none

Online Award Application Award Information

Profile Information

Applicant

	Current Profile	Application Profile
APS ID	[redacted]	[redacted]
APS Member?*	Yes	Yes
E-mail Address*	[redacted]	[redacted]
First Name*	Pooneh	Pooneh
Middle Name		
Last Name*	Bagher	Bagher
Institution*	[redacted]	[redacted]
Department		
Address*	[redacted]	[redacted]
City*	[redacted]	[redacted]
State/Province	[redacted]	[redacted]
Zip/Postal	[redacted]	[redacted]
Country*	[redacted]	
Work Phone	[redacted]	[redacted]
Home Phone		
Mobile Phone		[redacted]
Fax		[redacted]
Citizenship*	[redacted]	
Other Citizenship		

APS Section	**Primary:** Cardiovascular Section **Secondary:** Environmental & Exercise Physiology Section **Tertiary:** Cell & Molecular Physiology Section
Ed/Professional*	Early Career Professional
Degrees*	2007 - PhD: Doctor of Philosophy (Cornell University)
Year of Birth*	[redacted] 1982
Gender*	[redacted]
Ethnicity*	Not Hispanic or Latino
Race(s)*	Asian

Do you have a physical, mental, or learning disability that substantially limits one or more major life activities?*

I prefer not to answer this question

Undergrad Only: Do you come from a family with an annual income below established low-income thresholds?*

N/A or I prefer not to answer this question

Undergrad Only: Do you come from a social, cultural, or educational environment such as that found in certain rural or inner-city environments that have demonstrably and recently directly inhibited the individual from obtaining the knowledge, skills, and abilities necessary to develop and participate in a research career?*

N/A or I prefer not to answer this question

Undergrad Only: Are you a first generation student?*

Undergrad Only: If you answered yes to any of the questions above, please describe.

Application Information

Application Date: 5/2/2016 **Last Modified:** 5/13/2016

Have you been an APS member in good standing for the past 2 years?*
Yes

What is your professional rank?*
Assistant Professor

Description of proposed project and/or Course outline*
PB_APS_Proposal_160515.pdf

Description of current and future research program*
PB_APS_Research_160515.pdf

Has your application been reviewed and approved by an institutional oversight committee?*
Choice Not Made

Justification of Requested Funds (not to exceed $20,000)*
PB_APS_Justification_160515.pdf

List of current and pending research support*
PB_APS_Other_Support_160515.pdf

Letter of Support from Department Chair or equivalent. *
PB_APS_Letter_DCZ_1600515.pdf

Letter of Support from Host Laboratory
PB_APS_Letter_BEI_160515.pdf

Biosketch of the Chief of the Host Laboratory (not to exceed 5 pages)
PB_APS_Biosketch_BEI_160515.pdf

Curriculum Vitae*
PB_APS_CV_160515.pdf

none

Introduction

Regulation of blood flow is required to maintain tissue perfusion throughout the body in proportion to metabolic demand. Resistance arterioles, which are comprised of vascular smooth muscle cells (SMCs), endothelial cells (ECs) and perivascular nerves (PVNs), are the site of regulation, with subtle changes in diameter resulting in significant alterations in flow. In recent years, our understanding of the subtle interplay between ECs, SMCs and PVNs has been significantly improved due to advancements in imaging technology. Using electron microscopy, it has been demonstrated that ECs and SMCs of resistance vessels are directly coupled via gap junctions present at the myoendothelial junction [(MEJ); extensions of the EC plasmalemma through perforations in the internal elastic lamina (IEL)], allowing for transfer of hyperpolarization and small molecules between these two cell types.[1-3] Using calcium indicator molecules and confocal microscopy in isolated arterioles, myself and others have observed elementary calcium signaling events preferentially localized within the MEJ of ECs, that trigger downstream pathways to modulate blood flow.[4-6] These data clearly demonstrate a significant role for the MEJ as a signaling microdomain, and thus highlight the need to study these cell types as a functional unit.

