DJ, Jena BP.
Cell Biol Int. 2002;26(1):35-42.
PMID: 11779219

4. The atomic force microscope in the study of membrane fusion and exocytosis.
Jena BP, **Cho SJ.**
Methods Cell Biol. 2002;68:33-50. No abstract available.
PMID: 12053737

5. SNAREs in opposing bilayers interact in a circular array to form conducting pores.
Cho SJ, Kelly M, Rognlien KT, Cho JA, Hörber JK, Jena BP.
Biophys J. 2002 Nov;83(5):2522-7.
PMID: 12414686

6. New structure involved in transient membrane fusion and exocytosis.
Cho SJ, Wakade A, Pappas GD, Jena BP.
Ann N Y Acad Sci. 2002 Oct;971: 254-6. Review.
PMID: 12438127

7. Structure and composition of the fusion pore.
Jena BP, **Cho SJ**, Jeremic A, Stromer MH, Abu-Hamdah R.
Biophys J. 2003 Feb;84(2 Pt 1):1337-43.
PMID: 12547814

8. Reconstituted fusion pore.
Jeremic A, Kelly M, **Cho SJ**, Stromer MH, Jena BP.
Biophys J. 2003 Sep;85(3):2035-43.
PMID: 12944316

9. Regulation of the water channel aquaporin-1: isolation and reconstitution of the regulatory complex.
Abu-Hamdah R, Cho WJ, **Cho SJ**, Jeremic A, Kelly M, Ilie AE, Jena BP.
Cell Biol Int. 2004;28(1):7-17.
PMID: 14759764

10. Calcium drives fusion of SNARE-apposed bilayers.
Jeremic A, Kelly M, Cho JA, **Cho SJ**, Horber JK, Jena BP.
Cell Biol Int. 2004;28(1):19-31.
PMID: 14759765

11. Addendum to "Regulation of the water channel aquaporin-1: isolation and reconstitution of the regulatory complex" [Cell Biol. Int. 2004(1):7-17].
Abu-Hamdah R, Cho WJ, **Cho SJ**, Jeremic A, Kelly M, Ilie AE, Jena BP.
Cell Biol Int. 2004;28(5):421. No abstract available.
PMID: 15270024

12. Patch clamped single pancreatic zymogen granules: direct measurements of ion channel activities at the granule membrane.
Kelly ML, Abu-Hamdah R, Jeremic A, **Cho SJ**, Ilie AE, Jena BP.
Pancreatology. 2005;5(4-5):443-9.
PMID: 15985770

13. Secretory vesicle swelling by atomic force microscopy.
Cho SJ, Jena BP.
Methods Mol Biol. 2006;319:317-30.
PMID: 16719363

2001-2006

J.K. Hörber, Ph.D.
Professor, University of Bristol, UK
Research Professor, Physiology, Wayne State University School of Medicine
Publications:
1. SNAREs in opposing bilayers interact in a circular array to form conducting pores.
Cho SJ, Kelly M, Rognlien KT, Cho JA, **Hörber JK**, Jena BP.
Biophys J. 2002 Nov;83(5):2522-7.
PMID: 12414686

2. Calcium drives fusion of SNARE-apposed bilayers.
Jeremic A, Kelly M, Cho JA, Cho SJ, **Hörber JK**, Jena BP.
Cell Biol Int. 2004;28(1):19-31.
PMID: 14759765

3. Secretory vesicles in live cells are not free-floating but tethered to filamentous structures: a study using photonic force microscopy.
Abu-Hamdah R, Cho WJ, **Hörber JK**, Jena BP.
Ultramicroscopy. 2006 Jun-Jul;106(8-9):670-3.

PMID: 16713090

2001-2003

S. Dash, Ph.D.
Scientist, Iowa State University
Research Associate, Jena Lab., Wayne State University School of Medicine
Publications:
1. Aquaporin 1 regulates GTP-induced rapid gating of water in secretory vesicles.
Cho SJ, Sattar AK, Jeong EH, Satchi M, Cho JA, **Dash S**, Mayes MS, Stromer MH, Jena BP.
Proc Natl Acad Sci U S A. 2002 Apr 2;99(7):4720-4.
Erratum in: Proc Natl Acad Sci U S A 2002 Oct 1;99(20):13357.
PMID: 11917120

2. Structure and dynamics of the fusion pore in live cells.
Cho SJ, Quinn AS, Stromer MH, **Dash S**, Cho J, Taatjes DJ, Jena BP.
Cell Biol Int. 2002;26(1):35-42.
PMID: 11779219

2002-2005

M.L. Kelly, Ph.D.
Associate Professor, Ball State University
Research Associate, Jena Lab., Wayne State University School of Medicine
Publications:
1. SNAREs in opposing bilayers interact in a circular array to form conducting pores.
Cho SJ, **Kelly M**, Rognlien KT, Cho JA, Hörber JK, Jena BP.
Biophys J. 2002 Nov;83(5):2522-7.
PMID: 12414686

2. Reconstituted fusion pore.
Jeremic A, **Kelly M**, Cho SJ, Stromer MH, Jena BP.
Biophys J. 2003 Sep;85(3):2035-43.
PMID: 12944316

3. Regulation of the water channel aquaporin-1: isolation and reconstitution of the regulatory complex.
Abu-Hamdah R, Cho WJ, Cho SJ, Jeremic A, **Kelly M**, Ilie AE, Jena BP.
Cell Biol Int. 2004;28(1):7-17.
PMID: 14759764

4. Calcium drives fusion of SNARE-apposed bilayers.
Jeremic A, **Kelly M**, Cho JA, Cho SJ, Horber JK, Jena BP.
Cell Biol Int. 2004;28(1):19-31.
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5. Addendum to "Regulation of the water channel aquaporin-1: isolation

and reconstitution of the regulatory complex" [Cell Biol. Int. 2004(1):7-17].
Abu-Hamdah R, Cho WJ, Cho SJ, Jeremic A, **Kelly M**, Ilie AE, Jena BP.
Cell Biol Int. 2004;28(5):421. No abstract available.
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6. Vesicle swelling regulates content expulsion during secretion.
Kelly ML, Cho WJ, Jeremic A, Abu-Hamdah R, Jena BP.
Cell Biol Int. 2004;28(10):709-16.
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7. Patch clamped single pancreatic zymogen granules: direct measurements of ion channel activities at the granule membrane.
Kelly ML, Abu-Hamdah R, Jeremic A, Cho SJ, Ilie AE, Jena BP.
Pancreatology. 2005;5(4-5):443-9.
PMID: 15985770

2002-2006

A. Jeremic, Ph.D.
Associate Professor, George Washington University
Postdoctoral Fellow, Jena Lab., Wayne State University School of Medicine
Publications:

1. Reconstituted fusion pore.
Jeremic A, Kelly M, Cho SJ, Stromer MH, Jena BP.
Biophys J. 2003 Sep;85(3):2035-43.
PMID: 12944316

2. Regulation of the water channel aquaporin-1: isolation and reconstitution of the regulatory complex.
Abu-Hamdah R, Cho WJ, Cho SJ, **Jeremic A**, Kelly M, Ilie AE, Jena BP.
Cell Biol Int. 2004;28(1):7-17.
PMID: 14759764

3. Calcium drives fusion of SNARE-apposed bilayers.
Jeremic A, Kelly M, Cho JA, Cho SJ, Horber JK, Jena BP.
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6. Patch clamped single pancreatic zymogen granules: direct measurements of ion channel activities at the granule membrane.
Kelly ML, Abu-Hamdah R, **Jeremic A**, Cho SJ, Ilie AE, Jena BP.
Pancreatology. 2005;5(4-5):443-9.
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7. Involvement of water channels in synaptic vesicle swelling.
Jeremic A, Cho WJ, Jena BP.
Exp Biol Med (Maywood). 2005 Oct;230(9):674-80.
PMID: 16179736

8. Size of supramolecular SNARE complex: membrane-directed self-assembly.
Cho WJ, **Jeremic A**, Jena BP.
J Am Chem Soc. 2005 Jul 27;127(29):10156-7.
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9. Cholesterol is critical to the integrity of neuronal porosome/fusion pore.
Jeremic A, Jin Cho W, Jena BP.
Ultramicroscopy. 2006 Jun-Jul;106(8-9):674-7.
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10. Energy-dependent disassembly of self-assembled SNARE complex: observation at nanometer resolution using atomic force microscopy.
Jeremic A, Quinn AS, Cho WJ, Taatjes DJ, Jena BP.
J Am Chem Soc. 2006 Jan 11;128(1):26-7.
PMID: 16390104

11. Neuronal fusion pore assembly requires membrane cholesterol.
Cho WJ, **Jeremic A**, Jin H, Ren G, Jena BP.
Cell Biol Int. 2007 Nov;31(11):1301-8.
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12. Nano-scale imaging and dynamics of amylin-membrane interactions and its implication in type II diabetes mellitus.
Cho WJ, Jena BP, **Jeremic A**.
Methods Cell Biol. 2008;90:267-86. doi: 10.1016/S0091-679X(08)00813-3.
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13. Involvement of vH(+)-ATPase in synaptic vesicle swelling.
Shin L, Basi N, **Jeremic A**, Lee JS, Cho WJ, Chen Z, Abu-Hamdah R, Oupicky D, Jena BP.
J Neurosci Res. 2010 Jan;88(1):95-101. doi: 10.1002/jnr.22180.
PMID: 19610106

14. 3D organization and function of the cell: Golgi budding and vesicle biogenesis to docking at the porosome complex.

Wang S, Lee JS, Bishop N, **Jeremic A**, Cho WJ, Chen X, Mao G, Taatjes DJ, Jena BP.
Histochem Cell Biol. 2012 Jun;137(6):703-18. doi: 10.1007/s00418-012-0948-x.
PMID: 22527693

2004-2009

W-J. Cho, Ph.D.
Scientist, Wayne State University
Research Associate, Jena Lab., Wayne State University School of Medicine
Publications:

1. Regulation of the water channel aquaporin-1: isolation and reconstitution of the regulatory complex.
Abu-Hamdah R, **Cho WJ**, Cho SJ, Jeremic A, Kelly M, Ilie AE, Jena BP.
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2. Addendum to "Regulation of the water channel aquaporin-1: isolation and reconstitution of the regulatory complex" [Cell Biol. Int. 2004(1):7-17].
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3. Vesicle swelling regulates content expulsion during secretion.
Kelly ML, **Cho WJ**, Jeremic A, Abu-Hamdah R, Jena BP.
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Cho WJ, Jeremic A, Jena BP.
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7. Secretory vesicles in live cells are not free-floating but tethered to filamentous structures: a study using photonic force microscopy.
Abu-Hamdah R, **Cho WJ**, Hörber JK, Jena BP.

Ultramicroscopy. 2006 Jun-Jul;106(8-9):670-3.
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8. Energy-dependent disassembly of self-assembled SNARE complex: observation at nanometer resolution using atomic force microscopy.
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11. EM 3D contour maps provide protein assembly at the nanoscale within the neuronal porosome complex.
Cho WJ, Ren G, Jena BP.
J Microsc. 2008 Oct;232(1):106-11. doi: 10.1111/j.1365-2818.2008.02088.x.
PMID: 19017207

12. Circular dichroism (CD) spectroscopy of the assembly and disassembly of SNAREs: The proteins involved in membrane fusion in cells.
Cook JD, **Cho WJ**, Stemmler TL, Jena BP.
Chem Phys Lett. 2008 Sep 1;462(1-3):6-9.
PMID: 19412345

13. Porosome in astrocytes.
Lee JS, **Cho WJ**, Jeftinija K, Jeftinija S, Jena BP.
J Cell Mol Med. 2009 Feb;13(2):365-72. doi: 10.1111/j.1582-4934.2008.00334.x.
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14. Structure of membrane-associated neuronal SNARE complex: implication in neurotransmitter release.
Cho WJ, Shin L, Ren G, Jena BP.
J Cell Mol Med. 2009 Oct;13(10):4161-5. doi: 10.1111/j.1582-4934.2009.00895.x.
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15. Nanoscale 3D contour map of protein assembly within the astrocyte porosome complex.

