NanoBioScience Institute (NBSI)

http://www2.med.wayne.edu/physiology/nanobioscience/nanobioscience.htm

School of Medicine

Wayne State University

Progress Report prepared by Prof. Bhanu P. Jena, Director, NBSI

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NBSI was established in 2000 at the School of Medicine immediately after my arrival from Yale University School of Medicine and is the first and only existing NanoBioScience institute on our campus in this cutting-edge technology. 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, with no seed funding from the University, NBSI continues to contribute to the academic and research progress in the field, and to bring recognition to the School of Medicine and to Wayne State University. Some of the continuing contributions of NBSI are highlighted below:

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, NIH, DOD, and private sources.**
3. **Developed a team-taught, across campus interdisciplinary NanoBioScience Course (PSL7215) in the Dept. of Physiology at the Medical School, which is in its 11th year of offering. The class size continues to grow, and in the current class, we had 30 students from across campus. Students from other schools including from the University of Michigan are attracted to this course, and many have opted to continue their higher education as Ph.D. and MD students at Wayne State University.**

4. **NBSI has been selected as one of the top four Nano Institutes in the US. PROVIDED AT THE END OF THIS REPORT (http://www2.med.wayne.edu/physiology/nanobioscience/pdfs/Nanotechnology%20Standing.pdf).**
5. **The NBSI Director together with the late Prof. Ahmed H. Zewail (1999 Nobel Laureate in Chemistry) has helped establish the $150 million Asian NanoScience Institute in South Korea and served as its Co-Director (2002-2006).**
6. **The NBSI Director was organizer and Chair of the *International Nano Science Symposium* in 2002 at Wayne State University.**
7. **The NBSI Director was Co-organizer and Co-Chair of the *International Nano Science Symposium* in 2002 at Pusan National University in South Korea (Supported by Samsung and Govt. of Korea).**
8. **The NBSI Director was organizer and Chair of an *International Conference on Nano Science in the Understanding of Nature* in 2005 in Aiche, Japan, at the World Expo to show case the Medical School and Wayne State University. WSU President and Michigan Governor attended the conference. (Supported by a $250,000 grant from Toyota Corp.)**
9. **The NBSI Director was selected by the National Science Foundation (2003-2009) to serve as one of the 4-member Site Visit Team to assist in the establishment of the Nano Biotechnology Center at Cornell University in Ithaca.**
10. **The NBSI Director and NBSI member and collaborator Prof. Charles Manke, Associate Dean of Engineering, WSU, were both invited in 2015 by the President of Târgu Mureș University in Romania, to help establish a Nano Science Institute in that university and to establish strong collaborative research partnership with NBSI, which is on going.**
11. **The NBSI Director together with Prof. Roger Kornberg (2006 Nobel Laureate in Chemistry) serves in the Advisory Board and is helping in the establishment of a $6B STEM University in India, funded by the Anil Agarwal Foundation: (https://www.med.wayne.edu/news/2016/07/13/bhanu-jena-invited-to-contribute-to-indias-3-billion-vedanta-university-project/).**

    This has helped initiate the establishment of both research and clinical ties between NBSI, WSU School of Medicine, and the proposed Medical School of the Vedanta University.

12. **NBSI has fostered the establishment of several national and international scientific collaborations, grant applications, and meetings.**
13. **The NBSI Director was invited in 2017 by the Rustaveli National Science Foundation of the Republic of Georgia, together with the NBSI international collaborator Prof. Mzia G. Zhvania, Head of Chemical Neuroscience, Ilia State University, Tbilisi, Georgia, to establish a nano neuroscience Ph.D. program, where Ph.D. students funded by the foundation will visit NBSI to work in various member laboratories. This proposal was funded, resulting in annual international scientific meetings and student exchange and research collaborations:**
    https://cellularneurosciencephd.iliauni.edu.ge/?lang=en
    http://bnsma2019.iliauni.edu.ge

14. **NBSI Director has published five books on Nano Science and over 170 scientific papers in the field, some which are listed below. Completion of two additional books is in progress.**

15. **The NBSI Director received the Honorary Scientist Award from the 130-year old "*Victor Babes National Institute of Pathology*" [https://www.ivb.ro/v3/] of Romania and invited to serve on its Advisory Board. Research collaborations between NBSI and the Victor Babes National Institute initiated.**

    https://today.wayne.edu/medicine/news/2017/11/29/romanian-institute-of-research-and-development-in-pathology-honors-dr-jena-30000

16. **NBSI establishes research collaborations with Delhi University, where the NBSI Director serves as an Honorary Professor for life.**

    https://today.wayne.edu/medicine/news/2017/04/10/delhi-university-names-bhanu-jena-lifetime-honorary-professor-29786

Collaborative Studies at the NBSI

Some International NBSI Collaborations

NBSI-Ilia State University & I. Beritashvili Center, Tbilisi, Georgia

Zhvania-Jena Collaboration (2003-present): Prof. Mazia G. Zhvania, Professor of Neuroscience, Ilia State University & Head of Laboratory of Brain Ultrastructure and Nanoarchotecture, 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:

1. Cho, W.J., Lee, J-S., Ren, G., Zhang, L., Shin, L., Manke, C.W., Potoff, J., Kotaria, N., Zhvania, M.G., Jena, B.P. (2011) Membrane-directed molecular assembly of the neuronal SNARE complex. *J. Cell. Mol. Med.* 15:31-37.

2. Cho, W-J., Jeremic, A., Rognlien, K. T., Zhvania, M.G., Lazrishvili, I., Tamar, B., Jena, B.P. (2004). Structure, isolation, composition and reconstitution of the neuronal fusion pore. *Cell Biol. Int.* 28:699-708.

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

participated by Jena and colleagues. Jena and Zhvania have applied for an NIH-Fogarty Foundation grant. In May 2017, a new Nano neuroscience Ph.D. Program was launched in Ilia State University in Tbilisi, Georgia through funding from the Georgian Government's Rustaveli Science Foundation. Graduate student are expected to come and work in NBSI Lab's funded by the Georgian Govt.