Whereas Ca^{2+} signals in SMCs have been recognized as critical in modulating myogenic tone and vessel constriction, Ca^{2+} signals in ECs center on vasodilation. Calcium imaging studies in mouse models have been hindered by the inability to selectively load ECs and SMCs specifically without interference from the other cell layer. Due to the MEJ and the physical coupling between ECs and SMCs, conventional 1,2-bis(o-aminophenoxy)ethane-N,N,N'N'-tetraacetic acid (BAPTA)-based calcium indicators rapidly leave ECs and load adjacent SMCs. To overcome this problem Dr. Michael Kotlikoff's group at Cornell University has developed transgenic mice expressing genetically encoded calcium indicators (GECI). To date, mice expressing a SMC-specific red fluorescent based calcium indicator (RCaMP1.07) and mice expressing an EC-specific green fluorescent based calcium indicator (GCaMP2) have been generated. I am currently in the process of obtaining these mice, and have utilized a portion of my start-up fund from Texas A&M to buy a sensitive laser scanning confocal microscope to image tissues from these mice. Crossing these two strains will result in a dual sensor mouse which allows for dynamic imaging of calcium events in both ECs and SMCs simultaneously. As GCaMP2 and RCaMP1.07 have distinct excitation/emission spectra, technical challenges traditionally associated with cell loading and bleedthrough of signal during simultaneous imaging of ECs and SMCs can be eliminated allowing for precise examination of heterocellular communication. As defects in heterocellular communication underlies disease states such as hypertension[8] and the vascular dysfunction associated with aging,[9] the development of techniques to tease out molecular signaling pathways at the MEJ is crucial for development of novel therapeutics.

Background and Aims

To date the majority of microvascular calcium studies utilize *in vivo* preparations, isolated blood vessels or freshly dissociated cells; however, Brant Isakson at the University of Virginia has developed and validated a unique vascular cell co-culture (VCCC) technique whereby the interactions between ECs and SMCs can be readily examined.[10] In brief, vascular smooth muscle cells and endothelial cells are cultured on opposite sides of a Transwell membrane. These cells spontaneously form MEJs within holes in the membrane and therefore are coupled electrically and physically as they would be *in vivo*. Using this technique, Dr. Isakson has performed calcium imaging experiments (Figure 1A) which have focused on global calcium signaling events in the monolayer of cells (Figure 1 B). Since imaging technology, in particular calcium indicator and confocal microscope sensitivities have improved tremendously over the 5-

8 years, the aim of the current application is to examine focal calcium signaling events with the MEJ in the Transwell membrane of the VCCC. In addition, Dr. Isakson's group has developed a technique for specifically isolating mRNA and protein from the EC monolayer, SMC monolayer, and the MEJ fraction. This is a very powerful technique, which allows for the identification of key proteins that are highly expressed within the MEJ. Dr. Isakson's group has utilized both primary cell cultures as well as established cell lines in the VCCC, thus this procedure can be modified for use with numerous cell lines and/or tissues freshly isolated from animal models of human disease, such as hypertension. Although I aim to use GECIs, I have extensive experience with BAPTA-based dyes and can utilize these for control experiments and to validate the GECIs.

