Biographical Sketch
NAME: Tamer M A Mohamed
eRA COMMONS USER NAME: T0MOHA02
POSITION TITLE: Assistant Professor
EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Zagazig University, Egypt	B.S.	05/1999	Pharmacy
Zagazig University, Egypt	M.S.	03/2003	Biochemistry
University of Manchester, United Kingdom	Ph.D.	05/2008	Molecular Cardiology
University of Manchester, United Kingdom	Postdoctoral	11/2013	Signaling in cardiac hypertrophy and failure
Gladstone Institutes, University of California, San Francisco	Postdoctoral	06/2016	Cardiac regeneration and epigenetics

A. Personal Statement
I am confident that my expertise, training, and ambition have prepared me to complete the proposed research project. I have broad expertise in molecular cardiology and drug screening, and have recently completed training in cardiac regeneration and epigenetics.

During my research endeavors, I have studied novel mechanisms and therapies for cardiac hypertrophy and heart failure in animal models. During my doctoral and first postdoctoral training, I identified the role of the plasma membrane calcium ATPase isoform 4 (PMCA4) in cardiac physiology and pathophysiology. As a pharmacist, I have a special interest in translating my findings into human drug therapies for heart disease. Thus, I started screening drugs to identify the first specific inhibitor for PMCA4, which could be used as a novel treatment for cardiac hypertrophy and heart failure. Recently, in collaboration with the Fraunhofer Institute in Germany, the Medical Research council in the UK, and the drug company Astra Zeneca, we created a program to identify new drugs that treat heart failure by targeting PMCA4.

To expand my expertise in cardiac regeneration, I joined Prof. Deepak Srivastava's laboratory at the Gladstone Institutes in November 2013. In Srivastava lab I acquired training on cutting-edge technology for direct cardiac reprogramming, and profiling single-cell genomes and epigenomes during the reprogramming process. The skills that I have learned while working with Prof. Srivastava will be invaluable to running my independent laboratory. I worked on two parallel approaches to induce endogenous heart repair: direct cardiac reprogramming and inducing cardiomyocyte proliferation. Both approaches were highly successful. The direct reprogramming project was highly recognized by our scientific community, as it was awarded a Scientist Development Grant award from the AHA, manuscript was published in Circulation and this work was chosen as finalist at the Louis N. and Arnold M. Katz Basic Science Research Prize for Young Investigators from The AHA in 2016. In addition, the cardiomyocyte proliferation project was accepted for publication in Cell and awarded the March 22, 2018 issue cover for the journal. In October 2016, Dr. Srivastava founded a new start up (Tenaya Therapeutics) with $50 million investment from the column group to develop new therapies for heart failure based on my findings. Therefore, I was the first scientist recruited to the company to lead the efforts of direct cardiac reprogramming where I enjoyed the unique industry experience in building a start up from scratch. Due to the quick success in Tenaya, the research and development section ended very soon and now the major focus on scaling up viral manufacturing and filing IND which is away from my interest. Therefore, I have decided to go back to academia to initiate new discovery programs for heart failure therapy mainly focusing on understanding the regulation of cardiomyocyte proliferation. Furthermore, my laboratory established a novel system for long term culture of human and pig heart slices and efficiently demonstrating the efficacy of direct cardiac reprogramming in such pre-clinical models (Ou et al., Circulation Research, *2019*). During the past year we established all the necessary tools to enable conducting the proposed research.

B. Positions and Honors

Positions and Employment

2001–2003 Demonstrator, Department of Biochemistry, Faculty of Pharmacy, Zagazig University, Egypt
2003–2005 Assistant Lecturer, Department of Biochemistry, Faculty of Pharmacy, Zagazig University, Egypt
2006–2008 Teaching Assistant, Faculty of Life Sciences, University of Manchester, United Kingdom
2013–2016 Post Doctoral Research Scholar, J David Gladstone Institute for Cardiovascular Disease, University of California – San Francisco, CA
2008– Visiting Lecturer, Department of Biochemistry, Faculty of Pharmacy, Zagazig University, Egypt
2015– Honorary Lecturer, Cardiovascular Research Institute, Faculty of Medical and Human Sciences, University of Manchester, United Kingdom
2016–2016 Staff Scientist, J David Gladstone Institute for Cardiovascular Disease, University of California – San Francisco, CA
2016–2018 Scientist II, Tenaya Therapeutics – South San Francisco, CA
2018– Assistant Professor, University of Louisville, Louisville, KY