NBSI-Karolinska Institute, Stockholm, Sweden

Larsson-Jena Collaboration (2012-present): Prof. Lars Larsson, Professor of Physiology, Karolinska Institute, Stockholm, Sweden and the Jena group have collaborated in several aspects of muscle physiology and published the following study:

1. Li M, Deguchi T, Näreoja T, Jena BP, Hänninen P, Larsson L. (2015) Nanometric features of myosin filaments extracted from a single muscle fiber to uncover the mechanisms underlying organized motility. *Arch Biochem Biophys*. 2015 Oct 1;583:1-8. doi: 10.1016/j.abb.2015.06.010. PMID: 26116379

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

Funded by the Karolinska Institute, Post-Doctoral Student Dr. Mishan Lee has visited the Jena lab. to conduct research on muscle efficiency. Results from the study (March-April, 2017) and earlier studies, was part of the manuscript #2 (above), and was used to put together a proposal to NIH for joint funding.

NBSI-University of Windsor, Windsor, Ontario, Canada

Trant-Jena Collaboration (2017-present): Prof. John F Trant and the Jena lab. have been collaborating on determining optimal carbohydrate formulations as cell and tissue cryoprotectants the molecular level mechanisms involved in such protections. This is an ongoing collaboration.

NBSI-University of Melbourne, Melbourne, Australia

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.

1. Smith S.A., Kalcic C.L., Safran K.A., Stemmer P.M., Dantus M., Reid G.E.: Enhanced characterization of singly protonated phosphopeptide ions by femtosecond laser-induced ionization/dissociation tandem mass spectrometry (fs-LID-MS/MS). J Am Soc Mass Spectrom. 21:2031-40, 2010. PMID: 20888783
2. Palumbo, A.M., Smith, S.A., Kalcic, C.L., Dantus, M., Stemmer, P.M. and Reid, G.E.: Tandem Mass Spectrometry Strategies for Phosphoproteome Analysis. Rev. Mass Spectrom Rev. 2011, 30(4):600-25. PMID: 21294150

3. Lu, Y., Zhou, X., Stemmer, PM., Reid, GE.: Sulfonium Ion Derivitization, Isobaric Stable Isotope Labeling and Data Dependent CID- and ETD-MS/MS for Enhanced Phosphopeptide Quantitation, Identification and Phosphoprylation Site Characterization. J Am Soc Mass Spectrom. 2012, 23(4):577-93. PMID: 21952753; PMCID: PMC4228788
4. Zhou X, Mester C, Stemmer PM, Reid GE. Oxidation-induced conformational changes in calcineurin determined by covalent labeling and tandem mass spectrometry. Biochemistry. 2014 Nov 4;53(43):6754-65. doi: 10.1021/bi5009744. Epub 2014 Oct 20. PMID: 25286016

NBSI-University of Windsor, Windsor, Canada

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.

1. Mrinalini Pandit, Mina Maleki, Nicholas J Carruthers, Paul M. Stemmer, Luis Rueda. Prediction of Calmodulin-binding Proteins

The Director together with NBSI colleagues continue to participate in international institution building, gaining international recognition and visibility to Wayne State University, and expand research and academic collaborations on various fronts in nanobioscience and nanomedicine:

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 NanoBioScience Institute in Tbilisi, Georgia (ongoing).
4. Invited to help establish a $6 billion Vedanta University, Odisha, India (ongoing).
5. Development of the "Center for Metabolism and Movement", focused on the 'Human Skeletal Muscle Cell Atlas', Wayne State University, (ongoing).

Selected National NBSI Collaborations

NBSI-Lawrence Berkeley Laboratory, CA

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. Three additional manuscripts are in preparation.

1. Cho, W.J., Lee, J-S., Ren, G., Zhang, L., Shin, L., Manke, C.W., Potoff, J., Kotaria, N., Zhvania, M.G., Jena, B. P. (2011). Membrane-directed molecular assembly of the neuronal SNARE complex. *J. Cell. Mol. Med.* 15:31-37.
2. Cho, W-J., Shin, L., Ren, G., Jena, B. P. (2009). Structure of membrane-associated neuronal SNARE complex: Implication in neurotransmitter release. *J. Cell Mol. Med*. 13:4161-4165.

3. Cho, W-J., Ren, G., Lee, J-S., Jeftinija, K., Jeftinija, S., Jena, B.P. (2009). Nanoscale three-dimensional contour map of protein assembly within the astrocyte porosome complex. *Cell Biol. Int.* 33:224-229.
4. Cho, W-J, Ren, G., Jena, B.P. (2008). EM 3D contour maps provide protein assembly at the nanoscale within the neuronal porosome complex. *J. Microscopy* 232:106-111.
5. Cho, W-J, Jeremic, A., Jin, H., Ren, G., Jena, B. P. (2007). Neuronal fusion pore assembly requires membrane cholesterol. *Cell Biol. Int.* 31:1301-1308.

NBSI-University of Vermont, Burlington, VT

Taatjes-Jena Collaboration (2000-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 11 research publications.