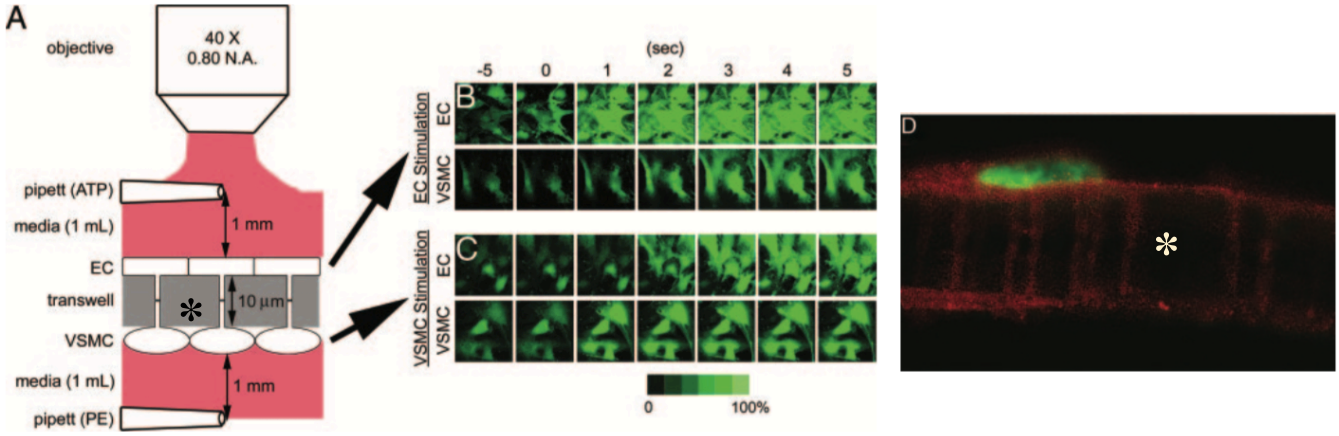

Figure 1. VCCC assay for calcium imaging. (A) ECs and VSMCs were plated on opposite sides of a Transwell membrane. Note the *in vitro* MEJ is present within the Transwell (indicated with a *). Both cell types were loaded with Fluo-4, AM (a BAPTA-based calcium indicator), and then stimulated with ATP (B) or phenylephrine (PE, C) to stimulate calcium activity in ECs and VSMCs, respectively. Images were acquired with a 40x 0.80 NA objective, using an Olympus confocal microscope. Once the VGCC protocol is established at Texas A&M, we can utilize a higher NA objective, and more sensitive detectors on our confocal microscope then used previously. (D) Calnexin was used to stain the ER (nucleus in green) and was found to be expressed in the *in vitro* MEJ. These data demonstrate that calcium stores are present in the MEJ, and thus are likely to be initiating focal calcium signals. Figure modified from Isakson, et al.[7]

In addition, Dr. Isakson's group has developed a method for transfecting isolated arteries,[11] that taken together with my previous experience in calcium imaging and examination of arterial function in diseased and non-diseased states, will allow me to be competitive for grants and will allow me to ask and answer novel questions in the field of microcirculation. The overarching goal of the Research Career Enhancement award is to spend time in the laboratory of Dr. Isakson to learn the VCCC and the transfection protocols so that I can establish these protocols at Texas A&M where I am currently an Assistant Professor. The overarching goal is to establish *in vitro* assays and further develop techniques in isolated vessels to identify signaling events within the MEJ in health and disease. The specific aims that I hope to achieve are found below:

Aim 1: Transfect cultured ECs and SMCs with a GCamP and RCaMP sensor, respectively, to establish an *in vitro* model to correspond with the dual-sensor transgenic mice described above. The main questions to be answered are:

a. Can focal events be observed in culture as in isolated arteries?
b. Can we observe signals (such as calcium) transfer between one cell type and another?
c. Are key calcium signaling molecules highly localized to the MEJ?

Aim 2: Transfect isolated blood vessels with constructs to allow for the knockdown of proteins specific to the calcium signaling cascade in SMCs and/or ECs. In particular, the aim is to by-pass issues with non-specific pharmacological blockers. The question to be answered is:

a. Can we observe functional and calcium signaling defects in arteries when MEJ specific signaling pathways are impaired?

Physiological Significance

It is worth noting that focal calcium events in the VCCC system have not been imaged previously, likely due to the limitations of confocal microscopes (working distance of objectives, intensity of fluorescence, detection of indicators). One extremely novel aspect of this project will be our ability to address many of these issues (long working distance (>1.5 mm), high NA objectives, distinct GECIs for resolution of cell-type specific events and high sensitivity GaAsP detectors), thus allowing for the spatiotemporal resolution of events that would not have been observable previously. Therefore, it is possible to study focal calcium events, which are are now considered key signals in health and disease. Long term, this model could be used to screen and develop pharmaceutical and/or therapeutic treatments for various vascular disorders.