Other Experience

04/2012–07/2012 International Research Fellow, University of Gottingen, Germany.
Advisors: In Prof. Gerd Hasenfuss and Dr. Kaomei Guan
Description: Received specialized training on human stem cells and induced pluripotent stem cells and their differentiation into cardiomyocytes

08/2011 Visitor Research Fellow, European Screening Port (Currently, Fraunhofer Institute IME-SP), Hamburg, Germany
Description: Received specialized training on high-throughput drug screening

06/2007–07/2007 Visitor Research Fellow, Glasgow, United Kingdom
Advisor: Prof. Manuela Zaccolo
Description: Received specialized training on compartmentalized imaging of cAMP, cGMP, and calcium

Professional Memberships and Services

2006– Member, American Heart Association
2006– Member, British Society of Cardiology
2006– Member, British Society of Cardiovascular Research
2007– Member, European Society of Cardiology
2007– Member, European Society of Heart Failure
2015– Guest Editor, Biomedical Research International
2012– Reviewer, British Journal of Pharmacology
2012– Grant Reviewer, Medical Research Council, United Kingdom
2014– Reviewer, Pharmacology Research & Perspectives
2012– Reviewer, Journal of Pharmaceutical Biology
2016- Senior Editor, Scientific Reports
2019- Guest Editor, Toxicology and Applied Pharmacology
2019- AHA TPA grant review committee member

Honors

2004–2008 Post-graduate Research Scholarship from the Egyptian government to complete PhD in the United Kingdom
2007 BCVS International Travel Award for best abstract, American Heart Association (AHA) Scientific Sessions, 2007, Orlando, Florida
2008 Basic Scientist Travel Award for best abstract, European Society of Cardiology (ESC) main congress, ESC Council on Basic Cardiovascular Science, 2008.
2009 Basic Scientist Travel Award for best abstract, ESC main congress, ESC Council on Basic Cardiovascular Science, 2009.
2010 Young Investigator Award, ESC main congress, 2010
2010–2013 Postdoctoral Fellowship, Medical Research Council, UK
2012 International Scholar Training Fellowship, NHS Biomedical Research Centre, United Kingdom
2013–2015 The University of Manchester Travel Fellowship, The University of Manchester
2014 Invited Speaker, Cardiology 2014, San Antonio, Texas

2017 Louis N. and Arnold M. Katz Basic Science Research Prize for Young Investigators from the American Heart Association
2018 Invited Speaker, 6th Annual Midwest Conference on Cell Therapy & Regenerative Medicine, Kansas City, Kansas
2019 Invited Speaker, Cardiovascular Grand Rounds, Department of Cardiology, University of Kentucky

