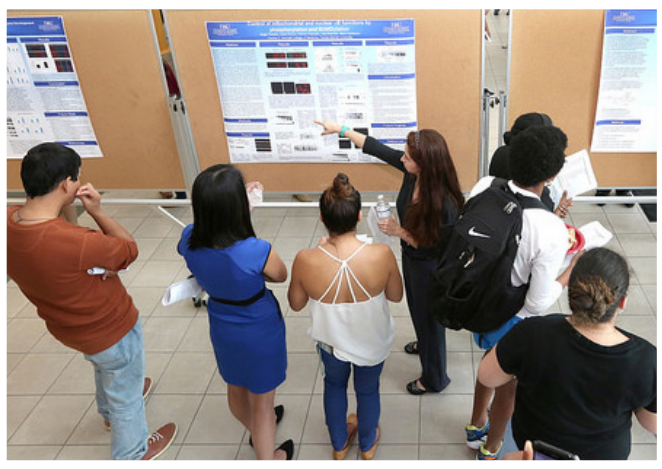
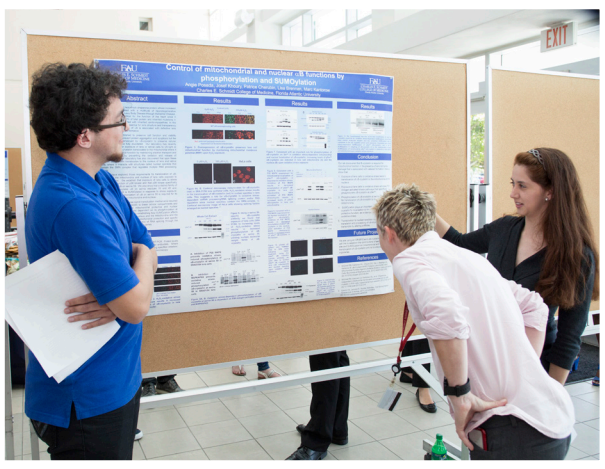
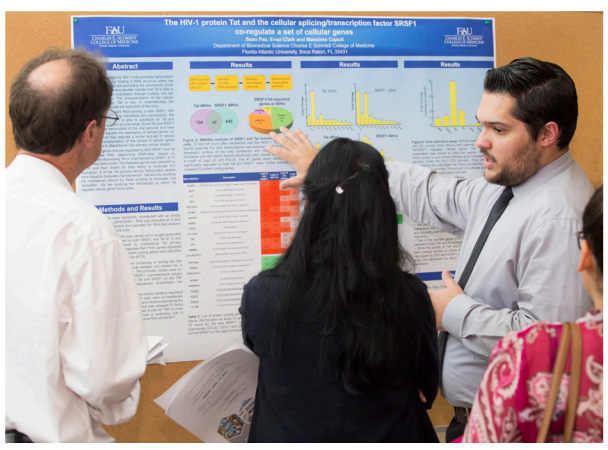
FLORIDA ATLANTIC UNIVERSITY™

CHARLES E. SCHMIDT COLLEGE OF MEDICINE

Biomedical Science Self-Study







Florida Atlantic University
Academic Program Review
Self-Study Report Biomedical Science

Program:	Biomedical Science
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TABLE OF CONTENTS

Preamble

The College of Medicine Master of Science in Biomedical Science Program provides a vital contribution to the mission of the Charles E Schmidt College of Medicine, Florida Atlantic University and the South Florida Community by proving innovative educational, research and career development opportunities for student success in a wide-range of biomedical science fields. The College of Medicine Master of Science in Biomedical Science Program has served the needs of approximately 40-55 graduate students enrolled in the program each year since its inception in 2004. In addition to meeting the educational goals of students directly enrolled in the program, the program also serves to meet the educational goals of students across the university enrolled in a wide variety of disciplines including engineering, biology, psychology, chemistry, business, neuroscience and more. The program is also vital to the Florida community by providing a central hub of biomedical science knowledge and resources.

A. Accomplishments since last review

- Established a centralized Graduate Student Advising Office with open-door access for student support.
- Recruited a Professional Coordinator of Graduate Programs.
- Developed Core Learning Requirements for the Program.
- Established Standardized Program of Study Requirements and Student Progress Assessment Tools.
- Developed Four Content-Based Core Courses to Provide a Common Learning Experience for all students in the program.
- Developed Standardized Syllabi.
- Developed Eight New Biomedical Science MS courses.
- Established Yearly Advising Requirements for all students In the Program by the Assistant Dean of Graduate Programs.
- Developed a Biomedical Science Distinguished Lecturer Series with attendance required by all students in the program.
- Developed a Biomedical Science Graduate Student Research Symposium.
- Developed an Annual Retreat for students in the program.

B. Metrics for Success

(SPOT data available up to 2014-2015)

- Biomedical Science MS Program Courses “as a whole” received an average student SPOT rating of 92% “excellent” in 2015 relative to an average rating of 40% “excellent” in the previous year and relative to a university-wide rating of 43% “excellent” in 2015.
- Biomedical Science MS Program Instructors “overall-effectiveness” received an average student SPOT rating of 92% “excellent” in 2015 relative to an average rating of only 46% “excellent” in the previous year and relative to a university-wide rating of 54% “Excellent” in 2015.
- The percentage of minority students in the Biomedical Science MS Program rose to a level of 67.9% for 2015-2016 relative to a level of 44.8% in 2014-2015 and relative to a university-wide minority level of 49%. *FAU has been designated as a Hispanic Serving Institution.
- First year retention rates for students in the biomedical science program 2015-2016 rose to 100% relative to 78.9% in 2011-2012 and 87.6% university-wide in 2014-2016.
- Three-year graduation rates for full-time MS Biomedical Science students rose to 91.3% 2013-2014 relative to 84.2% in 2011-2012 and relative to a university-wide level of 65% in 2013-2014.
- The MS Biomedical Science program awarded 139 MS degrees from 2010-2015 making the program 11th out of 66 master programs at the university in the number of degrees awarded.

C. Needs for Continued Advancement

- The program is not at its full teaching capacity. There are many unfilled seats in our courses. To fill theses seats, and increase the impact of the program, enrollment in the program must increase.

- A major obstacle for enrollment, and student success in the program, is a lack of student tuition and cost of living support. This lack of scholarships, research assistantships (RAs) and teaching assistantships (TAs) available to our students is a major obstacle for increasing enrollment and ensuring student success in the program.

- Another obstacle for the growth and success of the program is limited classroom space and dedicated study areas for students. Presently, there is only one classroom in the College of Medicine building available for scheduling graduate courses and no designated study areas. Identifying additional dedicated classroom space and study space for graduate students would advance the growth and impact of the program.

- Another obstacle for the growth and success of the program is lack of a centralized student body and a lack of representation in the college and at the university. Many students report that their process in the program is limited by a lack of recognition. Strategies are needed to improve student representation and provide a cohesive learning environment for students in the program.

- The ability of the program to serve student needs is hampered by a lack of administrative support for the program. Currently only one full-time administrative staff person is assigned to meet the needs of the entire program. Additional staff support would greatly facilitate the ability of the program to grow and meet the needs of students.

D. Mission of the Charles E. Schmidt College of Medicine Biomedical Science MS Program

The mission of the Charles E. Schmidt College of Medicine's MS Biomedical Science program is to provide students with the education and skills they need to pursue multiple careers in the biomedical sciences ranging from post-graduate studies in medicine and biomedical research to direct employment in education and industry. The Biomedical Science program is at the cornerstone of the mission of the Charles E. Schmidt College of Medicine that is to educate physicians and scientists to meet the healthcare needs of Florida, to conduct biomedical research to advance knowledge, to improve patient care, and to serve patients and communities with competence, compassion and respect.

E. Purpose of the Biomedical Science MS Program

The purpose of the Master of Science degree in Biomedical Science is to prepare students for post-graduate opportunities in the health sciences and biomedical research and to prepare students for direct entry into biomedical science-related careers. The program offers both thesis and non-thesis options. The thesis option is designed for students wishing to focus on biomedical research. The non-thesis option is designed for students whose primary interest is in preparing for professional school, preparing for careers in biomedical science-related industries and preparing for careers in science education. The program also offers a certificate in biomedical science for students in other graduate programs wishing to complete a biomedical science concentration.

F. Accreditation of the Biomedical Science MS Program

Florida Atlantic University (FAU) is accredited by the Southern Association of Colleges and Schools Commission on Colleges (SACSCOC) every 10 years to award degrees at the baccalaureate, master's, etc. level.

In December 2013, the Commission on Colleges of the Southern Association of Colleges and Schools (SACS) reaffirmed Florida Atlantic University's accreditation for a period of 10 years.

The MS Biomedical Science program was approved by the FAU Board of Trustees in approximately 2004 and was approved by the Board of Governors in approximately the same year.

G. Instruction of the Biomedical Science MS Program

Establishment of Student Learning Outcomes (SLOs)

Students enrolled in the MS in biomedical science degree are expected to have a thorough understanding of core biomedical science concepts, biomedical science applications and biomedical research skills. The Master of Science of Biomedical Science program in the College of Medicine (COM) has strong assessment plans in place for monitoring student success in these areas ranging from direct examinations both written and oral and through hands-on observations of student performance. Overall, the Florida Board of Governor's (BoG's) mandated key core Student Learning Outcomes (SLOs) in the areas of: content knowledge, critical thinking and communication skills. Courses in the program are designed to meet these SLO requirements through a variety of traditional and innovative teaching strategies. Examples of the best practices and assessment methods used to successfully quantify and evaluate student performance in these areas are:

1) Field-tested analytic rubrics developed by faculty are used for evaluating student written work. We have implemented this in individual course assessments and these are also a key component and for thesis related activities. In addition, we have implemented a required writing course (Biomedical Writing) that all students in the MS Biomedical Science program take and benefit from.

2) Analytic rubrics for oral presentations were developed by faculty and are implemented throughout the curriculum. These range from in class oral presentations through oral research competitions through traditional these and research credit defenses.

4) The MS Biomedical Science program has further met these SLOs through continues quality improvement efforts in annual revision and assessment of all courses taught in the program and through the development and implementation of required capstone (core) courses that touch on all of these assessments and provide core learning experience for all students enrolled in the MS Biomedical Science program. Core courses directly implementing the SLOs are Biomedical Writing and Biomedical Data and Informatics. Core courses that provide a core foundation for biomedical knowledge and skills are Human Genetics and Advanced Molecular and Cell Biology. In these core courses, and throughout the curriculum, cumulative assessment of student performance in all three SLOs including content knowledge, critical thinking and communication skills are evaluated in depth.

5) The MS Biomedical Science program implements a required Distinguished Lecturer Seminar Series throughout the academic year where faculty and distinguished lecturers present specific research topics to the students. This helps with student improvement and learning and gives them the opportunity to learn and discover broad-based research and critical thinking skills.

6) Students in the MS program also have the opportunity to perform laboratory research in state-of-the art biomedical science research areas as either thesis students preparing a scholarly proposal or non-thesis students in specialized directed independent study programs. The MS Biomedical Science program in COM conforms to the highest standards of nationally accepted research and educational practices. Our assessment practices conform to those across the university and align with nationally accepted standards for equivalent graduate MS science programs.

7) Students in the program must demonstrate substantial professional skills in the biomedical sciences, as evidenced by scholarly interactions with professionals in the field, including participation in professional organizations and activities such as scholarly presentations at the annual Research Day and Distinguished Lecturer Seminar Series attendance.

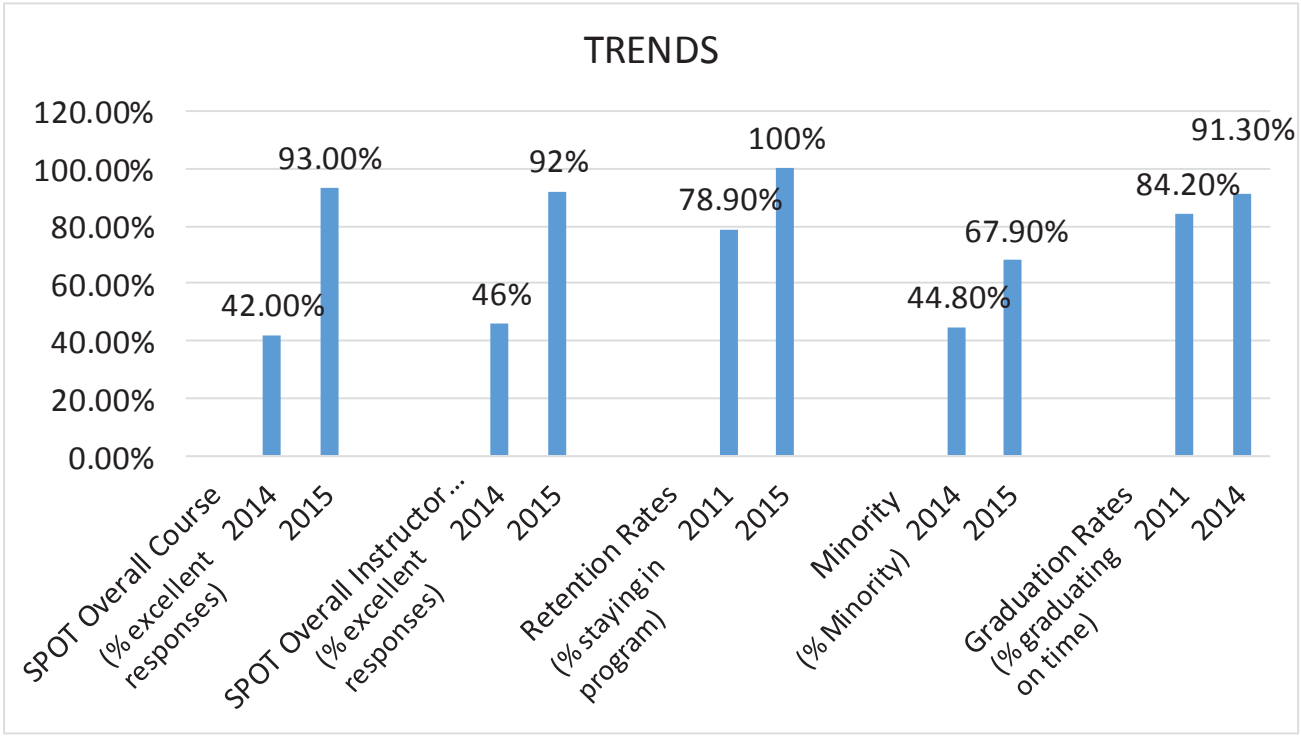
8) Students enrolled in the thesis option conduct original research and perform in-depth analysis, in cutting-edge biomedical research areas as demonstrated by the successful completion of a Master's Thesis. Specifically, students demonstrate: 1) current knowledge of their field of study and the ability to critically review and interpret scientific literature. 2) the ability to develop hypothesis, design and execute scientific experiments, and draw logical conclusions from data. 3) the ability to write scientific reports and communicate same effectively in oral presentations. Overall evaluation of student thesis work in the Biomedical Science Program is performed by a thesis committee in accordance with the guidelines of the academic department of the faculty advisor. A thesis committee reviews the thesis proposal and thesis defense presentations, which are open to all faculty. The advanced procedural and technical skills of the student are evaluated and reported by the thesis committee in accordance with the guidelines of the academic department of each student's faculty advisor.

The above achievements are representative of the MS Biomedical Science program and are a testimony to the high levels of dedication, coordination and cooperation between COM faculty. Additional support from the Chairs, Assistant Dean of Graduate Programs, Senior Associate Dean for Research and Dean reinforce these high standards of excellence.

Assessment of SLOs and Program Improvement

In addition to the above strategies for assessing students SLOs and beginning in 2015, the Coordinator of Graduate Programs, Assistant Dean of Graduate Programs, Senior Associate Dean for Research and Dean have continually monitored and worked together to develop and implement more standardized approaches to assess and document graduate student performance, progress, achievements and attainment of educational and career goals. These include the ongoing development and implementation of a rigorous advising program carried out by the Assistant Dean of Graduate Programs and Coordinator of Graduate Programs and the development and implementation of the key core courses described above that standardize the knowledge base, critical thinking skills assessment and advancement of our students. We are currently in the process of developing further academic, research and long-term goal assessment strategies to even better monitor and enhance student progress and outcomes. These and our other tools of assessment implement and advance these SLOs and we continue to develop further standardized and quantitative assessment metrics to meet and ultimately exceed these important expectations.

All courses in the Biomedical Science department are periodically evaluated for content and level of instruction through examination of course syllabi, enrollment figures, and SPOT evaluations by the Department Chairs and the Office of Graduate Programs (OGP). In consultation with the instructors and the graduate faculty, the OGP has begun to introduce new courses that are aligned with emerging science and medical science trends to keep the program innovative, impactful and current. These include new courses in precision medicine, genomic technology and other important areas.



H. Graduate Programs

Description of Biomedical Science Program Requirements:

i. Prerequisites:

The Prerequisites for the master's degree include:

- One year of biology
- One year of chemistry
- One year of physics
- One semester of organic chemistry
- One semester of biochemistry
- At least two upper-division (3000-4000 level) biology classes. For example, microbiology, genetics, molecular and cell biology, immunology, virology.

ii. Limited Access:

N/A

iii. Admissions Criteria:

In addition to meeting all of the University and College requirements for admission to graduate study, applicants for the MS Biomedical Science degree must meet the following criteria:

1. The student must have a baccalaureate degree from an accredited college or university or foreign equivalent;
2. The student must have competitive Graduate Record Examination scores or foreign equivalent;
3. The student must have a minimum 3.0 average in the last 60 credits of undergraduate work or foreign equivalent; and
4. The student must be approved for admission to the program by the Graduate Admissions Committee.

The admissions criteria is shown below in Appendix A and the brochure for the M.S. degree is in Appendix B. The Department's graduate admissions committee prefers students who exceed the minimum requirements.

Students in the MS Biomedical Science program typically bachelor's degrees in either biology chemistry micro or neuroscience a smaller percent have a bachelor's degrees in education, psychology, and public health.

Average Scores and GPA of Applicants for the 2016-2017 year

Average GRE Verbal	150
Average GRE Quantitative	150
Average Last 60 credits GPA	3.3
Average Science GPA	3.1

The table below illustrates the percentage of students from FAU and outside institutions from Fall 2016-Fall 2017. The majority of students come from Florida Atlantic University and other Florida institutions.

Applicants former institutions Fall 2016 Fall 2017

FAU	70%
Florida institutions (UF, FSU, UCF, UNF, UM, NOVA)	25%
Out-of-state	3%
Foreign	2%

The table below displays the acceptance ratio of all applicants in the last two years.

2015-2016	2016-2017
Accepted = 65%, Denied = 35%	Accepted = 72%, Denied = 28%

iv. Enrollment Information:

The headcount total enrollment information for graduate students in the program is shown in Table 1 (below).

The data below indicates that the number of MS Biomedical Science graduate students has remained close to the same over the last two years at 58 and 53. This corresponds to ~1.2 % of all graduate students in the university in the academic year 2015-2016.

The Headcount Total for graduates' students in the program

Annual Headcount (program CIP: 260102)	2013-2014	2014-2015	2015-2016	University Total 2015-2016
MS Biomedical Science	68	58	53	**4,474**

The table below displays billable semester credits hours generated by the program in the last five years.

Grad Level 1 MS Biomedical Semester credit hours (SCH) taken by students per Academic Year

Academic Year	Count
2011-2012	750
2012-2013	921
2013-2014	863
2014-2015	897
2015-2016	907

The table below is an estimate of the 5-year tuition revenue obtained by FAU MS Biomedical Science program. Listed are the direct revenues obtained by MS Biomedical Science students and other students taking MS Biomedical Science courses.

5-year tuition revenue report

	2011-2012	2012-2013	2013-2014	2014-2015	2015-2016	Total 5 year summary
MS Biomedical Science Students	$475,879.14	$564,929.49	$520,551.09	$473,472.90	$432,395.85	$2,467,228.47
Undergraduate DIS	$12,077.40	$9,661.92	$17,512.23	$18,116.10	$19,927.71	$77,295.36
Other Graduate Students	$26,627.04	$26,627.04	$26,627.04	$26,627.04	$26,627.04	$133,135.20
Non-Degree Seeking	$22,189.20	$22,189.20	$22,189.20	$22,189.20	$22,189.20	$110,946.00

v. Average Class Size and Faculty/Student Ratio:

For the 2015-2016 academic year there were 24 graduate faculty in the College of Medicine teaching graduate courses in the program out of 46 total graduate faculty eligible to train students in research thesis or directed independent study in the college of medicine. Using the 24 faculty engaged in classroom teaching alone, the student headcount was 53 students to 24 faculty resulting in 1:2 faculty/student ratio.

During the academic years from 2013-2014 to 2015-16, the Biomedical Science department offered an average of 18 graduate lecture/seminar courses with an average enrollment of about 13 students/course.

vi. Quality of Instruction

University-Wide SPOT Scores Summer 2015 compared to MS Biomedical Science SPOT Scores

- For the course as a whole, the Biomedical Science SPOT scores in the excellent rating were 92.73% compared to the University which was 42.80%.
- For the Instructor's overall effectiveness, the Biomedical Science SPOT scores in the excellent rating was 92.50% compared to the University which was 54.42%.

Average ratings for courses in the program were 1.7 (excellent) and 2.0 (very good) on a 5.0-point scale, with 1.0 being the highest on the core assessments of “quality of the course (item 20)” and “instructor overall effectiveness (item 21)”, respectively. Shown below are the SPOT results for items 20 and 21 for the 2014-2015 academic year. These results demonstrate a significant increase in course quality over the previous academic year.

2014-2015 SPOT Results for Item 20 (Course as a whole) and 21 Instructor’s overall effectiveness

SPOT Fall 2014

STUDENT PERCEPTION OF TEACHING

Number of Classes: 6

Number of Respondents: 63

Percentage of Enrolled Students Responding: 51.7%

20. This course as a whole was:

MS Biomedical Science SPOT

	Mean	Percentage of Students Selecting Response					
		Excellent (1)	Very Good (2)	Good (3)	Fair (4)	Poor (5)	No Response
		%	%	%	%	%	%
	1.85	41.77	36.26	17.02	4.95	0.00	N/A

21. Rate the instructor's overall effectiveness in this course:

MS Biomedical Science SPOT

	Mean	Percentage of Students Selecting Response					
		Excellent (1)	Very Good (2)	Good (3)	Fair (4)	Poor (5)	No Response
		%	%	%	%	%	%
	1.77	46.62	37.40	9.84	4.85	1.28	N/A

Spring 2015

STUDENT PERCEPTION OF TEACHING

Number of Classes: 8

Number of Respondents: 72

Percentage of Enrolled Students Responding: 71.2%

20. This course as a whole was:

MS Biomedical Science SPOT

	Mean	Percentage of Students Selecting Response					
		Excellent (1)	Very Good (2)	Good (3)	Fair (4)	Poor (5)	No Response
		%	%	%	%	%	%
	1.51	61.97	25.67	11.63	0.74	0.00	0.00

21. Rate the instructor's overall effectiveness in this course:

MS Biomedical Science SPOT

	Mean	Percentage of Students Selecting Response					
		Excellent (1)	Very Good (2)	Good (3)	Fair (4)	Poor (5)	No Response
		%	%	%	%	%	%
	1.40	68.93	23.22	7.12	0.74	0.00	0.00

Summer 2015

STUDENT PERCEPTION OF TEACHING

Number of Classes: 6

Number of Respondents: 44

Percentage of Enrolled Students Responding: 88.8%

20. This course as a whole was:

MS Biomedical Science SPOT

	Mean	Percentage of Students Selecting Response					
		Excellent (1)	Very Good (2)	Good (3)	Fair (4)	Poor (5)	No Response
		%	%	%	%	%	%
	1.08	92.73	3.33	2.08	0.00	0.00	1.85

21. Rate the instructor's overall effectiveness in this course:

MS Biomedical Science SPOT

	Mean	Percentage of Students Selecting Response					
		Excellent (1)	Very Good (2)	Good (3)	Fair (4)	Poor (5)	No Response
		%	%	%	%	%	%
	1.08	92.50	7.50	0.00	0.00	0.00	0.00

University SPOT

20. This course as a whole was:

	Mean	Percentage of Students Selecting Response					
		Excellent (1)	Very Good (2)	Good (3)	Fair (4)	Poor (5)	No Response
		%	%	%	%	%	%
	2.00	42.80	28.18	17.28	7.27	3.71	0.77

21. Rate the instructor's overall effectiveness in this course:

University SPOT

	Mean	Percentage of Students Selecting Response					
		Excellent (1)	Very Good (2)	Good (3)	Fair (4)	Poor (5)	No Response
		%	%	%	%	%	%
	1.81	54.42	22.62	12.67	6.06	3.52	0.70

vii. Core Curriculum:

All Biomedical Science graduate students are required to take four core courses (12 credits) that address the state mandated SLOs, provide a common learning experience for students in the program and provide students with the core skills and knowledge requirement needed to attain competence in the area of Biomedical Science. These courses are:

Biomedical Writing	PCB 6933	3
Human Genetics	PCB 6665	3
Biomedical Data & Informatics	BSC 6459	3
Advanced Molecular & Cell Biology	PCB 5532	3

A Description of these courses is provided below:

Biomedical Writing (PCB 6933) 3 credits - Ewa Wojcikiewicz, Ph.D.
Prerequisite: Permission of instructor
Biomedical Science is a broad field comprising many applied sciences geared toward the development of new approaches in healthcare or public health. This course is designed for graduate students headed toward a broad array of post-graduate vocational opportunities to enhance their writing, professional and organizational skills in order to excel in areas ranging from professional education, health care and scientific fields through business. Students will be instructed in basic writing skills, argument formation, debate and presentation skills.
Taught by Ewa Wojcikiewicz, Ph.D., Assistant Professor of Biomedical Science,
Degree: Physiology and Biophysics, University of Miami Miller School of Medicine, Miami, FL, 2004.
Research: Biophysical mechanisms of inflammatory leukocyte recruitment.

Human Genetics (PCB 6665) 3 credits
Prerequisite: Permission of instructor
Designed to provide students with a functional understanding of the field of human genetics as it applies to progressive research and medicine. Emphasizes the integrated understanding and application of genetic analysis, diagnosis and mechanisms in human disease.
Taught by Marc Kantorow, Ph.D. Professor of Biomedical Science, Assistant Dean of Graduate Programs
Degree: Ph.D., Genetics, The George Washington University, Washington, D.C. 1991
Research: The molecular genetics of eye diseases including age-related human cataract and age-related macular degeneration

Biomedical Data & Informatics (BSC 6459) 3 credits
Prerequisite: Permission of instructor
This course teaches essential concepts and methodology for biomedical data acquisition and analysis with an emphasis on the analysis of massive data. The course sets up the foundation for students' careers in biomedical informatics in a wide range of fields including biomedical academia, pharmaceutical and biotechnology industries.
Taught by Zhongwei Li, Ph.D. Professor of Biomedical Science
Degree: Ph.D., Microbiology, Chinese Academy of Sciences 1989
Research: RNA metabolism, RNA therapy, Bacterial Genomics, Regulation of gene expression by natural products

Advanced Molecular & Cell Biology (PCB 5532) 3 credits
Prerequisites: CHM 2210, PCB 4023, BCH 3033 and permission of instructor
Course is designed to provide students with a basic background and advanced topics in cell and molecular biology. Emphasis is placed on human physiology and disease.
Taught by Andrew Oleinikov, Ph.D. Associate Professor of Biomedical Science
Degree: Ph.D. in Biology, Moscow State University, Moscow, Russia, 1989
Research: Malaria studies with emphasis on mechanisms of sequestration of infected erythrocytes, protective immune response and vaccine development, anti-adhesion drugs

viii. Electives:
The M.S Biomedical Science program offers 19 elective courses in a wide-range biomedical science disciplines. Non-thesis students are required to take 18 total credits of electives (6 courses) while thesis students are required to take 9 elective credits (3 courses).

COLLEGE OF MEDICINE BIOMEDICAL SCIENCE ELECTIVE GRADUATE COURSES

Integrated Morphology 1 (BMS 6102C) 4 credits
Prerequisite: Permission of instructor
This course involves the developmental, microscopic, and gross anatomical features of the organs located in the thorax and abdomen of the human. A laboratory includes a cadaveric dissection experience and examination of tissue samples using virtual microscopy.
Taught by Rainald Schmidt-Kastner, M.D. Associate Professor of Integrated Medical Science
Degree: 1984: MD-Doktor der Medizin (Dr.med.) by thesis (summa cum laude), Medical Faculty, University of Düsseldorf, Düsseldorf, Germany
Research: Brain ischemia and hypoxia; selective vulnerability of the hippocampus; status epilepticus; retinal ischemia; optic nerve atrophy; gene x hypoxia interactions in neurodevelopmental disorders and neurodegeneration; teaching tools in medical neuroscience

Integrated Morphology 2 (BMS 6104C) 4 credits
Prerequisite: Permission of instructor
This course involves the gross anatomical features of the structures of the back, limbs, head, and neck of the human. A laboratory includes a cadaveric dissection experience.
Taught by Darin P. Trelka, M.D., Ph.D. Assistant Professor of Integrated Medical Science
Degree: 1999: Ph.D. Anatomy, Pathology, Cell Biology, Thomas Jefferson University, Philadelphia, PA; 2002: M.D. MCP-Hahnemann University Philadelphia, PA
Research: Consist of gross- and microscopic anatomy as well as assisting in the pathology laboratory curriculum and facilitating both PBL and IQ group learning activities.

Autonomic Function and Diseases (BMS 6523) 3 credits
Prerequisite: Permission of instructor
Course covers both the physiological and clinical study of the autonomic nervous system (ANS) emphasizing the neural circuitry aspects of systemic regulation. Topics are introduced in lectures and followed up by recent journal articles.
Taught by Rui Tao, Ph.D. Associate Professor of Biomedical Science
Degree: Ph.D., Physiology and Neurobiology, Rutgers University, NJ, 2000
Research: Pharmacology of selective serotonin reuptake inhibitors in midbrain raphe and forebrain

Fundamentals of General Pathology (BMS 6601) 3 credits
Covers the basic pathophysiology of mechanisms of disease in medicine and incorporates gross pathologic, microscopic and radiologic material to assist in understanding fundamental disease.
Taught by Morton Levitt, M.D. Professor of Clinical Biomedical Science
Degree: 1972: M.D., Duke University, Durham, North Carolina
Research: Mechanisms of carcinogenesis

Brain Diseases: Mechanism and Therapy (BMS 6736) 3 credits *
Prerequisite: Permission of instructor
Discussion of the molecular and cellular basis of brain diseases and of the current status of therapeutic intervention for those diseases.
Taught by Jang Yen Wu, Ph.D. Professor of Biomedical Science
Degree: Ph.D., Biochemistry, University of California, San Francisco Medical Center, 1968
Research: Neuroscience, Neurotransmitters and neurological disorders

Macromolecules and Human Disease (GMS 6301) 3 credits
Prerequisite: BCH 3033 or PCB 4023 or equivalent
Explores structure and function of biological macromolecules with emphasis on DNA, RNA and proteins.
Taught by Keith Brew, Ph.D. Professor of Biomedical Science
Degree: Ph.D., University of London, Courtauld Inst. of Biochemistry, London, U.K., 1966
Research: Protein engineering, with an emphasis on regulatory protein-protein interactions and the role of protein dynamics in such interactions

Molecular Basis of Disease and Therapy (GMS 6302) 3 credits
Prerequisites: BCH 4035 and (PCB 4023 or PCB 4522)
Explores the molecular basis of selected viral pathogens, genetic diseases and cancer through lectures and presentations by faculty in the College of Science and Biomedical Science, Scripps Florida and private industry representatives. Discusses novel technologies aimed at developing therapeutics together with the activity of modern biotechnology in drug development.
Taught by Massimo Caputi, Ph.D. Professor of Biomedical Science
Degree: Ph.D., Molecular Genetics, International School for Advanced Studies, Trieste Italy 1996
Research: mRNA processing, mRNA splicing regulation, HIV-1 replication, Bcl apoptotic gene family regulation

Host Defense and Inflammation (MCB 6208) 3 credits
Prerequisite: PCB 4233 or equivalent with a minimum grade of "B-"
Course covers the immunology emphasizing mechanisms of host defense and inflammation in chronic inflammatory diseases. Mechanisms emphasized are roles of macrophages that are heterogeneous and diverse populations regulating host defense and inflammation. Mycobacterial infections and allergic asthma are presented as disease models of chronic inflammatory diseases.
Taught by Yoshimi Shibata, Ph.D. Professor of Biomedical Science
Degree: Ph.D. Department of Bacteriology, Tohoku University School of Medicine, Bacteriology, Sendai, Japan 1982
Research: Mechanisms regulating ontogenic and functional heterogeneity of macrophage populations.

Advanced Cell Physiology (PCB 6207) 3 credits
Prerequisite: Permission of instructor
Course describes in-depth membrane physiology, intracellular signaling pathways, and cellular function, with an emphasis on neurons and human muscle cells (skeletal, smooth, and cardiac muscle cells).
Taught by Wen Shen, Ph.D. Associate Professor of Biomedical Science
Degree: Ph.D., Physiology and Biophysics, State University of New York at Buffalo, 1998.
Research: Electrophysiology of channels and receptors

Molecular Basis of Human Cancer (PCB 6235) 3 credits
Prerequisites: Graduate standing and PCB 4023 or BCH 3033 or PCB 6207 with minimum grade of "B-"
Course covers current concepts and knowledge of cancer, exploring the molecular and cellular mechanisms underlying cancer progression with an aim to understand the processes of tumorigenesis.
Taught by Michael Lu, Ph.D. Professor of Biomedical Science
Degree: Ph.D., Molecular and Cellular Biology, University of Massachusetts, Amherst., 1988
Research: Hormone-regulated signal transduction

Problem-Based Immunology (PCB 6238) 3 credits
Prerequisites: Graduate standing and PCB 4233 or equivalent with a minimum grade of "B-"
Course provides an up-to-date understanding of the basic science of immunology and how that science applies to the realities of patient care. The fundamental mechanisms of immunity are illustrated by cases of genetic defects in the immune system, immune complex diseases, immune mediated hypersensitivity reactions and autoimmune and alloimmune diseases.
Taught by Mahyar Nouri-Shirazi, D.V.M., Ph.D. Professor of Integrated Medical Science
Degree: 1992: D.V.M., Tottori University, School of Veterinary Medicine, Japan; 1996: Ph.D., Immunology, Chiba University, School of Medicine, Japan
Research: Dendritic cells (DCs)-based immunomodulation for treatment of cancer and allograft rejection

Tumor Immunology (PCB 6239) 3 credits
Prerequisites: Graduate standing and PCB 4233 or equivalent with a minimum grade of "B-"
Explores the role of the immune system in cancer and the implications for the host. The effect of the tumor-host interactions on the developing neoplasm are studied by considering related topics, such as angiogenesis, MMPs, chemokines, and metastasis. Additionally, the course explores the role of the immune system in defense against the tumors and the mechanism by which cancer cells escape the surveillance system.
Taught by Vijaya Iragavrapu –Charyulu, Ph.D. Associate Professor of Biomedical Science
Degree: PhD, Microbiology and Immunology, University of Miami School of Medicine, Miami, Florida, 1980
Research: Role of Semaphorins (axonal guidance molecules) in breast cancer

Molecular Biology of the Cardiovascular System and Cardiac Disease (PCB 6705) 3 credits*
Prerequisites: BCH 3034, PCB 4023, or permission of instructor
Examination of the molecular biology of cellular function focused on tissue adaptation in cardiovascular disease. Investigation of survival responses to cellular stress in atherosclerosis, cardiac hypertrophy, myocardial ischemia and hypertension.
Taught by Howard Prentice, Ph.D. Associate Professor of Biomedical Science
Degree: Ph.D., Biochemistry, University of London, England, 1987
Research: Determination of regulatory characteristics of specific gene/promoter elements in normal and disease-stressed myocardial tissue with particular attention to the skeletal alpha actin and myosin heavy chain gene promoters and to hybrid hypoxia responsive/tissue specific promoters. Incorporation of hypoxia responsive promoters into regulated gene therapy vectors for ischaemia heart disease.

Adult Neurogenesis (PCB 6848) 3 credits
Prerequisites: Graduate standing and PSB 6037 or PSB 6345 or equivalent
The background of stem cells and neuroscience is covered followed by several aspects of neurogenesis, including where neurogenesis happens in the brain, how it happens, why it happens, and, more importantly, how it might help the brain heal itself.
Taught by Jianning Wei, Ph.D. Associate Professor of Biomedical Science
Degree: Ph.D., Biochemistry, University of Kansas, Lawrence, KS, USA, 2003
Research: To investigate protein-protein interaction using a combination of biochemical methods and mass spectrometry.

Physiology of the Heart (PCB 6885) 3 credits
Prerequisites: BCH 3034, PCB 4023, or permission of instructor
Course emphasizes the relationship between the biochemical properties of the individual constituents of the heart cell (myocardium), the biophysics of cardiac muscle function, and the performance of the intact heart. The course format will involve lectures, journal club presentations, round table discussions, invited speakers as well as special projects
Taught by Huang Xupei, Ph.D. Professor of Biomedical Science
Degree: Ph.D., Biochemistry, University of Paris XII, France, 1992
Research: Intracellular signal pathways, protein phosphorylation and cellular function

Clinical Microbiology (BMS 6303) 3 credits
Prerequisite: MCB 3020
Students learn the relevant facts and principles underlying bacteria, parasites, pathogenicity and host resistance. Armed with this fundamental information, students will then be capable of understanding and utilizing contemporary modes of treatment and prevention.
Taught by Gary J. Rose, M.D. Associate Professor of Surgery
Degree: 1977: M.D., George Washington University School of Medicine
Published: Rose, G.J., New Directions in Laser Therapy, Clinics in Plastic Surgery, Vol.29 53-79, 2002.; Rose, G.J., Male Body Contouring and Gynecomastia Surgery , Operative Techniques in Plastic and Reconstructive Surgery 8:67-83, 2002.

Developmental Neurobiology (PSB 6515) 3 credits
Prerequisites: PSY 1012 and PSB 3002
In-depth coverage of the principles and recent advances in the development of the brain and nervous system, including nerve cell migration, axon outgrowth, specificity, plasticity, neurotrophism, nerve cell death, and the influence of experience on the nervous system.
Taught by Kathleen Guthrie, Ph.D. Associate Professor of Biomedical Science
Degree: Ph.D., University of California, Irvine, 1989
Research: Neurotrophic interactions in the brain during development and regeneration; Axon growth, targeting and sensory mapping

Neurobiology of Addiction (PCB 5844) 3 credits
Prerequisite: Permission of instructor
This course provides graduate students with fundamental information on molecular, cellular and neurocircuitry systems in the brain that are responsible for drug addiction. Common neurobiological elements are emphasized that provide novel insights into how the brain mediates the acute rewarding effects of drugs of abuse and how it changes during the transition from initial drug use to compulsive drug use and addiction.
Taught by Ceylan Isgor, Ph.D. Associate Professor of Biomedical Science
Degree: Ph.D., Animal Learning and Behavior, Indiana University, 1997.
Research: Neuromorphological, behavioral and molecular consequences of chronic, variable stress during peripubertal-juvenile period in rats.

Directed Independent Study (PCB 6905) 1-3 credits
Prerequisite: Permission of instructor and department
Independent research.

Special Topics (PCB 6933) 1-8 credits
Prerequisite: Permission of instructor
Topics of interest to students in Biomedical Science, such as protein misfolding and disease, molecular biology laboratory techniques and clinical microbiology.

Students may also fulfill their elective requirements by taking the following graduate electives taught by other colleges at FAU including:

COLLEGE OF SCIENCE BIOLOGY: ELECTIVE GRADUATE COURSES

Advanced Immunology (PCB 6236) 3 credits
Prerequisite: PCB 4233
A study of the chemical and biological natures of antigens and antibodies: their preparation and reactions in vivo and in vitro, their applications in basic science and therapy, and the immunochemical and experimental methods involved with tagged or free immunologic products. It is a lecture course.

Bioinformatics (BSC 6458C) 4 credits
Prerequisite: Permission of instructor
A practical approach to accessing nucleic/protein databases, management of databases, identification of genes, and electronic expression profiling.

COLLEGE OF SCIENCE PSYCHOLOGY: ELECTIVE GRADUATE COURSES

Biological Vision (PSB 5117) 3 credits
Visual perception is studied through its basis in retinal and cortical neurophysiology, with emphasis on the Fourier domain in early processing and co-operative neural interactions in pattern formation.

Principles of Neuroscience (PSB 6037) 3 credits
A survey of principles of neuroscience as they relate to behavior. Topics include morphology and connectivity of neural cells, biological potentials, gross structure of the central and peripheral nervous system, and sensory, motor, and higher-order integrative functions.

Neuroscience 1 (PSB 6345) 3 credits
A course of in-depth coverage of the principles of neural science, including functional neuroanatomy, sensory processes, higher brain function, and development of the nervous system.

Neuroscience 2 (PSB 6346) 3 credits
A course of in-depth coverage of the principles of neural science, including functional neuroanatomy, sensory processes, higher brain function, and development of the nervous system.

COLLEGE OF SCIENCE COMPLEX SYSTEMS: ELECTIVE GRADUATE COURSES

Cognitive Neuroscience (ISC 5465) 3 credits
An interdisciplinary survey of the neural basis of cognitive functions such as perception, attention, memory, and language.

ix. Degree Requirements:

The M.S. Biomedical Science degree at FAU require at least 30 semester credits beyond the baccalaureate degree. Students must maintain a program GPA of 3.0 as well as a cumulative GPA of 3.0 to remain a student in good standing and meet degree requirements. The following are requirements for the M.S. degrees with Thesis and Non-Thesis options in Biomedical Science.

x. Thesis Option

The writing of a thesis represents the culmination of study and research by a graduate student. Once a student has made the decision to complete a thesis track the student must find a faculty member to serve as their thesis advisor. The next step is for the student and the thesis advisor to discuss and choose a research project and additional faculty members to serve on the committee.

The thesis option for students require them to write a scholarly research paper with the assistance of their thesis advisor. Once the thesis advisor and the student have chosen a research project the student must prepare a proposal of how they are going to approach the research project (methods, literature review, data analysis, hypothesis, etc.). Once the proposal has been approved by the advisor and the committee the student will have the opportunity to work further on their research project to produce results which the student will later defend to the committee. Master's students must confirm additional thesis requirements with their advisers and follow the Graduate College thesis guidelines.

Thirty credits of coursework with the following requirements:

1. Must complete the four core courses (12 credits): Human Genetics, Biomedical Data & Informatics, Advanced Molecular & Cellular Biology, Biomedical Writing
2. The elective courses must be 5000, 6000, or 7000 level courses in biomedical science, biology, complex systems, psychology, or approved cognates.

3. A minimum of 3 Thesis-Related Research credits are required for graduation. Students may take up to 6 Thesis-related research credits to count towards graduation requirements. The Thesis-related research credits must be taken during the first year of study and cannot be counted towards a non-thesis M.S. degree.

4. A minimum of 6 credits of master's thesis are required for graduation. Students may take up to 12 credits of master's thesis.

5. Courses designated as proficiency or remedial may not be used to satisfy the course requirement.

6. Thesis students are required to make a formal research proposal to their committees within their

first year prior to enrollment in Thesis credits (Admission to Thesis Candidacy).

7. Upon completion of the research, Thesis students must make a formal thesis presentation and defense in the semester they plan to graduate.

8. The defense must be completed at least one week before the university's thesis submission deadline.

9. Thesis documents must be submitted to committee members two weeks before the scheduled defense.

Below are some examples of recent thesis titles from students in the program:

Identifying and Characterizing the Immune Cell Populations of Atlantic Bottlenose Dolphins (Tursiops Truncatus) by Brittany Bible *(PI Dr. Mahyar Nouri-Shirazi)*

Mitochondrial regulation pathways in the lens: PINK1/Parkin-AND BNIP3L-Mediated Mechanisms by Kerem Aktan *(PI Dr. Marc Kantorow)*

The effects of Toll-like receptor (TLR) agonists on human nicDC-NK mediated memory/effector T-cell development by Saba Tamjidi *(PI Dr. Mahyar Nouri-Shirazi)*

Recent Awareness and Use of the Great American Smokeout and Variation across Socioeconomic Status, Age and Gender by Joshua Lovelace *(PI Dr. Michelle Pergadia)*

Over-Expression of BDNF Does Not Rescue Sensory Deprivation-Induced Death of Adult-Born Olfactory Granule Cells by Rachel Berger *(PI Dr. Kathleen Guthrie)*

A Study on the Potential Role of Stress Granules and Processing Bodies In Eliminating Oxidatively Damaged RNA By Delaram Pourkalbassi *(PI Dr. Zhongwei Li)*

Peptidomic Analysis and Charactization of the Venom from Conus Purpurascens by Alena Rodriguez

Mechanisms of Placental Dysfunction in Pregnancy Malaria by Jared Lybbert *(PI Dr. Andrew Oleinikov)*

Integrin AVB5-Mediated Removal of Apoptotic Cell Debris by the Eye Lens and Its Inhibition by UV-Light Exposure by Olga Bakina *(PI Dr. Marc Kantorow)*

Chitin Microparticles (CMPs) Induce M1 Macrophage Activation via Intracellular TLR2 Signaling Mechanism by Spring Davis *(PI Dr. Yoshimi Shibata)*

Below are some titles of MS Biomedical Science graduate student titles for Research Day 2017:

The Role of Antioxidant Therapy in Treatment & Prevention of Diabetic Complications by Toni-Kaye McDougall

The HIV-1protein Tat and the cellular splicing/transcri ption factor SRSFI co-regulate a set of cellular genes by Sean Paz

Physical Activity Improves Cognition by Mediating BDNF Levels by Nareka Trewick

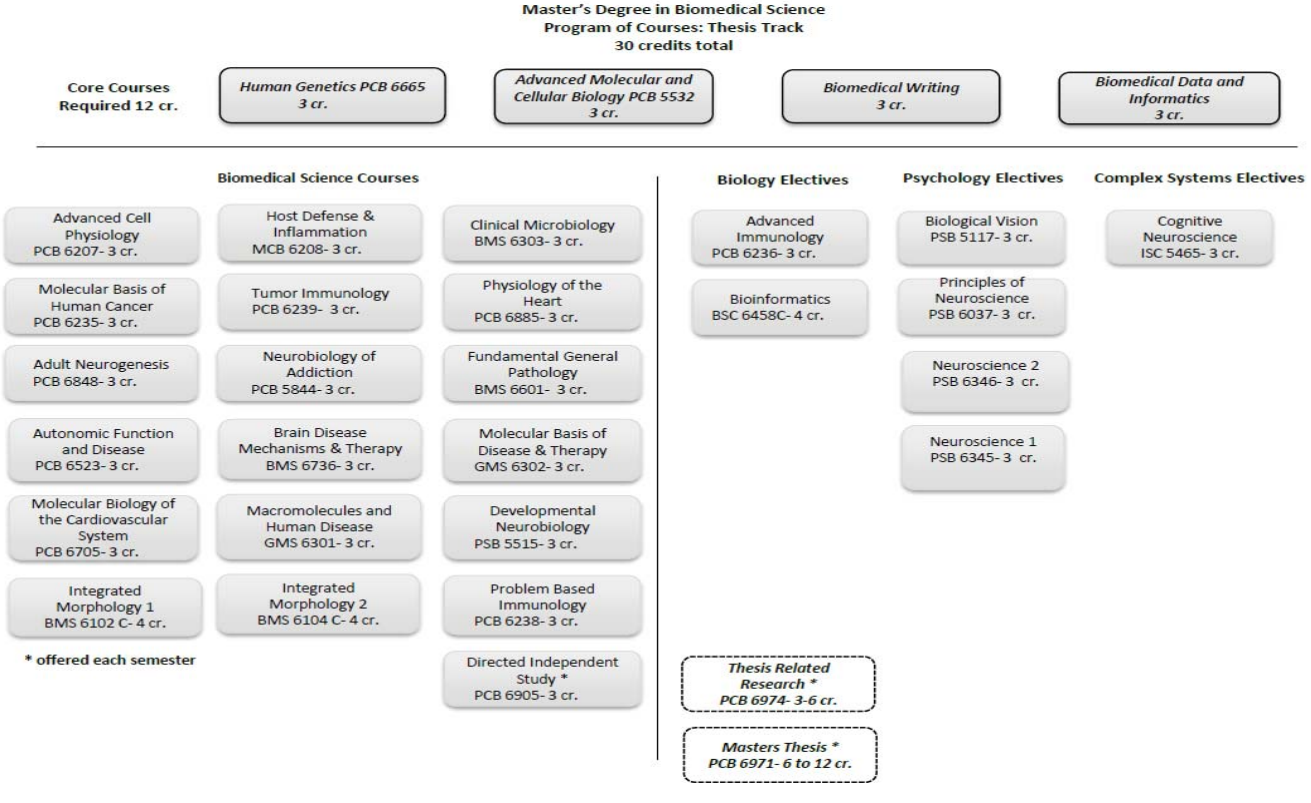
The Effects of MsrA and MsrB in Anoxia Tolerance in Aging Drosophila melanogaster by Nirthieca Suthakaran

G-CSF as a potential therapeutic agent for Alzheimer's disease by Carolyn Coles

Control of mitochondrial and nuclear alphaB functions by phosphorylation and SUMOylation by Angie Posada

A Schematic summaries of thesis and non-thesis programs of study for students in the Biomedical Science MS Program are listed below:

Thesis MS Biomedical Science Program Sheet



xi. Non-Thesis Option

Thirty credits of course work with the following requirements:

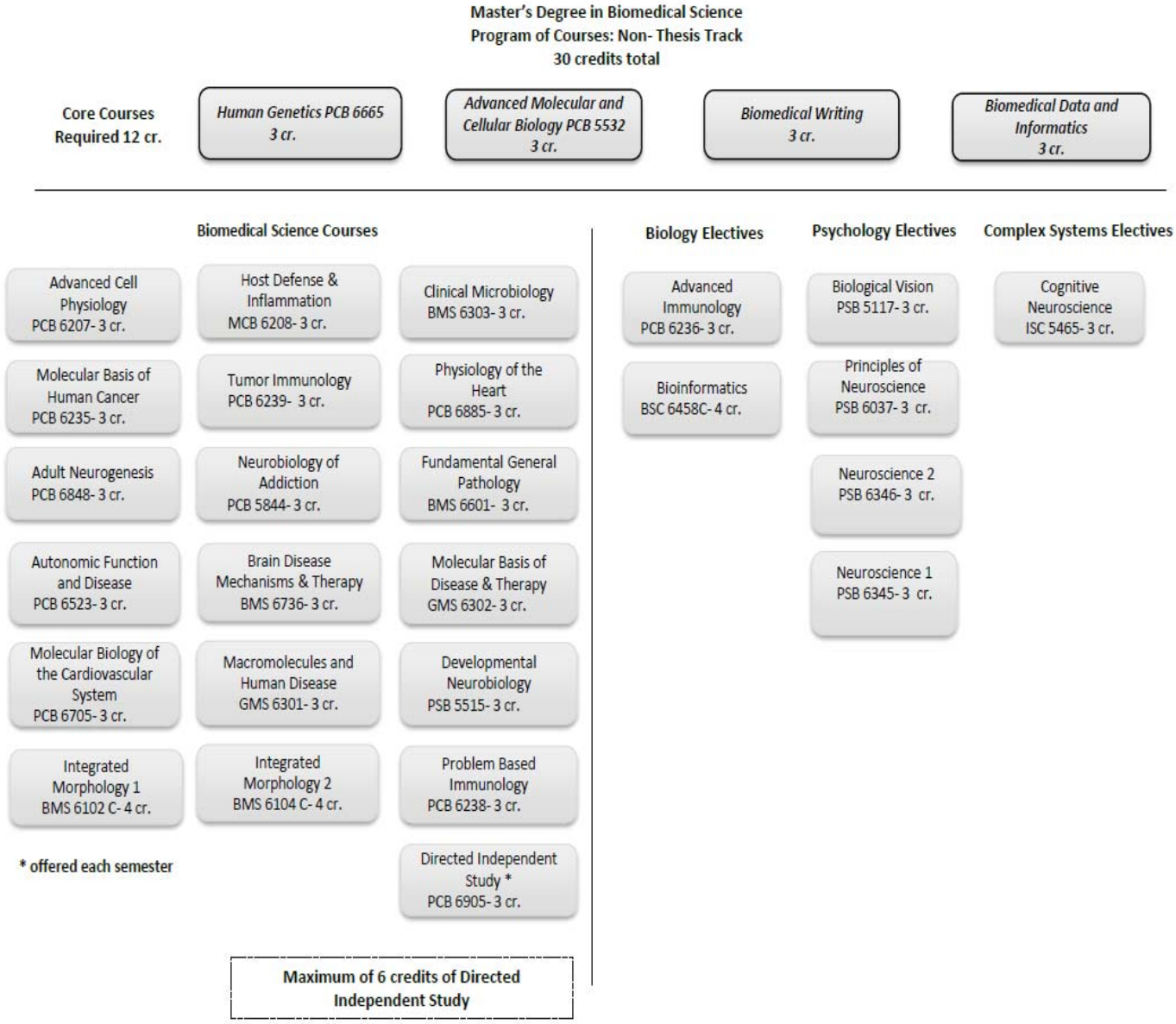
1. Must complete the four core courses (12 credits): Human Genetics, Biomedical Data & Informatics, Advanced Molecular & Cellular Biology, Biomedical Writing

2. The elective courses must be 5000, 6000, or 7000 level courses in biomedical science, biology, complex systems, psychology, or approved cognates.

3. A maximum of 6 DIS credits can count towards the graduation requirements.

4. Courses designated as proficiency or remedial may not be used to satisfy the course requirement.

Non-thesis MS Biomedical Science Program Sheet



xii. Cross-listings

The MS Biomedical Science program offers cross listing of two courses for co-enrollment of both advanced undergraduate and graduate students including Molecular Biology of the Cardiovascular System and Cardiac Disease and Brain Diseases: Mechanism and Therapy. Cross-listed courses have different requirements and learning outcomes for graduate and undergraduate including additional writing assignments, course presentations and self-study requirements for graduate students enrolled in these courses. These courses are denoted with an asterisk in the course descriptions listed above.

xiii. Direct Independent Study

Students are able to receive research experience in the College of Medicine through either volunteering in a research lab or receiving Direct Independent Study credits toward their MS Biomedical Science program. Students will have the opportunity to work closely with faculty members and also receive college credit. Students are able to receive Direct Independent Study credit in many ways:

- Working on research in a laboratory
- Publishing a paper
- Writing a research paper

The majority of students that are working with faculty are being supported in their research through a NIH grant or others grant that supports their research activity.

xiv. Scholarships and Fellowships

For the past 2 years the MS Biomedical Science program has provided up to three summer stipends of up to $5,000 to thesis students to increase opportunities to perform research.

The Graduate College has also provided two Provost Fellowship scholarships ($2,500).

xv. Teaching Assistantships

Graduate students can apply for teaching assistantships in other colleges including the College of Science Departments of Biology and Chemistry. Although, these teaching assistantships are not guaranteed to students in the program, approximately 40% of the students enrolled in the program earn teaching assistantships in these and other departments at FAU. These teaching assistantships provide tuition benefits and up to $18,000/yr. in stipend support. Although a small number of grant-funded research assistantships have been available to students in the program, and a small number of summer stipends for student research are directly available for a limited number of students, a major challenge for the growth of the program is the availability of direct student support.

Other Program Requirements

College of Medicine Distinguished Lecturer Seminar Series- Students are required to attend the Biomedical Science seminar series to expose them to state of the art researchers and topics in Biomedical Sciences and to provide them a core learning experience and a unified scholarly community. There is an average of 7-9 distinguished lecturers' speakers from both internal and external institutions speaking in this series during the academic year.

Fall Retreat – Students attend a social gathering where they have the opportunity to interact, network and receive mentorship advice from faculty.

