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<tr>
<td>SHAH, KEVIN - #2668 - VPCAT Application Kevin Shah Cardiology</td>
<td>1</td>
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<tr>
<td>VPCAT 2021 Senior Mentor Selection Form</td>
<td>5</td>
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<tr>
<td>VPCAT 2021 Combined PDF Application</td>
<td>6</td>
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</table>
# Application Summary

## Competition Details

<table>
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<tr>
<th>Competition Title</th>
<th>2021 Vice President's Clinical and Translational (VPCAT) Research Scholars Program Application</th>
</tr>
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## Application Information

<table>
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<tr>
<th>Submitted By</th>
<th>KEVIN SHAH</th>
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<tr>
<td>Application ID</td>
<td>2668</td>
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## Personal Details

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<tbody>
<tr>
<td>Applicant First Name</td>
<td>KEVIN</td>
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<tr>
<td>Applicant Middle Initial</td>
<td>S</td>
</tr>
<tr>
<td>Applicant Last Name</td>
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<tr>
<td>Applicant Alias (i.e., Name Applicant Prefers to Go By)</td>
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<tr>
<td>Applicant Degree(s)</td>
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</tr>
<tr>
<td>Academic Rank (i.e., Primary Appointment Title)</td>
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<tr>
<td>Division</td>
<td>Cardiovascular Medicine</td>
</tr>
<tr>
<td>Work Address</td>
<td>30 North 1900 East, Rm 4A100, Salt Lake City, UT 84132</td>
</tr>
<tr>
<td>Email Address</td>
<td><a href="mailto:kevin.shah@hsc.utah.edu">kevin.shah@hsc.utah.edu</a></td>
</tr>
<tr>
<td>Work Phone Number</td>
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<tr>
<td>ORCID Identifier # (if applicant does not have an ORCID, please register for a unique ID via <a href="http://www.orcid.org">www.orcid.org</a>):</td>
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<tr>
<td>Twitter Handle (if applicant does not have one, list &quot;none&quot;):</td>
<td>@KevinShahMD</td>
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<tr>
<td>Gender Identification:</td>
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<td>Separating each with a semicolon, list up to 5 key SCIENTIFIC TERMS aligned to your research interests that we could use to search for funding opportunities via online systems (i.e., Grants.gov, NIH, Pivot, etc.):</td>
<td>biomarkers; cardiovascular disease; heart failure; covid-19</td>
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<td>Separating each with a semicolon, list up to 5 FUNDING AGENCIES you are interested in submitting an application for funding considerations. NOTE: if you are interested in the National Institute of Health (NIH), provide the name of the specific institute.:</td>
<td>NIH: National Heart, Lung, and Blood Institute</td>
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<td>Are you a Scholar in one of the following programs?:</td>
<td>None of the Above</td>
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<tr>
<td>Administrative Assistant First Name:</td>
<td>Sandra</td>
</tr>
<tr>
<td>Administrative Assistant Last Name:</td>
<td>Martinez</td>
</tr>
<tr>
<td>Administrative Assistant Email:</td>
<td><a href="mailto:sandra.martinez@hsc.utah.edu">sandra.martinez@hsc.utah.edu</a></td>
</tr>
<tr>
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</table>
Pre-Award Support Staff  Janet
First Name (This person should be the individual in your division/department that supports you with the submission of grants. If unknown, state ‘Unknown’):

Pre-Award Support Staff  Janet
Last Name:  Hood
Pre-Award Support Staff  Janet
First Name (This person should be the individual in your division/department that supports you with accounting/payroll. If unknown, state ‘Unknown’):

Post-Award Support Staff  Janet
Last Name:  Hood
Post-Award Support Staff  Janet
First Name (This person should be the individual in your division/department that supports you with accounting/payroll. If unknown, state ‘Unknown’):

Post-Award Support Staff  Janet
Last Name:  Hood
Post-Award Support Staff  Janet
Email:  janet.hood@hsc.utah.edu

Application Details

Proposal Title
VPCAT Application Kevin Shah Cardiology

Scientific Mentor Unid (U of U ID number/u0000000. If none, list "Not Applicable")
u0330352

Scientific Mentor First Name
Stavros

Scientific Mentor Middle Initial
G

Scientific Mentor Last Name
Drakos

Scientific Mentor Alias (i.e., Name Mentor Prefers to Go By)

Scientific Mentor Degree(s)
MD, PhD

Scientific Mentor Academic Rank (i.e., Primary Appointment Title)
Professor

If selected "Other Title," please designate Mentor’s Primary Appointment Title

Scientific Mentor Secondary Appointment Title (i.e., clinic director, chair, chief, etc.)
Medical Director of Cardiac Mechanical Support/Aritificial Heart Program
Scientific Mentor College or School
University of Utah

Scientific Mentor Department
Internal Medicine

Scientific Mentor Division
Cardiovascular Medicine

Scientific Mentor Email Address
Stavros.Drakos@hsc.utah.edu

Scientific Mentor Work Phone Number

Scientific Mentor eRA Commons UserID

Scientific Mentor ORCID Identifier # (if mentor does not have an ORCID, please register for a unique ID via www.orcid.org)
0000-0002-1223-327X

Comments to Competition Coordinators

Acknowledgment

Applicant Acknowledgement Statement
[Acknowledged] As an applicant to the Vice President's Clinical and Translational (VPCAT) Research Scholar Program, I acknowledge that everything I have written and included within my application is a true and accurate representation of the work that I have done and aim to do if chosen to be a part of the program. I acknowledge that my application will be reviewed by VPCAT senior mentors and members of the VPCAT Alumni Advisory Committee. I understand that upon submission, I will not be allowed to make any further changes to my application.
Michael A. Rubin, MD, PhD, MS  
Director, VPCAT Program  
University of Utah Health  
SVPHS Education Office  
EHSEB 5515

Dear Dr Rubin and VPCAT Committee

I am writing to express my interest and submit my formal application for the upcoming Vice President’s Clinical and Translational (VPCAT) Research Scholar’s Program. I am an Assistant Professor of Medicine within the Division of Cardiovascular Medicine, practicing as a Heart Failure & Transplant Cardiologist. I joined faculty as my first post-training position at the University of Utah in September of 2019. I specifically chose to join the University of Utah because of the opportunities this institution provides to develop as a junior physician-investigator. I have a track record of research productivity and more recently, obtaining grant funding. Specifically, I was a recipient of a Young Investigator Data Seed Grant from the American Heart Association. Furthermore, I was selected for a Seed Grant from the University of Utah Immunology, Inflammation, & Infectious (3i) Disease Initiative COVID-19 during my first year here as faculty. I believe the VPCAT program will provide me the structure and direction to competitively apply for an NIH K23 Mentored Patient-Oriented Research Career Award.

My prior training prior to joining the University of Utah consisted of clinical training in Internal Medicine, Cardiovascular Disease, and Heart Failure & Transplant Cardiology. During this time, I developed my interest in clinical research focusing primarily on investigations relating heart failure outcomes, heart transplantation, and cardiovascular biomarkers. I received focused training to become facile in biostatistics analysis utilizing both IBM SBSS and Systat SigmaPlot. These interests and efforts have led me to successfully publish multiple peer-reviewed manuscripts, abstracts, and deliver local and international research presentations. The next professional step I am hopeful to work towards is the development of a competitive application for an extramural funding building upon my track record and developing my professional and research network at the University of Utah.

I am a board-certified Cardiologist and board-eligible in Heart Failure & Transplant Cardiology. With respect to my current allotment of time and efforts, this is listed in the following table. My division and my department leadership are committed to provide sufficient time in order to participate with the VPCAT program over a 2-year course. I anticipate further time commitment allotted towards research/investigation if I were successful in obtaining NIH funding during this time period.
Since joining faculty at the University of Utah last year, much of the scientific world has shifted their efforts towards the COVID-19 pandemic. Similarly, I was fortunate to have been selected for a seed grant from the University of Utah 3i team on the topic “The Role of Inflammation and Myocardial Injury Leading to Cardiac Deterioration in Patients with COVID-19.” We will shortly begin enrolling patients in our study at the University of Utah with COVID-19 to help better understand the predictors of adverse cardiovascular events, a critical issue in identifying patients at highest risk for events who are infected with the novel corona virus. This project will allow me to leverage my prior skillset with heart failure, cardiovascular outcomes, and biomarkers, in order to improve our understanding regarding how a virus can precipitate cardiovascular disease. I am fortunate to work with a mentorship team on this project which includes Dr Stavros Drakos (Director of Research for the Division of Cardiology), Dr James Fang (Chief of Cardiovascular Service Line), and Dr Robin Shaw (Director of the Nora Eccles Harrison Cardiovascular Research & Training Institute (CVRTI). Additional co-investigators include Dr Rashmee Shah (a graduate of the VPCAT program) and Dr Ezster Lazar-Molnar, Director of the H&I Lab at ARUP/Department of Pathology. They have been instrumental in my initial stages as a junior faculty here as well as the development of my proposal with regards to COVID-19 and the cardiovascular system.

