

# **Final Scientific/Technical Report**

## **DOE Grant DE-PS02-09ER-01**

Establishment of Center for Diagnostic Nanosystems

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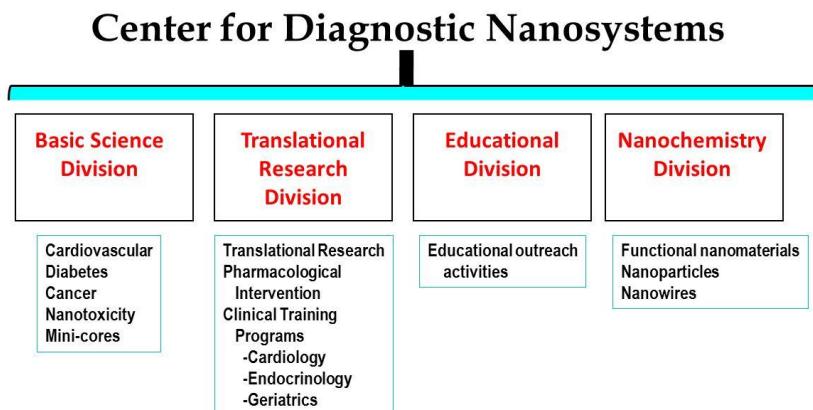
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Center for Diagnostic Nanosystems  
Final scientific/Technical Report 2015

## Executive Summary

### Introduction

The Center for Diagnostic Nanosystems was *formally* established at Marshall University in August of 2010 with the goal of developing novel molecular-based diagnostic tests that can be used by individuals and public health systems to facilitate personalized medicine (Figure 1). The primary disease focus of the Center for Diagnostic Nanosystems is on those disorders that are the most prevalent in West Virginia and Appalachia and include cancer, cardio-vascular disorders, and diabetes. The formation of the Center for Diagnostic Nanosystems was a result of intensive planning and was built on the base of previous funding from the National Science Foundation EPSCoR and National Institutes of Health COBRE / INBRE that had been used to significantly improve the biomedical research infrastructure at Marshall University. The Center for Diagnostic Nanosystems has been highly interdisciplinary in nature and has been staffed by scientists and researchers with expertise in the basic sciences, nanotechnology, and clinical medicine. One major aim of the Center was to develop partnerships with industry and other external partners in ways that further the mission of the Center and Marshall University. Work was also closely coordinated with related initiatives at Marshall University and within the state of West Virginia. Over the past years, the center has begun to merge new technologies from the nanosciences and engineering with genomics and molecular biology. Projects here include the identification of new biomarkers that could be used to track muscle wasting, cardiovascular dysfunction and progress in the development of new sensor platforms that could be used to interrogate blood or serum samples for makers of chronic disease. This fusion has been accomplished by linking biomedical scientists at Marshall University with nano-scientists and engineers at Michigan Technological University. Other successes include the ongoing development of the Translational Research Division whose mission was to facilitate the development of new clinical diagnostic techniques and novel clinical therapeutics. This work also serves as a bridge linking researchers across Marshall University to physician faculty at the Joan C. Edwards School of Medicine and the Erma Ora



**Figure 1. Organizational structure of the Center for Diagnostic Nanosystems.** The center is comprised of four divisions. Each division is or will be led by a senior scientist that oversees a team of other scientists, clinicians, technicians, and students and whose goal is to translate basic knowledge and discoveries into new treatments and devices that can be used to diagnose, follow, and treat chronic disease.

Byrd Clinical Center. This division addressed an *unmet need* in West Virginia and at Marshall University by aligning clinical and basic science activities and by providing a concrete mechanism to functionally bridge diverse disciplines for translational research. Other work in this division was centered on providing training and mentoring experiences for the next generation of clinical and translational researchers. This effort provided a significant increase in the amount and medical significance of research at Marshall University. Key clinical research initiatives within this portion of the Center were used to improve the excellence of clinical research programs at Marshall University and attract new students to clinical education and health care. Increased research associated with clinical activities at Marshall University provided an increase in opportunities for the clinical education of students in West Virginia. Finally, the Translational Research Division investigated a wide range of clinically relevant studies to help improve the treatment of our growing, and underserved, statewide population of elderly, the chronically ill, and our veterans.

Other activities within the Center of Diagnostic Nanosystems included the development of the Nanochemistry Division whose goal was to engineer new types of nanoparticles for drug delivery and to develop new types of nanomaterials and sensors that can be used to diagnose and treat chronic disease. Sensors studies conducted included foundational research for devices with the potential to obtain diagnostic information regarding chronic disease status non-invasively through either the analysis of exhaled biomarkers or saliva. Collaborations included work with Michigan Technological University, the University of South Carolina, the University of Delaware, the University of Western Australia, Walter Reed Hospital, Takasaki University of Health and Welfare, and the Beijing Higher Institution Engineering Research Center. Additional developments within the Center included the pursuit of collaborations with the Robert C. Byrd Institute for Advanced Flexible Manufacturing (RCBI) to lay the foundation for the development of a nano-safety training program. This program will be used to educate industry here in West Virginia and to support the development of nanosafety best practices and will be charged with the identification of existing occupational and environmental risk guidance information with the hopes of assisting small, medium and large businesses in developing environmental health and safety guidelines to minimize potential risk and any corresponding regulatory and legal exposures.