C. Contribution to Science

Calcium Signaling in the Heart Modulates Cardiac Function: As a PhD student, I continued investigating novel and potentially 'druggable' proteins that regulate cardiac hypertrophy and heart failure. In 2005, one of the proteins with unknown function in the heart was the plasma membrane calcium ATPase pump isoform 4 (PMCA4), which transports calcium out of the heart cell, but does not contribute to contraction/relaxation. I explored the role of PMCA4 with cellular models and transgenic and knock-out mice, which revealed that PMCA4 indirectly regulates cardiac contractility by modulating neuronal nitric oxide synthase (nNOS). This work produced three publications in highly recognized journals and several oral and poster presentations at international cardiovascular conferences. Furthermore, my PhD work formed the scientific basis of a research grant awarded by the Medical Research Council (MRC; G0802004, 01/2010–12/2012, £580,000).
a. Williams, J.C., Armesilla, A.L., Mohamed, T., Hagarty, C.L., McIntyre, F.H., Schomburg, S., Zaki, A.O., Oceandy, D., Cartwright, E.J., Buch, M.H., Emerson, M., & Neyses, L. (2006). The sarcolemmal calcium pump, alpha-1 syntrophin, and neuronal nitric-oxide synthase are parts of a macromolecular protein complex.
Journal of Biological Chemistry, 281(33), 23341–23348.
b. Mohamed, T., Oceandy, D., Prehar, S., Alatwi, N., Hegab, Z., Baudoin, F., Pickard, A., Zaki, A., Nadif, R., Cartwright, E., & Neyses, L (2009). Specific role of neuronal nitric-oxide synthase when tethered to the plasma membrane calcium pump in regulating the beta-adrenergic signal in the myocardium.
Journal of Biological Chemistry, 284(18), 12091–12098.
c. Oceandy, D., Pickard, A., Prehar, S., Zi, M., Mohamed, T., Stanley, P., Baudoin-Stanley, F., Nadif, R., Tommasi, S., Pfeifer, G., Armesilla, A., Cartwright, E., & Neyses, L. (2009). Tumor suppressor Ras-association domain family 1 isoform A is a novel regulator of cardiac hypertrophy.
Circulation, 120(7), 607–616.

Novel Calcium Signaling Pathways Modulate Cardiac Hypertrophy: In my first postdoctoral position, I expanded my interest from pure molecular biology to live imaging of subcellular compartments—one of the most fascinating developments in modern heart research. There, I trained for several months with Prof. M. Zaccolo at the University of Glasgow, and I started collaborating with Prof. Michael I. Kotlikoff (Cornell University, USA). Through these relationships, I learned new tools to assess changes in local calcium, cAMP, and cGMP to explore the role of PMCA4 in modulating compartmentalized cardiac signalling during cardiac hypertrophy and failure. For example, I gained valuable skills in live-cell bio-imaging techniques involving fluorescence resonance emission transfer (FRET). Then, I independently transferred this complex technology to Manchester (Bio-imaging Facility, Smith Building), where I first described a locally confined cAMP, cGMP, and calcium space near PMCA4 in myocardial caveolae. This work has been highly recognized, which led to my receiving one of the three Young Investigator Awards (Basic Science) at the European Society of Cardiology Congress in 2010, the largest cardiology conference in the world. I was also interviewed by Circulation, the leading international cardiovascular journal (European Perspectives in Cardiology. Circulation. 2010; 122(10):f55-60). My work has contributed to several publications, some are listed below:
a. Mohamed, T., Baudoin-Stanley, F., Abou-Leisa, R., Cartwright, E., Neyses, L. & Oceandy, D. (2010). Measurement of plasma membrane calcium-calmodulin-dependent ATPase (PMCA) activity.
Methods in Molecular Biology, 637, 333–342.
b. Mohamed, T., Oceandy, D., Zi, M., Prehar, S., Alatwi, N., Wang, Y., Shaheen, M., Abou-Leisa, R., Schelcher, C., Hegab, Z., Baudoin, F., Emerson, M., Mamas, M., Di Benedetto, G., Zaccolo, M., Lei, M., Cartwright, E. & Neyses, L. (2011). Plasma membrane calcium pump (PMCA4)/neuronal nitric oxide synthase complex regulates cardiac contractility through modulation of a compartmentalized cyclic nucleotide microdomain.
Journal of Biological Chemistry, 286(48), 41520–41529.