My background across multiple training universities prior to my joining the University of Utah has given me a broad perspective on how to successfully begin my career as an independent clinical investigator. My track record of scientific publications and research dissemination are evidence of my commitment to not only a career in academic medicine, but a career as a clinical investigator. The VPCAT program will provide me the network, tools, and environment to launch this aspect of my professional career. Thank you for your consideration of my application.

Sincerely,

Kevin S Shah, MD, FACC
Assistant Professor of Medicine
Heart Failure & Transplant Cardiology
University of Utah Health Sciences Center
Kevin.Shah@hsc.utah.edu
Curriculum Vitae

PERSONAL DATA
Name: Kevin S. Shah, M.D.

EDUCATION

<table>
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<tr>
<th>Years</th>
<th>Degree</th>
<th>Institution (Area of Study)</th>
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<tbody>
<tr>
<td>2018 - 2019</td>
<td>Fellow</td>
<td>Cedars-Sinai Medical Center (Advanced Heart Failure, Transplant Cardiology) Los Angeles, CA</td>
</tr>
<tr>
<td>2015 - 2018</td>
<td>Fellow</td>
<td>University of California, Los Angeles School of Medicine (Cardiovascular Disease) Los Angeles, CA</td>
</tr>
<tr>
<td>2012 - 2015</td>
<td>Intern/Resident</td>
<td>University of California, San Diego School of Medicine (Internal Medicine) San Diego, CA</td>
</tr>
<tr>
<td>2008 - 2012</td>
<td>M.D.</td>
<td>University of California, Irvine School of Medicine (Medicine) Irvine, CA</td>
</tr>
<tr>
<td>2003 - 2007</td>
<td>B.S.</td>
<td>University of California, San Diego (Human Biology) San Diego, CA</td>
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BOARD CERTIFICATIONS
10/10/2018 - Present American Board of Internal Medicine (Sub: Cardiovascular Disease), Certified
08/12/2015 - Present American Board of Internal Medicine, Certified
02/15/2019 - Present National Board of Echocardiography (Adult Comprehensive Echocardiography), Diplomate

CURRENT LICENSES/CERTIFICATIONS
2017 - Present American College of Cardiology Foundation/American Heart Association Level II Training in Cardiovascular Computed Tomography: Certificate/License
2019 - 2022 State License (UT) - Physician (MD)
2013 - 2021 State License (CA) - Physician (MD)

UNIVERSITY OF UTAH ACADEMIC HISTORY
Internal Medicine (Cardiovascular Medicine), 09/01/2019 - Present
09/01/2019 Assistant Professor (Clinical)

PROFESSIONAL EXPERIENCE
Full-Time Positions
2019 - Present Assistant Professor, University of Utah, Salt Lake City, UT

Editorial Experience

Shah, Page 1
2020 - 2023  ACC.org Heart Failure and Cardiomyopathies Clinical Topic Collection Associate Editorial Team Lead
2018 - 2019  FIT Section Editor for American College of Cardiology: Heart Failure Editorial Fellow
2018  Volunteer Editor for Journal of American College of Cardiology (JACC)

Reviewer Experience
JACC: Case Reports Guest Assistant Editor Reviewer
Assistant Reviewer for Circulation: Cardiovascular Quality and Outcomes

SCHOLASTIC HONORS
2018  William W. Parmley Young Author Achievement Award, Journal of the American College of Cardiology
2016  Young Investigator Research Seed Grant: Project under Dr. Gregg Fonarow, American Heart Association
2016  Fellow’s Teaching Award-Nominee: Chosen by the Housestaff, University of California, Los Angeles, Los Angeles, CA
2015  House Officer of the Year: Chosen from a pool of all residents (500+), University of California San Diego, San Diego, CA
2014  Kaiser Excellence in Teaching Award (House Staff): Chosen from a pool of all residents (500+)
2011  Gold Humanism Honor Society member: based on peer nomination
2010  Medical Student Scholarship Recipient, Indian Medical Association of Southern California
2008  Medical Student Scholarship Recipient, American Association of Physicians of Indian Origin

ADMINISTRATIVE EXPERIENCE
Professional Organization & Scientific Activities
2020 - Present  Editorial Review Board, American College of Cardiology, ACC.org Heart Failure and Cardiomyopathies Clinical Topic Collection Editorial Team
2018  Trainee Member, American Society of Transplantation, Thoracic and Critical Care Community of Practice Executive Committee
2018  Committee Member, American College of Cardiology/American Heart Association, Task Force on Clinical Data Standards
2016  Member, American Heart Association, Writing Group: Atherosclerotic Heart Disease in South Asians in the U.S.

Symposium/Meeting Chair/Coordinator
2020 - Present  Co-Chair of AHA/ACC Task Force on Race & Ethnicity in Clinical Trials
2020  New Cardiovascular Horizons Salt Lake City Meeting Heart Failure Track Director

PROFESSIONAL COMMUNITY ACTIVITIES
2020 - Present  Member, United Network for Organ Sharing, Heart Review Board. Local board member of UNOS Heart Transplant Review Board for Region 5
2018 Interviewee, Player FM, Circulation Fellow in Training Podcast Interview on REDUCE-LAP 1 HF trial
2018 Interviewee, American College of Cardiology, Two William W. Parmley Young Author Achievement Awardees Selected Kevin S. Shah and Jason M. Tarkin to be honored by American College of Cardiology
2018 Interviewee, TCTMD, Keeping Up With Cardiology: Old-School Learning Versus the Twittersphere
2017 Interviewee, MedicalResearch.com, Regardless of Ejection Fraction, Hospitalization for Heart Failure Linked to Increased Risk of Death
2016 Interviewee, CardioBrief, Time for Cardiologists to Start Prescribing Diabetes Drugs

SERVICE AT PREVIOUS INSTITUTIONS
2017 Interviewee, University of California, Los Angeles, Heart’s pumping function is not an indicator of heart failure survival rates. University of California, Los Angeles Research Alert

CURRENT MEMBERSHIPS IN PROFESSIONAL SOCIETIES
American College of Cardiology
American Heart Association
American Society of Transplantation
Heart Failure Society of America

FUNDING
Active Grants
09/01/20 - Present The Role of Inflammation and Myocardial Injury Leading To Cardiac Deterioration in Patients with COVID-19 Direct Costs: $25,000 Total Costs: $25,000 University of Utah Immunology, Inflammation, and Infectious Diseases Initiative Role:

Past Grants
01/01/16 - 12/31/16 Young Investigator Research Seed Grant Five Year Outcomes in Patients with Heart Failure with Preserved, Borderline, and Reduced Ejection in The Medicare Population American Heart Association Role: Lead Investigator

Clinical Studies
2020 - Present Local Principal Investigator of RELIEVE-HF TRIAL: REducing Lung congestIon Symptoms Using the v-wavE Shunt in adVancEd Heart Failure

TEACHING RESPONSIBILITIES/ASSIGNMENTS
Course Lectures
2018 Instructor, Ultra-Fest Echocardiography, University of California, Los Angeles, One-Day Event

Shah, Page 3
2017 Instructor, Project Based Learning, University of California, Los Angeles, 10 weeks

**Didactic Lectures**

2020 Cardiovascular Manifestations of COVID-19

**Internal Teaching Experience**

2018 Endomyocardial Biopsy and Rare Complications, Cardiology Cath Conference Lecture, University of California, Los Angeles

2018 Left Ventricular Thrombus, Cardiology Conference Lecture, University of California, Los Angeles

2017 Cardiovascular Disease and Periodontal Disease, University of California, Los Angeles, Medical and Dental Students

2017 An Atypical Case of a Common Cardiomyopathy, Cardiology Fellows Conference Lecture, University of California, Los Angeles

2016 Cardiology Board Review, Internal Medicine Conference, University of California, Los Angeles

2016 Coronary Embolism, Cardiology Cath Conference Lecture, University of California, Los Angeles

2016 MitraClip in End-Stage Heart Failure, Cardiology Cath Conference Lecture, University of California, Los Angeles

**CE Courses Taught**

2017 Not the Model Minority (of Health): Cardiovascular Disease and South Asians, Association of Los Angeles Physicians of Indian Origin (ALAPIO)

**PEER-REVIEWED JOURNAL ARTICLES**


**NON PEER-REVIEWED JOURNAL ARTICLES**


**REVIEW ARTICLES**


**BOOK CHAPTERS**


**ADDITIONAL PUBLICATIONS**

**Case Reports**


**Editorials**


**Multimedia**


PENDING PUBLICATIONS

Book Chapters


RECENTLY PUBLISHED ABSTRACTS (LAST 3 YEARS)


POSTER PRESENTATIONS

2019 Shah KS, Patel J, Levine R, Dimbil S, Passano E, Kobashigawa J. Increasing Use of Pain Medications as a Risk Factor for Outcomes After Heart Transplantation - OPIATES UPDATE. Poster session presented at Cutting Edge of Transplantation Meeting (CEoT), Phoenix, AZ.