1. Cho, S.-J., Quinn, A.S., Stromer, M.H., Dash, S., Cho, J., Taatjes, D.J., Jena, B.P. (2002). Structure and dynamics of the fusion pore in live cells. *Cell Biol. Int.* 26:35-42.
2. Jeremic, A., Quinn, A.S., Cho, W-J., Taatjes, D.J., Jena, B. P. (2006). Energy-dependent disassembly of self-assembled SNARE complex: observation at nanometer resolution using atomic force microscopy. *J. Am. Chem. Soc.* 128:26-27.
3. Wang, S., Lee, J-S., Bishop, N., Jeremic, A., Cho, WJ., Chen, X., Mao, G., Taatjes, D.J., Jena, B.P. (2012). 3D organization and function of the cell: Golgi budding and vesicle biogenesis to docking at the porosome complex. *Histochem. Cell Biol.* 137:703-718.
4. Lee, J-S., Hou, X., Bishop, N., Wang, S., Flack, A., Cho, WJ., Chen, X., Mao, G., Taatjes, D.J., Sun, F., Zhang, K., Jena, B.P. (2013). Aquaporin-assisted and ER-mediated mitochondrial fission: A hypothesis. *Micron* 47:50-58.
5. Taatjes, D.J., Rand, J.H., Jena, B.P. (2013). Atomic force microscopy: high resolution dynamic imaging of cellular and molecular structure in health and disease. *J. Cell Physiol.* 228:1949-1955.
6. Hou, X., Lewis, K.T., Wu, Q., Wang, S., Chen, X., Flack, A., Mao, G., Taatjes, D.J., Sun, F., Jena, B.P. (2014). Proteome of the porosome complex in human airways epithelia: Interaction with the cystic fibrosis transmembrane conductance regulator (CFTR). *Journal of Proteomics* 96:82-91.
7. Kovari, L.C., Brunzelle, J.S., Lewis, K.T., Cho, W.J., Lee, J-S., Taatjes, D.J., Jena, B.P. (2014). X-ray solution structure of the native neuronal porosome-synaptic vesicle complex: Implication in neurotransmitter release. *Micron* 56:37-43.
8. Lewis, K.T., Maddipati, K.R., Taatjes, D.J., Jena, B.P. (2014). Neuronal porosome lipidome. *J. Cell. Mol. Med.* 18:1927-1937.
9. Jena, B. P., Taatjes, D.J. (2014). NanoCellBiology: Multimodal Imaging in Biology & Medicine *Pan Sanford Publishing Pte. Ltd.* p1-400, ISBN: 9789814411790.
10. Rajagopal, A., Kulkarni, S., Lewis, K.T., Chen, X., Maarouf, A., Kelly, C.V., Taatjes, D. J., Jena, B.P. (2015). Proteome of the insulin-secreting Min6 porosome complex: Involvement of Hsp90 in its assembly and function. *Journal of Proteomics* 114:83-92.
11. Naik, A.R., Kulkarni, S.P., Lewis, K.T., Taatjes, D.J., Jena, B.P. (2016) Functional reconstitution of the porosome complex in live cells. *Endocrinology* 157:54-60.
12. Jena, B. P., Gatti, D. L., Arslanturk, S., Pernal, S., Taatjes, D. J. (2019) Human Skeletal Muscle Cell Atlas: Unraveling Cellular Secrets Utilizing 'Muscle-on-a-Chip', Differential Expansion Microscopy, Mass Spectrometry, Nanothermometry and Machine Learning. *Micron* 177: 55-59.

NBSI-Northwestern University & Synchrotron Research Center, Chicago, IL

Brunzelle-Jena Collaboration (2014-present): Prof. Joseph S Brunzelle, 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.

1. Kovari, L.C., Brunzelle, J.S., Lewis, K.T., Cho, W.J., Lee, J-S., Taatjes, D.J., Jena, B.P. (2014). X-ray solution structure of the native neuronal porosome-synaptic vesicle complex: Implication in neurotransmitter release. *Micron* 56:37-43.

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 8 publications.

1. Dzul, S.*; Rocha, A.; Rabat, S.; Kandegedara, A.*; Kusowski, A.*; Pain, J.; Murari, A.; Pain, D.; Dancis, A.; Stemmler, T.L.; "In vitro characterization of a novel Isu homologue from *Drosophila melanogaster* for de novo FeS-cluster formation." *Metallomics*, 2017,*9*, 48-60.
2. Rodrigues, A.V.*; Kandegedara, A.*; Rotondo, J.A.*; Dancis, A.; Stemmler, T.L. "Iron Loading Site on the Fe-S Cluster Assembly Scaffold Protein is Distinct from the Active Site" *BioMetals,* 2015, *28,* 567-76.
3. Pandey, A.; Gordon, D.M.; Pain, J.; Stemmler, T.L.; Dancis, A.; Pain, D. "Frataxin directly stimulates mitochondrial cysteine desulfurase by exposing substrate-binding sites and a mutant Fe-S cluster scaffold protein with frataxin-bypassing ability acts similarly." *J. Biol. Chem.*, 2013, *288*, 36773-86.
4. Cook, J.D.*; Kondapalli, K.C.*; Rawat, S.*; Childs, W.C.*; Murugesan, Y.*; Dancis, A.; Stemmler, T.L. "Molecular details of the yeast frataxin-Isu1 interaction during mitochondrial Fe-S cluster assembly" *Biochem.,* 2010, *49* (3), 8756-65.
5. Stemmler, T.L.; Lesuisse, E.; Pain, D.; Dancis, A. "Frataxin and mitochondrial Fe-S cluster biogenesis" *J. Biol. Chem.,* 2010, *285* (35), 26737-43.
6. Kondapalli, K.C.*; Dancis, A.; Stemmler, T.L. "Molecular interaction between Frataxin and Ferrochelatase during Heme Assembly" in Bioinorganic Chemistry; Cellular Systems and Synthetic Models, ACS Symposium Series 1012, Eric C. Long and Michael J. Baldwin, Eds., American Chemical Society, 2009, 17-30.
7. Kondapalli, K.C.*; Kok, N.M.*; Dancis, A.; Stemmler, T.L. "Drosophila Frataxin: an iron chaperone during cellular [2Fe-2S] cluster bioassembly" *Biochem.*, 2008, *47,* 6917-27.
8. He, Y.*; Alam, S.L.; Proteasa, S.V.*; Zhang, Y.*; Lesuisse, E.; Dancis, A.; Stemmler, T.L. "Yeast Frataxin Solution Structure, Iron Binding and Ferrochelatase Interaction," *Biochem.*, 2004, *43,* 16254-62.

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 methantropic 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 15 publications.