Cho WJ, Ren G, Lee JS, Jeftinija K, Jeftinija S, Jena BP.
Cell Biol Int. 2009 Feb;33(2):224-9. doi: 10.1016/j.cellbi.2008.11.008.
PMID: 19084606

16. Involvement of cholesterol in synaptic vesicle swelling.
Lee JS, **Cho WJ**, Shin L, Jena BP.
Exp Biol Med (Maywood). 2010 Apr;235(4):470-7. doi: 10.1258/ebm.2010.009259.
PMID: 20407079

17. Membrane lipids influence protein complex assembly-disassembly.
Shin L, **Cho WJ**, Cook JD, Stemmler TL, Jena BP.
J Am Chem Soc. 2010 Apr 28;132(16):5596-7. doi: 10.1021/ja101574d.
PMID: 20373736

18. Conformation states of the neuronal porosome complex.
Cho WJ, Lee JS, Jena BP.
Cell Biol Int. 2010 Nov;34(11):1129-32. doi: 10.1042/CBI20100510.
PMID: 20939833

19. Involvement of vH(+)-ATPase in synaptic vesicle swelling.
Shin L, Basi N, Jeremic A, Lee JS, **Cho WJ**, Chen Z, Abu-Hamdah R, Oupicky D, Jena BP.
J Neurosci Res. 2010 Jan;88(1):95-101. doi: 10.1002/jnr.22180.
PMID: 19610106

20. Involvement of β-adrenergic receptor in synaptic vesicle swelling and implication in neurotransmitter release.
Chen ZH, Lee JS, Shin L, **Cho WJ**, Jena BP.
J Cell Mol Med. 2011 Mar;15(3):572-6. doi: 10.1111/j.1582-4934.2010.01026.x.
PMID: 20132410

21. Membrane-directed molecular assembly of the neuronal SNARE complex.
Cho WJ, Lee JS, Zhang L, Ren G, Shin L, Manke CW, Potoff J, Kotaria N, Zhvania MG, Jena BP.
J Cell Mol Med. 2011 Jan;15(1):31-7. doi: 10.1111/j.1582-4934.2010.01152.x.
PMID: 20716122

22. 3D organization and function of the cell: Golgi budding and vesicle biogenesis to docking at the porosome complex.
Wang S, Lee JS, Bishop N, Jeremic A, **Cho WJ**, Chen X, Mao G, Taatjes DJ, Jena BP.
Histochem Cell Biol. 2012 Jun;137(6):703-18. doi: 10.1007/s00418-012-0948-x.
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23. Aquaporin-assisted and ER-mediated mitochondrial fission: a hypothesis.
Lee JS, Hou X, Bishop N, Wang S, Flack A, **Cho WJ**, Chen X, Mao G, Taatjes DJ, Sun F, Zhang K, Jena BP.
Micron. 2013 Apr;47:50-8. doi: 10.1016/j.micron.2013.01.005.
PMID: 23416165

24. X-ray solution structure of the native neuronal porosome-synaptic vesicle complex: Implication in neurotransmitter release.
Kovari LC, Brunzelle JS, Lewis KT, **Cho WJ**, Lee JS, Taatjes DJ, Jena BP.
Micron. 2014 Jan;56:37-43. doi: 10.1016/j.micron.2013.10.002.
PMID: 24176623

2007-2010 **J-S. Lee, Ph.D.**
Sr. Research Associate, UT Southwestern Medical Center
Postdoctoral Fellow, Jena Lab., Wayne State University School of Medicine
Publications:

1. Porosome in astrocytes.
Lee JS, Cho WJ, Jeftinija K, Jeftinija S, Jena BP.
J Cell Mol Med. 2009 Feb;13(2):365-72. doi: 10.1111/j.1582-4934.2008.00334.x.
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2. Nanoscale 3D contour map of protein assembly within the astrocyte porosome complex.
Cho WJ, Ren G, **Lee JS**, Jeftinija K, Jeftinija S, Jena BP.
Cell Biol Int. 2009 Feb;33(2):224-9. doi: 10.1016/j.cellbi.2008.11.008.
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3. Involvement of cholesterol in synaptic vesicle swelling.
Lee JS, Cho WJ, Shin L, Jena BP.
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4. Conformation states of the neuronal porosome complex.
Cho WJ, **Lee JS**, Jena BP.
Cell Biol Int. 2010 Nov;34(11):1129-32. doi: 10.1042/CBI20100510.
PMID: 20939833

5. Involvement of vH(+)-ATPase in synaptic vesicle swelling.
Shin L, Basi N, Jeremic A, **Lee JS**, Cho WJ, Chen Z, Abu-Hamdah R, Oupicky D, Jena BP.
J Neurosci Res. 2010 Jan;88(1):95-101. doi: 10.1002/jnr.22180.
PMID: 19610106

6. Involvement of β-adrenergic receptor in synaptic vesicle swelling and implication in neurotransmitter release.
Chen ZH, **Lee JS**, Shin L, Cho WJ, Jena BP.
J Cell Mol Med. 2011 Mar;15(3):572-6. doi: 10.1111/j.1582-4934.2010.01026.x.
PMID: 20132410

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Cho WJ, **Lee JS**, Zhang L, Ren G, Shin L, Manke CW, Potoff J, Kotaria N, Zhvania MG, Jena BP.
J Cell Mol Med. 2011 Jan;15(1):31-7. doi: 10.1111/j.1582-4934.2010.01152.x.
PMID: 20716122

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Histochem Cell Biol. 2012 Jun;137(6):703-18. doi: 10.1007/s00418-012-0948-x.
PMID: 22527693

9. Aquaporin-assisted and ER-mediated mitochondrial fission: a hypothesis.
Lee JS, Hou X, Bishop N, Wang S, Flack A, Cho WJ, Chen X, Mao G, Taatjes DJ, Sun F, Zhang K, Jena BP.
Micron. 2013 Apr;47:50-8. doi: 10.1016/j.micron.2013.01.005.
PMID: 23416165

10. X-ray solution structure of the native neuronal porosome-synaptic vesicle complex: Implication in neurotransmitter release.
Kovari LC, Brunzelle JS, Lewis KT, Cho WJ, **Lee JS**, Taatjes DJ, Jena BP.
Micron. 2014 Jan;56:37-43. doi: 10.1016/j.micron.2013.10.002.
PMID: 24176623

Faculty Mentored (Recent):

2013-2014 **G. Lawes**, Associate Professor of Physics, Wayne State University.
Promoted to Professor of Physics in 2015
Sabbatical in the Jena Group: Gain experience on various molecular, cellular, and biophysical approaches.

2011-2016 **X. Chen**, Assistant Professor of Physiology, Wayne State University School of Medicine

Received first NIH R01 Grant in 2016

Collaborative Publications:

1. 3D organization and function of the cell: Golgi budding and vesicle biogenesis to docking at the porosome complex.
Wang S, Lee JS, Bishop N, Jeremic A, Cho WJ, **Chen X**, Mao G, Taatjes DJ, Jena BP.
Histochem Cell Biol. 2012 Jun;137(6):703-18. doi: 10.1007/s00418-012-0948-x.
PMID: 22527693

2. Neuronal porosome proteome: Molecular dynamics and architecture.
Lee JS, Jeremic A, Shin L, Cho WJ, **Chen X**, Jena BP.
J Proteomics. 2012 Jul 16;75(13):3952-62. doi: 10.1016/j.jprot.2012.05.017.
PMID: 22659300

3. Aquaporin-assisted and ER-mediated mitochondrial fission: a hypothesis.
Lee JS, Hou X, Bishop N, Wang S, Flack A, Cho WJ, **Chen X**, Mao G, Taatjes DJ, Sun F, Zhang K, Jena BP.
Micron. 2013 Apr;47:50-8. doi: 10.1016/j.micron.2013.01.005.
PMID: 23416165

4. CXCR2 macromolecular complex in pancreatic cancer: a potential therapeutic target in tumor growth.
Wang S, Wu Y, Hou Y, Guan X, Castelvetere MP, Oblak JJ, Banerjee S, Filtz TM, Sarkar FH, **Chen X**, Jena BP, Li C.
Transl Oncol. 2013 Apr;6(2):216-25. Erratum in: Transl Oncol. 2013 Dec;6(6):erratum.
PMID: 23544174

5. Proteome of the porosome complex in human airway epithelia: interaction with the cystic fibrosis transmembrane conductance regulator (CFTR).
Hou X, Lewis KT, Wu Q, Wang S, **Chen X**, Flack A, Mao G, Taatjes DJ, Sun F, Jena BP.
J Proteomics. 2014 Jan 16;96:82-91. doi: 10.1016/j.jprot.2013.10.041.
PMID: 24220302

6. Proteome of the insulin-secreting Min6 cell porosome complex: involvement of Hsp90 in its assembly and function.
Rajagopal A, Kulkarni S, Lewis KT, **Chen X**, Maarouf A, Kelly CV, Taatjes DJ, Jena BP.
J Proteomics. 2015 Jan 30;114:83-92. doi: 10.1016/j.jprot.2014.11.010.
PMID: 25464371

7. COPII-Dependent ER Export: A Critical Component of Insulin Biogenesis and β-Cell ER Homeostasis.
Fang J, Liu M, Zhang X, Sakamoto T, Taatjes DJ, Jena BP, Sun F, Woods J, Bryson T, Kowluru A, Zhang K, **Chen X**.
Mol Endocrinol. 2015 Aug;29(8):1156-69. doi: 10.1210/me.2015-1012.
PMID: 26083833

2012-2016 **Christopher V. Kelly**, Assistant Professor of Physics & Astronomy, Wayne State University
Received NSF Career Award in 2016

Collaborative Publications:

1. Proteome of the insulin-secreting Min6 cell porosome complex: involvement of Hsp90 in its assembly and function.
Rajagopal A, Kulkarni S, Lewis KT, Chen X, Maarouf A, **Kelly CV**, Taatjes DJ, Jena BP. J Proteomics. 2015 Jan 30;114:83-92. doi: 10.1016/j.jprot.2014.11.010.
PMID: 25464371

2015-18 **Robert J. Wessells**, Assistant Professor of Physiology, Wayne State University School of Medicine
Joint Submission of one NIH and NSF Grant

Collaborative Publications:

1. Nano thermometry measure of muscle efficiency.
Laha SS, Naik AR, Kuhn ER, Alvarez M, Sujkowsky A, **Wessells RJ**, Jena BP. ACS Nano Letters 2017 Jan 23. **DOI:** 10.1021/acs.nanolett.6b05092.

2016-17 **Korosh Torabi**, Assistant Professor of Chemical Engineering & Materials Science, Wayne State University
Joint NSF Grant Submitted (2017)

2018-pr **Suzan Arslanturk**, Assistant Professor of Computer Science, Wayne State University College of Engineering
Joint Submission of one NIH and one Chan-Zuckerberg Grant

Collaborative Publications:

1. Skeletal muscle remodeling in immobilized patients: Determined using a parameter estimation histomorphometric approach.
Gatti DL, Larsson L, **Arslanturk S**, Jena BP.
*bioRxiv.*2020.06.17.157438; doi: https://doi.org/10.1101/2020.06.17.157438**.**

2. Cystic fibrosis transmembrane conductance regulator (CFTR) inhibition results in mucus accumulation in human airway epithelia Calu-3 cells: Experimental and machine learning studies.
Laethem BS, Lewis KT, Ramos R, Hou X, Sun F, Taatjes DJ, Jena BP, **Arslanturk, S.**
*bioRxiv.*2020.06.17.157438; doi: https://doi.org/10.1101/2020.06.17.157438**.**

3. Nanoscale imaging using differential expansion microscopy.
Pernal, S.P., Liyanaarachchi, A., Gatti, D.L., Formosa, B., Pulvender, R., Kuhn, E.R., Ramos, R., Naik, A.R., George, K., **Arslanturk, S.**, Taatjes, D.J., Jena BP.
Histochem Cell Biol. (2020)153: 469-480. ***(Cover Illustration & Editorial).***

4. Res-CR-Net, a residual network with a novel architecture optimized for the semantic segmentation of microscopy images.
Hassan Abdallah, H., Liyanaarachchi, A., Saigh, M., Silvers, S., **Arslanturk, S.,** Taatjes, D.J., Larsson, L., Jena,B.P., Gatti, D.L.
aRxiv (2020)http://arxiv.org/licenses/nonexclusive-distrib/1.0/.

5. Human Skeletal Muscle Cell Atlas: Unraveling Cellular Secrets Utilizing 'Muscle-on-a-Chip', Differential Expansion Microscopy, Mass Spectrometry, Nanothermometry and Machine Learning.
Jena BP, Gatti DL, **Arslanturk S**, Pernal S, Taatjes DJ.
Micron https://doi.org/10.1016/j.micron.2018.11.002

6. Differential expansion microscopy.
Pernal, S.P., Liyanaarachchi, A., Gatti, D.L., Formosa, B., Pulvender, R., Kuhn, E.R., Ramos, R., Naik, A.R., George, K., **Arslanturk, S.**, Taatjes, D.J., Jena BP. (2019) *bioRxiv* 699579; doi: https://doi.org/10.1101/699579

7. Deep learning stretegies for differential expansion microscopy.
Gatti, D.L., **Arslanturk, S**., Lal, S., Jena BP. (2019) DOI:
bioRxiv 743682; doi: https://doi.org/10.1101/74368

Report of Teaching and Education Innovations

2000 **Founder-Director, NanoBioScience Institute, Wayne State University.**
NBSI was established in 2000 at the School of Medicine immediately after my arrival from Yale University School of Medicine. The primary objective of the institute was to establish a strong interdisciplinary program in the Nano Sciences & Nano Medicine at the Medical School and the University. In summary, NBSI has made the following contributions to Wayne State University and the School of Medicine: **(1)** Continues to bring together a large group of cross-campus interdisciplinary faculty and student groups to study Nano Science, Nano Medicine, & Nano Technology. **(2)** Has resulted in joint grant applications and funding from the NSF and NIH. **(3)** Developed a NanoBioScience Course (PSL7215), which is in its 10th year of offering. **(4)** NBSI has been selected as one of the top four Nano Institutes in the US. **(http://www2.med.wayne.edu/physiology/nanobioscience/pdfs/Nanotechnology%20Standing.pdf). (5)** Has helped establish the $150 million Asian NanoScience Institute in South Korea and the NBSI Director has served as its Co-Director (2002-2006). **(6)** The NBSI Director has recently been invited to help in the establishment of a $6 billion Vedanta University in India, and to establish a "Named Molecular Medicine Institute" in the US. **(7)** NBSI has fostered the establishment of several national and international scientific collaborations. **(8)** NBSI has published five books on Nano Science and scores of scientific papers in the field involving over 50 national and international investigators.

2002 **Co-Founding Director, Asian & Korean Institute of Nanoscience & Technology, Pusan, Korea.** The institute was established in 2002 in Pusan National University, involving

100 scientists from 25 academic institutions from Korea and overseas [http://macdiarmid.ac.nz/interface_article/new-nanobioscience-institute/]. The South Korean Government partially financed the institute with additional funding from private industrial sector. A major focus was to train students in nano science and technology, by first developing courses and research projects in the field. Korea greatly benefited from this nano stimulus project both academically and economically. Within a decade of the establishment of the Asia Nano Institute, research and teaching in nanoscience began to be performed in every major academic institution in South Korea.

2006 **Developed the PSL7215 NaboBioScience Course,** serving as Course Director of this multidisciplinary course, Wayne State University School of Medicine. The course is offered once a year, and each year, 12-15 students register for the course. New and tools and technologies used in the study of NanoBioScience, and new discoveries and developments made in the field, are the focus of this course.