The interdisciplinary nature of the Center for Diagnostic Nanosystems is unique. This Center was the first of its kind in the state of West Virginia and *one of a very few nationwide* that was predicated on bringing together biomedical, nanoscientists and industry together to work on health related problems. This well-poised research capacity – and the focus on diseases and disorders prevalent in West Virginia – has resulted in the formation of a new and growing group of nanoscience researchers and scientists at Marshall University. These efforts, have laid the foundation for the development of new research programs at the Marshall University School of Pharmacy in the key areas of clinical, basic, health safety, and translational research.

## **Description of research activities and best successes**

### **Basis Science Division**

Research in the Basic Science Division has focused on better understanding the diabetic disease process, the identification of new biomarkers for the detection of cardiovascular disease, and on investigating the efficacy of using nanoparticles to treat chronic disease and sepsis. The following studies have been conducted over the life of this funding:

#### **Animal studies**

1. Effects of insulin resistance on muscle miRNA expression and the adaptation of skeletal muscle to increased loading.
2. Regulation of apoptosis in slow and fast twitch muscles of aged female F344BN rats
3. Hyperglycemia induced changes in vascular pressure-induced apoptosis in the rat inferior vena cava
4. Effects of cancer cachexia on cardiac remodeling in the APC min mouse.
5. Role of reactive oxygen species on the development of obesity.
6. Molecular Mechanisms of Age-Related Cardiac Hypertrophy in the F344XBN Rat Model
7. Cerium Oxide nanoparticle aggregates effect stress response and Function of *C. elegans*

### **Translational Medicine Division**

Research in the Translational Medicine Division has focused on better understanding the diabetic disease process in humans, how disease may affect endothelial expression, the identification of new biomarkers for the detection of cardiovascular disease, and on investigating the efficacy of several pharmaceutical agents for the treatment of hyperglycemia, renal disease, iron overload, and diabetes-induced bone loss.

#### **Human studies**

1. Effects of cardiovascular disease on endothelial function and miRNA expression.
2. Severe hypoglycemia and coronary artery calcification during the diabetes control and complications trial/epidemiology of diabetes interventions and complications (DCCT/EDIC) study

### Animal studies

1. Establishing obese Zucker rats (*Lepr<sup>fa/fa</sup>*) as a model of cardiovascular dysfunction
2. Establishing the efficacy of acetaminophen for the prevention or attenuation of cardiovascular and skeletal muscle dysfunction in metabolic syndrome.
3. Role of reactive oxygen species in renal remodeling.
4. Role of iron deposition in the development of hepatic fibrosis.
5. Effects of increased reactive oxygen species on diabetes-induced bone loss.
6. Examining the toxicity of cerium oxide nanoparticles on the heart, liver, and kidney.
7. Examining the toxicity of yttrium oxide nanoparticles on the kidney.

### Nanomedicine Division

Research in the nanomedicine division has been primarily centered on developing a new types of nanoparticles for the treatment of chronic and acute disease. In addition to these efforts, other work in the Nanomedicine Division has been centered animal studies to investigate the cytotoxic and therapeutic effects of nanoparticles.

### Animal studies

1. Cytotoxicity and genotoxicity caused by yttrium oxide nanoparticles in HEK293 cells
2. Effects of inhaled cerium oxide nanoparticles on the rat lung, heart, liver and kidney.
3. Efficacy of cerium oxide nanoparticles for the treatment of cardiac hypertrophy.
4. Efficacy of cerium oxide nanoparticles for the treatment of pulmonary hypertension.
5. Efficacy of cerium oxide nanoparticles for the treatment of microbial induced sepsis.

### Education Division

Efforts in the Education Division provided education and research opportunities for 6 PhD student, 9 masters students, 7 Post-doctoral fellows, 4 clinical fellows, 7 PhD rotation and 4 undergraduate students. In addition the Center has provided opportunities to 2 visiting scientists to gain valuable training and research experience in the field on nanotechnology. The center also conducted a lecture series to educate the public about nanotechnology.

## **Comparison of the actual accomplishments with the goals and objectives of the project.**

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This project was composed of two strategic goals:

**Strategic Goal 1: Achieve critical mass in research capacity at the interface between the nano- and biomedical sciences.** We will invest in people and the new ideas that will arise from them to serve as the means to accomplish this goal. With the proposed funding, the Center for Diagnostic Nanosystems will recruit two targeted research professors and three postdoctoral fellows. These positions will be used to fill existing and critical gaps in scientific expertise. The faculty and fellows of the quality we anticipate recruiting will be highly competitive for extramural grants. The recruitment of these lead investigators and postdoctoral fellows will be used to propel current research capabilities to enhance competitiveness for extramural funding.

Actual accomplishments here include the hiring of a two research assistant professors and several postdoctoral fellows. While employed at Marshall both of the research assistant professors were quite successful in publishing their work. Efforts by Dr. Wu resulted in obtaining a 5 year NASA-EPSCoR grant to examine the use of nanoparticles for the treatment of simulated space travel and exposure to radiation. This work is ongoing. The first research assistant professor left after one year at Marshall for a tenure track appointment at the University of Delaware. The work of the postdoctoral fellows has led to the development of a new research direction examining the use of nanoparticles for treating chronic and acute disease. This work has resulted in several publications and a patent application for using cerium oxide nanoparticles for the treatment of sepsis.