1. Fisher, O.S.; Kenney, G.E.; Ross, M.O.; Ro, S.Y.; Lemma, B.E.; Batelu, S.*; Thomas, P.M.; Sosnowski, V.C.; DeHart, C.J.; Kelleher, N.L.; Stemmler, T.L.; Hoffman, B.M.; Rosenzweig, A.C. "Characterization of a long overlooked copper protein from methane- and ammonia-oxidizing bacteria", *Nature Comm.,* 2018, *9,* 4276-88.
2. Ro, S.Y.; Ross, M.O.; Deng, Y.W.; Batelu, S.*; Lawton, T.J.; Hurley, J.D.; Stemmler, T.L.; Hoffman, B.M.; Rosenzweig, A.C.; "From micelles to bicelles: effect of the membrane on particulate methane monooxygenase activity." *J. Biol. Chem*., 2018, *293*, 10457-10465. PMID: 29739854.
3. Purohit, R.; Ross, M.O.; Batelu, S.*; Kusowski, A.*; Stemmler, T.L.; Hoffman, B.M.; Rosenzweig, A.C. "A Cu^{+}-specific CopB transporter: Revising P_{1B}-type ATPase classification." *Proc. Natl. Acad. Sci, U.S.A.*, 2018, *115.* 2108-13.
4. Smith, A.T.; Barupala, D.*; Stemmler, T.L.; Rosenzweig, A.C. "Discovery and characterization of a novel metal binding domain involved in cadium, cobalt, and zinc transport" *Nature Chemical Biology,* 2015, *11,* 678-84.
5. Sirajuddin, S.; Barupala, D.*; Helling, S.; Marcus, K.; Stemmler, T.L.; Rosenzweig, A.C. "Effects of Zinc on Particulate Methane Monooxygenase Activity and Structure" *J Biol Chem,* 2014, *289,* 21782-94.
6. Zielazinski, E.L.: González-Guerrero, M.; Subramanian, P.*; Stemmler, T.L.; Argüello, J.M.; Rosenzweig, A.C. "Sinorhizobium meliloti Nia is a P(1B-5)-ATPase expressed in the nodule during plant symbiosis and is involved in Ni and Fe transport." *Metallomics*, 2013, *12*, 1614-23.
7. Zielazinski, E.L.; Cutsail III, G.E.; Hoffman, B.M.; Stemmler, T.L.; Rosenzweig, A.C. "Characterization of a Cobalt-Specific P_{1B}-ATPase" *Biochem.,* 2012, *51* (40), 7891-900.
8. Smith, S.M.; Rawat, S.*; Telser, J.; Hoffman, B.M.; Stemmler, T.L.; Rosenzweig, A.C. "Crystal structure and characterization of particulate methane monooxygenase from *Methylocystis* species strain M" *Biochem.*, 2011, *59* (1), 10231-40.
9. Traverso, M.E.; Subramanian, P.*; Davydov, R.; Hoffman, B.M.; Stemmler, T.L.; Rosenzweig, A.C. "Identification of a hemerythrin-like domain in a P1B-type transport ATPase" *Biochem.,* 2010, *49* (33), 7060-8.
10. Balasubramanian, R.; Smith, S.M.; Rawat, S.*; Yatsunyk, L.A.; Stemmler, T.L.; Rosenzweig, A.C. "Oxidation of methane by a biological dicopper center" *Nature,* 2010, *465,* 115-9.
11. Hakemian, A.S.; Kondapalli, K.C.*; Telser, J; Hoffman, B.M.; Stemmler, T.L.; Rosenzweig, A.C. "The metal centers of particulate methane monooxygenase from *Methylosinus trichosporium* OB3b" *Biochem.,* 2008, *47,* 6793-801.
12. Sazinsky, M.H.; LeMoine, B,; Orofino, M.; Davydov, R.; Bencze, K.Z.*; Stemmler, T.L.; Hoffman, B.M.; Argüello, J.M.; Rosenzweig, A.C. "Characterization and Structure of a Novel Zn^{2+} and [2Fe-2S]-Containing Copper Chaperone from *Archaeoglobus fulgidus,*" *J. Biol. Chem.*, 2007, *282,* 25950-9.
13. Lieberman, R.L.; Kondapalli, K.C.*; Shrestha, D.B.; Hakemian, A.S.; Smith, S.M.; Telser, J.; Kuzelka, J.; Gupta, R.; Borovik, A.S.; Lippard, S.J.; Hoffman, B.M.; Rosenzweig, A.C.; Stemmler, T.L. "Characterization of the particulate methane monooxygenase metal centers in multiple redox states by X-ray absorption spectroscopy," *Inorg. Chem.*, 2006, *45,* 8372-81.
14. Hakemian, A.S.; Tinberg, C.E.; Kondapalli, K.C.*; Tesler, J.; Hoffman, B.M.; Stemmler, T.L.; Rosenzweig, A.C. "The copper chelator methanobactin from *Methylosinus trichosporium* OB3b binds copper(I)," *J. Am. Chem. Soc.*, 2005, *127*, 17142-3.
15. Lieberman, R.L.; Shrestha, D.B.; Doan, P.E.; Hoffman, B.M.; Stemmler, T.L.; Rosenzweig, A.C. "Purified particulate methane monooxygenase from *Methylococcus capsulatus* (Bath) is a dimer with both mononuclear copper and a copper-containing cluster," *Proc. Natl. Acad. Sci, U.S.A.*, 2003, *100,* 3820-3825.

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 8 publications.

1. Pawitwar, S.; Nadar, V.; Kandegedara, A.*; Stemmler, T.L.; Rosen, B.; Yoshinaga, M. "Biochemical characterization of ArsI: a novel C-As lyase for degradation of environmental organoarsenicals." *Environmental Science and Technology,* 2017, *51,* 11115-25
2. Kumar, N.V.; Yang, J.; Pillai, J.K.; Rawat, S.*; Solano, C.; Kumar, A.; Grotli, M.; **Stemmler, T.L.**; Rosen, B.P.; Tamas, M.K. "Arsenic directly binds to and activates the yeast AP-1-like transcription factor Yap8" *Molecular and Cellular Biology,* **2016**, *36,* 913-922.
3. Ye, J.; He, Y.*; Skalicky, J.; Rosen, B.P.; **Stemmler, T.L.** "Resonance assignments and secondary structure predictions of the As(III) metallochaperone ArsD in solution" *BioMol. NMR Assn.,* **2011**, *5* (1), 109-112.
4. 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.
5. Kandegedara, A.; Thiyagarajan, S.; Kondapalli, K.C.*; **Stemmler, T.L.;** Rosen, B.P. "Role of bound Zn(II) in the CadC Cd(II)/Pb(II)/Zn(II)-responsive repressor," *J. Biol. Chem.,* **2009**, *284,* 14958-65.
6. Ordóñez, E.; Thiyagarajan, S.; Cook, J.D.*; **Stemmler, T.L.;** Gil, J.A.; Mateos, L.M.; Rosen, B.P. "Evolution of metalloid binding sites in transcriptional regulators" *J. Biol. Chem.*, **2008**, *283,* 25706-14.
7. Qin, J.; Fu, H.-L.; Ye, J.; Bencze, K.Z.*; **Stemmler, T.L.;** Rawlings, D. E.; Rosen, B. P. "Convergent Evolution of a New Arsenic Binding Site in the ArsR/SmtB Family of Metalloregulators", *J. Biol. Chem.*, **2007**, *282,* 34346-55.
8. Ramírez-Solís, A.; Mukopadhyay, R.; Rosen, B.P.; **Stemmler, T.L.** "Experimental and Theoretical Characterization of Arsenite in Water: Insights into the Coordination Environment of As-O," *Inorg. Chem.,* **2004**, *43*, 2954-9.

