Some Examples of Collaborative Studies at NBSI

International Collaborations

Zhvania-Jena Collaboration (2003-present): Prof. Mazia G. Zhvania, Professor of Neuroscience, Ilia State University & Head of Laboratory of Brain Ultrastructure and Nanoarchitectonics, I. Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia, and Prof. Jena’s group have been collaborating for over a decade on the structure-function of the neuronal porosome complex. Prof. Zhvania is a leading investigator in the cutting-edge technology and field of Nano Science and Nano Medicine, focused on neurobiology and neuronal diseases, critical in the development of new neurological treatment modalities, drug development, and therapy. Prof. Mzia G. Zhvania is also a leading expert on the ‘porosome’, a supramolecular structure involved in neurotransmission, and is one of the first to establish the field of Nano Science in Georgia. The expertise and instrumentation available in the Zhvania group and her Georgian colleagues have provided high-resolution electron microscopy (EM), and EM tomography capabilities for the study of the brain, individual neurons, and supramolecular structures at the nerve terminal such as the porosome, the secretory portal for neurotransmission. The Jena laboratory has helped train students from the Zhvania group in atomic force microscopy and associated biophysical approaches, and in the recent past, Dr. Nato Kotaria and Ms. Vera Okuneva from the Zhvania group received fellowship from Georgia to come and spend 6 and 3 months respectively, to training in the Jena laboratory at WSU. This collaboration between the Zhvania and the Jena group has resulted in the publication of two scientific papers listed below:


In the past decade, Prof. Zhvania has received grant funding to host three international meetings on nano medicine involving neurons and neurological disorders, which were attended and participated by Jena and colleagues.

Jena participation in international institution building:

1. Established the Asian NanoScience Institute in South Korea and served as its Co-Director (2002-2006).

2. Development of the Institute of NanoMedicine in University of Delhi, India (ongoing).

3. Development of the Membrane Biology Institute in JNU, Delhi, India (ongoing).

4. Invited to help establish a $3 billion Vedanta University, Odisha, India (ongoing).

Reid-Stemmer Collaboration (2009-present): Development and testing of new chemical labeling strategies for mass spectrometry based analysis of biomolecules. Over the last few years I have had the good fortune to collaborate with Dr. Gavin Reid from The University of
Melbourne in Melbourne Australia. Gavin and I have complementary research interests and backgrounds. His group has developed novel chemical labeling strategies and has examined the behavior of novel chemical entities in the gas phase during MS analysis. I have contributed by evaluating the new reagents in my lab with a focus on novel approaches to analysis of phosphopeptides. The field of signaling and signal transduction research has benefited from this work and it has laid the groundwork for additional advances in targeted proteomic analysis.


Rueda-Stemmer Collaborations (2014-present): Bioinformatics for interpretation of omic data sets. Dr. Luise Rueda from the University of Windsor in Windsor CA has been a valued collaborator for the past three years. Our work is focused on interpretation of proteomic data sets that have hundreds to thousands of quantified elements. Our first project together was presented at the 2016 Great Lakes Bioinformatics and the Canadian Computational Biology Conference in Toronto.


National Collaborations

Ren-Jena Collaboration (2004-present): Dr. Gary Ren, Lawrence Berkeley Laboratory, CA, have been collaborating on t-/v-SNARE and porosome structures using cryo-EM. This ongoing collaboration has resulted in the funding of one DOE User Proposal and the following 5 research publications.


**Taatjes-Jena Collaboration (1998-present):** Prof. Douglas J. Taatjes, Department of Pathology, University of Vermont College of Medicine, VT, have been collaborating on t-/v-SNARE and porosome structures using various imaging modalities. This ongoing collaboration has resulted in the funding of one NIH grant and the following 10 research publications.


**Stemmler-Dancis Collaboration (2002-present):** Prof. Andrew Dancis, Division of Hematology, Department of Medicine at the University of Penn, Philadelphia has been collaborating with Dr. Timothy Stemmler, Department of Pharmaceutical Sciences, WSU to
elucidate the molecular and atomic basis for cellular metal regulation using a variety of Biophysical techniques. This work has been NIH funded for the past 11 years and resulting in 11 publications.


Stemmler-Rosenzweig Collaboration (2003-present): Prof. Amy Rosenzweig, Department of Chemistry at Northwestern University has collaborated with Dr. Stemmler to characterize the molecular and atomic characteristics of particulate methane monooxygenase, a protein isolated from several methanotrophic bacteria that converts methane to methanol. In the process of removing the green house gas methane, it converts the gas to a viable liquid energy source, methane. This work, as well as additional collaborations, has resulted in 12 publications.


Stemmler-Rosen Collaboration (2001-present): Prof. Barry Rosen, Department of Cellular Biology and Pharmacology, Florida International University, collaborates with Dr. Stemmler to better understand the molecular and atomic details of how As binding proteins regulate metalloid homeostasis and drive methylation of the metalloid. There work together has developed into 7 publications.


3. Yang, J.; Rawat, S.*; Stemmler, T.L.; Rosen, B.P. “Arsenic binding and transfer by the ArsD As(III) metallochaperone” Biochem., 2010, 49 (17), 3658-66.


