

GRANT NUMBER

T32 EB005969

TITLE

Interdisciplinary Training in Biomedical Imaging

GRANTEE ORGANIZATION

Georgia Institute of Technology

PROJECT PERIOD

09/01/2007 – 08/31/2012

Principal Investigator

Xiaoping P. Hu, Ph.D.

FINAL PROGRESS REPORT

PROGRAM EVALUATION

We plan to evaluate the training program in the following manners. First, we will obtain feedback from current and former trainees with regard to the effectiveness and value of the training program. Second we will collect specific data in terms of their publications, awards, graduation dates, and job placements after graduation. As a major goal of our program is to provide interdisciplinary training, we will assess the achievement in this regard by highlighting trainee publications in interdisciplinary journals.

1. The overall objective of this training program is to provide interdisciplinary predoctoral training in biomedical imaging to Ph.D. students enrolled in our graduate programs. Specifically, trainees will be trained with didactic course work in core imaging methodologies and application areas and in-depth research experience specializing in one core methodology as well as an application area.

For the current funding year, we have supported 4 trainees: William Alexander Calhoun, Jeenah Jung, Adrian Lam, and Jason Lamanna. All the trainees have made significantly progress in their research. In particular, Jeenah Jung has authored or co-authored 3 journal publications. All of the students have passed their Ph.D. qualifying exam, passing a major milestone towards their Ph.D. Adrian Lam has also passed his Ph.D. thesis proposal, allowing him to focus on dissertation research.

2. There are two courses currently offered for the students and mentors. These courses have been taken by most of our trainees. Trainees who have not taken them will do so soon.

The first course is offered at Georgia Institute of Technology. This one-credit course is the latest in a series of developments concerning research ethics training for graduate students. As the director of Graduate Research Ethics Programs, a joint appointment between the Office of the Vice Provost for Research and the School of Public Policy, Prof. Jason Borenstein developed resources and courses that help to meet the ethics educational needs of graduate students. The course is designed to help satisfy federal requirements for research ethics training. Several trainees have taken this course or an equivalent course and other trainees will take this course as part of their training. In addition, an online course is also made available (<http://www.researchethics.gatech.edu>) at Georgia Tech for students and faculty to be properly trained.

At Emory, the course for the trainees to take is Values in Science (IBS/Chem 606). This is an intensive two-day course in research ethics sponsored and coordinated by the Graduate School of Arts and Sciences and the Center for Ethics. It is offered prior to both the Fall and Spring semesters. The course satisfies the ethics training requirements of the National Institutes of Health and is designed for graduate students, post-doctoral fellows and others interested in addressing the objectives. Specifically, the course is intended to improve behavior outcomes related to ethical decision making, to improve moral reasoning, to increase knowledge of ethical theory, to develop core competencies in the responsible conduct of research, to increase appreciation for ethical guidelines, standards, and etiquette, to increase awareness of ethical guidelines, rules, and regulations related to the practice of research, and to increase the understanding of making and responding to allegations

of misconduct.

3. The trainees currently enrolled in this training program were recruited from our graduate student pool. Our graduate Admissions committee is very active and successful in attracting, identifying, and recruiting women and under-representative minority students into our programs. Taking advantage of our diverse graduate student body, the present training program has actively sought the participation of highly diversified trainees and has been successful in this regard. In year 5, one of the trainees is female.

TRAINEES RESEARCH PROJECT & COURSE WORK

Calhoun, William Alexander

Long-Term Two-Photon Imaging of Neuronal Cultures

His project under this training grant was to develop a two-photon imaging system suitable for long-term (over days to weeks) continuous imaging of living neurons with simultaneous electrical recording and stimulation through micro-electrode arrays. This included developing custom two-photon hardware and software, environmental controls, and image processing techniques necessary to probe the development and function of cultured neural networks. We are currently using this system to investigate changes in morphology induced by chronic closed-loop electrical stimulation by long term imaging of neurons in vitro expressing fluorescent proteins.

Course Work: His training was also supported by coursework in systems, cellular, and theoretical neuroscience, medical imaging and image processing, and advanced digital signal processing.

President's Fellowship (Georgia Tech) August 2010 – present

Jung, Jeenah

In medical imaging courses, Medical Imaging Systems and Medical Image Processing, she has studied the technology behind acquiring and processing various medical imaging data. In cellular engineering courses, Cellular Engineering and Cellular and Biomolecular Engineering, she has examined in depth the imaging and biochemical methods for investigating cells. By developing a firm understanding of medical imaging and cellular engineering in her course work, under the guidance of Dr. Philip Santangelo, she has found success in her research to create novel tools for more accurate and efficient detection of pathology at the cellular level. As presented in a recent publication in *Nucleic Acids Research* (2012), she has developed a method for imaging and quantifying interactions between an RNA and its regulatory protein *in situ*. This technique can be used to detect potentially pathologic gene expression at the mRNA level before the proteins are produced on a per cell basis. Early detection of disease-causing gene expression in a small number of cells is useful in diagnosing disorders, such as cancer and viral infection.