**Strategic Goal 2: Improve competitiveness for research and development funding in the nano- and biomedical sciences.** This goal will be met by facilitating interactions between researchers at Marshall University and scientists at Michigan Technological University. These interactions will be facilitated by monies that will be used to fund joint research projects between the two universities. Other funds will be used to support the travel of investigators from Marshall University to travel to other universities and centers to share scientific research ideas and experimental approaches. It is anticipated that if these two mechanisms are implemented in a coordinated manner, increased, long-term extramural funding will result, leading to a self-sustaining center.

Over the course of the grant several different projects were pursued between researchers at Marshall University and Michigan Technological University. These projects included the isolation of micro-RNA from biological samples and the modeling of DNA interactions with carbon nanowires. This work led to the submission of two NSF IGERT grants however neither were

funded. Also supported by this effort was the travel of researchers from Marshall to MTU and vice versa.

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### ***Summary of Project activities.***

#### Infrastructure development:

Funding from this project was used to develop several “mini-cores” that contained shared equipment that could be used by researchers at Marshall University. Equipment purchased during this project included: a fluorescent microplate reader, FTIR system, UV-Vis spectrophotometer, and DNA/RNA analyzer. Other deliverables included the funding of several graduate and undergraduate students, postdoctoral fellows and two research assistant professors.

#### Research development:

Projects supported by this funding included studies performed at the whole animal, organ, cellular and nano level. Several different types of researchers were supported including undergraduates, graduates, postdoctoral fellows and research assistant professors. The main outcomes of this work was the development of new types of nanoparticles that could be used for the treatment of pulmonary arterial hypertension and sepsis. Additional efforts to develop these projects are ongoing.

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### **Products developed under the award**

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Protective Effect of Acetaminophen on Renal Dysfunction in Obese Zucker Rat. C. Wang, Eric R. Blough, R. Arvapalli, S. Paturi, N. Manne, and MiaoZong Wu. American Associate of Colleges of Pharmacy, 2012.

Acetaminophen reduces lipid accumulation and improves cardiac function in the obese Zucker rat. M. Wu, R. Arvapalli, C. Wang, S. Paturi, N. Manne, L. Dornon, P. Wehner and Eric R. Blough. American Associate of Colleges of Pharmacy, 2012.

Expression of Titin, CCN and Extracellular Matrix Proteins in Smooth Muscle are Altered by Mechanical Stretch. E. Carte, A. Karunathilake, R. Harris and E. R. Blough. WVAS, June, 2012

Effect of dimethyl sulfoxide on bone hemostasis with obesity. O. Akhtar, Eric R. Blough, A. Yaqub, R. Arvapalli, S. Paturi, N. Manne, P. Herndon, and MiaoZong Wu. AACE, 2012.

Evaluation of Nano-Structured Surface Coatings for Improving Orthopaedic Implant Integration. A. H. Slocum, Jr., K. M. Rice, A. T. Paxson, A. Akono, K. K. Varansi, and Eric R. Blough, MUSOM Research Day, Marshall University, 2012.

Evaluation of oxidative stress and apoptosis in the liver following a single intratracheal instillation of cerium oxide nanoparticles in male Sprague Dawley Rats. S. K. Nalabotu and Eric R. Blough. Society of Toxicology, March 12, 2012.

Nano-Structured Contoured Porous Coatings for Orthopedic Implants. A. H. Slocum, Jr., A. T. Paxson, A. Akono, K. M. Rice, Eric. R. Blough, and K. K. Varansi, Materials Research Society, Boston, 2011

Physiological constituents of coping mechanisms: Relation to problem-solving and academic performance. S. Wemm, A. Fanenan, A. Baker, D. Mandich, Eric R. Blough, S. Mewaldt, and M. Bardi. Society for Neuroscience, Chicago, 2011.

MicroRNA nanosensor systems for early detection of disease in humans. T. Shokuhfar, T. Daunais, R. Tewari, X. Zhong, W. Slough, W. Douglas, Eric R. Blough, A. Kumar, R. Pandey, P. Bergstrom, C. Choi, S. Nalabothu, and C. Friedrich. Lab on a chip world congress. San Francisco, CA, September, 2011.

Efficacy of curcumin nanoparticles on monocrotaline induced pulmonary arterial hypertension and right ventricular hypertrophy. Madhukar B. Kolli, Arun Kumar, Feras Elbash, Radhakirshna Para, Siva Nalabotu, Nandini D.P.K. Manne, Geeta Nandyala, Paulette Wehner, and Eric R. Blough. American Heart Association, High Blood Pressure Research, Orlando, FL, 2011.

Resveratrol Attenuates Hypertrophy of Vascular Smooth Muscle Cells. R.P. Nagmal , R.T. Harris, K.M. Rice, and Eric R. Blough. 2011 Biennial National Land Grant Research Symposium. Washington DC.

Resveratrol attenuates fluprostenol induced hypertrophy of vascular smooth muscle cells. Rahul P. Nagmal, James R. Tchabo, Eric R. Blough, Robert T. Harris . Biophysical Journal 98(3) Supplement 1: 4330, 2011. 55<sup>th</sup> Annual Biophysical Society Meeting.