c. Mohamed, T., Abou-Leisa, R., Baudoin, F., Stafford, N., Neyses, L., Cartwright, E. & Oceandy, D. (2013). Development and characterization of a novel fluorescent indicator protein PMCA4-GCaMP2 in cardiomyocytes.
Journal of Molecular and Cellular Biology, 63:57–68.
d. Mohamed, T., Zakeri, S., Baudoin, F., Wolf, M., Oceandy, D., Cartwright, E., Gul, S. & Neyses, L. (2013). Optimisation and validation of a high throughput screening compatible assay to identify inhibitors of the plasma membrane calcium ATPase pump–a novel therapeutic target for contraception and malaria.
Journal of Pharmacy and Pharmaceutical Sciences, 16(2), 217–230.
e. Mohamed, T., Zi, M., Prehar, S., Maqsood, A., Abou-Leisa, R., Nguyen, L., Pfeifer, G., Cartwright, E., Neyses, L. & Oceandy, D. (2014). The tumour suppressor Ras-association domain family protein 1A (RASSF1A) regulates TNF-α signalling in cardiomyocytes.
Cardiovascular Research, 103(1), 47–59.
f. Mohamed, T., Abou-Leisa, R., Stafford, N., Maqsood, A., Zi, M., Prehar, S., Baudoin-Stanley, F., Wang, X., Cartwright, E., Neyses, L., Oceandy, D. (2016). The Plasma Membrane Calcium ATPase 4 Signaling in Cardiac Fibroblasts Mediates Cardiomyocyte Hypertrophy.
Nature Communications, *7:11074.*

Endogenous Heart Repair Using Cardiac Reprogramming and Cardiomyocyte Proliferation
In August 2013, I was awarded the University of Manchester's travel Fellowship to further train with Prof. Deepak Srivastava at the Gladstone Institutes on cutting-edge technologies in iPS-CM and direct cardiac reprogramming, as well as single-cell genome and epigenome profiling during the reprogramming process. At the Gladstone institute of cardiovascular disease I focused my research on finding novel treatment of heart failure to replace the loss of cardiomyocytes during myocardial infarction using two approaches:
1- The first strategy depends on optimization and enhancement of direct cardiac reprogramming approaches where we can convert the existing fibroblasts in the heart into new heart cells (cardiomyocytes) to replace the loss in heart cells after heart attack with the ultimate aim for heart failure treatment. This work was highly recognized by our scientific community, as it was awarded a Scientist Development Grant award from the AHA, manuscript was published in Circulation and this work was chosen as finalist at the Louis N. and Arnold M. Katz Basic Science Research Prize for Young Investigators from The AHA in 2016.
2- The second approach is based on stimulating the existing heart cells to proliferate (divide) to replace the loss of the heart cells following heart attack using a gene delivery approach. This approach is based on my discovery that overexpression of four cell cycle genes in cardiomyocytes is sufficient to induce cell division of cardiomyocytes following a screen of 30 cell cycle genes. Based on these results, it is contemplated that this cocktail of genes could be implemented for regenerative therapies by inducing endogenous cardiac cells to proliferate and thus repair or replace damaged or diseased cardiac tissue. Given the scope of congestive heart failure and lack of any pharmaceutical treatment approaches, there is a long-felt need for a curative process. This approach has just been patented and the patent application was entitled "METHOD FOR INDUCING CELL DIVISION OF CARDIOMYOCYTES ". Currently, the manuscript was published in Cell and awarded the March 22, 2018 issue cover of the journal.
Since October 2016 Dr. Srivastava has founded a new start up with $50 million investment from the column group to develop new therapies for heart failure based on cardiac regeneration approaches. I was the first scientist recruited to the company to lead the efforts of direct cardiac reprogramming where I enjoyed the unique industry experience in building a start up from scratch. In Tenaya I was able to establish novel system for long term culture of human heart slices and efficiently demonstrating direct cardiac reprogramming in such pre-clinical models. In addition, I was able to reduce the number of essential reprogramming factors in human cardiac fibroblasts to 3 essential factors where they are now under preclinical testing for in vivo efficiency in large animals (pigs). Due to the quick success in Tenaya, the research and development section ended very soon, and the major focus is shifted towards scaling up viral manufacturing and filing IND which is away from my interest. Therefore, I decided to go back to academia mainly focusing on understanding the reprogramming process and cell cycle regulation of cardiomyocyte proliferation.
a. Mohamed T., Ang Y., Radzinsky E., Zhou P., Huang Y., Elfenbein A., Foley A., Magnitsky S., Srivastava D. Regulation of Cell Cycle to Stimulate Adult Cardiomyocyte Proliferation and Cardiac Regeneration.
Cell, 2018 Mar 22;173 (1):104–116
b. Mohamed T., Stone N., Radzinsky E., Yu P., Huang Y., Wang H., Ding S., Srivastava D. Chemical Enhancement of Direct Cardiac Reprogramming In Vitro and In Vivo.
Circulation. 2017 Mar 7;135(10):978-995.