2019 **Developed a "Biophysics and Biomaterials Concentration",** serving as Director of this multidisciplinary and multi departmental program, Wayne State University. The objective of this integrated *Biophysics & Biomaterial Sciences Concentration* is to bring together researchers in the field to closely collaborate and submit joint research and training proposals. Students with backgrounds in biomedical sciences, physics, chemical engineering, and computational sciences and with interest in utilizing physical sciences to solve fundamental and medically relevant problems in biology and medicine will be attracted into this program. Wayne State University faculty from the departments of Physiology, Physics, and Chemical Engineering & Materials Sciences, with a long history of productivity in research, course development, and teaching accomplishments in this field, will participate in the program. The initial phase of development will focus on establishing a new joint concentration in *Biophysics and Biomaterial Sciences* in the PhD programs between the participating departments.

2016 **Advisory Board Member**, **& Academic Program Director**, Vedanta University. Establishment of Colleges, Departments & Institutes, for the University.

2016 **Advisor**, Development of new Neuroscience Ph.D. Program, Tbilisi State University, Georgia.

2018 **Founding-Director, "Named Molecular Medicine Institute", (US Institution to be identified).**

Teaching Strategy and Philosophy: My involvement in teaching is multi-faceted and takes place in several settings. Laboratory mentorship and thesis advisor, research seminar organizer and moderator and class lecturer are my primary teaching responsibilities. Most of my formal classroom teaching is aimed primarily at medical and graduate students. As an organizer and moderator of a research seminar, I have the opportunity to interact with a number of students, postdoctoral fellows and faculty from different departments having similar research interests. As a laboratory mentor, I have worked with students starting from high school through undergraduate, graduate and postdoctoral levels. To achieve perfection in these activities are part of my career academic goals. In view of the unique requirements of each of the above mentioned, teaching venues, necessitates the following teaching plan which I have adopted.

As a laboratory mentor, my emphasis is on teaching students how to think objectively, critically question and analyze results. The greatest challenge in scientific

research is identifying interesting research problems and formulating meaningful ways to examine them. I believe that the best way for students to develop the attributes to address these challenges is through the process of reasoning by design and interpretation of their own research. Through discussions, I guide them to arrive at their own effective problem-solving approach rather then mine. An extremely interactive and didactic journal club, which I have instituted in the laboratory, helps to provide students with insight into the tools they need to design and execute their research projects. Participation in seminars, lectures and multi-group laboratory meetings besides enabling my students develop their presentation and communication skills, help in fostering collaborations. Collaborative effort between multidisciplinary research groups, further the success of a project by pulling together both intellectual and material resources.

My participation in lecture classes encompasses topics in general cell biology, both general and clinical endocrinology, neuroendocrinology, nanobioscience and nanomedicine, signal recognition and transduction, and the biochemistry and biophysics of intracellular vesicle transport and fusion. My teaching plan emphasizes the structure-function relationship, and therefore my lectures are designed to elucidate the relationship between cellular function and cellular and sub-cellular structure.

National and international collaborative efforts and cooperative arrangements (2014-present): My laboratory has established strong on campus, national and international collaborations and partnerships, which has helped provide an enriched education, research, and training experience for student and faculty alike. In the past decade at WSU, my laboratory has published research papers and obtained joint research funding and team-taught with more than 10 on campus collaborators. With ***Prof. J. Potoff*** and ***Prof. C. Manke*** in Chem. Engineering at WSU, our collaboration has resulted in the publication of several research papers and succeeded in obtaining one internal and two NSF grants (one continuing). My group has collaborated with the groups of ***Prof. T. Stemmler*** and ***Prof. L. Kovari*** in Pharmacy and in the Dept. of Biochemistry at WSU, resulting in several publications. Research grant applications are in progress with the Kovari group. With ***Prof. Gary Ren*** formerly at UCSF and currently at the Lawrence Berkeley Laboratory, we have collaborated in research resulting in the publication of several papers, succeeded in obtaining a DOE user grant, and have recently applied for an NIH grant. Our continuing collaboration with ***Prof. Douglas J. Taatjes*** at the University of Vermont has similarly resulted in a large number of collaborations and successful obtaining of a NIH grant. Similarly, we continue to collaborate with ***Prof. Mzia G. Zhvania*** of the I.Beritashvili Institute of Physiology, Georgian Academy of Science, Tbilisi, Republic of Georgia, and with whom we recently submitted a proposal to the Georgian National Science Foundation to establish a doctoral program in Neuroscience at Ilia State University in Tbilisi, Georgia, which was funded. This funding will allow doctoral students in Neuroscience to visit my research group at Wayne State University and our NanoBioScience Institute, to carry our joint research funded by the Georgian National Science Foundation. We have published several papers and obtained two Georgian grants for her students to do research for a period of 4-6 months in my laboratory at WSU. Additionally, my laboratory has collaborations with the laboratory of ***Prof. Phil Andrews*** at the University of Michigan

School of Medicine. Similarly, within the Dept. of Physiology here at WSU, my laboratory has actively engaged in collaborative research with the laboratories of ***Prof's. Chen, Wessells, and Sun***, and plan joint R01's to NIH in the near future. We have established strong and long standing collaborations with Prof. Potoff and Prof. Manke in Chemical Engineering & Materials Science, resulting in several publications and more in preparation; with ***Prof. Chris Kelly*** in Physics, with whom we have published a research paper and two more are in preparation, and with whom we have received the Richard Barber Research Award; with ***Prof. Pancharatnam Jayasuria*** and ***Prof. Jenifer Condon*** at the C. S. Mott Center for Human Growth & Development; and with ***Prof. Hyeong-Reh Kim*** of Pathology, with whom we have published a paper and plan in submitting joint NIH proposals shortly. These inter- and intra-department collaborations have resulted in joint research publications and the application for both intramural and extramural funding. These are just a few examples of the extent of collaboration and interaction of my group, both within campus, as well as nationally and internationally in the past three years.

After nearly 25 years of studies focused on understanding various aspects of secretion and membrane fusion in cells, it has become increasing clear that besides the conventional secretory apparatus and process involved in secretion from eukaryotes, intra-luminal vesicles in cells called 'exosomes' containing proteins and nucleic acids present within multi-vesicular bodies are released into the extracellular fluid and have also been implicated in cell-cell communication. Exosome chemistry, its cellular distribution and release mechanisms, and its role in health and disease is the subject of one of the current focus in the laboratory, in collaboration with ***Professors Alan Dombkowski, Joyce A. Benjamins and Robert P. Lisak*** in the School of Medicine at Wayne State University [Benjamins JA, Nedelkoska L, Touil H, Stemmer, Carruthers NJ, Jena BP, Naik AR, Bar-Or A, Lisak RP. (2019) *Neurology(R) Neuroimmunology & Neuroinflammation*. 6: e550. PMID 31044144 DOI: 10.1212/NXI.0000000000000550]. The other focus in the laboratory is to understand the structure and energetics associated with protein-protein and protei n-ion interactions, and the ratio of the various components comprising a supramolecular complex, its assembly and stability in cells, dictate numerous life processes. Among such process is the assembly and dynamics of the thick filament in skeletal muscles, composed of different myosin isoforms, whose chemistry and interactions are in dynamic flux, and is influenced in-part, by age, exercise, and disuse, of which much remains to be understood. Since muscle disuse-induced myopathy is of frequent occurrence in the intensive care unit (ICU) resulting in approximately 5% increase in health care costs, a staggering $180 billion in the US alone, there is urgency in the development of new treatment and management modalities. We have therefore focused our attention in the past two years, to understand the molecular mechanism of myosin remodeling in muscle disuse myopathy, and the consequence of this remodeling on muscle structure-function. To be able to accomplish this goal, we have established close collaborations with the leading human muscle biology group of ***Prof. Lars Larsson*** in the Department of Physiology, at the Karolinska Institute, in Sweden [Kuhn ER, Naik AR, Lewis BE, Kokotovich KM, Li M, Stemmler TM, Larsson L, Jena BP. *ACS Nano Letters* October 22, 2018, DOI: 10.1021/acs.nanolett.8b02989; Cacciani N, Salah H, Li M, Akkad H, Backeus A,

Hedstrom Y, Jena BP, Bergquist J, Larsson L. (2019) *Acta Physiologica (Oxford, England)*. e13425. PMID 31799784 DOI: 10.1111/apha.13425]. Prof. Larsson has been working on muscle wasting in humans, especially in ICU patients for the past 40 years, and out joint groups have pooled our resources, experience, and expertise, to study disuse-induced myopathy in skeletal muscle. Additionally, we have established collaborative studies with ***Prof. R.J. Wessells*** with Drosophila genetics and exercise physiology expertise [Laha, S.S., Naik, A.R., Kuhn, E.R., Alvarez, M., Sujkowsky, A., Wessells, R.J., Jena, B.P. (2017), and a human skeletal muscle-on-a-chip platform. Nano thermometry measure of muscle efficiency. *ACS Nano Letters* 17 (2):1262-1268], and powerful proteomics approaches [Naik AR, Pernal S, Lewis KT, Wu Y, Wu H, Carruthers NJ, Stemmer PM, Jena BP. (2019) *ACS Biomaterials Science & Engineering* 2019 DOI: 10.1021/acsbiomaterials.8b01338.] to study muscle disuse-induced myopathy. We have further established collaborative ties with a number of laboratories, for example with ***Prof. Howard Matthews*** in Chemical Engineering at WSU for the biogenesis of human bone tissue in therapy.

A comprehensive understanding of different cells that constitute the human body and their various dynamic states is required to provide a reference map for the early diagnosis and treatment of various disease, and in the development of precision therapeutics. Skeletal muscles being the most abundant tissue and the largest locomotor and metabolic organ in the human body, requires a global understanding of its native structure, composition, and function in the sedentary and exercised states, to establish a 'Human Skeletal Muscle Cell Atlas'. To achieve this long-term objective, we have initiated collaborative studies to determine the remodeling of myosin motor proteins, and the energy-producing organelle the mitochondria in human skeletal muscle cells during development and growth, under conditions of activity and inactivity. This objective has necessitated the use and development of precise yet rapid and cost-effective approach of combined multimodal imaging, including our new and novel 'Differential Expansion Microscopy', our 'Nanoscale Thermometry', combined with 'Mass Spectrometry', 'Motility Assay' and 'Machine Learning'. We have achieved the first iteration of this objective by utilizing our stretchable micropatterned 3D human skeletal muscle platform that recapitulates organized and parallel growth of muscle fibers and cells expressing key myogenic proteins such as myoferlin for myoblast fusion required in muscle tissue formation, and proteins involved in biogenesis of the mitochondrial. We have begun utilizing this initial information to train our neural network. These studies involving machine learning and neural network, are in collaboration with the laboratories of ***Prof. Domenico L. Gatti*** in the School of Medicine at Wayne State University, and ***Prof. Suzan Arslanturk*** in the Dept. of Computer Science at Wayne State University [Jena BP, Gatti DL, Arslanturk S, Pernal S, Taatjes DJ. *Micron* https://doi.org/10.1016/j.micron.2018.11.002; Pernal, S.P., Liyanaarachchi, A., Gatti, D.L., Formosa, B., Pulvender, R., Kuhn, E.R., Ramos, R., Naik, A.R., George, K., Arslanturk, S., Taatjes, D.J., Jena BP. (2019) *bioRxiv* 699579; doi: https://doi.org/10.1101/699579; Gatti, D.L., Arslanturk, S., Lal, S., **Jena BP**. (2019) DOI: *bioRxiv* 743682; doi: https://doi.org/10.1101/74368].

Our published studies have successfully utilized atomic force microscopy, electron

microscopy, differential expansion microscopy, immunofluorescence confocal and TIRF microscopy, optical tweezers, small angle X-ray solution scattering, mass spectrometry, molecular biology, membrane electrophysiology, computational modeling, simulations and machine learning and neural network.

Other Educational Activities Beneficial to both Faculty & Students (2014-2016): Co-organizer with Prof. Charles Manke (Chair, Chemical Eng., WSU), the annual Zewail Award & Lecture. Attended by 400-500 students and faculty. Award recipients have always been Nobel Laureates or distinguished scholars worthy of receiving the Nobel Prize.

Report of Technological and Other Scientific Innovations

2016

Title: Nanometer scale thermometry of cells and biomolecules
Contribution: PI
Innovation Description: Despite recent advances in thermometry, determination of temperature at the nanometer scale in single molecules to live cells remains a challenge that holds great promise in disease detection among others. In a recent study [**ACS Nano Letters 2017 Jan 23. DOI: 10.1021/acs.nanolett.6b05092**], we use a new approach to nanometer scale thermometry with a spatial and thermal resolution of 80 nm and 1 mK respectively, capable of determining muscle efficiency, cancer, and with promise for early diagnosis and treatment of various metabolic disorders. [Patent: US 62/498,015].

2016

Title: Potentiation of gas transport in red blood cells
Contribution: PI
Innovation Description: Existing drug formulation for treatment of a different disease has been identified to potentiate gas transport in red blood cells, with promise for the treatment of various cardiovascular disorders and for potential use in high altitude and space flights. [**Patent Protection Filed**].

2017

Title: "Human Muscle-on-a-Chip" stretchable 3D microphysiological platform
Contribution: PI
Innovation Description: Improvements in modern critical care have led to improved survival, leading to a growing need for intensive care units (ICUs). It is predicted that ICUs will occupy one third of hospital beds by 2020, with staggering rehabilitation costs. No treatments are currently available for skeletal muscle atrophy and metabolic disorders as a consequence of disuse in ICU patients and in microgravity during extended space flights, and in diabetes. While animal models of disease and drug testing for use in treatment and therapy in human have provided a wealth of

information, over 75% of drugs with stellar results in animals demonstrate alarmingly low efficacy in human trials. Since drug testing on humans is prohibitory, we have developed a stretchable microphysiological 3D platform replicating native skeletal muscle, to test how sedentary and exercised muscles respond to the overexpression of the exercise-induced PGC-1□ gene (peroxisome proliferator-activated receptor coactivator 1□), an important regulator of mitochondrial biogenesis, to drugs identified to stimulate the PGC-1□ gene product, and to insulin.