Course Work: Medical Imaging Systems and Medical Image Processing; Cellular Engineering and Cellular and Biomolecular Engineering.

Lam, Adrian

His research project supported under this training grant was to determine the blood flow in the aorta after aortic valve bypass surgery, a surgery for high-risk patients with severe

aortic stenosis who cannot undergo aortic valve replacement. This surgery uses a bioprosthetic valve and a conduit to re-route blood flow from the apex of the heart to the descending aorta. In this project, he was trained to be capable in multiple software programs necessary to reconstruct a 3D model of the aorta and conduit from 2-D MR images, to simulate the blood flow patterns within these vessels, and to analyze the blood flow after computer simulation. These programs include Geomagic, ICEM, FLUENT, and Tecplot. This led to a poster presentation at SCMR as well as a poster presentation at the NIBIB Conference for Imaging Trainees, and we have submitted a manuscript to JACC Imaging (currently under review) titled, "Post-surgical Hemodynamics of the Aortic Valve Bypass Operation Evaluated with Phase Contrast Magnetic Resonance".

Course Work: During the period of support, he took courses on imaging systems, signal and image processing and fluid dynamics, biochemistry and applied physiology.

Lamanna, Jason

He is a fourth-year MD/PH.D student at Emory University and currently in the second year of the Emory/Georgia Institute of Technology combined Biomedical Engineering Ph.D. Program. The underlying mission of my research is to overcome the technical and immunological barriers preventing the successful translation of cellular therapies for disorders of the central nervous system to the clinic. Specifically, he is interested in tracking cells in vivo with cellular contrast agents and reporter genes for magnetic resonance imaging (MRI), developing non-invasive, MR-guided technologies for transplanting cells in to the spinal cord, and elucidating the mechanisms underlying cellular graft rejection in the central nervous system. His dissertation work includes tissue culture of human neural stem cells, diseased transgenic animal models, large animal models, medical device design, MRI, molecular imaging, and molecular and cell-based therapies, all with a focus on translation. His Ph.D. dissertation work was conducted under the guidance of a co-mentorship with Dr. Nicholas Boulis and Dr. John Oshinski.

TRAINEE PUBLICATIONS

Calhoun, William Alexander

Conference poster: Custom multiphoton microscope for long-term imaging of plasticity in neurons under chronic closed-loop stimulation, NIBIB Training Grantees Meeting, 2012

Jung, Jeenah

Jung J, Lifland AW, Zurla C, Alonas EJ and Santangelo, PJ. (2012) Quantifying RNA-protein interactions in situ using modified-MTRIPs and proximity ligation. *Nucleic Acids Res.* [Epub ahead of print] PMID: 22952158

Lifland AW, Jung J, Alonas E, Zurla C, Crowe JE Jr and Santangelo PJ. (2012) Human respiratory syncytial virus nucleoprotein and inclusion bodies antagonize the innate immune response mediated by MDA5 and MAVS. *J Virol*, 86(15): 8245-8258. PMID: 22623778

Santangelo PJ, Alonas E, Jung J, Lifland AW and Zurla C. (2012) Probes for intracellular RNA imaging in live cells. *Methods Enzymol*, 505: 383-399. PMID: 22289464

Lam, Adrian

Conference Poster: Post-surgical Hemodynamics of the Aortic Valve Bypass Operation Evaluated with Phase Contrast Magnetic Resonance, 2012

Lamanna, Jason

None

Table 12A. Predoctoral Trainees Supported by this Training Grant (Renewal Applications and Non-Competing Continuation Progress Reports Only)

Predoctoral (and MSTP) Trainees (Listed sequentially by Entering Class):

Trainee, Year of Entry Prior Degree & Institution (Mentor - Department/program)	Source(s) of Support Each Grant Year/Academic Year										Title of Research Project or Research Topic	Degree(s) Received (Year)	Current Position and Institution (grant support obtained)
	-01 07-08	-02 08-09	-03 09-10	-04 10-11	-05 11-12	-06	-07	-08	- 09	- 10			
Muir, E. R., 2008, BS, Georgia Tech, (Dr. Tim Duong-Yerkes/Emory-BME)	*TG/TA **TG/TA (01/08 – 12/08)										*MRI in Alzheimer's Disease Mouse Model **Anatomical & Physiological MRI of the Retina	BS (05/06) Ph.D. (2010)	N/A
Robledo, B., 2008, BS, Harvard University (Dr. Xiaoping Hu – Emory-BME)	TG (01/08 - 12/08)										Characterizing a Novel MRI Molecular Marker	BA (06/05)	Research Assistant/Graduate Student, Emory University & Georgia Tech.
Roller, B. T., 2008, BS. Georgia Tech, (Bellamkonda- Georgia Tech-BME)	*TG/UF (01/08 – 12/08)	**TG (01/09 – 07/09)									*Chemical Exchange Saturation Transfer (CEST) and Applications in MRI Imaging **Intraoperative Visualization of Brain Tumor	BS (05/07)	Ph..D. Student, Georgia Tech
Wen, M., 2008, BS, Johns Hopkins, (Dr. Shuming Nie, Emory-BME)	TG/RG/F (Georgia Tech Fellowship)	TG/RG/F (Georgia Tech Fellowship)									In Vivo Cancer Imaging	BS (05/07)	Ph..D. Student, Georgia Tech