Autonomous nanocargo transport system using actin bundle-myosin bionanomotor. H. Takatsuki, K. M. Rice, S. Nalabotu, M. Kolli, K. Kohama, P. Famouri, M. Norton, and Eric R. Blough. ACS Nano, Central Regional Meeting, Indianapolis, IN., 2011

Intratracheal instillation of nanoceria induced systemic toxicity in rats. S. Nalabothu, J. Ma, W. Triest, M. Kolli, P. Wehner and Eric R. Blough. Society of Toxicology, 2011.

Resveratrol attenuates fluprostenol induced hypertrophy of vascular smooth muscle cells. Rahul P. Nagmal, James R. Tchabo, Eric R. Blough, and Robert T. Harris. Biophysical Society 55th Annual Meeting 11-L-4330-BPS, 2011.

Long term efficacy of deferasirox in preventing cardiovascular complications in the iron overloaded gerbil. Long term efficacy of deferasirox in preventing cardiovascular complications in the iron overloaded gerbil. Al-Rousan RM, Manzoor K, Paturi S, Arvapalli R, Laurino JP, Dornon L, Ernest M. Walker EM, and Eric R. Blough. American Pharmacists Association (APhA) Annual Meeting and Exposition, March 25-28, 2011, Seattle, WA.

Anti-arrhythmic effect of chronic acetaminophen treatment in the aging Fischer Brown Norway rat involves gap junction protein connexin 43. F. Elbash, S. Kakarla, P. Wehner, and Eric R. Blough. ACC Symposium (Charleston, WV, March, 2011).

Aging associated cardiac hypertrophy is mediated via Akt/mTOR signaling. S. Elbash, S. Kakarla, P. Wehner, and Eric R. Blough. ACC Symposium (Charleston, WV, March, 2011).

Resveratrol Attenuates Hypertrophy of Vascular Smooth Muscle Cells. R. P. Nagmal, R.T. Harris, K.M. Rice, and Eric R. Blough. 16th Biennial Research Symposium of the Association of 1890 Research Directors (Atlanta; April 2011).

M. Tanner, R. Ragland, E. R. Blough and S. Day. The functionalization of actin filaments for nano cargo delivery systems. Sigma Xi Research Day, Marshall University, 2012

Autonomous nanocargo transport system using actin bundle-myosin bionanomotor. H. Takatsuki, K. M. Rice, S. Nalabotu, M. Kolli, K. Kohama, P. Famouri, M. Norton, and Eric R. Blough. ACS Nano, Central Regional Meeting, Indianapolis, IN., 2011

Intratracheal instillation of nanoceria induced systemic toxicity in rats. S. Nalabothu, J. Ma, W. Triest, M. Kolli, P. Wehner and Eric R. Blough. Society of Toxicology, 2011.

Resveratrol attenuates fluprostenol induced hypertrophy of vascular smooth muscle cells.

Rahul P. Nagmal, James R. Tchabo, *Eric R. Blough*, and Robert T. Harris. Biophysical Society 55th Annual Meeting 11-L-4330-BPS, 2011.

Long term efficacy of deferasirox in preventing cardiovascular complications in the iron overloaded gerbil. Long term efficacy of deferasirox in preventing cardiovascular complications in the iron overloaded gerbil. Al-Rousan RM, Manzoor K, Paturi S, Arvapalli R, Laurino JP, Dornon L, Ernest M. Walker EM, and *Eric R. Blough*. American Pharmacists Association (APhA) Annual Meeting and Exposition, March 25-28, 2011, Seattle, WA.

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Resveratrol Attenuates Hypertrophy of Vascular Smooth Muscle Cells. R. P. Nagmal, R.T. Harris, K.M. Rice, and *Eric R. Blough*. 16th Biennial Research Symposium of the Association of 1890 Research Directors (Atlanta; April 2011).

Targeted delivery of nano-teranostics (TNT) to lungs for diagnosis and treatment of lung disease. A. Kumar, M. Glaum, *Eric R. Blough* and D. F. Cameron. 2010 Nanomedicine Symposium. October, 2010. (Cleveland Clinic, Cleveland, OH).

Potential role of 7,8-dihydro-8-oxoguanine-DNA glycosylase activity in mediating cardiomyocyte survival signaling during aging in Huntington's Disease. Curtis Adams, Emily N. Whitt, Kevin Rice, Saba Keshavarzian, Saeed Keshavarzian, Anjaiah Katta, Cynthia McMurray, Paulette Wehner and *Eric R. Blough*. INBRE Symposium, Morgantown, WV, 2010.

Mechanisms of resveratrol action on vascular smooth muscle cells. Rahul Nagmal, Hari Addagarla, Anjaiah Katta, *Eric R. Blough*, and Robert Harris. INBRE Symposium, Morgantown, WV, 2010.

Vascular Smooth Muscle Cell Function, Morphology, and Angiogenic Properties are Altered by Resveratrol. Dawn Turner, Anthony Johnson, Rahul Nagmal, *Eric R. Blough*, and Robert Harris. INBRE Symposium, Morgantown, WV, 2010.

