Dissertation Defense

April 14, 2016; 3:00 PM

Proteomic Profile of Extracellular Vesicles Post-Myocardial Infarction

DERRICK EDEM AKPALU

PhD/MSCR Candidate

Under the direction of

Gale Newman, Ph.D.

Associate Professor, Department of Microbiology, Biochemistry & Immunology

In partial fulfillment of the requirements for the degrees

Doctor of Philosophy in Biomedical Sciences

Master of Science in Clinical Research

Clinical Research Center, Multidisciplinary Research Center, Room G14.

MOREHOUSE SCHOOL OF MEDICINE

720 Westview Drive SW, Atlanta, GA 30310

Graduate Education in Biomedical Sciences

Final Examination of

DERRICK EDEM AKPALU

For the Degrees

DOCTOR OF PHILOSOPHY IN BIOMEDICAL SCIENCES

MASTER OF SCIENCE IN CLINICAL RESEARCH

DISSERTATION COMMITTEE

Gale Newman, Ph.D., Research Advisor
Department of Microbiology, Biochemistry & Immunology
Morehouse School of Medicine

David Feldman, M.D., Ph.D.
Division of Cardiology
University of Cincinnati Medical Center

Elizabeth Ofili, M.D.
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Clinical Research Center
Morehouse School of Medicine

PROFESSOR IN CHARGE OF RESEARCH

Gale Newman, Ph.D.
Department of Microbiology, Biochemistry & Immunology
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FIELDS OF STUDY

Major Subject: **Biomedical Sciences**

Analysis of Frequency Data
Biochemistry
Biomedical Genetics
Biomedical Science Presentation I & II
Clinical Trails
Community Engaged Health Disparities in Clinical Research
Critical Thinking and Scientific Communication I & II
Dissertation Research
Ethics of Clinical Research
Fundamentals of Biostatistics
Human Biology
Integrated Biomedical Science
Introduction to Epidemiology
Laboratory Rotation I & II
Medical Informatics in Clinical Research
Mentored Research Project
Principles in Clinical Research
Special Topics in Immunology
Scientific Integrity in Research
Scientific Writing & Communication
Seminar in Biomedical Sciences I-VI

Research Focus: **Myocardial Infarction; Proteomic Profiling of Extracellular Vesicles**

BIOGRAPHICAL SKETCH

Undergraduate Study:
B.Sc., June 2006; University of London, Queen Mary, London, England, U.K.
Major: Biochemistry with Microbiology

Graduate Study:
MRes., Aug. 2009; University College London, London, England, U.K.
Major: Biomedicine

Ph.D. / M.S.C.R Candidate, Morehouse School of Medicine (MSM), Atlanta, GA, 2012-present; *Biomedical Science & Clinical Research*

Professional Memberships

2015-present	The American Heart Association
2015-present	International Atherosclerotic Society
2009-present	Institute of Biomedical Science (IBMS)
2009-present	Institute of Clinical Research (ICR) - Affiliate

Professional Service

2010-present	Amicus Capital Management – (Biotech Portfolio Advisor)
2011-present	Clinical Research Center, MSM – Research Assistant
2013-2014	Biochemistry Lab Teaching Assistant, MSM
2013-2014	Genetics Lab Teaching Assistant, MSM

Recent Fellowships & Awards

2015	Johnson and Johnson Consumer R&D Scientist Mentoring Program Awardee, Skillman, NJ. (Oct. 2015)
2015	Health Connect South, Atlanta, GA, Rapid Fire Session Panelist & Student Presenter
2015	Janssen R&D Scientist Mentoring Program (Drug Discovery and Development Training) Spring House, PA. (Sept. 2015)
2015	Janssen Biotherapeutics, Pharmaceutical Scientists Career Development Workshop, Spring House, PA. (Aug. 2015)
2015	International Center for Professional Development - Scientist Mentoring & Diversity Program (SMDP) Scholarship (2015-2016 Biotech)

Fellowships & Awards cont'd.

2014 NIH-Minority Health and Health Disparities International Research Training (MHIRT) Fellowship

2014 International Center for Professional Development - Scientist Mentoring & Diversity Program (SMDP) Scholarship (2014-2015 MedTech)

Select Presentations

Akpalu D.E., Brice M., Powell M., Singh R., Quarshie A., Ofili E., Feldman D.S., Newman G. Proteomic profiling of tissue factor microparticles in a chronic ischemic cardiomyopathy model. Poster presentation abstract, 2016 Curtis Parker Student Research Symposium, Morehouse School of Medicine, Atlanta, GA.