	(01/08 – 12/08)	(01/09 – 07/09)																
Magnuson, M., 2009 Louisiana Tech University, (Dr. Shella Keilholz – BME/BME)		TG (01/09 – 12/09)	TG (01/10 – 07/10)											Mapping Functional Connectivity in the Anesthetized Rat.	BS (05/06) Ph.D. (2010)		N/A	
Perez, D., 2008 BS, University of Miami (Hu – Biomedical Engineering)		TG (01/09 – 04/09)												Quantitative MRI for Acupuncture Induced Brain Activity	BS (05/08)		Biomedical Engineer- Research Dept. of Cardiovascular Surgery Miami Children's Hospital	
Suever, J. 2008, BS BME, University of Alabama at Birmingham (John Oshinski – Emory University, Radiology/BME)		TG (05/09 - 12/09)	TG (01/10- 07/10)											Optimizing Contrast-Enhanced Magnetic Resonance Imaging of the Coronary Veins	BS (05/08)		NSF - Training Fellowship	
Julie Johnson, 2009, Biomedical Engineering BS from Texas A&M University		TG 08/09-12/09	TG (01/10 – 12/10)	TG 01/11 – 07/11										Nanoparticle Attachment to Atherosclerotic Plaques under In Vivo Flow Conditions	BS (05/09)		GRA at Georgia Institute of Technology	
Zhan, Mei, 2009, B.S Biomedical Engineering, Texas A&M University		TG 08/09-12/09	TG (01/10 – 12/10)	TG 01/11 – 07/11										Transcriptional Stochasticity in Aging	B.S. in Biomedical Engineering (2009)		GRA at Georgia Institute of Technology	
Calhoun, W. Alexander 2010, BS, NC State University (Potter-BME)			TG 08/10- 12/10	TG 01/11 – 12/11	TG 01/12 – 07/12									Two-Photon Imaging of Neuronal Networks	BS (05/2010)		In Training	
Lam, Adrian 2010, B.S. in Biomedical Engineering at University of California, Davis (Dr. John Oshinski – Biomedical Engineering/Bioengineering			TG 08/10- 12/10	TG 01/11 – 12/11	TG 01/12 – 07/12									Combined Magnetic Resonance Imaging and CFD simulation of flow in patients with apico-aortic	BS - BME (2010)		Graduate Research Assistant, Georgia Institute of Technology	

											conduit		
Jeenah Jung, Entry Spring 2011 (Philip Santangelo – BME/GA Tech)					TG 09/11 – 08/12						Imaging post-transcriptional Regulation of mRNA		MSTP trainee (GA Tech)
Jason Lamanna, 2009, B.S. University of Florida (John Oshinski and Nicholas Boulis, Biomedical Engineering, MD/PhD)					TG 09/11 – 08/12						Overcome the technical and immunological barriers preventing the successful translation of cellular therapies for disorders of the central nervous system to the clinic.	B.S. (2009)	MD/PhD Candidate (Emory University and Georgia Institute of Technology)

Trainee Diversity Report

This report format should NOT be used for data collection from trainees.

Training Grant Title: Interdisciplinary Training in Biomedical Imaging

Total Number of Appointed: 4

Grant Number: 1 T32 EB005969-05

PART A. TOTAL TRAINEE APPOINTMENTS REPORT: Number of Trainees Appointed by Ethnicity and Race				
Ethnic Category	Females	Males	Sex/Gender Unknown or Not Reported	Total
Hispanic or Latino				**
Not Hispanic or Latino	1	3		4
Unknown (individuals not reporting ethnicity)				
Ethnic Category: Total of All Trainees*	1	3		4 *
Racial Categories				
American Indian/Alaska Native				
Asian	1	1		
Native Hawaiian or Other Pacific Islander				
Black or African American				
White		2		
More Than One Race				
Unknown or Not Reported				
Racial Categories: Total of All Trainees*	1	3		4 *
PART B. HISPANIC TRAINEE APPOINTMENTS REPORT: Number of Hispanics or Latinos Appointed				
Racial Categories	Females	Males	Sex/Gender Unknown or Not Reported	Total
American Indian or Alaska Native				
Asian				
Native Hawaiian or Other Pacific Islander				
Black or African American				
White				
More Than One Race				
Unknown or Not Reported				
Racial Categories: Total of Hispanics or Latinos**				**
PART C. TRAINEES WITH DISABILITIES OR FROM DISADVANTAGED BACKGROUNDS				
Number of Trainees with Disabilities:				0
Number of Trainees from Disadvantaged Backgrounds:				0

(*) (**) These totals must agree.