Spring Research Day- Students have the opportunity to present their thesis or DIS research though a poster and/or talks. Spring Research Day provides these students the opportunity to share

their research with other faculty, students, and peers to establish collaborations and to get advice on their research projects. As an incentive for participation awards are given for the best talk and poster selected through student voting.

xvi. Pedagogy/pedagogical innovations

Pedagogy in the MS Biomedical Science program is continuously developed and enhanced through the interactive review of all course content and syllabi between faculty, the Coordinator of Graduate Programs, The Assistant Dean of Graduate Programs, the Senior Associate Dean of Graduate Programs and the Dean.

Syllabi and learning objectives for each course are updated every year and cooperatively reviewed by the instructor, Department Chair and the Assistant Dean of Graduate Programs to ensure that each course is current and meeting the learning goals of the students.

Over the last four years a significant number of pedagogical innovations have been devised to advance the impact of the program on student learning. These include but are not limited to:

1. Development and Implementation of Capstone Core Courses That Optimize SLO Objectives:

In the last four years, we have developed and implemented as core learning requirements, four required core courses that serve as remediation and capstone courses for students in the program. These include: Biomedical Writing, Human Genetics, Biomedical Data & Informatics and Advanced Molecular and Cellular Biology

These courses were developed after careful review of the skills and backgrounds of students entering the program by the Dean and a Task Force Committee appointed by the Dean assigned to identify deficiencies in the skills and knowledge of incoming students and make recommendations to provide increased student performance in the identified areas and meet state mandated SLOs. Based on the grades, GRE verbal and writing scores and skills demonstrated by incoming students, it was identified that incoming students were deficient in communication and writing skills. To address this deficiency, a Biomedical Writing Course was developed to provide students with increased writing and communication skills through the writing of research papers and the preparation of scientific presentations.

Deficiencies were also identified in student analytical and math skills and since big data analysis and bioinformatics are emerging areas in the biomedical science field, a second core course was developed in Bioinformatics and Data Analysis. This course gives students competency in math and data analysis and provides them with proficiency in understanding bioinformatics and large scale data research.

Finally, since the fields of Genetics and Cell and Molecular Biology are central to every area of modern biomedical science two additional core courses were developed for these areas to ensure that all students have common core knowledge and mastery of these key areas.

2. Development of New Elective Courses:

In order to continuously improve the impact of the program on the learning and success of our students, new courses are continuously being developed. This year alone, five new courses representing state of the art and emerging areas in biomedical science have been developed including:

Fundamental Topics of Human Health
Translational Applications in Human Disease
Genomics and Precision Medicine
Biomedical Science Core Technologies Laboratory
Pharmacology

3. Distinguished Lecturer Seminar Series: Students are required to attend the Biomedical Science seminar series to expose them to state of the art researchers and topics in Biomedical Sciences and to provide them a core learning experience and a unified scholarly community. There is an average of 7-9 distinguished lecturers' speakers from both internal and external institutions speaking in this series during the academic year.

4. Research day: Students have the opportunity to present their thesis or DIS research though a poster and/or talks. Spring Research Day provides these students the opportunity to share their research with other faculty, students, and peers to establish collaborations and to get advice on their research projects. As an incentive for participation awards are given for the best talk and poster selected through student voting.

xvii. Comparison to Peer Programs

The MS Biomedical Program is unique among peer institutions in the state of Florida since it is the only Biomedical Science MS program in the State of Florida that offers thesis and non-thesis tracks that combines coursework and research opportunities to prepare students for a wide-range of post-graduate education and career options in the biomedical sciences.

- Nova Southeastern University in Davie, FL offers a specific pre-professional MS Biomedical Science program designed to specifically prepare students for entrance into their Dental and Osteopathic Medicine programs.

- University of Central Florida MS Biomedical Science offers only a non-thesis track program without research opportunities.

- Florida State University offers a PhD in Biomedical Science but only a MS Biomedical Science Engineering degree.

- University of Florida offers a PhD of Biomedical Science but only offers an MS Biomedical Engineering degree.

- University of South Florida offers a Master of Science in Medical Sciences but offers no specific degree in Biomedical Science.

xviii. Scope of institutional contributions

All Biomedical Science courses taught by our faculty attract a large number of graduate students from other undergraduate and graduate programs at FAU including Anthropology, Biology, Experimental Psychology, Integrative Biology, Integrative Biology Neuroscience, and Biomedical Engineering (COE).

- The Biomedical MS program is the 11th highest contributor of graduate degrees among 66 master programs at FAU.

- The Biomedical science program is a central part of the educational and research mission of the college of medicine.
- The Biomedical MS program provides a unique learning experience and educational background for students who go on to studies in the COM medical program, the Integrative Biology PhD program (including the new PHD Biomedical Science track), and other program across the university.
- The Biomedical MS program also provides an opportunity for FAU faculty to have outstanding research students work in their laboratories and their research programs.
- The Biomedical MS students contribute to the teaching mission of FAU by serving as teaching assistants.
- The Biomedical MS students form the foundation for research activities in the college including DNA day, and College of Medicine Research Day.
- Finally, The Biomedical MS program is central to the College of Medicine Distinguished Lecturer Seminar Series that attracts across FAU and at Scripps, Max Planck, and other partner institutions.

xix. Student Profile

The majority of MS Biomedical Science students come directly from FAU but many also come from other Florida universities including Florida Atlantic University, Nova Southeastern University, Florida International University, Florida State University, and University of Central Florida. The table below shows the percent of students in the program from FAU and other institutions:

Applicants Fall 2016-Fall 2017 University Attended

FAU	70%
Other Florida Universities (UF, FSU, UCF, UNF, UM, NOVA)	25%
Out-of-state	3%
Foreign	2%

Background and Ethnicity.

The MS Biomedical Science program is a highly diverse population with 47% of students reporting non-white backgrounds. This diversity is increasing. For Example, in 2013-2014 the Black or African American ethnicity percentage in the program was 13.2% and but has increased to 17% in the 2015-2016 academic year. In 2013-2014 the Hispanic or Latino ethnicity percentage in the program was 10.3% but has increased to 24.5% in the 2015-2016 academic year. Numbers for the 2013-2014 school year are shown below:

2013-2014 MS Biomedical Science Program Race/Ethnicity Count

Academic Year	Race/Ethnicity	Count	% of Subtotal
2013-2014	Asian	10	14.7%
2013-2014	Black or African American	9	13.2%
2013-2014	Hispanic or Latino	7	10.3%
2013-2014	Nonresident alien	3	4.4%
2013-2014	Race and ethnicity unknown	2	2.9%
2013-2014	Two or more races	1	1.5%
2013-2014	White	36	52.9%
2013-2014	**Total**	**68**	**100%**

2014-2015 MS Biomedical Science Program Race/Ethnicity Count

Academic Year	Race/Ethnicity	Count	% of Subtotal
2014-2015	Asian	6	10.3%
2014-2015	Black or African American	5	8.6%
2014-2015	Hispanic or Latino	10	17.2%
2014-2015	Nonresident alien	4	6.9%
2014-2015	Two or more races	1	1.7%
2014-2015	White	32	55.2%
2014-2015	**Total**	**58**	**100%**

2015-2016 MS Biomedical Science Program Race/Ethnicity Count

Academic Year	Race/Ethnicity	Count	% of Subtotal
2015-2016	Asian	7	13.2%
2015-2016	Black or African American	9	17.0%
2015-2016	Hispanic or Latino	13	24.5%
2015-2016	Nonresident alien	3	5.7%
2015-2016	Two or more races	4	7.5%
2015-2016	White	17	32.1%
2015-2016	**Total**	**53**	**100%**

xx. Advising Procedures:

Biomedical MS Graduate student advising is centralized in the Charles E. Schmidt College of Medicine (COM) Office of Graduate Programs located on the second floor of the College of Medicine main building. Both the Assistant Dean of Graduate Programs and the Coordinator of Graduate Programs directly advise students on at least an annual basis and an open-door advising policy is in place.

There are two tiers of advising. Student programs of study are developed before matriculation and reviewed again within the first month of entering the program. In addition, all students meet with the Coordinator of Graduate Programs and the Dean of Graduate Programs, usually within the first semester, to provide not only course advising but career advising and success monitoring. Thesis-students in the program are also advised by Coordinator of Graduate Programs and the Dean of Graduate Programs in the selection of thesis research opportunities. Following these initial opportunities students are encourage to meet with the Coordinator and the Assistant Dean of Graduate Programs on at least a yearly basis where their progress is monitored and their programs of study adjusted according to their goals.

i. Student Placement Profile:

Our students have diverse career objectives. Although the majority seek entrance into medical school or other professional programs, many seek other career opportunities ranging from PhD studies to direct employment opportunities in education, industry and other areas.

STUDENT TRACKING

In the three years we have been tracking students which is done by advising. Based on this, the percentage of students that want to go to medical school entering the program is about 65% and 35% apply to other programs.

Medical School	22
Pharmacy School	1
Dentistry School	2
Physician Assistant School	1
Industry	1
PhD Program	4
Post-Doctoral	1
Veterinary School	1
Fellowship Program	1

The table above is an estimate of post-graduation choices polled from available 2014-2017 graduates of the program.

Examples of Biomedical Science Graduates Students Post-Graduation Choices:

Academics/Federal agencies/Industry: FAU Medical School, Physician Assistant School at Nova Southeastern, Post-Doctoral Fellowship at National Institutes of Health, University of Illinois-Chicago MSTP, Wayne State University Medical School, University of Florida Dentistry School, Ph.D. at Helmholtz Zentrum in Munich, Germany, M.D. program at St. George's University in Grenada, Nova Medical School, FIU Medical School, Howard University College of Medicine, VCOM South Carolina, and Modernizing Medicine.

Graduates of the MS Biomedical Science Program and where they are now

ii. Retention Rates:

Tables below illustrate the MS Biomedical Science retention rates for full-time biomedical science master students. Our current program retention rate (almost 100%) is higher than the university-wide retention rate (87.6%) and increased significantly over the last years from a low of 78.9% in 2011. Below is a table of the retention rates for MS Biomedical Science students:

New Fulltime MS Biomedical Science Students 1 Year Retention

Entering Cohort	New Master Students	1 Yr Retention
2011-2012	19	78.9%
2012-2013	32	90.6%
2013-2014	23	91.3%
2014-2015	16	100.0%
2015-2016	10	100.0%

University Wide Fulltime New Master Students 1 Yr Retention

Entering Cohort	New Master Students	1 Yr Retention
2011-2012	739	85.9%
2012-2013	695	84.7%
2013-2014	716	86.0%
2014-2015	767	88.4%
2015-2016	800	87.6%

iii. Graduation Rates:

Tables below illustrate the MS Biomedical Science graduation rates for new, full-time, and part-time students. MS Biomedical Science program graduation rates are higher relative to university wide graduation rates. For example, our new full-time MS Biomedical Science students in the 2013-2014 2nd year cohort had a 87% graduation rate that is almost double the university graduation rate of 42.7%.

Overall MS Biomedical Science 2 & 3 Yr Grad Rates

Entering Cohort	New Master Students	2 Yr Grad Rate	3 Yr Grad Rate
2011-2012	23	82.6%	87.0%
2012-2013	40	80.0%	87.5%
2013-2014	27	85.2%	88.9%

Fulltime MS Biomedical Science 2 & 3 Yr Grad Rates

Entering Cohort	New Master Students	2 Yr Grad Rate	3 Yr Grad Rate
2011-2012	19	84.2%	84.2%
2012-2013	32	78.1%	84.4%
2013-2014	23	87.0%	91.3%

Part-time MS Biomedical Science 2 & 3 Yr Grad Rates

Entering Cohort	New Master Students	2 Yr Grad Rate	3 Yr Grad Rate
2011-2012	4	75.0%	100.0%
2012-2013	8	87.5%	100.0%
2013-2014	4	75.0%	75.0%

Tables below display university wide graduation rates for overall master students that are new, full-time, and part-time.

Overall University Wide Masters 2 & 3 Yr Grad Rates

Entering Cohort	New Master Students	2 Yr Grad Rate	3 Yr Grad Rate
2011-2012	1797	40.8%	62.8%
2012-2013	1793	37.8%	62.3%
2013-2014	1711	42.7%	65.3%

Fulltime University Wide Masters 2 & 3 Yr Grad Rates

Entering Cohort	New Master Students	2 Yr Grad Rate	3 Yr Grad Rate
2011-2012	739	57.1%	75.0%
2012-2013	695	56.0%	73.2%
2013-2014	716	61.2%	77.1%

Part-time University Wide Masters 2 & 3 Yr Grad Rates

Entering Cohort	New Master Students	2 Yr Grad Rate	3 Yr Grad Rate
2011-2012	1058	29.5%	54.3%
2012-2013	1098	26.3%	55.4%
2013-2014	995	29.4%	56.9%

Total number of Graduates produced relative to the rest of the university

The data below shows a 5 year of the number of Masters Degrees awarded at FAU. Our program graduated 139 students from 2010-2015 placing 11th out of 66 master programs at the university.

5 Year Summary of Degrees Awarded by FAU				Total Degrees Awarded for 5 year period		
					by Degree Level	
2010-2015	as of 6/2/2015	Threshold Criteria less than	30	20	10	20
CIP CODE	COLLEGE	Program Classification	Baccalaureate Degree	Masters Degree	Doctoral Degree	Other
030104	C.E. Schmidt Coll of Science	Environmental Science		43		
040201	Coll Design and Social Inquiry	Architecture	209			
040301	Coll Design and Social Inquiry	Urban & Regional Planning	197	65		
040401	Coll Design and Social Inquiry	Environmental Design/Architect	67			
050207	D. F. Schmidt Col Arts Letters	Women's Studies		17		
090101	D. F. Schmidt Col Arts Letters	Communication (Mass)	733	17		
090199	D. F. Schmidt Col Arts Letters	Communications and Media Studi		32		
090702	D. F. Schmidt Col Arts Letters	Multimedia Studies	549	3		
110101	Coll Engineering Computer Sci	Computer/Info Science, General	386	141	12	
	College of Business	Computer/Info Science, General	1			
110103	Coll Engineering Computer Sci	Information Technology		14		
130101	College of Education	Education, General	197	7		
130301	College of Education	Curriculum & Instruction		149	35	8
130401	College of Education	Ed. Admin/Leadership, General		377	75	97
130901	College of Education	Social Foundations of Ed		79		
131001	College of Education	Special Ed, General	116	38	10	
131101	College of Education	Counselor Ed./Student Counseli		176	21	27
131202	College of Education	Elementary Teacher Ed	1632	86		
131302	D. F. Schmidt Col Arts Letters	Art Teacher Ed.		1		
131305	College of Education	English Teacher Ed.	75			
131311	C.E. Schmidt Coll of Science	Mathematics Teacher Ed.		23		
	College of Education	Mathematics Teacher Ed.	22			
131312	College of Education	Music Teacher Ed.	25			
131315	College of Education	Reading Teacher Ed.		110		
131316	College of Education	Science Teacher Ed.	27			
131317	College of Education	Social Science Teacher Ed.	94			
131399	College of Education	Tchr Ed., Spcfc Academic & Voc		38		
131401	College of Education	Teaching English As A Second L		32		
140501	Coll Engineering Computer Sci	Biomedical Engineering		28		
140801	Coll Engineering Computer Sci	Civil Engineering	253	54		
140901	Coll Engineering Computer Sci	Computer Engineering	136	56	17	
141001	Coll Engineering Computer Sci	Electrical, Electronics Engin.	200	49	17	
141901	Coll Engineering Computer Sci	Mechanical Engineering	230	42	5	
142401	Coll Engineering Computer Sci	Coastal & Ocean Engineering	124	93	12	
143801	Coll Engineering Computer Sci	Surveying Engineering	15			
151202	Coll Engineering Computer Sci	Information Systems Technology	30			
160102	D. F. Schmidt Col Arts Letters	Linguistics	93	51		
160501	D. F. Schmidt Col Arts Letters	German	1			
160901	D. F. Schmidt Col Arts Letters	French	37	9		
160905	D. F. Schmidt Col Arts Letters	Spanish	46	28		
230101	D. F. Schmidt Col Arts Letters	English, General	640	71		
231302	D. F. Schmidt Col Arts Letters	Creative Writing		53		
240101	D. F. Schmidt Col Arts Letters	Liberal Arts & Sciences	408	8		
240199	H.L. Wilkes Honors College	New College/Honors College	314			
260101	C.E. Schmidt Coll of Science	Biology	1658	103	46	
260102	C.E. Schmidt Coll Med	Biomedical Sciences		139		
261201	C.E. Schmidt Coll of Science	Biotechnology		11		
270101	C.E. Schmidt Coll of Science	Mathematics, General	153	71	27	
270301	C.E. Schmidt Coll of Science	Applied Math/Math Sciences		8		
300000	C.E. Schmidt Coll of Science	Multi / Interdisciplinary Stud	5			
	Coll Design and Social Inquiry	Multi / Interdisciplinary Stud	3			
	Coll Engineering Computer Sci	Multi / Interdisciplinary Stud	3			
	College of Business	Multi / Interdisciplinary Stud	10			
	College of Education	Multi / Interdisciplinary Stud	17			
	D. F. Schmidt Col Arts Letters	Multi / Interdisciplinary Stud	1			
309999	D. F. Schmidt Col Arts Letters	Independent/Interdisc./Compara			37	

**** The table above displays is a screen shot of the 5 year summary of degrees awarded displayting the COM Biomedical Science program awarding 139 degrees from 2010-2015***

iv. Student Recruitment

Recruiting Initiatives:

To recruit qualified students the department is implementing innovative recruitment strategies. These include:

- Attend Graduate Fairs hosted by other Colleges and Universities to promote the MS Biomedical Science program to potential students.
- Attend campus-based programs hosted by the Graduate College, Career Center, and the College of Science to give information to interested students.

- Attend club meetings and present a brief information session on the program
- Create a 2-3 minute marketing video to recruit students from FAU and other Florida universities.
- Attend the Pre-Professional undergraduate course and present a brief information session on the program.
- Create marketing materials for COM website, bulletin boards, and Graduate Program Office.
- Identifying feeder institutions for direct mail or email advertising to institutions sponsoring an undergraduate biology, psychology, engineering, and chemistry.
- Target Historically black colleges and universities (HBCU) and Hispanic serving universities (HSUs)
- Target Southeast colleges and universities, particularly those in Florida
- Target FAU undergraduates to include:
    - Undergraduate majors in Biological Sciences
    - Undergraduate majors in Psychology
    - Undergraduate majors from FAU High School
    - Masters students in relevant FAU programs
- Create and distribute brochures to handout to campus visitors (also used during recruitment) containing single sheet inserts for the Biomedical Science Ph.D. track
- Support and organize visits of faculty to feeder institutions to discuss program with students/faculty
- Create website landing page dedicated to the FAU Graduate Biomedical Science Program
- Create marketing posts for Social Media – Facebook, Twitter, etc.

A number of other creative initiatives are under way:

- Advertise through via Google keywords. Desire to see FAU Graduate Biomedical Science Program to appear early in Google searches when prospective students search for opportunities.
- Identify students with certain GRE scores to target visibility to students likely to qualify for graduate training
- Advertise to international feeder institutions particularly those with undergraduate biology programs
- Coordinate international collaborators of training program faculty to help advertise to foreign students
- Emphasize a main focus to recruit Florida Atlanitc University High School.

Recruitment Incentives

The past 2 years the Biomedical Science has received $2,000 annually of Recruitment Grant Funds from the Graduate College that has supported our recruiting initiatives above.
Our recruitment efforts face the challenge of little resources such as teaching assistantships, research assistantships, and scholarship funds which makes the MS Biomedical Science program uncompetitive relative to other FAU graduate programs that offer more financial support. We have also recently received two Provost Fellowship scholarship ($2,500) to use for “one time” for newly admitted students for the 2017-2018 academic year from the Graduate College.

Student Testimonials

“I was accepted into Wayne state university school of medicine. I will be starting this coming Monday. I just wanted to take a moment to thank you for every interaction that we have had together. It is nice having people who actually care about you on this journey. I am also thankful for having been invited to work in your lab. That was a special moment for me.”
-Alexander Voitkov

"My time here included great challenges. Nevertheless, I had invaluable experiences that fostered both personal and academic growth. I wholeheartedly believe that the program played a major role in me getting accepted into medical school. Moreover, the education I received in the biomed program has improved my confidence as I look ahead towards a career in medicine. I will forever be grateful for my time spent here and look forward to including you all in my future endeavors."
-Allan Joseph

I. Faculty

i. Administrative Structure:

All programs in the College of Medicine are directed by the Dean of the College of Medicine (Dr. Phillip Boiselle). The Biomedical Science MS Program is administered by the Assistant Dean of Graduate Programs (Dr. Marc Kantorow) whose activities are directed by the Dean of the College of Medicine (Dr. Phillip Boiselle) and The Interim Senior Associate Dean of Research (Dr. Janet Robishaw). The daily activities of the program are coordinated by the Coordinator of Graduate Programs (Ms. Bridget Statler) under the direction of the Assistant Dean of Graduate Programs. Further support for the program is also provided by Dr. Lisa Brennan (Assistant Research Professor) whose activities are directed by The Assistant Dean of Graduate Programs.

Guidance for the program is also provided by The College of Medicine Graduate Program Committee that is elected by the faculty of the College of Medicine and serves to make recommendations to the Dean on new graduate courses, decides on student admissions and awards teaching and research assistantships if available. In addition to the Graduate Committee, a Graduate Task Force Committee appointed by the Dean also provides the Dean input on the Biomedical Science MS program including strategic planning for future program initiatives, approval of speakers for the Distinguished Lecturer Seminar Series, planning of Graduate Student Research Day and planning of other program related events.

ii. Faculty Profile:

As of 2015-2016, the College of Medicine (COM) has 42 graduate faculty members whose status allows them to supervise the research activities of students in the program and teach graduate courses in the program. Of the 42 faculty members, 24 faculty have appointments in the Department of Biomedical Science, 16 have appointments in the Department of Integrated Medicine, and 1 is appointed in the Department of Surgery. All graduate faculty in of the COM are eligible to train students for thesis research and DIS credits for Biomedical Science MS program. Of the total 42 graduate faculty in the COM 24 faculty from all three departments in the College directly teach graduate courses for the Biomedical Science MS Program.

Male: Female Ratio

Our faculty is 56% male and 44% female. A listing of all Graduate Faculty participating in Biomedical Science program is located in Appendix B.

ii. COM Graduate Faculty Teaching Load in Biomedical Science Program:

Faculty teaching courses in the program teach one course every academic year. Many also participate in group taught courses, supervise thesis-related research, supervise direct independent

study credits, and serve as research advisors for students in Biomedical Science program.

Below is the list of courses offered in Biomedical Science for Fall 2016-Summer 2017.

MS Biomedical Science Program Fall 2016-Summer 2017 Course

Fall 2016

Course	Title	Cr Hrs	Instructor
PCB 6207	Advanced Cell Physiology	3	Dr. Shen
PCB 6933	Biomedical Data/ Informatics	3	Dr. Li
PCB 6665	Human Genetics	3	Dr. Kantorow
PCB 5844	Neurobiology of Addiction	3	Dr. Isgor
PCB 6705	Molecular Bio Cardio System	3	Dr. Prentice
PCB 6848	Adult Neurogenesis	3	Dr. Wei

Spring 2017

Course	Title	Cr Hrs	Instructor
PCB 5532	Advanced Mol & Cell Biology	3	Dr. Oleinikov
GMS 6301	Macromolecules and Human Disease	3	Dr. Brew
MCB 6208	Host Defense and Inflammation	3	Dr. Shibata
PSB 6515	Developmental Neurobiology	3	Dr. Guthrie
PCB 6665	Human Genetics	3	Dr. Kantorow
PCB 6933	Biomedical Writing	3	Dr. Wojcikiewicz
BMS 6523	Autonomic Function & Disease	3	Dr. Tao

Summer 2017

Summer 2 May 15th-jun 26th

Course	Title	Cr Hrs	Instructor
BMS 6102C	Integrated Morphology 1	4	Dr. Schmidt-Kastner
BMS 6303	Clinical Microbiology	3	Dr. Rose
PCB 6235	Molecular Basis of Human Cancer	3	Dr. Lu
PCB 6239	Tumor Immunology	3	Dr. Iragavarapu
PCB 6885	Physiology of the Heart	3	Dr. Huang

Summer 3 June 27th-August 7

Course	Title	Cr Hrs	Instructor
GMS 6302	Molecular Basis of Disease & Therapy	3	Dr. Caputi
PCB 6238	Problem Based-Immunology	3	Dr. Nouri-Shirazi
BMS 6601	Fund. General Pathology	3	Dr. Levitt
BMS 6104 C	Integrated Morphology 2	4	Dr. Trelka

The average enrollment for the MS Biomedical Science courses is 14. A breakdown for enrollments in each course for 2016-2017 year is listed below.

Enrollment for MS Biomedical Science Program Fall 2016-Summer 2017 Course

Fall 2016

Course	Title	Cr Hrs	# Enrolled	Instructor
PCB 5844	Neurobiology of Addiction	3	8	Dr. Isgor
PCB 6207	Advanced Cell Physiology	3	15	Dr. Shen
PCB 6665	Human Genetics	3	7	Dr. Kantorow
PCB 6705	Molecular Bio Cardio System	3	23	Dr. Prentice
PCB 6848	Adult Neurogenesis	3	6	Dr. Wei
PCB 6933	Biomedical Data/ Informatics	3	28	Dr. Li

Spring 2017

Course	Title	Cr Hrs	# Enrolled	Instructor
PCB 5532	Advanced Mol & Cell Biology	3	31	Dr. Oleinikov
GMS 6301	Macromolecules and Human Disease	3	7	Dr. Brew
MCB 6208	Host Defense and Inflammation	3	14	Dr. Shibata
PSB 6515	Developmental Neurobiology	3	14	Dr. Guthrie
PCB 6665	Human Genetics	3	22	Dr. Kantorow
PCB 6933	Biomedical Writing	3	30	Dr. Wojcikiewicz
BMS 6523	Autonomic Function & Disease	3	14	Dr. Tao

Summer 2017

Summer 2 May 15th-jun 26th

Course	Title	Cr Hrs	# Enrolled	Instructor
BMS 6102C	Integrated Morphology 1	4	16	Dr. Schmidt-Kastner
BMS 6303	Clinical Microbiology	3	7	Dr. Rose
PCB 6235	Molecular Basis of Human Cancer	3	4	Dr. Lu
PCB 6239	Tumor Immunology	3	7	Dr. Iragavarapu
PCB 6885	Physiology of the Heart	3	15	Dr. Huang

Summer 3 June 27th-August 7

Course	Title	Cr Hrs	# Enrolled	Instructor
GMS 6302	Molecular Basis of Disease & Therapy	3	cancelled	Caputi
PCB 6238	Problem Based-Immunology	3	4	Nouri-Shirazi
BMS 6601	Fund. General Pathology	3	18	Levitt
BMS 6104 C	Integrated Morphology 2	4	15	Trelka

iv. Summary of Faculty Research Productivity:

Faculty from all three Departments at the College of Medicine (Biomedical Science, Integrated Medical Science and Surgery) participate in the program. Their individual faculty research productivity profiles are listed below:

Over the past 5 years, the Biomedical Science Departmental research activities resulted in 93 peer-reviewed publications, 30 other publications, 62 presentations at professional meetings or conferences, 139 submitted grant proposals and a total of $2,768,216.00 in received grant funds.

Over the past 5 years, the Integrated Medicine Science Departmental research activities resulted in 147 peer-reviewed publications, 92 other publications, 222 presentations at professional meetings or conferences, 88 submitted grant proposals and a total of $3,632,089.00 in received grant funds.

No data is available is available for the Department of Surgery.

Tabulated data is shown in the tables shown for the research section (below).

v.Strategic Planning for Hires:

Faculty are recruited for multiple roles at the College of Medicine and are not specifically recruited for teaching in the Biomedical Science MS Program. Faculty participation in the Biomedical Science MS program is made in consultation with their Chairs.

vi. Abbreviated faculty CVs:

Faculty CV's are included in Appendix B.

J. Research

Many students in the program engage in thesis, directed independent study, volunteer and other research opportunities. Although their research experiences are diverse, the majority receive state-of the-art hands on laboratory experience in a biomedical science-related research laboratory under the direction of a graduate program faculty member. Resources for this research is generally provided by external grant funding obtained by the research advisor. Most students not only receive research training but also have the opportunity to present and publish their work. These experiences provide them with invaluable skills and optimize their credentials to achieve their goals.

Below are some examples of publications by graduate students in the program:

Yuejin Li, Lei Zhang, Pierre-Yves Jean-Charles, Changlong Nan, Guozhen Chen, Jie Tian, J.-P., Jin, Ira J. Gelb, **Xupei Huang**. Dose-dependent diastolic dysfunction and early death in a mouse model with cardiac troponin mutations, J. Mol. Cell. Cardiology, 62:227-236, 2013.

Liu Xiaoyan., Lei Zhang, Daniel Pacciulli, Jianquan Zhao, Changlong Nan, Wen Shen, Junjun Quan, Jie Tian, **Xupei Huang**. Restrictive cardiomyopathy caused by troponin mutations: application of disease animal models in translational studies. Front. Physiology, 7:629, doi: 10.3389/fphys.2016.00629.

Rush, D., Leon, R., McCollum, M., Treu, R., Wei, J. (2012) Palmitoylation and trafficking of GAD65 is impaired in a cellular model of Huntington disease. *Biochem J*. 442(1) 39-48. PMCID: PMC4646170.

McCollum, M., Leon, R., Rush, D., Guthrie, K., Wei, J. (2013) Striatal oligodendrogliogenesis and neuroblast recruitment is increased in the R6/2 mouse model of Huntington's disease. *Brain Res*. 1518, 91-103. PMCID: PMC3684253.

Sean Paz and **Massimo Caputi**. (2015) SRSF1 inhibition of HIV-1 gene expression. ***Oncotarget.*** *6(23):19362-63.*

Sean Paz, Michael L. Lu, Hiroshi Takata, Lydie Trautmann and **Massimo Caputi**. (2015) The SRSF1 RNA Recognition Motifs of are strong inhibitors of HIV-1 replication. ***J. Virology.*** *89(12):6275-86.*

Sean Paz, Adrian R. Krainer and **Massimo Caputi**. (2014) HIV-1 transcription is regulated by splicing factor SRSF1. **Nucleic Acids Res.** 42:13812-13823

Jacques Jean-Philippe, Sean Paz, Michael L. Lu and **Massimo Caputi**. (2014) A truncated hnRNP A1 isoform, lacking the RGG-box RNA binding domain, can efficiently regulate HIV-1 splicing and replication. ***BBA-Gene Regul. Mech***. 1839(4):251-8

Jacques Jean-Philippe, Sean Paz and **Massimo Caputi** (2013) hnRNP A1: the Swiss Army Knife of Gene Expression. ***Int. J. Mol. Sci***. 14, 18999-19024

Parkin elimination of mitochondria is important for maintenance of lens epithelial cell ROS levels and survival upon oxidative stress exposure. Brennan L, **Khoury J**, Kantorow M. Biochim Biophys Acta. 2017 Jan;1863(1):21-32. doi: 10.1016/j.bbadis.2016.09.020. Epub 2016 Oct 1.

Integrin αVβ5-mediated Removal of Apoptotic Cell Debris by the Eye Lens and Its Inhibition by UV Light Exposure. Chauss D, Brennan LA, **Bakina O**, Kantorow M. J Biol Chem. 2015 Dec 18;290(51):30253-66. doi: 10.1074/jbc.M115.688390. Epub 2015 Nov 2.

Spatial expression patterns of autophagy genes in the eye lens and induction of autophagy in lens cells. Brennan LA, Kantorow WL, **Chauss D,** McGreal R, He S, **Mattucci L,** Wei J, Riazuddin SA, Cvekl A, Hejtmancik JF, Kantorow M. Mol Vis. 2012;18:1773-86. Epub 2012 Jun 30.

αB-crystallin/sHSP protects cytochrome c and mitochondrial function against oxidative stress in lens and retinal cells. McGreal RS, Kantorow WL, **Chauss DC**, Wei J, Brennan LA, Kantorow M.Biochim Biophys Acta. 2012 Jul;1820(7):921-30. doi: 10.1016/j.bbagen.2012.04.004. Epub 2012 Apr 12.

Focus on Molecules: methionine sulfoxide reductase A. Kantorow M, Lee W, **Chauss D.**Exp Eye Res. 2012 Jul;100:110-1. doi: 10.1016/j.exer.2010.09.007. Epub 2010 Oct 1. Review.

Thiyagarajan, N., Pham, TTK. Stinson, B., Sundriyal, A., Tumbale, P., Lizotte-Waniewski, M., Brew, K., and Acharya, K.R. (2012) Molecular structure of a metal-independent bacterial glycosyltransferase that catalyzes the synthesis of histo-blood group A antigen. *Scientific Reports*, **2**: 940

Pham, T.T.K., Stinson, B., Thiyagarajan, N., Lizotte-Waniewski, M., Brew, K., and Acharya, K.R. (2014) Structures of Complexes of a Metal-independent GT6 from *Bacteroides ovatus* with UDP-GalNAc and its Hydrolysis Products. *J. Biol. Chem.* **289**, 8041-8050.

Zou, H., Wu, Y., and Brew, K. (2016) Thermodynamic basis of selectivity in the interactions of tissue inhibitors of metalloproteinases N-domains with matrix metalloproteinases -1, -3 and -14. *J Biol. Chem* **291**, 11348- 11358

Nouri-Shirazi M, Bible B, Zeng M, Tamjidi S, and Bossart G. Phenotyping and comparing the immune cell populations of free-ranging Atlantic bottlenose dolphins (Tursiops truncatus) and dolphins under human care. BMC VETERINARY RESEARCH Mar 27, 2017 Volume: 13 Issue: 1 Pages 78-92

Nouri-Shirazi M, Tamjidi S, and Nourishirazi E. TLR8/7 combined withTLR3 or TLR4 enhances DC-NK driven effector T cells THE JOURNAL OF IMMUNOLOGY Abstract 2328 May 2017

Nouri-Shirazi M, Tamjidi S, and Nourishirazi E. Selected TLR agonists act in synergy to reprogram DC-NK cross-talk and generate effector T cells in nicotinic environment. THE JOURNAL OF IMMUNOLOGY May1, 2016 vol. 196 no.1 Supplement 215.17

Nouri-Shirazi M, Abu-Nuwar E, and Nourishirazi E. Genetic background influences the Cellular and humoral responses to vaccines. THE JOURNAL OF IMMUNOLOGY May1, 2016 vol. 196 no.1 Supplement 215.16

Nouri-Shirazi M, Bible B, Zeng M, Tamjidi S and Bossart G. Characterizing Immune Cells of Atlantic Bottlenose Dolphins. JOURNAL OF IMMUNOLOGY 2014 192:1 Suppl. 1

Nouri-Shirazi M, Zeng M, Bible B, Tamjidi S. Genetic background influences the NK recruitment and Th1 polarization in response to TLR agonists. JOURNAL OF IMMUNOLOGY 2014 192:1 Suppl. 1

Nouri-Shirazi M, Nourishirazi E, Lang K, and Guinet E. Candidate adjuvant restores DC-NK cross-talk and improves immunization outcomes in nicotine-exposed hosts. JOURNAL OF IMMUNOLOGY 188 MAY 2012

i. Review of Part II of the Department Dashboard Indicators:

Faculty of the departments participating in the program have brought a total of $6,994,550 in grant support over the past 5 years and have produced a large number of publications and other scholarly contributions. These are listed in detail below:

Departmental research activities for faculty in Biomedical Science

		Dept of Biomedical Science			College Total	University Total
		2013-2014	2014-2015	2015-2016	2015-2016	2015-2016
1. Books (including monographs & compositions)	**#**	0	0	0	0	105
2. Other peer-reviewed publications	**#**	44	49	0	0	1,124
3. All other publications	**#**	29	1	0	0	582
4. Presentations at professional meetings or conferences	**#**	37	25	0	0	1,377
5. Productions/Performances/Exhibitions	**#**	0	0	0	0	233
6. Grant Proposals Submitted	**#**	15	31	37	56	419
7. Organized Research	**#**	$2,466,408	$301,808	$0	$0	$0
8. Sponsored Instruction	**#**	$54,147	$80,368	$0	$0	$0
9. Other Sponsored Activities	**#**	$0	$0	$0	$0	$0

Departmental research activities for faculty in Integrated Medicine

		Dept of Integrated Medical Science			College Total	University Total
		2013-2014	2014-2015	2015-2016	2015-2016	2015-2016
1. Books (including monographs & compositions)	#	4	11	0	0	105
2. Other peer-reviewed publications	#	54	93	0	0	1,124
3. All other publications	#	19	73	0	0	582
4. presentations at professional meetings or conferences	#	73	149	0	0	1,377
5. productions/Performances/Exhibitions	#	3	13	0	0	233
6. Grant proposals Submitted	#	17	12	3	56	419
7. Organized Research	#	$1,579,603	$2,052,486	$0	$0	$0
8. Sponsored Instruction	#	$91,268	$49,892	$0	$0	$0
9. Other Sponsored Activities	#	$151,262	$167,308	$0	$0	$0

ii. Interdisciplinary Efforts:

Teaching
The Biomedical Science MS Program serves multiple other programs at FAU whose students take the program's courses as electives. These departments include, Bioengineering, Biology, Psychology, Chemistry, Engineering, and Business.

Research
Students in the program perform research not only in the College of Medicine but also in the College of Science.

K. Service and Community Engagement

i. Distinguished Lecturer Seminar Series - We successfully operated and instituted a Graduate Student-focused Distinguished Lecturer series to meet graduate student seminar requirements and expose students and faculty to Distinguished outside speakers in Biomedical Science. Students, faculty, and staff are welcome to attend the seminar series which creates a university community and creating a service that provides knowledge in the fields of science and medicine.

ii. The MS Biomedical Science program created a Graduate Student Research Day where students have the opportunity to present their research to their peers, community, staff, and faculty.

iii. The MS Biomedical Science program has created a DNA day where we invite middle and high schools to attend FAU College of Medicine to learn about science careers and participate with hands-on experiments.

iv. The MS Biomedical Science program is in the process of coordinating the identification, development and implementation of new student internships and post-graduation educational opportunities for MS Biomedical Students

L. Other Program Goals

Course Development:

A major goal of the program is to develop new courses that will strengthen the educational, research and vocational opportunities available to our students, provide new teaching opportunities for our faculty and enhance the value of the program to the College of Medicine and the University.

There are three emerging areas that are being targeted for the development of new courses. These areas align with the strategic plans of the college and support the FAU strategic pillars. They include Genomic and Precision Medicine, Pharmacology, Translational Applications in Human Disease and Biomedical Science Technology.

The program is now developing these areas and new courses in Pharmacology, Genomics and Precision Medicine, Translational Applications in Human Disease and a new Biomedical Science Technology course will be taught this year.

In addition to developing new courses another goal of the program is to revise and innovate existing courses and this process is underway through the integrated efforts of the faculty, Department Chairs, Office of Graduate Programs, Assistant Dean of Graduate Programs, Senior Associate Dean of Research and the Dean.

Student Development:

A major goal of the program is to enhance the learning opportunities of students and ensure their success in attaining their educational and vocational goals. To increase success in these areas, new and innovative research opportunities, internships, teaching opportunities and personnel development opportunities are being developed. The office of graduate programs is reaching out to employers to seek internships including Modernizing Medicine, Biorassi, IBM, Palm Beach County Schools, Broward County Schools, PBSC and more. Plans are underway

to enhance student development ranging from identifying personalized learning opportunities to providing direct assistance from the OGP in identifying scholarship opportunities, aid in applications to graduate and professional programs and job placement assistance. Our office would like to create a week long career development series including mini career workshops using the career center resources.

Faculty Development:

Another goal of the program is to provide increased support for faculty teaching initiatives, faculty teaching assistance and faculty engagement. Working with the Dean and department Chairs opportunities for achieving this goal are being identified.

Gain final approval and implement the new COM MS On the Way Program

Work with the Associate Dean of Graduate Programs in the College of Science to formalize the ongoing development of a Biomedical Science Masters on the Way Program for PhD students performing their thesis research in the newly created COM-IBBS track and other PhD programs whose research is performed with COM faculty in COM-sponsored labs.

Increase financial assistance for top-quality students

Develop financial assistance programs to attract and retain top-quality students for the program including additional FAU fellowships, internships and summer stipend opportunities. Increase the number of summer stipends offered.

Develop Performance Monitoring and Tracking Methods for COM Graduate Students

Tracking of students' perception of teaching, performance, graduation rates, research compliance and post-graduation success are being developed and will be implemented. Our goal is to establish a database of student success that can be used to enhance the existing program and increase its impact on the students. Appendix D includes our current COM Graduate Survey that will be used to track Alumni.

M. Strengths and opportunities that support achievement of program goals for Biomedical Science Program

- Biomedical Science and its subspecialties from precision medicine through bioinformatics is a high impact emerging area attracting students from multiple backgrounds with multiple vocational goals and will continue to be a hot topic for the near future.
- The Colle of Medicine is growing and the Masters of Science Program is an Integral Component of the colleges expansion and mission.
- The Program has strong support from the Dean and the College leadership.
- The program is supported by 46 actively experts in wide-ranging disciplines in biomedical science actively engaged in scholarship.
- The faculty of the program are actively engaged in publications with students and dedicated to student success.
- The faculty are well-supported with over 12 NIH-funded research programs and multiple state-funded research programs that offer unique research opportunities for students in the program.
- The program is flexible accommodating both thesis students who desire a traditional research-based masters degree and a non-thesis track for students who desire a pre-professional background that advances their ability to be accepted into pre-professional programs.
- The program has been successful in placing students in a wide-range of post-graduation

opportunities including, medical school, graduate school and teaching.
- The program a student to faculty ratio of almost 1:1 providing an unparalleled ability to address individual student needs and provide individualized learning.
- The program offers a wide-array of over 22 courses providing a custom-tailored program of study for students to achieve their individual goals and directed independent study opportunities are available for custom-tailored learning and hands-on research opportunities.
- Class sizes in the program are small averaging about 13 students in each class providing an outstanding learning environment.
- The program has a 100% graduation among the highest in the university.
- The program is 11th out of 66 programs at the university in number of graduate degrees produced over the last five years.
- The program has an intensive and open-door advising program to ensure student success.
- The program provides a valuable resource for the community providing faculty expertise and outreach for the state STEM initiative by providing faculty representation at Palm Beach County STEM events, FAU high school and other local schools.
- The program sponsors the DNA event attending by multiple local high schools and their students.
- The program provides infrastructure for the educational and intellectual culture of the College of Medicine and FAU by providing an annual research symposium and seminar series attending by not only students and faculty in the program but students and faculty across the university, Scripps Research Institute, Max Planck Research Institute and other biomedical science partners.

N. Weaknesses and threats that impede program progress for Program

Infrastructure
Growth of the program has been impeded by a lack of classroom space. More classroom space is needed. The program does not presently have a designated program office or central advising facility. These re currently restricted to a faculty and staff office. A central office for the program would benefit its activities. Finally, there is a lack of student study and work areas and no formal student lounge or common area is available. These student areas would greatly benefit the program. The entire program is administered by only one supporting staff member, the Coordinator of Graduate Programs and additional staff support is needed to carry out the diverse responsibilities of administrating the program.

Student Support
Although the majority of students in the program receive teaching assistantships from outside departments and colleges, the only financial support for students in the program is in the form of four summer research assistantships available for thesis students working in COM labs. Additional TA or RA support and other financial assistance would greatly benefit the program.

Research Support
Most research either thesis or directed independent study performed by students in the program is supported by direct grant funding to faculty. The program would greatly benefit from direct financial support for student research activities that is independent of faculty grant support. In addition, there is no direct support for student travel that is needed by the students.

The majority of our students seek to enter medical school however acceptance rates are low. Given that our students represent high GPA and test scores, we need to develop an intensive alternate career development resources. Although we have been developing internship opportunities and have strengthen advising opportunities to achieve this goal, we need to formalize career development programs. This can include a week long focus advising and exposing students to alternate careers such as pharmacy, physician assistant, dentistry, physical therapy, nursing, teaching, medical administration, medical policy, and medical law. This can also include a Princeton Review for the MCAT.

Also, graduate students that obtain assistantships at Florida Atlantic University receive low stipends that are not equivalent to the cost of living and FAU does not provide health insurance. With the low stipends and no health insurance for the Graduate Teaching Assistantships it is difficult to recruit students when several Florida state schools including Florida International University, Florida State University, University of Central Florida, University of Florida, and University of South Florida, cover an estimate of 75% of health insurance to their graduate assistants, teaching assistants, and research assistants.

O. Resource analysis for Program

Resources for all aspects of the program are currently providing by the Dean from the College of Medicine Budget.

P. Future directions for Program *(required questions for review team)*

- How can strategies be devised for increasing enrollment in the program?
- How can we increase tuition and cost of living support for students in the program?
- How can additional classroom and study space be obtained for students in the program?
- How can we provide better integration and representation for students in the program at the COM and at FAU?
- How can we identify resources for additional administrative support for the program?
- How can we better develop formal career development opportunities for our students?
- How can we explore BS/MS or other combined degree partnerships across the university?

Appendix A: MS Biomedical Science Brochure

Charles E. Schmidt College of Medicine at Florida Atlantic University offers graduate education programs that provide students with the skills and knowledge that will enable them to engage the forefront of basic, applied, and translational research or to continue their studies toward professional degrees in the health sciences.

College of Medicine biomedical science faculty are active experts in their respective biomedical science fields and will support development of the students' research in the areas of human genetics and genomics; cancer biology and prevention; microbiology, immunology and infectious disease; HIV/AIDS mechanisms and treatments; respiratory physiology and biophysics; age-related eye diseases including cataract and age-related macular degeneration; breast cancer mechanisms and therapy; cardiometobolic risk in psychiatry; Huntington's disease mechanisms; Alzheimer's disease mechanisms and therapy; vaccine development; osteoarthritis prevention and treatment; prostate cancer mechanisms; reducing premature death and disability from heart attacks and stroke; restrictive cardiomyopathy mechanisms; childhood malaria mechanisms and therapy development; in children; and, others.

Students interested in pursuing a Master's Degree in Biomedical Science will be able to choose the thesis or non-thesis option.

The thesis option is oriented towards those students interested in pursuing biomedical research careers in industry or academia and can provide a stepping stone to the Ph.D. degree. The non-thesis option is designed for students seeking in-depth exposure to biomedical science or to solidify their knowledge base in preparation for a broad range of career options, including further study in professional schools.

Please contact:
Graduate Program Coordinator
Bridget Statler
bstatler@health.fau.edu
561.279.4549

Assistant Dean of Graduate Programs
Dr. Marc Kantorow
mkantoro@health.fau.edu
561.297.2910

Vice Dean for Research and Innovation
Dr. John Newcomer
jnewcomer@health.fau.edu

FAU
CHARLES E. SCHMIDT COLLEGE OF MEDICINE
Florida Atlantic University

Master of Science Degree of Biomedical Science

Advanced Thesis-And Non-Thesis MS Degree Programs In Biomedical Science At The Rapidly Growing New College Of Medicine At FAU.

FAU
CHARLES E. SCHMIDT COLLEGE OF MEDICINE
Florida Atlantic University

*The **Charles E. Schmidt College of Medicine Master of Science program in biomedical science** is designed to advance students' academic and career goals through innovative course offerings, advanced research opportunities, and personalized advising and mentoring programs. Building upon a solid foundation of essential biomedical core courses, students in the Charles E. Schmidt College of Medicine Master of Science gain the credentials, skills and advanced knowledge they need to be successful for professional and graduate admissions, scientific and educational careers and beyond.*

We welcome your interest in our program and encourage you to contact us to learn more about program admission, course offerings and available research opportunities.

Biomedical Science Application Information

The University's general graduate admission requirements must be achieved, including:

- A minimum grade point average of 3.0 in the last 60 credits.
- Completion of the GRE (with competitive scores)

Prerequisites for the master's degree include:

- One year of biology
- One year of chemistry
- One year of physics
- One semester of organic chemistry
- One semester of biochemistry
- At least two upper-division (3000-4000 level) biology classes. For example, microbiology, genetics, molecular and cell biology, immunology, virology.

Application to the Graduate College:

- Go to *wise.fau.edu/graduate/*

Application for Graduate Studies in Biomedical Science:

- Complete the online application: *bioserv.biomed.fau.edu/grad_app/*
- Compose a 1-2 page personal statement explaining your career goals.
- Request 3 letters of recommendation.
- For additional information on research conducted in the College of Medicine, please visit *med.fau.edu/research/focus.php*

Fall deadline: April 1st
Spring deadline: October 1st
Summer deadline: March 1st

Appendix B: Abbreviated Faculty CVs & NIH Bio

Interim Associate Dean of Research: Dr. Janet Robishaw
Assistant Dean of Graduate Programs: Dr. Marc Kantorow
Biomedical Science Faculty: (alphabetical order)
Dr. Randy Blakely
Dr. Lisa Brennan
Dr. Keith Brew
Massimo Caputi, Ph.D.
Jim Galvin, M.D., M.P.H.
Kathleen Guthrie, Ph.D.
Xupei Huang, M.D., Ph.D.
Vijaya Iragavarapu-Charyulu, Ph.D.
Ceylan Isgor, Ph.D.
Morton Levitt, M.D.
Zhongwei, Li. Ph.D.
Michael Lu, Ph.D.
Mahyar Nouri-Shirazi, D.V.M., Ph.D.
Andrew Oleinikov, Ph.D.
Michele Pergadia, Ph.D.
Howard Prentice, Ph.D.
Rainald Schmidt-Kastner, M.D.
Wen Shen, Ph.D.
Yoshimi Shibata, Ph.D.
Rui Tao, D.V.M, Ph.D.
Darin Trelka, M.D., Ph.D.
Jianning Wei, Ph.D.
Ewa Wojcikiewicz, Ph.D.
Jang-Yen Wu, Ph.D.

Janet Robishaw, Ph.D.
Interim Associate Dean of Research, Department of Biomedical Science

Education

- 1979: B.S., Chemistry and biology, Central Michigan University, Mt. Pleasant, MI
- 1983: Ph.D. Cellular and Molecular Biology, Pennsylvania State University, College of Medicine, Hershey, PA

Research Interests

- Research focuses on G-protein coupled receptor signaling pathways that represent targets for more than 60% of all biomedical drugs on the market. Particularly abundant in the brain, GPCR signaling pathways must integrate many cellular functions to produce a coordinated neurological response.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Robishaw, Janet

eRA COMMONS USER NAME (agency login): jdrobishaw

POSITION TITLE: Professor and Chair, Biomedical Science; Senior Associate Dean for Research

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Central Michigan University, Mt. Pleasant, MI	BS	08/1979	Chemistry and Biology
Pennsylvania State University, College of Medicine, Hershey, PA	PHD	08/1983	Cellular and Molecular Physiology
University of Texas Health Science Center, Dallas, TX	Postdoctoral Fellow	06/1987	Pharmacology Dr. Alfred Gilman *Nobel Laureate*

A. Personal Statement

The Geisinger Health System has laid the foundation for its own precision medicine effort with the establishment of a large research cohort whose genomic information is linkable to a searchable clinical data warehouse. As the former Associate Director of the Weis Center for Research for the health system, I led a variety of initiatives revolving around the incorporation of genetic information into improvements in patient care. As a former Senior Scientist, I spent the last several years building the infrastructure and gaining specific expertise in both genomics- and phenomics- based strategies understand the genetic architecture of chronic pain and response to prescription opioids. As a current Professor of Biomedical Science, College of Medicine, Florida Atlantic University, I will continue these efforts as part of the multi-PI team on four NIH awards.

Briefly, my laboratory uses genotype, whole exome sequence, and clinical phenotype data to perform both common and rare variant association strategies. These pipelines allow the rapid identification of genetic variants that are significantly associated with clinical phenotypes (e.g., disease diagnoses, physiological traits, clinical lab values, and medications). Subsequently, we perform functional screening to assess the causality of the observed associations. This analysis runs the gamut from assessing the functional impact of a genetic variant in heterologous expression systems, to genome editing and study in native cells, to isolating human induced pluripotent cells carrying the genetic variant and modeling the disease in culture. By identifying genetic variants that are causally linked to clinical outcomes, we are able to facilitate the rapid translation of laboratory based discoveries into medically informed practices. To further maximize the clinical and therapeutic benefit, my laboratory focuses on G-protein coupled receptor (GPCR) signaling pathways that are dysregulated in many diseases and are proven drug targets. With more than 25 years of experience in this field, we utilize the full range of approaches to better understand how these signaling components contribute to common diseases that represent a significant public health burden. Investigating the genetic linkages and mechanistic bases between GPCR signaling components and common diseases will improve molecular diagnoses and identify new therapeutic targets in the coming years.

1. Gerhard GS *et al*. Genomic and Personalized Medicine. Second ed. Ginsburg GS, Willard HF, editors. United Kingdom: Elsevier; 2013. Chapter 24, Electronic Health Records for Genomic Medicine; p.287-294. 483p.

2. Metpally R *et al.* Disease Associations of Common and Rare Calcium Sensing Receptor Variants in a Cohort of 51,289 Individuals. Under revision for *New England Journal of Medicine.*

B. Positions and Honors

Positions and Employment

1985 - 1986	Research Assistant Professor, Pharmacology, University of Texas Health Science Center, Dallas, TX
1987 - 1996	Staff Scientist, Weis Center for Research, Geisinger Health System, Danville, PA
1996 - 1997	Senior Staff Scientist, Weis Center for Research, Geisinger Health System, Danville, PA
1997 - 2000	Professor, Physiology, Pennsylvania State University, Medical School, Hershey, PA
2000 - 2016	Senior Scientist, Weis Center for Research, Geisinger Health System, Danville, PA
2005 - 2016	Associate Director, Weis Center for Research, Geisinger Health System, Danville, PA
2016 - present	Professor and Chair, Biomedical Science, College of Medicine, Florida Atlantic University, Boca Raton, FL
2017 – present	Interim Senior Associate Dean for Research, College of Medicine, Florida Atlantic University, Boca Raton, FL

Other Experience and Professional Memberships

1987 -	Member, American Society of Biochemistry and Molecular Biology
2000 -	Member, American Society of Pharmacology and Therapeutics

Honors

1980-1983	Pre-doctoral Training Grant Recipient, National Institutes of Health
1983-1987	Post-doctoral Training Grant Awardee, National Institutes of Health
1989-1992	Signal Transduction Study Section, Chartered Member, American Cancer Society (National)
1989-1994	Established Investigator, American Heart Association (National)
1990-1995	Whittaker Foundation
1991	USA/USSR Scientific Exchange Representative, National Institutes of Health
1991-1995	Pharmacology Study Section, Chartered Member, National Institutes of Health
1993	Neuroscience Advisory Panel , National Institutes of Health
1993-1998	Editorial Board Member, Journal of Biological Chemistry
1996	Cardiovascular Study Section Ad hoc Reviewer, National Institutes of Health
1996-1999	Molecular Signaling Study Section, Chartered Member, American Heart Association (National)
1999-2003	Pharmacology Study Section, Chartered Member, National Institutes of Health
2001-2004	Executive Committee for Cardiovascular Physiology, Member, American Society of Pharmacology and Therapeutics
2007-2011	Molecular and Integrative Signal Transduction Study Section, Chartered Member, National Institutes of Health
2013	Hypertension Study Section, Ad Hoc Member, National Institutes of Health

C. Contribution to Science

1. Importance of G-protein Coupled Receptor (GPCRs) in Health and Disease.

   The estimated 865 members of the human G-protein coupled receptor (GPCR) family regulate many biological functions, contribute to numerous diseases, and represent targets for nearly half of prescribed drugs. This complexity has raised question regarding the biological functions of these receptors and the impact of genetic variation on receptor function, disease risk, and treatment response. Our early use of gene “knockout” strategies in mice and zebrafish have revealed important functions for both known and orphan receptors in context of heart disease and development. Our more recent identification of human “knockouts” lacking certain receptors in the Geisinger population is providing important insights into their clinical relevance. Altogether, our findings constitute a new source of drug targets that are long sought by the pharmaceutical industry.

a. Ivanova-Nikolova TT, Nikolov EN, Hansen C, Robishaw JD. Muscarinic K+ channel in the heart. Modal regulation by G protein βγ subunits. J Gen Physiol. 1998 Aug;112(2):199-210. PubMed PMID: 9689027; PubMed Central PMCID: PMC2525744.

b. Richardson M, Robishaw JD. The α_{2A}-adrenergic receptor discriminates between Gi heterotrimers of different βγ subunit composition in Sf9 insect cell membranes. J Biol Chem. 1999 May 7;274(19):13525-33. PubMed PMID: 10224121.

c. McWhinney C, Wenham D, Kanwal S, Kalman V, Hansen C, Robishaw JD. Constitutively active mutants of the α_{1a}- and the α_{1b}- adrenergic receptor subtypes reveal coupling to different signaling pathways and physiological responses in rat cardiac myocytes. J Biol Chem. 2000 Jan 21;275(3):2087-97. PubMed PMID: 10636913.

d. Leung T, Humbert JE, Stauffer AM, Giger KE, Chen H, Tsai HJ, Wang C, Mirshahi T, Robishaw JD. The orphan G protein-coupled receptor 161 is required for left-right patterning. Dev Biol. 2008 Nov 1;323(1):31-40. PubMed PMID: 18755178.