Report of Funded and Unfunded Projects

Funding Information Summary:

GRANTS, CONTRACTS, AND OTHER FUNDING
Indicate role (PI, Co-PI, Co-I, etc.), title, source, total period of support, total direct costs.

RECENT BRIEF GRANT HISTORY: JENA, Bhanu P. (PI & Co-PI)

1. Secured $12 million 5-year research funding (2021-2025) from QPathology LLC [https://qpathology.com] to Wayne State University School of Medicine, focused on diabetes and cancer research.

ACTIVE

1. The Foundation4Humanity Endowment, Jena (PI), Invited in 2021 to serve as President & Director, Molecular Medicine Institute, Cambridge, MA [$10.45 billion, 10-year period]. (*Pending Initiation*); MMI: https://cms9.revize.com/revize/moleculartx/

2. NIH 2R56 NS079429-04A1 Jena (Co-I) 12/01/19-07/31/21 5% effort [$539,000]
TITLE: The role of non-coding RNAs in epilepsy of tuberous sclerosis complex and focal cortical dysplasia type 2B.

3. Received the 2018-2019 Graduate Research Assistant Competition (GRA)

4. Shota Rustaveli National Science Foundation Jena (Collaborator) 09/01/2017 - 08/31/2027; Ph.D. Program in Neuroscience, Ilia State University, Tbilisi, Georgia (Co-Mentor Two Doctoral Students/year).

PENDING

1. NIH R01 GM137395-01A1 Jena (PI) 04/01/2021-03/31/2026 20% effort [$3,507,866]
TITLE: Differential expansion microscopy and machine learning in diagnostic pathology.

RECENT COMPLETED

1. NSF CBET Jena (Co-PI) 09/01/2011 - 08/31/2017 2.5% effort [$330,000]
TITLE: Elucidation of Membrane Fusion Mechanisms Using a Combined Stimulation and Experimental Approach

2. Richard Barber Foundation; Jena (Co-PI) 05/2015 - 08/2017 [$23,500]
TITLE: Determining the Macromolecular Structure of the Porosome complex in insulin-secreting cells.

3. OVPR Post-Doctoral Fellow Support; Jena (PI) 09/2015 - 08/2016 [$47,000]
TITLE: Single molecular thermometry.

4. DOE 1194 Jena (PI) 06/01/11 – 05/31/12
TITLE: Electron crystallography and X-ray determination of t-/v-SNARE structures

This proposal support is from the Molecular Foundry of DOE at the Lawrence Berkeley National Laboratory, CA. The overall objective of the study is to determine the chemistry of [Ca^{+2}]-lipid interactions underlying membrane fusion, and the molecular assembly of SNARE proteins enabling this process. This project is renewable.

5. WSU Bridge Funding Jena (PI) 09/01/11 - 08/31/12

6. NSF EB00303 Jena (Co-PI) 09/11/07 – 08/31/11
TITLE: Bioengineering and molecular simulation studies to understand membrane fusion

Results from experiments suggest that in presence of calcium, t-SNARE vesicles are able to interact with v-SNARE vesicles allowing formation of calcium-phosphate bridges between the opposing bilayers, resulting in the expulsion of water due to disruption of the water shell around the calcium ion. This removal of water leads to lipid mixing and membrane fusion. The objective of this application is to test this hypothesis using molecular simulation. Graduate and undergraduate students are actively participating in this project.

7. WSU Presidential Award Jena (PI) 08/01/07 - 07/31/10

8. WSU Deans Award Jena (PI) 04/01/08 - 03/31/11

9. NIH NS-39918 Jena (PI) 09/16/00 - 02/31/07
TITLE: Understanding Membrane Fusion: A Bioengineering Approach.
Percent Effort (PI): 30%
Objective: The objective of our application was to (1) determine the role of coiling and super-coiling in membrane fusion, (2) determine the nature of coiling of SNAREs, (3) determine the role of the 'new structure' in membrane fusion, and (4) determine the biochemical composition of the 'new structure'.

Results from the study: Six post doctoral students (Sang Joon Cho, Aleksander Jeremic, Marie Kelly, Sudhansu Dash, A.K.M. Abdus Sattar, and Won-Jin Cho) and five graduate students participated 50% to full time in the project. Additionally, six undergraduate students received their summer fellowship working on various aspects of the project. All proposed specific aims in the grant were addressed during the specified funding period, except for the determination of the biochemical composition of the 'new structure'. During the course of the study, more than 50 papers, reviews, and abstracts were published.
CURRENT ACTIVITY: In preparation for submission as a new proposal.

10. NIH DK-56212 Jena (PI) 09/16/00 - 07/31/06
Percent Effort (PI): 30%
Objective: Our goal was to determine the function and composition of the porosome structure.
Results from the study: Five post doctoral students (Sang Joon Cho, Aleksander Jeremic, Marie Kelly, Sudhansu Dash, and A.K.M. Abdus Sattar) and two graduate students participated 50% to full time in the project. All proposed specific aims in the proposal were addressed during the specified funding period.

Funding Information Detail:

Funded Projects Completed in the Recent Past

1999-2006 **Grant Title:** Exocytosis: Using Nanosurgery and Bioengineering
Grant type and number: NIH R01 DK56212
Role in Project: PI
Description of the major goal: The long-term goal of our research plan is to understand the molecular mechanism of exocytosis. Using atomic force microscopy (AFM), a new group of plasma membrane structures called 'pits' and 'depressions', have been identified and implicated in exocytosis in live pancreatic acinar cells. Our immediate research goal is to characterize and determine the involvement of these structures in the exocytotic process.

2000-2007 **Grant Title:** Understanding Membrane Fusion: A Bioengineering Approach
Grant type and number: NIH R01 NS39918
Role in Project: PI
Description of the major goal: The long-term goal of this research plan is to understand the molecular mechanism of exocytosis. Using electron microscopy, atomic force microscopy and immunoisolation procedures of a "new structure" associated with the neuronal fusion machinery.

2007-2011 **Grant Title:** Bioengineering and molecular simulation studies to understand membrane fusion
Grant type and number: NSF EB00303
Role in Project: Co-PI
Description of the major goal: Utilize both experimental and simulation studies, to determine the molecular mechanism of membrane fusion in cells.
(1) Determine if there is direct interaction between hydrated [Ca^{+2}] and [PO^{-}_{4}]-lipid head groups in the same and opposing bilayers.
(2) Determine if divalent cations especially [Ca^{+2}], alter interaction between

opposing bilayers.
(3) Determine if divalent cations especially [Ca^{+2}], influence binding interactions between membrane-associated t-/v-SNAREs.
(4) Determine the thermodynamics and phase transitions during membrane fusion.
(5) Provide research opportunity and experience for undergraduates and graduates.

2011-2012 **Grant Title:** Electron crystallography and X-ray determination of t-/v-SNARE structures
Grant type and number: DOE 1194
Role in Project: PI
Description of the major goal: The overall objective of this study is to determine the chemistry of [Ca^{+2}]-lipid interactions in membrane fusion, and the molecular assembly of the SNARE ring complex enabling this interaction.

2011-2016 **Grant Title:** Elucidation of Membrane Fusion Mechanisms Using a Combined Stimulation and Experimental Approach
Grant type and number: NSF CBET 1066661
Role in Project: Co-PI
Description of the major goal: The *objective* of this work is to understand membrane fusion at the atomic level.
(1) Determine the effect of Ca^{+2} on interactions between opposing lipid bilayers and membrane interfacial tension.
(2) Determine the role of Ca^{2+} concentration gradient and the subsequent formation of water pores on membrane fusion.
(3) Elucidate the role of synaptotagmin-1 in the regulation of membrane fusion.

Current

2015-2017 **Grant Title:** Use of QD's in single molecular thermometry in early disease detection and therapy
Grant type and number: Richard Barber Foundation Award
Role in Project: PI
Description of the major goal: In the last decade, zero-dimensional semiconductor nanoparticles, better known as quantum dots (QDs) have attracted considerable attention for their promising applications in major technological and biomedical areas ranging from optoelectronics to medical diagnostics. These small-sized QDs with enhanced photo-stability and better brightness quality are considered superior than standard organic dyes, green fluorescent proteins and lanthanide based chelates for the careful investigation of essential life processes at nanometer resolution. In the recent past, several studies have reported the potential use of quantum dots as nano-thermometers (NThs) for sensitive probing of local temperatures in fundamental biological systems. The emitted fluorescence (FL) intensity and the spectral wavelength shifts of the QDs are the two vital

parameters for the purpose of temperature sensing. It has been reported that the FL intensity of the QDs decreases following an increase in temperature, while a temperature rise could also manifest as a spectral red shift causing minor alterations in the emission color of these tiny particles. Studies have shown the possible use of a single CdSe quantum dot as an effective NTh (resolution of ~ 1^{o}C) depending on the spectroscopic studies based on wavelength shifts. In order to achieve better accuracy, recent studies have also been conducted on CdSe-CdS quantum dot/ quantum rod based NThs for recording temperatures of fundamental intracellular events with a minimum resolution of 0.2^{o}C. Studies also report CdTe QDs as a promising candidate especially when it comes to temperature sensing of essential biological activities with a high degree of precision (~0.2^{o}C). Cancer cells exhibit a higher metabolic rate, hence their detection using CdTe QDs. The proposed research will require very little training to master by an undergraduate and or graduate student, while providing very simple and elegant approaches in life-saving disease detection and therapy.

Projects Submitted for Funding

1. NIH Pioneers Award Jena (PI) 09/30/19-07/31/24 55% effort [$5,000,000]
TITLE: Engineered Human Skeletal Muscle for Engraft and Drug Screening.
(Focused on human ICU patients and biopsy samples)

2. Chan-Zuckerberg Jena (PI) 06/01/19 - 05/31/22 5% effort [$1,345,5000]
TITLE: Profiling the human skeletal muscle cell atlas.

3. NSF-CASIS Jena (PI) 09/01/2019 - 08/31/2022 5% effort [$400,000]
(Selected for submitting complete proposal)
TITLE: Understanding Myopathy in Microgravity and Gravity Using Engineered Human Skeletal Muscle

4. NMSS Jena (Co-PI) 10/01/2019 - 09/30/2022 3% effort [$1,091,491]
TITLE: B Cell Secretory Factors and Neuronal and Oligodendroglia Toxicity.

Unfunded Current Projects

2014-pr **Title:** Nanometer scale thermometry of cells and biomolecules
Role in Project: PI
Project Description: Despite recent advances in thermometry, determination of temperature at the nanometer scale in single molecules to live cells remains a challenge that holds great promise in disease detection among others. In a recent study (**manuscript submitted**), we use a new approach to nanometer scale thermometry with a spatial and thermal resolution of 80 nm and 1 mK respectively, capable of determining muscle efficiency, cancer, and with promise for early diagnosis and treatment of various metabolic disorders. [**Patent Protection Filed**].

2014-pr **Title:** Membrane biogenesis in cells
Role in Project: PI
Project Description: In addition to delimiting the cell and its intracellular compartments, biological membranes and their biogenesis govern a wide range of life processes including cell division, development, growth, and motility. From recent studies we have gained molecular understanding of membrane biogenesis in cells (**manuscript in preparation**).

2015-pr **Title:** Secretory vesicle-associated heterotrimeric GTP-binding G-proteins on insulin secretion
Role in Project: PI
Project Description: Heterotrimeric GTP-binding G-proteins present at the beta cell plasma membrane and membrane of the insulin secretory granule (ISG) implicated in glucose-stimulated insulin secretion have become primary candidates for drug targets in the treatment of Type-2 diabetes. Although our understanding of the role of G-proteins associated at the beta cell plasma membrane has greatly advanced, the function of ISG-associated Gi and Gs in the distal secretory pathway of glucose-stimulated insulin release is poorly understood. The objective of the proposed study is to (1) determine the signaling pathways upstream and downstream of ISG-associated Gi/Gs that are important for the regulation of glucose-stimulated insulin secretion in beta cells; and (2) determine how ISG-associated Gi and Gs proteins participate in glucose-stimulated insulin secretion.