Persechini-Stemmer Collaboration (1995-present): Dr. Anthony Persechini from the University of Missouri Kansas City has been a valued collaborator for over 20 years. Our work is focused on the biochemical mechanisms of calmodulin-dependent signaling. Calmodulin is a key regulator of almost every process in mammalian cells. The work I have done to detail the mechanisms by which calmodulin binds with positive cooperativity in a Ca2+-dependent manner to the calmodulin-binding domains of target proteins and to delineate the role of the different Ca2+ binding sites in calmodulin are shown in the following papers. Our current work is focused on profiling the full calmodulin binding proteome using crosslinking and LC-MS/MS.


Wayne State University Collaborations

Potoff-Jena-Manke (2007-2011): NSF Supported Project (2007-2011)– Prof. Jeffrey Potoff (PI)/Jena (Co-PI)/Manke (Co-PI); NSF-CBET 0730768 – Bioengineering and Molecular Simulation Studies to Understand Membrane Fusion. Results from experiments and simulations funded by this work are described in detail in the preliminary data. This grant provided partial funding for two graduate students Mrs. Zeena Issa (Chemical Engineering) and Ms. Leah Shin (Physiology), and undergraduate student, Rebecca Lindsey (Chemical Engineering). To date, this ongoing project has produced 6 peer-reviewed manuscripts [1-6], one of which was featured on the cover of the Journal of Physical Chemistry B [2]. Four scientific presentations were made at national and international meetings.

Potoff-Jena-Manke (2011-2016): NSF Supported Project (2011-2016) – Potoff (PI)/Jena (Co-PI)/Manke (Co-PI); NSF-CBET 1066661 – Elucidation of Membrane Fusion Mechanisms Using a Combined Simulation and Experimental Approach. The Jena component of this grant provided partial funding for two graduate students Ms. Amanda Flack (Physiology, who graduated with a Ph.D. in June 2014) and Mr. Kenneth T. Lewis (Physiology, current doctoral candidate). With support from the Dept. of Physics & Astronomy, two graduate students Ms. Maheshika Perera (Physics) and Mr. Suvra S. Laha (Physics). Laha successfully completed his doctoral program in the laboratory, and is doing post-doctoral studies. Undergraduate students, Ms. Sanjana Kulkarni (Biology); Ms. Amulya Rajagopal (Physics); Mr. Brandon Laethem (Biology); and Mr. Malek Ghandour (Biology), continue to work on various associated projects in the laboratory. A manuscript submitted with Amulya Rajagopal and Sanjana Kulkarni as lead authors, has been published [6], and a second manuscript with Sanjana Kulkarni as co-author with Graduate Student Akshata Naik (Physiology) is published [8] in the journal *Endocrinology*. Studies by Rajagopal and Kulkarni were twice selected and funded for their participation at the 2014 NCUR Kentucky, and the 2015 NCUR Washington Conference. Additionally, Ms. Rajagopal received the prestigious 2014 “George B. & Eveline R. Beard Endowed Student Prize” for her work. Ms. S. Kulkarni is completing her Senior Thesis in the lab. In the past three years, besides the three graduate and four undergraduate students, four high school students (Rohin Patel, Alina Shafikova, Naveen Karthik, and Cara Skrzycki) have actively participated in summer research in the laboratory, with Naveen Karthik making the Semifinalist in the 2014 Siemens Math & Science Competition. Ms. Alina Shafikova now a freshman, continues to progress her work in the laboratory, and proposes to work toward her Senior Thesis dissertation in the lab. To date, this ongoing project has produced 8 peer-reviewed manuscripts [1-8], one [2] of which was featured on the cover of the Journal of Histochemistry and Cell Biology, and another published in the Journal of Proteomics [4] was selected as F1000 prime. Additional manuscripts with Brandon Laethem as lead author in one, and Kenneth T. Lewis as lead author in three manuscripts, are in preparation. Eight scientific presentations were made at national and international meetings during this funding period.


**Stemmler-Jena Collaboration (2008-present):** Prof. Timothy L. Stemmler, Department of Pharmaceutical Sciences, have been collaborating on t-/v-SNARE structure-function in neurons using CD spectroscopy. This ongoing collaboration has resulted in the following research publications.


**Chen-Jena Collaboration (2012-present):** Prof. Xuequn Chen, Department of Physiology, have been collaborating on composition of the porosome complex using mass spectrometry. This ongoing collaboration has resulted in the following research publications.


**Sun-Jena Collaboration (2014-present):** Prof. Fei Sun, Department of Physiology, have been collaborating on composition of the porosome complex in human airways epithelia. This ongoing collaboration has resulted in the following research publication.


**Maddipati-Jena Collaboration (2014-present):** Prof. Krishna R. Maddipati, Director, Lipidomics, have been collaborating on determining the lipid composition of the porosome complex and in membrane biogenesis. This ongoing collaboration has resulted in the following research publication.