2. Specificity of G-protein Signaling in Health and Disease

Acting downstream of this vast number of receptors, the heterotrimeric G-proteins serve as on-off switches for enzymes and ion channels that produce the “second messengers” leading to the appropriate cellular response. It was not until the 1970s that the existence of such transducing proteins was seriously considered and our efforts contributed to the initial purification of the founding members of the G-α subunit family (αs, αi, αo proteins). Subsequently, our efforts led to the cloning and functional characterization of additional members of the α, β, and γ subunit families. This diversity has raised fundamental questions regarding the functional significance of this large number of potentially distinct G-αβγ heterotrimers. Establishing the first *in vivo* proof that specific G-αβγ combinations not only exist but contribute to the specificity of signaling underlying biological functions, we showed that: 1) receptors require specific G-αβγ combinations in the intact cell setting; 2) G-protein assembly occurs by an ordered process that is driven by the γ subtype.; and 3) the amount of the γ protein controls the cellular abundance of the whole G-protein and the net output of the signaling pathway. Altogether, our findings have transformed understanding of how these signaling pathways are assembled and how they maintain the specificity of physiological processes. Moreover, they offer a surprisingly diverse family of γ subtypes as novel drug targets for selectively manipulating these signaling pathways in health and disease.

a. Sternweis PC, Robishaw JD. Isolation of two proteins with high affinity for guanine nucleotides from membranes of bovine brain. J Biol Chem. 1984 Nov 25;259(22):13806-13. PubMed PMID: 6438083.

b. Robishaw JD, Russell DW, Harris BA, Smigel MD, Gilman AG. Deduced primary structure of the α subunit of the GTP-binding stimulatory protein of adenylate cyclase. Proc Natl Acad Sci U S A. 1986 Mar;83(5):1251-5. PubMed PMID: 3081893; PubMed Central PMCID: PMC323053.

c. Ray K, Kunsch C, Bonner LM, Robishaw JD. Isolation of cDNA clones encoding eight different human G protein γ subunits. J Biol Chem. 1995 Sep 15;270(37):21765-71. PubMed PMID: 7665596.

3. Organismal Functions and Disease Mechanisms

My training and extensive background in regulatory mechanisms and physiology allows me to see the “big picture” and to explore the interplay between genes, environment, and human biology. As evidenced by both my publication and funding records, my laboratory has the necessary approaches to go full circle between genes, molecules, cells, organ systems, and organismal function. Of particular relevance to this application, I have specific expertise in dopamine and opioid receptor signaling pathways that function in the reward system underlying addictive behaviors.

a. Schwindinger WF, Betz KS, Giger KE, Sabol A, Bronson SK, Robishaw JD. Loss of G-protein γ_7 alters behavior and reduces striatal G-α_{olf} level and cAMP production. J Biol Chem. 2003 Feb 21;278(8):6575-9. PubMed PMID: 12488442.

b. Schwindinger WF, Mihalcik LJ, Giger KE, Betz KS, Stauffer AM, Linden J, Herve D, Robishaw JD. Adenosine A_{2A} receptor signaling and G-olf assembly show a specific requirement for the γ7 subtype.

J Biol Chem. 2010 Sep 24;285(39):29787-96. PubMed PMID: 20639202; PubMed Central PMCID: PMC2943273.

c. Schwindinger WF, Borrell BM, Waldman LC, Robishaw JD. Mice lacking the G-protein γ3 subunit show resistance of opioids and diet induced obesity. Am J Physiol Regul and Integ Comp Physiol. 2009 Nov;297(5): R1494-502. PMID: 19759336 ; PMCID: PMC2777785.

d. Schwindinger WF, Mirshahi UL, Baylor KA, Sheridan KM, Stauffer AM, Usefof S, Stecker MM, Mirshahi T, Robishaw JD. Synergistic roles for G-protein γ_3 and γ_7 subtypes in seizure susceptibility as revealed in double knock-out mice. J Biol Chem. 2012 Mar 2;287(10):7121-33. PubMed PMID: 22207761; PubMed Central PMCID: PMC3293587.

e. Moon AM, Stauffer AM, Schwindinger WF, Sheridan K, Firment A, Robishaw JD. Disruption of G-protein γ_5 subtype causes embryonic lethality in mice. PLoS One. 2014;9(3):e90970. PubMed PMID: 24599258; PubMed Central PMCID: PMC3944967.

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/myncbi/1t3-9mx25aTkp/bibliography/48222423/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

NIH R01 GM114665
ROBISHAW, JANET D (PI)
04/01/15-03/31/19
Novel Aspects of Golf Signaling
Role: PI

NIH R01 GM111913
ROBISHAW, JANET D (MPI)
05/01/15-04/30/19
An integrated approach to study GPCR variants associated with complex diseases
Role: Multi-PI

NIH R01 HL134015
ROBISHAW, JANET D
12/01/16-11/30/20
Approaches to Genetic Heterogeneity of Obstructive Sleep Apnea
Role: Multi-PI

NIH R01 DA044015
ROBISHAW, JANET D
04/01/17-03/31/22
Clinical and Genetic Study of Prescription Opioid Addiction
Role: Multi-PI

Marc Kantorow, Ph.D.
Professor of Biomedical Science and Assistant Dean of Graduate Programs

Education

- B.S. Biology, Cum Laude from Towson State University, Towson, MD 1985
- Ph.D., Genetics, George Washington University, Washington, D.C. 1991

Research Interests

- Eye tissue development and molecular genetics including the etiology of age-related human cataract and age-related macular degeneration.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Kantorow, Marc

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

POSITION TITLE: Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Towson State University, Towson Md.	BS (cum laude)	1985	Biology
George Washington University, Wash. D.C.	PhD	1991	Genetics
National Eye Institute, NIH, Bethesda, MD	Senior Staff Fellow	1997	Ocular Biology
Jules Stein Eye Institute, UCLA, Los Angeles, CA	Assistant Research Ophthalmologist	1999	Ocular Biology

A. Personal Statement

My long-term goal has been to identify and functionally define the genetic, protective, repair and regulatory mechanisms that coordinate the development, differentiation and function of the eye lens and to establish how environmental damage and aging of the lens contributes to cataract formation. Since many of these mechanisms are conserved between the lens and more complex tissues, I have applied the knowledge gained from these studies towards understanding how retinal pigmented epithelium (RPE) cells maintain their homeostatic function in the retina. In early studies, we identified those transcription factor binding (promoter binding site analysis) and DNA structural requirements (in vivo chromatin accessibility) required for expression of the small heat-shock protein αA-crystallin that is required for lens transparency. We discovered how key post-translational mechanisms (phosphorylation and methionine oxidation) regulate the chaperone and protective functions of α-crystallin. We used high-throughput genomic and computational biology approaches to discover key genes altered upon human and mouse cataract formation (metallothionein II, Protein phosphatase 2a, osteonectin, ARK receptor kinase and others). We established that key mitochondrial repair enzymes and reducing systems (MsrA, TXNL6) are required to maintain lens mitochondrial function, lens cell homeostasis and lens cell survival. We found that deletion of MsrA results in oxidative stress-induced cataract formation. We demonstrated that other repair (MsrB1, MsrB2 and MsrB3) and antioxidant (peroxiredoxin 3) enzymes defend lens cells against oxidative stress damage. We demonstrated that MsrA can repair and restore the chaperone function of α-crystallin. We discovered that MsrA repairs lens cytochrome c to prevent its release from the mitochondria and the initiation of apoptosis. We demonstrated that MsrA provides mitochondrial protection and increased survival of RPE cells exposed to oxidative stress treatment suggesting it plays an important role in RPE and retinal function. We found that the same molecular mechanisms used by the RPE to phagocytize photoreceptor cell debris are employed by lens epithelial cells to phagocytize apoptotic and necrotic debris to ensure lens cell survival. We defined the conditions and molecular events required for differentiation of human embryonic lens cells into lens-like structures. We used high throughput genomic analysis and bioinformatic strategies to demonstrate that specific autophagy and mitophagy pathways operate at discrete stages of lens differentiation to orchestrate the loss of organelles required for lens cell maturation

and transparency. We have defined key autophagy/mitophagy proteins required for the specific elimination of lens mitochondria during lens differentiation (BNIP3L and Parkin) and have begun to examine how these proteins link mitochondrial elimination with that of other lens organelles. We discovered that mutation of at least one autophagy gene (FYCO1) causes inherited human cataract formation. We discovered that the lens nucleus is degraded during lens differentiation by a novel structure that we have named the nuclear excisosome. We have demonstrated that specific modifications of αB-crystallin (phosphorylation and sumoylation) specify its mitochondrial localization and that its translocation to the mitochondria preserves mitochondrial function in RPE cells. We have demonstrated that αB-crystallin specifically interacts with cytochrome c in the mitochondria where it regulates low levels of caspase 3 activity required for lens differentiation. We demonstrated that specific chromatin remodeling proteins are required for regulating differentiation during lens development.

B. Positions and Honors

Positions and Employment

1987-1991 Research Associate, Center for Advanced Research in Biotechnology, NIST, Rockville, MD
1991-1995 Intramural Research Fellow, Laboratory of Molecular and Developmental Biology, NEI, NIH
1995-1997 Senior Staff Fellow, Laboratory of Molecular and Developmental Biology, NEI, NIH
1997-1999 Assistant Research Ophthalmologist, Jules Stein Eye Institute, Los Angeles, CA
1999-2003 Assistant Professor, Dept of Biology, West Virginia University, Morgantown, WV
2004-2007 Associate Professor, Dept of Biomedical Sciences, Florida Atlantic University, Boca Raton, FL
2005-2007 Associate Chair, Dept of Biomedical Sciences, Florida Atlantic University, Boca Raton, FL
2007-present Professor, Dept of Biomedical Sciences, Florida Atlantic University, Boca Raton, FL
2013-2016 Director of Graduate Programs, Charles E. Schmidt College of Medicine
2016-present Assistant Dean of Graduate Programs, Charles E. Schmidt College of Medicine

Other Experience

2007-2010: ARVO Lens Program Committee Member (as Chair 2010)
2008 Young Investigator Session Organizer ICER Meeting
2010: Co-Chair Lens Program Organizer ICER Meeting`
2012: Ad-Hoc Reviewer: NIH Special Emphasis Study Section (As Chair)
2010-2013 ARVO Members in Training Committee
2013: Ad-Hoc Reviewer: NIH Special Emphasis Panel
2013: Ad-Hoc Reviewer: NIH Basic Visual Science Study Section
2013: Invited Participant: National Eye Institute Audacious Goals Planning Meeting
2012-present Editorial Board Member Molecular Vision
2013 Ad-Hoc Reviewer: NIH Special Emphasis Panel
2014 Ad-Hoc Reviewer: NIH Special Emphasis Panel
2014 Ad-Hoc Reviewer: NIH Basic Visual Science Study Section
2014-presentt International Society Eye Research Members in Training Committee
2015 Ad-Hoc Reviewer: NIH Basic Visual Science Study Section
2016 Ad-Hoc Reviewer: NIH Basic Visual Science Study Section
2015 Ad-Hoc Reviewer: NIH Basic Visual Science Study Section
present Chair NIH Special Emphasis Vision study section
present Co-Chair International Conference on the Lens Bi-annual meeting

Honors

2002: Cataract Research Award- National Foundation for Eye Research- (May 20-ARVO)
2003: Eberly College of Arts and Sciences, West Virginia University-Outstanding Researcher Award.
2005: Charles E. Schmitt College of Science -Researcher of the Year, FAU
2005: Florida Atlantic University- Associate Professor Researcher of the Year
2012: Silver Fellow: Association for Research in Vision and Ophthalmology
2014: Gold Fellow: Association for Research in Vision and Ophthalmology

C. Contribution to Science

URL for published work: http://www.ncbi.nlm.nih.gov/pubmed/?term=kantarow+m

Mechanisms Underlying Cell Survival in the Lens and Retina

Our lab has increased our understanding of how lens AND retinal pigmented epithelium (RPE) cells maintain their function upon exposure to age- and environmental-associated insults. We demonstrated that MsrA provides mitochondrial protection and increased survival of lens and RPE cells exposed to oxidative stress treatment suggesting it plays an important role in lens and retinal function. In more recent studies, we have explored novel mechanisms controlling lens cell differentiation, lens cell survival and novel functions for α-crystallin in regulation of the mitochondria and the nucleus.

1. McGreal RS, Kantorow WL, Chauss DC, Wei J, Brennan LA, **Kantorow M**. αB-crystallin/sHSP protects cytochrome c and mitochondrial function against oxidative stress in lens and retinal cells. Biochim Biophys Acta. 2012 Jul;1820(7):921-30.
2. Brennan LA, **Kantorow M**. Mitochondrial function and redox control in the aging eye: role of MsrA and other repair systems in cataract and macular degenerations. Exp Eye Res. 2009 Feb;88(2):195-203.
3. **Kantorow M, Hawse JR, Cowell TL, Benhamed S, Pizarro GO, Reddy VN, Hejtmancik JF.** Methionine sulfoxide reductase A is important for lens cell viability and resistance to oxidative stress.
4. Proc Natl Acad Sci U S A. 2004 Jun 29;101(26):9654-9. Epub 2004 Jun 15

Development and Maintenance of the Lens

In early studies, we identified those transcription factor binding (promoter binding site analysis) and DNA structural requirements (in vivo chromatin accessibility) required for expression of the small heat-shock protein αA-crystallin that is required for lens transparency. We discovered how key post-translational mechanisms (phosphorylation and methionine oxidation) regulate the chaperone and protective functions of α-crystallin. We used high-throughput genomic and computational biology approaches to discover key genes altered upon human and mouse cataract formation (metallothionein II, Protein phosphatase 2a, osteonectin, ARK receptor kinase and others). We established that key mitochondrial repair enzymes and reducing systems (MsrA, TXNL6) are required to maintain lens mitochondrial function, lens cell homeostasis and lens cell survival.

1. Chauss D, Basu S, Rajakaruna S, Ma Z, Gau V, Anastas S, Brennan L, Hejtmancik JF, Menko AS, **Kantorow M.** Differentiation state-specific mitochondrial dynamic regulatory networks are revealed by global transcriptional analysis of the developing chicken lens. *Genes, Genomes and Genetics G3 (Bethesda)*. 2014. 13;4(8):1515-27.
2. Yang C, Yang Y, Brennan L, Bouhissira E, **Kantorow M,** Cvekl A. Efficient generator of lens progenitor cells and lentoid bodies from human embryonic stem cells in chemically defined conditions. *FASEB J.* 2010. 24:3274-83.
3. Brennan LA, **Kantorow M.** Mitochondrial function and redox control in the aging eye: role of MsrA and other repair systems in cataract and macular degenerations. *Experimental Eye Research. 2009* Feb;88(2):195-203.
4. He S, Limi S, McGreal RS, Xie Q, Brennan LA, Kantorow W, Kokavec J, Majumdar R, Hou H, Edelmann W, Liu W, Padam RA, Zavadil J, **Kantorow M,** Skoultchi Am Stopka T, Cvekl A. Chromatin remodeling enzyme Snf2h/Smarca5 regulates embryonic lens differentiation and denucleation. *Development*. 2016. 143(11):1937-47.

Role of Mitochondrial Proteins in Ocular Function and Development

We found that deletion of MsrA results in oxidative stress-induced cataract formation. We demonstrated that other repair (MsrB1, MsrB2 and MsrB3) and antioxidant (peroxiredoxin 3) enzymes defend lens cells against oxidative stress damage. We demonstrated that MsrA can repair and restore the chaperone function of α-crystallin. We also discovered that MsrA repairs lens cytochrome c to prevent its release from the mitochondria and the initiation of apoptosis. Finally, we demonstrated that MsrA provides mitochondrial protection and increased survival of RPE cells exposed to oxidative stress treatment suggesting it plays an important role in RPE and retinal function. In more recent studies, we have explored novel mechanisms controlling lens cell differentiation, lens cell survival and novel functions for α-crystallin in regulation of the mitochondria and the nucleus. We found that the same molecular mechanisms used by the RPE to phagocytize photoreceptor cell debris are employed by lens epithelial cells to phagocytize apoptotic and necrotic debris to ensure lens cell survival. We defined the conditions and molecular events required for differentiation of human embryonic lens cells into lens-like structures. We used high throughput genomic analysis and bioinformatic strategies to demonstrate that specific autophagy and mitophagy pathways operate at discrete stages of lens differentiation

to orchestrate the loss of organelles required for lens cell maturation and transparency. We have defined key autophagy/mitophagy proteins required for the specific elimination of lens mitochondria during lens differentiation (BNIP3L and Parkin) and have begun to examine how these proteins link mitochondrial elimination with that of other lens organelles.

1. Brennan LA, Khoury J, **Kantorow M.** Parkin elimination of mitochondria is important for maintenance of lens cell ROS levels and survival upon oxidative stress exposure. *Biochimica Biophysica Acta (BBA)* Molecular Basis of Disease. 2017.
2. McGreal R, Brennan LA, Kantorow WL, Wilcox J, Wei J, Chauss D, **Kantorow M.** Chaperone-independent mitochondrial translocation and protection by αB-crystallin in RPE cells. *Experimental Eye Research*. 2013. 110:10-7.
3. McGreal R, Kantorow WL, Chauss D, Wei J, Brennan LA, **Kantorow M.** αB-crystallin/sHSP protects cytochrome c and mitochondrial function against oxidative stress in lens and retinal cells. *Biochim Biophys Acta.* 2012. 1820(7):921-30
4. Sagher D, Brunell D, Hejtmancik JF, **Kantorow M,** Brot N, Weissbach H Thionein can serve as a reducing agent for the methionine sulfoxide reductases. Proc Natl Acad Sci U S A. 2006 Jun 6;103(23):8656-61.

D. Research Support

Current:

NIH R01 EY 026478 **2015-2019**
Repurposing Classical Death Pathways for Signalling Roles in Lens Differentiation
The goal of this study is to identify novel lens cell differentiation pathways.
Senior/Key Person & their responsibilities: Kantorow, M, Role: PI and Menko, A. S. Role: PI

Completed:

The Rand Eye Institute **2014-2015**
Mechanisms of Ocular Differentiation
The goal of this study was to establish the mechanisms regulating RPE development.
Senior/Key Person & their responsibilities: Kantorow, M. Role: PI

Florida Atlantic University Research Corporation **2014-2015**
Mechanisms of Retinal Cell Differentiation
The goal of this study was to establish the pathways that initiate the differentiation of embryonic stem cells into RPE cells.
Senior/Key Person & their responsibilities: Kantorow, M. Role: PI

NIH R01 EY13022 (renewal) **2009-2015**
Molecular Analysis of Microdissected Human Lenses (Renewal)
The goal of this study was to determine function of the mitochondrial repair gene MsrA in α-crystallin chaperone and mitochondrial function, lens cell function and lens transparency.
Senior/Key Person & their responsibilities: Kantorow, M Role: PI

NIH R01 EY13022 (renewal) **2004-2009**
Molecular Analysis of Microdissected Human Lenses (Renewal) The goal of this study was to identify genes required for lens homeostasis and transparency.
Senior/Key Person & their responsibilities: Kantorow, M Role: PI

NIH R01 EY13022 **1999-2004**
Molecular Analysis of Microdissected Human Lenses (Renewal)
The goal of this study was to identify and functional characterize genes causing cataract.
Senior/Key Person & their responsibilities: Kantorow, M Role: PI

Randy D. Blakely, Ph.D.
Professor of Biomedical Science, Director of FAU Brain Institute

Education

- B.A. in Philosophy summa cum laude from Emory University
- Ph.D. in Neuroscience from the Johns Hopkins School of Medicine
- Postdoctoral training at the Yale/HHMI Center for Molecular Neuroscience

Research Interests

- Dr. Blakely has pursued studies of the genetics, structure, regulation and pathophysiology of synaptic transporters, work that appears in more than 300 research articles and scholarly reviews. In recent years, his work has focused on the identification of transporter mutations that alter neurotransmitter inactivation and/or drug recognition, leading to the generation of animal models of multiple neuropsychiatric disorders such as autism, OCD, ADHD and Major Depression.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: **Randy D. Blakely**

eRA COMMONS USER NAME: **blakelrd**

POSITION TITLE: **Professor of Biomedical Science, Charles E. Schmidt College of Medicine**

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Emory University	B.A.	05/1981	Philosophy
The Johns Hopkins School of Medicine	Ph.D.	12/1986	Neuroscience
HHMI/Yale University School of Medicine	Postdoc	08/90	Molecular Neurobiology

A. Personal Statement

My research focuses on the molecular neurobiology of neurotransmitter signaling at central and peripheral synapses, and the contribution made by membrane transporter proteins to synaptic neurotransmitter homeostasis and brain disorders. Our work began as the molecular era of neurotransmitter transporter biology was beginning, efforts we contributed to in the cloning multiple human, rodent and invertebrate neurotransmitter transporters, including norepinephrine, dopamine, serotonin, proline, taurine and choline transporters. We have uncovered multiple regulatory pathways that function in cells to control the surface expression and transport capacity of neurotransmitter transporter proteins, basic research findings that merged with translational studies of transporter protein contributions to autism, ADHD, OCD, depression, cardiovascular and gastrointestinal disorders. My work has led to the creation of important animal models that allow for the study of neurotransmitter transporter mutations *in vivo* and how genetic alterations impact physiology and behavior and can support the development of novel diagnostic and therapeutic strategies. With reference to the current R25 application, **Miami Neural Engineering (MiNE) Training Program to Develop a Diverse Research Workforce**, I have significant experience in mentoring trainees at the graduate, postdoctoral and faculty level and was for more than a dozen years the Director of the Vanderbilt Training Program in Functional Neurogenomics, where I worked to expose my trainees to cutting edge technologies and career development opportunities ranging from the diversity of career pathways to issues related to personnel and laboratory management. As Executive Director of the FAU Brain Institute, I now lead programs seeking to expand neuroscience research and training programs at our university and to link our efforts to Research Institute and University Affiliates. I am delighted to contribute my energies to this impactful initiative.

B. Positions and Honors

Positions: Assistant Professor, Dept of Anatomy and Cell Biology, Emory University (1990-1994), Associate Professor, Dept. of Anatomy and Cell Biology, Emory University (1995), Associate Professor, Dept. of Pharmacology, Vanderbilt School of Medicine (1995-1998); Director, Center for Molecular Neuroscience, Vanderbilt School of Medicine (1996-2011), Professor, Dept. of Pharmacology, Vanderbilt School of Medicine (1997-present); Director, NIMH Cellular and Molecular Neuroscience Training Program (2001-2002); Director, Neurogenomics Postdoctoral Training Program (2002-present); Professor of Psychiatry, Vanderbilt School of Medicine (2004-present); Director (Interim), Vanderbilt Brain Institute (2006-2007); Director, NIMH Silvio O. Conte Center for Neuroscience Research (2007-present); NIMH Board of Scientific Counselors (2011-2014, Chair 2012-2014), Professor, Biomedical Sciences, Florida Atlantic University (2016-present), Executive Director, FAU Brain Institute (2016-present), National Advisory Mental Health Council (2017-present).

Other Experience and Professional Memberships: Society for Neuroscience, American Association for the Advancement of Science (Elected Fellow)**,** American Society for Pharmacology and Experimental Therapeutics (Member)**,** American Society of Human Genetics (Member)**,** American College of Neuropsychopharmacology (Elected Fellow), International Society for Psychiatric Genetics (Member), Middle Tennessee Chapter, Society for Neuroscience (Member), Brain and Behavioral Research Foundation (Scientific Council), Genetics Society of America (Member), International Behavioral and Neural Genetics Society (Member), Vanderbilt Institute of Chemical Biology (Investigator), Vanderbilt Institute of Chemical Biology (Investigator), Vanderbilt Kennedy Center for Research on Human Developmental Disabilities (Investigator), Dana Alliance for Brain Initiatives (elected Member)

Honors: National Merit Scholar (1977), John Gordon Stipe Scholar, Emory University (1977-1981), Macy Fellowship for Foreign Study (1981), National Finalist, Rhodes Scholarship (1981), *Phi Beta Kappa* (1981), Rotary Scholar (1981), *Sigma Xi* Research Award (1982*),* Mallinckrodt Young Investigator Award (1991-1994), Herrick Award, Outstanding Young Investigator in Neuroscience (1992), Allan D. Bass Endowed Chair, Dept. of Pharmacology, Vanderbilt School of Medicine (1995-present), Grass Lecturer, University of British Columbia (1996), NARSAD Established Investigator Award (1996), Grass Lecturer, Univ. Of Mississippi Med. Ctr., (1997), Vice-Chair, Catecholamine Gordon Conference (1999), ACNP Daniel H. Efron Award for Excellence in Basic Research (1999), Chair, Catecholamine Gordon Research Conference (2001), ASPET Ray Fuller Lecturer (2003), Charles R. Park Prize for Research, Vanderbilt University (2003), ASPET Julius Axelrod Symposium Lecturer (2004), NIMH MERIT Award (2004), NARSAD Distinguished Investigator Award (2005), Alzheimer's Association Zenith Award (2005), Inaugural Ray Fuller Lecturer in the Neurosciences, ASPET (2005), Grass Lecturer, Ohio State (2007), LSU Chancellor's Lecturer in Neuroscience (2007), Julius Axelrod Prize, ASPET (2008), ASPET-Astellas Award in Translational Pharmacology (2008), F. Peter Guengerich Award for Postdoctoral Mentoring, Vanderbilt University (2009), Fellow-American Academy for the Advancement of Science (2009), F.C. MacIntosh Endowed Lectureship, McGill University (2011), Robert M. Hearin Distinguished lectureship, University of Mississippi Medical School (2013), Booney Vance Memorial Lecture, Quinlan College of Medicine, East Tennessee State Univ (2013), SFB35 Symposium, Keynote Speaker (2013), Brain In Flux ISN Satellite Meeting, Keynote Speaker (2013), Chancellor's Award for Research, Vanderbilt University (2013), Cozart Heritage Lecture, Meharry Medical College (2014), University of Montana Innovation and Imagination, Keynote Speaker (2014), Founder's Lecturer, American Academy of Child & Adolescent Psychiatry (2014), Delores Shockley Award for Minority Research Mentorship (2015). Romer Foundation for Research on Childhood Genetic Diseases of the Brain (2017).

C. Contributions to Science

1. As an undergraduate and predoctoral student at Emory University, working in the laboratories of Dr. Raymond Duvarney, Dr. James Herndon, Dr. Joseph Justice and Dr. Daryl Neill I pursued studies related to systemic hormonal changes and CNS neurotransmitter homeostasis in response to behavioral and pharmacological challenges in rodents and non-human primates,. With Dr. Herndon, I utilized telemetry-based sampling to determine changes in testosterone behavior during reproductive behavior in male monkeys. With Drs. Herndon, Justice and Neill, I utilized *in vivo* voltammetry to obtain the first measures of extracellular dopamine in the striatum of the rhesus monkey. To broaden the utility of *in vivo* voltammetry, I worked with Dr. Duvarney to develop the first microcomputer controlled system for multi-electrode *in vivo* voltammetry. Using *in vivo* microdialysis, I was among the first to monitor changes in extracellular dopamine, dopamine metabolites and ascorbic acid in the brain of freely moving rodents.

Herndon, J.G., Allen, W.C., and **Blakely, R.D.** Increases in testosterone levels and in copulatory behavior of male rhesus monkeys following treatment with human chorionic gonadotrophin, **Horm Behav**, 14:337-347, 1980. [PMID: 7216185]

Lindsay, W.S., Herndon, J.G., Jr., **Blakely, R.D.**, Justice, Jr., J.B., and Neill, D.B. Voltammetric recording from neostriatum of behaving rhesus monkey, **Brain Res,** 220:391-396, 1981. [PMID: 7284764]

Blakely, R.D., and Duvarney, R.C. A microcomputer controlled system for monitoring multiple voltammetric electrodes *in vivo*, **Brain Res Bull**, 10:315-320, 1983. [PMID: 6133600]

Blakely, R.D., Wages, S.A., Justice, Jr., J.B., Herndon, J.G., and Neill, D.B. Neuroleptics increase striatal catecholamine metabolites but not ascorbic acid in dialyzed perfusate, **Brain Res**, 308:1-8, 1984. [PMID: 6206916]

2. In my doctoral studies at the Johns Hopkins School of Medicine working with Dr. Joseph Coyle, I evaluated the neurotransmitter status of the brain peptide N-acetyl-aspartyl-glutamate (NAAG). In this effort, I discovered that the peptide was rapidly cleaved to produce free glutamate by an enzyme that postdoctoral fellow Michael Robinson and I purified and characterized as N-acetylated-alpha-linked acidic dipeptidase (NAALADase), also known as glutamate carboxypeptidase II (also prostate specific antigen (PSA). I determined that the release of free glutamate. Drugs that block the activity of NAALADase were later found to prevent ischemic brain injury and be effective in models of ALS and neuropathic pain, among other uses. I also generated antibodies against NAAG that provided the first cellular localization of the peptide, including its synthesis in multiple classes of glutamatergic and non-glutamatergic neurons.

Blakely, R.D., Ory-Lavollée, L., Thompson, R.C., and Coyle, J.T. Synaptosomal transport of radiolabel from N-acetyl-aspartyl-[^{3}H]glutamate suggests a mechanism of inactivation of an excitatory neuropeptide, **J Neurochem**, 47:1013-1019, 1986. [PMID: 2875126]

Blakely, R.D., Ory-Lavollée, L., Grzanna, R., Koller, K.J., and Coyle, J.T. Selective immunocytochemical staining of mitral cells in rat olfactory bulb with affinity purified antibodies against N-acetyl-aspartyl glutamate, **Brain Res**, 402:373-378, 1987. [PMID: 2435366]

Robinson, M.B., **Blakely, R.D.**, Couto, R., and Coyle, J.T. Hydrolysis of the brain dipeptide N-acetyl-L-aspartyl-L-glutamate: Identification and characterization of a novel N-acetylated a-linked acidic dipeptidase activity from rat brain, **J Biol Chem**, 262:14498-14506, 1987. [PMID: 3667587]

Blakely, R.D., Robinson, M.B., Thompson, R.C., and Coyle, J.T. Hydrolysis of the brain dipeptide N-acetyl L-aspartyl-L-glutamate: Subcellular and regional distribution, ontogeny, and the effect of lesions on N-acetylated-alpha-linked acidic dipeptidase activity, **J Neurochem**, 50:1200-1209, 1988. [PMID: 3346674]

3. As a postdoctoral fellow in the laboratory of Dr. Susan Amara and the HHMI/Yale University Center for Molecular Neuroscience, I pursued the expression cloning of the norepinephrine transporter (NET, *SLC6A2*). As an independent investigator, I cloned and characterized multiple neurotransmitter transporter genes, including those encoding serotonin, dopamine, and choline transporters, and developed novel animal models to study contributions of transporter function and dysfunction *in vivo*.

Pacholczyk, T., **Blakely, R. D.**, and Amara, S. G. Expression cloning of a cocaine- and antidepressant-sensitive human noradrenaline transporter, **Nature**, 350:350-354, 1991. [PMID: 2008212]

Blakely, R.D., Berson, H.E., Fremeau, Jr., R.T., Caron, M.G., Peek, M.M., Prince, H.K., and Bradley, C.C. Cloning and expression of a functional serotonin transporter from rat brain, **Nature**, 354:66-70, 1991. [PMID: 1944572]

Nass, R., Hall, D.H., Miller, III, D.M., and **Blakely, R.D.** Neurotoxin-induced degeneration of dopamine neurons in *Caenorhabditis elegans*, **Proc Natl Acad Sci USA**, 99:3264-3269, [PMID: 11867711]

Ferguson, S.M., Bazalakova, M., Savchenko, V., Tapia, J.C., Wright, J., **Blakely, R.D.** Lethal impairment of cholinergic neurotransmission in hemicholinium-3-sensitive choline transporter knockout mice, **Proc Natl Acad Sci USA**, 101:8762-8767, 2004. [PMID: 15173594]

4. For more than 25 years since founding my laboratory, I have worked to elucidate molecular mechanisms that define the gene and protein networks underlying transporter regulation, utilizing classical biochemical approaches and pursuing insights from model genetic systems (*C. elegans* and mouse).

Ramamoorthy, S. and **Blakely, R.D.** Phosphorylation and sequestration of serotonin transporters differentially modulated by psychostimulants, **Science**, 285:763-766, 1999. [PMID:10427004]

Carneiro, A.M.D., Airey, D.C., Thompson, B., Zhu, C., Lu, L, Chesler, E.J., Erikson, K.M., **Blakely, R.D.,** Functional coding variation in recombinant inbred mouse lines reveals novel serotonin transporter-associated phenotypes, **Proc Natl Acad Sci USA**, 106:2047-2052, 2009. [PMID: 19179283, PMCID: 2632716]

Ye, R., Carneiro. A.M.D., Airey, D., Sanders-Bush, E.,, Han, Q., Zhang, B., Williams, R.W., Lu, L., Wang, J., Zhang, B., **Blakely, R.D.** Quantitative trait loci mapping and gene network analysis implicate protocadherin-15 as a determinant of brain serotonin transporter expression, **Genes, Brain and Behavior**, 13: 261-275, 2014 [PMID: 24405699; PMCID: 4436591]

Hardaway, A.J., Sturgeon, S.M., Snarrenberg, C.L., Li, Z., Xu, X.C.S., Bermingham, D. P., Odiase, P., Spencer, W.C., Miller III, D. M., Carvelli, L., Hardie, S.L., **Blakely, R.D**., Glial expression of the *Caenorhabditis elegans*

gene Swip-10 supports glutamate dependent control of extrasynaptic dopamine signaling, **J. Neurosci** 35: 9409-9423, 2015 [PMID: 26109664 PMCID: 4478255]

5. A major contribution of our lab has been the elucidation of heritable variation in human neurotransmitter transporters and the demonstration *in vitro* and *in vivo* that this variation impacts transporter localization and function, providing insights into neurotransmitter-specific contributions to risk for brain disorders and their comorbidities.

Shannon, J.R., Flattem, N.L., Jordan, J., Jacob, G., Black, B.K, Biaggioni, I., Blakely, R.D., and Robertson, D. Orthostatic intolerance and tachycardia associated with norepinephrine transporter deficiency, **New Engl J. Med**, 342:541-549, 2000. [PMID: 10684912]

Sutcliffe, J.S., Delahanty, R.J., Prasad, H., McCauley, J.L., Han, Q., Jiang, L., Li, C., Folstein, S.E., Blakely, R.D. Allelic heterogeneity at the serotonin transporter gene (SLC6A4) confer susceptibility to autism and rigid-compulsive behaviors, **Am J Hum Genet**, 77:265-279, 2005. [PMID:15995945; PMCID: 1224529]

Mergy, M.A., Gowrishankar, R., Gresch, P.J., Wheeler, C.A., Davis, G.L., Jessen, T.N., Wright, J., Stanwood, G.D., Blakely, R.D. The rare DAT variant Val559 perturbs DA neuron function, changes behavior and alters *in vivo* responses to psychostimulants, **Proc Natl Acad Sci USA**, 111:E4779-88, 2014, [PMID: 25331903; PMCID: 4226116]

Margolis, K.G, Li, Z., Stevanovic, K., Saurman, V., Israelyan, N., Veenstra-VanderWeele, J., Blakely, R.D., Gershon, M.D. Serotonin transporter variant drives preventable gastrointestinal abnormalities in development and function, **J. Clin Investigation**, Apr 25. pii: 84877. doi: 10.1172/JCI84877, 2016 [PMID: 27111230; PMCID: In Progress]

Full Publication list: http://www.ncbi.nlm.nih.gov/myncbi/collections/bibliography/44851091/

D. Research Support

Ongoing Research Support:

5 R01 MH094527 (Blakely) 08/01/17-06/30/22
NIH/NIMH
Regulation of Serotonin Transporters: This project explores the ability of inflammatory cytokine and p38 MAPK signaling to impose a biased conformation on the serotonin transporter (SERT), modulating transporter activity state, and mimicking the functional impact of autism-associated SERT mutations.

5 R01 MH105094 (Blakely) 09/01/14-08/31/19
NIH/NIMH
Knock-In Mouse Model of Dopamine Dysfunction Underlying Traits of ADHD: This project explores the biochemical, physiological and behavioral perturbations in the DAT Val559 mouse model of ADHD.

SFARI Award, Simons Foundation (Blakely) 09/01/14-08/31/17
Immune p38 MAPK Activation: Convergent Mechanism Linking ASD Models: This project examines p38 MAPK as a mechanism by which maternal immune activation in a mouse model produces features of autism and whether these features show similarities to genetic insults.

Neurocrine Biosciences, Inc (Blakely) 11/01/17-04/30/18
Evaluation of the Valbenazine Analog NBI-641449 For Normalization of Locomotor and Psychostimulant Responses in the DAT Val559 Mouse Model. This project seeks to evaluate the impact of VMAT2 inhibitors on the behavioral response of DAT Val559 mice to psychostimulants.

Completed Research Support:

5 T32 MH65215 (Blakely) 07/11/01-06/30/18
NIH/NIMH
Postdoctoral Training Program in Functional Neurogenomics: This project supports the training of five postdoctoral fellows per year at Vanderbilt in the use of genomic and proteomics tools for the analysis of

neuron function and disease. Dr. Blakely was the Director of the Program. He stepped down from directing the project in May of 2016 upon relocation to FAU.

1 P50 MH096972 (Blakely) 07/01/12-06/30/17
NIH/NIMH
Silvio O. Conte Center for Neuroscience Research: Enduring Effects of Early Life Signaling: This Center grant, directed by Dr. Blakely, sought to elucidate the impact of early life changes in serotonin signaling in the brain and periphery on brain biochemistry, physiology and behavior. The Blakely Project seeks to develop conditional SERT KO and KI mouse models that permit interrogation of the role played by CNS and peripheral serotonin transporters on brain development and function.

1 R01 MH095044 (Blakely) 05/01/12-04/30/17
NIH/NIMH
Presynaptic Regulation of *C. elegans* Dopamine Transporter
This project supported both forward and reverse genetic analyses of presynaptic mechanisms that control dopamine signaling in general and the dopamine transporter in particular using the model system *C. elegans*

Dystonia Foundation (Blakely) 08/01/14-07/31/16
Development of Novel Reagents to Augment Cholinergic Signaling in Dystonia: This project sought to develop and characterize novel choline transporter antagonists for the treatment of dystonia.

Lundbeck (Blakely) 11/01/14-02/29/16
Dissection of the Role of the Presynaptic Serotonin Transporter in the Chronic Actions of Vortioxetine: This project utilized transgenic mice bearing a mutation that confers reduced antidepressant binding to SERT proteins to explore the transporter-specificity of chronic vortioxetine action.

5 R37 MH073159-09 (Blakely) 06/01/09-05/31/14
NIH/NIMH (MERIT Award)
Molecular Analysis of Presynaptic Choline Transporters: This project investigated the subcellular distribution, trafficking, and physiology of brain choline transporters using in-vitro biochemical approaches, CHT knockout mice, and transgenic *C. elegans* lines.

5 R01 MH086530 (Sarter) 07/15/10-02/28/15
NIH/NIMH
Choline Transporter Capacity Limits Motivated Behavior of Mice, Rats and Humans: This project examined the physiological and cognitive impact of genetically imposed reduction in the presynaptic choline transporter.

Lundbeck (Blakely) 11/01/13-10/31/14
Dissection of the Role of the Presynaptic Serotonin Transporter in the Acute Actions of Vortioxetine: This project utilized transgenic mice bearing a mutation that confers reduced antidepressant binding to SERT proteins to explore the transporter-specificity of acute vortioxetine action.

NeuroDetective, Inc (Blakely) 11/18/13-02/17/14
Evaluation of Novel DAT Inhibitors: Kinetics for Uptake Inhibition and Capacity for Dopamine Release: Studies were supported to test novel DAT-targeted drugs *in vitro* for possible therapeutic use in mental illness.

Lisa Brennan, Ph.D.
Research Associate Professor

Education

- B.Sc. (Honors) Biomedical Sciences, University of Ulster, Coleraine, Northern Ireland, 1992.
- Ph.D., Biomedical Sciences, University of Ulster, Coleraine, Northern Ireland, 1996.

Research Interests

- The contribution of oxidative stress to diseases of the aging eye.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.

Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Brennan, Lisa Ann	POSITION TITLE Research Associate Professor
eRA COMMONS USER NAME (credential, e.g., agency login)	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of Ulster, Northern Ireland.	BSc	1992	Biomedical Sciences
University of Ulster, Northern Ireland.	Ph.D	1996	Cancer Biology
University of Ulster, Northern Ireland.	Post-doc	1996-2000	Cancer biology
Northwestern University, Chicago, IL.	Post-doc	2000-2001	Neonatology

A. PERSONAL STATEMENT

I have worked on mitochondrial regulation for the last 15 years and for the last 8 years I have worked with Dr. Marc Kantorow at the FAU College of Medicine on eye lens mitochondrial protective, repair and mitophagy systems including novel functions for mitochondrial regulation by alpha-crystallin and regulation of mitochondrial degradation in the eye lens. I believe my almost 10 years working in the area of lens cell biology and regulatory mechanisms makes me uniquely qualified to collaborate on the successful completion of the aims proposed in this application. I have been productive in the area investigated having co-authored 11 papers on our labs only grant that expired this year and is my sole means of support. I am particularly excited about this proposal since the aims proposed will establish entirely new mechanisms for initiation of lens cell differentiation, the role of alpha-crystallin in lens cell differentiation initiation, the role of mitochondrial membrane potential in lens cell differentiation, novel signaling requirements for initiation of lens cell differentiation and formation of the organelle-free zone of the lens. I am particularly excited about our collaboration with Dr. Menko who is a pioneer in the area of signal transduction and whose knowledge and expertise perfectly complements and balances the skills of our laboratory. Our laboratory is state of the art and we are experts at primary chick lens culture, chick lens explant analysis, molecular biology of lens cells, biochemistry of lens cells, siRNA and shRNA gene silencing, RCAS expression in embryonic chicken lenses and all aspects of lens mitochondrial biology and alpha-crystallin function. We are extremely well-equipped with a state of the art multi-laser confocal microscope and imaging station just 50-feet from our physical lab. We have developed and in many cases had to invent the approaches, techniques and assays proposed in this application making us uniquely qualified to carry out the work. Their utility for the success of the aims proposed is exemplified by the large amount of preliminary data we have generated for this application and the high number of peer-reviewed publications relevant to this application. The multiple papers we have co-authored with Dr. Menko attests to our ability to successfully collaborate.

Positions and Employment

1996-2000 Postdoctoral Research Officer, Biomedical Sciences, University of Ulster, Northern Ireland.
2000-2001 Research Fellow, Feinberg School of Medicine, Northerwestern University, Chicago, IL.
2001-2007 Research Scientist, Randox Laboratories, Crumlin, Northern Ireland.
2007-present Research Associate Professor, Dept of Biomedical Sciences, Florida Atlantic University, Boca Raton, FL

Other Experience

Reviewer - Experimental Eye Research

Reviewer - International Journal of Radation Biology

Reviewer - Cell Biology and Toxicology

Reviewer - International Journal of Biological Sciences

Professional Memberships

American Association for Research in Vision and Ophthalmology.

International Society for Eye Research

C. SELECTED PEER-REVIEWED PUBLICATIONS (Selected from 52 peer-reviewed publications)

MOST RELEVANT MANUSCRIPTS TO THE CURRENT APPLICATION

Papers (most to least recent):

1. **Brennan LA**, Chauss D, Kantorow M. Integrin aVb5-mediated Phagocytosis by Eye Lens Epithelial Cells Enhances Cell Viability Under Apoptotic Conditions. Journal of Biological Chemistry. *In revision.*
2. Chauss D, Basu S, Rajakaruna S, Ma Z, Gau V, Anastas S, **Brennan LA**, Hejtmancik JF, Menko AS, Kantorow M. Differentiation state-specific mitochondrial dynamic regulatory networks are revealed by global transcriptional analysis of the developing chicken lens. G3 (Bethesda). 2014 Jun 13. pii: g3.114.012120.
3. Costello MJ**, Brennan LA**, Basu S, Chauss D, Mohamed A, Gilliland KO, Johnsen S, Menko AS, Kantorow M. Autophagy and mitophagy participate in ocular lens organelle degradation. Exp Eye Res. 2013 Nov;116:141-50.
4. **Brennan LA,** McGreal RS, Lee Kantorow W, Wilcox, JD, Wei J, Chauss DC, Kantorow M. Chaperone-independent mitochondrial translocation and protection by αB-crystallin in RPE cells. Exp Eye Res. 2013 May;110:10-7.
5. **Brennan LA**, Kantorow WL, Chauss D, McGreal RS, He S, Matucci L, Wei J, Riazuddin SA, Cvekl A, Hejtmancik JF, Kantorow, M. Spatial expression patterns of autophagy genes in the eye lens and induction of autophagy in lens cells. Molecular Vision 2012; 18:1773-1786.
6. McGreal RS, Lee Kantorow W, Chauss DC, Wei J, **Brennan LA**, Kantorow M. αB-crystallin/sHSP protects cytochrome c and mitochondrial function against oxidative stress in lens and retinal cells. Biochim Biophys Acta. 2012 Jul; 1820(7):921-30. Epub 2012 Apr 12.
7. Yang C, Yang Y, **Brennan L**, Bouhassira EE, Kantorow M, Cvekl A. Efficient generation of lens progenitor cells and lentoid bodies from human embryonic stem cells in chemically defined conditions. FASEB J. 2010 Sep; 24(9):3274-83. Epub 2010 Apr 21.
8. **Brennan LA**, Lee W, Kantorow M. TXNL6 is a novel oxidative stress-induced reducing system for methionine sulfoxide reductase a repair of α-crystallin and cytochrome C in the eye lens. PLoS One. 2010 Nov 4; 5(11):e15421.

9. **Brennan LA**, Lee W, Giblin FJ, David LL, Kantorow M. Methionine sulfoxide reductase A (MsrA) restores alpha-crystallin chaperone activity lost upon methionine oxidation. Biochim Biophys Acta. 2009 Dec; 1790(12):1665-72. Epub 2009 Sep 3.
10. **Brennan LA**, Lee W, Giblin F and Kantorow M. Deletion of mouse MsrA results in HBO-induced cataract: MsrA repairs mitochondrial cytochrome c. Mol. Vis. 2009 15:985-999.
11. Dizon, MLV, **Brennan LA,** Black SM. Ethanol Induces Cytotoxic Oxidative Stress in PC12 Cells: Protection by Reactive Oxygen Species Scavengers. Journal of Pharmacology and Toxicology 2006; 1 (5): 418-428.
12. Wedgwood S, Steinhorn RH, Bunderson M, Wilham J, Lakshiminsushimha S, **Brennan LA** and Black SM. Increased hydrogen peroxide downregulates soluble guanylate cyclase in the lungs of lambs with persistent pulmonary hypertension of the newborn. Am J Physiol Lung Cell Mol Physiol. 2005 Oct; 289(4):L660-6. Epub 2005 Jun 3.
13. Ravi, K., **Brennan, LA**, Levic, S, Ross, PA and Black SM. S-nitrosylation of endothelial nitric oxide synthase is associated with monomerization and decreased enzyme activity. Proc. Natl. Acad. Sci. U.S.A. 2004 Feb 24; 101(8):2619-24
14. Wainwright MS, **Brennan LA**, Dizon ML, Black SM. p21ras activation following hypoxia-ischemia in the newborn rat brain is dependent on nitric oxide synthase activity but p21ras does not contribute to neurologic injury. Dev Brain Res. 2003 Dec 19; 146(1-2):79-85.
15. **Brennan LA**, Wedgwood S, Bekker JM, Black SM. Nitric oxide activates p21ras and leads to the inhibition of endothelial NO synthase by protein nitration. DNA Cell Biol. 2003 May; 22(5):317-28.
16. **Brennan LA,** Steinhorn RH, Wedgwood S, Mata-Greenwood E, Roark EA, Russell JA, Black SM. Increased superoxide generation is associated with pulmonary hypertension in fetal lambs: a role for NADPH oxidase. Circ Res. 2003 Apr 4; 92(6):683-91.
17. **Brennan LA**, Wedgwood S, Black SM. The overexpression of catalase reduces NO-mediated inhibition of endothelial NO synthase. IUBMB Life. 2002 Nov; 54(5):261-5.
18. **Brennan LA**, Wedgwood S, Bekker JM, Black SM. The overexpression of copper-zinc superoxide dismutase protects NOS III from nitric oxide-mediated inhibition. DNA Cell Biol. 2002 Nov; 21(11):827-38.
19. **Brennan, LA**, Morris, GM., Wasson, GR, Hannigan, BM and Barnett, YA. The effect of vitamin C or vitamin E supplementation on basal and H_2O_2-induced DNA damage in human lymphocytes. Br J Nutr. 2000 84(2):195-202.
20. **Brennan, LA**, Hannigan, BM and Barnett, YA. The Effect of Antioxidant Supplementation on the Oxidant-Induced Stress Response in Human Lymphocytes. Biochemical Society Transactions. 1996 24 (1): S75.
21. O'Farrell, F, **Brennan, LA**, Barnett, YA and Hannigan, BM. An Investigation of the Oxidative Stress Response in Human Lymphoid Cells. British Journal of Radiobiology. 1995 68 (809): 559.
22. Barnett, YA, **Brennan, LA**, O'Farrell, F. and Hannigan, BM. The Oxidant Induced Stress Response in Lymphoid Cells. Biochemistry and Molecular Biology International. 1995 37 (2): 273-281.

Reviews (most to least recent):

1. Oxidative stress defense and repair systems of the ocular lens. **Brennan LA**, McGreal RS, Kantorow M. *Frontiers in Bioscience (Elite Ed).* 2012 Jan 1;4:141-55. Review.

2. Mitochondrial function and redox control in the aging eye: role of MsrA and other repair systems in cataract and macular degenerations. **Brennan LA**, Kantorow M. *Experimental Eye Research. 2009* Feb;88(2):195-203. Review.

D. RESEARCH SUPPORT

NONE

Keith Brew, Ph.D.
Professor and Chair of Biomedical Science Schmidt Senior Fellow

Education

- B.Sc. (Honors), University College London, Biochemistry, London, U.K.,1962.
- Ph.D., University of London, Courtauld Inst. of Biochemistry, London, U.K., 1966

Research Interests

- Protein engineering, with an emphasis on regulatory protein-protein interactions and the role of protein dynamics in such interactions.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Brew, Keith

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

POSITION TITLE: Professor, Department of Biomedical Science

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University College, London (UK)	B.Sc.	07/62	Biochemistry
University of London	Ph.D.	01/66	Biochemistry
Duke University Medical Center	Postdoctoral	01/68	Biochemistry

A. Personal Statement

I have been interested for many years in the relationship of structure to activity and evolution in proteins. The recent research of my group has involved protein engineering, with an emphasis on specificity in regulatory protein-protein interactions and in biophysical and (collaborative) structural studies of the basis of such interactions. Currently we are studying the tissue inhibitors of metalloproteinases (TIMPs) and evolutionary relationships between vertebrate and microbial glycosyltransferases. My collaborations with Drs K Ravi Acharya (crystallography) and Hideaki Nagase (matrix biology) are reflected I these two reviews. Areas of interest include glycobiology, and bioinformatics together with the thermodynamics and dynamics of protein-protein interactions and extracellular matrix metabolism. Over many years, my research has encompassed studies of β-1,4 galactosyltransferase, the α-lactalbumin/lysozyme superfamily, protein N-glycosylation, transferrin, lipocalins, and metalloproteases and their inhibitors. I have a continuing interest in graduate education and have graduated, to date, more than 20 PhD students

.

1. Brew, K., Tumbale, P., and Acharya, K.R. (2010) Family 6 Glycosyltransferases in vertebrates and bacteria: inactivation and horizontal gene transfer may enhance mutualism between vertebrates and bacteria. *J. Biol. Chem.* **258**, 37121-37127
2. Brew, K and Nagase, H., (2010) The tissue inhibitors of metalloproteinases (TIMPs): an ancient family with structural and functional diversity. *Biochim. Biophys. Acta* **1803***, 55-71*

B. Positions and Honors

Positions and Employment

1967-74 Lecturer, Department of Biochemistry, Leeds University, UK.
1974-77 Associate Professor, Department of Biochemistry, University of Miami, FL
1977-2001 Professor, Department of Biochemistry and Molecular Biology, University of Miami, FL
2001- Schmidt Senior Fellow, and Distinguished Professor, Department of Biomedical Science, FAU
2007-2015 Chair, Department of Biomedical Science, Charles E. Schmidt College of Medicine, FAU.

Other Experiences and Professional Memberships

1974- Member, ASBMB
2004- Member, Society for Glycobiology

1976-1980 Member, NIH Physiological Chemistry Study Section
1978-83, 1996-01, 2006-11 Member, Editorial Board, Journal of Biological Chemistry
1982-87 Member, NSF Biochemistry Review Panel
1982, 84, 86, 88 Chair, DRR Shared Instrumentation Grant (NIH) Ad hoc Review Panels
1994-98 Member, American Cancer Society Personnel for Research B Review Panel

Honors

1966 Welcome Trust Research Travel Grant
1972 EMBO Research Travel Grant (1972)
1975-80 NIH Research Career Development Award

C. Contributions to Science

1. My early publications document work on lactose synthase, the enzyme system that catalyzes the biosynthesis of lactose. This emerged from my PhD studies and continued during my postdoctoral fellowship and beyond. I discovered that α-lactalbumin, a milk protein that is a component of lactose synthase, is homologous with the type-c lysozymes, and functions in modifying the substrate specificity of a β-1,4-galactosyltransferase so that it can bind glucose and catalyze lactose synthesis. Related publications report an early homology-based model for α-lactalbumin (collaboration with DC Phillips), the subcellular organization of lactose synthase that explains how lactose is secreted and its production regulated. Subsequent work included mechanistic and structure-function relationships in lactose synthase including investigations of the structural role of a Ca^{2+} required for the folding of α-lactalbumin. My continuing interest in the evolution of structure and function in proteins led to studies of serum transferrin and other proteins. that another milk protein, β-lactoglobulin, is related to proteins that bind non-polar ligands, including serum retinol binding protein. We designated the members of this large functionally divergent family "lipocalins".

a. Brew, K., Vanaman, T.C. and Hill, R.L. (1968) The role of α-lactalbumin and the A Protein in Lactose Synthesis: A Unique Mechanism for the Control of a Biological Reaction. Proc. Natl. Acad. Sci. Wash. 59, 491-497.

b. Browne, W.J., North, A.C.T., Phillips, D.C., Brew, K., Vanaman, T.C. and Hill, R.L. (1969) A Possible Three-dimensional Structure of Bovine α-Lactalbumin Based on that of Hen's Egg-White Lysozyme. J. Mol. Biol. 42, 65-86.

c. Brew, K. (1969) Secretion of α-Lactalbumin into Milk and Its Relevance to the Organization and Control of Lactose Synthetase. Nature 223, 671-672.

d. Chrysina, E.D., Brew, K., and Acharya, K.R. (2000) Crystal structures of apo- and holo- bovine reveal an effect of calcium on inter-lobe interactions. J. Biol. Chem. 275, 37021-37029.

e. Pervaiz, S. and Brew, K. (1985) Homology of ß-lactoglobulin, serum retinol-binding protein and protein HC. Science 228, 335-337.

f. Greene, L.H., Chrysina, E.D., Irons, L.I., Papageorgiou, A.C., Acharya, K.R. and Brew, K. (2001) Role of conserved residues in structure and stability: tryptophans of human serum retinol-binding protein, a model for the lipocalin superfamily. Protein Science, 10, 2301-2316.