Acetaminophen improves protein translational signaling in aged skeletal muscle. Wu M, Liu H, Fannin J, Katta A, Wang Y, Arvapalli RK, Paturi S, Kakarla SK, , Rice KM, and *Eric R. Blough*. 39th Annual Meeting of the American Aging Association; Portland, Oregon. June 2010.

Katta A, Kundla S, Kakarla S, Wu, M. Diabetes alters vascular mechanotransduction: pressure induced regulation of phosphatase and tensin homologue (PTEN) in rat inferior vena cava. Price, B, Rice, KM, Kakarla, SK, Katta, A., Preston, D.L., Wehner, P., and *Eric R. Blough*. MUSOM Research Day, Marshall University, 2010.

Acetaminophen diminishes age-associated increases in cardiac oxidative stress in the male Fischer 344 x Brown Norway Rats. Almahaasneh, F., Kakarla, S., Narula, S., Decker, J., Katta, A., Rice, K.M, Wehner, P., and *Eric R. Blough*. MUSOM Research Day, Marshall University, 2010.

Effect of iron chelation on cardiac function in the iron overloaded Mongolian gerbil. Maru, M., Dornon, L., Al-Rousan, R., Manzoor, K., Laurino, J, Walker, EM and *Eric R. Blough*. MUSOM Research Day, Marshall University, 2010.

Chronic acetaminophen attenuates age-associated increases in cardiac ROS and apoptosis in the Fischer Brown Norway rat. Kakarla, S.K., Fannin, J.C., Katta, A., Paturi, S., Rice, K.M., and *Eric R. Blough*. MUSOM Research Day, Marshall University, 2010.

Impaired overload-induced hypertrophy is associated with diminished mTOR signaling in insulin resistant obese Zucker Rat. Katta A, Kundla S, Kakarla S, Wu M, Paturi S, Gadde MK, Arvapalli R, Kolli M, Siva K, Rice KM, and *Eric R. Blough*. Presented at the 57<sup>th</sup> annual Meeting of American College of Sports Medicine; Washington, DC. June 2010.

E. Schleser, P. Manne and *E. R. Blough*. Passive exposure of *carnorhabditis elegans* to cerium oxide nanoparticles in culture alters age-related metabolic decline. Sigma Xi Research Day, Marshall University, 2010

A. Litchfield, B. Wang, *E. R. Blough* and S. Thulluri. Age associated changes in mRNA expression of SOD-2, HO-1, APP, BACE-1 and alpha-synuclein in the hippocampus of male and female rat brains. Sigma Xi Research Day, Marshall University, 2010

M. Tanner, E. R. Blough and B. S.Day. The functionalization of actin filaments for a nano-cargo delivery system. Sigma Xi Research Day, Marshall University, 2010

D. L. Preston and *E. R. Blough*. Effects of acute contractile exercise on MAPK signaling in the soleus and extensor digitorum longs muscles of syndrome-X obese and normal lean zucker rats. Undergraduate Research Day at the Capital.

Design of nanofiber scaffolds for regulating cell behaviors. Xie, J and B. Ma (Abstract submitted for The 9th World Biomaterials Congress, Chengdu, China, June 1-5, 2012. Accepted as an oral presentation.)

Design of electrospun nanofiber scaffolds for tissue engineering applications. Xie, J. Department of Orthopaedics, Joan C. Edwards School of Medicine, Marshall University, July 20<sup>th</sup> 2011 (Invited seminar).

Bin Wang<sup>†</sup>, Characterization and comparison of cytosine-rich RNA domains, *The 241<sup>st</sup> American Chemical Society National Meeting & Exposition, Anaheim, CA*, March 27-31, 2011. (Poster Presentation)

Bin Wang<sup>†</sup>, Structural determination of an iron-responsive element in the 5' untranslated region of alpha-synuclein mRNA, *The 242<sup>nd</sup> American Chemical Society National Meeting & Exposition, Denver, CO*, August 28-September 1, 2011. (Oral Presentation)

Srinivasarao Thulluri<sup>#</sup>, MiaoZong Wu, Eric R. Blough, Nandini D.P.K. Manne<sup>#</sup>, Ashley B. Litchfield<sup>\*</sup>, Bin Wang<sup>†</sup>, Regulation of iron-related molecules in the rat hippocampus, *The 242<sup>nd</sup> American Chemical Society National Meeting & Exposition, Denver, CO*, August 28-September 1, 2011. (Poster Presentation)

Bin Wang<sup>†</sup>, Michael S. Thompson<sup>\*</sup>, Kevin M. Adkins<sup>\*</sup>, Development of RNA nanostructures for drug delivery, *The 243<sup>rd</sup> American Chemical Society National Meeting & Exposition, San Diego, CA*, March 25-29, 2012. (Oral Presentation)

Tyler E. Dickson<sup>\*</sup>, Srinivasarao Thulluri<sup>#</sup>, Bin Wang<sup>†</sup>, Age- and sex-associated changes in mRNA expression of Alzheimer's disease-related molecules in the hippocampus of rat brains, *The 243<sup>rd</sup> American Chemical Society National Meeting & Exposition, San Diego, CA*, March 25-29, 2012. (Poster Presentation)