Report of Scholarship

Peer-Reviewed Scholarship in print (Selected):
Research Investigations (Selected):

1. Regulation of Hepatic Circadian Metabolism by the E3 ubiquitin ligase HRD1-controlled CREBH/PPARα Transcriptional Program.
Kim H, Wei J, Song, Z, Mottillo E, Samavati L, Zhang, R, Li L, Chen, X, **Jena BP**, Lin JD, Fang D, Zhang, K. (2021) *Molecular Metabolism.*
https://doi.org/10.1016/j.molmet.2021.101192

2. Skeletal muscle remodeling in immobilized patients: Determined using a parameter estimation histomorphometric approach.
Formosa, B., Liyanaarachchi, A., Silvers, S., Gatti, D.L., Larsson, L., Arslanturk, S., **Jena, B.P.**
*bioRxiv.*2020.06.17.157438; doi: https://doi.org/10.1101/2020.06.17.157438**.**

3. Cystic fibrosis transmembrane conductance regulator (CFTR) inhibition results in mucus accumulation in human airway epithelia Calu-3 cells: Experimental and machine learning studies.
Laethem BS, Lewis KT, Ramos R, Hou X, Sun F, Taatjes DJ, **Jena BP**, Arslanturk, S. *bioRxiv.*2020.06.17.157438; doi: https://doi.org/10.1101/2020.06.17.157438**.**

4. Nanoscale imaging using differential expansion microscopy.

Pernal, S.P., Liyanaarachchi, A., Gatti, D.L., Formosa, B., Pulvender, R., Kuhn, E.R., Ramos, R., Naik, A.R., George, K., Arslanturk, S., Taatjes, D.J., **Jena, B.P.** (2020) *Histochem Cell Biol.* doi:https://doi.org/10.1007/s00418-020-01869-7

5. Res-CR-Net, a residual network with a novel architecture optimized for the semantic segmentation of microscopy images.
Abdallah, H., Liyanaarachchi, A., Saigh, M., Silvers, S., Arslanturk, S., Taatjes, D.J., Larsson, L., **Jena, B.P.**, Gatti,D.L. (2020) *arXiv*; doi: https://arxiv.org/abs/2004.08246v1

6. vH-ATPase-induced intracellular acidification is critical to glucose-stimulated insulin secretion in beta cells.
Naik AR, Formosa BJ, Pulvender RG, Liyanaarachchi AG, **Jena BP**. (2019) *Histochemistry and Cell Biology*. PMID 31901974 DOI: 10.1007/s00418-019-01841-0

7. Chaperone co-inducer BGP-15 mitigates early contractile dysfunction of the soleus muscle in a rat ICU model.
Cacciani N, Salah H, Li M, Akkad H, Backeus A, Hedstrom Y, **Jena BP**, Bergquist J, Larsson L. (2019) *Acta Physiologica (Oxford, England)*. e13425.
PMID 31799784 DOI: 10.1111/apha.13425

8. Self-Assembly and Biogenesis of Cellular Membrane is Dictated by Membrane Stretch and Composition.
Naik AR, Kuhn ER, Lewis KT, Kokotovich KM, Maddipati KR, Chen X, Hörber JHK, Taatjes DJ, Potoff J, **Jena BP**. (2019) *The Journal of Physical Chemistry. B*. 123(32): 6997-7005. PMID 31322890 DOI: 10.1021/acs.jpcb.9b04769

(A comprehensive understanding of the biogenesis of additional membrane to pre-existing cellular membrane determined by the study)

9. Exosome- enriched fractions from multiple sclerosis B cells induce oligodendrocyte death.
Benjamins JA, Nedelkoska L, Touil H, Stemmer, Carruthers NJ, **Jena BP**, Naik AR, Bar-Or A, Lisak RP. (2019) *Neurology(R) Neuroimmunology & Neuroinflammation*. 6: e550. PMID 31044144 DOI: 10.1212/NXI.0000000000000550

10. Human skeletal muscle cells on engineered 3D platform express key growth and developmental proteins.
Naik AR, Pernal S, Lewis KT, Wu Y, Wu H, Carruthers NJ, Stemmer PM, **Jena BP**. (2019) *ACS Biomaterials Science & Engineering* 2019 DOI: 10.1021/acsbiomaterials.8b01338.

11. Differential expansion microscopy.
Pernal, S.P., Liyanaarachchi, A., Gatti, D.L., Formosa, B., Pulvender, R., Kuhn, E.R., Ramos, R., Naik, A.R., George, K., Arslanturk, S., Taatjes, D.J., **Jena BP**. (2019) *bioRxiv* 699579; doi: https://doi.org/10.1101/699579

(Demonstrated that in expansion microscopy (ExM), anisotrophic expansion is observed between tissues, between cells, between cellular organelles, and even within organelles themselves, hence called differential expansion microscopy (DiExM))

12. Deep learning strategies for differential expansion microscopy.
Gatti, D.L., Arslanturk, S., Lal, S., **Jena BP**. (2019) DOI:
bioRxiv 743682; doi: https://doi.org/10.1101/74368

13. Nanothermometry Reveals Calcium-Induced Remodeling of Myosin.
Kuhn ER, Naik AR, Lewis BE, Kokotovich KM, Li M, Stemmler TM, Larsson L, **Jena BP**.
ACS Nano Letters October 22, 2018, DOI: 10.1021/acs.nanolett.8b02989

(Enthalpy changes in the motor protein myosin, and the consequent loss in the alpha helical content of the protein demonstrated following calcium binding)

14. Human Skeletal Muscle Cell Atlas: Unraveling Cellular Secrets Utilizing 'Muscle-on-a-Chip', Differential Expansion Microscopy, Mass Spectrometry, Nanothermometry and Machine Learning.
Jena BP, Gatti DL, Arslanturk S, Pernal S, Taatjes DJ.
Micron https://doi.org/10.1016/j.micron.2018.11.002

15. Valproate inhibits glucose-stimulated insulin secretion in beta cells.
Yedulla NR, Naik AR, Kokotovich KM, Yu W, Greenberg ML, **Jena BP**.
Histochem Cell Biol. 2018 Aug 25. doi: 10.1007/s00418-018-1713-6. PMID: 30145684

(First demonstration of the reduction of glucose-stimulated insulin secretion in beta cells following exposure to Valproate, an FDA approved drug that has been used clinically for decades, in treating migraines, bipolar disorder, and epileptic seizures.)

16. Secretion induces cell pH dynamics impacting assembly-disassembly of the fusion protein complex: A combined fluorescence and atomic force microscopy study.
Lewis KT, Naik AR, Laha SS, Wang S, Mao G, Kuhn E, **Jena BP**. *Semin Cell Dev Biol.* 2018 Jan;73:57-63. doi: 10.1016/j.semcdb.2017.08.003. Epub 2017 Aug 3. PMID: 28779980

(Secretion induces pH dynamics of cells impacting assembly-disassembly of the membrane-associated t-SNAREs and v-SNARE complex complex)

17. Molecular architecture of mouse and human pancreatic zymogen granules: protein components and their copy numbers.
Lee JS, Caruso JA, Hubbs G, Schnepp P, Woods J, Fang J, Li C, Zhang K, Stemmer PM, **Jena BP**, Chen X.
Biophys Rep. 2018;4(2):94-103. doi: 10.1007/s41048-018-0055-1. Epub 2018 Apr 26. PMID: 29756009

18. *Porosome:* Supramolecular Structures at the Synaptosome Membrane Involved in Vesicle Docking, Fusion, and Neurotransmitter Release.
Jena BP.
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Fang J, Liu M, Zhang X, Sakamoto T, Taatjes DJ, **Jena BP**, Sun F, Woods J, Bryson T, Kowluru A, Zhang K, Chen X.
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Rajagopal A, Kulkarni S, Lewis KT, Chen X, Maarouf A, Kelly CV, Taatjes DJ, **Jena BP**.
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Kovari LC, Brunzelle JS, Lewis KT, Cho WJ, Lee JS, Taatjes DJ, **Jena BP**.
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J Am Chem Soc. 2005 Jul 27;127(29):10156-7.
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(t-SNAREs and v-SNAREs present in opposing bilayers interact to form a rosette or ring complex. The size of the rosette is directly proportional to the curvature of the SNARE-associated membrane, hence smaller the vesicle higher its curvature, and smaller the size of the t-/v-SNARE rosette)

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Kelly ML, Abu-Hamdah R, Jeremic A, Cho SJ, Ilie AE, **Jena BP**.
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(First demonstration that secretory vesicle swelling is a requirement for content release during cell secretion)

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SNARE vesicles, allowing the formation of calcium-phosphate bridges between the opposing bilayers, resulting in the expulsion of water due to disruption of the water shell around the calcium ion, enabling lipid mixing and membrane fusion)

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Jena BP.
J Endocrinol. 2003 Feb;176(2):169-74.
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(Demonstration that t-SNARE is present at the base of the cup-shaped porosome complex facing the cytosol)

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Biophys J. 2002 Nov;83(5):2522-7.
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Sattar AA, Boinpally R, Stromer MH, **Jena BP**.
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Cho SJ, Sattar AK, Jeong EH, Satchi M, Cho JA, Dash S, Mayes MS, Stromer MH, **Jena BP**.
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(First demonstration that secretory vesicle volume increase is via the water channel or aquaporin, which is a GTP-mediated event)

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Cho SJ, Jeftinija K, Glavaski A, Jeftinija S, **Jena BP**, Anderson LL.
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(Immuno-AFM studies localizing secretory antibody-conjugated gold against secreted protein, demonstrate that the pores present at the cell surface of pancreatic acinar cells are secretory portals)

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Cho SJ, Cho J, **Jena BP**.
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Nathan JD, Zdankiewicz PD, Wang J, Spector SA, Aspelund G, **Jena BP**, Seymour NE, Geibel JP, Andersen DK.
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Schneider SW, Egan ME, **Jena BP**, Guggino WB, Oberleithner H, Geibel JP.
Proc Natl Acad Sci U S A. 1999 Oct 12;96(21):12180-5.
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Jeong EH, Webster P, Khuong CQ, Abdus Sattar AK, Satchi M, **Jena BP**.
Cell Biol Int. 1998;22(9-10):657-70.
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Sritharan KC, Quinn AS, Taatjes DJ, **Jena BP**.
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Schneider SW, Yano Y, Sumpio BE, **Jena BP**, Geibel JP, Gekle M, Oberleithner H.
Cell Biol Int. 1997 Nov;21(11):759-68.
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Proc Natl Acad Sci U S A. 1997 Nov 25;94(24):13317-22.
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131. Jena, B.P. (2020). Chaperonin: Protein Folding Machinery in Cells *Natures Engineered Marvels*. *Springer Nature* p49-56, ISBN: 9783030444952

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Abstracts, Poster Presentations at Professional Meetings (Recent):

176. 2019 EBM (ASBMB): Human Skeletal Muscle-on-a-Chip; *Naik, A. R., Pernal, S., Lewis, K.T., Wu, Y., Wu, H., Stemmer, P.M., Jena, B.P.*

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178. 2019 International Neuroscience Conference, Tbilisi, GEORGIA: Differential Expansion Microscopy Techniques; *Pernal, S., Kuhn, E.R., Pulvender, R., Formosa, B., Ramos, R., Naik, A.R.,* Liyanaarachchi, A., George, K., Rajagopalan, R., Jena, B. P. (**Selected for Oral Presentation)**

179. 2018 EBM (ASBMB): Valporate inhibits glucose-stimulated insulin secretion in beta cells; *Yedulla, N. R.; Naik, A. R.; Kokotovich, K. M.; Yu, W.; Greenberg, M. L.; Jena, B. P.*

180. 2018 EBM (ASBMB): Membrane Biogenesis in Cells. *Akshata R. Naik, Eric R. Kuhn, Kenneth T. Lewis, Kieth M. Kokotovich, Krishna R. Maddipati, Xuequn Chen, J.H.K. Hörber, Douglas J. Taatjes, Jeffrey J. Potoff, Bhanu P. Jena (Selected for oral presentation)* (**Selected for Oral Presentation)**

181. 2018 NCUR: Valporate inhibits glucose-stimulated insulin secretion in beta cells; *Yedulla, N. R.; Naik, A. R.; Kokotovich, K. M.; Yu, W.; Greenberg, M. L.; Jena, B. P.* (Received Travel Fellowship to NCUR, Oklahoma, to Nikhil Yedulla)

182. 2017 EBM: Machinery Mediating Kiss-and-Run Mechanism of Cell Secretion; *Bhanu P. Jena*

183. 2017 EBM: Different Lipids in Synaptic Vesicle and Synaptosome Membrane. *Kenneth T. Lewis†, Krishna R. Maddipati, Akshata R. Naik, Bhanu P. Jena (Selected for oral presentation)*

184. 2017 EBM: Functional Reconstitution of the Beta Cell Porosome. *Akshata R. Naik, Kenneth T. Lewis, and Bhanu P. Jena*

185. 2016 NCUR: Insulin Secretion in Min6 Cells Reconstituted with the Porosome Complex. *Sanjana Kulkarni, Bhanu Jena,* (Received Travel Fellowship to NCUR, North Carolina & Best Poster in Undergraduate Research Day to S. Kulkarni)

186. 2015 NCUR: Molecular mechanism of regulated insulin release from □-cells.

Sanjana Kulkarni, Bhanu Jena, (Received Travel Fellowship to NCUR, Kentucky)

187. 2015 EBM: Porosome: Involvement of Hsp90 in its Assembly and Function. *Bhanu Jena, Amulya Rajagopal, Sanjana Kulkarni, Kenneth Lewis, Xuequn Chen and Douglas Taatjes* FASEB J April 2015 29:975.6

188. 2014 NCUR: Proteome of the insulin-secreting Min6 cell porosome complex: Involvement of Hsp90 in its assembly and function. *Amulya Rajgopal, Bhanu Jena,* (Received Travel Fellowship to NCUR, Washington, D.C.).

Invited Presentations (Recent/Selected from over 400):

National

2002 Prof. Ahmed H. Zewail Guest Lecture on “Porosome Discovery”, Laboratory for Molecular Sciences, California Institute of Technology. Pasadena, CA. (Sponsored).

2002 Wise & Hellen Burroughs Foundation Lecture, Iowa State University, IA. (Sponsored).

2003 Invited Speaker, “Discovery of the Porosome” Department of Physiology & Cellular Biophysics, Columbia University College of Physicians & Surgeons, NY. (Sponsored).

2005 Sir Aaron Klug Distinguished Lecture & Award, Mississippi State University, MS. (Sponsored).

2005 George E. Palade Distinguished Lecture & Award, Wayne State University School of Medicine, Detroit, MI. (Sponsored).

2006 Keynote Lecture, Genome Science & Technology, Student Research Day, University of Tennessee & Oak Ridge National Laboratory, Knoxville, TN (Sponsored)

2007 Keynote Speaker, International Conference on Biological Sensorics: Critical Technologies for Future Biosystems, Minneapolis, MN (Sponsored).

2008 Plenary Lecture, International Scanning Probe Microscopy Meeting, Seattle, WA (Sponsored)

2008 Distinguished Lecture, Molecular Basis for Disease, Georgia State University, Atlanta, GA (Sponsored).

2008 Invited Lecture, “Porosome: The universal secretory machinery in cells” at the 48th ASCB Meetings, Seattle, WA. (Sponsored).

2009 Invited Lecture on “Porosome Discovery”, Department of Physiology & Biophysics, Case Western Reserve University School of Medicine, Cleveland, OH. (Sponsored).

2009 Invited Lecture on “Porosome Discovery”, Department of Physiology, University of Michigan School of Medicine, Ann Arbor, MI. (Sponsored).

2011 Invited Colloquia Lecture, “Discovery of the Porosome: The Universal Secretory Machinery in Cells”, Department of Physics, University of Wisconsin-Milwakee, WI. (Sponsored).