2018  Shah KS, Heikali D, Bokhoor PI. Dizziness, Clots, And Heart Failure: Reasons To Stay Out Of The Lymelight. Poster session presented at American Heart Association Scientific Sessions, Chicago, IL.

2018  Shah KS, Ziaeian B, Mody F, Nsair A, Fonarow GC. Perceived Barriers to Sacubitril/Valsartan Use in Patients with Heart Failure. Poster session presented at Heart Failure Society of Annual Scientific Meeting, Nashville, TN.


2017  Shah KS, Vucicevic D, Honoris L, Baas A. A Rare Case of an Idiopathic Cardiomyopathy Complicated by Acute Pulmonary Emboli in the Setting of Antiphospholipid Syndrome with Successful Bridge to Heart Transplantation via BIVAD Implantation. Poster session presented at International Society for Heart & Lung Transplantation (ISHLT), San Diego, CA.


2015  Iwaz J, Shah K, Peacock WF, Filippatos GS, Maisel AS. Heart Failure Patients with Elevated Pro-Endothelin Have Improved Mortality on Statin Therapy. Poster session presented at American College of Cardiology, San Diego, CA.


ORAL PRESENTATIONS

Keynote/Plenary Lectures


Meeting Presentations


2009  Shah K. Mid-region pro-atrial natriuretic peptide and the diagnosis of heart failure in the setting of atrial fibrillation: an exploratory analysis of the biomarkers in acute heart failure (BACH) trial. European Society of Cardiology (ESC) Congress, Barcelona, Spain


2019  Shah K, Patel J. Treatment of the Sensitized Heart Patient Pre-Transplant: What's the Right Thing?. Cutting Edge of Transplantation (CEoT), Phoenix, AZ


2016  Shah K. Panel Discussant. Diagnostic and Therapeutic Modalities in Heart Failure, Advances in Managing End State Heart Failure, Kohala Coast, HI

Local/Regional
2020 - Present Shah, K. Heart Failure Updates in 2020. Noon Lecture for Internal Medicine Residents and Cardiology Fellows. VA Las Vegas Medical Center, Las Vegas, NV.

Invited/Visiting Professor Presentations

International


2014 Shah K. Proenkephalin Predicts Acute Kidney Injury in Coronary Artery Bypass Grafting Patients. International Academy of Cardiology, Boston, MA

Local/Regional


Grand Rounds Presentations


2014 Shah K. Serial Sampling of Copeptin levels improves diagnosis and risk stratification in patients presenting with chest pain. Internal Medicine Grand Rounds, University of California San Diego, San Diego, CA

Outreach Presentations

2020 - Present From Shock to Chronic Heart Failure: Acute & Chronic Management

OTHER SCHOLARLY ACTIVITIES

Additional Research/Scholarship Contributions

2018 Attendee: Consensus Conference on Critical Care in Thoracic Transplantation, American Society of Transplantation, Seattle, WA

2017 Attendee: Future Leaders in Heart Failure (HFSA), Miami, FL

2016 Attendee: US Ten Day Seminar on The Epidemiology and Prevention of Cardiovascular Disease Stroke, Lake Tahoe, CA
Career Plan

Career Statement

I am a heart failure and transplant cardiologist beginning my second year as an Assistant Professor of Medicine with a career goal of developing into an independently funded clinical researcher. Specifically, I have a prior track record in performing clinical and translational cardiovascular biomarker and heart failure research. I plan to develop and implement clinical studies which establish causal pathways in the development of heart disease and clinical heart failure. I have two areas of interest: 1) the cardiorenal syndrome and 2) the connection between viral infection and subsequent heart disease. With the support of my mentors, Drs. Drakos and Shaw, and the VPCAT program, I will combine my experience in biomarker research and advanced heart failure management to transition from early career to independent clinician-scientist.

Career Goals and Objectives

My overarching career goal is to improve our understanding of the pathogenesis of cardiovascular disease and heart failure through the study of biomarkers. My objectives in participating in the VPCAT Research Scholars program will be to develop and submit a competitive NIH K23 Award (Mentored Patient-Oriented Research Career Award). I am motivated to complete the program because I recognize the importance of developing other aspects of my professional growth, including leadership training and career development. With respect to the research objectives the program, I will aim to develop a grant submission for extramural funding based on pilot data from a research seed grant awarded to our team in April of 2020. This seed grant is funded by the University of Utah Immunology, Inflammation, & Infectious (3i) Disease Initiative under the category of Special Emphasis: Emerging COVID-19/SARS-CoV-2 Research.

The overarching goal of this project will be to use the opportunity from the global pandemic to identify risk factors associated with the development of adverse cardiovascular events in patients infected with SARS-CoV2. Furthermore, we will longitudinally study the risk of development of cardiovascular disease and heart failure to shed light on the link between viral infection and cardiomyopathy. For this project, we are planning to begin recruitment of human subjects in September of 2020 and have been requested to submit for extramural funding by April of 2021. The important research niche we will address with this project will be the association between viral infection and acute as well as chronic cardiovascular disease.

As a junior faculty member, I would benefit from the intensive mentorship/support and training afforded by this program to help develop in to an independent principal investigator. My additional goals if selected for the program include:

1) Pursue formal training in biostatistics by taking the course MDCRC 6000 (Introduction to Biostatistics) and formalize my training in statistical analysis by taking the course MDCRC 6030 (Computer Practicum)

2) Formalize my clinical research productivity and develop professional relationships within the pool of research mentors. As a newer faculty member to the University of Utah, participating in a program like this will allow me to broaden my professional network locally including senior and peer mentors.

3) Improve leadership training specifically by enrolling in the three-day course Leadership Fundamentals when available in Spring of 2020.
Scientific Mentoring Plan

I will work with Stavros Drakos MD PhD as my primary scientific mentor for the VPCAT Research Scholar Program. Dr. Drakos currently serves as the Co-Director of the Heart Failure & Transplant Program and Director of Research for the Division of Cardiology. His track record for success in research includes over 150 peer-review publications in the fields of heart failure, mechanical circulatory support, and cardiogenic shock. Furthermore, he has had success from a funding perspective having multiple NHLBI R01 grants as well as the NIH T32 program, which helps train the next generation of investigators in cardiovascular disease at the University of Utah. As evident from his CV (funding and publication record) he has helped guide the following young investigators towards independence: (1) Tracy M. Frech, MD, Associate Professor of Medicine/Rheumatology, University of Utah, (2) Junco Warren. PhD, Assistant Professor of Medicine, CVRTI/U of Utah, (3) Omar Weyer-Pinzon, MD, Assistant Professor of Medicine/Cardiology, University of Utah, (4) Palak Shah, MD, Assistant Professor of Medicine/Cardiology, George Washington University, Inova Heart and Vascular Center, (5) Michael J. Bonios, MD/PhD, Faculty of Medicine, Onassis Cardiac Center & University of Athens, Greece, (6) Anna Catino, MD, Assistant Professor of Medicine/Cardiology, University of Utah

Dr. Drakos will help with the development of my research career specifically by serving as a mentor in my efforts towards developing formal submissions for independent funding. He will help in my moving my research plan forward by providing guidance on the enrollment of patients, data collection, and interpretation. We have recently begun to write manuscripts together. We have a manuscript on cytokines predicting myocardial improvement in patients on mechanical circulatory support as well as a review paper on COVID-19 and the cardiovascular system in review. I will emphasize moving forward to ensure we have developed a greater number of publications and collaboration to help support our efforts towards extramural funding.

Dr. Robin Shaw MD PhD will serve as my co-mentor for this program. Dr Shaw currently serves as the Director of the Cardiovascular Research Training Institute (CVRTI) at the University of Utah. Dr Shaw has a research background defining the mechanisms by which the cytoskeleton delivers ion channels to their respective subregions on the cardiac membrane, and how delivery is changed during heart failure. Dr. Shaw has a track record of independent funding from the NHLBI. Moreover, he has been instrumental in helping guide young investigators towards extramural funding including TingTing Hong PhD and Joseph Palatinus MD PhD, who have been recruited from Cedars Sinai to join the team here at the University of Utah. Dr Shaw has helped develop the research biomarker cBIN1 which will be investigated as a potential link between viral infection and subsequent clinical cardiac pathology within our proposed project. We have a manuscript in review on COVID-19 and the cardiovascular system and we will continue to emphasize our efforts in ongoing collaboration on additional manuscripts to strengthen my candidacy for independent funding.

Mentoring Plan

Dr. Drakos will be my primary methodologic mentor on this project. We will meet on a monthly basis to monitor progress, set goals, and continue to identify funding opportunities. Dr. Shaw will serve as my co-mentor and we will also meet on a monthly basis in similar fashion. I will meet with both Dr. Drakos and Shaw for additional pressing matters as needed.

In addition to Dr Drakos, I plan to continue to collaborate with the following individuals (who are co-investigators on the planned project):

- **Dr. Rashmee Shah MD MS** (Assistant Professor of Medicine Division of Cardiovascular Disease): Dr. Shah is beginning her transition from early career to independent funding, and current holds 3 grants as Principal Investigator and serves on NIH study sections. Peer mentorship within the Division is critically important in academic success, as made clear by the VPCAT program. Dr. Shah has a track record in publishing as a data scientist and we are currently collaborating on a manuscript on COVID-19 from the American Heart Association Get with The Guideline COVID-19 registry.