Citations

1. Dora, K. A. *et al.* Myoendothelial gap junctions may provide the pathway for EDHF in mouse mesenteric artery. *J Vasc Res* **40**, 480-490, doi:74549 (2003).
2. McSherry, I. N. *et al.* A role for heterocellular coupling and EETs in dilation of rat cremaster arteries. *Microcirculation* **13**, 119-130, doi:10.1080/10739680500466400 (2006).
3. Billaud, M. *et al.* Regulation of cellular communication by signaling microdomains in the blood vessel wall. *Pharmacol Rev* **66**, 513-569, doi:10.1124/pr.112.007351 (2014).
4. Bagher, P., Garland, C. J. & Dora, K. A. Ca2+ influx through vascular smooth muscle cell voltage-gated Ca2+ channels increases endothelial cell Ca2+ to evoke vasodilation. *FASEB J* **29**, 795.794 (2015).
5. Bagher, P. *et al.* Low intravascular pressure activates endothelial cell TRPV4 channels, local Ca2+ events, and IKCa channels, reducing arteriolar tone. *Proc Natl Acad Sci U S A* **109**, 18174-18179, doi:10.1073/pnas.1211946109 (2012).
6. Sonkusare, S. K. *et al.* Elementary Ca2+ signals through endothelial TRPV4 channels regulate vascular function. *Science* **336**, 597-601, doi:10.1126/science.1216283 (2012).
7. Isakson, B. E., Ramos, S. I. & Duling, B. R. Ca2+ and inositol 1,4,5-trisphosphate-mediated signaling across the myoendothelial junction. *Circ Res* **100**, 246-254, doi:10.1161/01.RES.0000257744.23795.93 (2007).
8. Sonkusare, S. K. *et al.* AKAP150-dependent cooperative TRPV4 channel gating is central to endothelium-dependent vasodilation and is disrupted in hypertension. *Sci Signal* **7**, ra66, doi:10.1126/scisignal.2005052 (2014).
9. Boerman, E. M., Everhart, J. E. & Segal, S. S. Advanced age decreases local calcium signaling in endothelium of mouse mesenteric arteries in vivo. *Am J Physiol Heart Circ Physiol*, ajpheart 00038 02016, doi:10.1152/ajpheart.00038.2016 (2016).
10. Isakson, B. E. & Duling, B. R. Heterocellular contact at the myoendothelial junction influences gap junction organization. *Circ Res* **97**, 44-51, doi:10.1161/01.RES.0000173461.36221.2e (2005).
11. Straub, A. C. *et al.* Endothelial cell expression of haemoglobin alpha regulates nitric oxide signalling. *Nature* **491**, 473-477, doi:10.1038/nature11626 (2012).

The goal of the current proposal is to develop high-resolution imaging techniques to examine elementary calcium signaling events in the established vascular cell co-culture (VCCC) assay. Dr. Brant Isakson's group at the University of Virginia has developed the VCCC assay and I am currently applying for an APS Research Career Enhancement Award to go and learn this technique. In brief, endothelial cells are seeded on one side of a transwell membrane, while vascular smooth muscle cells are seeded on the opposite side of the membrane. Small holes within the transwell membrane allows for extension of the two cell types to penetrate and interact, in a manner very similar to how these cells interact and communicate *in vivo*. To date focal calcium events have yet to be resolved using the VCCC technique; however, I believe the technical expertise in calcium imaging I developed as a post-doctoral fellow can overcome these challenges. I have previous research experience in molecular biology, calcium imaging and microvascular physiology with a particular focus on blood flow regulation. Although I have skills in a wide range of experimental techniques, one aspect of my research program is currently lacking, namely a cell culture assay to examine heterocellular communication between endothelial cells and vascular smooth muscle cells of the vascular wall. Using my expertise in calcium imaging, the aim is to resolve focal calcium events using the VCCC technique. Below I have detailed my academic career to date and have highlighted the techniques and questions that defines my current research program at Texas A&M Health Science Center. There are two key areas of interest that I am currently developing in the lab, both of which can be strengthened by incorporating the techniques I will learn as a Research Career Enhancement Fellow. The two key areas (highlighted further below) that I am pursuing are 1) calcium imaging in GECI mice and 2) examination of elementary calcium events in rodent models of hypertension.

Career Development

My career to-date has involved collaboration with some of the leading scientists in my field. During my doctoral work at Cornell University, which utilized primarily molecular biological techniques, I examined the role of an E3 ubiquitin ligase in cardiac development under the mentorship of Dr. Teresa Gunn. Professor Michael Kotlikoff, who was the Departmental Chair, focused heavily on developing mouse models expressing genetically encoded calcium indicator (GECI) molecules, thus sparking my interest in calcium imaging. I then joined the laboratory of Professor Steven Segal as a postdoctoral fellow at the University of Missouri where I examined blood flow regulation in the microcirculation *in vivo*, in particular in 1) mice expressing a GECI and 2) mouse models of Duchenne Muscular Dystrophy. This interest in imaging calcium in GECI mice has continued, and has advanced with the development of improved indicators. Although my research group is in its early days, we aim to utilize GECI-mice to examine calcium activity in blood vessels in non-diseased and diseased states. We have access to a wide range of GECI-mouse lines and indeed are beginning to acquire and breed the mice to establish colonies at Texas A&M Health Science Center.