Persechini-Stemmer Collaboration (2000-present): Dr. Anthony Persechini from the University of Missourri 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.

1. Persechini A, Yano K, Stemmer PM.: Ca(2+) binding and energy coupling in the calmodulin-myosin light chain kinase complex. J Biol Chem. 2000 Feb 11;275(6):4199-204. PMID: 10660583
2. Persechini A, Stemmer PM.: Calmodulin is a limiting factor in the cell. Trends Cardiovasc Med. 2002 Jan;12(1):32-7. PMID: 11796242
3. Ohashi I, Pohoreki R, Morita K, Stemmer PM.: Alcohols increase calmodulin affinity for Ca2+ and decrease target affinity for calmodulin. Biochim Biophys Acta. 2004 May 3;1691(2-3):161-7. PMID: 15110996

Some NBSI Collaborations Within Wayne State University

Jena-Potoff-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 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.

1. Cho, W.J., Lee, J-S., Ren, G., Zhang, L., Shin, L., Manke, C.W., Potoff, J., Kotaria, N., Zhvania, M.G., Jena, B. P. (2011). Membrane-directed molecular assembly of the neuronal SNARE complex. *J. Cell. Mol. Med.* 15:31-37.
2. Issa, Z., Manke, C.W., Jena, B. P., Potoff, J.J. (2010). Ca^{2+} bridging of apposed phospholipid bilayer *J. Phys. Chem.* 114:13249-13254.
3. Potoff, J.J., Issa, Z., Manke Jr, C.W., Jena, B. P. (2008). Ca^{2+}-Dimethylphosphate complex formation: providing insight into Ca^{2+} mediated local dehydration and membrane fusion in cells. *Cell Biol. Int.* 32:361-366.
4. Jena, B. P. (2009). Porosome: the secretory portal in cells. *Biochemistry*. 49:4009-4018.
5. Jena, B.P. (2010) Secretory vesicles transiently dock and fuse at the porosome to discharge contents during cell secretion. *Cell Biol. Int.* 34:3-12.
6. Jena, B.P. (2009) Functional organization of the porosome complex and associated structures facilitating cellular secretion. *Physiology* 24:367-376.

Jena-Potoff-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-lead author with Graduate Student Akshata Naik (Physiology) is published [8] in the journal *Endocrinology*. Studies by Rajgopal 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.

1. Lee, J-S., Jeremic, A., Shin, L., Cho, WJ., Chen, X., Jena, B.P. (2012). Neuronal porosome proteome: Molecular dynamics and architecture. *J. Proteomics* 75:3952-3962.
2. Wang, S., Lee, J-S., Bishop, N., Jeremic, A., Cho, WJ., Chen, X., Mao, G., Taatjes, D.J., Jena, B.P. (2012). 3D organization and function of the cell: Golgi budding and vesicle biogenesis to docking at the porosome complex. *Histochem. Cell Biol.* 137:703-718.
3. Kovari, L.C., Brunzelle, J.S., Lewis, K.T., Cho, W.J., Lee, J-S., Taatjes, D.J., Jena, B.P. (2014). X-ray solution structure of the native neuronal porosome-synaptic vesicle complex: Implication in neurotransmitter release. *Micron* 56:37-43.
4. Hou, X., Lewis, K.T., Wu, Q., Wang, S., Chen, X., Flack, A., Mao, G., Taatjes, D.J., Sun, F., Jena, B.P. (2014). Proteome of the porosome complex in human airways epithelia: Interaction with the cystic fibrosis transmembrane conductance regulator (CFTR). *Journal of Proteomics* 96:82-91.
5. Jena, B. P. (2015) Porosome Discovered Nearly 20 Years Ago Provide Molecular Insights into the Kiss-and-Run Mechanism of Cell Secretion. *J Cell Mol. Med.* J. 2015 May 28. PMID: 26033351.
6. Rajagopal, A., Kulkarni, S., Lewis, K.T., Chen, X., Maarouf, A., Kelly, C.V., Taatjes, D. J., Jena, B.P. (2015). Proteome of the insulin-secreting Min6 porosome complex: Involvement of Hsp90 in its assembly and function. *Journal of Proteomics* 114:83-92.
7. Naik AR, Lewis KT, Jena BP. (2015) The Neuronal Porosome Complex in Health and Disease. *Exp. Biol. Med.* (Maywood) OnlineFirst, published on August 11, 2015 as doi:10.1177/1535370215598400.
8. Naik, A.R., Kulkarni, S.P., Lewis, K.T., Taatjes, D.J., Jena, B.P. (2016) Functional reconstitution of the porosome complex in live cells. *Endocrinology* 157:54-60.
9. Laha SS, Naik AR, Kuhn ER, Alvarez M, Sujkowsky A, Wessells RJ, Jena BP. (2017) Nano thermometry measure of muscle efficiency. *Nano Letters* 2017 Jan 23. DOI: 10.1021/acs.nanolett.6b05092
10. Lewis KT, Maddipati KR, Naik AR, Jena BP. (2017) Unique lipid chemistry of synaptic vesicle and synaptosome membrane revealed using mass spectrometry. *Chemical Neuroscience*. 2017 DOI: 10.1021/acschemneuro.7b00030. PMID: 28244738.
11. Arachchige MP, Laha SS, Naik AR, Lewis KT, Naik R, Jena BP. (2017) Functionalized nanoparticles enable tracking the rapid entry and release of doxorubicin in human pancreatic cancer cells. Micron. 2017 Jan;92:25-31. doi: 10.1016/j.micron.2016.10.005. PMID: 27846432.
12. Jena BP, Stemmer PM, Wang S, Guangzhao M, Lewis KT, Walz DA. (2017) Human platelet vesicles exhibit distinct size and proteome. J. Proteom Res. DOI: 10.1021/acsjproteom. 7b00309.