- **Dr. Eszter Lazar-Molnar PhD** (Division of Clinical Pathology, Director of Histocompatibility and Immunogenetics Laboratory): Dr Lazar-Molnar will provide guidance regarding the inflammatory biomarkers and guidance on data analysis. Furthermore, she will serve as a collaborative connection
between my team and Associated Regional and University Pathologists (ARUP) Laboratories, which will serve as the central lab to run analyses for our proposed project.

- Dr. James Fang MD (Chief of Cardiovascular Medicine) will supervise manuscript authorship and seek out additional funding opportunities. Dr Fang will provide overall mentorship and guidance for this project and in general as Chief of my Division.
Specific Aims

Severe Acute Respiratory Syndrome Coronavirus-2 was declared a global pandemic on March 11 2020 by the World Health Organization (WHO) (1,2). This single-stranded RNA virus is the cause of a viral respiratory syndrome with high associated morbidity and mortality (3). As of September 2020, 950,000 people have died among 30,000,000 confirmed cases worldwide (4). Patients with cardiovascular (CV) comorbidities are at greater risk for morbidity and mortality compared to patients without CV comorbidities (5). In patients with COVID-19, adverse cardiac events during hospitalization occurred including cardiac injury, acute heart failure, arrhythmias and cardiac arrest (6,7). Reports of fulminant myocarditis and cardiogenic shock related to COVID-19 have been reported (8,9). The mechanisms driving this acute heart failure phenotype in patients with COVID-19 infection are poorly understood.

Patients with COVID-19 have a high prevalence (20%-28%) of severe myocardial injury (6,7). Preliminary observations in COVID-19 patients as well as evidence from other viral causes of myocarditis suggest that both (a) a primary, direct myocardial invasion, and (b) a secondary inflammatory response, play key roles in driving this severe myocardial injury (7,9). Biomarker blood testing can provide insights into the contribution from both primary myocardial injury as well as the secondary hyper-inflammatory response. Accumulating evidence has demonstrated a subgroup of patients with severe COVID-19 develop a cytokine storm syndrome with elevations in both c-reactive protein and interleukin-6 (IL-6) (5,10,11). While the degree of cytokine involvement is controversial (12), measurement of specific immune cells and cytokines in patients diagnosed with COVID-19 infection may identify those at risk for decompensation and serious CV adverse events.

Cardiac bridging integrator 1 (cBIN1) is a membrane-scaffolding protein found in cardiomyocytes discovered by Dr Robin Shaw. cBIN1 organizes the microdomains at transverse tubules responsible for systolic and diastolic calcium transients (13). cBIN1 Score is a regulator of cardiac contractile and diastolic function and an emerging novel biomarker of cardiomyocyte health. Plasma concentrations of cBIN1 are increased in patients with cardiomyopathy (14-16). Given the ability of this biomarker to detect cardiomyocyte injury and remodeling, measurement of this protein could serve a complementary role in understanding the nature and time course of myocardial injury relative to the systemic inflammatory milieu of COVID-19 and provide insight into those at particular risk for CV complications.

As the burden of disease from COVID-19 continues to increase, there is a critical unmet need and knowledge gap to phenotype and risk stratify these patients for adverse CV events and advance our understanding of the involved mechanisms. We propose to assess the value of traditional cardiac risk markers, cBIN1, and specific soluble and cell surface-bound immune and inflammatory biomarkers in patients with COVID-19. My long-term goal is to identify clinical risk factors which predict adverse CV events in patients admitted with COVID-19 infection. Our overarching hypothesis is that both primary myocardial injury and secondary inflammatory-mediated myocardial injury are involved in this process. We will characterize the time course and degree of involvement at different phases and advance our ability to prognosticate and manage the CV sequelae of the COVID infection. We will follow patients during their hospitalization and long-term for future cardiac events. We will prospectively collect blood specimens from COVID-19 infected patients upon hospital admission, weekly, and upon discharge. We will store peripheral blood mononuclear cells (PBMCs) and plasma samples for biomarker studies. Major immune cell populations, including innate (monocytes) and adaptive (lymphocyte) subsets from cryopreserved PBMCs will be analyzed by flow cytometry for the expression of immune activation markers and intracellular cytokines.

**Aim #1**: Identify clinical risk factors associated with adverse CV events in patients hospitalized with COVID-19 infection. The working hypothesis is that age, pre-existing CV comorbidities, serum cardiac troponin and serum natriuretic peptide levels will predict adverse CV events. We will use traditional regression models, as well as random forest and Bayesian network analyses to identify the associations.

**Aim #2**: Identify the additive value of the novel biomarker cBIN1 and specific inflammatory mediators in predicting adverse CV events. The working hypothesis is that elevations of specific soluble inflammatory biomarkers and cBIN1, as well as immune activation status of lymphocytes/monocyte subsets will be independently associated with adverse CV events and occur earlier than traditional markers of clinical decompensation.
Significance & Rigor of Prior Research

The topic of focus for my research for this program will be combining prior areas of interest including biomarkers and heart disease and applying them to a new problem which has had a major global impact. Specifically, the COVID-19 pandemic has had an impact on global health with social, economic, and cultural ramifications. Emerging trends with regards to COVID-19 and the cardiovascular (CV) system have emerged. Identification of individuals at high risk for adverse CV events beyond recognition of medical comorbidities may help further refine public health direction regarding which patients are at greatest risk for severe consequences. With respect to the inflammatory cascade, an inflammatory “signature” including measurement of IL-6 and TNF-alpha have been identified in small cohorts and risk stratification markers in patients with COVID-19 (11). A weakness of prior research published on this topic has been primary focus on either myocardial injury or inflammatory markers. Our efforts will merge these two complementary pathways in their contribution and time course towards clinical events. Furthermore, we will focus on both short and long-term cardiovascular events, to help determine the association between prior viral infection and future cardiomyopathy and chronic heart failure development.

If our proposed aims are achieved, we will describe a more detailed immunologic signature by deep immune profiling with flow cytometry. Furthermore, we will provide complimentary information with the incorporation of traditional CV biomarkers (troponin and natriuretic peptide). This combination effort of examining both established cardiac injury markers as well as markers of inflammation has not been studied in patients with COVID-19. We will improve our scientific knowledge of both the timing and contribution of myocardial injury and systemic inflammation as we follow our patients for both short and long-term events. The gap in clinical practice this project will help fill include the potential identification of therapeutic targets in patients who demonstrate greater activation of the immune system prior to CV events.

Prior Research Efforts

Biomarkers can aid in the diagnosis, prognosis, and potentially serve as therapeutic targets in cardiovascular disease. During my time as a medical student and trainee, I have published multiple manuscripts focusing on novel biomarkers (e.g., proenkephalin, copeptin, mid-regional pro-adrenomedullin) as well as established heart failure and cardiovascular biomarkers (B-type natriuretic peptide and troponin). These efforts have served to help enrich the current tools cardiovascular disease experts have within their patient care armamentarium as well as optimize our ability to use contemporary, established biomarkers. Furthermore, as a heart failure cardiologist I have worked to improve our understanding of heart failure outcomes by developing a project on five-year outcomes of heart failure separated by ejection fraction, based on the American Heart Association (AHA) Get with The Guidelines Registry. This project was selected for an AHA Young Investigator Data Seed Grant Award and the associated manuscript was recognized by the American College of Cardiology as the top manuscript by a young author (William W. Parmley Young Author Achievement) in 2018.

With respect to the proposed project, we will begin consenting human subjects in September of 2020. There remains a large number of patients in the Utah area being infected with and being admitted to the University of Utah Medical Center with COVID-19. This project will provide the preliminary data for the larger mentioned proposal.

Future Research Plan

This project will serve as the basis to collect and present preliminary data to lead to larger funding opportunities potentially in 2021. Specifically, our team will begin to understand the foundation regarding the interplay between primary and secondary acute myocardial injury which may a) reveal therapeutic targets for a future interventional study/grant proposal and b) understand pathophysiologic changes that may inform us on the pathogenesis of COVID-19 myocarditis and potential subsequent cardiomyopathy, and chronic heart failure. Specifically, future steps would include following patients to advance our understanding regarding the association between acute viral infection and idiopathic dilated cardiomyopathy.
In addition to the described protocol, addendums to this IRB approved project are in development. This will include the use of cardiac magnetic resonance imaging (CMR) of the heart in patients who recover from COVID-19. There is a growing interest to characterize myocardial tissue in these patients to help learn the degree of inflammation that may occur directly or indirectly as a result of viral infection. Beyond this effort, we have a proposal under review with the Utah Department of Health to study histologic slides and/or fixed tissue fragments of medical examiner cases within the state of Utah which identify COVID-19 as a clinical problem. This is a separate IRB proposal in review with Dr Elizabeth Hammond as a co-investigator. Our efforts here will shed light on the incidence of histologic evidence of myocarditis in patients who have died from (or with) COVID-19.
References


Plan for Transition into an Independent Investigator

This Memorandum of Understanding identifies the commitment of Dr Shah to pursue extramural funding as outlined in this application for the VPCAT Research Scholars Program. If he is selected for the program, he will make his best efforts to adjust his schedule without affecting clinical care beginning in 2021 to ensure he is able to attend programs and workshops associated with this rigorous program.