Tyler Dickson<sup>†</sup>, Srinivasarao Thulluri, Bin Wang, Age- and sex-associated changes in mRNA expression of Alzheimer's disease-related molecules in the hippocampus of rat brains, *The 21<sup>st</sup> Annual Sigma Xi Research Day, Marshall University, Huntington, WV*, April 29, 2011. (Poster Presentation, winner of the Best Poster Award)

Kevin Adkins<sup>†</sup>, Bin Wang, RNA nanotechnology, *Marshall University Chemistry Summer Research Program Symposium, Huntington, WV*, July 22, 2011. (Oral Presentation)

Irfan Khan<sup>†</sup>, Bin Wang, Development of microchip-based platform for dynamic monitoring of cellular response to environmental toxins, *Marshall University Chemistry Summer Research Program Symposium, Huntington, WV*, July 22, 2011. (Oral Presentation)

Kevin Adkins<sup>†</sup>, Bin Wang, RNA nanotechnology, *The WV SURE Symposium, Marshall University, Huntington, WV*, July 29, 2011. (Poster and Oral Presentations)

Kevin Adkins<sup>†</sup>, Bin Wang, RNA nanotechnology, *Department of Chemistry, Marshall University, Huntington, WV*, October 14, 2011. (Oral Presentation)

Michael Thompson<sup>†</sup>, Bin Wang, Self-assembly of ribonucleic acid nanostructures, *Department of Chemistry, Marshall University, Huntington, WV*, March 16, 2012. (Oral Presentation)

Irfan Khan<sup>†</sup>, Colton Koontz, Masudur Rahman, David Neff, Bin Wang, Elmer Price, Michael Norton, Designing a microfluidic cell culture system for growing endothelial cells, *The West Virginia STaR Symposium, West Virginia State University, WV, April 21-22, 2012.* (Oral Presentation)

Irfan Khan<sup>†</sup>, Masudur Rahman, David Neff, Colton Koontz, Bin Wang, Elmer Price, Michael Norton, Monitoring the effect of bradykinin and cadmium chloride on endothelial cell nitric oxide production via fluorescence microscopy, *The 22<sup>nd</sup> Annual Sigma Xi Research Day, Marshall University, Huntington, WV, April 27, 2012.* (Poster Presentation)

Colton Koontz<sup>†</sup>, Irfan Khan, Bin Wang, Design and simulation of microfluidics for endothelial cell culture, *The 22<sup>nd</sup> Annual Sigma Xi Research Day, Marshall University, Huntington, WV, April 27, 2012.* (Poster Presentation)

#### ***Grants Awarded***

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“Establishing the efficacy of empagliflozin for the prevention of cardiac and renal dysfunction during the development of metabolic syndrome in the obese Zucker rat.”

Principal Investigator: Eric Blough

Agency: Boehringer Ingelheim Pharmaceuticals

\$394,627; (7/1/2015-6/30/2017)

“Mechanical unloading and irradiation-induced musculoskeletal loss and dysfunction: molecular mechanisms and therapeutic nanoparticles.”

Principle Investigator: MiaoZong Wu, Ph.D., co-PI and PI-mentor: Eric Blough, Ph.D.

Agency: NASA-EPSCoR

\$750,000 (Direct costs); (10/1/13-9/31/16)

“Effects of cerium oxide nanoparticles on X-ray irradiated human keratinocytes”

Principal Investigator: Nicole Winston, PharmD, Eric Blough Ph.D. (co-investigator)

Agency: West Virginia, Space Grant Consortium

\$10,000 (Direct costs); (6/15/2013-6/14/2014)

Obesity-induced alteration of bone structure and function: molecular mechanisms and DMSO intervention”

Principal Investigator: MiaoZong Wu, Ph.D., Eric Blough Ph.D. (co-investigator)

Agency: West Virginia, Space Grant Consortium

\$20,000 (Direct costs); (6/15/2012-6/14/2013)

“Evaluation of niacin to improve vascular endothelial function in dialysis patients”

Principal Investigator: MiaoZong Wu, Ph.D., Eric Blough Ph.D. (co-PI)

Agency: Rezulin funding for translational initiatives.  
\$10,000 (Direct costs); (11/1/2012-10/31/2013)

Title: "The efficacy of trichostatin A to improve bone quality and function in hindlimb unloaded rats."

PI: MiaoZong Wu, Eric Blough Ph.D. (co-investigator)

Agency: *NASA WV EPSCoR*

Award: \$20,000

Date range: 06/2012-06/2013

Title: "Trichostatin A as a countermeasure to aortic dysfunction following hindlimb unloading."

PI: MiaoZong Wu, Eric Blough Ph.D. (co-investigator)

Agency: *NASA WV EPSCoR*

Award: \$20,000

Date range: 06/2011-06/2012

Title: "Examine and validate whole genome mRNA expression in skeletal muscle following hindlimb unloading and trichostatin A intervention."

PI: MiaoZong Wu, and Robert Harris (Co-PI)

Agency: *NASA WV EPSCoR*

Award: \$20,000

Date range: 06/2011-06/2012

"Development of an Integrated Microfluidic Device for Cargo Transport Using an Actin-Myosin System"

PI: B. Scott Day, Student: Rebecca Ragland.

Agency: NASA West Virginia Space Grant Consortium, Graduate Research Fellowship Program.

Award: \$12,000.