2. My interest in glycosyltransferases still continues and is currently focused on structural, mechanistic and evolutionary relationship between metal-independent family 6 glycosyltransferases from Gram-negative bacteria and their metal-dependent homologues found in vertebrates and some prokaryotes. In collaboration with Ravi Acharya, we have explored the structural basis of catalysis and specificity of bovine α-1,3 galactosyltransferase, which catalyzes the synthesis of the α-gal epitope (xenoantigen). This enzyme is inactive in humans, resulting in the presence of a large fraction of circulating antibodies against this epitope. This enzyme and its vertebrate homologues depend on a Mn^{2+} cofactor for activity but most of their bacterial homologues, epitomized by an enzyme from *Bacteroides ovatus* are metal-independent. Products of the bacterial enzymes on the surface of gastrointestinal bacteria promote humans to synthesize anti-glycan antibodies that provide protection against potentially pathogenic enveloped viruses from other species. Our studies, involving mutagenesis and crystallography, are aimed at determining the basis of metal-dependence/independence in this family and the role of the metal in catalysis.

a. Zhang, Y., Swaminanthan, G.J., Deshpande, A., Natesh, R., Boix, E., Xie, Z., Acharya, K.R., and Brew, K. (2003), Roles of individual enzyme-substrate interactions by α -1,3 galactosyltransferase in catalysis and specificity. *Biochemistry* **42**, 13512-13521.
b. Tumbale, P., and Brew, K. (2009) Characterization of a metal-independent CAZy family 6 glycosyl-transferase from *Bacteroides ovatus. J. Biol. Chem*. 284, 25126-25134.
c. Thiyagarajan, N., Pham, TTK. Stinson, B., Sundriyal, A., Tumbale, P., Lizotte-Waniewski, M., Brew, K., and Acharya, K.R. (2012) Molecular structure of a metal-independent bacterial glycosyltransferase that catalyzes the synthesis of histo-blood group A antigen. *Scientific Reports*, 2: 940
d. Pham, T.T.K., Stinson, B., Thiyagarajan, N., Lizotte-Waniewski, M., Brew, K., and Acharya, K.R. (2014) Structures of Complexes of a Metal-independent GT6 from *Bacteroides ovatus* with UDP-GalNAc and its Hydrolysis Products. J. Biol. Chem. 289, 8041-8050.

3. Tissue inhibitors of metalloproteinases (TIMPs), a family of proteins that regulate the activities of the matrix metalloproteinases and are relevant to an array of pathological processes including tumor cell metastasis and invasion and arthritis. These proteins inhibit members of the large matrix metalloproteinase (MMP) family, as well as disintegrin metalloproteinases and have distinct roles in regulating cell growth, inhibiting angiogenesis, and in the structure of extracellular matrices. In collaboration with Dr. Hideaki Nagase, Kennedy Institute, Oxford University, and others, we have determined the structural basis of the inhibition of metalloproteinases by TIMPs and identified TIMP mutants that are selective inhibitors of metalloproteinases involved in key human diseases including osteoarthritis.

Mutational Study of the Amino-Terminal Domain of Human Tissue Inhibitor of Metalloproteinases 1 (TIMP-
a. Huang, W., Meng, Q., Suzuki, K., Nagase, H. and Brew, K. (1997) Locates an Inhibitory Region for Matrix Metalloproteinases. J. Biol. Chem. 272, 22086-22091.
b. Gomis-Ruth, F-X., Maskos, K., Betz, M., Bergner, A., Huber, R., Suzuki, K., Yoshida, N., Nagase, H., Brew, K., Bourenkow, G.B., Bartunik, H., and Bode, W. (1997) Mechanism of inhibition of the human matrix metalloproteinase stromelysin-1 by TIMP-1. *Nature* **389**, 77-81.
c. Wei, S., Kashiwagi, M., Kota, S., Xie, Z., Nagase, H., and Brew, K. (2005) Reactive site mutations in Tissue Inhibitor of Metalloproteinases-3 disrupt inhibition of matrix metalloproteinases but not tumor necrosis factor-α-converting enzyme. *J. Biol. Chem*. 280, 32877-82.
d. Bahudhanapati, H., Zhang, Y., Sidhu, S.S., and Brew, K. (2011) Phage display of Tissue Inhibitor of Metalloproteinases-2 (TIMP-2): Identification of selective inhibitors of Collagenase-1 (MMP-1). *J. Biol. Chem.* **286**, 31761-31770.
e. Wu, Y., Wei, S., Van Doren, S.R., and Brew, K. (2011) Entropy increases from different sources support the high-affinity binding of the N-terminal inhibitory domains of tissue inhibitors of metalloproteinases (N-TIMPs) to the catalytic domains of matrix metalloproteinases (MMPs) -1 and-3. *J. Biol. Chem*. **286**, 16891-16899.

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

NIH RO1GM21363-01 to -20, P.I. K Brew (1977-1994). Title: 1977-1990 “Chemical Studies of Enzymes and Proteins”. Title: 1990-1995; “Structure and Function of Lactose Synthase”
NIH 1S10RR006376 (1991) P.I. K Brew Title: “Peptide Synthesis and Amino Acid Analysis Facility” (equipment grant)
NIH RO1GM058773-01 to -04 (2000-2004) P.I. K. Brew Title: “Galactosyltransferases-Structure and Regulation” (Total budget $739,099)
NIH AR 40994 P.I. K. Brew, 35% effort; “TIMP Engineering and Application to Arthritis”. NIH, National Institute of Arthritis and Musculoskeletal and Skin Diseases. Total funding period 9/01/1991 to 3/31/2008. Years 10-14 Total budget: $2,033,551.
NIH AR 40994 P.I. K. Brew, 35% effort; Years 15-19. (4/1/09-3/31/15) Title: Structure, Function and Application of Metalloproteinase Inhibitors in Osteoarthritis. Total award: $2,623,959
James and Esther King Biomedical Research Program (Florida Department of Health) Team Science Award, P.I. K. Brew, 20% effort (co-Investigators, Drs. C Isgor and V. Iragavarapu). 7/1/08-6/30/10. Total budget $820,800.

Massimo Caputi, Ph.D.
Professor of Biomedical Science

Education

- 1992: Degree in Biological Science (magna cum laude), University of Trieste, Italy
- Ph.D., Molecular Genetics, International School for Advanced Studies, Trieste Italy 1996

Research Interests

- mRNA processing
- mRNA splicing regulation
- HIV-1 replication
- Bcl apoptotic gene family regulation

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Massimo Caputi

eRA COMMONS USER NAME (credential, e.g., agency login): CAPUTI0627

POSITION TITLE: Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Trieste (Italy)	B.S.	07/1992	Molecular Biology
International School for Advanced Science, Trieste (Italy)	Ph.D.	02/1996	Molecular Genetics
University of California, Santa Cruz, CA	Postdoc	10/2001	Molecular Biology

A. Personal Statement.

For the past 15 years my research focused on uncovering the complex regulation of HIV splicing and transcription and the connections between the cellular splicing and transcription machineries. In the past years I have characterized several key cellular factors and viral sequences required for efficient HIV-1 splicing and developed novel methodologies and reduced systems to study the transcription and regulation of the viral transcripts. Currently my research has shifted from the study of viral minigenes in model cell culture systems toward a more physiological approach with the utilization of replication competent viral strains and primary lymphocytes. Recent collaborations with Dr. Krainer at CSHL, Dr. Trautman at VGTI Florida (now HMRP), Dr. Stevenson at the University of Miami and Dr. O'Doherty (The Hospital of University of Pennsylvania) have been aimed at the development and study of novel cellular assays to characterize the activity of therapeutic compounds that target different aspects of HIV replication. I have ongoing collaborations with several experts in the fields of HIV replication and drug development both in the US and abroad as attested by my publication record. In summary, I have the experience, track record, and expertise needed to accomplish the objectives of this proposal.

B. Positions and Honors.

Employment

2007 – Present: Associate Professor, Florida Atlantic University, Biomedical Science Department, Charles E. Schmidt College of Medicine.
2003 –2007: Assistant Professor, Florida Atlantic University, Basic Science Department, College of Biomedical Science.
2004-2010: Adjunct Assistant Professor. University of Miami, Miami School of Medicine, Microbiology Department Miami (FL).
2001- 2003: Associate Research Scientist, The Johns Hopkins University, Baltimore MD.

Fellowships and Honors

European Economic Union, Erasmus fellowship (1990)
Award of the Italian Society for Biochemistry and Molecular Biology for the best degree thesis. (1992)
ISAS predoctoral fellowship (1992-1995)
Postdoctoral fellowship from the Lucille P. Markey Charitable Trust (1996)
Human Frontier Science Program long term fellowship (1997-1999)

Other Professional Experience
Grant Reviewer:
NIH/NHGRI P01 (2015)
NIH/NIAID R01- ZRG1 AARR-M (2015)
NIH/NIGMS R01- Special Emphasis Panel "Competing Revisions for Macromolecular Interactions in Cells" (2014)
NIH/NIAID R01-US-China Biomedical Collaborative research (2013)
NIH/NIAID R15-ZRG1 (2012)
Danish Council for Independent Research – DFF Mobilex grant (2015)
Biomedical Research Council AStar applications (Singapore) (2010)
AIDS FONDS. Grant Applications (The Netherlands) (2011-2012)
ACS IRG (Florida) (2011-1013)

Editorial Board member: Journal of virology since 2013-present.
Editorial Board member: PLOS One since 2013-present.
Editorial Board member: Journal Biological Science (2004 - 2007)

Ad hoc reviewer for: Journal of Biological chemistry, Nucleic Acids Research, New England Journal of medicine, PLOS Biology, PLOS One, Journal of Virology, Retrovirology, Biochemical and Biophysical Acta, Experimental Cell Research, Virus Research, FEBS letters, AIDS Research and Retroviruses, International Journal of Cancer, Scandinavian Journal of Virology, Pharmacology, Future Oncology, Journal of General Virology, mBio, PLOS Pathogens.

C. Contribution to Science.

1) Defined the role of the SRSF1 gene in HIV-1 replication. The cellular machineries regulating the transcription and processing of eukaryotic RNAs are intimately coupled but little is known on the mechanisms that couple transcription and RNA processing in HIV-1. In the past decade my lab has focused on the role of several RNA binding proteins in HIV replication and determined that the SRSF1 gene product is a key regulator of both HIV-1 transcription and splicing. We also determined that overexpression of certain subdomains of SRSF1 can shut down viral replication in cellular systems. Given the therapeutic implications of the discovery these findings have been featured in a recent editorial and a patent application has been filed. I was the sole PI in this work.

References:

Sean Paz and Massimo Caputi. (2015) SRSF1 inhibition of HIV-1 gene expression. Oncotarget. 6(23):19362-63.

Sean Paz, Michael L. Lu, Hiroshi Takata, Lydie Trautmann and Massimo Caputi. (2015) The SRSF1 RNA Recognition Motifs of are strong inhibitors of HIV-1 replication. J. Virology. 89(12):6275-86.

Sean Paz, Adrian R. Krainer and Massimo Caputi. (2014) HIV-1 transcription is regulated by splicing factor SRSF1. Nucleic Acids Res. 42:13812-13823

Provisional patent. Title "Inhibition of HIV-1 replication by delivery of the complete or partial human SRSF1 gene or protein sequence".
Inventor: Caputi Massimo.
Filed :5/05/2015

2) Described the role of hnRNP A/B proteins in HIV-1 RNA processing. This project, started during my postdoctoral training and followed up by my group during my tenure as an independent PI, led to the discovery and characterization of one of the first examples of cellular splicing silencing mechanism. Utilizing a novel set of techniques we characterized the cellular proteins (hnRNPs A/B) interacting with a viral cis-acting sequence, which is required to regulate the complex splicing of the HIV messengers and ultimately viral replication.

References:

Jacques Jean-Philippe, Sean Paz, Michael L. Lu and Massimo Caputi. (2014) A truncated hnRNP A1 isoform, lacking the RGG-box RNA binding domain, can efficiently regulate HIV-1 splicing and replication. BBA-Gene Regul. Mech. 1839(4):251-8

Joseph A. Jablonski and Massimo Caputi. (2009). Role of cellular RNA processing factors in human immunodeficiency virus type 1 mRNA metabolism, replication, and infectivity. J. Virology 83, 981-992.

Alan M. Zahler, Christian K. Damgaard, Jorge Kjems and Massimo Caputi (2004). SC35 and hnRNPs A/B binding to a juxtaposed ESE/ESS element regulates HIV-1 tat exon 2 splicing. J. Biol. Chem., 279, 10077-10084.

Massimo Caputi, Akila Mayeda, Adrian R. Krayner and Alan M. Zahler (1999) hnRNP A/B proteins are required for inhibition of HIV-1 pre-mRNA splicing. EMBO J., 18, 4060-67.

3) Determined the role and functions of the H family of heterogenous ribonucleoproteins in cellular and viral gene expression. We determined the RNA binding specificity and the mechanism of action of the 5 members of the hnRNP H protein family (hnRNP H, F, 2H9 and GRSF1) in HIV-1 splicing and replication. These studies have been followed up by several laboratories and were seminal in the structural and functional studies aimed at characterizing the activity of this protein family in cellular gene expression. I initiated these studies as a postdoctoral fellow and I have followed them up as an independent PI.

References:

Joseph A. Jablonski and Massimo Caputi. (2009). Role of cellular RNA processing factors in human immunodeficiency virus type 1 mRNA metabolism, replication, and infectivity. J. Virology 83, 981-992.

Michael Schaub, Suzette L. Lopez and Massimo Caputi. (2007) Members of the heterogeneous nuclear ribonucleoprotein (hnRNP) H family activate splicing of an HIV-1 splicing substrate by promoting formation of ATP-dependent spliceosomal complexes. J. Biol. Chem. 282, 13617-26.

Massimo Caputi and Alan M. Zahler (2002) SR proteins and hnRNP H family members regulate the splicing of the HIV-1 tev-specific exon 6D. EMBO J., 21, 845-855.

Massimo Caputi and Alan M. Zahler (2001) Determination of the RNA Binding Specificity of the Heterogeneous Nuclear Ribonucleoprotein (hnRNP) H/H'/F/2H9 Family. J. Biol. Chem., 276, 43850-43859.

4) Developed novel techniques to study RNA – RNA binding proteins interactions *in-vitro* and *in-vivo*. Starting as a postdoctoral fellow I have developed a set of novel biochemical techniques to study the binding of RNA binding proteins onto their target RNA sequences in native conditions. The technique named RAC (RNA affinity chromatography) has been utilized by over a dozen laboratories to study the binding of specific proteins onto their target RNAs in *in-vitro* conditions that resemble the complex cellular environment. More recently we have developed a novel technique based on FRET (named RB-FRET) to study RNA-protein interactions *ex-vivo* in cultured cells.

References:

Martina Huranová, Joseph A. Jablonski, Aleš Benda, Martin Hof, David Staněk and Massimo Caputi (2009) In vivo detection of RNA-binding protein interactions with cognate RNA sequences by fluorescence resonance energy transfer. RNA. 15, 2063-71.

Michael Schaub, Suzette L. Lopez and Massimo Caputi. (2007) Members of the heterogeneous nuclear ribonucleoprotein (hnRNP) H family activate splicing of an HIV-1 splicing substrate by promoting formation of ATP-dependent spliceosomal complexes. J. Biol. Chem. 282, 13617-26.

Jeremy E. Wilusz, Sean C. Devanney and Massimo Caputi. (2005) Chimeric peptide nucleic acid compounds modulate splicing of the bcl-x gene in vitro and in vivo. Nucleic Acids res. 33(20): 6547-54.

Massimo Caputi, Akila Mayeda, Adrian R. Krayner and Alan M. Zahler (1999) hnRNP A/B proteins are required for inhibition of HIV-1 pre-mRNA splicing. EMBO J., 18, 4060-67.

A full list of my published material can be found at:
https://www.ncbi.nlm.nih.gov/sites/myncbi/massimo.caputi.1/bibliography/52235418/public/?sort=date&direction=ascending

D. Research Support (for the past 3 years)**.**

NIH/NIAID: R15AI120882. 09/01/2015 – 08/31/2018
Principal Investigator: Massimo Caputi Ph.D.

Title: Inhibition of HIV-1 replication by delivery of the SRSF1 RNA Recognition Motifs
Total cost awarded: $ 443,000
The major goal of the project is to utilize peptides derived from the SRSF1 protein to inhibit HIV replication in infected primary T cells.

NIH/NIAID: 1R15AI122975 06/20/2016 –5/31/2019
Principal Investigator Asghar, Waseem; Co-PI Caputi, Massimo
Total cost awarded: $ 447,000
Development of disposable and refrigeration-free microchip technology for CD4+ T cell counting at point-of-care settings

Florida Department of Health 5/01/2017 –4/30/2018
Co-PI Caputi, Massimo; PI Asghar, Waseem
Total cost: $ 220,000
Rapid Detection of Zika Virus as Point of Care Settings

NIH/NIAID: R15 AI093229. 03/01/2011 – 02/28/2015
Principal Investigator: Massimo Caputi Ph.D.
Title: hnRNP A1 inhibition of HIV-1 replication
Total cost awarded: $ 433,000
The Major goal of this grant is to characterize the mechanism by which hnRNPA1 inhibits HIV-1 replication.

James E. Galvin, M.D., M.P.H.
Professor of Integrated Medical Science and Associate Dean for Clinical Research

Education

- 1986: B.A., Chemistry, New York University, New York, NY.
- 1988: M.S., Nutrition, Rutgers University, New Brunswick, NJ.
- 1992: M.D., Nutrition, UMDNJ-New Jersey Medical School, Newark, NJ.
- 2004: M.P.H., Nutrition, Saint Louis University, St Louis, MO

Research Interests

- Dr. Galvin's research focusing on older adults is well positioned to address a growing crisis facing US healthcare systems. Much of the discussion on aging has centered on the impact the demographic shift will have on healthcare delivery, however we must also seek to recast the role of this segment of society as a productive one. Aging, as it currently stands, is often viewed by society as a problem rather than an opportunity. However, it is now as meaningful to speak of vitality, well-being, and healthfulness as it is to the degrees of impairment, sickness, and disability. Dr. Galvin's research program is a transdisciplinary, multi-school, evidence-based approach to translational research on healthy aging based on four "cornerstones" that will drive our clinical and research themes: (1) Health Maintenance with behavioral changes to reduce risk, limit disability, and promote adaptive aging; (2) Models of Excellence testing innovative peer-led programs to improve older adult well-being; (3) Promoting Recovery linking inpatient and outpatient care to improve health outcomes, and reduce unnecessary acute care utilization; and (4) Facilitating Life Transitions by developing programs to lead a productive life upon retirement and other transition periods (e.g., widowhood, change in living situation).

Kathleen Guthrie, Ph.D.
Associate Professor of Biomedical Science

Education

- B.S. Biology, Fort Lewis College, Durango, Colorado, 1980
- B.S. Chemistry, Fort Lewis College, Durango, Colorado, 1982
- Ph.D., University of California, Irvine, 1989

Research Interests

- Neurotrophic interactions in the brain during development and regeneration
- Axon growth, targeting and sensory mapping
- Adult neural stem cells, neurogenesis and neuronal survival.
- Plasticity of sensory systems in response to brain injury, with a focus on the olfactory forebrain.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: KATHLEEN GUTHRIE, Ph.D.

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

POSITION TITLE: ASSOCIATE PROFESSOR of Biomedical Science

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Fort Lewis College, Durango, Colorado	B.S.	1980	Biology
Fort Lewis College, Durango, Colorado	B.S.	1982	Chemistry
University of California, Irvine	Ph.D.	1989	Psychobiology/ Neuroscience

A. Personal Statement

My long-term interests center on mammalian olfactory-limbic systems, brain areas that display unique and remarkable plasticity. My research goals are to investigate how these brain circuits are constantly remodeled in adults, and yet maintain normal functions in the face of adaptive, neuronal replacement through adult neurogenesis, and the accompanying reorganization of circuitry that sculpts adult networks to the meet needs of the adults in response to their environments. Identifying factors that regulate these processes holds promise for understanding how new neurons can successfully integrate into pre-established circuitry, potentially for therapeutic benefit. I am equally interested in how aberrant adult neurogenesis or circuit integration can go wrong, to the detriment of normal circuit function, as occurs when abnormal hippocampal neurogenesis contributes to seizure vulnerability.

B. Positions and Honors

Positions and Employment:

1989-1994 Postdoctoral Fellow, Dept. of Anatomy and Neurobiology, University of California, Irvine
1994-2001 Assistant Res. Prof., Dept. of Anatomy and Neurobiology, University of California, Irvine
2001-2007 Assistant Professor, Dept. of Biomedical Sciences, Florida Atlantic University
2007-present Associate Professor, Dept. of Basic Biomedical Science, Florida Atlantic University

Other Experience and Professional Memberships:

1985- Member, Society for Neuroscience
1985- Member, American Association for Chemoreceptive Sciences
1987-1989 NIMH Predoctoral Fellow, University of California, Irvine
1992 NIDCD Postdoctoral Fellow, University of California, Irvine
2002- Member, Center for Molecular Biology and Biotechnology, FAU
2004-2006 Scientific Advisory Board Member, Matrixx Intitatives, 2004-2006
2005 Grant Review, NIH/NIDCD Communications Disorders Study Section
SEP for Postdoctoral/K99 applications.
2010-2012 Member European Chemosensory Research Organization

2013	Member, Palm Beach Chapter of Society for Neuroscience
2014-	Editorial Board Member, *Scientific Reports* (Nature Publishing Group)
2016-2017	NIH Grant Review- Special Emphasis Panel, ZRG1-F03A-N(20), *Neurodevelopment, Synaptic Plasticity, and Neurodegeneration.*
2017	NIDCD Grant Review, Special Emphasis Panel, *Chemosensory Fellowships.*

Honors:

1990	Career Development Award, University of California, Irvine
1991	Winter Conference on Brain Research Fellowship Award
1992	Career Development Award, University of California, Irvine
1996	Career Development Award, University of California, Irvine
1998	Career Development Award, University of California, Irvine
1998	European Chemosensory Research Organization Fellowship Award
2001	FAU Division of Sponsored Research Initiation Award
2010	FAU College of Biomedical Science, Excellence in Teaching Award

C. Contribution to Science

1. My early work included the first demonstration that odor stimulation in awake rodents induced expression of the immediate early gene (IEG) c-fos (mRNA and protein) in specific, topographically-distributed neuronal ensembles in the main olfactory bulb. This approach was rapidly and widely adopted in the field of olfactory neurobiology, as it provided clear localization of individual activated olfactory bulb neurons, with significantly better resolution than had been obtained with other sensory mapping approaches, such as 2-deoxyglucose administration. I also showed that other IEGs, including the activity-regulated cytoskeletal protein Arc, could be sensory-induced in this system, identifying a mechanism for activity-dependent structural plasticity in activated neuronal populations. I served as primary author on the following publications:

a. Guthrie KM, Anderson AJ, Leon M, Gall C. (1993) Odor-induced increases in c-fos mRNA expression reveal an anatomical unit for odor processing in olfactory bulb. *Proc. Natl. Acad. Sci.,*USA 90: 3329-3333. PMCID: PMC46293.

b. **Guthrie KM** and Gall CM. (1995) Functional mapping of odor-activated neurons in the olfactory bulb. *Chem. Senses*, 20:271-282. *Solicited by the editors.*

c. Guthrie KM and Gall CM. (1995) Odor increases Fos in olfactory bulb neurons including dopaminergic cells*. NeuroReport.* 6:2145-2149.

d. Wilson DA, Sullivan R, Gall CM, and **Guthrie KM.** (1996) NMDA receptor modulation of lateral inhibition and c-fos expression in olfactory bulb. *Brain Research* 719: 62-71

e. Guthrie KM, Rayhanabad J, and Gall CM. (2000) Odor regulation of Arc expression in neuronal ensembles engaged in odor coding. *NeuroReport*, 11: 1809-1813.

f. **Guthrie KM** and Gall CM. (2003) Anatomical mapping of neuronal odor responses in the developing rat olfactory bulb. *J. Comp. Neurol.* 455: 56-71.

2. I documented the distribution of neurotrophic factor gene expression in forebrain areas, and demonstrated that this expression could be altered by brain lesions (repair responses) and changing neuronal activity (epileptic seizures). This included the first demonstration of induced trophic factor expression spatially-localized to regions of the dentate gyrus undergoing entorhinal cortical axon sprouting following injury. These collaborative studies emphasized the potential role of endogenous neurotrophic mechanisms in multiple forms of structural CNS plasticity. I served as corresponding author or co-author on the following publications:

a. Guthrie KM and Gall CM. (1991) Differential expression of mRNAs for the NGF-family of neurotrophic factors in the adult rat central olfactory system. *J. Comp. Neurol.* 313: 95-102.

b. **Guthrie KM**, Nguyen T, Gall CM. (1995) Insulin-like growth factor-1 mRNA is increased in deafferented hippocampus: Spatiotemporal correspondence of a trophic event with axon sprouting. *J. Comp. Neurol.* 352:147-160.
c. Gall CM, Lauterborn JC, **Guthrie KM** and Stinis CT. (1997) Seizures and the regulation of neurotrophic factor expression: Associations with structural plasticity in epilepsy. In: Neuronal Regeneration, Reorganization, and Repair, Advances in Neurology, vol. 59, F.J. Seil, Ed., Raven Press, N.Y., pp. 9-24. *Solicited by the editor.*
d. **Guthrie KM**, Woods AG, Nguyen T, Gall C. (1997) Astroglial CNTF expression is increased in fields of axonal sprouting in deafferented hippocampus. *J. Comp. Neurol.* 386: 137-148.
e. Woods AG, **Guthrie KM,** Kurwala M and Gall C. (1998) Neurotrophic responses during sprouting are attenuated in the aged rat hippocampus. *Neuroscience* 83: 663-668.

3. In recent work I have shown how chronic alterations in BDNF trophic signaling engage mechanisms that remodel functional circuitry in forebrain. Using BDNF over-expressing mice, I have quantified effects on adult stem cell proliferation, neuron survival and morphology, and functional connectivity in vivo. The impact on adult neurogenesis under both normal and pathological circumstances (mutant huntingtin expression) are minimal, however morphological effects of sustained increases in BDNF are significant. In collaboration with Dr. C. Isgor, we have documented structural remodeling in the olfactory-limbic system that compromise normal circuit function. In the hippocampus this includes significant expansion of mossy fiber innervation in CA3, increases in the numbers of dentate granule cells, and increases in granule cell spine density. These structural changes emerge in the absence of chemical or physiological seizure induction, and we have shown that they are highly correlated with the gradual emergence of spontaneous seizures. These findings demonstrate that dysregulation of endogenous trophic signaling drives aberrant functional reorganization of hippocampal networks over time, potentially by compromising the gating functions of dentate granule cell population. This would promote increased propagation of excitatory drive throughout and beyond the hippocampus. Increased BDNF levels, as well as similar morphological changes, are seen in both epileptic patients, and in those at high risk of developing seizures after traumatic brain injury. In parallel work on these BDNF mice, I have found that increased BDNF does not rescue impairments in adult neurogenesis in a mouse model of Huntington's disease. am corresponding author or co-author on the following publications:

a. Isgor C, Pare C, McDole B, Coombs P, **Guthrie K**. (2015) Expansion of the dentate mossy fiber-CA3 projection in the brain-derived neurotrophic factor enriched hippocampus. *Neuroscience*, **288**:10-23. PMC:4324623. NIHMS652724.
b. McDole B, Isgor C, Pare C, **Guthrie K**. (2015) BDNF over-expression increases olfactory bulb granule cell dendritic spine density in vivo. *Neuroscience,* 304: 146-160. doi:10.1016/j.neuroscience. 2015.07.056. PMID: 26211445. PMC4547863. NIHMS710570.
c. McCollum MH, Leon RT, Rush DB, **Guthrie KM**, Wei J. (2013) Striatal oligodendrogliogenesis and neuroblast recruitment are increased in the R6/2 mouse model of Huntington's disease. *Brain Research*, 1518:91-103. PMC3684253
d. Smail S, Bahga D, McDole B, **Guthrie, K**. (2016) Increased olfactory bulb BDNF expression does not rescue deficits in olfactory neurogenesis in the Huntington's disease R6/2 mouse. *Chem. Senses*. 41:221-232. PMID:26783111.

Additional published work listed in MyBibliography at:
http://www.ncbi.nlm.nih.gov/sites/myncbi/kathleen.guthrie.1/bibliograpahy/47609532/public/?sort=date&direction=ascending

D. Research Support

Completed: 3/3/14-12/30/16 (extended) Role: PI (K. Guthrie)
FAU Division of Research Seed Grant Award: "Trophic mechanisms promoting the emergence of pro-epileptic hippocampal circuitry".
The goal of this work is to obtain data in support of the hypothesis that increased endogenous brain-derived neurotrophic factor (BDNF) drives the age-related formation of abnormal hippocampal circuitry leading to development of spontaneous seizures in a transgenic mouse model of epilepsy.

Xupei Huang, Ph.D.
Professor of Biomedical Science

Education

- M.D., Nanjing Medical University, Nanjing, China, 1985
- Ph.D., Biochemistry, University of Paris XII, France, 1992

Research Interests

- Intracellular signal pathways, protein phosphorylation and cellular function
- Gene expression profiling and gene regulation in the heart
- Functional evaluation of cardiac genes
- Transgenic and gene knockout animal models

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Xupei Huang

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

POSITION TITLE: Professor of Biomedical Science

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Nanjing Medical University, Nanjing, China	MD.(Equal)	1982	Medicine
University of Paris XII, Creteil, France	Ph.D.	1992	Biochemistry
University of Wisconsin, Madison, WI	PostDoc	1993-1998	Physiology/Cardiology

A. Personal Statement

The long-term goal of our laboratory is to investigate the mechanisms underlying cardiomyopathies and heart failure that are related to myofibril protein mutations. Our laboratory has been among the first to begin to define the effect of cardiac troponin I (cTnI) mutation on the development of diastolic dysfunction and heart failure. As a PI, I have the expertise, leadership and motivation necessary to successfully carry out the proposed work. I have a broad background in myofibril proteins and the mutations of these proteins caused cardiac dysfunction in the heart. As a postdoctoral fellow at University of Wisconsin-Madison, I have received a comprehensive training in molecular cardiology and cardiovascular physiology. When I joined Florida Atlantic University in 2001 as a young faculty member, I had set up a research laboratory there equipped with instruments and facilities that allow us to perform cardiac function measurements at cellular, organ and whole animal levels. As PI or co-Investigator on several previous NIH- and AHA-funded grants, I laid the groundwork for the proposed research by developing *in vitro* cell-based experiments, telemetric ECG measurement on conscious mice and data analyses, and whole animal cardiac function measurement by echocardiography and P-V loop measurements. During the past 16 years, over 50 papers have been published on cardiac myofibril protein studies and I was promoted to Associate Professor in 2005 and Professor in 2012. Furthermore, I have collaborated with Dr. Jin (Wayne State University), Dr. Solaro (University of Illinois at Chicago) and Dr. Jose Pinto (Florida State University) to explore the mechanisms underlying troponin mutation caused cardiac dysfunction and inherited cardiomyopathies, such as restrictive and hypertrophic cardiomyopathies. The results obtained from the collaborative work have been recently produced several research papers in various journals in the field. The current proposal is a logical extension of the common interest from our laboratory in defining the mechanisms of diastolic dysfunction and exploring therapeutic potentials for heart failure, especially diastolic heart failure (HFpEF).

4 peer reviewed publications that highlight my qualification:

1. **Huang X.P.**, Pi YQ, Lee KJ, Henkel AS, Gregg RG, Powers PA, Walker JW. (1999) Cardiac troponin I gene knockout: A mouse model of myocardial troponin I depletion. Circulation Research, 84: 1-8. PMID: 9915769 [PubMed_Link]
2. **Huang X.P.,** Lee KJ, Riedel B, Zhang C, Lemanski LF, Walker JW (2000) Thyroid hormone regulates ssTnI inactivation in cTnI deficient mouse hearts. J. Mol. Cell. Cardiology, 32:2221-2228. PMID: 11112997 [PubMed_Link]

3. Du J., C. Zhang, J. Liu, C. Sidky, **X.P. Huang**. (2006) A point mutation (R192H) in the C-terminus of human cardiac troponin I causes diastolic dysfunction in transgenic mice. Archives of Biochemistry and Biophysics, 456:143-150.
PMID: 17027633 [PubMed Link]
4. Liu Xiaoyan., Lei Zhang, Daniel Pacciulli, Jianquan Zhao, Changlong Nan, Wen Shen, Junjun Quan, Jie Tian, **Xupei Huang**. (2016) Restrictive cardiomyopathy caused by troponin mutations: application of disease animal models in translational studies. Front. Physiology, 7:629, doi: 10.3389/fphys.2016.00629.

B. Positions and Honors

Positions and Employment

09/1985–11/1987	Assistant Professor, Preclinical Drug Research Center, Nanjing Medical Univ., Nanjing, China
11/1987–12/1988	Research Fellow, Roussel Uclaf Co., Romainville, France
09/1992–08/1993	Postdoctoral Research Fellow, Hospital Saint Lazare, Paris, France
09/1993–09/1998	Postdoctoral Fellow, Dept. of Physiology, Medical School, Univ. of Wisconsin, Madison, WI
10/1998–08/2001	Asst. Professor (research track), Dept. of Med. Phys., College of Med., Texas A&M Univ., College Station, TX
08/2001-05/2005	Assistant Professor (tenure track), Dept. of Biomedical Sciences, Florida Atlantic Univ., Boca Raton, FL Assistant Professor, Dept. of Biological Sciences, Center for Molecular Biology and Biotechnology, Florida Atlantic University, Boca Raton, FL Adjunct Assistant Professor, Department of Cellular and Molecular Pharmacology, University of Miami Miller School of Medicine, Miami, FL
05/2005-05/2012	Associate Professor (with tenure), Dept. of Biomedical Science, Florida Atlantic University, Boca Raton, FL Adjunct Associate Professor, Department of Molecular and Cellular Pharmacology, University of Miami Miller School of Medicine, Miami, FL
05/2012-	Professor (with tenure), Dept. of Biomedical Science, Charles E. Schmidt College of Medicine, Florida Atlantic University, Boca Raton, FL
2013	Visiting Professor, Dept. Pediatrics, Stanford University School of Medicine, Palo Alto, CA

Other Experience and Professional Memberships

2005	NIH-NIGMS MBRS Cardiovascular Physiology Review Panel
2009	NIH-NIGMS MBRS Neuroscience & Physiology Review Panel
2012	NIH-NHLBI ZRG1 CVRS-B (90) Grant Review Panel
2013	NIH-NHLBI ZRG1 CVRS-Q (90) Grant Review Panel
2014	NIH-NHLBI ZRG1 CVRS-Q (80) Grant Review Panel
2015	VA/ORD EPID Grant Review Panel
2016	VA/ORD EPID Grant Review Panel
2017	VA/ORD EPID Grant Review Panel
2005 - 2007	AHA-Florida/Puerto Rico Affiliate Grant Review Group 1A
2006 - 2009	AHA-National Grant Review Panel, Basic Cell Biology Group 3
2008 - 2009	AHA Region 2 Peer Review, Basic Cell & Molecular Biology 2
2010 - 2013	AHA Region 2 Peer Review, Basic Cell – Proteins & Crystallography

Professional Affiliations

Member of the Biophysical Society
Member of the American Society for Cell Biology
Professional member of the American Heart Association
Fellow of American Heart Association (FAHA)
Associate Editor and Editorial Board, *Cardiology*, since 2006

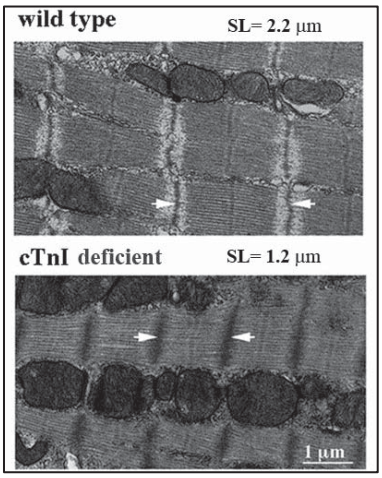
C. Contribution to Science

For past 20 years, my research mainly focuses on physiological function of myofibril proteins and pathological outcomes related to the mutations of these proteins, in particular, the thin filament protein troponin. My major contributions to science in the field include 5 aspects: 1) generate cTnI knockout mouse

model to identify the physiological function of cTnI; 2) generate transgenic mice modeling cTnI mutations in human cardiomyopathy patients; 3) using these animal models to reveal mechanisms underlying diastolic dysfunction and heart failure; 4) propose novel concept of sensitization and desensitization; 5) explore chemical molecules for the prevention and treatment of diastolic dysfunction and heart failure.

C1. The PI generate cTnI knockout mouse model to identify the physiological function of cTnI in the heart

In the end of last century, I generated the first cTnI gene knockout mouse model using loss-of-function techniques in University of Wisconsin-Madison. Our study have demonstrated, for the first time that cTnI deficiency is lethal that can result in restricted ventricles due to the impaired relaxation and high ventricular pressure. Increased tension inside of myocardial cells even in a relaxing solution is a major pathological feature in the heart with cTnI deficiency, which causes a sarcomere shortening and pressure increasing. The homozygous mutant mice 100% die about 18 days after birth, whereas the heterozygous mutants can survive without significant phenotypes. We use the homozygous mutant mice to monitor the development of diastolic dysfunction and heart failure, while use the heterozygous mutant mice to produce double mutant mice by crossing with other transgenic mice expressing various mutant cTnI protein. For example, by crossing cTnI heterozygous mutant mice with our later generated cTnI R193H transgenic mice (cTnI^{193His}), we obtained double transgenic mice expressing different concentrations of cTnI R193H in the heart, which allows us to study the dose-dependent effect of the R193H mutation in the heart. I also shared this mouse model with many researchers from other institutes, for example, Dr. J-P Jin at Wayne State University and Dr. Brandon Biesiadecki at Ohio State University. They use our animal models to create various double transgenic mice at a wild type cTnI null background and developed novel research projects in their interesting.



1. **Huang X.P.**, Pi YQ, Lee KJ, Henkel AS, Gregg RG, Powers PA, Walker JW. (1999) Cardiac troponin I gene knockout: A mouse model of myocardial troponin I depletion. Circulation Research, 84: 1-8. PMID: 9915769 [PubMed_Link]
2. **Huang X.P.,** Lee KJ, Riedel B, Zhang C, Lemanski LF, Walker JW (2000) Thyroid hormone regulates ssTnI inactivation in cTnI deficient mouse hearts. J. Mol. Cell. Cardiology, 32:2221-2228. PMID: 11112997 [PubMed_Link]

C2. Our lab generate transgenic mouse lines modeling human cTnI mutations in RCM patients

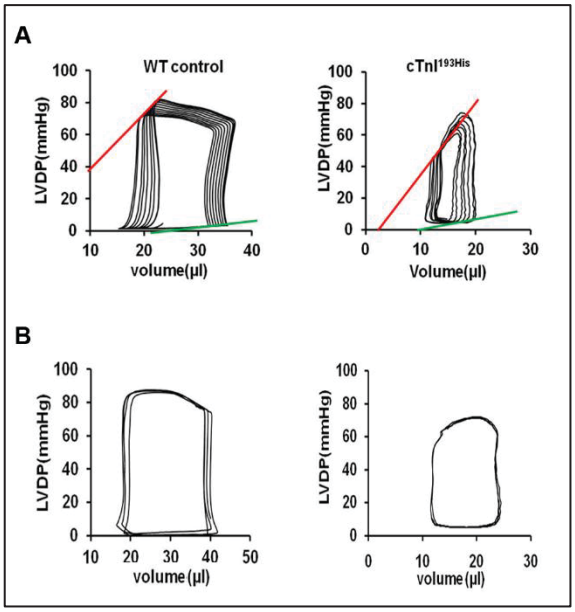
In 2003, Morgensen et al reported the association of cTnI C-terminal mutations with human restrictive cardiomyopathy (RCM). Our laboratory generated the first transgenic mouse lines modeling human cTnI K178E and R193H (K179E and R193H in mouse sequence) mutations. Characterization of the transgenic mouse lines has demonstrated that cTnI C-terminus is highly conserved and one point mutation in this region can result in cardiac dysfunction, especially diastolic dysfunction. The phenotype of these transgenic mouse lines with cTnI K179E or R193H mutation in the heart is, morphologically, bi-atrial enlargement and ventricles with no significant changes and, functionally, impaired relaxation and significantly reduced left ventricular end diastolic dimension (LVEDD) without significant changes in systolic function. The mortality in these transgenic mice is significantly higher compared to wild type mice and sudden death occurs commonly. Our data indicate that these animal models are valuable tools to study the mechanisms underlying diastolic dysfunction and diastolic heart failure in genetic cardiomyopathies. We provided the mouse models and cardiac samples to other researchers for their studies.

1. Du J., C. Zhang, J. Liu, C. Sidky, **X.P. Huang**. (2006) A point mutation (R192H) in the C-terminus of human cardiac troponin I causes diastolic dysfunction in transgenic mice. Archives of Biochemistry and Biophysics, 456:143-150. PMID: 17027633 [PubMed_Link]
2. Du J., J. Liu, H.Z. Feng, M.M. Houssain, N. Gobara, C. Zhang, Y. Li, P. Jean-Charles, J.P. Jin, **X.P. Huang**. Impaired relaxation is the main manifestation in transgenic mice expressing a restrictive cardiomyopahty mutation, R193H, in cardiac TnI. Am. J. Physiol. Heart Circ. Physiol. 294:H2604-H2613, 2008. PMID: 18408133 [PubMed_Link]

3. Liu J., J. Du, C. Zhang, J.W. Walker, **X.P. Huang**. (2007) Progressive troponin I loss impairs cardiac relaxation and causes heart failure in mice. American Journal of Physiology Heart and Circulation Physiology, 293:H1273-H1281.
PMID: 17526646 [PubMed_Link]

C3. Our lab proposes novel concept about the role of myofibril sensitivity to Ca^{2+} in cardiac diastolic function

In the past, the definition for heart failure is that a heart is too weak to pump enough blood to meet the need of the body. Thus, the focus was always concentrated on restoring cardiac muscle contractility. Recently most researchers and cardiologists have realized that almost half of the heart failure patients suffer from diastolic dysfunction with normal or almost normal systolic performance, i.e. preserved ejection fraction. This phenomenon is more common in older patients. Diastolic dysfunction, as a cause of heart failure, is as important as systolic dysfunction. Based on the studies from our and other laboratories, we demonstrate that the down-stream part in myocardial cells, i.e. contractile myofibril proteins such as troponin and tropomyosin, etc. play critical roles in cardiac function, especially the diastolic function by regulating the myosin-actin cross-bridge formation and modifying the myofibril sensitivity to Ca^{2+}. Based on these studies, we can see a significant advancement of scientific knowledge in cardiovascular research and heart failure studies, which shifts our attention from systolic to the role of diastolic function in the development of heart failure. The results obtained from the proposed study will enrich further our scientific knowledge on the treatment of diastolic dysfunction and diastolic heart failure due to impaired ventricular relaxation.



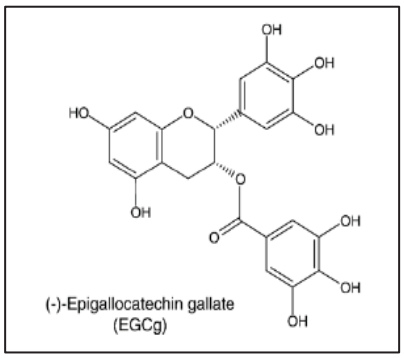
1. Shirin Akhter, Kenneth Bueltmann, Jr., **Xupei Huang**, J-P. Jin. (2013) Restrictive cardiomyopathy mutations demonstrate functions of the C-terminal end-segment of troponin I. Arch Biochem Biophys. doi:http://dx.doi.org/10.1016/j.abb.2013.12.001.
PMID: 24326031 [PubMed_Link]
2. Yuejin Li, Lei Zhang, Pierre-Yves Jean-Charles, Changlong Nan, Guozhen Chen, Jie Tian, J.-P., Jin, Ira J. Gelb, **Xupei Huang**. (2013) Dose-dependent diastolic dysfunction and early death in a mouse model with cardiac troponin mutations, J. Mol. Cell. Cardiology, 62:227-236.
PMID: 23810866 [PubMed_Link]

C4. Our lab tests the novel concept of sensitization and desensitization in normal and diseased hearts

Now we know that different cardiomyopathies are resulted from different causes. The main pathophysiological feature of dilated cardiomyopathy (DCM) is systolic dysfunction. Whereas hypertrophic cardiomyopathy (HCM) and restrictive cardiomyopathy (RCM) share a common pathological feature, i.e. diastolic dysfunction. So the treatment should be different. For DCM, enhance the myofibril sensitivity to Ca^{2+} would increase cardiac contractility. Whereas reduce the myofibril sensitivity to Ca^{2+} would correct the Ca^{2+} hypersensitivity in HCM and RCM and improve diastolic function. We have tested the concept by reducing myofibril sensitivity to Ca^{2+} in RCM mice and demonstrated that desensitization is useful and beneficial to RCM hearts and can rescue the phenotype.

1. Li Y., P. Jean-Charles, C. Nan, JR. Pinto, Y. Wang, J. Liang, G. Wu, J. Tian, H. Feng, JD. Potter, JP. Jin, **X.P. Huang**. (2010) Correcting diastolic dysfunction by Ca^{2+} desensitizing troponin in a transgenic mouse model of restrictive cardiomyopathy. J. Mol. Cell. Cardiology, 49:402-411.
PMID: 20580639 [PubMed_Link]
2. Feng H, G. Chen, C. Nan, X.P. Huang, J.P. Jin. (2014) Abnormal splicing in the N-terminal variable region of cardiac troponin T impairs systolic function of the heart with preserved Frank-Starling compensation. Physiological Report 2 (9), 2014, e12139, doi: 10.14814/phy2.12139.
PMID: 25194024 [PubMed_Link]

C5. Our lab explores the desensitizing chemicals for the treatment of diastolic dysfunction in genetic RCM



We have applied green tea extract catechins (active molecule EGCg) to RCM mice to test our hypothesis that desensitization is useful to reverse the Ca^{2+} hypersensitivity and impaired relaxation in our RCM mouse models. Our data confirm that EGCg can compete with Ca^{2+} to bind with troponin C so that to accelerate the Ca^{2+} drop off rate and to reduce the Ca^{2+} hypersensitivity in RCM hearts.

1. Zhang L., C. Nan, Y. Chen, J. Tian, P. Jean-Charles, C. Getfield, X. Wang, **X.P. Huang** (2015) Calcium desensitizer catechin reverses diastolic dysfunction in mice with restrictive cardiomyopathy. Arch. Biochem. Biophysi, 573: 69-76.
2. Liu Xiaoyan., Lei Zhang, Daniel Pacciulli, Jianquan Zhao, Changlong Nan, Wen Shen, Junjun Quan, Jie Tian, **Xupei Huang** (2016) Restrictive cardiomyopathy caused by troponin mutations: application of disease animal models in translational studies. Front. Physiology, 7:629, doi: 10.3389/fphys.2016.00629.
3. Pan B, J. Quan, L. Liu, Z Xu, J Zhu, **X.P. Huang**, J. Tian. Epigallocatechin gallate reverses cTnI-low expression-induced age-related heart diastolic dysfunction through histone acetylation modification. J Cell Mol Med. 2017 Apr 6. doi: 10.1111/jcmm.13169. [Epub ahead of print] PubMed PMID: 28382690.

A full list of my published work (70+ peer reviewed original research papers) is publicly available in the NCBI digital database:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1H7Wib4oVgz57/bibliography/51964023/public/?sort=date&direction=descending

D. Research Support

(Current)

1RO1HL119199-01A1 J.-P. Jin (PI) 04/01/16-03/31/21
NIH/NHLBI
Regulation of troponin I in cardiac adaptation & failure
The research studies the role of N-terminal truncated cTnI in cardiac physiology and pathology.
There is no scientific or budgetary overlap of the current application.
Role: Consultant

(Pending)

1R21 AG058897-01 Xupei Huang (PI) 02/01/18-01/31/20
NIH/AG
Efficacy of green tea extract catechines in the treatment of diastolic dysfunction in the aging heart
This research investigates desensitizer green tea extract catechines on cardiac function in the aging hearts.
There is no scientific or budgetary overlap of the current application.
Role: PI

Vijaya Iragavrapu –Charyulu, Ph.D.
Associate Professor of Biomedical Science

Education

- B.A., Biological Sciences, University of Miami, Miami, Florida, 1975
- PhD., Microbiology and Immunology, University of Miami School of Medicine, Miami, Florida, 1980
- BSMT, Florida Atlantic University, Boca Raton, Florida, 1998

Research Interests

- Tumor immunology
- Role of Semaphorins (axonal guidance molecules) in breast cancer
- Effect of chitinase-3-like-1 (CHI3L1) molecule in breast cancer progression
- Chitin and immune modulation to inhibit tumor growth and metastasis
- Effect of nicotine on breast cancer growth and metastasis

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Iragavarapu-Charyulu, Vijaya	Associate Professor
eRA COMMONS USER NAME (credential, e.g., agency login) iragavar	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of Miami, Miami, FL	BA	1975	Biology
University of Miami, Miami, FL	Ph.D.	1980	Microbiology/Immunology
Florida Atlantic University, Boca Raton, FL	BSMT	1998	Clinical Lab Sci

A. Personal Statement

The goal of my proposed research is to determine the mechanisms involved in accelerated metastasis of breast cancer. I am studying the influence of comorbidities such as allergen pulmonary inflammation with breast cancer. I have the expertise, leadership, extensive training and the motivation that is necessary to successfully carry out all the Aims proposed in this research project. I have a broad background in tumor immunology, tumor biology and molecular cell biology and other key research areas for this application. My expertise is in inflammatory mediators that include CHI3L1, cytokines, chemokines & MMPs and how these molecules play crucial roles in tumor growth, angiogenesis and metastasis. I have extensive expertise in understanding the role of CHI3L1 in inflammation associated with pulmonary allergic inflammation and tumor-associated inflammation. My initial work with CHI3L1 laid the foundation for this proposal to delineate the synergistic effect of pulmonary and tumor-associated inflammation in contributing to tumor growth and metastasis. As a research associate at University of Miami, I studied how tumor-derived factors affect cytokine production by lymphocytes leading to understanding the role cachexia in tumor bearers. I have geared my laboratory at Florida Atlantic University to focus on the role of inflammation in accelerating breast cancer metastasis. I have been continuously funded by Florida Department of Health and NIH. From these funded grants, I laid the groundwork for the proposed research that includes generation of chimera mice. In addition, I successfully administered the projects (e.g. staffing, research protections, budget), collaborated with other researchers, and have published from each of these projects. From my previous R-15 grants, I have successfully trained undergraduate students in scientific research. As a result, these students have gone on to further their scientific careers by entering into either graduate or medical programs.

1. Jennifer L. Owen, M. F. Criscitiello, S. Libreros, R. Garcia-Areas, K. Guthrie, M. Torroella-Kouri, S. Libreros, R. Garcia-Areas, and * V. Iragavarapu-Charyulu. 2011. Expression of the inflammatory chemokines CCL2, CCL5 and CXCL2 and the receptors CCR1-3 and CXCR2 in T lymphocytes from mammary tumor-bearing mice. *Cellular Immunology, 270: 172-182,* PMC3156845 .
2. Roberto Carrio, Marta Torroella-Kouri, Stephania Libreros, Ramón A. García-Areas, Vijaya Iragavarapu-Charyulu, and Diana M. López. 2011. Decreased accumulation of immune regulatory cells is correlated to the antitumor effect of IFN-γ overexpression in the tumor, *Int. J. Oncology, 39(6): 1619-1627,* PMID 21874231.
3. Stephania Libreros, R. Garcia-Areas**,** Y.Shibata, R. Carrio, and *V. Iragavarapu-Charyulu. 2011. Induction proinflammatory mediators by CHI3L1 is reduced by chitin treatment: decreased tumor metastasis in a breast cancer model, *Int. J. Cancer, Vol. 131 (2): 377-386,* PMC3288379.
4. Stephania Libreros, R. Garcia-Areas, and V. Iragavarapu-Charyulu. 2013. CHI3L1 plays a role in cancer through enhanced production of pro-inflammatory/pro-tumorigenic and angiogenic factors. *Immunol. Research, 57 (1-3): 99-105,* PMC3966554.
5. Rodriguez, D., Silvera, R., Carrio, R. Nadji, M. Caso, R., Iragavarapu-Charyulu, V., and Torroella-Kouri, M. 2013. Tumor microenvironment profoundly modifies functional status of macrophages: peritoneal and tumor-associated macrophages are two very different subpopulations. *Cell. Immunol., 283 (1-2): 51-60,* : PMC3771500.

6. Stephania Libreros, R. Garcia-Areas, P. Keating, R. Carrio, and V. Iragavarapu-Charyulu, 2013. Exploring the role of CHI3L1 in "pre-metastatic" lungs of mammary tumor-bearing mice. *Fron. Vasc. Physiol.* 4: article 392: 1-13, PMC3872303.
7. Garcia-Areas R, Libreros S, Amat S, Keating P, Carrio R, Robinson P, Blieden C, Iragavarapu-Charyulu V. 2014. Semaphorin 7A promotes tumor growth and exerts a pro-angiogenic effect in macrophages of mammary tumor-bearing mice. *Front Vasc.Physiol. 5*: article 17: 1-13, PMC3914020.
8. Michal A Rahat, Hemmerlein B., and Iragavarapu-Charyulu, V. 2014. The regulation of angiogenesis by tissue cell-macrophage interactions. *Fron.Vasc. Physiol., 5: 262-264.*
9. Stephania Libreros, R. Garcia-Areas, P. Keating, Robinson, P., Humbles, A., and Iragavarapu-Charyulu, V. 2015. Allergen induced pulmonary inflammation enhances mammary tumor growth and metastasis: role of CHI3L1. *J Leukoc Biol*. *97: 929-940.*
10. Stephania Libreros and Iragavarapu-Charyulu, V. 2015. YKL-40/CHI3L1 drives inflammation on the road of tumor progression*. J Leukoc Biol. In Press.*

B. Positions and Honors

Positions and Employments

1975-1980 Graduate student asst.; University of Miami School of Medicine, Miami, FL
1980-1981 Post-doctoral associate; Mount Sinai Medical Center, NY, NY
1993-1995 Post-doctoral associate; University of Miami School of Medicine, Miami, FL
1995-1999 Instructor; University of Miami School of Medicine, Miami, FL
1996 Adjunct Professor; Florida Atlantic University (FAU), Boca Raton, FL
1999-2002 Assistant Professor; Dept. of Medical Technology; FAU, Boca Raton, FL
1999-Present Voluntary Professor, University of Miami School of Medicine, Miami, FL
2002-2008 Assistant Professor, Dept of Biomed Sci., FAU, Boca Raton, FL
2008-Present Associate Professor, Dept of Biomed Sci, FAU, Boca Raton, FL
2006 Secondary appointment, Dept. of Biological Sciences, FAU, Boca Raton, FL

Honors, Awards and Memberships

1995 American Cancer Society Institutional Grant in Cancer Research at University of Miami School of Medicine, Miami, Florida
2001 Research Initiation Award, Florida Atlantic University, Boca Raton, Florida
2000 American Society for Clinical Pathology
2002 American Association for Cancer Research
2005-Present American Association of Immunologists
2002-Present Center for Molecular Biology and Biotechnology, Florida Atlantic University, Boca Raton, FL
2003 The Society for Leukocyte Biology
2004 FAU Division of Sponsored Research Initiation Award
2004-Present Integrative Biology, Florida Atlantic University, Boca Raton, FL
2009-2010 Excellence in Graduate Mentoring, Florida Atlantic University, Boca Raton, FL
2010 Teacher of the Year, Charles E. Schmidt College of Medicine, FAU
2011 Excellence in Graduate Mentoring, Florida Atlantic University, Boca Raton, FL
2013 Florida Atlantic University's Researcher of the Year, Boca Raton, FL.
2013 Associate Editor, Journal of Vascular Physiology

Other Experience

1981-1993 Family leave of absence

C. Contribution to Science

My early contributions addressed the role of immune cells such as B and T lymphocytes promoting tumor progression.