Akpalu D.E., Powell M., Singh R., Quarshie A., Ofili E., Feldman D.S., Newman G. Proteomic profiling of tissue factor microparticles in a chronic ischemic cardiomyopathy model. Poster presentation abstract, 2015 Janssen Biotherapeutics: Pharmaceutical Scientists Career Development Workshop & Open House, Spring House, PA.

Akpalu D.E., Powell M., Singh R., Quarshie A., Ofili E., Feldman D.S., Newman G. Tissue Factor-Bearing Microparticle Release Post-Myocardial Infarction. Poster presentation abstract, 2015 Health Connect South, Atlanta, GA,

Akpalu D.E., Powell M., Singh R., Quarshie A., Ofili E., Feldman D.S., Newman G. Proteomic profiling of tissue factor microparticles in a chronic ischemic cardiomyopathy model. Poster presentation abstract, 2015 Johnson and Johnson R&D Training and Career Development Session, Skillman, NJ.

Akpalu D.E., Brice M., Powell M., Singh R., Quarshie A., Ofili E., Feldman D.S., Newman G. Tissue Factor-Bearing Microparticle Release Post-Myocardial Infarction. Poster presentation abstract, 2015 Curtis Parker Student Research Symposium, Morehouse School of Medicine, Atlanta, GA.

Akpalu D.E., Brice M., Powell M., Singh R., Quarshie A., Ofili E., Feldman D.S., Newman G. Tissue Factor-Bearing Microparticle Release Post-Myocardial Infarction. Poster presentation abstract, 2014 Curtis Parker Student Research Symposium, Morehouse School of Medicine, Atlanta, GA.

Publications

Akpalu D.E., Newman G., Brice M., Powell M., Singh R., Quarshie A., Ofili E., Fonger J., Chronos, N, Feldman D.S. Proteomic profiling of tissue factor microparticles in a chronic ischemic cardiomyopathy model. *In submission.*

Akpalu D.E., Jackson K., Oliver-Commey J. A., Powell M., Quarshie A., Ofili E., Feldman D.S., Newman G., Proteomic profile of extracellular vesicles following an acute myocardial infarction in Humans.
In preparation.

DISSERTATION ABSTRACT

Akpalu, Derrick Edem, Morehouse School of Medicine, April 2016. Myocardial Infarction; Proteomic Profiling of Extracellular Vesicles. Chair of Committee: Gale Newman.

Following a myocardial infarction (MI), activation of beta adrenergic receptors (β-ARs) causes acute changes in myocardial signaling. Chronic β-AR signaling that may cause cardiotoxicity and pathological remodeling is less well studied in a large animal model (up to six months). We investigated the release and proteomic profile of tissue factor microparticles (TF MPs) prospectively following a MI in a chronic porcine model to establish their utility in tracking cellular level activities, which predict physiologic outcomes. This porcine model was developed to emulate many of the conditions and temporal signaling of humans as the animals were followed for 6 months after their infarct. It was imperative to develop this model since the majority of current chronic models of signaling are largely in smaller animal models with a limited duration and poorly represent the actual conditions seen in chronic HF in human patients. Our animal groups (n=6-8) consisted of control, non-infarcted (negative control); infarcted only (positive control); and infarcted animals treated with cardiac resynchronization therapy (CRT) and a β-blocker (BB) (metoprolol succinate). Additionally, we determined the proteomic content of extracellular vesicles (EVs) obtained from acute MI patients and healthy controls. Human plasma samples were obtained at one time point for 16 healthy controls and at 24hrs; 48hrs; and 72hrs post-infarction for 22 acute MI patients. The number of TFMPs and EVs in circulation were determined by flow cytometry and their protein content determined by mass spectrometry. We found different protein profiles in TFMPs between the control, infarcted only group, and the CRT + BB group with predictive impact on the outward phenotype of pathological remodeling after a MI within and between groups. Our study on human EVs also indicated that the proteins contained in EVs of the healthy controls predominantly inhibit inflammation and cell death, while those from the infarcted patients contained apoptotic and inflammatory mediators. These results indicate that the proteomic profile of TFMPs and EVs may be a useful diagnostic and/or prognostic tool in elucidating β-AR signaling, inflammatory and apoptotic pathways activated following a MI. Furthermore, this novel approach of monitoring cellular level activities by profiling the content of TF MPs and EVs has the potential of addressing one cardinal shortfall of the current crop of cardiac biomarkers, which is the inability to dynamically capture composite molecular changes associated with chronic maladaptive signaling in a spatial and temporal manner.

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