Furthermore, if he is successful in achieving research independence by obtaining extramural funding, he will adjust his workload by increasing time dedicated to non-clinical work from 30 (current) to 50%.

Kevin S Shah, MD, FACC
Assistant Professor of Medicine
Heart Failure & Transplant Cardiology
Division of Cardiovascular Medicine

James C Fang, MD, FACC, FAHA, FHFSF
Professor of Medicine
John and June B. Hartman Endowed Chair
Chief, Division of Cardiovascular Medicine
Executive Director, Cardiovascular Service Line
September 23 2020

RE: Kevin S Shah, MD – VPCAT Research Scholars Program Letter of Support

Dear Review Committee,

I am delighted to serve as the Primary Mentor for Dr. Kevin Shah and to provide this letter reflecting my full commitment for his candidacy for the highly competitive VPCAT Research Scholars Program. Dr. Shah was recruited to join our Heart Failure and Transplant Section in September of 2019. Part of our efforts in recruiting Dr. Shah was that he has the phenotype to develop into a strong academic clinical researcher and he has demonstrated these efforts in his time with our team.

I am a Heart Failure cardiologist with extensive clinical and research experience in the fields of heart failure, mechanical circulatory support (MCS) and heart transplantation. Over the years, it has become clear to me that interdisciplinary collaborations can fuel really innovative research efforts. Part of the genesis of Dr. Shah’s ability to obtain seed grant funding for our project in response to the COVID-19 pandemic was his ability to collaborate across departments and divisions within our institution. By merging areas of expertise and efforts to include individuals from the Department of Pathology as well as the Nora Eccles Harrison Cardiovascular Research and Training Institute (CVRTI), this collaborative effort can help to begin answering questions about the interaction of the novel corona virus and the heart.

I am a Professor of Internal Medicine and a Nora Eccles Treadwell Investigator, Co-Chief of the Heart Failure and Transplant Section, and Director of Cardiovascular Research at the University of Utah. I have a national and international reputation in clinical and translational research focused on understanding the mechanisms underlying myocardial recovery in chronic heart failure. I have led as PI multiple extramural awards from the NIH (R01 grants, CCTS/CTSA award), AHA (16SFRN29020000 HF Network-Clinical Grant and CV Genome Phenome Discovery Award), European Union Marie Curie Grant-FP7 (#276776), VA Merit Review Awards, Doris Duke Physician Scientist Development Grant, and others.

Since my recruitment back at the U of Utah as tenure-track cardiology faculty in 2009, I founded and have been fully committed to advancing the award winning Utah Cardiac Recovery program (UCAR). UCAR is a clinical and translational research program aimed at characterizing the clinical and molecular profile of the failing versus recovered heart to understand, predict and manipulate cardiac recovery. My lab was the first to challenge the widely held view that left ventricular assist device (LVAD)-induced unloading is associated with disuse myocardial atrophy. I am co-chairing the NHLBI Working Group on Myocardial Recovery and to facilitate progress in the field of recovery I have been co-organizing for the last 7 years the Annual International Utah Cardiac Recovery Symposium, which attracts every year over 500 attendees and faculty from around the globe and features high quality clinical and translational research. The resources available through UCAR are
ideal for the project Dr. Shah is proposing.

My clinical and translational research experience makes me well-suited for my role in this career development training grant. Over the years I have mentored over 25 trainees including post-doctoral fellows, medical students and junior faculty members. As the Contact PI of our NHLBI Cardiovascular Research Training Grant (5T32HL007576-32), I play a central role in preparing trainees, with MD, PhD or MD/PhD degrees, for an academic career in cardiovascular medicine. Our T32 training program has been in existence for over 25 years and before becoming the PI I had served for several years on its executive board. I am also the Director and PI of an AHA-funded Institutional Undergraduate Student Research Fellowship Program for performing cardiovascular research at the University of Utah (i.e. essentially this is an AHA funded “T-32”). Furthermore, I have a strong history of one-on-one scientific mentorship. Nine individuals I have mentored have successfully transitioned to faculty positions and developed independent academic careers. In 2017, I was presented the Department of Internal Medicine Outstanding Faculty Mentorship Award (sole recipient).

Dr. Shah is a new member of our team but has a strong track record of publications and notoriety within the field of heart failure prior to our arrival. During his time as an Internal Medicine Resident at the University of California San Diego, he was selected as the House Officer of the Year and received the Kaiser Teaching Award from medical students. While he was a fellow in Cardiovascular Disease at University of California Los Angeles, he received the William W. Parmley Young Author Achievement Award as recognition for a top paper of the year in the Journal of American College of Cardiology. Dr. Shah has authored multiple manuscripts on cardiovascular biomarkers and heart failure outcomes as well as had prior success in obtaining grant funding including the American Heart Association Young Investigator Data Seed Grant in 2016.

Dr. Shah joined our team initially focusing his efforts on the cardiorenal syndrome, as we have a working collaborative effort between the Divisions of Cardiovascular Medicine and Nephrology to develop projects focusing on heart and kidney interactions. While he has been an active member of our consortium here, he was ready and able to adjust his focus to incorporate his strengths in clinical and translational research with the current COVID-19 pandemic, leading to a seed grant from the University of Utah Immunology, Inflammation, & Infectious Disease Initiative for a project we will begin enrolling patients at the University of Utah. In addition to this effort, he has led a comprehensive review paper with myself and others on the topic of COVID-19 and the cardiovascular system which is under review. In addition, he and one of our senior pathologists, Dr Elizabeth Hammond, have a protocol under review with the Utah Department of Health IRB specifically to study prior post-mortem autopsy samples of patients who have died in Utah from COVID-19. Collectively, Dr Shah is showing a keen effort here to direct his efforts on the intersection between viral infection and heart disease.

I have read and can meet the expectations and required responsibilities to serve as a primary mentor for this program if Dr. Shah is selected. Dr. Shah will have the minimum of 30% FTE dedicated to research and career development efforts. He will ensure his schedule can accommodate the sessions associated with this program without compromising clinical care during this time. Furthermore, he is committed to pursuing extramural funding and this program and the mentor network will provide valuable tools to help him achieve this career goal. During this program, Dr Shah and I will meet on a monthly basis to discuss progress, barriers, and importantly, papers to collaborate upon. We have two papers under review at this time and he and I will place an emphasis on increasing our efforts to author additional manuscripts together as this will be important to strengthen his pursuit for extramural funding. Dr Robin Shaw, the Director of the Nora Eccles Harrison CVRTI, has agreed to serve as a co-mentor and he will routinely meet with Dr Shah as well to help monitor his progress and provide additional support. I also routinely interact with Dr Shaw as we are colleagues within the CVRTI and we will join our efforts to ensure Dr Shah is on track to continue to grow professionally.

In summary, Dr. Shah is a very qualified candidate for this highly competitive research and mentorship program. His prior research training is strong and his academic productivity and track record to date is impressive. Under the guidance of the mentoring team and structure program provided by VPCAT Research Scholars program, he will gain the skills to take the next step in his young career. I support this application with
the highest possible enthusiasm.

Sincerely,

Stavros G. Drakos, MD, PhD, FACC
September 22, 2020

Michael A. Rubin M.D., Ph.D.
Professor and Vice-Chair for Faculty Development
Department of Internal Medicine
Director, VPCAT Program
University of Utah Health Science Center

Re: Kevin S Shah M.D. - VPCAT Scholar Application

Dear Dr. Rubin,

I am thrilled to provide this enthusiastic letter of support for Kevin Shah M.D. as he applies for this upcoming cohort for the VPCAT Research Scholars Program. I am the Director of the Nora Eccles Harrison CVRTI (Cardiovascular Research and Training Institute) and Professor of Medicine having joined the University of Utah in 2019.

Dr. Shah went to medical school at the University of California Irvine and completed his training in Internal Medicine at the University of California San Diego. He went on to complete fellowships in Cardiovascular Disease and Heart Failure & Transplant Cardiology at University of California Los Angeles and Cedars Sinai Heart Institute, respectively. I have known Dr. Shah since he was an Advanced Fellow at Cedars Sinai in Los Angeles (2018-2019). While he is early in his career, he has demonstrated commitment to science, publishing multiple peer-reviewed manuscripts in high impact journals, including the Journal of American College of Cardiology and Circulation. Dr. Shah is an aspiring clinician scientist and being selected for this program will be an asset to him as he continues his early career growth.