c. Ang Y., Rivas R., Ribeiro A., Srivas R., Rivera R., Stone N., Pratt K., Mohamed T., Fu J., Spencer I., Tippens N., Li M., Narasimha A., Radzinsky E., Moon-Grady A., Yu H., Pruitt B., Snyder M., Srivastava D. Disease Model of GATA4 Mutation Reveals Transcription Factor Cooperativity in Human Cardiogenesis.
Cell. 2016 Dec 15;167(7):1734-1749.e22
d. Stone N., Gifford C., Thomas R., Pratt K., Samse-Knapp K., Mohamed T., Radzinsky E., Schricker A., Ye L., Yu P., van Bemmel J., Ivey K., Pollard K., Srivastava D. Context-Specific Transcription Factor Functions Regulate Epigenomic and Transcriptional Dynamics during Cardiac Reprogramming.
Cell Stem Cell. 2019 Jul 3;25(1):87-102.

Developing novel tool for testing gene therapy in human heart tissue: Preclinical testing of cardiotoxicity and efficacy of novel heart failure therapies currently faces a major limitation; the lack of an *in situ* culture system that emulates the complexity of human heart tissue and maintains viability and functionality for prolonged time. Recently, we developed a novel medium throughput biomimetic culture system that maintains full viability and functionality of human and pig heart slices (300 µm thickness) for 6 days in culture through optimization of the medium and culture conditions with continuous electrical stimulation at 1.2 Hz and oxygenation of the medium.
a. Ou Q., Jacobson Z., Abouleisa R., Tang X., Hindi S., Kumar A., Ivey K., Giridharan G., Al-Baz A., Brittian K., Rood B., Lin Y., Watson S., Perbellini F., McKinsey T., Hill B., Jones S., Terracciano C., Bolli R., Mohamed T. A Physiological Biomimetic Culture System for Pig and Human Heart Slices
Circulation Research 2019 Aug 30;125(6):628-642.

For full list of publication: https://www.ncbi.nlm.nih.gov/pubmed/?term=Tamer+M+A+Mohamed

D. Research Support
Current
NIH P30-GM127607 Research Pilot Project Program Mohamed (PI) 10/01/18-06/30/20
Mechanistic Study to Decipher the Correlation Between Metabolism and Cardiomyocyte Proliferation
The goal of this study to investigate the correlation between cardiomyocyte ability to proliferate with the metabolic switch between fatty acid oxidation and glycolysis.

University of Louisville SOM Collaborative Research Grant Mohamed (PI) 10/01/19-09/30/20
Development of Efficient Biomimetic Human Heart Slice Culture Systems
The goal of this grant is to develop a reliable extended culture system for human heart slices for testing cardiotoxicity and efficacy of novel heart failure therapies.

Completed
16SDG29950012, American Heart Association (AHA) Mohamed (PI) 07/01/16–06/30/19
Targeting WNT and TGF-β signaling to enhance direct cardiac reprogramming
The goal of this study is to identify the mechanisms by which the WNT and TGF-β signaling regulate cardiac reprogramming process.
(Returned to the AHA on March 2017 due to my job transfer to Tenaya Therapeutics)

R116066, NC3Rs, UK Mohamed (PI) 10/01/13–04/30/15
Novel and reliable method to screen for drug cardiac toxicity using human pluripotent stem cell derived cardiomyocytes (hPS-CM)
The goal of this study was to test the efficiency of Using human pluripotent stem cell derived cardiomyocytes (hiPSC-CM) to test drug cardiac toxicity in collaboration with the Fraunhofer institute in Germany.

PG/13/12/30017, British Heart Foundation (BHF) Oceandy (PI) 05/01/13–06/30/15
Signal modulation in cardiac fibroblasts by the plasma membrane calcium ATPase 4 (PMCA4) controls cardiac hypertrophy.
The goal of this project is to investigate the mechanism by which PMCA4 modulates cardiac hypertrophy.
Role: Co-Investigator