In early 2011, I moved to the University of Oxford to work as a postdoctoral fellow in the laboratory of Profs. Kim Dora and Christopher Garland where I became proficient at *in vitro* techniques for examining blood vessel function as well as measuring calcium changes in both endothelial and vascular smooth muscle cells. Our work has identified a novel role for endothelial cell Transient Receptor Potential Cation Channels Subfamily V Member 4 (TRPV4) in the modulation of arteriolar tone at low intraluminal pressure, which was published in the Proceedings of the National Academy of Sciences in late 2012 and has been highly cited since. This discovery has had major implications for our understanding of myogenic tone and the mechanism by which it is regulated normally, and under pathophysiological conditions, such as

hypertension. It also sparked my current interest and focus on rodent models of hypertension.

In September 2014, I transitioned from a postdoctoral fellow to an academic post (non-tenure track) at the University of Oxford, and in doing began to carve a niche for myself in studying the interface between perivascular nerves and the resistance arterioles they innervate. In my own group at the University of Oxford, I examined contractile responses to adrenergic receptor activation (both to exogenous and direct nerve activation) in pre-spontaneously hypertensive rats (preSHR). Preliminary data suggests even prior to alterations in blood pressure, pre-SHRs exhibit hyperreactivity to adrenergic stimulation compared to WKY control rats. One possibility is to alter the VCCC technique to also co-culture neuronal cells, making an assay even more representative of an intact arterial wall.

In March 2016, I transitioned to a tenure-track faculty position in the Department of Medical Physiology at Texas A&M Health Science Center; with the support of the Dean and the Departmental Chair I utilized a portion of my start-up funds to invest in the microscopy equipment required for the current application. Texas A&M has historically had strength in vascular and lymphatic physiology and thus is an ideal department to further develop the VCCC technique.

Current Funding

In 2014, I was awarded a Project Grant as a co-Principal Investigator, in conjunction with Profs. Kim Dora and Christopher Garland, from the British Heart Foundation (BHF) in the UK. This grant is based on a novel, technically challenging methodology, namely calcium imaging in freshly dissociated endothelial cell tubes, a technique which I learned during my initial post-doctoral fellowship at the University of Missouri and that I further established at the University of Oxford. Prior to leaving the University of Oxford, I was awarded a Medical Research Fund Pump-Priming Award from the University of Oxford to examine neurovascular defects in a rodent model of Duchenne muscular dystrophy (mdx). These awards highlight my ability to secure independent funding, a trend I hope will continue after I learn and implement the VCCC technique as a part of my research program. I believe that Texas A&M provides an outstanding infrastructure that would allow for the development of my academic career and the support to implement the techniques I would learn as a Research Career Enhancement Fellow.

Budget Justification

Travel/Lodging	Approximate Cost	
Travel	$600.00	
Lodging	$3,500.00	
	Sub-Total A	$4,100.00
Project Reagents	**Approximate Cost**	
Imaging Chamber	$800.00	
Cell Lines	$3,000.00	
Transfection Reagents	$3,500.00	
Culture Reagents	$3,500.00	
Calcium Indicators	$1,000.00	
Microdissection Instruments	$800.00	
Transwell Membranes	$300.00	
siRNA	$2,000.00	
	Sub-Total B	$14,900.00
	Total	**$19,000.00**

Current and Pending Support

Bagher, Pooneh

Active

PG/14/58/30998 (Bagher- Co-I) 01/01/15-12/31/17
British Heart Foundation $250,000 total project
Investigation of endothelial cell signaling in freshly isolated

Start Up Funding 2016-2019
Texas A&M Health Science Center $750,000 total start-up

Pending

16SDG30480000 (Bagher – PI) 07/01/16-06/30/19 1.8 cal mths
American Heart Assn. SW SDG $210,000 total project
Elementary Calcium Signaling Events in a Rodent Model of Hypertension
The aim of this application is to test the hypothesis that KCa-dependent feedback vasodilation is impaired and thus is a potential culprit in the etiology of hypertension.