These studies revealed that B cells produce cytokines such as IL-6 which was later discovered to be a cachetic factor. T cells on the other hand were found enhance tumor metastasis through production of MMP-9 which can degrade extracellular matrix. Towards this goal we focus our studies on determining alterations in lung microenvironment, recruited inflammatory cells and production of inflammatory products that aid in accelerated metastasis to the lungs and lymph nodes.

1. Charyulu, V. and D.M. Lopez. (2000). Elevated GM-CSF levels in tumor bearing mice upregulate IL-6 production by B cells via a mechanism independent of TNF-alpha. *Int J.of Oncol., 16:161-167.*
2. Charyulu, V., and D.M. Lopez. (1999). Abnormal binding pattern and composition of the NF-κB complex components are involved in increased TNF-α production by tumor bearers' B cells. *Intl. J. Mol. Med., 3:411-416.*
3. Owen, J., Iragavarapu-Charyulu, V., Gunja-Smith, Z., Herbert, L., Grosso, J., and Lopez, D.M. (2003). Upregulation of Matrix metalloproteinase-9 in T lymphocytes of mammary tumor bearers: Role of tumor derived factors. *J. Immunol. 171: 4340,* PMID14530359

These early findings on the role of lymphocytes in tumor responses led to the understanding how immune cells are attracted to the tumor and their recruitment via chemokine signals. We were one of the early investigators who found that T cells actually produce CCL2, a monocyte chemoattractant. In collaboration with others in the field we discovered the signaling pathways involved in dysregulated cytokine production.

1. Owen, J., Lopez, D.M. and Iragavarapu-Charyulu, V. (2005). The expression of CCL2 by T lymphocytes of mammary tumor bearers: Role of tumor-derived factors. *Cellular Immunology, 235: 122-135* PMID16243300.
2. Marta Torroella-Kouri, Xiaojing Ma, Giselle Perry, Milena Ivanova, Pedro J. Cejas, Jennifer L. Owen, Vijaya Iragavarapu-Charyulu and Diana M. Lopez. (2005). Altered NF-kB and C/EBP signaling pathways underlie the dysregulation of cytokines and receptor gene expression in macrophages of mammary tumor-bearing mice. *Cancer Research, 65 (22): 10578-84.*
3. Owen,J., Torroella-Kouri, M., Handel-Fernandez, M., and Iragavararpu-Charylulu, V. 2007. GM-CSF up-regulates the expression of CCL2 by T lymphocytes in mammary tumor-bearing mice. International Journal of Molecular Medicine, *20 (1): 129-135,* PMID17549399.
4. Garcia-Areas R, Libreros S, Amat S, Keating P, Carrio R, Robinson P, Blieden C, Iragavarapu-Charyulu V. 2014. Semaphorin 7A promotes tumor growth and exerts a pro-angiogenic effect in macrophages of mammary tumor-bearing mice. *Front Vasc.Physiol. 5*: article 17: 1-13, PMC3914020.

Since I along with others in the field found that chemokines can attract monocytes, I explored the functions of monocytes/macrophages in the context of breast cancer. In collaboration, we discovered the plasticity of macrophages in mammary tumor bearing mice and that macrophages depending on environmental influences, can exhibit different functional properties. My role in these studies was to direct some of the studies and data interpretation and manuscript preparation.

1. Marta Torroella-Kouri, Risset Silvera, Dayron Rodriguez, Raul Caso, Alwi Shatry, Shannon Opiela, Dan Ilkovitch, Reto A. Schwendener, Vijaya Iragavarapu-Charyulu, Yoslayma Cardentey, Natasa Strbo, and Diana M. Lopez. 2009. Identification of a Subpopulation of Macrophages in Mammary Tumor-Bearing Mice That Are Neither M1 nor M2 and Are Less Differentiated. *Cancer Research, 69 (11): 4800-09.,* PMID19458073
2. Giselle Perry, V. Iragavarapu-Charyulu, E.W. Harhaj, and M.Torrella-Kouri. 2010. Role of the proteosome in the downregulation of transcription factors NF-*k*B and C/EBP in macrophages from tumor hosts. *Oncology Reports, 23 (3): 875-881,* PMID20127032.
3. Roberto Caso, R. Silvera, R. Carrio, V. Iragavarapu-Charyulu, RR Gozalez-Perez, and M. Torroella-Kouri. 2010. Blood monocytes from tumor-bearing mice: early targets of tumor-induced immune suppression? *International J. Oncology, 37(4): 891-900,* PMID20811711
4. Rodriguez, D., Silvera, R., Carrio, R. Nadji, M. Caso, R., Iragavarapu-Charyulu, V., and Torroella-Kouri, M. 2013. Tumor microenvironment profoundly modifies functional status of macrophages: peritoneal and tumor-associated macrophages are two very different subpopulations. *Cell. Immunol., 283 (1-2): 51-60,* : PMC3771500.

My latest scientific findings concern how inflammation contributes towards tumor progression. My laboratory was one of the first to show that pre-existing pulmonary inflammation promotes tumor growth and accelerates metastasis. We also were the first to show that CHI3L1 is involved in this process. We are also one of the first to link breast cancer metastasis to CHI3L1 expression in lungs of allergen-induced mice. These studies have clinical implications in treatment of breast cancer patients with underlying inflammatory illnesses. In addition to the finding that CHI3L1 plays a role in metastasis to the lung, we have also discovered that a neurodevelopmental molecule known as Semaphorin 7A contributes to pulmonary metastasis. We developed a SEMA 7A knockout mouse model on BALB/c background. We were the first to show that implantation of SEMA7A silenced tumor cells into SEMA7A knockout mice results in decreased metastasis. We also showed that mesenchymal marker expression is reduced while epithelial marker expression is increased supporting the hypothesis that SEMA7A is involved in epithelial to mesenchymal transition associated with metastasis.

1. Libreros S, Garcia-Areas R, Shibata Y, Carrio R, Torroella-Kouri M & Iragavarapu-Charyulu V. 2012. *Induction of proinflammatory mediators by CHI3L1 is reduced by chitin treatment: decreased tumor metastasis in a breast cancer model. Int J Cancer 131, 377-386*, doi:10.1002/ijc.26379.
2. Stephania Libreros, R. Garcia-Areas, and V. Iragavarapu-Charyulu. 2013. CHI3L1 plays a role in cancer through enhanced production of pro-inflammatory/pro-tumorigenic and angiogenic factors. *Immunol. Research, 57 (1-3): 99-105,* PMC3966554.
3. Stephania Libreros, R. Garcia-Areas, P. Keating, R. Carrio, and V. Iragavarapu-Charyulu, 2013. Exploring the role of CHI3L1 in "pre-metastatic" lungs of mammary tumor-bearing mice. *Fron. Vasc. Physiol.* 4: article 392: 1-13, PMC3872303.
4. Michal A Rahat, Hemmerlein B., and Iragavarapu-Charyulu, V. 2014. The regulation of angiogenesis by tissue cell-macrophage interactions. *Fron.Vasc. Physiol., 5: 262-264.*
5. Libreros S, Garcia-Areas R, Keating P, Gazaniga N, Robinson P, Humbles A, Iragavarapu-Charyulu V. 2015. *Allergen induced pulmonary inflammation enhances mammary tumor growth and metastasis: Role of CHI3L1*. *J. Leukoc. Biol 97*,*929-940*, doi:10.1189/jlb.3A0214-114RR.
6. Libreros S, Iragavarapu-Charyulu V. 2015. *YKL-40/CHI3L1 drives inflammation on the road of tumor progression. J. Leukoc. Biol.* 98(6):931-6. doi: 10.1189/jlb.3VMR0415-142R.
7. Garcia-Areas R, Libreros S, Simoes M, Castro-Silva C, Gazaniga N, Amat S, Jaczewska J, Keating P, Schilling K, Brito M, Wojcikiewicz EP, Iragavarpu-Charyulu V. 2017. Suppression of tumor-derived Semaphorin 7A and genetic ablation of host-derived Semaphorin 7A impairs tumor progression in a murine model of advanced breast carcinoma. *Int J Oncol. 2017 Nov;51(5):1395-1404*. doi: 10.3892/ijo.2017.4144. PMID: 25765679.

D. Research Support

Ongoing Research Support

1. 2012 – 2015: NIH/NCI, PI: "Role of CHI3L1 in accelerating breast cancer metastasis". The overall goal of this project is to determine if preexisting inflammation in a target organ accelerates metastasis by breast cancer cells. The role of the PI is to oversee all of the experiments, plan the study, analyze data for publications and grant submissions.
2. 2011-2012: Boca Raton Regional Hospital Foundation, PI: "Exploring the Novel Role of Sema 7A in Breast Cancer".

Completed Research Support

3. 2013-2015: NIH/NCI, PI: "Role of CHI3L1 in accelerating breast cancer metastasis". Research Supplements to Promote Diversity in Health-Related Research Program for Stephania Libreros.

4. 2008-2010: Florida Biomedical Research, James & Esther King Biomedical Research Program; Co-PI; "A Rat Model of Individual Differences in Neuro-immune Responses to Nicotine and Stress". The overall goal of the project is to determine how the immune response is modulated by behavior using a

rat model of individual differences and nicotine addiction model. The role of the PI is to oversee all the experiments, plan the study, analyze data and submit NIH proposals.

5. 2009-2010: NIH/NCI (ARRA Supplement), PI: Interfering with CCL2 and CCR2 to limit tumor growth". The overall goal of this project is continuation of Project 1 with using fluorescent tagged siRNA to monitor the in vivo localization of siRNA and to determine the subsequent effect. The role PI is to oversee the budget, personnel and directing the experiments.

6. 2008-2009: Florida Biomedical Research, Bankhead-Coley Biomedical Research Program; PI: Use of selective PGD2 receptor antagonists to reduce MMP-9 secretion and decrease metastasis in a breast cancer model. The role of PI is to direct the experiments, oversee the budget, analyze the data and prepare manuscripts.

7. 2008-2010 (No cost extension 2011): NIH/NCI (R-15), PI: "Interfering with CCL2 and CCR2 to limit tumor growth". The overall goals of this project is to determine whether breast cancer growth & metastasis can be inhibited by silencing the gene for CCL2 and its receptor CCR2. The PI is responsible for directing the overall project, training undergraduate/graduate students in research as well as data analysis and manuscript preparation/submission.

Ceylan Isgor, Ph.D.
Associate Professor of Biomedical Science

Education

- 1990: University Degree, Business and Psychology, Bogazici University, Instanbul, Turkey
- 1993: B.A., Psychology, University of Maryland, College Park, MD
- 1999: Ph.D., Animal Learning and Behavior, Indiana University, Bloomington, IN

Research Interests

- Neuromorphological, behavioral and molecular consequences of chronic, variable stress during peripubertal-juvenile period in rats.
- Animal models for individual differences in the novelty-seeking or risk-taking behavior
- Gonadal and adrenal steroid regulation of the novel estrogen receptor beta in stress rele- vant brain nuclei

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME Ceylan Isgor, Ph.D.	POSITION TITLE Associate Professor
eRA COMMONS USER NAME CISGOR	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of Maryland at College Park, MD	B.S.	05/92	Psychology
Indiana University, Bloomington, IN	Ph.D.	08/97	Neuroscience
Mental Health Research Institute University of Michigan, Ann Arbor, MI	Post Doctoral Fellow	1998-2004	Behav & Mol Neurosci

A. Personal Statement: This is an application that uses a transgenic mouse strain that over-expresses BDNF in the forebrain with adult-onset, spontaneous seizure development. The model has an appreciable pre-seizure time period (~ 6 months) during when we previously reported progressive changes in the hippocampal mossy-fiber-CA3 connectivity. In this application, I will assess temporal progression of epileptiform phenomena in the emergence of convulsive seizures using EEG implants that contain subdural and intrahippocampal recording electrodes. I will use video monitoring along with EEG traces to survey genesis of distinct abnormal activity. Together with my Co-Investigator, Dr. Steve Danzer, I will examine EEG recordings together with video surveillance to pinpoint onset and maintenance of hippocampal/cortical hyperexcitability. I will also collect neural tissue from these mice to process for c-fos expression using the hallmark features of EEG as guides for determining time points for euthanization. These studies will delineate recruitment of distinct brain regions in the seizure prone circuitry in pre-epileptic and epileptic mice. My expertise will also be used for gross and cellular morphological analyses of hippocampal neurons. My laboratory has extensive experience in 3-D reconstruction of neurons and subsequent dendritic process assessments using the Neurolucida software, and design-based stereology including volume estimates and cell counts using Stereoinvestigator software. I have additional published expertise in rodent stereotaxic surgery, permanent cannula placement for microinjection of substances in specific brain regions for subsequent behavioral testing, immunohistochemistry using neurogenic markers and cell counts using such markers, in situ hybridization histochemistry and multitudes of hippocampal behavioral tests including learning and memory, stress & anxiety-like behaviors, HPA axis activation. My laboratory personnel obtained the entire data set submitted in this proposal including video/EEG surveillance for spontaneous seizure onset and severity, subthreshold EEG abnormalities on route to epilepsy, dendritic and spine morphology assessments following Golgi-Cox impregnation of mature hippocampal neurons, breeding and maintaining the GFP-GAD67 mice and tissue processing for a visual representation of adult-born granule neurons that transiently express the GFP protein in soma, dendritic tree, and mossy fibers with visible mossy fiber contacts on the target sites, and lastly tau-mCherry lentivirus infection of granule neurons demonstrating feasibility for downstream anatomical assessments. I will be primarily responsible for all behavioral/physiological data collection (video/EEG monitoring, analyses of seizure frequency, duration, intensity), stereotaxic surgeries involving lentivirus microinjection and EEG headmount implantation, 3-D reconstruction of hippocampal cells for structural analyses of dendritic and axonal maturation, maintaining the transgenic mice strains and conducting accurate cell counts using design-based stereology. Together with my Co-Investigator Dr. Steve Danzer, I will design, execute and collect data for tamoxifen-induced conditional TrkB knockdown experiment that will specifically implicate local BDNF-induced morphological changes in dentate granule neurons in epileptogenesis. I have over 15 years of expertise as a hippocampal neuroanatomist and behavioral neuroscientist and extensive experience with mentoring undergraduate research trainees in my laboratory as a former R15 AREA grant

awardee. This track record consisting of above outlined anatomical, behavioral and histological techniques coupled with my long-standing dedication and commitment to training undergraduate students on these techniques make my laboratory a suitable place for conducting the proposed experiments.

B. Position and Honors

Positions and Employment:

2004-2010 Assistant Professor, Florida Atlantic University, Boca Raton, FL

2010- Associate Professor (tenured), Florida Atlantic University, Boca Raton, FL

Professional Memberships and Other Experience:

1992- Member, Society for Neuroscience

2002- Member, International Behavioral Neuroscience Society

2005- Member, Center for Molecular Biology and Biotechnology, FAU

2014- Member, Palm Beach Chapter of Society for Neuroscience, FL

2015- Member, American Epilepsy Society

2015- Member, Sigma Xi Scientific Research Society

Honors:

1996-1997 Indiana University, Biomedical Research Grant

1996,1997 Indiana Academy of Sciences Grant-in-Aid of Research

1994-1996 Indiana University Center for Integrative Study of Animal Behavior Graduate Student Fellowship

1995,1996 Sigma Xi Grant-in-Aid of Research

1995,1996 Indiana University Center for Integrative Study of Animal Behavior Summer Support Fellowship

C. Contributions to Science:

Early work on neonatal gonadal steroid-dependent sexual dimorphism in hippocampal structure and function: My early work in neuroscience as a PhD student was concentrated on assessing effects of neonatal gonadal steroids on mediating sexual dimorphism in hippocampal structure and function. These studies focused on establishing the critical time window for organizational effects of androgens and estrogen on gross and cellular morphology of hippocampal neurons and their effects on adult spatial navigation. Adult spatial navigation shows sexual dimorphism in laboratory rodents associated with sex differences in structure of primary hippocampal fields and neurons. My work narrowed down critical time period for gonadal steroids to drive such sexual dimorphism to a range from embryonic day 16 to postnatal day 5. Androgens during this time regulate developmental effects such as somal growth, cell layer volume, neuronal differentiation (i.e., longer dendrites, increased dendritic complexity, spine density and number) all of which contribute to sex differences in adult spatial navigation. This work is the start of my interest and expertise building with unbiased stereological technique as well as 3-D reconstruction of hippocampal neurons and assessment of dendritic morphology. These studies required long-term tracking of rodent hippocampal behavior and established me in behavioral neuroscience.

Isgor, C., Sengelaub, D.R. (2003). Effects of neonatal gonadal steroids on adult CA3 pyramidal neuron dendritic morphology and spatial memory in rats. *Journal of Neurobiology* 55(2): 179-190. PMID: 12672016

Isgor, C., Sengelaub, DR. Prenatal gonadal steroids affect adult spatial behavior, CA1 and CA3 pyramidal cell morphology in rats. *Horm Behav* 34(2):183-98. PMID: 9799628.

Postdoctoral work on effects of chronic stress exposure during adolescence on hippocampal structure-function: At my postdoctoral post in University of Michigan with Drs. Huda Akil and Stanley J. Watson, I made a seamless transition to studying stress neurobiology, and specifically how stressful stimuli chronically present during the peripubertal-juvenile period can alter structural integrity of hippocampus that lasts into adulthood. At the time when I embarked on this, studies on how chronic stress during adolescence affects hippocampal structure and function was unknown. Teaming up with an excellent group of scientists, I found that chronic, variable and nonhabituating stress delivered intermittently through the peripubertal-juvenile period decelerated normally-occurring maturation in all hippocampal fields, and that some of these effects were reversible while others persisted into young adulthood. We further distinguished that type of stress exposure (i.e., physical vs. social) during adolescence made a difference in the reversibility of stress-induced structural changes. This time period marks my continued interest in morpho-behavioral correlations and how to devise studies that assess structure-function relationships. I also developed expertise on *in situ* hybridization histochemistry (both digoxigenin- and radioactively-labeled riboprobe versions of the technique). Also during this time, I learned how to deliver precise microinjections of substances into brain regions *in vivo* and test for behavior following or during surgery. Moreover, I gained expertise in using Neurolucida & Stereoinvestigator softwares from Microbrightfield (VT) as tools for video-interfaced, computer-assisted image analysis systems.

Isgor, C., Kabbaj, M., Akil, H., Watson, S.J. (2004). Delayed effects of chronic, variable stress during peripubertal-juvenile period on hippocampal morphology and on cognitive and stress axis functions in rats. *Hippocampus* 14:636-648. PMID:15301440

Isgor, C., Slomianka, L., Watson, S.J. (2004). Hippocampal mossy fiber terminal field size is differentially affected in a rat model of risk-taking behavior. *Behavioral Brain Research* 153:7-14. PMID: 15219701

Isgor, C., Cecchi, M., Kabbaj, M., Akil, H., Watson, S.J. (2003). Estrogen receptor β in the paraventricular nucleus of hypothalamus regulates the neuroendocrine response to stress and is regulated by corticosterone. *Neuroscience* 121(4):837-845. PMID: 14580933

Isgor, C., Shieh, K.R., Akil, H., Watson, S.J. (2003). Colocalization of estrogen β-receptor messenger RNA with vasopressin, oxytocin and orphanin FQ in the rat hypothalamic paraventricular and supraoptic nuclei. *Anatomy and Embryology* 206(6):461-469. PMID: 12690447

Vulnerability to nicotine relapse in an outbred rodent model of the novelty-seeking phenotype: I have established an independent, NIH-funded research program in Florida Atlantic University studying the neurobiological bases for individual differences in susceptibility to nicotine relapse. The outbred rodent model I use is based on simple behavioral screening for high novelty-seeking vs. low novelty-seeking. An arbitrary cut off at top one third of activity measured in a novelty chamber identifies high novelty-seeker (HR) population and the bottom third is categorized as low novelty-seekers (LRs). Based on this phenotype distinction we found that HRs displayed high nicotine abstinence-related negative affect and were more vulnerable to relapse due to dysregulated stress/anxiety systems. Our lab showed that mood dysregulation

was related to abstinence-induced effects seen in extracellular concentrations of hippocampal 5HT and structural alterations seen both at baseline and following nicotine exposure between LRs and HRs. Furthermore, these studies gave fruition to various therapeutic targets for correcting mood dysregulations induced by nicotine, specifically in high novelty-seeking/risk-taking individuals. This research program solidified my expertise in unbiased stereology, molecular techniques and experimentation with rodent behavior.

Bhatti, A.S., Hall, P., Ma, Z., Tao, R., **Isgor, C.** (2007). Hippocampus modulates the behaviorally-sensitizing effects of nicotine in a rat model of novelty-seeking: potential role for mossy fibres. *Hippocampus* 17:922-933. PMID: 17598146

Bhatti, A.S., Aydin C., Oztan O, Ma, Z., Hall, P., Tao, R., **Isgor, C.** (2009). Effects of a cannabinoid receptor (CB) 1 antagonist AM251 on behavioral sensitization to nicotine in a rat model of novelty-seeking behavior: correlations with hippocampal 5HT. *Psychopharmacology (Berl).* 203(1):23-32. PMID: 18936914

Aydin C., Oztan, O., **Isgor C.** (2012). Nicotine-induced anxiety-like behavior in a rat model of the novelty-seeking phenotype is associated with long-lasting neuropeptidergic and neuroplastic adaptations in the amygdala: effects of the cannabinoid receptor 1 antagonist AM251. *Neuropharmacology* 63(8):1335-45.

Aydin, C., Oztan, O., **Isgor C.** (2014). Hippocampal Y2 receptor-mediated mossy fiber plasticity is implicated in nicotine abstinence-related social anxiety-like behavior in an outbred rat model of the novelty-seeking phenotype. *Pharmacol Biochem Behav* 125:48-54. PMCID:PMC4183225

Evolution and emergence of spontaneous epilepsy using the TgBDNF model: This is a novel direction that our laboratory embarked upon with various collaborators both within FAU (Drs. Kathleen Guthrie & Robert Vertes) and outside of FAU (Dr. Steve Danzer, Co-Investigator on this proposal from Cincinnati Children's Hospital Medical Center/University of Cincinnati). We summarized published and preliminary work up to date in the **Significance** section of this application.

Complete list of published work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/ceylan.isgor.1/bibliography/49714330/public/?sort=date&direction=ascending

D. Research Support

Current: 05/01/2017-04/30/2018 Role PI (Team)

Florida Atlantic University, Brain Institute Pilot Grant

"Compromised neural activity of the nucleus pontis oralis of the brain stem leads to sudden unexpected death in epilepsy"

This application explores brainstem mechanisms in SUDEP.

Completed: 03/03/2014-06/30/2015 Role: PI (Team)

FAU Division of Research Seed Grant Award Florida Atlantic University

"Trophic mechanisms promoting the emergence of pro-epileptic hippocampal circuitry"

This application determines how trophic factor signaling (BDNF) promotes emergence of aberrant functional circuitry, leading to the development of seizures in a transgenic mouse model of epilepsy. Under this support from our University, video and EEG recording equipment were purchased and a transgenic mouse strain (GFP-GAD67) was recovered from cryopreservation. Aims focused on collecting data on anatomical effects (published in a 2015 article), and on establishing video recording facilities for surveying quantifying seizure behavior of individual mice over several months, as spontaneous seizures emerge. Additional aims included purchase a set up of mouse EEG recording station to monitor hippocampal activity in vivo, and recovery and in house breeding of GFP-GAD67 mice from cryopreservation (Jackson Labs) to successfully establish a local colony.

Completed: 12/01/2009-11/30/2011
NIH/NIDA (DA023675) Role: PI
“Individual differences in relapse to nicotine”
This research program investigates individual differences in locomotor sensitization to nicotine and subsequent morphological changes in the hippocampal mossy fibre system. Cannabinoid receptor 1 targeting drugs along with serotonergic agents are tested in their efficacy to aid in relapse to nicotine.

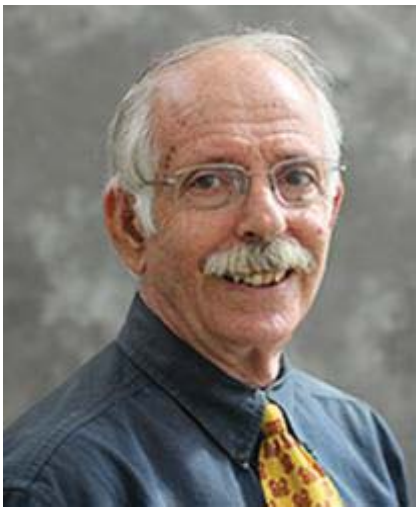
Pending: 09/01/2017-08/31/2019 Role: PI

NIH/NINDS

R21 NS101314
“Therapeutic potential for voluntary wheel running on emergence of epilepsy”
This application investigates anti-epileptic effects of voluntary wheel running and associated theta activity in a transgenic mouse model of adult-onset spontaneous seizures.

Pending: 08/01/2017-07/31/2019
Citizens United for Research in Epilepsy Sleep & Epilepsy Award Role: Co-PI
“Reversal of postictal electroencephalographic suppression with brainstem pontis oralis stimulation”
This application tests a novel neuromodulatory treatment for SUDEP.

R21 NIH/NIDCD 07/01/2017-06/30/2019 Role: Co-Investigator
“Role of Ube3a in neuronal maturation and synaptogenesis in adult-born neurons”.
This application investigates healthy versus pathological course of spine development/remodeling.



Morton Levitt, M.D.
Professor of Clinical Biomedical Science

Education

- 1968: B.S., Engineering, Princeton University, Princeton, New Jersey
- 1970: Certificate in Hospital Management, King's Fund College of Hospital Management, London, England
- 1972: M.D., Duke University, Durham, North Carolina
- 1973 -1974: Post Graduate Resident, Medical Education in Anatomic Pathology and Clinical Laboratory Medicine, Duke University, Durham, North Carolina
- 1980-1982: MHA, Duke University, Durham, North Carolina
- 1987-1989: Resident, Clinical Pathology and Laboratory Medicine, University of Chicago Hospitals and Clinics, Chicago, Illinois

Research Interests

Mechanisms of carcinogenesis; evaluation of environmental carcinogenic hazards; in vitro bioassay methodology; morphological and biochemical models for cancer pathogenesis studies; research planning in chemical carcinogenesis; pathogenesis of pancreatic cancer; experimental tumor pathology (particularly liver, colon, pancreas and prostate); occupational and environmental cancer and toxicology; cardiovascular and pulmonary pathophysiology; immunohematology, and laboratory administration, manpower utilization, and quality assurance.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: MORTON H. LEVITT, MD, MHA, FCAP

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

POSITION TITLE: Professor, Integrated Medical Science

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Princeton University	B.S.E.	05/1968	Engineering
Duke University	M.D.	05/1972	Medicine
Duke University	Resident	06/1974	Pathology, Anatomic
Duke University	M.H.A.	05/1981	Health Administration
University of Chicago	Resident	06/1989	Pathology, Clinical

A. Personal Statement

I have been a practitioner, medical educator, and administrator, for more than 30 years. My government service, including six years as an NIH researcher and program administrator, as well as my academic career in medical education, has always put me in a strong research environment. At NIH, in the late 70's, I was involved at the very highest levels of Federal research as a member of the NCI's Carcinogenesis Bioassay Testing Program (now the National Toxicology program, NIEHS). During that time I conducted and published my own research, oversaw extramural research programs, and evaluated food additives, cosmetics, and other common chemicals and agents, for their potential to cause cancer. That work involved analyzing vast amounts of research data, writing scientific reports, and testifying before Congressional committees and various Federal agencies. This opportunity gave me the opportunity to get to know NIH and its scientific missions extremely well, and instilled in me a lifelong interest in research, research funding, public education, and advocacy. For this reason, I see my work at Florida Atlantic University in the Biomedical Sciences Program a natural extension of my public service and networking experiences, spanning more than three decades, and bring to the Graduate School what I have learned from my service on the boards of my state and national professional societies, my involvement for 20 years in the uniformed services, and my employment in state universities of higher education.

B. Positions and Honors

C. 2014-Present: Professor of Clinical Biomedical Science, Florida Atlantic University, Charles E. Schmidt College of Medicine [CESCOM]
D. 2013-2014: Interim Senior Associate Dean, Faculty Affairs, and Professor of Clinical Biomedical Science, Florida Atlantic University, Charles E. Schmidt College of Medicine [CESCOM]
E. 2010-2013:Chair, Department of Pre Clinical Science and Medical Education [now, Integrated Medical Science Department], and Professor of Clinical Biomedical Science, Florida Atlantic University, Charles E. Schmidt College of Medicine [CESCOM]
F. 2007-2010:Clinical Professor of Biomedical Science, University of Miami, Miller School of Medicine@FAU and Affiliated Professor of Pathology, Boca Raton, Florida

G. University of Miami, Miller School of Medicine, Regional Campus at Florida Atlantic University, Boca Raton, FL, Charles E. Schmidt College of Biomedical Science, Department of Clinical Science and Medical Education
H. 2003-2007: Faculty Scholar in Pathology, Associate Professor, and Assistant Director for Pathology Curriculum, Florida State University, College of Medicine, Tallahassee, FL
I. 2001-2003: Associate Professor of Pathology and Course Director, PAO 2001; Associate Professor, Emerging Infectious Diseases Program (secondary), Uniformed Services University of the Health Sciences, Bethesda, Maryland (USUHS).
J. 1996-2003: Associate Professor of Pathology and Chief, Clinical Medical Education and Director, Medical Clerkships, Pathology 2001, Uniformed Services University of the Health Sciences, Bethesda, Maryland (USUHS).
K. 1997-2003: Senior Air Force Officer Advisor, Uniformed Services University of the Health Sciences, Bethesda, Maryland (USUHS).
L. 1991-1996 Assistant Chief of the Hospital Medical Staff, Malcolm Grow Medical Center (MGMC), Andrews Air Force Base, Maryland 20331-6600.
M. 1989-1996: Staff Pathologist and Chairperson (1990 – 1996), Department of Pathology and, Malcolm Grow Medical Center (MGMC), Andrews Air Force Base, Maryland 20331-6600.
N. 1990-1996:Medical Director, School of Medical Technology, Laboratory Officer Training Program; and Medical Director, Phase II Medical Training Program for Medical Laboratory Specialists; and Medical Director, School of Medical Technology, Laboratory Officer Training Program; and Medical Director, Phase II Medical Training Program for Medical Laboratory Specialists, Malcolm Grow Medical Center (MGMC), Andrews Air Force Base, Maryland 20331-6600.
O. 1987-1989: Resident in clinical pathology and laboratory medicine, University of Chicago Hospitals and Clinics, Chicago, Illinois
P. 1985-1987: Vice President, Medical Affairs, Jewish Hospital, Louisville, Kentucky
Q. 1985-1987: Associate Clinical Professor of Pathology, University of Louisville School of Medicine, Louisville, KY
R. 1984-1985: Vice President, Clinical Services, Research Medical Center, Kansas City, Missouri
S. 1982-1984: Assistant Vice President, Professional Services, Methodist Hospitals of Memphis, Memphis, Tennessee
T. 1981-1982: Special Assistant to the Chairman, Health Administration and Coordinator, the 19th National Forum on Hospital and Health Affairs, Duke Hospital, Duke University Medical Center, Durham, North Carolina
U. 1976-1980: Administrative Director, GI Tract/Prostate Cancer Program, National Cancer Institute, National Institutes of Health, Bethesda, Maryland
V. 1974-1976: Staff Associate, Office of the Director, National Cancer Institute, National Institutes of Health, Bethesda, Maryland

C. Contributions to Science

PUBLICATIONS

- **Levitt, M.H**., McCoy, R.C., and Fetter, B.F.,: Glomerulopathy in Medullary Sponge Kidneys: Case Presentation and Review of the Literature. J. Urol. 112: 710 to 713, 1974.
- Squire, R.A., and Levitt, M.H.: Classification of Specific Hepatocellular Lesions in Rats: Report of Workshop. Cancer Research 35: 3214 to 3223, 1975.
- **Levitt, M**., Harris, C.C., Squire, AR, Springer, S., Wenk, M. and Kingsburg, E.: Morphogenesis of Pancreatic Adenocarcinoma in the Syrian Golden Hamster. Lab. Invest. 34: 323, 1976.

- **Levitt, M**., Harris, C. C., Squire, R., and Wenk, M.: Introduction of Pancreatic Neoplasm in Syrian Golden Hamsters by 2, 2'-Dihydroxy di-N propylinitrosamine. Proc. Amer. Assoc. Cancer Research 17: 41, 1976.
- **Levitt, M.H**., Harris, C.C., Squire, R., Wenk, M., Mollelo, C., and Springer, S.: Experimental Pancreatic Carcinogenesis. I. Morphogenesis of Pancreatic Adenocarcinoma in the Syrian Golden Hamster by N-Nitroso-bis (2 hydroxypropyl) amine. Am. J, Pathol. 88: 5 to 28, 1977.
- **Levitt, M.H.**, Harris, C. C., Squire, R., Wenk, M., Mollelo, C., and Springer, S.: Experimental Pancreatic Carcinogenesis. II. Lifetime Carcinogenesis Studies in the Outbred Syrian Golden Hamster with N-Nitroso bis (2 hydroxypropyl)amine. J. Natl. Cancer Inst. 60: 701 to 705, 1978.
- Squire, R. A., Goodman, D. G., Valerio, M. G., Fredrickson, T., Strandberg, J. D., **Levitt, M. H.**, Lingeman, C. H., Harshbarger, J. C. and Dawe, C. J.: In: Pathology of Laboratory Animals, Vol. II, Chapter 12, pages 1252 to 1283, Benirschke, K., Garner, F. M., and Jones, T. C. (Eds). Springer-Verlag, New York, 1978.
- Cardesa, A., Bullon Ramirez, A., and **Levitt, M**.: Tumors of the Pancreas. In: Pathology of Tumors in Laboratory Animals, Vol. II Tumors of the Mouse, Turusov, V. S. (Ed.). IARC Scientific Publications No. 7, Lyon, France, 1978.
- Pour, P. and **Levitt, M.H**.: Tumors of the Pancreas. In: Handbook: Animal Models of Human Disease. Fasc. 7. Edited by T.C. Jones, D.B. Hackel and G. Migaki-Registry of Comparative Pathology, Armed Forces Institute of Pathology, Washington, D.C., 1979.
- Kurti, S.P., Rosenkranz, S.K., **Levitt, M.**, Cull, B. J., Teeman, C. S., Emerson, S. R., and Harms, C. A. BioMed Research International (Article ID 647952).

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

Editorial and Journal Review Activities

- 2014-present Reviewer, Cardiology [International Journal of Cardiovascular Medicine, Surgery, Pathology and Pharmacology]
- 1977 - 1980 Reviewer, Cancer Letters
- 1977 - 1980 Reviewer, Cancer Research
- 1975 - 1980 Reviewer, Journal of the National Cancer Institute

Peer Review and Management Activities

- 2002: Member (Scientist Reviewer), Clinical and Experimental Therapeutics Review Panel, CDMRP Prostate Review Panel (DOD, USAMRMC), Baltimore, MD, July 8-10
- 1975 - 1980 Member, Project Administration Committee, Contract NO1-CP-02199, Laboratory Services for the Support of NCI Long Term Studies in Carcinogenesis and Related Activities, Microbiological Associates, Inc., Bethesda, Maryland
- 1977 - 1980 Member and Chairman (1978), Pathology Working Group, Carcinogenesis Testing Program, National Cancer Institute
- 1977 - 1980 Member, Experimental Design Working Group, Carcinogenesis Testing Program, National Cancer Institute
- 1977 - 1980 Member, Data Evaluation Working Group, Carcinogenesis Testing Program, National Cancer Institut
- 1977 - 1980 Member (alternate), Carcinogenesis Testing Program Review Group, Division of Cancer Cause and Prevention, National Cancer Institute
- 1977 - 1980 Acting Manager, Tumor Pathology Branch (Segment), Carcinogenesis Testing Program, Division of cancer Cause and Prevention, National Cancer Institute
- 1978 Member, Ad Hoc Internal Review Committee on Smoking and Health Program, convened by Acting Director, Division of Cancer Cause and Prevention, National Cancer Institute

- 1976 - 1977 Acting Director, Gastrointestinal Tract Prostate Cancer Program, Office of the Coordinator for Collaborative Research, Carcinogenesis Program, Division of Cancer Cause and Prevention, National Cancer Institute

Scientific and Advisory Committees, Conferences and Workshops

- 1988 Presiding Officer, American College of Healthcare Executives, Congress on Administration, Chicago, Illinois, February 15 to 19, 1988
- 1979 - 1980 Member (Cause and Prevention Division Representative), Pathology Review Working Group for the Director, National Cancer Institute
- 1978 - 1980 Member, National Cancer Institute Bioassay Program Health and Safety Group, and principal medical advisor, Medical Monitoring Sub Group, National Cancer Institute Bioassay Program Health and Safety Group
- 1979 Chairman, Sub Group on Pathology, Program Development Meeting on Laboratory Monitoring, Toxicology Branch, Carcinogenesis Testing Program, Bethesda, Maryland, June 18 and 19, 1979
- 1978 Consultant, Bureau of Foods, Food and Drug Administration
- 1978 Participant, Carcinogenesis Testing Program Workshop on the Pathology of the F344 Rat and B6C3F1 Mouse, and Discussant, Rat-Liver Lesions and Mouse and Rat-Pancreatic Lesions, Bethesda, Maryland, June 7 and 8, 1978
- 1978 Participant, Program Officials Guide to Contracting, sponsored by the Office of the Secretary, Department of Health Education and Welfare, April 24 to 26, 1978
- 1977 Chairman, organizer and speaker, Program Development Meeting on Prostate Carcinogenesis, sponsored by the Biology Operational Unit, Office of the Coordinator for Collaborative Research, Carcinogenesis Program, Division of Cancer Cause and Prevention, National Cancer Institute, San Antonio, Texas, February 23 to 25, 1977
- 1977 Participant, Mouse Liver Tumor Workshop, sponsored by the National Cancer Institute, Carcinogenesis Testing Program, and the National Cancer Institute, Carcinogenesis Testing Program, and the National Cancer for Toxicological Research, Little Rock, Arkansas, November 3 to 4, 1977
- 1977 Participant, National Research Council, Institute of Laboratory Animal Resources, Sub Committee on Rat Liver Tumors, Committee on Histologic Classification of Laboratory Animal Tumors
- 1975 - 1976 Participant, Pathology Working Group, National Cancer Institute, Temporary Committee for the Review of Data on the Carcinogenicity of Cyclamate, for the Food and Drug Administration
- 1974 Participant, Prostate Carcinogenesis Workshop, sponsored by the Biological Models Segment, Office of the Coordinator for Collaborative Research, Carcinogenesis Program, Division of Cancer Cause and Prevention, National Cancer Institute, Denver, Colorado, September 5 and 6, 1974
- 1974 Participant and co-organizer, Rat Liver Tumor Workshop, sponsored by the Carcinogenesis Bioassay Program, Division of Cancer Cause and Prevention, National Cancer Institute, Silver Spring, Maryland, December 11 to 13, 1974
-

Summary of Academic Achievements, Charles E. Schmidt College of Medicine, Boca Raton, FL

- Selected by the Class of 2012 for the Dwight W. Warren “Excellence in Teaching” Award, 2009-2010
- Summary of Academic Achievements, Uniformed Services University of the Health Sciences, Bethesda, Maryland.
- Selected “Instructor of the Year” for USUHS, 2002
- Selected “Outstanding Pathology Lab Instructor,” 2002
- Selected “Outstanding Course Administrator” for USUHS, 2002

- Selected “Outstanding Student Advocate” for USUHS, 2002
- Awarded USUHS Commendable Service Medal, 2001
- Selected “Instructor of the Year” for USUHS Basic Sciences, 2001
- Top Laboratory Instructor (rated by students) in Pathology, 1999-2000 and 2000-2001 Academic years
- Awarded USUHS “Distinguished Services Award,” 2000

Major Research Interests

- Mechanisms of carcinogenesis; evaluation of environmental carcinogenic hazards; in vitro bioassay methodology; morphological and biochemical models for cancer pathogenesis studies; research planning in chemical carcinogenesis; pathogenesis of pancreatic cancer; experimental tumor pathology (particularly liver, colon, pancreas and prostate); occupational and environmental cancer and toxicology; cardiovascular and pulmonary pathophysiology; immunohematology, and laboratory administration, manpower utilization, medical education, and quality assurance.

Zhongwei Li, Ph.D.
Interim Associate Dean for Faculty Affairs
Professor of Biomedical Science

Education

- B.S., Microbiology, Liaoning University 1982
- M.S., Microbiology, Chinese Academy of Sciences 1984
- Ph.D., Microbiology, Chinese Academy of Sciences 1989
- M.S., Computer Science, University of Miami 2001

Research Interests

- RNA metabolism
- RNA therapy
- Bacterial Genomics
- Regulation of gene expression by natural products

OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES**.

NAME: Li, Zhongwei

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

POSITION TITLE: Professor of Biomedical Science

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Liaoning University, Shenyang, China	B.S	01/1982	Microbiology
Chinese Academy of Sciences, China	M.S.	01/1985	Microbiology
Chinese Academy of Sciences, China	Ph.D.	09/1989	Microbiology
University of Connecticut Health Center	Postdoctoral	08/1995	Biochemistry
Yale University School of Medicine	Postdoctoral	08/1996	Molecular Neuroscience
University of Miami	M.S.	05/2001	Computer Science

A. Personal Statement

My expertise in the field of microbiology, biomedical science and computational biology make me well suited for carrying out the proposed studies. My research relevant to identification of bacteria started in graduate schools where I isolated and characterized symbiotic bacteria for nitrogen fixation: Rhizobium and Frankia strains (MS thesis, Ph.D. dissertation). I continued to work with bacteria at the molecular level, including diverse species such as *Escherichia coli, Yersinia pestis, Mycoplasma genitalium, Citrobacter rodentium*, etc. In addition, my computer science background enables me to work with computer engineers in the development of analysis and automation of this device. I am currently teaching a required graduate course in FAU Biomedical Science Program titled “Biomedical Data and Informatics” which involves computational analysis of diverse data.

1. Lalonde MS, Zuo Y, Wang J, Gong X, Wu S, Malhotra A, and Li Z (2007) Exoribonuclease R in Mycoplasma genitalium can carry out both RNA processing and degradative functions and is sensitive to RNA ribose methylation. RNA 13:1957-1968. PMCID: PMC2040080.
2. Bartra SS, Gong X, Lorica CD, Jain C, Nair MKM, Schifferli D, Qian L, Li Z, Plano GV and Schesser K. (2012) The outer membrane protein A (OmpA) of Yersinia pestis promotes intracellular survival and virulence in mice. Microbial Pathogenesis 52:41-46.
3. Wu J, Jiang Z, Liu M, Gong X, Wu S, Burns CM and Li Z. (2009) Polynucleotide Phosphorylase Protects Escherichia coli against Oxidative Stress. Biochemistry 48:2012–2020.
4. Li Z, Gong X, Joshi VH and Li M. (2005) Co-evolution of tRNA 3' trailer sequences with 3' processing enzymes in bacteria (Bioinformatics). RNA 11:567-577.

B. Positions and Honors

Positions and Employment

1985-1986 Research Assistant, Institute of Forestry and Soil Science, Chinese Academy of Sciences, Shenyang, China

1989-1991 Assistant Investigator, Inst. Applied Ecology, Chinese Academy of Sciences, Shenyang, China
1996-2000 Research Assistant Professor of Biochemistry, University of Miami, Miami, FL
2000-2002 Specialist in Bioinformatics, DuPont Central Research and Development, Wilmington, DE
2002-present Assistant Professor (2002-2007), Associate Professor (2007-2013), and Professor (2013-present), Dept. of Biomedical Science, Florida Atlantic University, Boca Raton, FL

Other Experience and Professional Memberships

2001- Vice President, Association of Chinese Bioinformaticians
2002- Member, The RNA Society
2002- Member, American Society of Biochemistry and Molecular Biology
2010- Member, Overseas Chinese Society for Microbiology (Sino-Micro)
2011-2016 Board of Editors, Current Cellular Biochemistry
2013- NSF China Grant Reviewer
2013-2014 Board of Editors, Frontiers in Genomic Physiology
2016- Board of Editors, BAOJ Microbiology
2016- Board of Editors, The Scientific Pages of Biomedical Research

Honors

1982 Award for Outstanding Undergraduate Research, Liaoning University, China
1988 Outstanding Young Investigator Award, Joint Symposium of the 4th International Union of Biochemistry and Molecular Biology (IUBMB) and the 6th Chinese Biochemistry Conference, Nov. 6-11, 1988, Nanjing, China
1989 Presidential Distinguished Dissertation Award, Chinese Academy of Sciences
1990 Research Excellence Award, Institute of Applied Ecology, Chinese Academy of Sciences
2001 Way-to-Go Award, DuPont Central Research and Development
2008 Researcher of the Year Nominee, Florida Atlantic University

C. Contribution to Science

1. My early publications directly addressed the fact that substance abuse is often overlooked in older adults. However, because many older adults were raised during an era of increased drug and alcohol use, there are reasons to believe that this will become an increasing issue as the population ages. These publications found that older adults appear in a variety of primary care settings or seek mental health providers to deal with emerging addiction problems. These publications document this emerging problem but guide primary care providers and geriatric mental health providers to recognize symptoms, assess the nature of the problem and apply the necessary interventions. By providing evidence and simple clinical approaches, this body of work has changed the standards of care for addicted older adults and will continue to provide assistance in relevant medical settings well into the future. I served as the primary investigator or co-investigator in all of these studies.
    a. Gryczynski, J., Shaft, B.M., Merryle, R., & Hunt, M.C. (2002). Community based participatory research with late-life addicts. American Journal of Alcohol and Drug Abuse, 15(3), 222-238.
    b. Shaft, B.M., Hunt, M.C., Merryle, R., & Venturi, R. (2003). Policy implications of genetic transmission of alcohol and drug abuse in female nonusers. International Journal of Drug Policy, 30(5), 46-58.
    c. Hunt, M.C., Marks, A.E., Shaft, B.M., Merryle, R., & Jensen, J.L. (2004). Early-life family and community characteristics and late-life substance abuse. Journal of Applied Gerontology, 28(2),26-37.
    d. Hunt, M.C., Marks, A.E., Venturi, R., Crenshaw, W. & Ratonian, A. (2007). Community-based intervention strategies for reducing alcohol and drug abuse in the elderly. Addiction, 104(9), 1436-1606. PMCID: PMC9000292

2. In addition to the contributions described above, with a team of collaborators, I directly documented the effectiveness of various intervention models for older substance abusers and demonstrated the importance of social support networks. These studies emphasized contextual factors in the etiology and maintenance of addictive disorders and the disruptive potential of networks in substance abuse treatment. This body of work also discusses the prevalence of alcohol, amphetamine, and opioid abuse in older adults and how networking approaches can be used to mitigate the effects of these disorders.

a. Hunt, M.C., Merryle, R. & Jensen, J.L. (2005). The effect of social support networks on morbidity among elderly substance abusers. Journal of the American Geriatrics Society, 57(4), 15-23.
b. Hunt, M.C., Pour, B., Marks, A.E., Merryle, R. & Jensen, J.L. (2005). Aging out of methadone treatment. American Journal of Alcohol and Drug Abuse, 15(6), 134-149.
c. Merryle, R. & Hunt, M.C. (2007). Randomized clinical trial of cotinine in older nicotine addicts. Age and Ageing, 38(2), 9-23. PMCID: PMC9002364

3. Methadone maintenance has been used to treat narcotics addicts for many years but I led research that has shown that over the long-term, those in methadone treatment view themselves negatively and they gradually begin to view treatment as an intrusion into normal life. Elderly narcotics users were shown in carefully constructed ethnographic studies to be especially responsive to tailored social support networks that allow them to eventually reduce their maintenance doses and move into other forms of therapy. These studies also demonstrate the policy and commercial implications associated with these findings.

a. Hunt, M.C. & Jensen, J.L. (2003). Morbidity among elderly substance abusers. Journal of the Geriatrics, 60(4), 45-61.
b. Hunt, M.C. & Pour, B. (2004). Methadone treatment and personal assessment. Journal Drug Abuse, 45(5), 15-26.
c. Merryle, R. & Hunt, M.C. (2005). The use of various nicotine delivery systems by older nicotine addicts. Journal of Ageing, 54(1), 24-41. PMCID: PMC9112304
d. Hunt, M.C., Jensen, J.L. & Merryle, R. (2008). The aging addict: ethnographic profiles of the elderly drug user. NY, NY: W. W. Norton & Company.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/collections/public/1PgT7IEFIAJBtGMRDdWFmjWAO/?sort=date&direction=ascending

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

Ongoing Research Support

R01 DA942367 Hunt (PI) 09/01/08-08/31/16
Health trajectories and behavioral interventions among older substance abusers
The goal of this study is to compare the effects of two substance abuse interventions on health outcomes in an urban population of older opiate addicts.
Role: PI

R01 MH922731 Merryle (PI) 12/15/07-11/30/15
Physical disability, depression and substance abuse in the elderly
The goal of this study is to identify disability and depression trajectories and demographic factors associated with substance abuse in an independently-living elderly population.
Role: Co-Investigator

Faculty Resources Grant, Washington University 08/15/09-08/14/15
Opiate Addiction Database
The goal of this project is to create an integrated database of demographic, social and biomedical information for homeless opiate abusers in two urban Missouri locations, using a number of state and local data sources.
Role: PI

Completed Research Support

R21 AA998075 Hunt (PI) 01/01/11-12/31/13
Community-based intervention for alcohol abuse
The goal of this project was to assess a community-based strategy for reducing alcohol abuse among older individuals.
Role: PI

Michael Lu, Ph.D.
Professor of Biomedical Science

Education

- B.S., University 1982
- Ph.D., Molecular and Cellular Biology, University of Massachusetts, Amherst., 1988

Research Interests

- Hormone-regulated signal transduction
- Tumor metastasis
- Cell growth regulation

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Michael L. Lu

eRA COMMONS USER NAME (credential, e.g., agency login): mlu@rics.bwh.harvard

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
National Taiwan University, Taiwan R.O.C.	B.V.M.	06/1979	Veterinary Medicine
National Board, Taiwan, R.O.C.	D.V.M.	06/1981	Veterinary Medicine
University of Massachusetts, MA	Ph.D.	06/1988	Molecular Cell Biology
Dana Farber Cancer Institute	Post-Doctor	1988-1991	Cancer Biology

A. Personal Statement

I have the knowledge, leadership, training, expertise and motivation necessary to successfully carry out the proposed research project. I have a broad background in molecular cell biology, with specific expertise in steroid hormone signal transduction. My research focuses on androgen receptor signaling in malignancy progression including mapping the pathway of androgen receptor non-genomic signals and characterizing the molecular interactions between AR and its associated signaling molecules. As a PI on several federal funded grants, NIH and DOD, I have gained ample experiences in how to efficiently and successfully manage research projects. I successfully administered the projects (e.g. staffing, research protections, budget), collaborated with other researchers, and produced several peer-reviewed publications from each project. The current proposal is a logic extension from our previously NIH funded grant, Hormone-Regulated Prostate Cancer Cell Motility. The AR-interacting kinase PAK6 was identified more than a decade ago, but information related to its physiological role remains spares. Lack of proper tool, such as an antibody that can recognize the endogenous PAK6 at its native subcellular localization, may attribute to this impediment. Through many failed attempts, we have recently generated a new antibody that is able to recognize the native PAK6 protein and, for the first time, to identify PAK6's subcellular localization at centrosome and plasma membrane. The current project represents a new area of interest to our continue efforts on elucidating the physiological role of PAK6 in prostate cancer progression.

B. Positions and Honors

Positions and employment

1988-1991 Research Fellow Pathology, Harvard Medical School/Dana-Farber Cancer Institute
1991-2006 Director, Uro-Oncology Research, Brigham & Women's Hospital
1994-2006 Assistant Professor, Harvard Medical School
2006- Associate Professor, Florida Atlantic University

Other Experience and Professional Memberships

1999- Member, Society of Basic Urology Research
2007- Member, American Cancer Society
2002-2005 Scientific Reviewer Cancer Molecular Endocrinology CSR, Reproductive Endocrinology Study Section National Institute of Health

2003-2005 Scientific Reviewer, Cancer Biology Study Section, Breast Cancer Program, Department of Defense

2002- 2014 Scientific Reviewer, Cancer Cell Biology Study Section, Prostate Cancer Program, Department of Defense

Honors

1989-1990 Neuromuscular Disease Research Award, Muscular Dystrophy Association
1991-1992 National Research Service Award, National Institute of Health
2002 Hershey Prostate Cancer Research Fellow

C. Contribution to Sciences (Complete list, 42 total, of peer-reviewed publications can be found in PubMed link below)

1. In my early years of research work, my lab was the first to discover the evidence of androgen receptor (AR) non-genomic activities and that AR activation is regulated by a cross-talk with signal complexes associated with caveolin containing caveolae, a cholesterol-rich membrane domain. Caveolin expression, a scaffold protein associated with caveolae signaling microdomains, has been correlated with hormone resistance and metastasis in prostate cancer. We demonstrate in cellular models that modulation of caveolin or cholesterol levels alters the sensitivity of AR to androgen. Furthermore, a transient and dynamic direct interaction between AR and caveolin in response to androgen stimulation was also demonstrated. Our results laid the foundation for later field of research in understanding the AR non-genomic signaling prostate cancer progression.

a. Zhang X, Richie JP, Lu ML. Downreuglation of Androgen Receptor Transactivation Activity by Cholesterol Synthesis Inhibitor Lovastatin in Prostate Cancer Cells. Surgical Forum 1999; 50:698-9.

b. Lu ML, Schneider MC, Zhang X, Richie JP. Caveolin-1 interacts with androgen receptor: a positive modulator of androgen receptor mediated transactivation. J Biol Chem 2001; 276:13442-51.

c. Zhuang L, Lin J, Lu ML, Solomon KR, Freeman MR. Cholesterol-rich lipid rafts mediate Akt-regulated cell survival in prostate cancer cells. Cancer Res. 2002; 62:2227-31.

d. Freeman MR, Cinar B and Lu ML. Membrane rafts as potential sites of nongenomic hormonal signaling in prostate cancer. Trens Endocrin. Metabol. 2005, 16:273-279

2. Continue working to elucidate the androgen receptor (AR) signaling mechanism, with a team of collaborators, we identified and characterized a novel AR-interacting PAK6, a member of Group 2 PAK member. We have focused working on elucidate molecular pathways that lead to PAK6 activation. We determined that PAK6 is activated through a stress-related signal pathway. We also established a mechanistic link between AR and PAK6 activation through PAK6 and AR intermolecular interaction and a phosphorylation cascade to regulate pAK6 activities. To further delineate the PAK6 signal pathway, we have generated the first anti-PAK6 antibody recognize the endogenous native PAK6 and determined PAK6 subcellular localization at centrosome and plasma membrane. This new results revised the previous view of PAK6 being a cytosolic soluble kinase. These results will serve as the foundation for further exploring the 'newfound' role of PAK6 in contributing to genomic instability in response to hormone signaling.

a. Lee SR, Ramos SM, Ko A, Masiello D, Swanson KD, Lu ML, Balk SP. Androgen and Estrogen Receptor Interaction with a Novel p21 Activated Kinase (PAK6). Mol Endocrin 2002; 16:85-99.

b. Kaur R, Liu X, Gjoerup O, Zhang A, Balk SP, Yuan X, Schneider MC and Lu ML. Activation of p21 Activated Kinase (PAK6) by MAP kinase kinase 6 and p38 MAP kinase. J. Biol. Chem. 2005; 280:3323-3330.

c. Kaur R, Yuan X, Lu ML and Balk SP Increased PAK6 expression in prostate cancer and identification of PAK6 associated proteins. Prostate 2008; 68:1510-1516.

d. Liu X, Busby J, John C, Wei J, Yuan X, Lu ML. Direct Interaction between AR and PAK6 in Androgen-Stimulated PAK6 Activation. PLoSOne 2013 8(10): e77367.