Date range: July 2011- June 2012

"The efficacy of trichostatin A to improve bone quality and function in hindlimb unloaded rats."

Principal Investigator: MiaoZong Wu, Ph.D., Eric Blough Ph.D. (co-investigator)

Agency: West Virginia, Space Grant Consortium

\$20,000 (Direct costs)

(6/15/2012-6/14/2013)

"Establishing obese Zucker rats (*Lep<sup>fa/fa</sup>*) as a model of cardiovascular dysfunction for ONGLYZA (Saxagliptin) intervention. "

Principal Investigator: Eric Blough, Ph.D.  
Agency: Bristol Meyer Squibb  
\$85,050 (Direct costs)  
(4/1/2011-3/31/2012)

“Establishing the efficacy of TYLENOL for the prevention or attenuation of cardiovascular and skeletal muscle dysfunction in metabolic syndrome.”

Principal Investigator: Eric Blough, Ph.D.  
Agency: McNeil Pharmaceutical  
\$56,500 (Direct costs)  
(12/1/2010-11/30/2011)

“Effect of Exjade on hepatic fibrosis and iron regulatory protein expression following iron overload.

Principal Investigator: Eric Blough, Ph.D.  
Agency: Novartis Pharmaceutical  
\$49,500 (Direct costs)  
(11/15/20

“Influence of the HDAC inhibitor Trichostatin A on hypertrophic and atrophic responses of smooth and skeletal muscle.”

Principle Investigator: Robert Harris, Ph.D.; Co-PI: Eric Blough, Ph.D.  
Agency: NASA / WV Space Grant Consortium  
\$12,000  
Funding used to support graduate student (James Tchabo)  
(7/1/2010-6/30/2011)

The Design and Development of RNA Nanoparticles for Drug Delivery.  
Principal investigator: Bin Wang  
Agency West Virginia Research Proposal Mini-Grants program  
\$5,000

“Biomimetic Nanofiber Scaffolds seeded with Adipose-derived Stem Cells for Rotator Cuff Injury Repair”  
Principal investigator: Jingwei Xie  
University of Kentucky- Marshall University Translational Science Award Program.  
\$25,000 (Direct costs)  
January 2012

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***Patent applications, In process***

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“Nanofiber scaffolds and methods for repairing damaged cardiac tissue”, Xie, J. U.S. patent application number 61586866. (U.S. provisional patent application filed in January 2012).

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***Disclosures***

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“Induction actin bundle disassembly for release of molecular cargo” H. Takatsuki and *E. R. Blough\**

“Application of deferasirox for treatment and prevention of iron-induced tissue apoptosis and fibrosis” M. Wu and *E. R. Blough\**

“Use of acetaminophen for the prevention of age-associated cardiac dysfunction” S. Kakarla and *E. R. Blough\**

“Use of acetaminophen for treatment of muscle atrophy, improvements in meat quality and for increasing plant protein production.” M. Wu and *E. R. Blough\**

“Application of 3-mercaptopropyltrimethoxysilane (MPTMS) for non-contact photo patterning and site specific chemistry and reliable positioning of functional native proteins”, K. M. Rice and *E. R. Blough\**

“Development of chromatin actuator for nanoscale manipulation”, P, Georgel and *E. R. Blough\**

“Antioxidants alone or in combination with iron chelation treat and prevent protein S-nitrosylation related disorders and diseases”, M. Wu and *E. R. Blough\**

“Prevention of Akt / protein kinase B s-nitrosylation and improvement of Akt-associated disorders and diseases”, M. Wu and *E. R. Blough\**

“Application of acetaminophen for prevention and treatment of dysregulation of phosphatase and tensin homolog deleted on chromosome 10 (PTEN)”, M. Wu and *E. R. Blough\**

“Application of acetaminophen for prevention and treatment of dysregulation of mitogen-activated protein kinases (MAPK)”, M. Wu and *E. R. Blough\**

“Application of acetaminophen for improvement of glucose transporter (Glut) expression, prevent and treat hyperglycemia” M. Wu and *E. R. Blough\**“

“Application of actin bundle for actomyosin motor-based cargo transport system. H. Takatsuki and *E. R. Blough\**“

### ***Media Reports related to Laboratory Research***

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Nanoparticles Used as Additives in Diesel Fuels Can Travel from Lungs to Liver ScienceDaily (Nov. 17, 2011)

In vivo study reveals toxic effects of cerium oxide nanoparticles in liver Safenano; Europe Center of excellence on nanotechnology hazard and risk (21/11/2011)

Marshall Study: Efficiency Additive Linked to Liver Damage West Virginia State Journal (Nov 17, 2011)

“Revolutionizing Health Care for the Next Generation” . West Virginia Executive. Winter 2011, Pg. 20, Executive LLC Publication, 2011.