My role as a VPCAT scientific co-mentor will be to meet with him regularly as outlined in his application during his time in this program. He will reach out for additional questions or support throughout the process while he is in the program as well as for specific guidance with regards to our collaboration. Dr. Shah has worked with a team of us within the Division of Cardiovascular Medicine, CVRTI, and ARUP to obtain seed grant funding from the University of Utah Immunology, Inflammation, & Infectious Disease initiative; he will use this data as part of his application to pursue extramural funding.

Thank you for your consideration of Dr. Shah to this highly competitive program. I am very confident that he will do well in terms of his career growth and contributions to the clinical research and overall growth our academic efforts within the University of Utah.

Robin Shaw, M.D., Ph.D.
Director, Nora Eccles Harrison Cardiovascular Research and Training Institute
September 25, 2020

Dear VPCAT Research Scholars Program Committee,

I write to provide strong support for the application for Kevin Shah M.D. as a Vice President’s Clinical and Translational (VPCAT) Research Scholar. Kevin was recruited and joined our team on the Clinical Track in the Division of Cardiovascular Medicine in September of 2019. Kevin trained in Cardiovascular Medicine and Heart Failure & Transplant Cardiology at University of California Los Angeles and Cedars Sinai, respectively. Kevin had a very strong track record of clinical research productivity as a trainee and this was part of what made him an attractive candidate to recruit as junior faculty here. He has continued his dedication through his efforts with our team here.

I have full confidence that Kevin would be an excellent candidate for the VPCAT Research Scholars Program. He would benefit greatly from the research training and mentorship network. Furthermore, he is developing as a clinician investigator and I believe this program would be of great benefit to help him take the next steps forward in his career. Kevin has been successful in obtaining seed grant funding during his first year as faculty and his outlined Research Plan to take the next step forward is strong. He is committed to working with his primary mentor Dr. Stavros Drakos and co-mentor Dr. Robin Shaw to pursue extramural funding and he has arranged for a strong team of collaborators to help improve his chances for success. Dr. Drakos and Shaw both have strong track records of mentoring junior faculty towards independent funding and I am confident in their abilities and commitments towards helping Kevin be successful.

I attest that our commitment to Kevin meets eligibility criteria of the VPCAT program. As Division Chief, we will ensure Kevin has the time available to attend the required sessions for this program. Furthermore, he will devote a minimum of 30% FTE to the development of his career and research during the 2-year program period. I am strongly committed to Kevin’s ongoing professional development and success. Moreover, I believe Kevin will be a great asset to this program and he will continue to make strong academic contributions moving forward.

If you need additional information, please feel free to contact me.

Sincerely,

James C. Fang, MD, FACC, FAHA, FHFSU
Professor of Medicine
John and June B. Hartman Presidential Endowed Chair
Chief, Division of Cardiovascular Medicine
Executive Director, Cardiovascular Service Line
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: Drakos, Stavros G

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

POSITION TITLE: Professor of Medicine, University of Utah Health & School of Medicine

EDUCATION/TRAINING

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<td>Ph.D.</td>
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<td>Cardiovascular Medicine</td>
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<td>Residency</td>
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<td>Internal Medicine</td>
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<td>University of Utah/UTAH Cardiac Transplant Program, Salt Lake City, UT</td>
<td>Fellowship</td>
<td>07/2003</td>
<td>Heart Failure (HF) &amp; Transplant (Tx)</td>
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<td>National University of Athens &amp; “Harefield/Imperial College Athens Recovery Program” (HARP)</td>
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<td>University of Utah/Eccles Institute of Human Genetics, Salt Lake City, UT</td>
<td>Post-Doc</td>
<td>10/2009</td>
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A. Personal Statement

I am a heart failure (HF) cardiologist with a NIH-funded research team focused on understanding the mechanisms underlying myocardial failure and recovery in the experimental and clinical settings. I have clinical and research experience in the fields of advanced heart failure (HF), mechanical circulatory support and heart transplantation. My background includes: (a) M.D. (1991-97, Summa Cum Laude) and Ph.D. (1996-2000) both performed at the Univ. of Athens (most competitive institution in Greece - http://en.uoa.gr/ - PhD Thesis: “Pulsatile Vs. Non-Pulsatile mechanical circulatory support in a porcine model of HF – Institutional Award “Best PhD Thesis”, Mentor: John N. Nanas, MD/PhD, bench-to-bedside international leader in HF), (b) HF/Tx Fellowship (2001-2003) at the U of Utah and the affiliated Intermountain and VA Hospitals (i.e. the historic Utah Transplantation Affiliated Hospitals [U.T.A.H.] Cardiac Transplant Program), (c) Cardiology and Clinical Research training (2003-2007) at the U of Athens and the “Harefield/Imperial College Athens Recovery Program” (H.A.R.P.) under the mentorship of Sir Magdi Yacoub, MD, a living legend in CV diseases, and, (d) Translational Research training (2007-2009) at the Molecular Medicine Program, Eccles Institute of Human Genetics, U of Utah (Mentor: Dean Y. Li, MD/PhD, currently Senior VP Translational Medicine at Merck).

Since my recruitment as cardiology faculty at the University of Utah (2009) original work in the field of myocardial recovery generated by my research team both in the lab (www.cvrti.utah.edu/~drakos) and in the clinical arena led to the founding and establishment of the award-winning Utah Cardiac Recovery Program – UCAR (selected publications #1-12). UCAR is a clinical and translational research program aiming in characterizing the clinical and molecular profile of the failing versus recovered heart in order to understand, predict and manipulate cardiac recovery. My lab was the first to challenge the widely held view that ventricular assist device (VAD)-induced unloading is associated with disuse myocardial atrophy (publications #1, #2). UCAR is supported by extramural funding I secured as PI through the NIH (R01s and CCTS/CTSA award), AHA (HFSFR Network-Clinical Grant PI and Genome Phenome Grant), Doris Duke Physician Scientist Development Grant, European Union Marie Curie Grant-FP7, Dpt of Veterans Affairs and others. I am co-chairing the NHLBI Working Group on Myocardial Recovery (publication #3) – its members list and executive summary can be found at: https://www.nhlbi.nih.gov/events/2016/nhlbi-working-group-advancing-science-myocardial-recovery-mechanical-circulatory. Also, to facilitate progress in the field of myocardial recovery I have been co-organizing for the last 9 years the annual international Utah Cardiac Recovery Symposium (UCARS) http://medicine.utah.edu/cardiacrecoverysymposium/ which is attracting every year > 500 attendees and faculty from around the globe and features high quality clinical, translational and basic research.
I have a strong commitment to training and mentoring the next generation of physician investigators. In 2017, I was presented the U of Utah Department of Medicine Outstanding Faculty Mentorship Award (sole recipient). More than 30 publications included in my CV were authored by trainees under my mentorship who have now moved on to either independent faculty position (n=9) or are still under training in various institutions. In addition, I am the PI of the NHLBI Cardiovascular T32 grant and previously I had served for several years on the executive board of this grant. I am also the Director and PI of an American Heart Association-funded Institutional Undergraduate Student Research Fellowship Program for performing cardiovascular research at the University of Utah.

I feel that my clinical and research background alongside with my track record in mentoring position me well for my role in this award submitted by my colleague Dr. Kevin Shah.


**B. Positions and Honors**

**Positions and Employment**

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<td>Professor of Medicine, Division of Cardiology, U of Utah</td>
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<td>Director of Cardiovascular Research, Division of Cardiology, U of Utah</td>
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<td>09/2014-Present</td>
<td>Co-Chief, Heart Failure and Transplant Section, Division of Cardiology, U of Utah</td>
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<td>Associate Professor of Medicine (with award of tenure)</td>
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<td>10/2011-Present</td>
<td>Medical Director, Cardiac Mechanical Support Program, U of Utah Healthcare</td>
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<tr>
<td>10/2009-10/2014</td>
<td>Assistant Professor of Medicine, Division of Cardiology, U of Utah</td>
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**Professional Activities and Honors**


2017 Keynote Speaker at National Conference: INTERMACS 11th Annual Meeting and Scientific Sessions 2017, Atlanta, Georgia

2017 Outstanding Faculty Mentorship Award (sole recipient), Dpt of Internal Medicine, U of Utah

2017 Keynote Speaker at UT Southwestern Annual Cardiovascular Conference, Dallas, Texas

2017 Nora Eccles Treadwell Investigator, Nora Eccles Treadwell Foundation & U of Utah

2017 Chair, Annual ISHLT Mechanical Circulatory Support MASTERS Academy, San Diego, CA

2017 Member, NHLBI Clinical and Integrative Cardiovascular Sciences (CICS) study section


2017 Chair, Annual ISHLT Mechanical Circulatory Support MASTERS Academy, Washington DC

2012-19 Co-Director, Annual International Utah Cardiac Recovery Symposium (U-CARS) [http://medicine.utah.edu/cardiarecoverysymposium/](http://medicine.utah.edu/cardiarecoverysymposium/)

SHAH, KEVIN - #2668 33 of 42
As part of our work we investigated the potential of reverse remodeling and myocardial recovery appears to be very unlikely. Changes on the myocardial T-tubule system in human heart failure impairs excitation-contraction coupling and functional recovery by continuous mechanical unloading. We also discovered specific carbon metabolism (OCM). These findings advanced our understanding of the differential functional and increased flux through the cardioprotective metabolism pathways of pentose phosphate (PPP) and one carbon metabolism (OCM).


b). Impact of Mechanical Circulatory Support on Myocardial Recovery: Clinical Structure-Function Studies

As part of our work we investigated the impact of mechanical unloading and hemodynamic support on the structure, function and pathophysiology of the failing and recovering myocardium.


c). Pathophysiological Studies on Adverse Cardiovascular Remodeling and Reverse Remodeling in Chronic Heart Failure.