Bibliography:

http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/48942159/?sort=date&direction=descending

Research Support:

Ongoing Research Support:
Florida Atlantic University Research Corporation
Title: AR in Advanced Prostate Cancer
The goal of this project is to determine the role of AR in prostate cancer progression.

Recently Completed Research Support:
1R15CA143816 (7/1/11-6/30/13)
Title: Hormone–Regulated Prostate Cancer Cell Motility
The proposal aims at determining the role of AR in hormone-regulated cell motility and invasion.

Mahyar Nouri-Shirazi, D.V.M., Ph.D.
Professor of Integrated Medical Science

Education

- 1992: D.V.M., Tottori University, School of Veterinary Medicine, Japan
- 1996: Ph.D., Immunology, Chiba University, School of Medicine, Japan

Research Interests

Dr. Nouri-Shirazi is an immunologist with an interest in basic immunology, specifically the application of its principles to clinical settings. Research in his laboratory is focused on 1) dendritic cells (DCs)-based immunomodulation for treatment of cancer and allograft rejection and 2) TLR agonists as adjuvants to augment vaccine efficacy in immunocompromised individuals. Among his responsibilities, he teaches Immunology to M1 and M2 medical and graduate students, facilitates small group cases, and serves as director of the M2 Pathophysiology and Therapeutics 4 course

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Nouri-Shirazi, Mahyar

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

POSITION TITLE: Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Tottori University, School of Veterinary Medicine Tottori, Japan	D.V.M	1992	Veterinary Medicine
Chiba University, School of Medicine Chiba, Japan	Ph.D.	1996	Immunology
Baylor Institute for Immunology Research Dallas, Texas	Postdoctoral	2001	Immunology

A. Personal Statement

The ultimate goal of this project is to protect the public health from contagious disease by optimizing the efficacy of current and future vaccines in smokers through the use of an appropriate adjuvant. I have the motivation, expertise, and leadership necessary to successfully carry out the proposed work. I have a long standing interest in basic immunology, specifically the application of its principles to clinical settings. As a postdoctoral fellow at Baylor Institute for Immunology Research, I carried out research on designing dendritic cells (DCs)-based vaccine for patients with cancer. During my independent career, I expanded my research on the topic of cancer immunotherapy to include nicotinic effects on tumor immunosurveillance and immunotherapy with the hypothesis that the adverse effects of nicotine on the biological activities of DCs increase the susceptibility of individuals to cancer and infectious diseases and decrease the effectiveness of vaccination and consequently its herd effect. As a PI on several university and private- and NIH-funded grants, I laid the groundwork for the proposed research by developing and establishing all experimental methods proposed in this application. In addition, I successfully administered the projects, trained staff and students, produced biannual/final reports to the sponsor, and published original research articles in this field including the most recent one in the Journal of Immunology. As a result of these previous experiences, I am aware of the importance of constructing a realistic research plan, timeline, and budget. The current project builds logically on my previous and current work and I am prepared to lead this project of high relevance to public health. I am confident that with the support of this project at the highest level of our administration, my research team can complete the necessary tasks in a timely and successful manner.

1. **M. Nouri-Shirazi,** E. Guinet. Evidence for the immunosuppressive role of nicotine on human dendritic cell functions. IMMUNOLOGY 109 (3): 365-373 JUL 2003
2. Guinet, K. Yoshida and **M. Nouri-Shirazi.** Nicotinic environment affects the differentiation and functional maturation of monocytes derived dendritic cells (DCs). IMMUNOLOGY LETTERS 95 (1): 45-55 AUG 15 2004
3. **M. Nouri-Shirazi,** E. Guinet. A possible mechanism linking cigarette smoke to higher incidence of respiratory infection and asthma. IMMNUOLOGY LETTERS 103 (2): 167-176 MAR 15 2006

4. **M. Nouri-Shirazi**, R. Tinajero and E. Guinet. Nicotine alters the biological activities of developing mouse bone marrow-derived dendritic cells (DCs). IMMUNOLOGY LETTERS 109 (2): 155-164 MAR 9 2007
5. **M. Nouri-Shirazi** and E. Guinet. Exposure to nicotine adversely affects the dendritic cell system and compromises host response to vaccination. THE JOURNAL OF IMMUNOLOGY 188 (5): 2359-70 MAR 1 2012

B. Positions and Honors

Positions and Employment

1994-1996	Research Scientist, Columbia University, Department of Microbiology. New York, NY
1996-1998	Research Scientist, Bayer Pharmaceutical Ltd, Research Center Kyoto, Division of Autoimmunity. Kyoto, Japan
1998-2001	Senior Post-doctoral Fellow, Baylor Institute for Immunology Research. Dallas, TX
2001-2008	Assistant Professor, Texas A&M University System Health Science center, Baylor College of Dentistry, Department of Biomedical Sciences. Dallas, TX
2005-2008	Adjunct Assistant Professor, Baylor University, Waco, TX
2008-2011	Assistant Professor, Florida Atlantic University, Charles E. Schmidt College of Medicine, Boca Raton, FL
2008-	Director of Flow Cytometry Core Facility, Florida Atlantic University, Charles E. Schmidt College of Medicine, Boca Raton, FL
2008-2011	Affiliated Assistant Professor of Microbiology & Immunology, University of Miami Miller School of Medicine, Miami, FL
2011-2017	Associate Professor, Florida Atlantic University, Charles E. Schmidt College of Medicine, Boca Raton, FL
2011-	Professor, Florida Atlantic University, Charles E. Schmidt College of Medicine, Boca Raton, FL

Other Experience and Professional Memberships

2008	Abstract reviewer, American Society of Transplantation (ASTS/AST)
2000-	American Association of Immunologists (AAI)
2000-2004	International Association for Dental Research (IADR)
2001-	Lecturer, PBL Facilitator, and Course Director
2001-2010	American Association of Cancer Research (AACR)
2002-2008	American Association of Dental Research (AADR)
2002-2005	Consultant, US Oncology
2004-2005	Chair, Research Committee, Texas A&M University Health Science Center
2005-2008	American Association for the Advancement of Science (AAAS)
2005-2012	American Society of Transplantation (AST)
2005-2007	Consultant, Murex Pharmaceutical Inc.
2005-2008	Consultant, ODC Therapy Inc.
2005	Peer-reviewer, Transplant Immunology Journal, Clinical Immunology Journal
2005-2007	Peer-reviewer, Phillip Morris Inc., External Research Program
2006	Study Section reviewer, NIAID/NIH Transplantation, Tolerance and Tumor Immunology (TTT)
2006	Peer-reviewer, Expert Opinion on Drug Discovery
2010	Peer-reviewer, Cancer Immunology and Immunotherapy
2010-	Member, Faculty Affairs, LCME meeting, FAU- College of Medicine
2011-	Member, Admissions Committee, FAU-College of Medicine
2011-	Member, Research Committee, FAU-College of Medicine
2011-	Chair, Graduate Program Committee, FAU-College of Medicine
2011-	Member, College Promotion and Tenure Committee, FAU-College of Medicine
2012-	Member, College of Medicine Curriculum Committee, FAU-College of Medicine
2011-	Member, University Graduate Council, Florida Atlantic University
2012-	Member, M1/M2 Committee, FAU-College of Medicine
2013	Member, Ad Hoc IMS P&T committee, FAU-College of Medicine
2013-	Senator, University Faculty Senate, Florida Atlantic University
2013-	President, Faculty Assembly, FAU-College of Medicine

2013- Chair, Faculty Assembly Executive (FAX) committee, FAU-College of Medicine
2014 Peer-reviewer, Journal of Immunology Research
2014- Editorial Board, Journal of Annals of Vaccines and Immunization
2014- Member, Medical Student Promotions and Professional Standards Committee (MSPPSC), FAU-College of Medicine
2014- Member, Institutional Animal Care and Use Committee (IACUC), Florida Atlantic University
2015 Peer-reviewer, International Immunopharmacology, Analytical Cellular Pathology
2017 Peer-reviewer, Veterinary Immunology and Immunopathology

Honors and Awards

2016 AAI Travel Award, International Congress of Immunology 2016
2016 Nominated by the College for the Distinguished Mentor of the Year Award: Excellence in Undergraduate Research and Inquiry Mentorship
2015 AAI Laboratory Travel Award, The American Association of Immunologists
2014 AAI Laboratory Travel Award, The American Association of Immunologists
2013 Outstanding Problem-Based Learning (PBL) Facilitator Award, Charles E. Schmidt College of Medicine
2012 Researcher Excellence Award, American Association for Laboratory Animal Science
2012 AAI Laboratory Travel Award, The American Association of Immunologists
2011 Dwight W. Warren Award for Excellence in Graduate Teaching, Florida Atlantic University-Charles E. Schmidt College of Medicine
2011 Teaching and presentation Award, American Association for Laboratory Animal Science
2006-2007 Basic Science Faculty Research Award, Texas A&M University Health Science Center- Baylor College of Dentistry
1992-1996 Doctoral scholarship Award, Japan Ministry of Education
1986-1992 Graduate scholarship Award, Japan Ministry of Education

C. Contributions to Science

- In my early publications on dendritic-based cancer immunotherapy, I reported a methodology that could overcome the limitations associated with DC-based vaccination protocols, namely peptide restriction to a given HLA, immune diversification, and the need for an adequate amount of autologous tumor tissue as a source of tumor antigens. So far, the immunotherapies of cancer targeted toward tumor associated antigens have yielded limited clinical responses, suggesting that these antigens are unlikely to represent therapeutic targets *in vivo*. Therefore, it has been my belief that the success of cancer vaccine highly relies on the existence of the tumor specific antigens to which the patients have not developed tolerance.

  1. **M. Nouri-Shirazi,** J. Banchereau, J. Fay, and K. A. Palucka. Dendritic cell based tumor vaccine. IMMUNOLOGY LETTERS 74 (1): 5-10 Sp. Iss. SI SEP 15 2000
  2. **M. Nouri-Shirazi**, J. Banchereau, D. Bell, S. Burkeholder, E. T. Kraus, J. Davoust, and Karolina A. Palucka. Dendritic cells capture killed tumor cells and present their antigens to elicit tumor-specific immune responses. THE JOURNAL OF IMMUNOLOGY 165 (7): 3797-3803 OCT 1 2000
  3. F. Berard, P. Blanco, J. Davoust, E.M. Neidhart-Berard, **M. Nouri-Shirazi**, N. Taquet, D. Rimoldi, J.C. Cerot-tini, J. Banchereau, and A. K. Palucka. Cross-priming of naïve CD8+ T cells against melanoma antigens using dendritic cells loaded with killed allogeneic melanoma cells. JOURNAL OF EXPERIMENTAL MEDICINE 192 (11): 1535-1543 DEC 4 2000
  4. Zeng M, Nourishirazi E, Guinet E, and **Nouri-Shirazi M**. Genetic background influences the cellular and humoral immune responses to vaccines. CLINICAL AND EXPERIMENTAL IMMUNOLOGY Volume: 186 Issue: 2 Pages 190–204 Nov 2016
  5. **Nouri-Shirazi M**,Tamjidi S, Nourishirazi E, and Guinet E. *TLR8 combined withTLR3 or TLR4 agonists enhances DC-NK driven effector Tc1 cells.* Immunology Letters (In Press)

- I expanded our research on the topic of cancer immunotherapy to nicotinic effects on tumor immunosurveillance and immunotherapy, with the hypothesis that the adverse effects of nicotine on the biological activities of DCs increases the susceptibility of smokers to cancer and infectious diseases and decreases the effectiveness of vaccination. Our pioneering in vitro and in vivo work (indicated by asterisks) revealed that nicotine-induced defects in the differentiation and the biological activities of DCs diminishes

the development of antigen-specific effector memory Th1 cells and antibody production, leading to poor host response to an otherwise protective and therapeutic vaccine.

1. **M. Nouri-Shirazi,** E. Guinet. Evidence for the immunosuppressive role of nicotine on human dendritic cell functions. IMMUNOLOGY 109 (3): 365-373 JUL 2003
2. Guinet, K. Yoshida and **M. Nouri-Shirazi.** Nicotinic environment affects the differentiation and functional maturation of monocytes derived dendritic cells (DCs). IMMUNOLOGY LETTERS 95 (1): 45-55 AUG 15 2004
3. **M. Nouri-Shirazi,** E. Guinet. A possible mechanism linking cigarette smoke to higher incidence of respiratory infection and asthma. IMMNUOLOGY LETTERS 103 (2): 167-176 MAR 15 2006
4. **M. Nouri-Shirazi**, R. Tinajero and E. Guinet. Nicotine alters the biological activities of developing mouse bone marrow-derived dendritic cells (DCs). IMMUNOLOGY LETTERS 109 (2): 155-164 MAR 9 2007
5. **M. Nouri-Shirazi** and E. Guinet. Exposure to nicotine adversely affects the dendritic cell system and compromises host response to vaccination. THE JOURNAL OF IMMUNOLOGY 188 (5): 2359-70 MAR

- I addition, I introduced a method of presenting a broad spectrum of donor alloantigens by pharmacologically modified recipient DCs that lead to indirect pathway tolerance induction. I also investigated a DC-based requirement for *in vivo* expansion and maintenance of antigen specific regulatory T cells and their impact on graft rejection mediated by both direct and indirect pathways in naïve mice and mice with history of exposure to alloantigens.

1. **M. Nouri-Shirazi**, E. Guinet. Direct-, and Indirect Cross-Tolerance of Alloreactive T cells by Dendritic cells Retained in the Immature Stage. TRANSPLANTATION 74 (7): 1035-1044 OCT 15 2002
2. **M. Nouri-Shirazi,** AW. Thomson. Dendritic cells as promoters of transplant tolerance. EXPERT OPINION ON BIOLOGICAL THERAPY 6 (4): 325-339 APR 2006
3. M. Zeng, E. Guinet an**d M. Nouri-Shirazi.** B7-1 and B7-2 differentially control peripheral homeostasis of CD4+CD25+Foxp3+ regulatory T cells. TRANSPLANT IMMUNOLOGY 20 (3): 171-179 JAN 2009
4. M. Zeng, E. Guinet and **M. Nouri-Shirazi.** Comparative analysis of dendritic cells and anti-CD3/CD28 expanded regulatory T cells for application in transplantation. TRANSPLANT IMMUNOLOGY 22 (1-2): 82-92 December 2009

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

Research Support

- 1R03AI103750-01A1 Nouri-Shirazi (PI) 07/01/13-06/30/17
  NIH-NIAID
  Overcoming the degrading effects of nicotine on vaccine using TLR agonists
  The major goal of this proposal is to determine the mechanisms by which the TLR7/8 agonist exerts its unique adjuvant effects in nicotine-exposed mice.
  Role: PI

- Georgia Aquarium Nouri-Shirazi (PI) 08/01/2012-07/30/2018
  Characterization of Atlantic Bottlenose Dolphin Dendritic Cells.
  The major goal of this proposal is to generate a knowledge base to further study emerging diseases in this species and the possible negative influences of environmental stressors on their immune system and human who inhabit the same coastal ecosystems.
  Role: PI

- The National Natural Science Foundation of China (NSFC) Zeng (PI) 2014-2017
  Mechanisms by which resiquimod-mediated enhancement of DC-NK cross-leads to a strong Th1 immunity
  Role: Mentor

Completed Research Support

- 1R15NS066339 Jianning Wei (PI) 07/01/2009-06/30/2011
  NIH-NINDS

Regulation of BimEL phosphorylation in the pathogenesis of Huntington's disease.
The major goal of this proposal is to understand the molecular pathways that are altered by mHtt expression. Specifically the link between the pro-apoptotic BH3-only protein, BimEL, and mHtt aggregates.
Role: Collaborator

- Philip Morris External Research Program — Nouri-Shirazi (PI) — 08/01/2005-12/31/2010
  Phillip Morris Inc. USA
  The impact of nicotine on dendritic cells and host immunity.
  The goal of this project was to expand on our *in vitro* results and determine the physiological effects of nicotine on host response to model antigen.
  Role: PI
- K23 DE00-469-01 — Ezzo (PI) — 2001-2003
  NIH-NIDCR
  Dendritic Cells & Actinobacillus Actinomycetemcomitans
  Role: mentor
- R01CA78846-01A1 — Banchereau (PI) — 1999-2000
  NIH-NIAID
  Subpopulations of Human Dendritic Cell
  Role: Senior Postdoctoral Fellow
- CaPCURE — Banchereau (PI) — 1999-2000
  Generation of prostate carcinoma Specific T cell lines and clones using dendritic cells.
  Role: Co-investigator

Andrew Oleinikov, Ph.D.
Associate Professor of Biomedical Science

Education

- M.S. (honors) in Biophysics, St. Petersburg Polytechnical University, St. Petersburg, Russia, 1983
- Ph.D. in Biology, Moscow State University, Moscow, Russia, 1989

Research Interests

- Malaria studies with emphasis on mechanisms of sequestration of infected erythrocytes, protective immune response and vaccine development, anti-adhesion drugs.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Andrew V. Oleinikov

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

POSITION TITLE: Associate Professor of Biomedical Science

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
St. Petersburg Polytechnical University, St. Petersburg, USSR	M.S.	1983	Physics, Biophysics, Molecular Biology
Moscow State University, Moscow, USSR	Ph.D.	1989	Molecular Biology, Biochemistry

A. Personal Statement

1) I have experience and publication track record in four specific fields directly relevant to the proposed work: malaria studies concentrated predominantly on cytoadherence between malarial PfEMP1 proteins and host receptors (**Section C4** below); mechanistic studies on the normal functioning (including signaling) and related pathology of trans-membrane receptors (e.g. megalin) (**Section C2**); studies on novel technology development including high throughput screening approaches and on biophysical methods including electrochemical biosensors (**Section C3**); immunological studies (**Section C2 and C4**). My experience in these fields is reflected in the list of selected publications below (**Section C**) and in my complete list of publications (*link provided* below). Some of these works are highly cited in current literature; 2) I have experience in protein biochemistry and biophysics, cell biology including endocytosis, protein-ligand interactions, protein cross-linking, immunology, high throughput approaches, malaria parasite studies, and drug studies (publications **a-c** below in this section) - all expertise necessary to obtain and analyze data from suggested experiments.

a. Tcherniuk SO and Oleinikov AV – Pgp efflux pump decreases the cytostatic effect of CENP-E inhibitor GSK923295. (2015) ***Cancer Letters,*** V. 361 (1), p. 97–103

b. Tcherniuk SO, Chesnokova O, Oleinikov IV, Potopalsky AI, Oleinikov AV – Anti-malarial effect of semi-synthetic drug Amitozyn. (2015) ***Malaria Journal,*** V. 14, p. 425-434

c. Therniuk SO, Chesnokova O, Oleinikov IV, Oleinikov AV – Nicotinamide inhibits the growth of P. falciparum and enhances the antimalarial effect of artemisinin, chloroquine and pyrimethamine. (2017) **Mol. Biochem. Parasitol**. V. 216, p. 14-20

B. Positions and Honors

1985 – 1988 **Graduate Student**, Institute of Protein Research Russian Academy of Science, Pushchino, Russia. (Dissertation was defended at Moscow State University, Moscow, Russia).

1988 – 1990 **Research Scientist**, Institute of Protein Research Russian Academy of Science, Pushchino, Russia.

1991 – 1994 **Postdoctoral Researcher**, University of California, Davis, School of Medicine, Department of Biological Chemistry, Davis, CA.

1994 – 1996 **Postdoctoral Researcher**, University of California, Davis, School of Medicine, Department of Pediatrics, Davis, CA.

1997 – 2000 **Assistant Professor (Research Series)**, University of California, Davis, School of Medicine, Department of Pediatrics, Davis, CA.
2000 – 2003 **Principal Scientist and Group Leader**, CombiMatrix Corporation, Mukilteo, WA.
2004 – 2013 **Principal Scientist,** Seattle Biomedical Research Institute, Seattle, WA
2013 – present **Associate Professor (tenured)**, Charles E. Schmidt College of Medicine, Department of Biomedical Science, Florida Atlantic University, Boca Raton, FL

Honors

2015 Florida Atlantic University "Degree of Difference" Award for teaching graduate students

Other Experience and Professional Memberships

Ad Hoc NIH reviewer:

- ZRG1 BDCN-S(02) (**Panel reviewer**) (July 2017)
- PTHE (**Panel reviewer**) (February 2017)
- CNBT (**Panel reviewer**) (October 2015)
- ZRG1 BCMB-A (51) R (mail reviewer) (March 2015)
- ZGM1-TWD-6 (SC) (**Panel reviewer**) (March 2014)
- IRAP (**Panel reviewer**) (September 2014)
- ZRG1 IDM-U 56 R (Spesial Emphasis **Panel reviewer**) (November 2013)
- CNBT (**Panel reviewer**) (October 2012)
- ZRG1 AARR-D (42) (Special Emphasis **Panel reviewer**) (August 2012)
- ZRG1 BST-F (30) (Special Emphasis **Panel reviewer**) (October 2009)
- ZRG1 IDM-C (58) (mail reviewer) (July 2009)
- ZRG1 IMM-E (58) (mail reviewer) (July 2009)

Memberships

2002 American Society for Cell Biology
2006-present American Society for Tropical Medicine and Hygiene

C. Contribution to Science

1. In 1991-1998 contributed to studies of the process of ribosomal elongation during protein biosynthesis and structure-function relationship of ribosomal protein L7/L12 (the only tetramer on the ribosome present as 2 dimers) using genetic engineering of partial and hybrid molecules, chemical cross-linking, and a number of biochemical and biophysical techniques. These studies resulted in publication of 13 papers cited more than 400 times. The main contribution was the determination of how different domains of the L7/L12 molecule interact with other proteins on the ribosome and with elongation factors, the importance of the flexible hinge for protein activity, and demonstration that C-terminal domains work independently and a single-headed dimer of L7/L12 is fully functionally active (publications **b** and **c** below). As L7/L12 is the only protein on the ribosome not localized by X-ray crystallography due to its extreme mobility, our work remains an important source of information about this protein in studies of mechanisms of ribosomal functioning. I was the first author of these publications, the primary investigator and the corresponding author (*) in the third publication.

a. Oleinikov AV, Perroud B, Wang B, Traut RR - Structural and functional domains of *E. coli* ribosomal protein L7/L12. The hinge region required for activity. (1993) ***J.Biol.Chem.***,V.268, No.2, pp.917-922.

b. Oleinikov AV, Jokhadze GG, Traut RR - Escherichia ribosomal protein L7/L12 dimers remain fully active after interchain crosslinking of the C-terminal domains in different orientations. (1993*)* ***Proc. Nat. Acad. Sci. USA*****,** V.90, p.9828-9831.

c. Oleinikov AV*, Jokhadze GG, Traut RR – A single-headed dimer of E coli ribosomal protein L7/L12 supports protein synthesis. (1998) ***Proc. Nat. Acad. Sci. USA*****,** V.95, p.4215-4218.

2. In 1997-2000 contributed to studies of a giant endocytic receptor megalin belonging to the LDL-receptor superfamily and major autoantigen of Heymann nephritis (a model for human acute and chronic glomerular nephritis and end-stage renal failure) by identifying pathogenic B- and T-cell autoimmune epitopes (pub. **a** and **b**). We conducted seminal work on the identification of the first intracellular ligand of megalin, adaptor protein Disabled 2 (Dab2). Our hypotheses that megalin might be involved in signal transduction through Dab2 as well

as that Dab2 might serve as an adaptor protein for endocytosis opened a new avenue for studies of this endocytic/signal transduction system not only in kidney, but in a number of other organs and in embryonic development. This work (I was the primary investigator on this study and the first corresponding (*) author) was published in ***Biochemical Journal*** (pub. **c**) and is steadily cited (>160 times) for the last 16 years. I have continued these studies now in application to placental malaria (PM) starting in 2012, as megalin system is highly expressed in placenta (organ with a 3rd highest megalin expression). We have found that this system is affected during PM, which may play a role in low birth weight (pub. **d**). I was the primary investigator* on this study. It was further expanded to test samples from a different geographical area and to *in vitro* cellular studies, and is currently funded by NIH R21 grant.

a. Oleinikov AV, Feliz BJ, Makker SP – A small 60 kDa fragment of gp600/megalin, major autoantigen of active Heymann nephritis of rat, can induce full-blown disease. (2000) ***J.Am. Soc.Nephrol.,*** V.11, p.57-64.

b. Oleinikov AV and Makker SP – Increased expression of cytoplasmic tail-containing form of gp600/megalin in active Heymann nephritis. (2000) ***J. Pathol*****.** V.192, p.251-256.

c. Oleinikov AV*, Zhao J, Makker SP – Cytosolic adaptor protein Dab2 is an intracellular ligand of endocytotic receptor megalin. (2000) ***The Biochemical Journal,*** V.247, p.613-621.

d. Lybbert J, Gullingsrud J, Chesnokov O, Turyakira E, Dhorda M, Guerin PJ, Piola P, Muehlenbachs A, and Oleinikov AV* – Abundance of megalin and Dab2 is reduced in syncytiotrophoblast during placental malaria, which may contribute to low birth weight. (2016) ***Sci. Rep***, V.**6,** p. 24508

3. In 2000-2003 developed a number of novel technologies based on an addressable array of electrodes on semiconductor microchips: a) for protein microarray manufacturing using *in vitro* and *in situ* protein biosynthesis; b) for long gene synthesis and assembly; c) for anti-sense drug compound screening d) for fast and efficient preparation of siRNA mixtures usable in gene down-regulation by RNA interference and for drug discovery; e) for electrochemical detection of protein-ligand interactions. The work resulted in the publication of 3 papers (below) cited >160 times and a patent award. I was the primary investigator in these studies and awarded SBIR NIH grant as a PI to develop protein array technology. *These studies were the intellectual basis for the development of a high throughput screening system, described in the next paragraph and extensively used in my malaria studies including current proposal.*

a. Oleinikov AV*, Gray MD, Zhao J, Montgomery DD, Ghindilis AL, Dill K – Self-assembling protein arrays using electronic semiconductor microchips and *in vitro* translation. (2003) ***Journal of Proteome Research*** V. 2, p.313-319.

b. Dill K, Montgomery DD, Ghindilis AL, Schwarzkopf KR, Ragsdale SR, Oleinikov AV – Immunoassays Based on Electrochemical Detection Using Microelectrode Arrays. (2004) ***Biosensors and Bioelectronics*** V. 20, p.736-742.

c. Oleinikov AV*, Zhao J, Gray MD – RNA interference by mixtures of siRNAs prepared using custom oligonucleotide arrays. (2005) ***Nucl. Acid Res.*** V. 33, p. e92.

d. Oleinikov AV. "Microarray synthesis and assembly of gene-length polynucleotides". US Patents **#7,323,320** (issued 01-29-2008), **#7,563,600 B2** (issued 07-21-2009), **#8,058,004** (issued 11-15-2011), and **#9,023,601** (issued 05-0502015) by US Patent and Trademark Office, also filed with European Patent Office).

4. In 2006-2017 contributed to various aspects of malarial studies including identification of vaccine candidates in childhood and placental malaria (US patents #7,655,247 B2 and #8,012,493 B2), with the main focus on the structure and function of *P. falciparum* adhesins, PfEMP1 family of proteins linked to sequestration of *P. falciparum*-infected erythrocytes in microvasculature/placenta and severe forms of malaria. Published 13 papers (cited >200 times). The main contributions were i) development and application of a quantitative functional protein microarray platform for high throughput screening of receptors and antibodies interacting with a large family of PfEMP1 malarial surface proteins (publications **a-d** below); ii) identification of a novel ICAM-1-binding PfEMP1 domain (publication **b**) and relating the immune response to this domain to protection against severe malaria (publication **c**); iii) preparation of a complete (n=190 domains) functional PfEMP1 domain library from a parasite line (manuscript submitted and publications **a-c**); iv) development of a two-step system for and identification of anti-adhesion compounds that prevent sequestration of infected erythrocytes to the host receptors as a proof-of-principle (publication **d**). I served as the primary investigator and was the corresponding

author (*) in cited works below and the PI on a number of NIH grants (R21s, R56, R01s) awarded to study malaria including placental malaria (**Section D**).

a. Oleinikov AV*, Rossnagle E, Francis SE, Mutabingwa TK, Fried M, Duffy PE –Effects of sex, parity and sequence variation on seroreactivity to candidate pregnancy malaria vaccine antigens. (2007) ***J. Infect. Diseases*** V. 196, p.155-164.

b. Oleinikov AV*, Amos E, Frey TI, Rossnagle E, Mutabingwa TK, Fried M, Duffy PE – High throughput functional assays of the variant antigen PfEMP1 reveal a single domain in the 3D7 *P. falciparum* genome that binds ICAM1 with high affinity and is targeted by naturally acquired neutralizing antibodies. (2009) ***PLoS Pathogens***, V. 5, p. e1000386

c. Oleinikov AV*, Voronkova V, Frey TI, Amos E, Morrison R, Fried M, Duffy PE – A survey of naturally acquired antibody responses to 38 PfEMP1 domains in plasma of Tanzanian infants reveals frequent recognition of VAR2CSA. (2012) ***PLoS One***. V. 7, p.e31011.

d. Gullingsrud J, Milman N, Saveria T, Chesnokov O, Williamson K, Srivastava A, Gamain B, Duffy PE, Oleinikov AV* – High throughput screening platform identifies small molecules that prevent sequestration of *Plasmodium falciparum*-infected erythrocytes. (2015) ***J. Infect. Diseases*** V. 211 (7), p. 1134–43 (first published online: October 29, 2014)

Complete List of Published Work (43 publications) in My NCBI Collections:
http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/41133417/?sort=date&direction=ascending

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

ONGOING Research Support

1R21AI105506-01A1 (Oleinikov, PI) 02/01/2016 – 01/31/2018
NIH/NIAID
Mechanisms of placental dysfunction in pregnancy malaria
The proposal will test our hypothesis about potential role of proteins of the megalin transporting/signaling system in the placental transfer of nutrients and regulatory molecules, and association of their abundance/distribution with placental malaria and/or with low birth weight. One paper has been published.
Role: PI

1R21HD092779-01 (Du and Oleinikov, MPIs) 07/01/2017 – 06/30/2019
NIH/NICHD
Placenta-on-a-Chip Sensing Platform to Study Placental Malaria
This project will apply microfluidic organ-on-a-chip technology and biosensing technologies to develop novel placenta-on-a-chip sensing platform and validate it using placental malaria as a model.
Role: MPI

1R41AI129130-01A1 (Oleinikov, PI) 08/01/2017 – 06/30/2018
NIH/NIAID
Highly sensitive isothermal method and instrument for field diagnostics to facilitate malaria eradication
This project will adapt a novel and highly sensitive DNA diagnostics technology for early detection of the most virulent form of malaria caused by Plasmodium falciparum.
Role: PI

COMPLETED Research Support (selected relevant older grants on top)

R21AI064503-01A2 (Oleinikov, PI) 09/21/07-08/31/09
NIH/NIAID
High throughput analysis of malaria antigens
The goal of this study is to develop an array technology to study the antigenicity and function of surface proteins of *Plasmodium falciparum*. The main intended use of this technology was extensive seroepidemiology studies directed at identification of new vaccine candidates. This project has been completed successfully with development of the genome-wide array of PfEMP1 domains and resulted in several published papers.
Role: PI

1364 (Duffy, PI) 07/31/2005-12/31/2011
FNIH/Grand Challenges in Global Health
Protective immunity against severe malaria in young children (Consortium grant)
The goal of this project is to identify the immune responses that prevent severe disease and death due to malaria. The project involves a consortium of African, European, and American scientists who are evaluating phenotypes and gene/protein expression profiles of parasites causing severe disease, as well as the acquisition of immune responses that correlate with protection against malaria in longitudinal studies of young children. This project has been completed successfully with publication of several papers.
Role: Collaborator

47029 (Duffy, PI) 10/01/2007-10/01/2011
Bill and Melinda Gates Foundation
Malaria Antigen Discovery Program - Pregnancy Malaria Initiative (Consortium grant)
The goal of this project was to develop recombinant proteins that elicit functional antibodies against placental parasites as the next step in developing a pregnancy malaria vaccine. The project exploited existing consortium capabilities—human monoclonal antibodies; expression platforms; panel of CSA-binding laboratory parasites; field site to assess antisera against fresh placental parasites—to be rapid, efficient and comprehensive in achieving project goals. This project has been completed successfully with publication of several papers.
Role: Collaborator

R01HD058005 (Oleinikov, PI) 12/18/2008 – 11/30/2013
NIH/NICHD
Pathways of Maternal Anemia
I was appointed to complete the work on this grant started by previous PI. In malaria endemic areas, pregnancy malaria is a risk factor for maternal mortality due to anemia. Pregnancy malaria and maternal anemia are independent risk factors for low birth weight (LBW) deliveries that increase the risk of mortality during the neonatal period and infancy. The goal of this project is to identify potential immunological and transcriptional pathways and mediators that are pivotal in the pathogenesis of malaria associated maternal anemia. One published and two manuscripts are in preparation.
Role: New PI (from 2011 due to departure of the previous PI)

R56AI083668 (Oleinikov, PI) 09/24/2010-02/29/2012
NIH/NIAID
High throughput screening for anti-adhesion drugs to treat severe malaria
The goal of this project was *to develop a platform for screening* anti-adhesion compounds that block binding of infected erythrocytes *to endothelial cell receptors in vitro* to treat in future, as adjunctive therapy, various forms of severe malaria. Platform was successfully developed and a few inhibitory small molecules compounds were identified as a proof-of-principle using Petri dish binding inhibition assay. Three papers has been published, one more manuscript is in preparation.
Role: PI

R01AI092120-01 (Oleinikov, PI) 03/01/2011 – 02/28/2016
NIH/NIAID
Identification of vaccine candidates against severe malaria
The goal of this project is to better understand the protective humoral immune responses against PfEMP1 family of infected erythrocyte surface proteins in severe malaria in children and identify PfEMP1 domains as vaccine candidates against severe malaria syndromes. This proposal will exploit our recently-developed functional high throughput *in vitro* system to understand functional anti-PfEMP1 immune responses at the genome-wide level and plasma samples from longitudinal and hospitalization cohorts of children living in malaria endemic areas in Tanzania. Four publications resulted from this work, and a number of manuscripts are currently in preparation.
Role: PI

Michele Pergadia, Ph.D.
Associate Professor of Clinical Biomedical Science and Director of Health Behavioral Science

Education

- B.A., Biology and Psychology, Washington University, St. Louis, Missouri, 1987-1991
- M.S., Clinical Psychology, Finch University of Health Sciences/The Chicago Medical School, North Chicago, Illinois, 1994-1998
- Ph.D., Clinical Psychology, Finch University of Health Sciences/The Chicago Medical School, North Chicago, Illinois, 1998-2001
- Health Psychology Resident, Rush Presbyterian St. Luke's Medical Center, Chicago, Illinois, 2001
- Postdoctoral Research Fellow/Associate, Genetic Epidemiology, Washington University School of Medicine, St. Louis, Missouri, 2001-2004

Research Interests

Dr. Pergadia's research informs health related behaviors, such as smoking and associated factors such as depression. Her cross-disciplinary collaborations involve epidemiologic, genetic, human laboratory, and animal models to address these major public health problems. Her work also considers translation to practice, by examining dissemination and implementation of evidence-based treatments for smoking cessation. In addition to training and mentoring within that context, her track record as a principal investigator and co-investigator on National Institutes of Health and non-federal grants includes inves- tigations of smoking and related behaviors. Her collaborative work is reflected in over 70 publications, including papers in the *American Journal of Psychiatry* and *Nature Genetics*. An example of the inno-

vative translational approach is evident in one of her recent papers in *JAMA Psychiatry*, in which reward dysfunction during nicotine withdrawal was replicated across species using similar behavioral assessment procedures.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Michele L. Pergadia, Ph.D.

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

POSITION TITLE: Associate Professor of Integrated Medical Science

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Washington University	B.A.	05/1991	Biology & Psychology
Finch University of Health Sciences/ The Chicago Medical School	M.S.	06/1998	Clinical Psychology
Finch University of Health Sciences/ The Chicago Medical School	Ph.D.	06/2001	Clinical Psychology
Washington University School of Medicine	Post-doc	06/2004	Genetic Epidemiology

A. Personal Statement

My research interests concern biopsychosocial models of nicotine dependence and smoking cessation, including bidirectional relations with history of major depression and related psychiatric conditions. I am a psychologist whose clinical research spans epidemiologic, laboratory, treatment, and psychiatric genetic studies in the study of smoking-related behavior; with a focus to uncover the mechanisms underlying problems such as nicotine withdrawal and depression in human smokers. During my graduate training as a clinician-scientist at Chicago Medical School, I gained experience in laboratory studies and clinical trials involving cigarette smokers, including pharmacological and behavioral interventions, and diagnostic assessment of nicotine dependence and other psychiatric disorders. During my post-doctoral fellowship and the initial years of my K-award, I received extensive training at Washington University School of Medicine using comprehensive lifetime diagnostic assessments and analytical procedures applicable to large complex datasets, including genetic epidemiologic studies, with a focus on smoking-related behavior, particularly nicotine dependence, in addition to commonly co-morbid depression and other psychiatric conditions.

B. Positions and Honors

Positions and Employment

2004-06 Research Instructor, Washington University School of Medicine, St. Louis, MO
2006-12 Research Assistant Professor, Washington University School of Medicine, St. Louis, MO
2012-14 Research Associate Professor, Washington University School of Medicine, St. Louis, MO
2014 Associate Professor, Washington University School of Medicine, St. Louis, MO
2014- Associate Professor, Charles E. Schmidt College of Medicine, Florida Atlantic University, Boca Raton, FL

Other Experience and Professional Memberships

2006-2014 Research Associate Member, Siteman Cancer Center, Barnes-Jewish Hospital/Washington University School of Medicine, St. Louis, MO
2006-2014 Medical Staff/Department of Psychiatry, Barnes-Jewish Hospital/Washington University Medical Center, St. Louis, MO
2008-2014 Executive Board Member of the Missouri Family Registry
2008-2014 Member, Institute for Public Health, Washington University

2010-2014 Member, Diabetes Research and Training Center, Washington University

Professional Memberships:

1994- American Psychological Association
1998- Society of Behavioral Medicine
2000- Society for Research on Nicotine and Tobacco
2001- Behavior Genetics Association
2012- Association of Psychologists in Academic Health Centers

Honors/Awards

1998 Citation Award from Society of Behavioral Medicine
1999 Veterans Administration Predoctoral Fellowship
1999-00 American Heart Association Predoctoral Fellowship
2003-08 NIH Loan Repayment Program Award
2003 NIDA CPDD Women and Gender Junior Investigator Travel Award
2003 Society for Research on Nicotine and Tobacco Young Investigator Travel Award

C. Contributions to Science (selected from 80 peer-reviewed publications; 3 book chapters).

1. Phenotypic Refinement of Nicotine Dependence and Related Behavior.
A challenge in clinical research is identifying reliable and valid measures of complex outcomes, such a nicotine dependence in humans. Over the last 15 years I have led multidisciplinary approaches to characterize nicotine dependence and related behaviors, including epidemiologic and cross-translational human laboratory studies, in effort to converge on measures that indicate reliable influences on nicotine dependence.

a. Pergadia, M.L., Der-Avakian, A., D'Souza, M., Madden, P.A.F., Heath A.C., Shiffman, S., Markou, A., Pizzagalli, D.A. (2014). Association between nicotine withdrawal and reward responsiveness in humans and rats. JAMA Psychiatry, 71 (11), 1238-1245. PMID: 25208057 PMCID: PMC4353576

b. Pergadia, M.L., Agrawal, A., Heath, A.C., Martin, N.G., Bucholz, K.K., & Madden, P.A.F. (2010). Nicotine withdrawal symptoms in adolescent and adult twins. Twin Research and Human Genetics, 13 (4), 359-69. PMID: 20707706 PMCID: PMC3051418.

c. Pergadia, M.L., Heath, A.C., Agrawal, A., Bucholz, K.K., Martin, N.G., and Madden, P.A.F. (2006). The implications of simultaneous smoking initiation for inferences about the genetics of smoking behavior from twin data. Behavior Genetics, 36 (4), 567-576. PMID: 16477519.

d. Pergadia M.L., Heath A.C., Martin N.G., & Madden, P.A.F. (2006). Genetic analyses of DSM-IV nicotine withdrawal in adult twins. Psychological Medicine, 36 (7), 963-972. PMID: 16749946.

2. Molecular Genetic Studies of Nicotine Withdrawal and Related Smoking Behavior.
Following from phenotypic refinement research, I have led and collaborated on efforts to map nicotine withdrawal and other smoking-related behaviors to specific genetic regions within large linkage and genetic association studies, including work that supported the now widely replicated effect of rs16969968 (in *CHRNA5*) or its proxy rs1051730 (in *CHRNA3*) on smoking-related behavior.

a. Pergadia, M.L., Agrawal, A., Loukola, A., Montgomery, G.W., Broms, U., Saccone, S.F., Wang, J.C., Todorov, A.A., Heikkilä, K., Statham, D.J., Henders, A.K., Campbell, M.J., Rice, J.P., Todd, R.D., Heath, A.C., Goate, A.M., Peltonen, L., Kaprio, J., Martin, N.G., Madden, P.A.F. (2009). Genetic linkage findings for DSM-IV nicotine withdrawal in two populations. American Journal of Medical Genetics. Part B. Neuropsychiatric Genetics, 150B (7), 950-959. PMID: 19180564 PMCID: PMC2995916.
b. Lind*, P.A., Macgregor*, S., Vink*, J.M., Pergadia*, M.L., Hansell, N.K., de Moor, M. Smit, A.B., Hottenga, J., Heath, A.C., Martin, N.G., de Geus, E.J.C., Vogelzangs, N., Penninx, B.W., Whitfield, J.B., Montgomery, G.W., Boomsma, D.I., Madden, P.A.F. (2010). A genomewide association study of nicotine and alcohol dependence in Australian and Dutch populations. Twin Research and Human Genetics, 13 (1), 10-29. PMID: 20158304 PMCID: PMC3070599. **joint first authors;*

c. Thorgeirsson TE... Pergadia ML,….Stefansson K. (2010). Sequence variants at CHRNB3-CHRNA6 and CYP2A6 affect smoking behavior. Nature Genetics, 42(5):448-53. PMID: 20418888 PMCID: PMC3080600.

d. Saccone, N.L., Culverhouse, R.C., Schwantes-An, T., Cannon, D.S., Chen, X., Cichon, S., Giegling, I., Han, S., Han, Y., Keskitalo-Vuokko, K., Kong, X., Landi, M.T., Ma, J.Z., Short, S.E., Stephens, S.H., Stevens, V.L., Sun, L., Wang, Y., Wenzlaff, A.S., Aggen, S.H., Breslau, N., Broderick, P., Chatterjee, N., Chen, J., Heath, A.C., Heliövaara, M., Hoft, N.R., Hunter, D.J., Jensen, M.K., Martin, N.G., Montgomery, G.W., Niu, T., Payne, T.J., Peltonen, L., Pergadia, M.L., Rice, J.P., Sherva, R., Spitz, M.R., Sun, J., Wang, J.C., Weiss, R.B., Wheeler, W., Witt, S.H., Yang, B., Caporaso, N.E., Ehringer, M.A., Eisen, T., Gapstur, S.M., Gelernter, J., Houlston, R., Kaprio, J., Kendler, K.S., Kraft, P., Leppert, M.F., Li, M.D., Madden, P.A.F., Nöthen, M.M., Pillai, S., Rietschel, M., Rujescu, D., Schwartz, A., Amos, C.I., Bierut, L.J. (2010). Multiple independent loci at chromosome 15q25.1 affect smoking quantity: a meta-analysis and comparison with lung cancer and COPD. PLoS Genetics, 5; 6(8). pii: e1001053. PMID: 20700436 PMCID: PMC2916847.

3. Studies of Co-morbid Behavior: Major Depression.

Smoking-related behaviors, including nicotine withdrawal are highly co-morbid with depression. Thus, my work has also focused on gaining a better understanding of that phenotypic and genetic relationship. I have led large-scale efforts to map genomic correlates of depression in families of heavy smokers using genetic linkage analyses, in addition to collaborating on consortium efforts to pool samples across studies with the goal to identify genetic markers associated with major depression and other psychiatric problems.

a. Pergadia, M.L., Glowinski, A.L., Wray, N.R., Agrawal, A., Saccone, S.F., Loukola, A., Broms, U., Korhonen, T., Penninx, B.W.J.H., Grant, J.D., Nelson, E.C., Henders, A.K., Schrage, A.J., Chou, Y., Kaisu, K., Zhu, R. Gordon, S.D., Vink, J.M., de Geus, E.J., MacGregor, S., Liu, J.Z., Willemsen, G., Medland, S.E., Boomsma, D.I., Montgomery, G.W., Rice, J.P., Goate, A.M., Heath, A.C., Kaprio, J., Martin, N.G., Madden, P.A.F. (2011). A 3p26-3p25 genetic linkage finding for DSM-IV major depression in heavy smoking families. American Journal of Psychiatry, 168 (8), 848-852. PMID: 21572167 PMCID: PMC3433250.

b. Wray, NR, Pergadia, ML, Blackwood, DHR, Penninx, BWJH, Gordon SD, Nyholt, DR , Ripke, S, MacIntyre, DJ, McGhee, KA, Maclean, AW, Smit, JH, Hottenga, JJ, Willemsen, G, Middeldorp, CM, de Geus, EJC, Lewis, CM, McGuffin, P, Hickie, IB, van den Oord, EJCG, Liu, J, Macgregor, S, McEvoy, BP, Byrne, EM, Medland, SE , Statham, DJ, Henders, AK, Heath, AC, Montgomery, GW, Martin, NG, Boomsma, DI, Madden, PAF, Sullivan, PF. (2012). Genome-wide association study of major depressive disorder: New results, meta-analysis, and lessons learned. Molecular Psychiatry, 17(1), 36-48. PMID: 21042317 PMCID: PMC3252611.

c. Cross-Disorder Group of the Psychiatric Genomics Consortium, Lee SH…Pergadia ML, …Wray NR (2013) Genetic relationship between five psychiatric disorders estimated from genome-wide SNPs. Nature Genetics, 45 (9) 984-994. PMID: 23933821 PMCID: PMC3800159.

d. Korhonen, T., Loukola, A., Wedenoja, J., Nyman, E., Latvala, A., Broms, U., Häppölä, A., Paunio, T., Perola, M., Schrage, A., Vink, J., Pergadia, M.L., Madden, P.A.F., Kaprio, J. (2014) Nicotine Dependence Potentiates the Association between the Dopamine Receptor Gene DRD3 and Major Depressive Disorder. PLoS One. Jun 13;9(6):e98199. PMID: 24927283 PMCID: PMC4057087.

List of my published scientific papers available via PubMed:

https://www.ncbi.nlm.nih.gov/pubmed/?term=pergadia+m

D. Research Support

Active Research Support

1 R01 DA036032 (Gilbert-PI; Pergadia-PI of Subc. to FAU) 09/15/13-06/30/18
National Institute on Drug Abuse (NIDA)
"Predictors of Light Smoker Trajectories"
The goal of this study to examine the effects of brain, behavioral, genetic and self-report indices prior to and in response to acute nicotine and how these contribute to individual differences in smoking trajectories across a 18-month follow-up.
Role: Co-Investigator/Subcontract-PI

ACI-1541330 Pergadia (Co-PI) 03/15/16-03/14/18
National Science Foundation
(Principal Investigator: Dr. Jason O. Hallstrom, Florida Atlantic University;
other Co-PIs: Drs. Fraser Dalgleish, Gregg B. Fields & Borko Furht)
"CC*DNI Networking Infrastructure: Enabling Multi-Campus, Data-Driven Science and Engineering through a 10Gb FAU DMZ"
We are requesting support through the CC*DNI program to install intra- and inter-campus networking facilities to establish a 10Gb regional DMZ for research computing that will support data-intensive research and education in science and engineering.
Role: Co- Principal Investigator

Completed Research Support

Florida Atlantic University internal equipment grant Pergadia (PI) 05/22/2015
"Charles E. Schmidt College of Medicine Common Equipment Foundation Grant"
This proposal requests funds to purchase a computer cluster to be securely configured to handle data of a sensitive nature, such as that used in medical research.
Role: Principal Investigator

Project Award Funding Pergadia (PI) 07/01/13-08/17/14
Barnes-Jewish Hospital Foundation
"Smoking Cessation Services: An Integrated Care Model for the Primary Care Medicine Clinic"
The objectives of this proposal include piloting integrative smoking cessation services within the Primary Care Medicine Clinic (PCMC) of Barnes-Jewish Hospital (BJH).
Role: Principal Investigator

1 K08 DA019951 Pergadia (PI) 08/01/05-07/31/11
NIDA
"Refining Phenotypic Measures of Nicotine Withdrawal"
This K08 will help the PI develop an independent line of research to gain a greater understanding of both phenotypic characteristics and genetic influences on nicotine withdrawal in efforts to decrease morbidity and mortality in heavily dependent and relapsing smokers.
Role: Principal Investigator

2 R01 DA/CA12854 Madden (PI) 05/25/00-04/30/13
NIDA/National Cancer Institute (NCI)
"The Genetics of Vulnerability to Nicotine Addiction"
This project is a gene mapping study to identify specific chromosomal locations or candidate genes that have an effect on risk for addiction to nicotine.
Role: Collaborator

2 R01AA012640 Bucholz (PI) 04/01/00-04/30/13
National Institute on Alcohol Abuse and Alcoholism (NIAAA)
“Alcoholism: Epidemiologic High Risk Family Study”
This is a high risk genetic family study within an epidemiologic framework representing a novel paradigm for epidemiologic research on alcohol dependence. Oversampling of African -American families will permit testing of longstanding models of adolescent and young adult alcohol involvement based on majority youth.
Role: Collaborator

R01 DA020810 Xian (PI) 04/01/07-03/31/11
NIDA
“Environmental risk of smoking: A genetically informed children of twins design”
This study uses the offspring of twins design to identify environmental factors that contribute to the risk of smoking behaviors while accounting for genetic factors, including smoking initiation, regular smoking, nicotine withdrawal, cessation and nicotine dependence.
Role: Collaborator

R01 AA13321 Heath (PI) 09/29/01-08/31/07
NIAAA
“Molecular Epidemiology of Alcoholism 3 - EDAC Families”
This project (IRPG-3) is part of an IRPG for a program to localize genes that contribute to variation in heavy drinking and alcohol (and associated tobacco) dependence risk, using epidemiologically informative samples ascertained from general population surveys of the Australian Twin Register and their family members.
Role: Research Associate

DA020343 Pergadia (PI) 07/01/03-06/30/08
NIH, NIAAA/NIDA
Clinical Research-LRP
This initial award and subsequent competitive renewals repays educational loans for Principal Investigator Pergadia, who as a scientist-practitioner is pursuing clinically relevant alcohol and tobacco-related research.
Role: Principal Investigator

T32 AA07580 Heath (PI) 07/01/01-06/30/03
NIAAA
“Biomedical Training in Alcoholism Research”
Institutional National Research Service Award to support multidisciplinary postdoctoral training in alcoholism research, with special emphasis on neurobiology, epidemiology, and behavioral and statistical genetic approaches.
Role: Post-doctoral Fellow

910149Z Pergadia (PI) 07/01/99-06/30/01
American Heart Association
“The Effect of Tryptophan Depletion on Mood and Brain Activity in Depression-Prone Smokers”
Individual predoctoral fellowship to examine changes in mood and regional cerebral blood flow following tryptophan depletion in smokers with and without a history of depression.
Role: Principal Investigator

Howard Prentice, Ph.D.
Associate Professor of Biomedical Science

Education

- M.A., Experimental Psychology, Honors, University of Aberdeen, 1980.
- DEA. Neurobiology, L'INSERM, Paris, France 1981.
- M.Sc., Neurobiology, University of London, England, 1984
- Ph.D., Biochemistry, University of London, England, 1987

Research Interests

- Determination of regulatory characteristics of specific gene/promoter elements in normal and disease-stressed myocardial tissue with particular attention to the skeletal alpha actin and myosin heavy chain gene promoters and to hybrid hypoxia responsive/tissue specific promoters. Incorporation of hypoxia responsive promoters into regulated gene therapy vectors for ischaemia heart disease.
- Characterisation of the effects of cardiac hypertrophy on the expression of the calcium regulatory molecules SERCA2a and phos- pholamban. Analysis of the role of phosphodiesterase type 4 isoenzymes and myotonic dystrophy protein kinase in regulating phos- pholamban phosphorilation status and in modifying cardiac myocyte adaptations to hypertrophy.
- Examination of the effects on altered cardiac contractility of exoneous expression of contractile protein isoforms (troponin C fast, troponin T) in cardiac myocytes by means of adenoviral gene transfer into heart cells in culture and the myocardium in vivo.

OMB No. 0925-0001/0002 (Rev. 08/12 Approved Through 8/31/2015)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Howard M. Prentice

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

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Aberdeen	M.A. (Hons)	06/80	Exptl. Psychology
L'INSERM, Paris, France	D.E.A.	06/81	Neurobiology
University of London	M.Sc.	06/84	Neurochemistry
University of London	Ph.D.	08/87	Biochemistry
Stanford University School of Medicine, Palo Alto, California, Supervisor: Dr. Laurence H. Kedes. M.D.	Postdoctoral	09/87-01/89	Molecular Genetics
University of Southern California, Los Angeles, California, Supervisor: Dr. Laurence H. Kedes. M.D.	Postdoctoral	01/89-08/93	Molecular Genetics

A. Personal Statement

My research studies incorporate gene therapy approaches for retinal disease in addition to strategies for neuroprotection for stroke. In addition, using in vitro cell lines I have investigated protective interventions for preventing ER stress and apoptosis caused by glutamate induced excitotoxicity. These analyses provide the basis for understanding mechanism based protective strategies for neurodegenerative diseases (including Alzheimer's disease and Parkinson's disease) as well as ischemic stroke. With respect to neuronal function I am currently employing rodent stroke models to examine the mechanism of action of key ischemic preconditioning agents, neuro-protectants, gene therapy interventions and stem cell mobilizing agents. I have extensive experience of gene transfer using purified DNA or viral vectors into rodent models of heart disease. Hence my experience gene therapy models related to stroke in combination with my studies on retinal gene therapy have provided me with the necessary background to successfully carry out the current project addressing gene therapy for Alzheimer's disease.