Nanotechnology now: [http://www.nanotech-now.com/news.cgi?story\\_id=36572](http://www.nanotech-now.com/news.cgi?story_id=36572)

Nanowerk: <http://www.nanowerk.com/news/newsid=14645.php>

Science daily: <http://www.sciencedaily.com/releases/2010/02/10020211103.htm>

Nanopatents and Inventions:

<http://nanopatentsandinnovations.blogspot.com/2010/02/research-at-marshall-university-may.html>

Eureka Alert: [http://www.eurekalert.org/pub\\_releases/2010-02/murc-ram020210.php](http://www.eurekalert.org/pub_releases/2010-02/murc-ram020210.php)

Red orbit:

[http://www.redorbit.com/.../research\\_may\\_lead\\_to\\_new\\_ways\\_to\\_transport\\_and\\_manipulate/](http://www.redorbit.com/.../research_may_lead_to_new_ways_to_transport_and_manipulate/)

First science News: <http://www.firstscience.com/home/news/nanotechnology.html>

Genetic engineering and biotechnology news:

<http://www.genengnews.com/news/bnitem.aspx?name=74516295&taxid=34>

Innovations report: <http://www.innovations->

[report.de/html/berichte/biowissenschaften\\_chemie/research\\_marshall\\_university\\_lead\\_ways\\_transport\\_147880.html](http://report.de/html/berichte/biowissenschaften_chemie/research_marshall_university_lead_ways_transport_147880.html)

Feedzilla Nanotechnology Report: <http://www.feedzilla.com/latest-news/science/nanotechnology.html>

News Guide: <http://www.newsguide.us/education/science/Research-at-Marshall-University-may-lead-to-new-ways-to-transport-and-manipulate-molecules/>

Fars news: <http://english.farsnews.com/newstext.php?nn=8811140745>

Medical and Technology review: <http://cmumedteachandtech.blogspot.com/>

### ***Research Advising***

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#### Research Assistant Professor

Miaozong Wu

Center for Diagnostic Nanosystems

Arun Kumar

Center for Diagnostic Nanosystems

Selvaraj Vellaisamy

Center for Diagnostic Nanosystems (current)

#### Senior Scientists

Kevin Rice

Center for Diagnostic Nanosystems (current)

#### Post-Doctoral Fellows

Hideyo Takatsuki

Center for Diagnostic Nanosystems

Weingshang Liu

Center for Diagnostic Nanosystems

Shinichi Asano

Center for Diagnostic Nanosystems

Bing Ma

Center for Diagnostic Nanosystems

Prasanna Manne

Center for Diagnostic Nanosystems (current)

Ata Abbas

Center for Diagnostic Nanosystems

Selvaraj Vellaisamy

Center for Diagnostic Nanosystems

#### Visiting Scientists

Cuifen Wang, M.D. (Current)

Center for Diagnostic Nanosystems

Rao Indlamuri Mastran, M.D.

Center for Diagnostic Nanosystems

#### Research Technicians

Geeta Nandyala

Center for Diagnostic Nanosystems

Nirajan Nepal

Center for Diagnostic Nanosystems

#### PhD Students

Jackie Decker

Major advisor, Graduated

Madhukar Kolli

Major advisor, Graduated

Nandini Manne

Major advisor, Graduated

Siva Nalabothu	Major advisor, Graduated
Sunil Kakkarla	Major advisor; Graduated
Anjia Katta	Major advisor; Graduated

#### MS Students

Rebecca Ragland	Committee member, Graduated
Geeta Nandyala	Major advisor, Graduated
Niraj Nepal	Committee member, Graduated
Radhakrishna Para	Major advisor, Graduated
Sravanthi Bodapti	Major advisor, Graduated
Sudarasanam Kundla	Major advisor, Graduated
Nandini Manne	Major advisor, Graduated
Mani Maheshwari	Major advisor,
Vinay Bandarupalli	Major advisor,

#### Clinical Fellows:

Feras El-Bash, M.D.	(with Paulette Wehner, M.D., St. Mary's Hospital)
Brian A. Price, M.D.	(with Paulette Wehner, M.D., St. Mary's Hospital)
Muhammad Waqas, M.D.	(Marshall University Cardiology)
David Francke, M.D.	(Marshall University Cardiology)

#### PhD rotations

Prasanna Manne	JCESOM, Physiology, Pharmacology and Toxicology
Mike Brown	JCESOM, Physiology, Pharmacology and Toxicology
Sunil Kakkarla	JCESOM, Physiology, Pharmacology and Toxicology
Anjiah Katta	JCESOM, Physiology, Pharmacology and Toxicology
Megan Neal	JCESOM, Physiology, Pharmacology and Toxicology
Jackie Decker	JCESOM, Physiology, Pharmacology and Toxicology
Madhukar Kolli	JCESOM, Physiology, Pharmacology and Toxicology
Siva Nalabothu	JCESOM, Physiology, Pharmacology and Toxicology

#### Undergraduate research mentor

Erin Fankhanel	Marshall University
Ellie Andrews	Georgetown University, HHMI Undergraduate Fellow
Curtis Adams	University of North Carolina, INBRE
Zaira Riberiro	Marshall University

#### Seminar Series:

In conjunction with the RCBI Institute the Center for Diagnostic Nanosystems co-sponsored a lecture series to educate the public about different aspects of nanotechnology.

***Networks and Collaborations Fostered:***

Michigan Technological University  
Georgetown University  
University of North Carolina  
University of Kentucky  
University of Western Australia  
Walter Reed Hospital,  
Takasaki University of Health and Welfare,  
Beijing Higher Institution Engineering Research Center  
RCBI for Advanced Flexible Manufacturing.  
National Institute for Occupational Safety and Health