COLLEGE OF MEDICINE
TEMPLE CAMPUS

HEALTH SCIENCE CENTER

Department of Medical Physiology

TEXAS A&M UNIVERSITY

May 7, 2016

Re: Dr. Pooneh Bagher's Application for the APS Research Career Enhancement Award

To Whom It May Concern:

The applicant, Dr. Pooneh Bagher, is a new recruit to the Department of Medical Physiology at the Texas A&M University Health Science Center. Her appointment in our department at the rank of Assistant Professor began March 15, 2016. Prior to appointment in our department, Dr. Bagher was in a non-tenured faculty position at the University of Oxford in the United Kingdom. In this role in the UK, Dr. Bagher was successful in securing independent funding in the form of a Seed Award from the Medical Research Fund at the University of Oxford, as well as serving as a co-PI on a Project Grant from the British Heart Foundation (BHF), which is the United Kingdom equivalent to the American Heart Association. As a scientific trainee in the US, Dr. Bagher was successful in securing externally reviewed funding from the NIH as an F32 Ruth L. Kirschstein National Research Service Award Postdoctoral Fellow and as a Predoctoral Fellow from the Northeastern Affiliate of the AHA. This record provides a strong indication that even at this early stage in her scientific career she is a strong, successful grant candidate.

Dr. Bagher's application to the APS Research Career Enhancement Award is of particular importance as it provides her the opportunity to learn techniques in the laboratory of Dr. Brant Isakson at the University of Virginia, which will significantly strengthen her research program. In particular, she will learn the vascular co-culture technique developed by the Isakson group with the aim of developing an in vitro model that can be used in parallel to the mouse vascular models she has used previously and will continue to use for calcium imaging experiments. In particular, Dr. Bagher is currently in the process of acquiring and breeding mice expressing two unique genetically-encoded calcium indicators specifically in the cells that comprise the arterial wall (a GFP-based sensor in endothelial cells, and an RFP-based sensor in smooth muscle cells). She aims to express these same indicators in cultured endothelial cells and smooth muscle cells, respectively, and then perform high resolution calcium imaging studies. It should be noted that the unique imaging equipment required to complete the proposed experiments are provided through contributions made by the department, the TAMU Dean of Medicine, and the candidate's startup funding. Indeed, Dr. Bagher was the first individual in the world to purchase the new model of the Olympus FV3000 with significantly enhanced optics and detectors that have the capability to image these cells and tissues with higher spatial and temporal resolution than previously possible using genetically-encoded calcium indicators. Dr. Bagher is uniquely qualified to carry out the proposed experiments having trained in prominent molecular, *in vivo*, and *in vitro* physiology and pharmacology laboratories. In particular, Dr. Bagher has gained great experience with calcium imaging techniques through her training and has published her work in high-impact journals.

The Department of Medical Physiology is world leading in cardiovascular physiology, particularly in the arena of microcirculation research, and provides Dr. Bagher the infrastructure and support needed to establish the techniques she will learn at the University of Virginia in her own laboratory. Dr. Bagher has nearly 1200 square feet of lab space, in the form of 6 laboratory benches, a cell/tissue culture room, and 2 separate imaging rooms. In addition, several pieces of specialized equipment and resources are already available within the department to aid the proposed work including a significant

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[redacted]

number of other confocal, multiphoton, TIRF and scanning probe imaging workstations within the Integrated Microscopy and Imaging Laboratory Core headquartered in our department. Additionally, a suite of experimental equipment has been moved with Dr. Bagher's laboratory from the University of Oxford to Texas A&M University Health Science Center, which will provide further equipment required to establish the techniques she will learn at the University of Virginia.

Although she is an early career scientist, Dr. Bagher has been invited to speak at national and international meetings and symposia, has been asked to contribute as an expert panelist for webinars, as well as having been invited to write editorials for prominent cardiovascular journals. Dr. Bagher is making a name for herself in the fields of microcirculation, calcium imaging, and physiology, and her work represents both the state of the art as well as the future of calcium-dependent pathways in health and disease. She was recently invited to contribute to a book compiled by the Physiological Society (the United Kingdom equivalent to the APS), not only celebrating 100 years of women membership in the society, but also highlighting top female physiologists.