Earlier in my career I performed studies investigating aspects of adverse cardiovascular remodeling such as endothelial dysfunction (publ. #13), sympathetic innervation (publ. #14), and electrophysiology (publ. #16) and their relation to the potential of reverse remodeling (publ. #14-16).


d). Impact of Mechanical Circulatory Support on Acute and Chronic Heart Failure Outcomes.

I published 4 first-author clinical studies (2 of them listed below - publications #17 and #18) focused on the HLA allosensitization induced by VADs. Another significant problem in patients undergoing support with a left ventricular assist device is the development of right ventricular failure: in a highly cited publication we developed a predictive risk score for appropriate patient selection (publ. #19). I have also been interested in short-term MCS in acute HF/cardiogenic shock. Recently, I led the investigational effort to design and implement the first multidisciplinary SHOCK TEAM in the country (publ. #20).


Complete List of Published Work: https://www.ncbi.nlm.nih.gov/pubmed/?term=DRAKOS+S

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

Ongoing Support
AHA HF SFR Network - Clinical Project 1 Drakos (PI) 07/16/07/20
Title: Functional, Metabolic, and Patient-Centered Determinants of Recovery in Heart Failure
The goal of this project is to define determinants of cardiac recovery in chronic heart failure
Role: PI

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<td>Merit Review Award I01 CX002291</td>
<td>Drakos (PI)</td>
<td>01/21-01/25</td>
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<td>Department of Veterans Affairs</td>
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<tr>
<td>Title: Understanding Myocardial Recovery in Diabetes and Heart Failure</td>
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<tr>
<td>NHLBI 1R01HL156667-01</td>
<td>Drakos/Warren (MPI)</td>
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<tr>
<td>Title: Perm1 is a Novel Regulator of Cardiac Energetics and Function</td>
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<tr>
<td>Nora Eccles Treadwell Foundation</td>
<td>Drakos (PI)</td>
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<tr>
<td>Title: Improving Myocardial Salvage after Acute Myocardial Infarction with Simultaneous Mechanical Unloading and Reperfusion</td>
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<td>NIH T32 HL007576</td>
<td>Drakos/Weyrich (MPI)</td>
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<td>Training in Cardiovascular Research</td>
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<td>AHA Award #18UFEL3390022</td>
<td>Drakos (PI)</td>
<td>02/18-01/22</td>
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<td>Institutional Undergraduate Student Research Fellowship Program</td>
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<td>Role: Director and PI</td>
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<td>Merck Research Labs LKR173917</td>
<td>Drakos/Rutter (MPI)</td>
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<tr>
<td>Title: The Metabolic Basis of Human Heart Failure and Recovery</td>
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<td>Nora Eccles Treadwell Foundation</td>
<td>Rutter (PI)</td>
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<tr>
<td>Mitochondrial Pyruvate Metabolism: Structure and Role in Heart Failure</td>
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<tr>
<td>Role: Co-Investigator</td>
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<tr>
<td>AHA Fellowship Grant</td>
<td>Badolia (PI)/Drakos (Mentor)</td>
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<tr>
<td>Title: Altered monocarboxylate and glycolysis-dependent cardioprotective metabolism in the failing human heart.</td>
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<td>Role: Mentor</td>
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<td>NHLBI R01HL151924-01</td>
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<tr>
<td>Title: Role of cardiomyocyte KLF5 in heart failure</td>
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<tr>
<td>Role: Co-Investigator</td>
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<td>NHLBI-R01</td>
<td>DiBella (PI)</td>
<td>07/17-07/21</td>
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<tr>
<td>Title: Quantitative MRI for characterizing heart failure with preserved ejection fraction (HFpEF)</td>
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<td>Role: Co-Investigator</td>
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</table>
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: SHAW, ROBIN MARK

eRA COMMONS USER NAME (agency login): SHAWRO

POSITION TITLE: Professor (Medicine), Wasserman Endowed Chair in Cardiology

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

<table>
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<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE (if applicable)</th>
<th>Completion Date MM/YYYY</th>
<th>FIELD OF STUDY</th>
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<tbody>
<tr>
<td>Brown University, Providence, RI</td>
<td>BS</td>
<td>05/1990</td>
<td>Bioengineering</td>
</tr>
<tr>
<td>Case Western Reserve University, Cleveland, OH</td>
<td>PHD</td>
<td>01/1997</td>
<td>Bioengineering</td>
</tr>
<tr>
<td>Case Western Reserve University, Cleveland, OH</td>
<td>MD</td>
<td>05/1999</td>
<td></td>
</tr>
<tr>
<td>University of California, San Francisco, CA</td>
<td>Resident</td>
<td>06/2001</td>
<td>Internal Medicine</td>
</tr>
<tr>
<td>University of California, San Francisco, CA</td>
<td>Fellow</td>
<td>06/2004</td>
<td>Cardiology</td>
</tr>
<tr>
<td>University of California, San Francisco, CA</td>
<td>Postdoctoral Fellow</td>
<td>06/2006</td>
<td>Lily Jan Lab</td>
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A. PERSONAL STATEMENT

My laboratory is focused on basic myocardial biology. We define the mechanisms by which the cytoskeleton delivers ion channels to their respective subregions on the cardiac membrane, and how delivery is changed during heart failure. Our work defined the paradigm of Targeted Delivery which describes how the cytoskeleton delivers membrane proteins directly to their functional membrane subdomain and why there is less delivery in failing heart. Our models involve exploration of Connexin43 gap junction trafficking to the cardiomyocyte intercalated disc, with comparison to L-type calcium channel trafficking to cardiomyocyte T-tubules. In the process we identified that the mRNA of Cx43 is alternatively translated to generate endogenously up to six different truncated isoforms which are essential to trafficking. These isoforms we identified have a different biophysics and biology as Connexin43 and thus function as new proteins with important roles in basic cell biology. The most commonly translated isoform, GJA1-20k, is critical for Connexin43 forward trafficking as well as mitochondrial organization, transport and function. A major current focus of my group is to identify how GJA1-20k works with the actin cytoskeleton to regulate both membrane protein trafficking and metabolism. A second major focus involves another trafficking molecule Dr. TingTing Hong and I cloned, cardiac BIN1 (cBIN1, Nature Medicine 2014) which regulates L-type calcium channel trafficking, T-tubule folds and is also released into blood as T-tubule origin microparticles, and available as a biomarker of muscle health (JAMA Cardiology, 2018).

For VPCAT Research Scholars Program proposal, I will serve as Co-mentor for Dr. Shah. I am Director of the Cardiovascular Research and Training Institute (CVRTI) at the University of Utah, and thus am highly invested in maintaining a stellar cardiovascular training environment able to address emerging needs from Medicine. Furthermore, my group has developed the cBIN1 Score (CS) biomarker which is a first-in-class marker of cardiomyocyte remodeling. We have published the use of CS is heart failure patients, and have found, in transplant patients, it can predict antibody and cellular mediated rejection prior to clinical symptoms or biopsy. Dr. Shah will be utilizing CS in his original and highly innovative proposal.


B. POSITIONS AND HONORS

Positions and Employment
2004 – 2006 Assistant Adjunct Professor of Medicine, University of California, San Francisco, CA
2006 – 2012 Assistant Professor of Medicine, In Residence (full FTE), UCSF, San Francisco, CA
2009 – 2013 Investigator, Cardiovascular Research Institute, University of California, San Francisco, CA
2012 – 2013 Associate Professor of Medicine (tenure), University of California, San Francisco, CA
2014 – 2018 Associate Professor of Medicine in Residence, UCLA, Los Angeles, CA
2015 – 2019 Wasserman Endowed Chair in Cardiology, Cedars-Sinai Medical Center, Los Angeles, CA
2018 – 2019 Professor of Medicine in Residence, UCLA, Los Angeles, CA
2019 – present Nora Eccles Harrison Presidential Endowed Chair in Cardiology, U of Utah, Salt Lake City, UT
2019 – present Director, Cardiovascular Research and Training Institute, U of Utah, Salt Lake City, UT