Jena-Stemmler 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.

1. Shin, L., Cho, W-J., Cook, J., Stemmler, T., Jena, B. P. (2010). Membrane lipids influence protein complex assembly-disassembly. *J. Am. Chem. Soc*. 132:5596-5597.

2. Cook, J.D., Cho, W.J., Stemmler, T.L., Jena, B. P. (2008). Circular dichroism (CD) spectroscopy of the assembly and disassembly of SNAREs: the proteins involved in membrane fusion in cells. *Chem. Phys. Lett.* 462:6-9.
3. Kuhn, E. R., Naik, A. R., Lewis, B. E., Kokotovich, K. M., Li, M., Stemmler, T. M., Larsson, L., Jena, B. P. (2018) Nanothermometry reveals calcium-induced remodeling of myosin. *ACS Nano Letters* October 22, 2018, DOI: 10.1021/acs.nanolett.8b02989.

Jena-Chen 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. X. Chen, Associate Professor of Physiology, Wayne State University School of Medicine Received first NIH R01 Grant in 2016

1. Lee, J-S., Jeremic, A., Shin, L., Cho, WJ., Chen, X., Jena, B.P. (2012). Neuronal porosome proteome: Molecular dynamics and architecture. *J. Proteomics* 75:3952-3962.
2. Wang, S., Lee, J-S., Bishop, N., Jeremic, A., Cho, WJ., Chen, X., Mao, G., Taatjes, D.J., Jena, B.P. (2012). 3D organization and function of the cell: Golgi budding and vesicle biogenesis to docking at the porosome complex. *Histochem. Cell Biol.* 137:703-718.
3. Hou, X., Lewis, K.T., Wu, Q., Wang, S., Chen, X., Flack, A., Mao, G., Taatjes, D.J., Sun, F., Jena, B.P. (2014). Proteome of the porosome complex in human airways epithelia: Interaction with the cystic fibrosis transmembrane conductance regulator (CFTR). *Journal of Proteomics* 96:82-91.
4. Rajagopal, A., Kulkarni, S., Lewis, K.T., Chen, X., Maarouf, A., Kelly, C.V., Taatjes, D. J., Jena, B.P. (2015). Proteome of the insulin-secreting Min6 porosome complex: Involvement of Hsp90 in its assembly and function. *Journal of Proteomics* 114:83-92.
5. Fang J, Liu M, Zhang X, Sakamoto T, Taatjes DJ, Jena BP, Sun F, Woods J, Bryson T, Kowluru A, Zhang K, Chen X. (2015) COPII Dependent ER Export: a Critical Component of Insulin Biogenesis and Beta Cell ER Homeostasis. *Mol Endocrinol.* 29: 1156-1169.
6. Lee JS, Caruso JA, Hubbs G, Schnepp P, Woods J, Fang J, Li C, Zhang K, Stemmer PM, Jena BP, Chen X. Molecular architecture of mouse and human pancreatic zymogen granules: protein components and their copy numbers. *Biophys Rep.* 2018;4(2):94-103. doi: 10.1007/s41048-018-0055-1. Epub 2018 Apr 26. PMID: 29756009

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

1. Hou, X., Lewis, K.T., Wu, Q., Wang, S., Chen, X., Flack, A., Mao, G., Taatjes, D.J., Sun, F., Jena, B.P. (2014). Proteome of the porosome complex in human airways epithelia: Interaction with the cystic fibrosis transmembrane conductance regulator (CFTR). *Journal of Proteomics* 96:82-91.

Jena-Maddipati Collaboration (2014-present): Prof. Krishna R. Maddipati, Director, **Wayne State University Lipidomics Facility**, 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. An NIH grant proposal is in progress.

1. Lewis, K.T., Maddipati, K.R., Taatjes, D.J., Jena, B.P. (2014). Neuronal porosome lipidome. *J. Cell. Mol. Med.* 18:1927-1937.

2. Lewis KT, Maddipati KR, Naik AR, Jena BP. (2017) Unique lipid chemistry of synaptic vesicle and synaptosome membrane revealed using mass spectrometry. *Chemical Neuroscience*. 2017 DOI: 10.1021/acschemneuro.7b00030. PMID: 28244738.

Jena-Stemmer Collaboration (2016-present): Prof. Paul M. Stemmer, Director, **Wayne State University Proteomics Facility**, have been collaborating on determining the proteome of the porosome complex and secretory vesicle chemistry. This ongoing collaboration has resulted in the following research publication. An NIH grant proposal is in progress.

1. Jena BP, Stemmer PM, Wang S, Guangzhao M, Lewis KT, Walz DA. (2017) Human platelet vesicles exhibit distinct size and proteome. *J. Proteom Res.* DOI: 10.1021/acsjproteom. 7b00309.
2. Naik, A. R., Pernal, S., Lewis, K. T., Wu, Y., Wu, H., Carruthers, N. J., Stemmer, P. M., Jena, B. P. (2019) Human skeletal muscle cells on engineered 3D platform express key growth and developmental proteins. *ACS Biomaterials Science & Engineering* DOI: 10.1021/acsbiomaterials.8b01338.

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.

1. Kovari, L.C., Brunzelle, J.S., Lewis, K.T., Cho, W.J., Lee, J-S., Taatjes, D.J., Jena, B.P. (2014). X-ray solution structure of the native neuronal porosome-synaptic vesicle complex: Implication in neurotransmitter release. *Micron* 56:37-43.

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.

1. Najy A, Dyson G, Jena BP, Lin C-Y, Kim H-R. (2016) Matriptase Activation and Shedding through PDGF-D mediated Extracellular Acidosis. *Am J. Physiol Cell Physiol* 310: C293-C304.

Jena-Kelly Collaboration (2014-present): Prof. Chris Kelly, Department of Physics & Astronomy, have been collaborating on t-/v-SNARE 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.