2011 Invited Lecture on “Porosome Discovery”, Larry L. Hillblom Islet Research Center, UCLA, School of Medicine, Los Angeles, CA

2012 Keynote Speaker, American Physical Society, Detroit, MI. (Sponsored).

2014 Distinguished Lecture, Harvard College Undergraduate Research Association (HCURA), Cambridge, MA

2014 Invited Speaker, Gordon Research Conference, Cilia, Mucus, & Mucociliary Interactions, Galveston, TX. (Sponsored).

2014 Distinguished Lecture, Department of Pathology, Harvard Medical School, Boston, MA

2016 Distinguished Lecture, Harvard Medical School, Boston, MA

2017 Invited Lecture, Stanford Medical School, Stanford, CA (Sponsored).

2018 RALI Distinguished Lecture, Harvard Medical School, Boston, MA (Sponsored).

2019 Keynote Lecture, Nano Boston Conference, Boston, MA (Sponsored).

2020 Keynote Lecture, Nano Boston Conference, Boston, MA (Sponsored)

International

2001 Distinguished Lecture, Samsung Corporation, Seoul, Korea (Sponsored)

2001 State Guest & Distinguished Lecture on the “Power & Scope of Nano Science & Technology”, Korean National Assembly & Science Advisory Committee, Seoul, Korea (Sponsored)

2001 Distinguished Lecture, Korean National Academy of Science, Seoul, Korea (Sponsored)

2001 Keynote Lecture, International Meeting on Vascular Aging & Angiogenesis, Korea (Sponsored)

2002 Keynote Lecture, 6th International Conference on Fundamental & Applied Aspects of Physical Chemistry, Belgrade, Yoguslavia. (Sponsored).

2002 Distinguished Hallim Award Lecture jointly with Prof. Ahmed H. Zewail, Korean Academy of Science, Seoul, Korea. (Sponsored).

2002 Opening Plenary Lecture, Romanian Annual Cell Biology Society Meetings, Satu-Mari, Romania. (Sponsored).

2002 Distinguished Lecture, Serbian National Academy of Science, Belgrade, Yoguslavia.

2002 Distinguished Lecture, Vasile Goldis University, Romania (Sponsored).

2002 Distinguished Lecture, Vinca Research Institute, Yoguslavia. (Sponsored).

2003 Distinguished Lecture jointly with Prof. Günter Blobel, 'Babes-Bolyai' University, Romania (Sponsored).

2003 Distinguished Lecture, Georgian National Academy of Science, Tbilisi, Georgia (Sponsored).

2005 Distinguished Lecture, 'Carol Davila' University, Romania (Sponsored).

2005 Distinguished Lecture, University of Budapest, Hungary (Sponsored).

2006 Keynote Lecture, International NanoBioScience Conference, Pune, India. (Sponsored).

2006 Distinguished Lecture, Agarkar Research Institute, India (Sponsored).

2006 Plenary Lecture, International Meeting on Advanced Spectroscopies on Biomedical & Nanostructured Systems, Cluj-Napoca, Romania.

2008 Distinguished Lecture, 9th International Congress for Cell Biology, Seoul, South Korea. (Sponsored).

2008 Distinguished Lecture, Korea Vaccine Institute & Seoul National University, Korea. (Sponsored).

2008 Weizmann Institute Lecture, Rehovot, Israel (Sponsored & Invited by Prof. Ada Yonath).

2008 Department of Physiology Lecture, University of Toronto, Canada. (Sponsored).

2010 Keynote Speaker & Session Chair, International Neuroscience Meetings, Singapore.

2010 Keynote Lecture, International Garga Lectures, Tbilisi, Georgia.

2010 (Sponsored).

2010 Keynote Lecture, Neuroplasticity Conference, Tbilisi, Georgia. (Sponsored).

2010 Special Lecture, Karolinska Institute, Sweden. (Part-Sponsored).

2010 Special Lecture, Uppsala University, Sweden. (Part-Sponsored).

2011 Special Lecture, Lund University, Sweden. (Part-Sponsored).

2011 Keynote Lecture, Advanced Spectroscopies on Biomedical and Nanostructured Systems. Cluj-Napoca, Romania. (Sponsored).

2012 Indian Chemical Society Lecture, IIT, New Delhi, India. (Sponsored).

2012 Invited Speaker, 46th Annual Israeli Microscopy Society Meetings, Ben Gurion University, Israel. (Sponsored).

2012 Invited Speaker, University of Tel Aviv, Israel. (Sponsored).

2013 Keynote Speaker, ISTC International Scientific Seminar, Tbilisi, Georgia. (Sponsored).

2014 Keynote Lecture, International Garga Lectures, Tbilisi, Georgia. (Sponsored).

2014 “Distinguished Academy Lecture”: Georgian National Academy of Sciences, Tbilisi, Georgia. (Sponsored).

2014 Keynote Lecture, Annual Meeting of the Romanian Cell Biology Society,

Targu Mures, Romania. (Sponsored).

2014 Opening Plenary Lecture, International Neuroplasticity Meetings, Tbilisi, Georgia. (Sponsored).

2014 Distinguished Lecture, Indian Institute of Technology, Bhubaneswar, India. (Sponsored).

2014 Special Lecture, Department of Biochemistry, Delhi University, India (Part-Sponsored).

2015 Special Lecture, Indian Institute of Technology, New Delhi, India. (Part-Sponsored).

2016 Keynote Lecture, World Congress of Molecular & Cell Biology, Nanjing, China. (Sponsored).

2016 Distinguished GIAN Lecture Series (14 Lectures), Jawaharlal Nehru University, New Delhi, India. (Sponsored).

2017 Distinguished Lecture, Delhi University & Ambedkar Research Institute, Delhi, India. (Sponsored).

2017 Distinguished Lecture, University of Windsor, ON, Canada. (Invited/Accepted/ Sponsored).

2017 Rystaveli National Science Foundation Lectures (14 Lectures), Tbilisi, Georgia. (Invited/Accepted/ Sponsored).

2017 Opening Keynote Lecture, International Physiology Congress, Beijing, China. (Invited/Accepted/ Sponsored).

2017 Opening Keynote Lecture, Molecular Medicine World Congress, Xi'an, China. (Invited/Accepted/ Sponsored).

2017 Distinguished Lecture, School of Life Sciences, JNU, Delhi, India (Part Sponsored)

2017 Opening Keynote Lecture, 130th Year Anniversary, Victor Babes National Research Institute, Bucharest, Romania (Sponsored)

2017 Presidents Lecture, Georgian Section of the European Biochemical Society, Tbilisi, Georgia (Sponsored)

2018 Presidents Lecture, Georgian Section of the European Neuroscience Society, Tbilisi, Georgia (Sponsored)

2018 Vedanta University, Institute of Eminence Presentation, New Delhi, India (Sponsored)

2019 6th World Congress on Nanomedical Sciences, New Delhi, India

2019 “Distinguished Keynote Lecture”: International Neuroscience Meeting, Tbilisi, Georgia. (Sponsored).

2019 Keynote Lecture, Keynote Lecture, BIT 9th World Congress of Molecular & Cell Biology, Singapore. (Sponsored).

Narrative Research Report

A. CELL SECRETION

Summary: Secretion is a fundamental process through which cells communicate with their environment and exchange information in a multicellular context to reach homeostasis and sustain life. For decades, the prevailing worldview was that secretion operates as an all-or-none 'complete fusion' event, where vesicles are trafficked to the cell surface where the membrane encapsulating the secretory vesicle fuse and completely incorporate into the cell plasma membrane. The vesicle contents then diffuse out of the cell. This hypothesis, although attractive at first glance, had several key setbacks. First, it predicted a quantization of secretory products packaged into each secretory vesicle, when in fact, secretory vesicle size greatly vary even within the same cell, sometimes as much as 6-fold. Second, the level of additional regulation necessary to rapidly and precisely internalize and sequester vesicle-associated lipids and proteins following incorporation into the cell plasma membrane seem extraordinarily complex, given the tens of thousands of different membrane lipids and their differential distribution even between the same bilayer leaflets. Third, following a secretory episode, partially empty secretory vesicles accumulate within cells as observed in electron micrographs, demonstrating that secretory vesicles are capable of incomplete content release.

We therefore hypothesized some 25 years ago, the presence of a tunable dial at the cell plasma membrane for secretory vesicle docking and fusion without full collapse, and the generation of hydrostatic pressure within vesicles to drive vesicular contents to the cell exterior. Through the use of atomic force microscopy, we identified nanoscale transmembrane cup-shaped lipoprotein structures, and named them 'porosomes,' that have since been implicated in a wide range of secretory events. The family of proteins that make up the porosome has been biochemically identified and the mesoscale structure of the complex has been well characterized through electron microscopy and solution X-ray methods. Defects in one or more porosome components has measurable, often highly potent effects on the regulation of secretion, establishing links between point mutations and secretion-defective disease states such as cystic fibrosis that were previously correlative and are now causative. The discovery of the porosome solved the conundrum of fractional discharge of intravesicular contents from cells by providing an explanation for regulated graded secretion. Porosomes are cup-shaped supramolecular lipoprotein structures at the cell plasma membrane ranging in size from 15 nm in neurons, to 100-180 nm in endocrine and exocrine cells and composed of about 30-40 proteins. In comparison, the 120 nm nuclear pore complex is composed of nearly 1,000 protein molecules.

The discovery of the porosome, formation of SNARE ring complex at the porosome base to establish continuity between the porosome and the secretory vesicle membrane, and the molecular mechanism of secretory vesicle volume regulation, has brought about a clear and compelling understanding of the fractional intra-vesicular content release from cells during secretion. Additionally, it has raised new questions

that we continue to investigate: (a) What is the full set of cellular parameters regulating components of the porosome, and how do they act in concert to achieve a tuned output as a secretory portal? (b) Are porosomes serving multiple duties in cells beyond controlled fractional intra-vesicular release? (c) Are there different subclasses of porosomes where different secretory vesicles carrying different cargo dock and fuse? The impact and reach of the porosome discovery, and the associated findings ranging from understanding the fundamental cellular processes and the emergence of multicellularity, to detecting and preventing secretion-mediated disorders, have come to light.

Porosome Discovery & Cell Secretion Mechanism: Nearly 25 years ago, my laboratory made the fundamental discovery of a new cellular structure called the 'porosome', and since, has elucidated its morphology, composition, function as the universal secretory machinery in cells, and has functionally reconstituted the porosome complex in lipid membrane and in live cells.

A time line of the *porosome* discovery and its participation in cell secretion is briefly outlined: i.e., the elucidation of the porosome structure, its chemical composition, and functional reconstitution into artificial lipid membrane and in live cells (4-14, 43-45); the molecular assembly of membrane-associated t-SNARE proteins at the *porosome* base and v-SNARE proteins in the secretory vesicle membrane in a ring or rosette confermation resulting in the establishment of continuity between the opposing bilayers or ***'fusion pore'*** formation in the presence of calcium (15-23,38); and the molecular mechanism of secretory vesicle volume increase required for intra-vesicular content expulsion with great precision during cell secretion (24-30,42), provide a molecular understanding of the fractional release of intra-vesicular contents from cells during secretion. Consequently, publications of reported studies from other laboratories on the *porosome* complex and the involvement of various *porosome* proteins in secretion and in secretory defects (37,47-62), attest to the critical role played by the *porosome* in health and disease. It took nearly 20 years for the *porosome* to be included in textbooks.

Since the 50's, it was believed that secretory vesicles completely merge with the cell plasma membrane during secretion, resulting in release of the entire vesicular contents, an all or none mechanism. While this provides one mechanism for cell secretion, the observation of partially empty vesicles in cells following secretion [Fig. 1] is incompatible with complete vesicle merger, suggesting the presence of an additional mechanism that allows partial discharge of intra-vesicular contents during secretion. In a 1993 *Nature* article *[1993 Nature 363:497–498]* therefore, *Erwin Neher* wrote: *"It seems terribly wasteful that, during the release of hormones and neurotransmitters from a cell, the membrane of a vesicle should merge with the plasma membrane to be retrieved for recycling only seconds or minutes later."* We hypothesized that the proposed mechanism would involve a plasma membrane structure, which would serve to prevent the collapse of secretory vesicles at the cell plasma membrane, enabling the vesicle to instead transiently establish continuity with the cell plasma membrane, expel a portion of its contents, and disengage while remaining partially filled [Fig. 1a (√), 1b]. This

mechanism would enable the cell to retain the integrity of both the vesicle membrane and the cell plasma membrane.

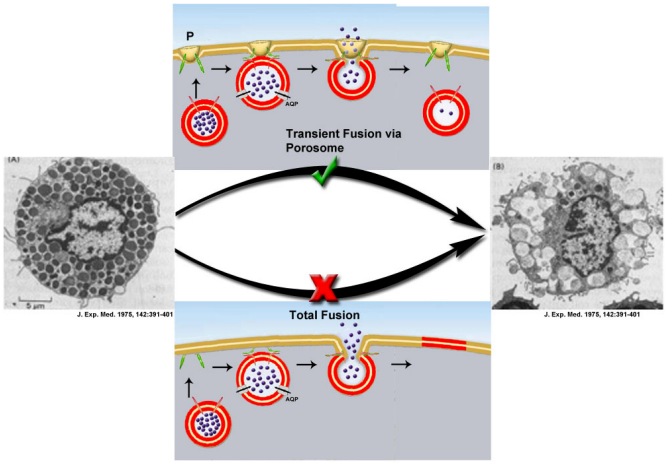

Fig. 1a. Electron micrographs of rat peritoneal mast cells, in resting (A, extreme left) and following secretion (B, extreme right). Note the fractional release of intravesicular contents following secretion (B) (*J. Exp. Med.* 1975, 142:391-401). This fractional release of intravesicular contents could only be achieved via the *porosome* (P)-mediated transient fusion mechanism shown (√).