Other Experience and Professional Memberships
2002 – Diplomate, American Board of Internal Medicine, Internal Medicine
2004 – Diplomate, American Board of Internal Medicine, Cardiovascular Disease
2006 – 2012 Electrophysiology & Arrhythmias/Regulation Peer Review Study Group, AHA
2007 Study Section (ad hoc), National Science Foundation
2010 Stage 1 Reviewer SC4 Applications, National Institutes of Health
2012 ESTA Study Section (ad hoc), National Institutes of Health
2013 SYN and ZRG1 Special Emphasis Panels, National Institutes of Health
2014 National Innovative Research Grant Study Group, American Heart Association
2014 – Editorial Board, Trends in Cardiovascular Medicine
2015 ESTA Study Section (ad hoc), National Institutes of Health
2015 AHA National Electrophysiology and Arrhythmia Study Group
2015 Department of Defense Health Program (Cardiovascular), Peer Review
2015 National Institutes of Health, ESTA / CCHF / MEM Special Emphasis Panel
2016 CCHF Study Section (ad hoc), National Institutes of Health (June and October)
2017 CICS Study Section (ad hoc) National Institute of Health (February and June)
2017 National Institutes of Health, CCHF Study Section (ad hoc, November)
2017 National Institutes of Health, CVRS-K (ESTA) Special Emphasis Panel (December)
2018 Co-Chair, AHA Basic Myocyte Biology and Electrophysiology Study Group
2018 National Institutes of Health, CVRS-K (ESTA) Special Emphasis Panel (July)
2018 National Institutes of Health, CCHF Study Section (ad hoc), (October)
2019 – 2023 CCHF Study Section, standing member

Honors
2003 "Golden Stethoscope", Best Clinical Cardiology Fellow, University of California San Francisco
2004 Fellow to Faculty Award, American Heart Association
2013 Established Investigator Award, American Heart Association
2014 Elected Member, American Society for Clinical Investigation (ASCI)
2016 Addgene, Blue Flame Award (100+ requests for a single plasmid)
2017 Addgene, Blue Flame Award (second plasmid, another 100+ lab requests)
2017 – 2020 Member, Katz Award Committee, AHA Council of BCVS
2018 Addgene, Blue Flame Award (third plasmid, another 100+ lab requests)
C. CONTRIBUTIONS TO SCIENCE

1. Gap Junction Communication and Ventricular Arrhythmogenesis. My early focus was to explore the role of gap junction mediated cell-cell communication in ventricular arrhythmogenesis. The resultant publications (my graduate work) helped establish the mechanisms of action potential propagation in ventricular muscle and identified that the level of gap-junction mediated cell-cell coupling in muscle has profound effects on traditional ion currents, even in the absence of changes to the other currents themselves. This influential body of work (reference d. below has 650 citations) helped establish gap junction communication as a major determinant of healthy, and diseased, cardiac electrophysiology.


2. Targeted Delivery, prior to GJA1-20k. Continuing to explore Cx43 biology, I asked the question how do the newly made and short-lived gap junction proteins arrive at the intercalated disc? The result of these mechanistic explorations is the Targeted Delivery model Cx43 trafficking but which newly formed hemichannels exit the Golgi and ride microtubule highways specifically to their destination membrane subdomains. Specificity of delivery is a combination of the channel protein, microtubule plus-end tracking proteins, and a membrane anchor. We have found Targeted Delivery occurs for Cx43 trafficking in cardiomyocytes, and is disrupted in conditions of oxidative stress, helping to explain decreased cell-cell coupling in failing myocardium, and that actin organized the microtubule highways by the alternatively translated GJA1-20k isoform. Targeted Delivery has become the prevailing model for channel trafficking in non-failing hearts and explains channel mislocalization in heart failure.


3. GJA1-20k in Trafficking and Metabolism. A byproduct of our Cx43 trafficking studies revealed that Cx43 mRNA which is the product of a single coding exon (hence no splicing), can generate not one but seven total proteins with the latter six encoded with internal AUG start sites and translated by Alternative Translation. Furthermore, translation of the smaller isoforms is mTOR dependent and the 20kd smaller isoform (GJA1-20k) is important for Cx43 forward trafficking. Further exploring the roles of the smaller isoforms, we are finding that actin is important to Cx43 forward delivery, and there gap junction trafficking affected but mitochondria as well. GJA1-20k affects mitochondria movement and promotes mitochondrial
biogenesis. Please refer to three recent papers listed in the Personal Statement of section A above. In addition, relevant manuscripts include:


4. **Calcium Channel Trafficking and T-tubule Regulation.** Studies in my laboratory have also expanded beyond Cx43 hemichannels to L-type calcium channels (Cav1.2). We chose Cav1.2 because it is a very important ion channel that needs to be at a specific subdomain (T-tubules) which is a different structure from the intercalated disc. We found the Cav1.2 channels follow Targeted Delivery and are trafficked on microtubules to the membrane anchor BIN1. Expanding our exploration of BIN1, we found that it is decreased in acquired heart failure, and itself generates small, overlapping folds within T-tubule membrane, affecting ionic flux, calcium transients, and arrhythmogenesis. These studies (below and those mentioned in biosketch section A above), done in collaboration with Dr. TingTing Hong and her group, have initiated a multifaceted exploration of dyad microdomains in healthy muscle and failing heart.


5. **Biomarker and Therapeutic Development for Heart Failure.** A translational component to our effort uses the lessons learned from mechanistic studies of cardiomyocyte trafficking to develop novel diagnostics and therapeutics. The most advanced of such studies is use of blood based BIN1 as an index of cardiac health. We have found that not only is BIN1 important to calcium hemostasis and electrical stability in ventricular cells, but is reduced in acquired heart failure and is turned over into blood in levels that reflect cardiac content. Dr. Hong’s group and mine have developed a cBIN1 score (CS) as a first of its kind biomarker of cardiac muscle health that could be used as a screen for heart failure, prognosticate heart failure outcomes, and prognosticate the occurrence of ventricular arrhythmia.


Kobashigawa JA, Hamilton M, Hong TT, Shaw RM. Plasma cBIN1 Score (CS) Identifies HFrEF and Can Predict Cardiac Hospitalization in Stable Ambulatory Patients 2018. Preprints. doi:10.20944/preprints201801.0040.v1


Complete List of Published Work in MyBibliography:

D. RESEARCH SUPPORT

Ongoing Research Support

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<td>R01 HL138577</td>
<td>Shaw (PI)</td>
<td>07/01/17 – 04/30/21</td>
<td>National Heart, Lung and Blood Institute (NHLBI)</td>
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<tr>
<td>“A New Non-Canonical for an Alternatively Translated Ion Channel Protein”</td>
<td>The goal of this study is to explore the role of the alternatively translated isoform GJA1-20k on the its role in mitochondrial biology. A supplemental to this proposal was awarded to explore the role of GJA1-20k in neurodegenerative disease.</td>
<td>Role: PI</td>
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<td>R01 HL138577S</td>
<td>Shaw (PI)</td>
<td>07/01/2018 – 4/30/2021 (one year supplement)</td>
<td>National Heart, Lung and Blood Institute (NHLBI)</td>
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<tr>
<td>“A New Non-Canonical for an Alternatively Translated Ion Channel Protein”</td>
<td>The goal of this Supplemental study is to explore the role of the alternatively translated isoform GJA1-20k on protecting against neurodegenerative disease.</td>
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<td>Shaw (PI)</td>
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<td>National Heart, Lung and Blood Institute (NHLBI)</td>
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<td>“Unlocking Trafficking Specificity for Cx43 Gap Junctions”</td>
<td>The goal of this study to examine how GJA1-20k contributes specificity of delivery for Cx43 gap junction being trafficked to the cardiac intercalated discs.</td>
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<td>R01 HL136463</td>
<td>Saffitz (PI)</td>
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<td>National Heart, Lung and Blood Institute (NHLBI)</td>
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<td>“Altered Cell-Cell Coupling in Arrhythmogenic Cardiomyopathy”</td>
<td>The goal of this translational study to examine known cytoskeleton trafficking pathways in the context of the clinical entity arrhythmogenic cardiomyopathy.</td>
<td>Role: Co-investigator</td>
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Completed Research Support (Last 3 years)

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<td>DoD PR150620</td>
<td>Marban (PI)</td>
<td>06/01/16-09/16/19</td>
<td>Department of Defense, CDMRP, Focused Program Award (similar to NIH Program Project)</td>
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Heart Failure With Preserved Ejection Fraction: Mechanisms and Novel Therapeutics
The goal of this program project is to determine the mechanisms of heart failure with preserved ejection fraction (HFrEF) as well as conduct a clinical trial in which cardiosphere based therapies are tested.
Role: **Subproject Co-PI (with T. Hong)**

13EIA4480016    Shaw (PI)    01/01/13-12/31/17
American Heart Association
Bench to Bedside Studies of Ion Channel Trafficking
The goal of this study to translate discoveries of the mechanisms of cardiac channel trafficking to new therapeutic approaches to arrhythmia and heart failure.
Role: PI

R01 HL094414    Shaw (PI)    12/01/08-10/31/19
National Heart, Lung and Blood Institute (NHLBI)
Novel Mechanisms of Cardiac Ion Channel Regulation
The goal of this study to understand the mechanisms trafficking, from internal translation, to forward delivery, to internalization of cardiac ion channels.
Role: PI