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

1. Rajagopal, A., Kulkarni, S., Lewis, K.T., Chen, X., Maarouf, A., Kelly, C.V., Taatjes, D. J., Jena, B.P. (2015). Proteome of the insulin-secreting Min6 porosome complex: Involvement of Hsp90 in its assembly and function. *Journal of Proteomics* 114:83-92.

Jena-Mao Collaboration (2012-present): Prof. Guangzhao Mao, Chair, 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.

1. Wang, S., Lee, J-S., Bishop, N., Jeremic, A., Cho, WJ., Chen, X., Mao, G., Taatjes, D.J., Jena, B.P. (2012). 3D organization and function of the cell: Golgi budding and vesicle biogenesis to docking at the porosome complex. *Histochem. Cell Biol.* 137:703-718.
2. Hou, X., Lewis, K.T., Wu, Q., Wang, S., Chen, X., Flack, A., Mao, G., Taatjes, D.J., Sun, F., Jena, B.P. (2014). Proteome of the porosome complex in human airways epithelia: Interaction with the cystic fibrosis transmembrane conductance regulator (CFTR). *Journal of Proteomics* 96:82-91.
3. Jena BP, Stemmer PM, Wang S, Guangzhao M, Lewis KT, Walz DA. (2017) Human platelet vesicles exhibit distinct size and proteome. *J. Proteom Res.* DOI: 10.1021/acsjproteom. 7b00309.

Jena-Walz Collaboration (2015-present): Prof. Daniel A. Walz and the Jena lab. have been collaborating on understanding the proteome of the human platelet and the different vesicles within.

1. Lee JS, Agrawal S, von Turkovich M, Taatjes DJ, Walz DA, Jena BP. (2012) Water channels in platelet volume regulation. *J Cell Mol Med.* 2012 Apr;16(4):945-9. doi: 10.1111/j.1582-4934.2011.01362.x. PMID: 21692982
2. Jena BP, Stemmer PM, Wang S, Guangzhao M, Lewis KT, Walz DA. (2017) Human platelet vesicles exhibit distinct size and proteome. *J. Proteom Res.* DOI: 10.1021/acsjproteom. 7b00309.

Jena-Gatti Collaboration (2018-present) Domenico L. Gatti, Associate Professor of Biochemistry, Microbiology and Immunology, and the Jena lab. have been collaborating to establish the Human Skeletal Muscle Cell Atlas. In addition to the following manuscript, they have jointly submitted an NIH R01 in 2019 and a Chan-Zuckerberg grant in 2018.

1. Jena BP, Gatti DL, Arslanturk S, Pernal S, Taatjes DJ., "Human skeletal muscle cell atlas: Unraveling cellular secrets utilizing 'muscle-on-a-chip', differential expansion microscopy, mass spectrometry, nanothermometry and machine learning.", *Micron.* 117, 55-59, 2019.

Jena-Arslanturk Collaboration (2018-present) Suzan Arslanturk, Assistant Professor of Computer Science, and the Jena lab. have been collaborating to establish the Human Skeletal

Muscle Cell Atlas. In addition to the following manuscript, they have jointly submitted an NIH R01 in 2019 and a Chan-Zuckerberg grant in 2018.

1. Jena BP, Gatti DL, Arslanturk S, Pernal S, Taatjes DJ., "Human skeletal muscle cell atlas: Unraveling cellular secrets utilizing 'muscle-on-a-chip', differential expansion microscopy, mass spectrometry, nanothermometry and machine learning.", *Micron.* 117, 55-59, 2019.

Jena-Matthew Collaboration (2018-present) Howard Matthew, Vice-Chair and Professor of Chemical Engineering & Materials Science and the Jena lab. are collaborating on a muscle-bone organoid.

Jena-Dombkowski Collaboration (2017-present) Alan Dombkowski, Associate Professor of Pediatrics and the Jena lab. are collaborating on The role of non-coding RNAs in epilepsy of tuberous sclerosis complex and focal cortical dysplasia type 2B in children. Jena serves as a Co-I in a new NIH grant on the subject where Dombkowski serves as PI. A joint manuscript is in preparation.

Jena-Lisak-Benjamins Collaboration (2017-present) Professor Joyce A. Benjamins and Professor Robert P. Lisak of Neurology and the Jena lab. are collaborating on B Cell Secretory Factors and Neuronal and Oligodendroglia Toxicity. They have jointly submitted a proposal to NMSS. Results of this collaboration have recently been published.

1. Benjamins JA, Nedelkoska L, Touil H, Stemmer PM, Carruthers NJ, Jena BP, Naik AR, Bar-Or A, Lisak RP. Exosome-enriched fractions from MS B cells induce oligodendrocyte death. *Neurol Neuroimmunol Neuroinflamm.* 2019;6:e550. doi:10.1212/NXI.0000000000000550

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 phophoproteome 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.

1. Caruso JA, Stemmer PM.: Proteomic profiling of lipid rafts in a human breast cancer model of tumorigenic progression. Clinical and Experimental Metastasis, 2011, 28(6):529-540. PMID: 21533873; PMCID: PMC3827680
2. Caruthers, N.J., Stemmer, P.M., Shin, N., Dombkowski, A., Caruso, J.A., Gill, R., Rosenspire, A.: Mercury Alters B-Cell Protein Phosphorylation Profiles. J Proteome Res. 2014, 13(2):496-505. PMID: 24224561; PMCID: PMC4167842
3. Caruso, J.A., Stemmer, P.M., Dombkowski, A., Caruthers, N.J., Gill, R., and Rosenspire, A.J.: A systems toxicology approach identifies Lyn as a key signaling phosphoprotein modulated by mercury in a B lymphocyte cell model. Toxicology and Applied Pharmacology, 2014;276(1):47-54. PMID: 24440445; PMCID: PMC4005802

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.

1. Dombkowski AA, Batista CE, Cukovic D, Carruthers NJ, Ranganathan R, Shukla U, Stemmer PM, Chugani HT, Chugani DC. Cortical Tubers: Windows into Dysregulation of Epilepsy Risk and Synaptic Signaling Genes by MicroRNAs. Cereb Cortex. 2014 Dec 1. PubMed PMID: 25452577.

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.