The late *Bruno Ceccarelli* was a pioneer in the field of 'transient' or 'kiss-and-run' mechanism of secretory vesicle fusion at the cell plasma membrane enabling fractional release of intravesicular contents. Ceccarelli proposed in 1973 the presence of such a process in cells (1). Then in 1990 *Wolfhard Almers* hypothesized that the *fusion pore* (continuity established between the vesicle membrane and the cell plasma membrane), results from a "preassembled ion channel-like structure that could open and close" (2). A later 1992 review (3) by *Julio Fernandez*, opined that the difficulty in observing such channel-like structures, was the lack of ultrahigh resolution imaging tools to directly monitor their presence and study their dynamics in live cells.

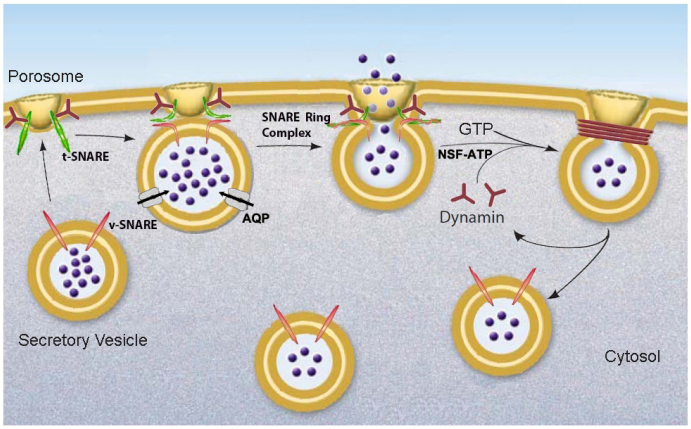

Fig. 1b: Schematic drawing of porosome-mediated fractional release of intravesicular contents from the cell during secretion. Secretory vesicles dock at the porosome base via t-SNAREs present at the pososome base and v-SNAREs present at the secretory vesicle membrane to form a ***t-/v-SNARE ring complex***, establishing continuity between the opposing membranes ***[fusion pore]*** through which pressurized intra-vesicular contents [intra-vesicular pressure established via active transport of water through aquaporin or water channels (AQP) at the secretory vesicle membrane] are expelled to the outside during cell secretion. Following secretion, the t-/v-SNARE rosette complex is disassembled by NSF-ATP and the fused lipid membrane is cleaved by dynamin-GTP. The resultant partially empty vesicle then dissociates from the porosome at the cell plasma membrane.

In the mid 1990's, motivated by the goal of identifying cellular structures at the plasma membrane involved in the regulated fractional release of intravesicular contents from cells, we employed the then newly developed imaging modality of AFM to study the morphology and dynamics of live pancreatic acinar cell surface at the nanometer scale during secretion. The major breakthrough came in 1995-1996, when circular pit-like structures containing 100-180 nm depressions or pores [Fig 2A,B] were observed at the

apical plasma membrane of pancreatic acinar cells, where secretion is known to occur. During secretion, the depressions or pores grew larger, returning to their resting size following completion of secretion. We reported these results on January 1, 1997 in the Proceedings of the National Academy of Sciences (4). Five years later, new results from our laboratory established that the observed depressions are secretory portals at the cell plasma membrane (5,6). In January 2002 and February 2003, we reported in two seminal studies, one in Cell Biology International (5), and the other in the Biophysical Journal (6), that following stimulation of cell secretion, gold-conjugated amylase antibodies (the starch-digesting enzyme amylase being a major intravesicular product secreted by the exocrine pancreas) accumulate at depressions, establishing depressions to be secretory portals in the cell (5,6) and the name *'porosome'* was therefore assigned to the structure. The study reported in the Biophysical Journal (6), further demonstrated the presence of t-SNAREs at the *porosome* base facing the cytosol, firmly establishing *porosome* structures to be secretory portals (6). Electron micrographs of *porosome* at the apical plasma membrane (PM) of pancreatic acinar cells with docked secretory vesicle called zymogen granule (ZG) is presented in Fig 2 (Fig 2 top left and right). In Fig 2A, the *porosome* membrane (POM, yellow arrowhead) associated with the ZG membrane (ZGM) is shown. In March 2002, our laboratory in collaboration with *Lloyd Anderson* reported in the journal Endocrinology (ref. 7, Fig 2 cover illustration lower right), the structure of *porosome* and their dynamics at the cell plasma membrane in growth hormone (GH) secreting cells of the pig pituitary, and the accumulation of GH-immuno-gold at *porosome* openings following cell secretion (7). These results further demonstrate *porosome* to be plasma membrane-associated secretory portals in cells. In the same year in a separate study, we reported *porosome* structure-dynamics in chromaffin cells (8), and in September of 2003 (9) following isolation of *porosome* from acinar cells of the exocrine pancreas, and determination of their composition and reconstitution into lipid membrane, the *porosome* was recognized as the universal secretory portal in cells (9). In the same study (9), morphological details of the *porosome* complex associated with docked secretory vesicles was revealed using EM (9) [Fig. 2A]. Finally in 2015-2016, isolated *porosomes* were functionally reconstituted in live cells (10) by our laboratory, establishing its critical function as the universal secretory machinery in cells and promise in therapy.

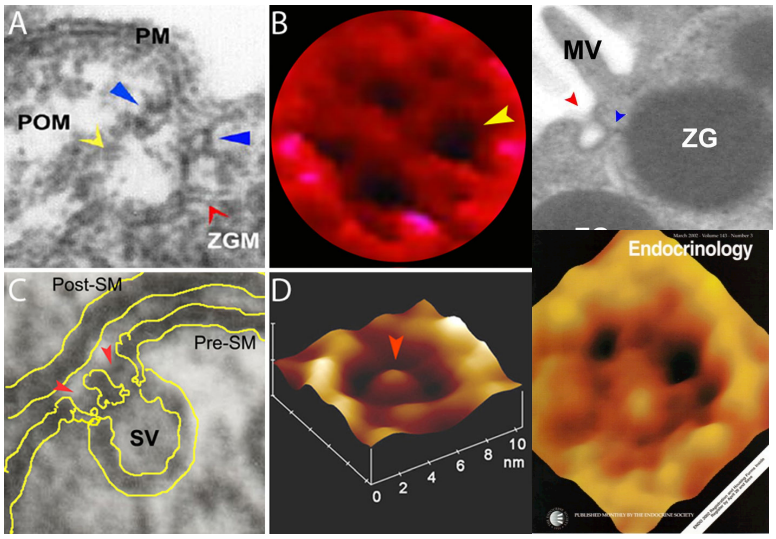

Fig. 2. Porosomes in the exocrine pancreas (A, B), neurons (C, D), growth hormone cell (Journal cover). (**A**) Electron micrograph of a single *porosome* at the apical plasma membrane (PM) of a pancreatic acinar cell showing the *porosome* membrane (POM, yellow arrowhead) associated with the membrane of a secretory vesicle called zymogen granule (ZGM). A circular ring structure (blue arrowhead) forms the neck of the *porosome* complex. (**B**) AFM micrograph of the apical surface topology of a live pancreatic acinar cell, demonstrating the presence of four openings or *porosomes* (one

indicated by the yellow arrowhead). *Porosomes* in the exocrine pancreas range in size from 100-180 nm in diameter. (**C**) Electron micrograph of a neuronal *porosome* (red arrowheads) with a docked synaptic vesicle (SV) at its base, in the presynaptic membrane (Pre-SM) of the nerve terminal. Note the central plug in the *porosome* complex. (**D**) AFM micrograph of a neuronal *porosome* at the presynaptic membrane in an isolated synaptosome. Note the central plug (red arrowhead). The neuronal *porosome* is an order of magnitude smaller (10-17 nm in diameter) in comparison to the *porosome* in the exocrine pancreas. (**Extreme Top Right**) Electron micrograph of *porosome* (Fig 2 top left and right) next to a microvilli (MV) at the apical plasma membrane (PM) of a pancreatic acinar cell with docked secretory vesicle or ZG. (**Extreme Lower Right**) AFM micrograph of the apical surface topology of a live GH cell from pig pituitary demonstrating the presence of 100-180 nm in diameter *porosomes* (black circular openings). [Images obtained from: *Proc Natl Acad Sci* 94:316-321 (1997); *Biophys J* 85:2035-2043 (2003); *Cell Biol Int* 28:699-708 (2004); *J Microscopy* 232:106-111 (2008); *Endocrinology* 143:1144-1148 (2003).

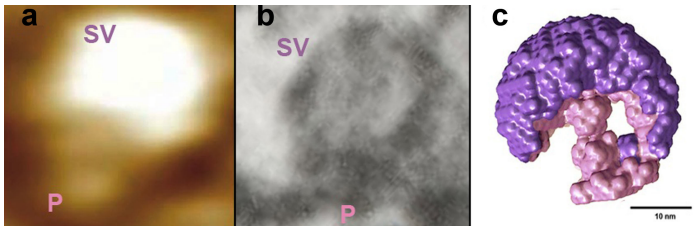

Fig. 3. **Docked synaptic vesicles at the neuronal *porosome*** in the presynaptic membrane of the nerve terminal, observed using AFM, EM, and small angle X-ray solution scattering (SAXS). (**a**) AFM micrograph obtained in fluid of a synaptic vesicle (SV) docked at the cup-shaped *porosome* complex (P) at the cytosolic compartment of the presynaptic membrane. Note the 35 nm SV docked to a 15 nm *porosome* complex. (**b**) An EM micrograph of a 35 nm SV docked to a 15 nm P at the presynaptic membrane [*Cell Biol. Int.* 28:699-708 (2004)]. Note the central plug of the *porosome* complex in the EM micrograph. (**c**) The averaged SAXS 3-D structure of synaptic vesicle (purple) docked at the cup-shaped neuronal *porosome* complex (pink) at the presynaptic membrane in isolated synaptosome is presented *(Bar = 10 nm)* [2014 *Micron* 56:37-43]. Note that AFM, EM, and SAXS, all demonstrate similarity in the docking and interaction of synaptic vesicles with the neuronal *porosome* complex.

In the past 20 years following the initial discovery of the *porosome*, employing a combination of approaches such as AFM, biochemistry, electrophysiology, conventional EM, mass spectrometry, and SAXS, we have reported the presence of *porosomes* in all secretory cells examined, including perhaps most significantly, neurons [Fig. 2C,D; Fig. 3] (11-14). Studies by our laboratory and those of other colleagues, establish this new cup-shaped supramolecular lipoprotein structure at the cell plasma membrane to be secretory portals that performs the specialized task of fractional release of intravesicular contents from cells during cell secretion (12-14). The discovery of the *porosome* provides new understanding on how cells secrete, resulting in a paradigm-shift in our understanding of the secretory process in cells.

The significance of the *porosome* discovery is reflected by the many publications on *porosomes* and associated transient fusion mechanism accompanied by fractional release of intravesicular contents from cells during secretion. In 2011 the *porosome* in hair cells was discovered by *Dennis Drescher* [*Cell Biol. Int. Rep.* (2011) 18:31-34.]; in 2010 *porosome* in RBL-2H3 and BMMC cells were reported by *Gang-yu Liu* [*J. Phys. Chem. B.* (2010) 114:5971-5982.]; *porosomes* in the exocrine pancreas have been further elaborated by the groups of *Elshennawy* in 2011[*J. Am. Sci.* (2011) 7:835-843.] and *Constantin Craciun* in 2013 [*Micron* (2013) 44:137-142.]

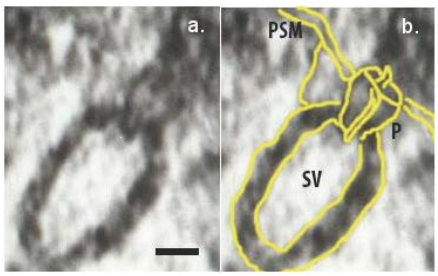

Fig. 4. Electron micrograph of docked synaptic vesicles (SV) at the base of a cup-shaped neuronal porosome complex (P) in the presynaptic membrane (PSM) of the nerve terminal, observed using electron microscopy. *Micron* (2012) 43:948-953.

Porosomes have also been discovered by the group of *Márcia Attias* in the unicellular pathogen *Toxoplasma Gondii* in 2011[*J. Stru. Biol.* (2011) 177:420-430.]; by *Mzia Zhvania* in normal and diseased cat and dog brain neurons in 2012 [*Brain. Res. Bull* (2012) 87(2-3):187; *Cell Tissue Biol.* (2012) 6:69-72.; *Micron* (2012) 43:948-953 [Fig. 4]; and by the group of *Ilan Hammel* and *Isaac Meilijson* in 2012 [J. R. Soc. Interface 2012, 9:2516-2526]. It has also been demonstrated in the exocrine, endocrine, and neuronal cells that "secretory granules are recaptured largely intact following stimulated exocytosis in cultured endocrine cells" [*Proc. Natl. Acd. Sci.* 2003, 100:2070-2075]; "single synaptic vesicles fuse transiently and successively without loss of identity" [*Nature* 2003, 423:643-647]; and "zymogen granule exocytosis is characterized by long fusion pore openings and preservation of vesicle lipid identity" [*Proc. Natl. Acd. Sci.* 2004, 101:6774-6779]. Similarly, in recent years, a great number of *porosome*-associated proteins such as chloride, calcium, and potassium channels, rabs, SNAREs, dystrophin, dynamine, NSF, heterotrimeric GTP-binding proteins, GAPs, and myosin, among others have been implicated in secretion and diseases resulting from secretory defects (37,47-62).

Membrane fusion and secretory vesicle volume regulation for fractional release of intravesicular contents from cells: In the past two decades, our laboratory has also contributed to our understanding of the fundamental molecular process involved in Ca^{+2} and SNARE-mediated membrane fusion (15-23), and on secretory vesicle volume regulation required for the regulated fractional release of intravesicular contents (24-30) via the *porosome* during cell secretion. This process enables cells to precisely regulate the discharge of a portion of their intravesicular contents during a secretory episode, while retaining full integrity of both the vesicle membrane and the cell plasma membrane.