1. Dougherty C, Smith G, Dorey CK, **Prentice H**, Webster KA, and Blanks J Robust Hypoxia-Selective Regulation of an RPE-Specific AAV Vector. Mol Vis. 2008 Mar 7;14:471-80
2. Moench I, **Prentice H,** Rickaway Z and Weissbach H. "Mechanisms of protection by sulindac against myocardial ischemic damage". 2009 Proc. Natl. Acad. Sci. USA. Nov 17;106(46):19611-6.

3. Mohammad-Gharibani P, Modi J, Menzie J, Jenova R, Ma Z, Chen PC, Tao R, **Prentice H** and Wu J.-Y. Mode of Action of S-Methyl-N, N-Diethylthiocarbamate Sulfoxide (DETC-MeSO) as a Novel Therapy for Stroke in a Rat Model. Molecular Neurobiology, 50(2):655-672 (2014), (DOI 10.1007/s12035-014-8658-0, 2014, Feb 28).
4. Gharibani P, Modi J, Menzie J, Alexandrescu A, Ma Z, Tao R, **Prentice H**, Wu JY. Comparison between single and combined post-treatment with S-Methyl-N,N-diethylthiolcarbamate sulfoxide and taurine following transient focal cerebral ischemia in rat brain. Neuroscience. 2015, 300:460-73. (Prentice, Tao and Wu corresponding authors).
5. Chou CC, Modi JP, Wang CY, Hsu PC, Lee YH, Huang KF, Wang AH, Nan C, Huang X, Prentice H, Wei J, Wu JY. Activation of Brain L-glutamate Decarboxylase 65 Isoform (GAD65) by Phosphorylation at Threonine 95 (T95). Mol Neurobiol. 2017 Mar;54(2):866-873. doi: 10.1007/s12035-015-9633-0.

B. Positions and Honors

Positions and Employment

2007 - Present	Associate Professor with Tenure, Department of Biomedical Science, Charles E. Schmidt College of Medicine, Florida Atlantic University, Boca Raton, FL.
7/1/13 – 6/30/14	Visiting Associate Professor, Harvard Medical School, Martinos Center for Molecular Imaging, Mass. General Hospital, Boston, MA.
2000 - 2007	Associate Professor, Biomedical Sciences, Charles E. Schmidt College of Science, Florida Atlantic University, Boca Raton, FL.
2007-Present	Member of the Center for Complex Systems and Brain Sciences, Florida Atlantic University, Boca Raton, FL.
2000-Present	Member of the Center for Molecular Biology and Biotechnology (CMBB) Florida Atlantic University, Boca Raton, FL.
1997 - 2000	Senior Lecturer with Tenure, Division of Molecular Genetics, Institute of Biomedical and Life Sciences, University of Glasgow, Scotland.
1993-1997	Lecturer (equivalent to Assistant Professor), Division of Molecular Genetics and Department of Medicine and Therapeutics, University of Glasgow, Scotland.

Honors

2016: Nominated as International Faculty for the International Congress on Coronary artery disease (2017 Congress).
2014: Nominated as International Faculty for the International Congress on Coronary artery disease (2015 Congress).
2012: Nominated as International Faculty for the International Congress on Coronary artery disease (2013 Congress).
2010: Nominated as International Faculty for the International Congress on Coronary artery disease (2011 Congress).
2009: Nominated as International Faculty for the International Congress on Coronary artery disease (2009 Congress).

Other Experience and Professional Memberships

Editorial Board Member of Scholarena Journal of Case Reports
Editorial Board Member of ISRN Vascular Medicine
American Heart Association Study Section Chair

C. Contribution to Science

1. My early contribution to science involved analysis of gene transfer and gene regulation related to gene therapy in the cardiovascular system. My studies indicated that regulatory domains of cardiac specific genes retained their gene activation capabilities using in vivo skeletal muscle and cardiac gene transfer models and correspond closely to activation characteristics found in cell culture models. Importantly hypoxia regulated promoter vectors were found to activate foreign gene expression in hypoxia/ischemia in vivo in a manner that induces high level gene activation and well as switching off of expression once hypoxia/ ischemia subsided.

1. Christensen, T.H., **Prentice, H.**, Gahlmann, R. and Kedes, L. Regulation of the human cardiac/slow twitch troponin C gene by multiple, cooperative, cell-type-specific and MyoD responsive elements. Mol. Cell. Biol. 13: 6752-6765 (1993).
2. **Prentice, H.M.**, Kloner, R.A., Newman, L., Li, Y., Christensen, T., Prigozy, E. and Kedes, L. Tissue restricted expression patterns of two muscle specific promoters are retained with direct DNA injection assay into cardiac and skeletal muscle. J. Mol. Cell. Cardiol. 26: 1393-1401 (1994).
3. **Prentice, H.**, Bishopric, N.H., Hicks, M.N., Discher, D.J., Wu, X., Wylie, A.A. and Webster, K.A. Regulated expression of a foreign gene targeted to the ischaemic myocardium. Cardiovascular Research - Focus on Gene Therapy Issue 567-574 (1997).

2. In exploring mechanisms of hypoxia sensing I have used a model of anoxia tolerance-the brain of the freshwater turtle. In this system I elucidated mechanisms of anoxic survival including controlled induction of heat shock protein mRNAs and suppression of transcription of mRNAs encoding voltage gated potassium channels.

1. **Prentice, H. M.**, Milton, S.L, Scheurle, D, Lutz, P.L. Voltage Gated Potassium Channel Gene Transcription Reversibly Regulated by Oxygen Supply. American Journal of Physiology, Regul. Integr. Comp. Physiol. 285(6): R1317-21 (2003).
2. **Prentice H. M.**, Milton, S.L., Scheurle, D., Lutz., P.L. The upregulation of cognate and inducible heat shock proteins in the anoxic turtle brain. J. Cerebral. Blood Flow and Metabolism 24: 826-828 (2004).
3. Milton SL, Dirk LJ, Kara LF, **Prentice HM**. Adenosine modulates ERK1/2, PI3K/Akt, and p38MAPK activation in the brain of the anoxia-tolerant turtle Trachemys scripta. J Cereb Blood Flow Metab. 2008 Aug;28(8):1469-77.

3. In applying the use of hypoxia regulated promoter domains to gene therapy for specific disorders including ischemic disorders I have investigated hypoxia regulated and cell specific expression of antiangiogenic molecules using models of diabetic retinopathy. Specific a hypoxia inducible and GFAP specific promoter was found to regulate endostatin expression in an vivo model of retinal hypoxia (Oxygen Induced Retinopathy) and the transgene was found to rescue the excessive angiogenesis associated with oxygen induced retinopathy.

1. **Prentice HM**, Biswal MR, Dorey CK, Blanks JC. Hypoxia-regulated retinal glial cell-specific promoter for potential gene therapy in disease. Invest Ophthalmol Vis Sci. 2011 Nov 1;52(12):8562-70. doi: 10.1167/iovs.10-6835.
2. Biswal MR, **Prentice HM**, Dorey CK, Blanks JC. A hypoxia-responsive glial cell-specific gene therapy vector for targeting retinal neovascularization. Invest Ophthalmol Vis Sci. 2014;55(12):8044-53.

4. In examining the effects of preconditioning mechanisms in using mild oxidative stress to activate tolerance against later severe ischemia I have employed the drug sulindac as pharmacological preconditioning agent. In an ex-vivo model of myocardial ischemia hearts that had previously been exposed to sulindac were dramatically protected against ischemic damage. The mechanisms of protection

involved Hsp27 and iNOS induction. In in vitro retinal pigment epithelium cell models (ARPE19 and primary RPE cells) it was found that sulindac protected RPE cells against oxidative stress. These RPE experiments point strongly to a preconditioning effect in retina that may be applicable to future treatments for age related macular degeneration.

1. Moench I, **Prentice H,** Rickaway Z and Weissbach H. "Mechanisms of protection by sulindac against myocardial ischemic damage". 2009 Proc. Natl. Acad. Sci. USA. Nov 17;106(46):19611-6.
2. Sur A, Kesaraju S, **Prentice H**, Ayyanathan K, Baronas-Lowell D, Zhu D, Hinton DR, Blanks J, Weissbach H. Pharmacological protection of retinal pigmented epithelial cells by sulindac involves PPAR-α. Proc Natl Acad Sci U S A. 2014;111(47):16754-9.

5. In translational research I have employed a glutamate receptor partial antagonist DETC-MeSO to elicit neuroprotection in the rat middle cerebral artery occlusion model. In addition I have employed the preconditioning agent sulindac in models of neuroprotection for stroke. For these two drugs the mechanisms of protection have involved firstly inhibition of ER stress pathways in the case of DETC-MeSO and activation of Hsp27 and Akt in experiments on sulindac.

1. Mohammad-Gharibani P, Modi J, Menzie J, Jenova R, Ma Z, Chen PC, Tao R, **Prentice H** and Wu J.-Y. Mode of Action of S-Methyl-N, N-Diethylthiocarbamate Sulfoxide (DETC-MeSO) as a Novel Therapy for Stroke in a Rat Model. Molecular Neurobiology, 50(2):655-672 (2014) (DOI 10.1007/s12035-014-8658-0, 2014, Feb 28).
2. Gharibani P, Modi J, Menzie J, Alexandrescu A, Ma Z, Tao R, **Prentice H**, Wu JY. Comparison between single and combined post-treatment with S-Methyl-N,N-diethylthiolcarbamate sulfoxide and taurine following transient focal cerebral ischemia in rat brain. Neuroscience. 2015, 300:460-73. (Prentice, Tao and Wu corresponding authors).
3. Ren, J. Q., Chen, I., Chen, P.-C., **Prentice, H.,** Wu, J.-Y. and Liu, P.K. Non-invasive evaluation of brain damage and repair by gene therapy. Gene Ther. 2016; 23(1):1-9. doi: 10.1038/gt.2015.81.
4. Modi, J.P., Gharibani PM., Ma Z, Tao R., Menzie J., **Prentice H** and Wu JY. Protective Mechanism of Sulindac in an Animal Model of Ischemic Stroke. Brain Res. 2014 Aug 12;1576:91-9. doi: 10.1016/j.brainres.2014.06.019.(Prentice, Tao, Wu –corresponding authors).

A complete list of my publications can be found at:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1v574UlUjtG55/bibliograpahy/48484106/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

1. Title of Research Project "Granulocyte colony-stimulating factor (GCSF) gene therapy for stroke". Amount of Award: $ 1,231,336.00; Source of support: State of Florida RC-1.Period covered: 04/01/2016-03/31/2019. Grant number: 6JK08. Role: Co-I.
2. Title of Research Project "Neuroprotection with active fractions of agent in PC 12 cell cultures". Amount of Award: $ 50,000.00; Source of support: Aeura, Inc. Period covered: 05/20/2015-11/19/2017. Role: PI

Completed Research Support

1. Title of Research Project: Multidrug therapy for stroke. Source of support: Florida Department of Health. Period covered: 01/01/2010-6/30/2013. Role in the project: Co-Principal Investigator-7% effort (John Wu- Principal Investigator).
2. Title of Research Project: FAU Research Priority Theme: Neuroscience. Source of Support: FAU Research Priority Theme. Period covered: 01/08/2010- 31/07/2013. Prentice –member and investigator. (P.I.: Janet Blanks).

Gary J. Rose, M.D.
Associate Professor of Surgery

Education

•1973: B.S., Zoology, George Washington University

•1977: M.D., George Washington University School of Medicine

•1977-1978: Internship in General Surgery, University of Miami School of Medicine

•1978-1981: Residency in Otolaryngology, University of Miami School of Medicine;1980-1981 Chief Resident

•1981-1983: Residency in Plastic Surgery, University of Florida School of Medicine, Jacksonville Division; 1982 1983 Chief Resident

Research Interests (Publications)

- Rose, G.J., New Directions in Laser Therapy, Clinics in Plastic Surgery, Vol.29 53-79, 2002.
- Rose, G.J., Male Body Contouring and Gynecomastia Surgery , Operative Techniques in Plastic and Reconstructive Surgery 8:67-83, 2002.
- Rose G.J., Temporary Tarsorrhaphy Suture to Prevent or Treat Scleral Show and Ectropion Secondary to Laser Resurfacing or Laser Blepharoplasty, Plastic and Reconstructive Surgery, 106:721, 2000.

Rainald Schmidt-Kastner, M.D.
Associate Professor of Integrated Medical Science

Education

- 1977-1983: Studies of Human Medicine, Medical Faculty, Universität Düsseldorf, Düsseldorf, Germany, completed by "Staatsexamen" (National Exam in Medicine)
- 1984: MD-Doktor der Medizin (Dr.med.) by thesis (summa cum laude), Medical Faculty, University of Düsseldorf, Düsseldorf, Germany
- 1992: Qualification to Lecture in Physiology and Evidence for Scholarly Research ("Habilitation" and "Privat-Dozent" - PD), Ruhr-Universität Bochum, Germany

Research Interests

- Brain ischemia and hypoxia; selective vulnerability of the hippocampus; status epilepticus; retinal ischemia; optic nerve atrophy; gene x hypoxia interactions in neurodevelopmental disorders and neurodegeneration; teaching tools in medical neuroscience

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Schmidt-Kastner, Rainald

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

POSITION TITLE: Associate Professor of Integrated Medical Science

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Duesseldorf, Germany	MD by thesis	1984	Medicine
Ruhr-University Bochum, Germany	Habilitation	1992	Physiology

A. Personal Statement

I hold an MD degree through thesis (neuroanatomy) from University of Duesseldorf and a research-teaching degree in physiology (Habilitation) from Ruhr-University Bochum, Germany. I serve as Course Director for Neuroscience and Behavior. I was a Section Editor for the international neuroscience journal, “Neuroscience” (2011-2016). My research interests are brain ischemia and hypoxia; selective vulnerability of the hippocampus; status epilepticus; retinal ischemia; optic nerve atrophy; gene x hypoxia interactions in neurodevelopmental disorders and neurodegeneration.

B. Positions and Honors

1983-1987 Scientific Assistant (postdoctoral), Max-Planck-Institute for Neurological Research, Germany
1987-1992 Scientific Assistant (postdoctoral), Ruhr-University Bochum, Dept. Neurophysiology, Germany
1990-1994 Visiting Scientist, Karolinska Institute, Depts. Histology-Neurobiology, and Neuroscience, Stockholm, Sweden
1994-1996 Visiting Scientist, University of Ottawa, Neuroscience Research Institute, Ottawa, Canada
1997-2002 Research Assistant Professor, University of Miami School of Medicine, Dept. of Neurology
2002-2004 Research Associate Professor, University of Miami School of Medicine, Dept. of Neurology
2005-2006 Scientist, FAU, Dept. of Biological Sciences
2006-2008 Visiting Clinical Assistant Prof., FAU, C.E. Schmidt College of Biomedical Science
2008-2010 Clinical Assistant Professor, FAU; Course Director Neuroscience and Behavior
2011-now Associate Professor of Clinical Biomedical Science

C. Contributions to Science

Schmidt-Kastner, R. Genomic approach to selective vulnerability of the hippocampus in brain ischemia-hypoxia. Neuroscience 309: 259-279, 2015

Schmidt-Kastner, R., van Os, J., Esquivel, G., Steinbusch, H.W.M., Rutten, B.P.F. An environmental analysis of genes associated with schizophrenia: hypoxia and vascular factors as interacting elements in the neurodevelopmental model. Molecular Psychiatry, 17 (12) 1194-1205, 2012 (Advance Online Publication, Jan. 31, 2012)

Schmidt-Kastner, R., Kreczmanski, P., Preising, M., Diederen, R., Schmitz, C., Reis, D., Blanks, J., Dorey, C.K. Expression of the diabetes risk gene wolframin (WFS1) in the human retina. Experimental Eye Res. 89: 568-574 (June 12 Epub ahead of print), 2009.

Schmidt-Kastner, R., Aguirre-Chen, C., Kietzmann, T., Saul, I., Busto, R., Ginsberg, M.D. Nuclear localization of the hypoxia-regulated pro-apoptotic protein BNIP3 after global brain ischemia in the rat hippocampus. Brain Res. 1001: 133-142, 2004.

Schmidt-Kastner, R., Truettner, J., Zhao, W., Saul, I., Busto, R., Ginsberg, M.D. Transient changes of brain-derived neurotrophic factor (BDNF) mRNA expression in hippocampus during moderate ischemia induced by bilateral common carotid artery occlusions in the rat. Mol. Brain Res. 92: 157-166, 2001.

Schmidt-Kastner, R., Truettner, J., Zhao, W., Belayev, L., Krieger, C., Busto, R., Ginsberg, M.D. Differential changes of bax, caspase-3 and p21 mRNA expression after transient focal brain ischemia in the rat. Mol. Brain Res.79: 88-101, 2000.

Schmidt-Kastner, R., Fliss, H., Hakim, A.M. Subtle neuronal death in striatum after short forebrain ischemia in rat detected by in situ end-labelling for DNA damage. Stroke 28: 163-170, 1997.

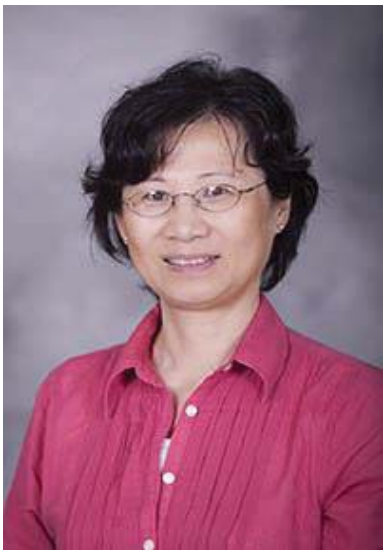
Wolf, H.K., Buslei, R., Schmidt-Kastner, R., Schmidt-Kastner, P.K., Pietsch, T., Wiestler, O.D., Blümcke, I. NeuN: A useful neuronal marker for diagnostic histopathology. J. Histochem. Cytochem. 44: 1167-1171, 1996.

Schmidt-Kastner, R., Wetmore, C., Olson, L. Comparative study of brain-derived neurotrophic factor (BDNF) mRNA and protein at the cellular level suggests multiple roles in hippocampus, striatum and cortex. Neuroscience 74: 161-183, 1996.

Schmidt-Kastner, R., Freund, T.F. Selective vulnerability of the hippocampus in brain ischemia. Commentary. Neuroscience 40: 599-636, 1991

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

N.a.



Wen Shen, Ph.D.
Associate Professor of Biomedical Science

Education

- Ph.D., Physiology and Biophysics, State University of New York at Buffalo, 1998.

Research Interests

- Electrophysiology of channels and receptors
- Transporters in neurodevelopment and adult system
- Signal transduction in retinal circuit

BIOGRAPHICAL SKETCH
DO NOT EXCEED FIVE PAGES.

NAME: Wen Shen

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

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	START DATE MM/YYYY	END DATE *(or expected end date)* MM/YYYY	FIELD OF STUDY
Shanghai University, Shanghai, China	BS	09/1979	06/1983	Electrical Engineering
SUNY at Buffalo, New York, USA	Ph.D	09/1994	12/1998	Physiology & Biophysics

A. Personal Statement

The long-term goal of my research is to explore neural function and mechanism that encode visual signals in the retina. We are addressing the critical questions about how the individual cell and complex of neuronal circuits interact at processing of visual information, using in vivo animal models and in intro retinal tissues. The proposed project focuses on the role of the network neurons - glycinergic interplexiform cells in regulation of visual function in retina. The results from the study will establish a new concept of how a network feedback as an important element in adjusting and fine-tuning visual sensitivity in the light adaptation, which will advance the research field. Multiple techniques are used in the study, including electrophysiology, photic stimulation, immunocytochemistry, Ca^{2+} imaging, quantitative-PCR, Western blotting. All necessary equipment are available either in my laboratory or in the college core facility at Florida Atlantic University. I have solid background in retinal physiology and pharmacology and have broad experiences in the research area of this application, which build my confident in completion of the proposed study. Over the years, as a PI, I received several research grants from both federal agents and private foundation, eg. NIH, NSF and Fight for Sight, Prevent Blindness of American. I have developed both research and administrative skills for carrying out the research projects. This study opens a new avenue for my laboratory to conjugate basic science and translational research.

Selected publications highlighting my expertise and qualification:

a. W Shen, C Nan, PT Nelson, H Ripps, MM Slaughter (2017) $GABA_B$ receptor attenuation of $GABA_A$ currents in neurons of the mammalian central nervous system. *Physiol Rep., 5(6).* PMCID: PMC5371550.

b. Z Jiang, JN Yang, LA Purpura, YF Liu, H Ripps, W Shen (2014) Glycinergic feedback enhances synaptic gain in the distal retina. *J Physiol. (London), 592: 1479-1492.* PMCID: PMC3979606

c. W Shen, LA Purpura, BQ Li, CL Nan, IJ Chang and H Ripps (2013) Regulation of synaptic Transmission at the photoreceptor terminal: A novel role for the cation-chloride cotransporter NKCC1. *J Physiol. (London), 591:133-147.* PMCID: PMC3630777

d. M JM Rowan, H Ripps and W Shen (2010) Fast glutamate uptake via EAAT2 shapes the cone-mediated light offset response in bipolar cells. *J Physiol.(London), 588(20): 3943-3956.* PMCID: PMC3000584

B. Positions and Honors

Positions and Employment:

1983-1988 Engineer, Institute of Environmental Control and Protection, Shanghai Municipal Bureau of Chemical Industry. Shanghai, China
1988-1993 Research Specialist, Shanghai Institute of Physiology, Chinese Academy of Science, China
1993-1998 Graduate Research Assistant, Department of Physiology and Biophysics, School of Medicine and Biomedical Science, State University of New York at Buffalo.
1998-1999 Research Associate, Department of Physiology and Biophysics, School of Medicine and Biomedical Science, State University of New York at Buffalo.
1999-2003 Research Assistant Professor, Department of Physiology and Biophysics, School of Medicine and Biomedical Science, State University of New York at Buffalo
2003-2007 Assistant Professor, Department of Biomedical Science, Florida Atlantic University
2007-present Associate Professor, Department of Biomedical Science, Florida Atlantic University

Awards and Honors:

1998 Mark Diamond Research Award
1998 Dean's Award for Outstanding Thesis Dissertation, School of Medicine and Biomedical Science, State University of New York at Buffalo
2000 ARVO-Retinal Research Foundation-Lawrence Travel Fellowship Grant
2001 Postdoctoral Research Fellowship Award, Fight for Sight, Prevent Blindness of America
2002 Grant-in-Aid, Fight for Sight, Prevent Blindness of America
2002 International Eye Research Congress Travel Fellowship, Geneva, Switzerland
2002 R01 research grant, National Eye Institute (NEI), NIH
2006 New Project Development Award, Florida Atlantic University
2010 NSF Research Grant Award
2011 Researcher of the Year 2010-2011, Florida Atlantic University
2011 Researcher of the Year 2010-2011, College of Medicine, Florida Atlantic University

Professional Memberships:

1994- present Member of Associate for Research in Vision and Ophthalmology
2004- present Member of Society for Neuroscience

C. Contribution to Science:

1. My early work addresses the neural mechanisms of visual signal processing. My study provided better understanding of the interactions of neurotransmitter receptors and voltage-gated Ca^{2+} channels that form the fundamentals of visual information processing and neural adaptation in retina. Both glutamate and GABA are known as the major neurotransmitters in the CNS; however, the functional role of these transmitters in visual signaling had not been well defined in early 90's when I was a graduate student. I discovered that the different subgroups of glutamate and GABA receptors located in the pre- and post-synaptic areas of retina regulate voltage-gated Ca^{2+} channels differentially, playing an important role in modulating neurotransmitter release in light- and dark-adapted conditions. The results from these studies laid a solid foundation for understanding the role of the neurotransmitter receptors in governing synaptic transmission and modulation in visual system. Most of the work was done in Dr. Malcolm Slaughter's lab at the Department of Physiology and Biophysics at State University of New York at Buffalo where I completed my Ph.D dissertation.

Selected publications:

a. J. Zhang, **W. Shen** and M.M. Slaughter (1997) Two metabotropic GABA receptors differentially modulated calcium currents in retinal ganglion cells. *J Gen. Physiol. 110:45-58.* PMCID: PMC2229361

b. **W. Shen** and M.M. Slaughter (1998) Metabotropic and ionotropic glutamate receptors regulate calcium channel currents in salamander retinal ganglion cells. *J Physiol.(London), 510(3): 815-828.* PMCID: PMC2231079

c. **W. Shen** and M.M. Slaughter (1999) Metabotropic GABA receptors facilitate L-type and inhibit N-type calcium channels in single salamander retinal neurons. *J Physiol.(London), 516(3):711-718*. PMCID: PMC2269297

d. **W Shen** and MM Slaughter (2001) Multireceptor GABAergic regulation of synaptic communication in amphibian retina. *J Physiol. (London), 530(1):55-67.* PMCID: PMC2278394

2. I started my independent laboratory in 2003 after I received a R01 grant from National Eye Institute, NIH. The long-term goal of my research focuses on understanding the cellular and molecular mechanisms underlying synaptic function and dysfunction in normal and diseased brain and sensory system. We use *in vivo* animal models and *in vitro* retinal tissues and human brain tissues to address the fundamental questions regarding neural plasticity in physiology and pathology of the CNS. Multiple techniques are used in my laboratory, including electrophysiological techniques (e.g. patch-clamp recording, intracellular recording, ERG), optogenetic applications, Ca^{2+}- and voltage-sensitive dye imaging, immuocyto-chemistry, confocal imaging, Western blotting and RT-PCR assays. Over the years, we successfully mapped the details of neuronal structure and synaptic connections of the network feedback neurons - glycinergic interplexiform cells in vertebrate retina. We studied the synaptic receptors, uptake transporters and light-evoked response patterns of the glycinergic interneurons, as well as the functions of glycine feedback in the synaptic complex between photoreceptors and their second-order neurons (bipolar and horizontal cells). Furthermore, we characterized the functions of the major Cl^- transporters, Na-K-2Cl co-transporter (NKCC) that serves to uptake Cl^- for maintaining a high Cl^- levels intracellularly in retinal neurons. Glycine feedback activates Cl^- permeable receptors in photoreceptor terminals, horizontal cells and the dendrites of the bipolar cells, leading to depolarizing effects in Cl^- efflux from the cells and cellular regions. Therefore, feedback of glycine in the distal retina enhances the synaptic gains between photoreceptors and second-order neurons, which improve visual sensitivity in retina. Importantly, we discovered that this positive feedback loop is facilitated under intermittent lights that have been found to be effectively enhancing contrast sensitivity in visual psychophysical tests. Thus, glycine feedback in network is an existed mechanism served for neural adaptation in retinas. This project is funded by NIH (R01) and NSF research grant.

Selected publications:

a. **W Shen** (2005) Repetitive light stimulation inducing glycine receptor plasticity in the retinal neurons. *J Neurophysiol.*, *94:2231-2238.* PMID: 16105957

b. M JM Rowan, H Ripps and **W Shen** (2010) Fast glutamate uptake via EAAT2 shapes the cone-mediated light offset response in bipolar cells. *J Physiol. (London), 588: 3943-3956.* PMCID: PMC3000584

c. **W Shen**, LA Purpura, Baoqin Li, CL Nan, IJ Chang and H Ripps (2013) Regulation of Synaptic Transmission at the Photoreceptor Terminal: A Novel Role for the Cation-Chloride Cotransporter NKCC1. *J Physiol. (London)*, *591:133-147.* PMCID: PMC3630777

d. Z Jiang, JN Yang, LA Purpura, YF liu, H Ripps, **W Shen** (2014) Glycinergic feedback enhances synaptic gain in the distal retina. *J Physiol. (London)*, 592: 1479-1492. PMCID: PMC3979606

3. In addition, my research interests are expand to the neurochemicals and neurotrophins that can serve as neuroprotective agents against cell degeneration in disease and pathological conditions. We investigate whether bone morphogenetic protein 7 (BMP-7) and taurine can serve as cytoprotective agents for retinal neuron survival in optic nerve stress in glaucomatous eyes. A hallmark of these disorders relates in important ways to which characterizes glaucoma, most notably the early onset of hypoxia/ischemia, and the neuronal release of glutamate. Of particular importance is an experimental study of the phenomenon of 'non-excitatory glutamate toxicity', the ability of very low levels of glutamate to allow Ca^{2+} to enter highly sensitive kainite receptors and cause widespread cell death of retinal ganglion cells. Significantly, both BMP-7 and taurine can reduce the rate of cell degeneration by suppressing glutamate-induced intracellular Ca^{2+} overload. Currently, we extend our study to exam the effects of these agents in protecting cone photoreceptors in the retinal degeneration mouse models, *rd1* and *rd10*. Importantly, BMP-7 can be delivered to the CNS through intravenous injection, and it has been used successfully to prevent the onset or spread of cell death after brain ischemia in humans and animal models. We anticipate that the outcome of our study will provide strong evidence leading to a clinic trial testing BMP-7 as a neuroprotective agent against cell degeneration in retinal diseases.

Selected publications:

a. **W Shen** and M.M. Slaughter (2002) A non-excitatory paradigm of glutamate toxicity. *J Neurophysiol., 87:1629-1634.* PMID: 11877532

b. **W. Shen**, S.G. Finnegan, P. Lein, S. Sullivan, M.M. Slaughter and D Higgins (2004) Bone morphogenetic proteins regulate ionotropic glutamate receptors. *Euro J Neurosci.*, 20:2031-2037. PMID: 15450082

c. S Bulley, YF Liu, H Ripps, and **W Shen** (2013) Taurine Activates Delayed Rectifier K_V Channels via a Metabotropic Pathway in Retinal Neurons". *J Physiol. (London), 591:123-132*. PMCID: PMC3630776

d. J Yang, CL Nan, H Ripps, **W Shen** (2015) Destructive Changes in the Neuronal Structure of the FVB/N Mouse Retina. *PLoS ONE 10(6): e0129719.* PMCID: PMC4475023

Complete List of Published Work in MyBibliography (Ctrl+Click to following link):
https://www.ncbi.nlm.nih.gov/sites/myncbi/wen.shen.1/bibliography/41166907/public/?sort=date&direction=descending

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

COMPLETED RESEARCH SUPPORT

NSF 1021646
Research Grant 08/01/2010 - 07-31/2015
Title: The function of glycine in modulation of cone visual sensitivity
The goal of this project is to discover a novel mechanism involved glycine network feedback for cone adaptation in dim and flicking light conditions.
Role: PI

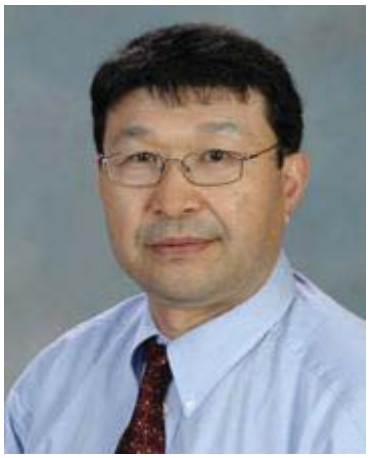
EY14161
R01 Research Grant
National Eye Institute, NIH 08/01/2002 – 07/31/2008
Title: Interplexiform Cell Function
The goals of this project are to explore the role of glycinergic interplexiform cells in retina and to determine the effect of glycine feedback on distal retinal neurotransmission.
Role: PI

NO. 1180-074
Florida Atlantic University
Division of Sponsored Research 01/01/2006-10/31/2007
Title: Bone Morphogenetic Proteins in Neuroprotection
The major goal of this project was to study effects of bone morphogenetic proteins in protection of glaucoma caused ganglion cells death
Role: PI

GA01032
Grant-in-Aid Research Award, Fight for Sight
Research Division of Prevent Blindness America 07/01/2001-06/30/2002
Title: Neuroprotective Effect of TGF-β Superfamily of Growth Factors in Human Retina
The major goal of this project was to define the regulation of glutamate receptors by bone morphogenic proteins, BMP-7, in human retinal horizontal cells.
Role: PI

PD20047

Postdoctoral research Fellowship, Fight for Sight
Research Division of Prevent Blindness America 07/01/2000-06/30/2001
Title: Kainate-preferring glutamate receptors in human retinal function and disease
The mean goal of this project was to study the mechanism of Ca^{2+} permeable kainate receptors in ganglion cell degeneration in human retina.
Role: PI



Yoshimi Shibata, Ph.D.
Professor of Biomedical Science

Education

- BS, Biology, Yamagata University, Yamagata, Japan 1973
- Ph.D., Department of Bacteriology, Tohoku University School of Medicine, Bacteriology, Sendai, Japan 1982

Research Interests

- Mechanisms regulating ontogenic and functional heterogeneity of macrophage populations.
- Macrophage-mediated regulation of innate and acquired immune responses.
- Intracellular trafficking of particles and activation of cellular signaling in phagocytosis.
- Development of a new Th1 adjuvant against infections and allergic asthma.
- Mechanisms of chronic inflammation in atherosclerosis.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Shibata, Yoshimi

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

POSITION TITLE: Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Yamagata University, Yamagata, Japan	B.S.	03/73	Biology
Tohoku University Med School, Sendai, Japan	Ph.D.	12/82	Immunology and Bacteriology
East Carolina University Med School, Greenville, NC	Postdoctoral	11/87	Hematopathology

A. Personal Statement

As PI of NIH-, DOD- and Florida Department of Heath- funded projects, I have demonstrated that chitin microparticles induce bactericidal macrophage activation in a phagocytosis-dependent manner. Dietary administration of chitin microparticles (CMPs) is further demonstrated to ameliorate asthma, infections and colitis. Ongoing projects are defining the process of macrophage proteins binding phagocytosed CMPs. I also studied macrophage heterogeneity and diversity for many years, and established mice depleted of bone marrow and blood monocytes, and phagocytosis-mediated macrophage activation in tissue macrophages and monocyte-derived macrophages. In summary, I have the expertise, leadership and motivation necessary to successfully carry out the proposed work. I have a demonstrated record of successful and productive research collaborations with colleagues including Drs. C Kathleen Dorey (Virginia Tech Carilion School of Medicine), and Zhongwei Li (FAUCOM) in areas that will directly allow me to explore the mechanism of host macrophage activation by chitin microparticles.

1. **Shibata Y**, WJ Metzger, QN Myrvik: Chitin particle-induced cell mediated immunity is inhibited by soluble mannan --- Mannose receptor-mediated phagocytosis initiates interleukin-12 production. J Immunol 159:2462-2467, 1997.
2. Nishiyama A, T Shinohara, T Pantuso, S Tsuji, M Yamashita, QN Myrvik, RA Henriksen, **Y Shibata**. Depletion of cellular cholesterol enhances macrophage MAPK activation by chitin microparticles but not by heat-killed Mycobacterium bovis BCG. Am J Physiol Cell Physiol 295:341-349, 2008.
3. Kogiso M, A Nishiyama, T Shinohara, M Nakamura, E Mizoguchi, Y Misawa, E Guinet, M Nouri-Shirazi, CK Dorey, RA Henriksen, **Y Shibata**. Chitin particles induce size-dependent but carbohydrate independent innate eosinophilia. J Leukocyte Biol 90:167-176, 2011.
4. Nagatani K, S Wang, V Llado, CW Lau, Z Li, A Mizoguchi, CR Nagler, **Y Shibata**, H-C Reinecker, JR Mora, E Mizoguchi. Chitin-microparticles for the control of intestinal inflammation. Inflammatory Bowel Diseases, 18:1698-1710, 2012.

B. Positions and Honors

Positions and Employment

1987-1989 Scientist, Assistant to Director, Fujisaki Cell Center, Hayashibara Biochemical Laboratories, Inc., Japan
1989-994 Research Assistant Professor, Dept. Pathology, East Carolina University School of Medicine,

	Greenville, NC
1994-1996	Associate Scientist/Associate Professor (Affiliate), Medical Sciences Res Inst, George Mason University, Herndon, VA
1996-2003	Research Associate Professor, Department of Physiology, East Carolina University School of Medicine, Greenville, NC
2003-2008	Associate Professor (tenured), Florida Atlantic University, Biomedical Science, Boca Raton, FL
2008 -	Professor (tenured), Florida Atlantic University College of Medicine, Boca Raton, FL

Other Experience, Honors, and Professional Memberships

1984- 2016	Member, Society of Leukocyte Biology
1994-	Member, The American Association of Immunologists
1998- 2003	Board Member, the Leonard Wood Memorial American Leprosy Foundation
2006- 2007	Researcher of the Year, Florida Atlantic University
2007- 2009	Peer Review Services for American Heart Association
2008- 2016	Member, American Physiological Society
2013-	Member, American Society for Microbiology

C. Contributions to Science

1. My early publications directly addressed the origin of tissue macrophages. My approaches included mice depleted of bone marrow and blood monocytes by administration of bone-seeking isotope, strontium-89. Not all tissue macrophages are derived from bone marrow through blood monocytes. My study clearly sorted out bone marrow -dependent and –independent macrophage populations. This observation has recently been confirmed by many other groups.

a. **Shibata Y,** and A. Volkman: The effect of bone marrow depletion on prostaglandin E producing suppressor macrophages in mouse spleen. J. Immunol., 135, 3897-3804, 1985.
b. **Shibata Y**, and A. Volkman: The effect of hemopoietic microenvironment on suppressor macrophages in the spleen in the congenitally anemic mice of the genotype Sl/Sld. J. Immunol., 135, 3905-3910, 1985.
c. **Shibata Y**, A. P. Bautista, S. N. Pennington, J.L. Humes, and A. Volkman: Eicosanoid production by peritoneal and splenic macrophages in mice depleted of bone marrow by 89Sr. Am. J. Pathol., 127, 75-82, 1987.
d. **Shibata Y**, and A. Volkman: Restorationof prostaglandin releasing macrophage populations in lethally irradiated mice with spleen cells from bone marrow-depleted donors. J Leukoc Biol 1991; 49:397-406.

2. Research characterizing tissue-dependent macrophage activation will continue to focus on prostaglandin E_2-releasing property. PGE_2 is a multifunctional inflammatory mediator that regulates processes such as local inflammation, Th1-to-Th2 shift, airway smooth muscle relaxation, and tumor progression. Prostaglandin G/H synthases (COX-1 and COX-2) is known to rate-limit the PGE_2 synthesis. Our study demonstrated that COX-1 and COX-2 functions induced under inflammation are dependent on tissue macrophages. Most importantly, the functions are also inactivated when macrophages are activated in vivo. This is because these enzymes are degraded immediately in the in vivo condition. Our observation provided a novel mechanism to understand a long-held view that activation of local macrophages by immunomodulators *in vivo* results in less production of PGE_2 compared with untreated local macrophages.

a. Yamashita M, A Nishiyama, QN Myrvik, RA Henriksen, S Tsuji, **Y Shibata**. Heat-killed Mycobacterium bovis BCG induces non-catalytic and catalytic cyclooxygenase 2 (COX-2) in resident tissue macrophages. Am J Physiol Cell Physiol 293: C184-90, 2007
b. Yamashita M, T Shinohara, S Tsuji, QN Myrvik, A Nishiyama, RA Henriksen, **Y Shibata**. Catatlycially inactive cyclooxygenase 2 (COX-2) and absence of PGE_2 biosynthesis in murine peritoneal macrophages following in vivo phagocytosis of heat-killed Mycobacterium bovis BCG. J Immunol.179:7072-7078, 2007.
c. Shinohara T, M Yamashita, T Pantuso, M Kogiso, S Shinohara, QN Myrvik, RA Henriksen, **Y Shibata**. Persistent inactivation of macrophage cyclooxygenase-2 in mycobacterial pulmonary inflammation. Am J Resp Cell Mole Biol 41:146-154, 2009.

d. Kogiso M, T Shinohara, CK Dorey, **Y Shibata**. Cholera toxin induces a shift from inactive to active cyclooxygenase 2 in alveolar macrophages activated by Mycobacterium bovis BCG. Infection and Immunity, 81:373-380, 2013.

3. Mechanisms of phagocytosis –dependent and -independent macrophage activation are studied in vitro and in mouse models of human diseases including asthma, colitis, and mycobacterial vaccination. My publications are cited by numerous studies addressing the effects of chitin on infections caused by chitin-containing fungi and parasites, and on allergic diseases caused by chitin-containing allergens.

a. **Shibata Y**: Prostaglandin E_2 release triggered by phagocytosis of latex particles--- A distinct association with prostaglandin synthase isozymes in bone marrow macrophages. *J. Immunol. 154:2878-2887, 1995.*
b. **Shibata Y**, LA Foster, WJ Metzger, Q N Myrvik: Alveolar macrophage priming by intravenous administration of chitin particles, polymers of N-acetyl-D-glucosamine, in mice. *Infect. Immunity 65:1734-1741, 1997.*
c. Huang C-J, KN Beasley, EO Acevedo, RL Franco, TL Jones, **Y Shibata**. Chitin enhances obese inflammation ex vivo. Hum Immunol, 75(1):41-6, 2014.
d. Kamba A, **Y Shibata**, E Mizoguchi. Potential roles of chitin in mucosal inflammation. pp 1853-1863, Book Chapter #56 Microbial pathogens and strategies for combating them: science, technology and education, Editor A. Méndez-Vilas, Vol 3: 978-84-942134-1-0, 2013.

Complete List of Published Work in MyBibliography: http://www.ncbi.nlm.nih.gov/sites/myncbi/1ZCfp_oS-hf56/bibliography/48069151/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

NIH R15 AT008252-01 Shibata (PI) 6/1/14-5/30/17 (no cost extension by 5/30/18)
Dietary anti-inflammatory chitin in colitis: The specific aims are to determine optimal forms of chitin preparations that ameliorate colitis and to determine whether the chitin preparation selected in Aim 1 ameliorates colitis in mice deficient of TLR2 or CD44.
Role: PI

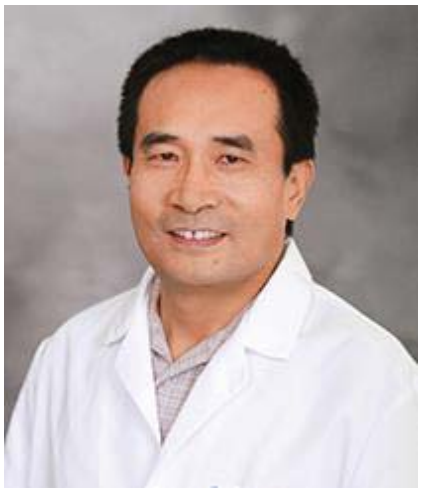
Completed Research Support

FAU Faculty Seed Grant Andrew V. Oleinikov (PI) 3/1/14 – 2/28/15
Mechanisms of interaction between malaria-infected erythrocytes and monocyte/macrophages and modulation of innate immune activity.
Role: Co-PI

2R15CA135513-02A1 V Iragavarapu-Charyulu (PI) 7/01/12 – 6/30/15
Role of CHI3L1 in acceleratiing breat cancer metastasis:The specific aims are to are: to determine if inflammation associated with CH13L1 in the lung alters the pulmonary environment to attract circulating breast tumor cells and accelerates metastatic growth; and to determine if inhibition of CH13L1 by either chitin microparticles, anti-CH13L1 neutralizing antibody or combination of these two decreases tumor metastasis.
Role: Co-PI

FAU Faculty Grant Shibata (PI) 1/01/2012 – 2/28/2015
Size- and mast cell- dependent anti-colitis effects of chitin particles: Major goals are to determine if the anti-colitis effects of oral larger chitin beads on intestinal bacterial infection into colonic epithelial cells in dextran sodium sulfate-induced colitis are greater than those obtained by an equal dose of oral chitin microparticles in a mast cell-dependent manner.
Role: PI

NIH/NIDDK 1R01 DK080070-01A2 E Mizoguchi (PI) 4/01/09-3/31/14
Role of mammalian chitinases in inflammatory bowel disease: The specific aims of this grant application are designed to define the biological role of mammalian chitinases including chitinase-3-like-1 and their substrate chitin in the pathogenesis and regulation of inflammatory bowel disease.
Role: Consultant



Rui Tao, Ph.D.
Associate Professor of Biomedical Science

Education

- Ph.D., Physiology and Neurobiology, Rutgers University, NJ, 2000

Research Interests

- Pharmacology of selective serotonin reuptake inhibitors in midbrain raphe and forebrain
- 5-HT and related effective disorders (such as depression, anxiety)
- Dorsal and median raphe neural circuitry including afferents and interneurons
- Physiology of opioidergic systerms (neurons, ligands and receptors)
- Role of opioids in the regulation of 5-HT release
- Relationship between exercise, 5-HT and opioid abuse
- The role of GABA and glutamate in opioid addiction

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Rui Tao

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

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Anhui Agricultural University, China	D.V.M	1984	Veterinary Medicine
Gothenburg University, Sweden		1991	Pharmacology
Rutgers University, NJ	Ph. D	2000	Physiol & Neurobiol
Harvard Medical School		2004	Psychiatry

A. Personal Statement

My research has been dedicated to the understanding of synaptic neurotransmissions involving 5-HT, DA, GABA and glutamate through *in vivo* neurochemical, electrophysiological, and behavioral analysis. I previously received NIDA R01 and R15 awards to study opioids and MDMA abuse.

The present grant proposal is to investigate why D1Rs, but not D2Rs, are involved in the stimulant effects of MDPV, a synthetic cathinone. This contrasts with amphetamine-like psychostimulants in which DA exerts more effects on D2Rs than D1Rs. We propose that the neural circuits and pathways used by MDPV are different from amphetamine-like psychostimulants. The differential role of D1Rs and D2Rs in MDPV abuse is a new area which needs to be explored. The idea that activation of DA receptor subtypes may be different between DA-based psychostimulants is also new. Therefore, this novel concept is worthy of investigation. The neuronal circuits and pathways involving D1Rs and D2Rs can be revealed by measuring neurotransmitters, such as DA, GABA and glutamate. Taken advantage of well-established setup of microdialysis and long experience, my lab can precisely measure different neurotransmitter effluxes in very specific brain nuclei, which is essential to pinpoint GABAergic projections to the global pallidus. Moreover, using modern techniques, including *in-situ* hybridization will help to validate the microdialysis findings. In summary, my knowledge and research experience makes me uniquely qualified to carry out this investigation.

Understanding the preferential role of D1Rs in MDPV abuse will not only add scientific knowledge, but also help clinicians to choose a specific treatment for patients intoxicated with synthetic cathinones (bath salts) in the emergency clinic. I am excited and looking forward to the opportunity of having a support for this project.

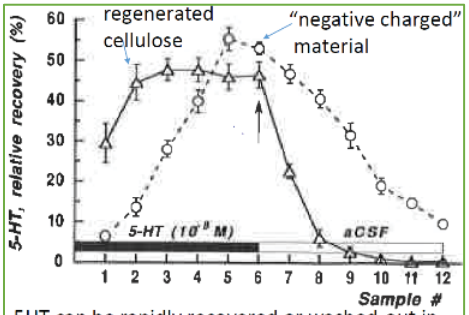
B. Positions and Honors

2008-present, Associate Professor, Florida Atlantic University, Boca Raton, FL
2004-2008, Assistant Professor, Florida Atlantic University, Boca Raton, FL
2001-2004, Instructor, Harvard Medical School VA Medical Center, Brockton, MA
2000-2001, Research Assistant Professor in Dept. of Cell biology and Neuroscience, Rutgers University, NJ

Honors: Oversee Scholarship of the Chinese Committee for Education (90'); Charles and Johanna Busch Memorial fellowship (91-94); Rutgers University Student Travel Award (98'); the NIH-funded basic ***sleep research training*** program at ***UCLA*** (01'); The Researcher of the Year award at the College of Medicine (formerly College of Biomedical Science; 07' & 08').
Professional activity: A mailed-in reviewer NIH ARRA1 study section (09'); A mail-in reviewer for 2011 NIH Director's Early Independence Award (DP5); Chair, College Research Committee

C. Contribution to Science

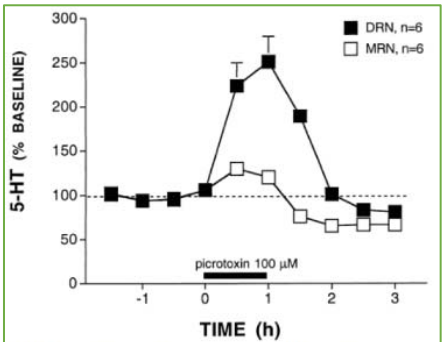
C1: Identify appropriate membrane materials used for building a microdialysis probe. Prior to this work, a debate existed about comparable data between labs using microdialysis technology. In a series of tests at the time when I was an exchange scholar at Gothenburg University Pharmacology Department, I found that some microdialysis probes had variable recovery rates by conducting 5HT microdialysis. As shown in the graph on the right, we reveled that all membrane materials except for regenerated cellulose could retain 5HT (and also dopamine) molecules to their membranes. This may be attributed to negative electric charges of those materials. Nevertheless, we found the cause resulting in data variables in a time- and pH-dependent manner. We concluded that regenerated cellulose hollow fibers are the appropriate material making microdialysis probe, which has a constant recovery rate. Then, we published two articles, which have been considered to be fundamental in this field. My role in this study as an investigator was to perform experiments. Since then, all microdialysis probes are made from the materials as we suggested, and all data between labs appear comparable.



5HT can be rapidly recovered or washed-out in the regenerated-cellulose hollow fibers, but not the "negative charged" materials

1. Hjorth S and **Tao R**, Microdialysis of 5-HT: comparison of the in vitro and in vivo performance of three common dialysis membranes. In: Monitoring Molecules in Neurosciences. Proceedings of the 5th International Conference on in vivo methods edited by H. Rollema, B. Westerink and W. J. Drijfhout (University Center for Pharmacy, Groningen) pp 242-246, 1991.
2. **Tao R** and Hjorth S, Differences in the in vitro and in vivo 5-hydroxytryptamine extraction performance among three common microdialysis membranes. *Journal of Neurochemistry* 59 (1992): 1778-1785.

C2: Neural circuits that regulate serotonergic neurons: In a mammalian brain, serotonergic cell bodies are found mainly in the dorsal (DRN) and median raphe nuclei (MRN). Despite 5HT utilized as a neurotransmitter, its functional role is different in two regions. For instance, DRN 5HT is critical to the sleep-wake cycle while MRN 5HT mediates mainly locomotion and food/water intake. Prior to our work, little was known about the neural base for their difference in functioning. We found the difference may be ascribed to the balance between inhibitory and excitatory inputs. To that end, we have published 8 articles. Briefly as shown in the graph on the right, DRN 5HT receives more inhibitory inputs than MRN 5HT. In contrast, MRN 5HT receives almost exclusively excitatory inputs. The results are critically used as the neural basis to understand functional difference in serotonergic neurons between two raphe nuclei. My role in those studies as an investigator was to design and perform experiments, and participate in manuscript writing.



Infusion of the $GABA_A$ receptor antagonist picrotoxin caused an increase in DRN 5HT, but not MRN 5HT, suggesting a strong inhibitory inputs to the DRN serotonergic neurons

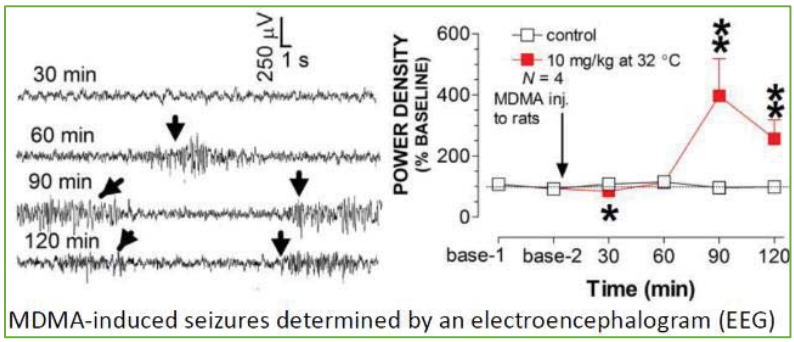
1. **Tao R** and Auerbach SB, 1996, Differential effect of NMDA on extracellular serotonin in rat midbrain raphe and forebrain sites. *Journal of Neurochemistry* 66: 1067-1075.
2. **Tao R**, Ma Z and Auerbach SB, 1996, Differential regulation of 5-hydroxytryptamine release by $GABA_A$ and $GABA_B$ receptors in midbrain raphe nuclei and forebrain of rats. *British Journal of Pharmacology* 119: 1375-1384.

3. **Tao R**, Ma Z and Auerbach SB, 1997, Influence of AMPA/kainate receptors on extracellular 5-hydroxytryptamine in rat midbrain raphe and forebrain. *British Journal of Pharmacology* 121: 1707-1715.
4. **Tao R,** Auerbach SB, 2002, GABAergic and glutamatergic afferents in the dorsal raphe nucleus mediate morphine-induced increase in serotonin efflux in the rat CSN. *Journal of Pharmacology and Experimental Therapeutic*s 303:704-710.

C3. 5HT involved in mood changes following drug abuse. Although dopamine is critical in mediating the negative motivational effect of drug abuse, less is known about 5HT that mediates mood swing and drug abuse-related depression. To fulfill this gap, we have investigated the 5HT response to psychoactive drugs, including opioids, nicotine, cannabinoids, or MDMA. We found each psychoactive drug has a characteristic effect on 5HT release in animal models of drug abuse. We reported that μ- and δ-opioids may cause an increase in 5HT outputs of dorsal raphe serotonergic neurons. In contrast, κ- or ORL1 opioids a reduction in brain 5HT. Utilizing a similar approach, we characterize 5HT the 5HT to nicotinic AChR agonists, cannabinoid CB1 receptor agonists or MDMA. We have published 10 articles regarding this aspect of research. I was a principal investigator to design, plan, and also execute a series of experiments.

1. **Tao R,** Karnik M, Ma Z, Auerbach SB, 2003, Effect of fentanyl on 5-HT efflux involves both opioid and 5-HT_{1A} receptors. *British Journal of Pharmacology* 139:1498-1504.
2. Ma Z, Strecker RE, McKenna J T, Thakkar MM, McCarley RW and **Tao R**, 2005, Effects of nicotine and dimethylphenylpiperazinium on extracellular 5-HT in the dorsal raphe and nucleus accumbens of freely behaving rats. *Neurosicence* 135:949-958.
3. Ma Z, Pearson E and **Tao R**, 2007, CART peptides increase 5-hydroxytryptamine in the dorsal raphe and nucleus accumbens of freely behaving rats. *Neurosci lett* 417:303-307.
4. **Tao R**, Ma Z. 2012, Neural circuit in the dorsal raphe nucleus responsible for cannabinoid-mediated increases in 5-HT efflux in the nucleus accumbens of the rat brain. ISNR Pharmacology 2012: 276902

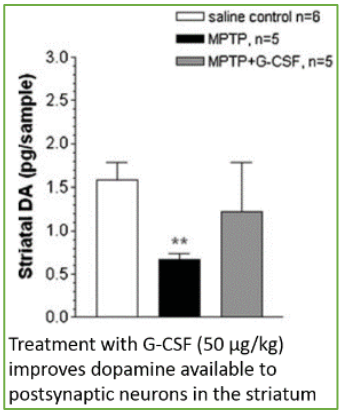
C4. Mechanisms underlying serotonin syndrome: Although a potential risk of serotonin syndrome is known for over three decades, little progress is made to understand the cause of the syndrome, except for excessive 5HT. For instance, it was not clear why the same drug dose produces a mild syndrome in one case but severe syndrome in others, or how high of serotonin is too much for brain to elicit a defensive or adverse response. We have made several contributions summarized as follows. 1) reveal mechanisms responsible for mild and severe syndromes; 2) find the 5HT threshold for the syndrome; 3) understand presynaptic and postsynaptic mechanisms of serotonin syndrome. Additionally, we have developed an animal model of serotonin syndrome that can be used for laboratory investigation. As shown in the graph above, this was the first time to replicate seizure activit under laboratory conditions by which syndrome induced by MDMA could be thoroughly investigated. We have published 7 research articles in this regard. My role in this work is the PI or research design, planning and also co-excution of experiments.