1. Lum, L.G., M. Ramesh, A. Thakur, S. Mitra, A. Deol, J.P. Uberti, and P.E. Pellett. 2012. Targeting cytomegalovirus infected targets with T-cells armed with anti-CD3 x anti-CMV bispecific antibody. Biology of Blood and Marrow Transplantation 18:1012-1022.

Jena-Pellett 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.

PATENT

1. Nano thermometry measure of muscle efficiency. Patent: US 62/498,015.
Establishes a novel approach to determine muscle efficiency, with promise for early diagnosis and treatment of various metabolic disorders including cancer.

CURRENT FOCUS

The current focus of NBSI is to establishment a "**Center for Metabolism and Motion", focused on the Human Skeletal Muscle Atlas.**

June 2006

Supplement to: Reed Business Information. Science Group

Reed Science Group ACADEMIC SOURCEBOOK

A Report on the State of Science in Universities and Colleges

- Industry/Academia Relationship
- Lab Design in Academia
- Generating Grant Proposals
- U.S. Student Exchange Issues
- Building Campus-based Nanotech Labs
- Funding and Collaboration Needs
- Federal Support for Academia
- Top Universities Worldwide

Academic Biotech Resources

Biotechnology Centers		
Boston Univ., Mass.	BioMolecular Engineering Research Center	http://bmerc-www.bu.edu
City Univ. of New York, N.Y.	Structural Biology Center	www.ccny.cuny.edu
Columbia Univ., N.Y., N.Y.	Northeast Biodefense Center	www.nbc.columbia.edu/
Cornell Univ., Ithaca, N.Y	Biotechnology Institute	www.biotech.cornell.edu
Florida Atlantic Univ., et al	Center for Biomedical and Marine Biotech	www.floridabiotech.org
Harvard Univ., Cambridge, Mass.	Harvard Biotech Club	www.thebiotechclub.org
Harvard Univ., Cambridge, Mass.	Bauer Center for Genomics Research	www.cgr.harvard.edu
Johns Hopkins Univ., Baltimore, Md.	Army Center for Biotech	www.jhuapl.edu/
Massachusetts Institute of Technology, Cambridge	Biotech Process Engineering Center	http://web.mit.edu/bpec/
Massachusetts Institute of Technology, Cambridge	Whitehead Center	www.wi.mit.edu
Michigan Technological Univ., Houghton	Biotech Research Center	http://biotech.mtu.edu
National Heart, Lung, and Blood Institute, NIH	Univ. Proteomics Centers	www.nhlbi-proteomics.org/centers
Northwestern Univ., Evanston, Ill.	Center for Biotechnology	www.kellogg.northwestern.edu/academic/biotech/index.htm
Ohio State Univ., Columbus	Plant-Microbe Genomics Facility	www.biosci.ohio-state.edu
Oklahoma State Univ., Stillwater	Plant Transformation Facility	www.ptf.okstate.edu
Rochester Institute of Technology, N.Y.	Center for Biotech Education and Training	www.bioinformatics.rit.edu
Rutgers, The State Univ. of N.J., New Brunswick	Biotech Center	www.cook.rutgers.edu
Stanford Univ., Calif.	Center for Law and the Biosciences	www.law.stanford.edu
State Univ. of N.Y., Buffalo	Center for Bioinformatics and Life Sciences	www.ccr.buffalo.edu
State Univ. of N.Y. Stony Brook	Center for Biotech	www.biotech.sunysb.edu
Tuskegee Univ., Ala.	Center for Plant Biotechnology Research	www.tuskegee.edu
Univ. of Cincinnati, Ohio	Genome Research Institute	http://medcenter.uc.edu
Univ. of Colorado, Denver	Center for Pharmaceutical Biotech	www.uchsc.edu/sop/biotech/overview.html
Univ. of Florida, Gainesville	Center for Regenerative Health Biotech	www.biotech.ufl.edu
Univ. of Idaho, Moscow	Environmental Biotech Institute	http://image.fs.uidaho.edu
Univ. of Illinois, Urbana-Champaign	Biotech Center	www.biotec.uiuc.edu
Univ. of Maryland, College Park	Biotechnology Institute	www.umbi.umd.edu
Univ. of Maryland, Rockville	Center for Advanced Research in Biotechnology	http://carb.umbi.umd.edu
Univ. of Maryland, Shady Grove	Center for Advanced Research in Biotech	http://shadygrove.umbi.umd.edu
Univ. of Minnesota, Minneapolis	Academic Health Center	www.ahc.umn.edu
Univ. of Southern California, Los Angeles	Center for Computational and Experimental Genomics	www-hto.usc.edu
Univ. of Tennessee, et al	Tennessee Biotech Association	www.tnbio.org
Univ. of Texas, College Station	Crop Biotech Center	http://cbc.tamu.edu
Univ. of Texas, Houston	Health Science Center	http://biotech.uth.tmc.edu
Univ. of Wisconsin, Madison	Biotechnology Center	www.biotech.wisc.edu
Utah State Univ., Logan	Center for Integrated Biosystems	www.biosystems.usu.edu
Virginia Polytechnic Institute and State Univ., Blacksburg	Fralin Biotech Center	www.biotech.vt.edu
Washington State Univ., Pullman	Center for Integrated Biotechnology	www.biotechnology.wsu.edu
Yale Univ., New Haven, Conn.	Keck Biotechnology Lab	http://keck.med.yale.edu
Nanobiotechnology		
Arizona State Univ., Tempe	BioDesign Institute	www.biodesign.asu.edu
California Institute of Technology, Pasadena	Nanosystems Biology Cancer Center	www.caltechcancer.org
Cornell Univ., Ithaca, N.Y.	Nanobiotechnology Center	www.nbtc.cornell.edu
Wayne State Univ., Detroit, Mich.	NanoBioScience Institute	www.med.wayne.edu/nanobioscience/
Web sites of interest		
Academic Microarray Core Facilities	www.nslij-genetics.org/microarray/core.html	
Biotechnology Educational Resources	www.nal.usda.gov/bic/Education_res	
Biotechnology on the Web	www.cato.com/biotech	
Biotech-Related WWW Sites and Documents	www.nal.usda.gov/bic/www.html	
GradSchools.com	www.gradschools.com/listings/menus/biotechnology_menu.html	