Role of SNAREs in membrane fusion: In 1988 *Richard Scheller* discovered a secretory vesicle associated membrane protein (VAMP-1 or v-SNARE) (31), and then in 1992 he and his team discovered another important protein present in the plasma membrane called syntaxin. Syntaxin is one of the two target SNARE or t-SNARE proteins (32). Then in 1989 Michael Wilson discovered SNAP-25, the other t-SNARE protein (33). Understanding the properties of the three SNARE proteins in membrane fusion requires a molecular understanding of their interactions, with the different SNARE proteins being present in opposing membranes (VAMP-1 in secretory vesicle membrane, and syntaxin and SNAP-25 in the cell plasma membrane). Since SNAREs are membrane-associated proteins, crystals of membrane-associated SNARE complex are required for X-ray crystallography. This has not been possible due to solubility problem of such membrane proteins. To circumvent issues associated with the solubility of membrane associated SNAREs, *Axel Brunger* and *Reinhard Jahn* in 1998 truncated the hydrophobic membrane anchoring domains of syntaxin and VAMP, to obtained crystals of a non-membrane associated t-/v-SNARE complex. Utilizing X-ray

crystallography, Brunger and Jahn determined the atomic structure of the soluble SNARE complex at 2.4Å, which they reported in Nature (34). It was unclear however, whether the structure of the resolved soluble SNARE complex was identical to the native membrane-associated SNARE complex.

To address this issue, we carried out high-resolution AFM studies combined with electrophysiological measurements. In a study reported in the Biophysical Journal in 2002 (15), we demonstrated that in the absence of membrane association, SNAREs fail to appropriately interact with each other or establish continuity between the opposing bilayers in presence of calcium. We further demonstrated for the first time that VAMP-1 proteins present in one membrane interact with syntaxin and SNAP-25 proteins present in an opposing membrane, and assemble in a rosette or ring configuration, establishing continuity between the opposing bilayers in the presence of calcium. While it had been hypothesized that the interaction between t-SNAREs and v-SNARE present in opposing bilayers form rosette or ring structures (35), the experiments confirming this was first reported by us in the 2002 in the Biophysical Journal (15) [Fig. 5], and further established using high resolution EM (18-23). This SNARE rosette arrangement between opposing bilayers during membrane fusion is now widely accepted as the fundamental structure of the t-/v-SNARE complex associated with membrane fusion and cell secretion, and is widely published (36,37).

Role of Ca^{2+} in membrane fusion: In the 1970's, the late *Demetrious Papahadjopoulos* had proposed the involvement of inter-membrane Ca^{2+}-phospholipid complex in the fusion of opposing lipid membranes (38). To determine the involvement of Ca^{2+} in membrane fusion at the atomic level, Professor Jena performed X-ray diffraction studies involving t- and v-SNARE reconstituted liposomes (16). Results from this study demonstrated that SNAREs overcome the repulsive forces between the opposing negatively charged lipid membranes to bring them within a distance of 2.8Å (16). We therefore concluded that if calcium was involved in the bridging of opposing bilayers via oxygen of the phospholipid head groups, calcium must be present at the site where the t-SNARE vesicles and v-SNARE vesicles make contact. t-SNARE vesicles and v-SNARE vesicles associated in the absence of calcium, would therefore fail to establish continuity between the opposing bilayers since hydrated calcium (with 6 water molecules surrounding it) measuring nearly 7Å would be unable to fit within the 2.8Å spacing separating the two opposing membranes. In 2004, this hypothesis was tested and confirmed experimentally by our laboratory (17).

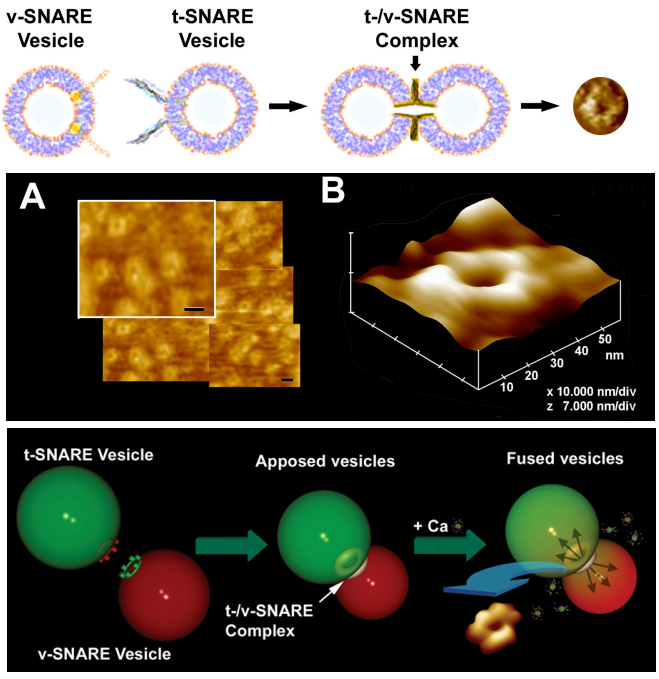

Fig. 5. Actual t-/v-SNARE ring complexes or

rosettes formed following the interaction between membrane-associated t-SNAREs and v-SNAREs. Top panel is a schematic drawing depicting the interaction between t-SNAREs and v-SNAREs in opposing vesicles. AFM micrographs of the actual SNARE complex rings or rosettes are presented in the top right panel, in the middle panel, and in the right lower panel (15,16).

From these results, we further hypothesized that following bridging of the opposing phospholipids by hydrated Ca^{2+}, the loss of coordinated water associated with the calcium ion as well as those associated with the oxygens of the phospholipid head groups must result in local dehydration, lipid mixing, and membrane fusion. In collaboration with *Jeff Potoff*, we tested this hypothesis using blind molecular dynamic simulations involving dimethyl phosphate (DMP), calcium, and water molecules (14). Confirming this hypothesis, results from the study demonstrated that hydrated Ca^{2+} is capable of bridging phospholipid head groups, and that this process results in the expulsion of water from both phospholipid head groups and the calcium ion (39). The simulation further demonstrated that the distance between the anionic oxygen in DMP bridged by calcium is 2.92Å, which is in close agreement with the 2.8Å reported from X-ray diffraction measurements (16). These findings provide new insights into our understanding of the chemistry of membrane fusion in cells.

Secretory vesicle volume increase, and regulated content expulsion during cell secretion: In the early 1990's it was reported that secretory vesicles undergo an increase in volume during cell secretion (40,41). However, the molecular mechanism underlying volume regulation of secretory vesicles, and the role of this volume increase on secretory vesicle function during cell secretion, was poorly understood. Studies by our laboratory showed that water channels or aquaporin in conjunction with several ion channels present at the secretory vesicle membrane regulate vesicle volume through GTP-binding G-proteins (24-30). The role of various ion channels at the secretory vesicle membrane was also demonstrated using single vesicle patch studies (42). In 2004, we reported that secretory vesicle volume increase is a requirement for the regulated release of intravesicular contents from cells (26). The relative increase in vesicle volume during cell secretion is proportional to the fraction of the intravesicular contents expelled.

In summary, studies by our laboratory in the past over 20 years demonstrate the presence of a new cup-shaped lipoprotein structure at the cell plasma membrane called *porosome*, -the universal secretory machinery in cells, and elucidated how the *porosome* is involved in the regulate fractional release of intravesicular contents from cells with exquisite precision involving membrane fusion and secretory vesicle volume regulation. We have isolated the *porosome* from a number of secretory cells including neurons, determined its composition, functionally reconstituted it in lipid membrane and live cells, and determined its dynamics and high-resolution structure using a variety of approaches including AFM, EM, and SAXS. Complementing the regulation of the *porosome* function, our studies have further contributed to our understanding of membrane fusion and secretory vesicle volume regulation, both required for the regulated fractional release of intravesicular contents during cell secretion. These results provide for the first time a molecular understanding of the regulated fractional release of intravesicular contents from cells during secretion. Recent studies by our laboratory using mass spectrometry, demonstrate interaction between the cystic fibrosis

trans-membrane conductance regulator (CFTR) and the *porosome* complex in human airways epithelia, shedding light on the possible regulatory role of CFTR on the quality of mucus secretion via the *porosome* complex (43). Results from this study provide critical insights into the etiology of CF disease and for potential therapies. Similarly, our recent studies using mass spectrometry provide understanding of the lipidome of the neuronal *porosome* complex (44), and the role of Hsp90 in *porosome* assembly and function (45), has enabeled further understanding of the *porosome* structure-function (46). To determine the distribution of proteins within the *porosome* complex, our laboratory is currently engaged in single particle electron crystallography, cryoelectron microscopy, X-ray solution and neutron scattering, and chemical cross linking followed by mass spectrometry. In a recent publication (10), we report for the first time the functional reconstitution of the insulin-secretion *porosome* complex into live insulin secreting cells, resulting in an increase in the potency and efficacy of glucose-stimulated insulin release, and a promise for therapeutic applications. In the past decade, there have been scores of publication by other laboratories on the *porosome* complex and the involvement of various *porosome* proteins in secretion and in secretory defects, some referenced here (37,47-62), attesting to the critical role played by the *porosome* in health and disease.

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CURRENT RESEARCH

B. Determine the distribution of proteins within the neuronal porosome complex utilizing chemical cross linking followed by mass spectrometry and molecular modeling.

C. Determine the structure and composition of the neuronal porosome complex during development.

D. Use of single molecule nanoscale thermometry to understand the enthalpy of protein-protein and protein-ion interactions, impact of cation binding on the structure-function of the motor protein myosin, in evaluating muscle efficiency, detection of metabolic diseases including cancer, single molecule calorimetry, and the detection of bacterial antibiotic resistance and pathogenesis.

E. Establish the ‘Human Skeletal Muscle Cell Atlas” utilizing ‘Machine Learning”.

F. Molecular mechanism of membrane biogenesis in cells.

G. Mitochondrial electron transport chain.

H. Exosome biology.

I. Differential Expansion Microscopy.

J. Determination of intracellular pH at the nanometer and milli-pH scale.

K. "Muscle-on-a-Chip" stretchable 3D microphysiological platform.

Institution-Building Activity:

TO BENEFIT HUMANITY: Educate, Innovate, Invent, Inspire

1. (Invited with $450 million initial funding and $10 billion in the next decade) Establishment of the Molecular Medicine Institute (MMI), Cambridge, MA. (Source of Funding: Philanthropy) [https://cms9.revize.com/revize/moleculartx/].
2. Develop an 'Astromedicine Program'.
3. Help in the establishment of Vedanta University in India. (Source of Resource: Philanthropy)
4. Help in the establishment of Nano Institute & Neuroscience Doctoral Program, Tbilisi, Georgia
5. Establish Nano Medicine Institute, Delhi University, Delhi, India
6. Co-Founder & President: QPathology [**https://www.qpathology.com**]

BRIEF BIOGRAPHY

I was born in Jajpur, a small town in Odisha, India, on November 1, 1955, to Manju and Prafulla Jena. My early childhood was spent in remote villages in Odisha, where my grandfather Braja Kishore practiced medicine. The dedication of my father and grandfather to science and medicine and their service to humanity greatly influenced me to choose a career in science. I majored in Chemistry, Zoology, and Botany, for my Undergraduate studies at BJB College in Bhubaneswar, Odisha (B.Sc., 1975) and completed Masters in Zoology (Endocrinology) from Utkal University, (M.Sc., 1978). I graduated top of my graduating class in the Masters of Science program and received the Prasant Ku. Memorial Prize and the Utkal University Gold Medal. In December of 1988, I received Doctorate Degree (Ph.D.) in Zoology (Molecular Endocrinology), and the Research Excellence Award from Iowa State University. Following postdoctoral training as a Fellow at Yale University, I accepted a faculty appointment at Yale University as an Assistant Professor, and in 2000, moved to the Department of Physiology, at Wayne State University School of Medicine, as a tenured full Professor, and Founder-Director of the Institute of NanoBioScience. In 2004, I was conferred the title of Distinguished Professor, and the George E. Palade University Professor by the Board of Governors of Wayne State University. I am the only living University Professor, and the second at Wayne State University's 160-year history.

Since high school, my passion has been to understand the workings of the unit of life, 'the cell'. At a very early age, I was fascinated by the complexity of 'the cell' in electron micrographs, similar to the complexity of a city, yet every aspect of its function is so precisely regulated. My scientific enquiry on how cells secrete, led to the discovery of the *"porosome"* -a new cellular structure and a molecular nanomachine, demonstrated to be the universal secretory portal in cells involved in the fractional release of intra-vesicular contents during secretion. Currently, the major focus of my laboratory is to determine the distribution of proteins within the porosome complex using single particle cryoelectron microscopy, and small angle x-ray solution and neutron scattering. In the past two decades, I have been involved in institution building to bring the benefits of science and education to society.

Among the honors and awards I have received: Distinguished Scientist Award from the Society for Experimental Biology and Medicine; Elected Foreign Member of the Georgian National Academy of Science; Fellow AAAS; Elected Foreign Member of the Korea Academy of Science & Technology; Elected Foreign Member of the National Academy of Medicine, Romania; Elected to the European Union Academy of Science; the Swebelius Cancer Research Award; the Hallim Distinguished Award Lecture jointly with the Prof. Ahmed H. Zewail; Sir. Aaron Klug Award; ASAS Basic Biological Science Award; Ranbaxy Basic Research in Medical Sciences Award; George E. Palade Gold Medal; Elected to the Academy of Scholars at Wayne State University; six Honorary Doctorates including one from Babes-Bolyai University, Romania, jointly with Prof's George E. Palade and Günter Blobel; and Distinguished Visiting Professorships in a number of institutions.

Throughout my career, I have been fortunate to avail the opportunity to learn from wonderful teachers and scholars, and to work with students and colleagues with a passion for science. My parents and my family have been a great source of peace, inspiration, and joy in my life.

"The three stages of truth: *At first it is ridiculed. Then, violently opposed and finally become accepted as self-evident*." Arthur Schopenhauer (1788-1860).