**Kovari-Jena Collaboration (2014-present):** Prof. Ladislau Kovari, and the Jena lab. have been collaborating on determining the molecular structure of the native neuronal porosome complex using solution X-ray and neutron scattering studies. This ongoing collaboration has resulted in the following research publication.


**Kim-Jena Collaboration (2015-present):** Prof. Hyeong-Reh Kim, Department of Pathology, have been collaborating on the use of pH- and temperature-sensitive nanoparticles in cancer detection and therapy. This ongoing collaboration has resulted in the following research publication.


**Kelly-Jena Collaboration (2014-present):** Prof. Chris Kelly, Department of Physics & Astronomy, have been collaborating on t-γ-SSNARE and porosome structure-function in beta cells of the endocrine pancreas using super resolution microscopy. Jointly, Prof’s. Kelly and Jena revealed the effects of HSP90 on the supramolecular structure of the porosome secretory portal. In brief, inhibition of HSP90 resulted in deformations in porosome assembly and function. They achieved this through complimentary methods in proteomics, optical imaging, and electron microscopy. Ongoing collaborative studies are exploring the effects of membrane bending on the organization of the porosome on the plasma membrane. Through engineering nanoscale membrane curvature and Polarized Localization Microscopy, preliminary data suggests a passive sorting and aggregation method of porosomes at membrane buds. Additionally, Profs. Kelly and Jena have jointly advised graduate and undergraduate students. In particular, Dr. Suvra S. Laha earned his Ph.D. in physics by studying the magnetic properties and biomedical applications of nanomaterials. Dr. Laha discovered mechanisms for regulating the relaxation rates and temperatures for supraparamagnetic nanoparticles by balancing the Brownian and Neel relaxation rates via diverse nanoparticle syntheses. This ongoing collaboration has resulted in the following research publication.


**Mao-Jena Collaboration (2012-present):** Prof. Guangzhao Mao, Department of Chemical Engineering & Material Science, and the Jena group have been collaborating on porosome structure-function using AFM. This ongoing collaboration has resulted in the following research publications.

Stemmer-Walz-Jena Collaboration (2015-present): Prof. Paul M. Stemmer, Director of Proteomics at Wayne State, Prof. Daniel A. Walz, and the Jena lab. have been collaborating on understanding the proteome of the human platelet and the different vesicles within.

Kelly-Potoff Collaboration (2015-present): Profs. Kelly and Potoff have an emerging collaboration to reveal the nanoscopic mechanisms of membrane bending. Prof. Potoff brings his expertise in computational simulations and revealing the molecular details of membrane organization. Prof. Kelly brings his expertise in super-resolution optical methods and nanoengineering. Jointly, they are exploring the mechanism by which lipids of varying shape and phase may contribute to spontaneous membrane bending and initiate endocytosis.

Kelly-Granneman Collaboration (2015-present): Professor James Granneman, Department of Molecular Medicine and Genetics, Wayne State University School of Medicine, specializes in adipose tissue cell and molecular biology, target identification and high throughput screening for novel obesity and diabetes therapeutics. This growing collaboration combines Prof. Granneman’s expertise in endocrinology and metabolism with Prof. Kelly’s expertise in nanoscale biological processes. Jointly, they aim to understand the supramolecular structures created on the phospholipid surface of lipid droplets within fat cells. Through revealing the cooperative protein behavior, they hope to further advance therapeutic approaches for regulating lipolysis.

Rosenspire-Caruso-Stemmer (2005-present): Analysis of Toxicant and disease mechanisms. Using mass spectrometry we have profiled phosphoproteomes and signaling molecules. The findings have been the first to demonstrate that the Lyn kinase is a key node in mercury toxicity. In this ongoing project we have performed discovery analysis by profiling mass spectrometry focused on the phosphoproteome and targeted quantitation using Multiple Reaction Monitoring (MRM) of phosphopeptides in Lyn kinase. We are expanding this project to examine the contribution of genetic background to mercury toxicity mediated by phosphorylation changes in Lyn kinase and Syk kinase. The following publications are papers from my research group in collaboration with Drs. Al. Rosenspire and Joe caruso.


Dombkowski-Stemmer Collaboration (2008-present): Dr. Alan Dombkowski and I have collaborated on various projects in which advanced analysis of proteomic data sets is required. Our shared publications are represented in the previous sections and also include the following.

**Pellett Collaborations:** Viruses are nanomachines that can be targeted for destruction by nanomachines designed for that purpose, as was done in a study performed in collaboration with Dr. Lawrence Lum and other investigators from the Karmanos Cancer Institute, Henry Ford Hospital, and the Wayne State Division of Infectious Diseases.


**Pellett-Jena collaborations:** Prof. Pellett has been studying how herpesvirus virions acquire their envelope and how newly enveloped virions are transported to, and then released from the cell surface. An ongoing project in the laboratory has included collaboration between the Pellett and Jena laboratories.

**Pellett-Kovari collaborations:** The Pellett laboratory is collaborating with the laboratory of Prof. Ladislau Kovari to study the structural aspects of the function of a conserved herpesvirus protein that is involved in virion envelopment and egress.