MDMA-induced seizures determined by an electroencephalogram (EEG)

1. Ma Z, Rudacille M, Prentice HM. and **Tao R**, 2013, Characterization of electroencephalographic and biochemical responses at the onset of serotonin syndrome induced by 5-HT promoting drugs in rats. J Neurochem, 125: 774-789
2. **Tao R,** Rudacille M, Zhang G and Ma Z, 2014, Changes in intensity of serotonin syndrome caused by adverse interaction between monoamine oxidase inhibitors and serotonin reuptake blockers. Neuropsychopharmacology 2014 Jul;39(8):1996-2007.
3. **Tao R**, Shokry IM, Callanan JJ, Adams HD, and Ma Z, 2014, Mechanisms and environmental factors that underlying the intensification of 3,4-methylenedioxymethamphetamine (MDMA, Ecstasy)-induced serotonin syndrome in rats. Psychopharmacology (Berl). 2015, 232:1245-1260
4. Shokry IM, Callanan JJ, Sousa J, **Tao R**, Rapid in situ hybridization using oligonucleotide probes on paraformaldehyde-prefixed brain of rats with serotonin syndrome. . J Vis Exp. 2015 Sep 23; (103)

C5. Neurodegenerative diseases and Stroke: Recently, my research interests have extended broadly to neurodegenerative diseases and stroke, through collaborative work with Dr. JY Wu's laboratories. To date, many drugs have developed to treat neurodegenerative diseases or stroke. However, their pharmacological effectiveness is quite limited, primarily limited to symptomatic improvement in the early stage of the disease and has a little effect in preventing or delaying the progression of the disease. In this context, developments of new therapeutic strategies that can delay loss of neurons or even replenish the lost neurons through neurogenesis are of clinical interest. We have developed a glutamate receptor partial antagonist, S-Methyl N, Ndiethylthiolcarbamate sulfoxide (DETC-MeSO) and demonstrated its efficacy in neuroprotection in seizure and stroke. In addition, we have developed a stem cell stimulator, granulocyte colony-stimulating factor (G-CSF) as an effective therapeutic agent for Parkinson's disease in both the animal model as well as in clinical setting. My role as a co-investigator is to determine changes in neurochemistry (serotonin, dopamine, or glutamate), and behavioral improvement following drug administration, or gene therapy.



Treatment with G-CSF (50 μg/kg) improves dopamine available to postsynaptic neurons in the striatum

1. McCollum M, Ma Z, Cohen E, Keon R, **Tao R**, Wu JY, Maharaj D, Wei J. 2010, Post-MPTP treatment with granulocyte colony-stimulating factor improves nigrostriatal function in the mouse model of Parkinson's disease. *Molecular Neurobiology* 2010 41(2-3) 410-9.
2. Buddhala C, Suarez M, Modi J, Prentice H, Ma Z, **Tao R**, Wu JY, 2012, Calpain Cleavage of Brain Glutamic Acid Decarboxylase 65 Is Pathological and Impairs GABA Neurotransmission. PLoS One. 7:e33002
3. Gharibani PM, Modi J, Menzie J, Genova R, Ma Z, **Tao R**, Howard Prentice, Jang-Yen Wu, 2014, Mode of Action of *S*-Methyl-*N*, *N*-Diethylthiocarbamate Sulfoxide (DETC-MeSO) as a Novel Therapy for Stroke in a Rat Model. Mol Neurology 2014 Oct;50(2):655-72. doi: 10.1007/s12035-014-8658-0.
4. Gharibani P, Modi J, Menzie J, Alexandrescu A, Ma Z, **Tao** R, Prentice H, Wu JY. 2015. Comparison between single and combined post-treatment with S-Methyl-N,N-diethylthiolcarbamate sulfoxide and taurine following transient focal cerebral ischemia in rat brain. Neuroscience. 2015 May 27;300:460-473. doi:

A complete list of my publications can be found at
https://www.ncbi.nlm.nih.gov/myncbi/collections/mybibliography/

D. Research Support

Ongoing supports

2016-2019 6JA08 James & Esther King Biomedical Program, State of Florida
"Granulocyte colony-stimulating factor (G-CSF) gene therapy for stroke"
Role: Co-PI (PI, Dr. Wu)
The goal of this project was to develop a gene therapy based on mechanisms related to facilitation of stem cells, anti-glutamate excitotoxicity and anti-oxidative stress.

2015-2017 University Research Grant
"Molecular pharmacology underlying susceptibility to serotonin poisoning"
In this proposal, our goal is to investigate the neural basis underlying the susceptibility to serotonin poisoning and relevant syndrome. Neural evidence for involvement in this topic is not only 5HTergic, but highly dependent on postsynaptic responses, including the thyrotropin-releasing hormone-containing (TRHergic) neurons. Our proposed hypothesis is that allostatic modulation of the TRHergic system in the caudal medullary raphe promotes the susceptibility to serotonin poisoning and syndrome induced by 5HT-promoting drugs. The 5HT promoting drugs used in this study to test our hypothesis are paroxetine (selective serotonin reuptake inhibitor, SSRI), fentanyl (mu-opioid receptor agonist) and MDMA (ecstasy; amphetamine derivative). Outcome of this hypothesis potentially leads to a major breakthrough in understanding serotonin poisoning and syndrome and reducing adverse effects of 5HT-promoting drugs.

Darin P. Trelka, M.D., Ph.D.
Assistant Professor of Integrated Medical Science

Education

- 1992: B.A. Psychology, Washington and Jefferson College, Washington, PA
- 1999: Ph.D. Anatomy, Pathology, Cell Biology, Thomas Jefferson University, Philadelphia, PA
- 2002: M.D. MCP-Hahnemann University Philadelphia, PA

Research Interests

Dr. Trelka joined the faculty at the Charles E. Schmidt College of Medicine in August 2014 where he teaches anatomical sciences in FAU's College of Medicine, which consist of gross- and microscopic anatomy as well as assisting in the pathology laboratory curriculum and facilitating both PBL and IQ group learning activities.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: **Darin P. Trelka, M.D., Ph.D.**

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

POSITION TITLE: **Assistant Professor of Clinical Biomedical Science and Director of Anatomical Programs**

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Washington and Jefferson College, Washington, PA	B.A.	05/1992	Psychology
Thomas Jefferson University, College of Graduate Studies, Philadelphia, PA	Ph.D.	06/1999	Anatomy, Pathology and Cell Biology
MCP-Hahnemann University, Philadelphia, PA.	M.D.	05/2002	Medicine
University of Virginia Health Sciences Center		06/2007	Post-graduate Residency training in Anatomic and Clinical Pathology
Medical College of Virginia/Office of the Chief Medical Examiner, Commonwealth of Virginia, Richmond VA		06/2006	Post-graduate Fellowship training in Forensic Pathology and Legal Medicine

A. Personal Statement:

I can comprehensively describe the goals of all of my teaching endeavors as being two-fold:
The first goal is to not only provide the learners/trainees fundamental information to get them started on their particular educational journey…but also to use my experience and expertise to give those fundamentals context and organization. This enables the students to better package the information into more meaningful quanta for effective recall and retrieval.
The second is to strive to become educationally unimportant to my students. This may appear on the surface to be counterintuitive, however, if I have done my job properly, the students should be armed with the data and skillset(s) to approach both academic and real-life challenges and find their own solutions. By approaching education in this manner, I have found that the students and trainees begin to develop their own experience earlier and are able to make better decisions based on their education and training, rather than simply mimicking mine. In doing so, they will naturally have fewer questions and will need less and less active guidance as they are now able to handle larger problems with greater complexity.
Thus, the less they require my assistance, the more successful I have been in educating and training them.

B. Positions and Honors:

Positions:

August 2014-Present

Assistant Professor of Clinical Biomedical Science and Director of Anatomical Programs
Florida Atlantic University
Charles E. Schmidt College of Medicine
Assistant Professor of Criminology and Criminal Justice (Secondary)
College for Design and Social Inquiry
777 Glades Road
Boca Raton, FL 33431
Office: 561.297.4667
dtrelka@health.fau.edu
Responsibilities:
Teaching Gross Anatomy and Histology.
Teaching histology review lectures for the Pathology curriculum.
Assisting in Gross Anatomy Laboratory Dissection.
Assisting in Pathology Curriculum.
Facilitating in Problem Based- and Inquiry small groups.
Chair of the Curriculum Integration and Program Evaluation Committee (CPIEC)
Co-Chair of the Faculty Review Advisory Committee
Serving on the M1 and M2 Curriculum Committee
Serving on the College of Medicine Curriculum Committee (COMCC)
Serving on the Learning Resources Committee
Serving on the College of Medicine Admissions Committee
Serving on the Academic Advisory Committee
Serving on the Arts and Medicine Committee
iPad Curriculum Integration
Support and Sponsoring of the Humane Anatomy research project with FAU medical student Emily Senderey as well as the Gross Anatomy "Seeding Ceremony"
Course developer and coordinator for Introduction to Forensic Science in the Criminal Justice curriculum, Florida Atlantic University.

January 2014-Present
Director Trelka Forensic- and Medicolegal Services
Provision of:
Expert case review, consultation and education for law enforcement, attorneys, health care providers, insurance companies and families.
Services include, but not limited to:
Autopsy/microscopy/medical record review and consultation;
"Cold Case" review and consultation;
Provision of expert witness testimony;
Trial preparation for attorneys;
Lecture/seminar series on medical, scientific and forensic topics;
Death investigation system analysis and process improvement to National Association of Medical Examiner's (NAME) standards;
Policy. Procedure and workflow improvements for Medical Examiner/coroner systems.

May 2011-November 2011; July 2012 to August 2014
Deputy Chief Medical Examiner
Broward County Medical Examiner and Trauma Services Division
Craig T. Mallak, M.D., J.D., Chief Medical Examiner
5301 SW 31st Ave
Fort Lauderdale, FL 33312
Office: 954.357.5232
Main: 954.357.5200
Fax: 954.327.6580
Responsibilities:

Adjudicating cause and manner of death through performance of autopsies, death scene examination, medical record review, and review of laboratory results. Expert witness testimony in criminal and civil cases. Training of the forensic pathology fellow. Teaching of medical and allied health students. Responsible for revising and updating the Broward County Medical Examiner and Trauma Services Policy and Procedure Manual. Director of office accreditation by the National Association of Medical Examiners. Pathologist on the committee for mass disaster response and preparedness. Supervision of Associate Medical Examiner physician staff. ACGME Fellowship Director (2012 to 2014).

November 2011 to July 2012
Interim District (Chief) Medical Examiner
Broward County Medical Examiner and Trauma Services Division
5301 SW 31st Ave
Fort Lauderdale, FL 33312
Office: 954.357.5232
Main: 954.357.5200
Fax: 954.327.6580
Responsibilities:
Adjudicating cause and manner of death through performance of autopsies, death scene examination, medical record review, and review of laboratory results. Expert witness testimony in criminal and civil cases. Training of the forensic pathology fellow. Teaching of medical and allied health students. Responsible for all the functions of the office with regard to death investigation and administration of Broward County policies. Re-writing, revision and establishment of new policy and culture within the office. Creation and submission of the FY2013 Operating and Capital Budget. Complete revision of office presence within the law enforcement community of Broward County with regard to death investigations.

2009-2011:
Associate Medical Examiner
Broward County Medical Examiner and Trauma Services Division
Joshua A. Perper, M.D., L.L.B, M.Sc, Chief Medical Examiner
5301 SW 31st Ave
Fort Lauderdale, FL 33312
Office: 954.357.5232
Main: 954.327.6500
Fax: 954.327.6580
Responsibilities:
Adjudicating cause and manner of death through performance of autopsies, death scene examination, medical record review, and review of laboratory results. Expert witness testimony in criminal and civil cases. Training of the forensic pathology fellow. Teaching of medical and allied health students. Responsible for updating the Broward County Medical Examiner and Trauma Services Policy and Procedure Manual. Director of office accreditation by the National Association of Medical Examiners. Pathologist on the committee for mass disaster response and preparedness. Pathologist on employment committees for a medical–legal death investigator and an autopsy technician.

Fall 2010:
Acting Medical Examiner for the U.S. Virgin Islands
Stephen J. Cina, M.D., P.C.-Director
Forensic Pathology Consultant
1305 S. Michigan Ave, Unit 608
Chicago IL 60605
(C) (970) 231-9207
(W) (312) 997-4500
E-mail:Stephen.Cina@cookcountyil.gov
Responsibilities:

Adjudicating cause and manner of death through performance of autopsies, death scene examination, medical record review, and review of laboratory results.

2007-2009:
Deputy Coroner and Forensic Pathologist
Cuyahoga County Coroner's Office,
Frank Miller III, M.D., Coroner
11001 Cedar Avenue
Cleveland, OH. 44106
Office: 216.698.5501
Fax: 216.707.3178
Responsibilities:
Adjudicating cause and manner of death through performance of autopsies, death scene examination, medical record review, and review of laboratory results. Expert witness testimony in criminal and civil cases. Training of the forensic pathology fellow. Teaching of medical and allied health students.

2006-2007:
Local Medical Examiner for Albemarle, Greene, and Nelson Counties,
Office of the Chief Medical Examiner
Marcella Fierro, M.D., Chief Medical Examiner
Commonwealth of Virginia
400 East Jackson Street
Richmond, Virginia 23219
804.786.3174
Responsibilities:
Adjudicating cause and manner of death through performance of autopsies, death scene examination, medical record review, and review of laboratory results. Expert witness testimony in criminal and civil cases.

2005-2006:
Local Medical Examiner for Richmond City, Henrico, Hanover, and Chesterfield Counties,
Office of the Chief Medical Examiner
Marcella Fierro, M.D., Chief Medical Examiner
Commonwealth of Virginia
400 East Jackson Street
Richmond, Virginia 23219
804.786.3174
Responsibilities:
Adjudicating cause and manner of death through performance of autopsies, death scene examination, medical record review, and review of laboratory results. Expert witness testimony in criminal and civil cases.

Academic Appointments:

Florida Atlantic University, Charles E. Schmidt College of Medicine, 777 Glades Road, Boca Raton, FL (2014 to Present)

Clinical Assistant Professor, Department of Surgery, Division of Pathology, Nova Southeastern University College of Osteopathic Medicine (2010-2014)

Nova Southeastern University College of Osteopathic Medicine Forensic Pathology Fellowship Program Director (2011-2014)

Grant Writing and Submissions:

Paul J. Coverdell Forensic Improvement Grant from the U.S.

Department of Justice award FY-2011-CD-BX-0064 for $148,778.

Grand Rounds:

University of Nebraska Medical Center: Pathology and Microbiology
Clinical Grand Rounds “Thinking Forensically in the Hospital Setting”.
June 3, 2015.

C. Contributions to Science

Publications:

Robinson RM, **Trelka DP.** Scene Investigation. eMedicine from WebMD. Updated January 16, 2011. Available at: http://emedicine.medscape.com/article/1680358-overview.

Baskurt, E., Raghavan P.,**Trelka, D.P.** Extramedullary hematopoiesis involving the bilateral lacrimal fossae. American Journal of Neuroradiology. 27(4):934-5, 2006 May.

Taraschi TF. O'Donnell M. Martinez S. Schneider T. **Trelka D.** Fowler VM. Tilley L. Moriyama Y. Generation of an erythrocyte vesicle transport system by Plasmodium falciparum malaria parasites. Blood. 102(9):3420-6, 2003 Nov 1.

Taraschi TF. **Trelka D.** Martinez S. Schneider T. O'Donnell ME. Vesicle-mediated trafficking of parasite proteins to the host cell cytosol and erythrocyte surface membrane in Plasmodium falciparum infected erythrocytes. International Journal for Parasitology. 31(12):1381-91, 2001 Oct.
Trelka DP. Schneider TG. Reeder JC. Taraschi TF. Evidence for vesicle-mediated trafficking of parasite proteins to the host cell cytosol and erythrocyte surface membrane in Plasmodium falciparum infected erythrocytes. Molecular & Biochemical Parasitology. 106(1):131-45, 2000 Feb 25.

Taraschi TF. **Trelka D.** Schneider T. Matthews I. Plasmodium falciparum: characterization of organelle migration during merozoite morphogenesis in asexual malaria infections. Experimental Parasitology. 88(3):184-93, 1998 Mar.

Goodyer ID. Pouvelle B. Schneider TG. **Trelka DP**. Taraschi TF. Characterization of macromolecular transport pathways in malaria-infected erythrocytes. Molecular & Biochemical Parasitology. 87(1):13-28, 1997 Jul.

Abstracts:

Taraschi, T.F., Goodyer, I.D., Pouvelle, B., **Trelka, D.P**., Nicholas, E., and Schneider, T. The Ins and outs of macromolecular transport in malaria-infected erythrocytes. Novartis Symposium, 1999

Textbooks:

Trelka, D.P. and Cummings, P. (Authors) Pearls and Pitfalls in Forensic Pathology: Infant and Child Death Investigation. Cambridge University Press 2016.
Collins, K.A. and Byard, R.W. (Eds) The Pathology of Infancy and Childhood. Chapter 26: Sports-Related Injuries and Deaths with Stephen J. Cina, M.D.. Springer Reference 2014.
Cummings, P. Trelka, D.P., and Springer, K. (Authors) Atlas of Forensic Histopathology. Cambridge University Press 2011.

Mark Songer (Ed). Practical Applications in Forensic Science. Death Investigation Chapter. Crime Ink Publishing LLC, 2011.

Webinars:

Capital Litigation Initiative: Crime Scene to Courtroom Forensics Training
Webinar 3: “Forensic Pathology Essentials.” Thursday, October 13, 2016. National Clearinghouse for Science, Technology and the Law at Stetson University College of Law.

D. Additional Information: Research Support and/or Scholastic Performance
None.

Jianning Wei, Ph.D.
Associate Professor of Biomedical Science

Education

- B.S., Organic Chemistry, University of Science and Technology of China, Hefei Anhui, P.R.China,1999
- Ph.D., Biochemistry, University of Kansas, Lawrence, KS, USA, 2003
- Postdoctoral Fellow, Florida Atlantic University, Boca Raton, FL, USA, 2003-2005

Research Interests

- To investigate protein-protein interaction using a combination of biochemical methods and mass spectrometry.
- Molecular mechanisms of age-related neurodegenerative diseases, such as Alzheimer's disease, Huntington's disease.
- The physiological function of Huntington interaction protein (HIP14) as a neuronal palmitoyl transferase.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Wei, Jianning

eRA COMMONS USER NAME (credential, e.g., agency login): jwei123

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Science and Technology of China, Hefei, P. R. China	B.S.	07/99	Organic Chemistry
University of Kansas, Lawrence, KS	Ph.D.	07/03	Biochemistry
Florida Atlantic University, Boca Raton, FL	Postdoctoral	07/06	Neuroscience

A. Personal Statement

The goal of the proposed research is to investigate activity-dependent synaptic changes in the pathogenesis of Huntington's disease (HD). Specifically, I plan to examine activity-dependent lysosomal distribution and its functional role in the nerve terminals of HD primary neurons cultured in a microfluidic chamber using a combination of biochemical genetic and optical imaging approaches. I have the expertise, leadership and motivation necessary to successfully carry out the proposed work. I have a broad background in neuroscience, with a specific training and expertise in biochemistry and molecular neurobiology, which are essential for the success of this application. My research group has been focusing on investigating the molecular pathogenesis of HD for more than ten years using a combination of biochemical, genetic and molecular approaches as demonstrated by my publications. My research has been supported by two consecutive NIH-funded AREA grants. In addition, I have served as the mentor for a number of graduate and undergraduate students in the field of HD research from different aspects in the past ten years. As a result of these previous experiences, I am aware of the importance of frequent communication about research designs, results and timeline between the mentor and students in successfully carrying out the proposed project. I have chosen Dr. Du from College of Engineering as the co-investigator, who will provide additional expertise in designing and fabricating microfluidic chamber required in this project. In summary, I have a demonstrated record of accomplished and productive research project in the area of HD research. My research expertise and experience in mentoring students and managing grants as the PI have prepared me to lead the proposed project.

B. Positions and Honors

Positions and Employment

08.2013-present Associate Professor, Dept. of Biomedical Science, Charles E. Schmidt College of Medicine, Florida Atlantic University, Boca Raton, FL.

08.2006-07. 2013 Assistant Professor, Dept. of Biomedical Science, Charles E. Schmidt College of Medicine, Florida Atlantic University, Boca Raton, FL.

01.2006-08.2006 Research Assistant Professor, Dept. of Biomedical Science, Florida Atlantic University, Boca Raton, FL.

Other Experience and Professional Memberships

2009-present The Society for Neuroscience, Member
2014-present Editorial member, SOJ Neurology

Honors

1997 P&G scholarship, University of Science and Technology of China
2002 Graduate Student Travel Award, Taiwanese Neuroscience Association
2002 Stanley L. Twomey Memorial Award. University of Kansas
2009 Excellence in Graduate Mentoring Award, Florida Atlantic University

C. Contribution to Science

1. My early work directly addressed how glutamate acid decarboxylase (GAD) activity is regulated in the brain. GAD is the rate-limiting enzyme in the synthesis of gamma-aminobutyric acid (GABA), the major inhibitory neurotransmitter in the CNS. Therefore, changes in GAD activity can directly affect GABA-mediated neurotransmission, which has been implicated in a number of neurological disorders, including Huntington's disease. My publications in this area document that GAD activity is regulated at different post-translational levels. We are the first to demonstrate that the two isoforms of GAD, GAD65 and GAD67, are regulated in opposite manner by protein phosphorylation and identified the phosphorylation sites and the responsible protein kinases. In addition, we also found that GAD65 can be cleaved *in vivo* and may have important physiological implications. In summary, this body of work provides new insight into the molecular mechanisms underlying the regulation of GAD activity and contributes to the understanding of GABA neurotransmission *in vivo*.
   a. Jin, H., Wu, H., Osterhaus, G., Wei, J., Davis, K., Sha, D., Floor, E., Hsu, C.C., Kopke, R.D., and Wu, J.Y. (2003) Demonstration of functional coupling between gamma-aminobutyric acid (GABA) synthesis and vesicular GABA transport into synaptic vesicles. *Proc. Natl. Acad. Sci. USA* 100, 4293-98.
   b. Wei, J., Davis, K.M., Wu, H., and Wu, J-Y. (2004) Protein phosphorylation of human brain glutamic acid decarboxylase (GAD)65 and GAD67 and its physiological implications. *Biochemistry* 43, 6182-89.
   c. Wei, J., and Wu, J-Y. Structural and Functional Analysis of Cysteine Residues in Human Glutamate Decarboxylase 65 (GAD65) and GAD67. (2005) *J. Neurochem.* 93 (3), 624-633.
   d. Wei, J., Lin, C-H., Wu, H., Jin, Y., Lee, Y-H., and Wu, J-Y. Activity Dependent Cleavage of Brain Glutamic Acid Decarboxylase 65 by Calpain (2006) *J. Neurochem.* 98(5), 1688-95.

2. My current research focuses on investigating the molecular pathways altered in Huntington's disease (HD). Our long-term goal is to understand the function of normal huntingtin and how mutant huntingtin interferes with it. We are the first to systemically study the role of Bim in the pathogenesis of HD using a combination of genetic, molecular and biochemical approaches. We report that Bim expression is increased in cellular and mouse models of HD. As a pro-apoptotic protein, Bim can directly participate in mHtt-induced cell death. In addition to Bim studies, we also investigate the molecular pathways that affect protein trafficking in HD. We demonstrate that GAD65 trafficking is impaired in HD, which may contribute to the impairment of GABA transmission reported in HD. Moreover, lysosomal trafficking is also affected. This body of work highlights the importance of huntingtin as a scaffold protein in protein trafficking and laid the groundwork for the proposed study in this application.
   a. Leon, R., Bhagavatula, N., Ulukpo, O., McCollum, M., Wei, J. (2010) BimEL as a possible molecular link between proteasome dysfunction and cell death induced by mutant huntingtin. *Eur J Neurosci.* 31, 1915-1925. PMCID: PMC2931320.
   b. Rush, D., Leon, R., McCollum, M., Treu, R., Wei, J. (2012) Palmitoylation and trafficking of GAD65 is impaired in a cellular model of Huntington disease. *Biochem J.* 442(1) 39-48. PMCID: PMC4646170.
   c. Erie C, Sacino M, Houle L, Lu M, Wei J. (2015) Altered lysosomal positioning affects lysosomal functions in a cellular model of Huntington's disease. *Eur J Neurosci*. 42(3): 1941-51. PMCID: PMC4523460.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/jianning.wei.1/bibliograpahy/49450739/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

1R01EB025819-01 (NIH/NIBIB) Wei (MPI) 9/15/2017-6/30/2021
Source: NIH/NIBIB
Title: SCH: INT: Virtual Neuroprosthesis: Restoring Autonomy to People Suffering From Neurotrauma.
The major goal of this project is to improve manipulation of robotic hands by testing the efficacy of tactile feedback in prosthetic limbs using a "virtual neural prosthetic." in which a facsimile of a neural implant is externalized and housed in a well-controlled microfluidic chamber, thereby abating the intrinsic limitations of highly invasive studies with neural implants. There is no overlap with the research proposed in the current application.
Role : MPI

FAU Brain Institute Pilot Grant Wei (PI) 03/10/2017-03/09/2018
Source: FAU
Title: Lysosomal Positioning in the Pathogenesis of Huntington's Disease.
The major goal of this project is to investigate lysosomal trafficking along axons of primary neurons and the role of lysosomes at nerve terminals. There is no overlap with the research proposed in the current application.
Role : PI

Seed grant Engeberg (PI) 12/20/2016-12/19/2017
Source: i-SENSE/FAU
Title: Robotic Symbiosis with Neuronal Action Potential Sensing Electrodes (ROBO-SYNAPSE): Network Connection To Link Living Systems with Robotic Devices
The major goal of this project is to (1) develop the novel ROBO-SYNAPSE between sophisticate tactile sensors on a dexterous robotic hand and a cutting edge microfluidic neuron-on-a-chip via a real-time inter-building network connection; (2) investigate neural plasticity with living nerves during robotic grasping experiments using microfluidic sensors under an action-based electrostimulation protocol; and (3) use a high-density electroencephalographic (EEG) sensing array to study cognitive plasticity by monitoring the dynamics of neural correlates during somatosensory restoration. There is no overlap with the research proposed in the current application.
Role: Co-PI.

Completed Research Support

2R15NS066339-02A1 Wei (PI) 07/01/2012-06/30/2016
Source: NIH/NINDS
Title: Regulation of BimEL phosphorylation in the pathogenesis of Huntington's disease.
The major goal of this proposal is to further investigate the molecular mechanism underlying the up-regulation of BimEL in Huntington's disease and its functional significance by behavioral analyses of the Bim-null R6/2 transgenic mouse model of HD. There is no overlap with the research proposed in the current application.
Role: PI.

1R15NS066339-01 Wei (PI) 07/01/2009-06/30/2012
Title: Regulation of BimEL phosphorylation in the pathogenesis of Huntington's disease.
The major goal of this proposal is to understand the molecular pathways that are altered by mHtt expression. We specifically hypothesize that the pro-apoptotic BH3-only protein, BimEL, is the molecule that functionally links mHtt aggregates formation and apoptosis. There is no overlap with the research proposed in the current application.
Role: PI.

R15DC012425-01A1 **Guthrie (PI)** **09/13/2012-09/12/2016**
Source: NIH/NIDCD
Title: BDNF over-expression and olfactory neurogenesis
The major goal of this project is to investigate the effect of BDNF on adult olfactory neurogenesis. Olfactory neurogenesis in R6/2 mice and R6/2 crossed with BDNF transgenic mice will be investigated. There is no overlap with the research proposed in the current application.
Role: Co-investigator.

R15DA029863 **Tao (PI)** **07/01/2010-06/30/2013**
Source: NIH/NIDA
Title: Mechanisms of sudden onset of malignant MDMA toxicity
The goal of this award is to understand the basic neural mechanisms of 5HT efflux related to MDMA neurotoxicity. There is no overlap with the research proposed in the current application.
Role: Co-Investigator

Ewa Wojcikiewicz, Ph.D.
Assistant Professor of Biomedical Science

Education

- B.S., State University of New York at Albany, Biochemistry and Molecular Biology, Albany, NY, 1997.
- Ph.D., University of Miami Miller School of Medicine, Physiology and Biophysics, Miami, FL, 2004.

Research Interests

- Biophysical mechanisms of inflammatory leukocyte recruitment.
- Nanomechanical changes associated with metastatic progression of cancer cells.
- Age-related changes in the mechanical properties of the eye accommodation apparatus.
- Atomic Force Microscopy.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Ewa P. Wojcikiewicz, PhD

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

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
State University of New York, Albany, NY.	B.S.	05/1997	Biochemistry/Mol. Biol.
University of Miami School of Medicine, Miami, FL	Ph.D.	05/2004	Physiology & Biophysics
University of Miami, School of Medicine, Miami, FL	Postdoc	06/2004-12/2005	Physiology & Biophysics

A. Personal Statement

My extensive experience in the biophysics and AFM fields as well as a good background and very strong interest in the biological sciences make me ideally suited to successfully carry out the proposed project. I have fourteen years of experience in the AFM field and was one of the first few people to advance single cell force spectroscopy (Helenius et al. 2008, JCS 121:1785). Specifically, I have extensive experience in cell to cell interactions including leukocyte/ endothelial interactions (Jaczewska et al., 2014). I have supervised four post-doctoral associates during my career, four graduate students and 14 undergraduate students. The undergraduate students trained include seven underrepresented minorities and two students from disadvantaged backgrounds. In summary, I am confident that I have the necessary expertise to successfully complete the proposed project.

B. Positions and Honors

Positions and Employment

8/17/2009- present Assistant Professor, Florida Atlantic University, Charles E. Schmidt College of Medicine, Basic Science Dept.

6/1/2006-8/14/2009 Research Assistant Professor, University of Miami Miller School of Medicine at the Dept. of Physiology and Biophysics.

1/1/2006-5/30/2006 Assistant Scientist, University of Miami Miller School of Medicine at the Dept. of Physiology and Biophysics.

9/1996-5/1997 Undergraduate Research Assistant, Department of Biochemistry and Cell Biology, SUNY Albany, Mentor: Dr. Robert Ossuna. (3 semesters)

5/1995-8/1996 Undergraduate Research, Department of Cell Biology at the Albert Einstein College of Medicine, Mentor: Dr. Carl Schildkraut. (2 summers)

6/1993-8/1993 Undergraduate Research Department of Cell and Molecular Biology at the Rockefeller University. Supervised by Dr. Maria Febbraio (consultant on proposed project), Mentor: Dr. James Darnell, Jr.(1 summer)

Awards

- Selected to serve as Session Chair at the Atomic Force Microscopy Nanomedicine Conference, Krakow, Poland, Travel Award

- Youth Travel Award, EMBO/FEBS workshop on AFM Applications in Biology, Oeiras, Portugal, Jul 2004.

Invited Seminars

1. Department of Chemistry and Biochemistry at FAU, Nov 2013
2. Southeastern Section of the American Physical Society, Bowling Green, KY, Nov 2013
3. Women's Leadership Conference, Boca Raton, FL , Mar 2013
4. FAU-VGTI Conference, Boca Raton, FL, Oct 2011
5. Atomic Force Microscopy Biomedical Conference, Paris, France, Aug 2011
6. Basic Science Dept. and CMBB at FAU, Boca Raton, FL, Feb 2010
7. Basic Science Dept. and CMBB at FAU, Boca Raton, FL, Feb 2009
8. Atomic Force Microscopy Conference in Barcelona, Spain, Oct 2008
9. Biophysical Society Conference in Long Beach, CA (platform session), Feb 2008
10. Bascom Palmer Eye Institute, Miami, FL, March 2007
11. Medical University of South Carolina, Charleston, SC, Apr 2005
12. VII Annual Linz Winter Workshop, Linz, Austria, Feb 2005

C. Contributions to Science

Leukocyte adhesion is mainly mediated by the interaction of LFA-1 and intercellular adhesion molecule-1 (ICAM-1). My work characterized the biophysical mechanisms of enhanced adhesion of leukocytes to ICAM-1. Using single cell force spectroscopy studies in conjunction with single molecule AFM measurements, our work revealed the very significant role of avidity modulation in enhanced cell adhesion. Avidity modulation is a measure of the overall binding strength of a system consisting of multiple receptors and multiple ligands. Enhanced cell adhesion results from a greater number of receptors being available for ligand binding. We were one of the first groups to pioneer single cell force spectroscopy, which is utilized in the proposed research.

1. Zhang, X, **Wojcikiewicz, E**, Moy V.T. (2002) Force spectroscopy of the leukocyte function-associated antigen-1/intercellular adhesion molecule-1 interaction. *Biophys J*.,83(4):2270-9.
2. **Wojcikiewicz, E.P.,** Zhang, X.H., Chen, A, Moy V.T. (2003) Contributions of molecular binding events and cellular compliance to the modulation of leukocyte adhesion. *J.Cell Sci*.,116(12):2531-2539.
3. **Wojcikiewicz, E.P.,** Zhang, X.H., Moy V.T. (2004) Force and compliance measurements on living cells using atomic force microscopy (AFM*). Biol Proced Online*.,6:1-9. Epub 2004 Jan 15.
4. **Wojcikiewicz, E.P.,** Moy V.T. (2006): Mechanisms of Avidity Modulation in Leukocyte Adhesion Studied by AFM. (p.169-180). F*orce Microscopy: Applications in Biology and Medicine,* John Wiley & Sons, Inc.

Later studies investigated the mechanisms of inflammatory leukocyte recruitment, a process mediated by adhesion receptors. This process is critical in a number of diseased states including atherosclerosis. The infiltration of leukocytes results in a release of cytokines and other factors causing the accumulation of fatty substances, cholesterol, cellular waste products, calcium and other substances and leading to plaque formation. We identified the molecular biophysical mechanisms that modulate leukocyte interactions with ICAM-1 and 2. Most recently, we elucidated the key role of the Junctional adhesion molecule-A in the early events of leukocyte transmigration. I served as the primary investigator on the latest of these studies.

1. Jaczewska, J., Abdulreda, M.H., Yau, C. Y., Shubert, I., Berggren, P.O., Weber, C., Koenen R.R., Moy, V.T., **Wojcikiewicz, E.P.** (2014) TNF-alpha and IFN-gamma promote lymphocyte adhesion to endothelial junctional regions facilitating transendothelial migration. *Journal of Leukocyte Biology,* 95(2):265-74.
2. **Wojcikiewicz, E.P.**, Koenen, R.R., Fraemohs, L., Minkiewicz, J., Azad, H., Weber, C., Moy, V.T. (2009) LFA-1 binding destabilizes the JAM-A homophilic interaction during leukocyte transendothelial migration. *Biophysical Journal,* 96(1):285-293.
3. **Wojcikiewicz, E.P.**, Abdulreda, M.H., Zhang, X., Moy, V.T. (2006) Force Spectroscopy of LFA-1 and its ligands, ICAM-1 and ICAM-2. *Biomacromolecules,* 7(11):3188-3195.
4. Zhang, X., **Wojcikiewicz, E.P.,** Moy, V.T. (2006) Dynamic adhesion of T- lymphocytes to endothelial cells revealed by Atomic Force Microscopy. *Experimental Biology and Medicine*, 231(8):1306-1312.

The formation of Beta amyloids is chiefly responsible for the pathology of Alzheimer's disease. I am participating in collaborative work to identify novel therapies aimed at disrupting A Beta peptides. AFM imaging is allowing us to visualize both peptide formation and disruption with potential novel therapeutics.

1. Liu, H., Lantz, R., Cosme, P., Rivera, N., Andino, C., Terentis, A., **Wojcikiewicz, E.P.,** Oyola, R., Du, D. Site-Specific Dynamics of Amyloid Formation and Fibrillar Configuration of Aβ1-23 Using an Unnatural Amino Acid. *Chem Commun (Camb)*. (2015) Apr 25;51(32):7000-3. doi: 10.1039/c5cc00149h.
2. Ojha,B., Liu, H., Dutta, S., Nekkar Rao, P.,**Wojcikiewicz, E.P.**, Du, D.(2013) Poly(4-styrenesulfonate) as an Inhibitor of ABeta40 Amyloid Fibril Formation. *Journal of Physical Chemistry, Part B,* 117(45):13975-84.
3. Elbassal, E.A., Liu, H., Morris C., **Wojcikiewicz, E.P.**, Du, D. Effects of Charged Cholesterol Derivatives on Aβ40 Amyloid Formation. J Phys Chem B. 2016 Jan 14;120(1):59-68. doi: 10.1021/acs.jpcb.5b09557. Epub 2015 Dec 23.PMID:26652010
4. Liu, H., Ojha, B., Morris, C., Jiang, M., **Wojcikiewicz, E.P.**, Rao, P.N., Du, D. Positively charged Chitosan and N-Trimethyl Chitosan Inhibit Aβ40 Amyloid Formation. Biomacromolecules. 2015 Aug 10;16(8):2363-73. doi: 10.1021/acs.biomac.5b00603. Epub 2015 Jul 14.PMID:26125953

Complete List of Published Work in MyBibliography:

http://www.ncbi.nlm.nih.gov/sites/myncbi/ewa.wojcikiewicz.1/bibliography/48023906/public/?sort=date&direction=ascending

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

Ongoing Research Support

Effects of Cell-penetrating Peptides on Cancer Cell Stiffness
OURI Undergraduate Research Grant (internal, FAU) 01/24/2017-1/23/2018
Undergraduate student: Mary Moussa

Effect of PAK6 Gene Knockout on Prostate Cancer Cell Stiffness
OURI Undergraduate Research Grant (internal, FAU) 03/01/2017-2/28/2018
Undergraduate students: Belinda Gerard and Nikolas Echeverry

Completed Research Support

Grant #:180259 Wojcikiewicz (PI) 01/01/2011-12/31/2011
Atomic Force Microscopy Studies of the Epithelial to Mesenchymal Transition
American Cancer Society Seed Money for Research to allow new investigators to generate preliminary data for national award application. The goal of this study was to determine if cell stiffness was a predictor of metastatic progression.

NIR-0612, FBRP:YR66253H Wojcikiewicz (PI) 07/01/2006-08/14/2009
Biophysical Determinants of Leukocyte Transmigration
The goal of this work was to determine the role of the numerous adhesion receptors found in endothelial junctions in promoting paracellular transendothelial migration under inflammatory conditions.

Jang Yen Wu, Ph.D.
Professor of Biomedical Science

Education

- B.S., Chemistry, National Taiwan University, 1963
- Ph.D., Biochemistry, University of California, San Francisco Medical Center, 1968
- Post-doctoral training, University of California, Los Angeles, 1968-1970

Research Interests

- Neuroscience, Neurotransmitters and neurological disorders

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Wu, Jang-Yen	Professor

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

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE	MM/YY	FIELD OF STUDY
National Taiwan University	B.S.	06/63	Chemistry
University of California, San Francisco, CA	Ph.D.	06/68	Biochemistry
University of California, Los Angeles, CA	Postdoctoral	07/70	Molecular Biology

A. Personal Statement

My research interest includes the basic study of neurotransmission with special emphasis on the regulation of GABA and glutamate neurotransmission at molecular and cellular levels and translational research to develop mechanism-based therapeutics for brain diseases including stroke, Parkinson's disease, Alzheimer's disease (AD) and other neurological disorders as documented in my publications. The overall goal of the proposed study is to test the hypothesis that the combination therapy consisted of granulocyte colony- stimulating factor (G-CSF) protein and GCSF gene is a novel therapeutic intervention for Alzheimer's disease (AD). Recently we have demonstrated that G-CSF is effective in restoring the function of dopamine neurons in Parkinson's disease animal model. In addition, we have also shown that G-CSF is also effective in reducing the infarct size and improving the brain function in stroke animal model. Protein therapy using GCSF is attractive because GCSF is well tolerated. However, its plasma half - life is about 4 hours. One alternative approach is to use a combination therapy consisted of GCSF protein and well regulated GCSF gene therapy. AS PI or Co-I of several NIH-funded, NSF-funded or State-funded grants, I have laid the ground work for the proposed research by developing cell cultures, stem cell and animal models as platforms for testing biological functions and the efficacy of therapeutic intervention. We have already demonstrated the proof of concept that combination therapy provides a higher efficacy in protecting the brain than the individual single therapy in stroke animal model. We have also demonstrated that GCSF protein therapy and GCSF gene therapy are effective in protecting cells in AD cell cultures model. Hence, we believe GCSF and G-CSF gene combination therapy will provide a novel new therapeutic intervention for AD. I have expertise and extensive experience in neurotransmitter systems e.g., GABA, glutamate and dopamine systems under physiological as well as pathological conditions. In addition, I have also developed several mechanism-based novel therapeutics for brain diseases e.g., Parkinson's disease, stroke, epilepsy and alcoholism. Hence, I believe that with my expertise and experience in the field I can lead this proposed project to a fruitful conclusion. Some relevant publications are listed below:

1. Jin, H., Wu, H., Osterhaus, G., Wei, J., Davis, K., Sha, D., Floor, E., Hsu, C.-C., Kopke, R.D. and Wu, J.-

Y. Demonstration of functional coupling between GABA synthesis and vesicular GABA transport into synaptic vesicles. *Proc. Natl. Acad. Sci. U.S.A.* 100: 4293-4298, 2003.
2. McCollum M., Ma Z., Cohen E., Leon R., Tao R., Wu J.Y., Maharaj D., Wei J. Post-MPTP Treatment with Granulocyte Colony-Stimulating Factor Improves Nigrostriatal Function in the Mouse Model of Parkinson's Disease. Mol Neurobiol. 2010, 41: 410-419. [2 1 Apr 2010, E-Pub ahead of print]
3. Buddhala, C., Suarez, M., Modi, J., Prentice, H., Ma, Z., Tao., R and Wu, J.-Y. Calpain cleavage of brain glutamic acid decarboxylase 65 is pathological and impairs GABA neurotransmission. PLoS ONE 7(3): e33002. doi:10.1371/journal.pone.0033002 (2012)
4. Gharibani, P.M., Modi, J., Menzie, J., Genove, R., Ma, Z., Tao, R., Prentice, H., and Wu, J.-Y Mode of action of S-Methyl-N, N-diethylthiocarbamate sulfoxide (DETC-MeSO) as a novel therapy for stroke in a rat model. Mol. Neurobiol., 50 (2): 655-672 (2014).((DOI 10.1007/s12035-014-8658-0, 2014, Feb 28)
5. Shu, S.-Y., Jiang, G., Zeng, Q.-Y., Wang, B., Li, H.,Ma, L., Steinbusch, H., Song, C., Chan, W.-Y., Chen, X.-H., Wu, Y.-M., Bao, R., Chen, Y.-C. and Wu, J.-Y. The Marginal Division of the Striatum and Hippocampus Has Different Role and Mechanism in Learning and Memory. Mol. Neurobiol. DOI 10.1007/s12035-014-8891-6 (2014).
6. Gharibani, P.M., Modi, J., Menzie, J., Alexandrescu, A., Ma, Z., Tao, R., Prentice, H., and Wu, J.-Y. Comparison between single and combined post-treatment with S-Methyl-N,N-diethylthiolcarbamate sulfoxide and taurine following transient focal cerebral ischemia in rat brain. Neuroscience, 300: 460-473 (2015).
7. Ren, J., Chen, I., Liu, C.H., Chen, P.C., Prentice, H., Wu, J.-Y., and Liu, P.K. (2015). Non-invasive tracking of gene transcript and neuroprotection after gene therapy. Gene Therapy, 1-9; (doi:10.1038/gt.2015.81; 24July, 2015).

B. Position and Honors

Position and Employment

1970-1975 Assistant, Associate & Research Scientist and Section Head, Division of Neurosciences, City of Hope National Medical Center, Duarte, CA.
1975-1983 Associate Professor (Tenured), Department of Cell Biology, Baylor College of Medicine, Houston, TX.
1983-1989 Professor, The Milton S. Hershey Medical Center, Department of Physiology The Pennsylvania State University, Hershey, PA.
1989-1995 Chairman and Professor, Department of Physiology and Cell Biology, University of Kansas, Lawrence, KS.
1995-2002 Professor, Department of Molecular Biosciences, University of Kansas, Lawrence, KS
2002- 2016 August, Schmidt Senior Fellow and Distinguished Professor, Charles E. Schmidt College of Medicine, Florida Atlantic University, Boca Raton, FL.
2016 August –Present, Professor, Charles E. Schmidt College of Medicine, Florida Atlantic University, Boca Raton, FL.

2005-2008 Senior Assistant Vice-President for Research, Florida Atlantic University, Boca Raton, FL.
2006-2009 Associate Dean for Research, Charles E. Schmidt College of Biomedical Science, Florida Atlantic University, Boca Raton, FL

Other Experience and Professional Memberships

1980	Study Section (Ad hoc), National Institute of Neurological and Communicative Disorders and Stroke, NIH.
1985	Study Section (Ad hoc), National Eye Institute, NIH.
1993-2003	Scientific Review Committee Board, National Health Research Institute, Taiwan.
1994-1997	Merit Review Board, Department of Veterans Affairs, U.S.A..
1987-1997	Editorial Board, Neurochemistry International.
1990-Present	Editorial Board, Newsletter on Neurochemistry.
1992-Present	Editorial Board and Editor, Journal of Biomedical Science.
2004-Present	Editorial Board, Journal of Biomed Science & Bioengineering.
2012-Present	Editorial Board, Peer J.
2013-Present	Editorial Board, Science Postprint
2013-Present	Editorial Board, Journal of Methodology
2009	Chair of the Organizing and Program Committee, International Taurine Conference
2009 -Present	Member of the Advisory Board, Academia Sinica, Taiwan.
2012- 2015	Member of External Review/Advisory Board, Jiao Tung University, Shanghai, China
2013- 2015	Member of the Advisory Board, China Medical University, Taiwan

Membership: Society for Neuroscience, International Society for Neurochemistry, American Society for Neurochemistry, AAAS

Honors

1965 C.T. Loo Fellowship, China Institute in America
1986 Taiwanese American Foundation Achievement Award in Science and Technology
1987 Instituto Venezolano de Investigacion Cientifica (IVIC) Award
1991 First Presidential Award in Basic Research, Chinese Neuroscience Society in America
2002 One of the world's most cited authors identified by Current Contents/ISI

C. Contribution to Science

(I). In GABA system: My early contribution to science is in neurotransmitter gamma-aminobutyric acid (GABA) system. I am the first one responsible for isolation, purification and characterization of the two key brain enzymes involved in synthesis and metabolism of GABA, namely, L-glutamate decarboxylase (GAD), and GABA-transaminase (GABA-T), respectively. This important work has laid the foundation for subsequent advances in GABA system including identification of GABA neurons and its neuronal circuitry in the brain. In addition, it also provides the new insight regarding the regulation of GABA transmission. Some representative publications are listed below:

1. Wu, J.-Y., Matsuda, T., and Roberts, E. Purification and characterization of glutamate decarboxylase from mouse brain. *J. Biol. Chem.* 248:3029-3034, (1973).
2. Davis, K.M., Foos, T., Bates, C.S., Tucker, E., Hsu, C.-C., Chen, W.Q., Schlooss, J.V., Tobin, A. and Wu, J.-Y. A novel approach for expression and large scale purification of human brain L-glutamate decarboxylase. *Biochem. Biophys. Res. Commun.* 267:777-782, (2000).
3. Jin, H., Wu, H., Osterhaus, G., Wei, J., Davis, K., Sha, D., Floor, E., Hsu, C.-C., Kopke, R.D. and Wu, J.-Y. Demonstration of functional coupling between GABA synthesis and vesicular GABA transport into synaptic vesicles. *Proc. Natl. Acad. Sci. U.S.A.* 100: 4293-4298, (2003).
4. Buddhala, C., Suarez, M., Modi, J., Prentice, H., Ma, Z., Tao., R and Wu, J.-Y. Calpain cleavage of brain glutamic acid decarboxylase 65 is pathological and impairs GABA neurotransmission. PLoS ONE 7(3): e33002. doi:10.1371/journal.pone.0033002 (2012).

(II). In Taurine system: In addition to GABA system, I have also played a major role in delineating the role of taurine in the brain. I discovered and purified of a specific taurine synthesizing enzyme, cysteinesulfinic acid/cysteic acid decarboxylase (CSAD/CAD) and taurine receptor in mammalian brain. These important findings have help establish that CSAD/CAD and GAD are two distinct proteins and that CSAD/CAD and GAD are responsible for synthesis of taurine and GABA, respectively. Similarly, taurine receptor is distinctly different from other amino acids receptors such as GABA receptors, glycine or glutamate receptors. In addition, I also elucidated the mode of action of taurine including regulation of calcium homeostasis, neuroprotection and anti-apoptotic process. Representative publications are listed below:

1. Wu, J.-Y. Purification and characterization of cysteic/cysteine sulfinic acids decarboxylase and L-glutamate decarboxylase in bovine brain. *Proc. Natl. Acad. Sci. USA* 79:4270-4274, 1982.

2. Wu, J.-Y., Liao, C., Lin, C.-J., Lee, Y.H., Ho, J.-Y., and Tsai, W.H. Taurine receptors in the mammalian brain. In: Functional Neurochemistry of Taurine, (Pasantes-Morales, H., ed.), Alan R. Liss Publishers, New York, pp. 147-156 (1990).

3. Chen, W.Q., Nguyen, M., Carr, J., Lee, Y.J., Jin, H., Foos, T., Hsu, C.C., Davis, K.M., Schloss, J.V., and Wu, J.-Y. Role of taurine in regulation of intracellular calcium level and neuroprotective function in cultured neurons. *J. Neurosci. Res.* 66:612-619,2001.

4. Leon, R., Wu, H., Jin, Y., Wei, J.N., Buddhala, C., Prentice, H., and Wu, J-Y., Mechanism of the effect of taurine on glutamate-induced apoptosis. *J. Neurosci. Res.,87 (5): 1185-1194, 2009.*

(III). In translational research: I have developed a glutamate receptor partial antagonist, S-Methyl N, N-diethylthiolcarbamate sulfoxide (DETC-MeSO) and demonstrated its efficacy in neuroprotection in seizure and stroke. In addition, I have developed a stem cell stimulator, granulocyte colony-stimulating factor (G- CSF) as an effective therapeutic agent for Parkinson's disease in both the animal model as well as in clinical setting. Some representative publications are listed below:

1. Nagendra, S.N., Faiman, M.D., Davis, K., Wu, J.-Y., Newby, X. and Schloss, J.V. Carbamoylation of brain glutamate receptor by a disulfiram metabolite. *J. Biol. Chem.* 272:24247-24251, 1997.

2. McCollum M., Ma Z., Cohen E., Leon R., Tao R., Wu J.Y., Maharaj D., Wei J. Post-MPTP Treatment with Granulocyte Colony-Stimulating Factor Improves Nigrostriatal Function in the Mouse Model of Parkinson's Disease. Mol Neurobiol. 2010, 41: 410-419. [2 1 Apr 2010, E-Pub ahead of print]

3. Gharibani, P.M., P.M., Modi, J., Menzie, J., Genove, R., Ma, Z., Tao, R., Prentice, H., and Wu, J.- Y Mode of action of S-Methyl-N, N-diethylthiocarbamate sulfoxide (DETC-MeSO) as a novel therapy for stroke in a rat model. Mol. Neurobiol., 50 (2): 655-672 (2014).((DOI 10.1007/s12035-014-8658-0, 2014, Feb 28)

4. Gharibani, P.M., Modi, J., Menzie, J., Alexandrescu, A., Ma, Z., Tao, R., Prentice, H., and Wu, J.-Y. Comparison between single and combined post-treatment with S-Methyl-N,N-diethylthiolcarbamate sulfoxide and taurine following transient focal cerebral ischemia in rat brain. Neuroscience, 300: 460-473 (2015).

5. Ren, J., Chen, I., Liu, C.H., Chen, P.C., Prentice, H., **Wu, J.-Y**., and Liu, P.K. (2015). Non-invasive tracking of gene transcript and neuroprotection after gene therapy. Gene Therapy, 1-9; (doi:10.1038/gt.2015.81; 24July, 2015).

A complete list of my publications cab be found at:

http://www.ncbi.nlm.nih.gov/myncbi/collections/bibliography/48173513/

D. Research Support

Ongoing Research Support

1. Title of Research Project “Granulocyte colony-stimulating factor (GCSF) gene therapy for stroke”. Amount of Award: $ 1,231,336.00; Source of support: James & Esther King Biomedical Program, State of Florida. (Grant #: 6JK08). Period covered: 04/01/2016-03/31/2019. Role: PI

Completed Research Support

1. 09KW-11 James & Esther King Biomedical Program, State of Florida, Amount of Award: $748,046.00. Period covered: 01/01/10 -12/31/12. Title of Research Project: “G-CSF, DETC-MeSO and Sulindac as Multi-drug Combination Therapy for TBI and Stroke”. Role: PI

The goal of this project was to develop a multi-drug combination therapy based on mechanisms related to facilitation of stem cells, anti-glutamate excitotoxicity and anti-oxidative stress.

2. Neuroscience Major Theme Grant, Florida Atlantic University, 01/01/11-12/31/13

The goal of this project is to study neurotransmission in physiological and pathological conditions. Role: Investigator, PI: Janet Blanks and Rodney Murphey

Appendix C: COM MS Biomedical Science Graduate Survey

College of Medicine Graduate Degree Recipients
We are interested in what you have been doing in the time between graduating from the Florida Atlantic University with your Master's Degree in Biomedical Science and now.

1) Currently, what is your highest educational degree earned?

- Master's degree
- Medical degree (MD, DO, DDS, DVM)
- Law degree (LLB or JD)
- PhD or EdD
- Other (specify):

2) Have you ever attended another graduate or professional school since obtaining your Master's degree?

Yes No

If yes:

Educational program:

Field of study:

Educational institution:

3) Have you worked since obtaining your Master's degree?

Yes No

If yes:

Job title (for your last job):

Employer:

City:

State:

If you are primarily employed, please answer the following questions:

Describe your present job.

- Part-time
- Full-time, temporary
- Full-time, not in career
- Full-time, in career field, but likely to change within the next two years
- Full-time, permanent in career field

What is your monthly income:

- Under $500
- $500-999
- $1000-1499
- $1500-1999
- $2000-2499
- $2500-2999
- $3000-3499
- $3500-3999
- $4000-4499
- $4500-4999
- $5000-5499
- Over $5500

Given your training and degree, how would you describe your job?

- Definitely beneath my level
- Somewhat beneath my level
- Appropriate for my level
- Too advanced for my level

Even though you are not primarily a student, are you attending or planning to attend school?

- Yes, post-graduate in my degree area
- Yes, career related, new area
- Yes, not career related
- No

Have you been working continuously (with the exception of time off for travel or family business) since obtaining your Master's degree from Florida Atlantic University?

Yes No

Your job title:

Your employer:

City :

State:

<u>If you are primarily a student</u>, please answer the following questions:

Which of the following best describes the level of your current educational program?

- Bachelor's degree
- Master's degree
- PhD or EdD
- MD,DO,DDS,DVM
- JD or LLB (law)
- BD of MDiv (divinity)
- Other (specify):

Are you employed while attending school?

- Yes, part-time by the school I attend
- Yes, part-time but not by the school I attend
- Yes, full-time but not by the school I attend
- No

Your educational program:

Your field of study:

Educational institution your are attending:

<u>If you are currently not working for pay and not a student</u>, please answer the following questions:

Why are you not currently working?

- ○ I am volunteering my skills and time
- ○ I am looking for work
- ○ I am raising a family
- ○ I am taking time off to decide what to do
- ○ I am taking care of an ill relative
- ○ I am taking time off for personal reasons
- ○ I am traveling or undertaking some other activity
- ○ I am disillusioned/discouraged about my job searches

For what type of work are you or will you be looking (if any)?