Our department has developed an intensive mentoring plan for our junior faculty that utilizes the expertise of internal and external successful senior faculty that meet with the junior faculty at least twice a year to provide feedback and guidance on their career trajectory, as well as other critical professional skills development. As part of this mentoring plan we expect the mentee to be preparing and submitting proposals to granting agencies by the end of their first year and position themselves to submit independent proposals to NIH by the end of year 2 of their probationary period. I believe this additional training opportunity will allow Dr. Bagher to submit a more competitive NIH proposal. The unique techniques she will learn from Dr. Isakson will provide the additional tools that will help her answer questions on vascular function at scales from the molecule to the whole animal level. I have known Pooneh since she was a senior graduate student and have specifically followed her career as I recognized her great potential as a future faculty. Thus I believe that Dr. Bagher has outstanding potential to develop a successful career as an independent scientific investigator and I have long thought she would eventually become a leader in her field. The opportunity provided by the APS in this grant program would be an excellent step for Dr. Bagher to advance her career as a PI and advance the cause of the APS to foster scientific research and develop the next generation of physiologists.

Sincerely,

David C. Zawieja, Ph.D.
Regents Professor and Interim Chair

UNIVERSITY of VIRGINIA
SCHOOL OF MEDICINE

The Robert M. Berne Cardiovascular Research Center

May 11, 2016

Re: Pooneh Bagher's Research Career Enhancement Application

To Whom It May Concern:

I am delighted to write this letter of invitation for Dr. Pooneh Bagher to visit my lab here at the University of Virginia in Charlottesville. Pooneh and I have interacted in many instances over the last 5 years and we share a long-standing common interest in microvasculature heterocellular communication.

My lab has an "open door" policy in terms of visiting faculty members and students, where we foster a transparent and mutual learning environment. This includes access to any of our resources and our techniques that could benefit Pooneh, especially as an early stage investigator. In the short 8 years since my lab started, we have hosted over 10 different foreign and domestic faculty members or students to learn various techniques (e.g., vascular cell co-culture, electron microscopy) for various amounts of time (2 weeks to 2 months). In particular, Pooneh would like to utilize our vascular cell co-culture technique (e.g., *Circ Res*, 2005; *Nature* 2012) to drive mechanistic and cellular concepts into her work. Pooneh would also like to attempt transfection of arterioles as we had previously reported (*Circ Res* 2012). We would of course be delighted to teach her the vascular cell co-culture model and our arterial transfection techniques. There is ample space for her to set up a "mini-office" during her time here and I have already commissioned a graduate student (Ms. Lauren Biwer) to help with the vascular cell co-culture, and a post-doc (Dr. Miranda Good) to help facilitate the arterial transfection work.

Lastly, in addition to time spent in my lab, Pooneh would also have the opportunity to discuss shared scientific concepts and ideas with other colleagues here at UVA including Swapnil Sonkusare, Gary Owens, Shayn Peirce-Cottler and Avril Somlyo. In particular, Drs. Somlyo and Sonkusare and I share a weekly journal club that Pooneh would certainly enjoy participating in.

I really look forward to getting underway!

Sincerely,

Brant E Isakson, PhD
Resident Faculty, Robert M. Berne Cardiovascular Research Center
Associate Professor, Dept of Molecular Physiology and Biophysics
University of Virginia School of Medicine
[redacted]

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: Brant E. Isakson

eRA COMMONS USER NAME (credential, e.g., agency login): BEI6NNIH

POSITION TITLE: Associate Professor in Molecular Physiology and Biophysics

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Gustavus Adolphus College, Saint Peter, MN	B.A.	05/1998	Biology
University of Wyoming, Laramie, WY	Ph.D.	12/2002	Physiology
University of Wyoming, Laramie, WY		2003	Cell-cell Communication
University of Virginia, Charlottesville, VA		2006	Cell-cell Communication

A. Personal Statement

My research has been focused on cellular communication throughout the length of my career, including *the means* by which cells communicate (e.g., connexins and pannexins) and *the how* of cell communication (e.g., ATP, IP_3/Ca^{2+} and nitric oxide), especially in the blood vessel wall of microcirculatory arterioles and venules. The combination of these projects has recently been synthesized into a broad discussion on their potential role in cellular signaling microdomains (*Pharm Rev*, 2014). The ethos of our lab focuses on moving the field forward with creative ideas supported by several different lines of evidence. This is usually done by employing several different methods and working from whole animal physiology down to biophysical protein behavior. The creates a laborious load, but it has been very rewarding with over 6 different editorials (e.g., in *Nature*, *Science Signaling* and *Circ Res*) accompanying our work over a 6 year time period.

B. Positions and Honors

Positions and Employment

2001	Visiting Scholar, Wales Heart Research Institute, University of Wales, Cardiff UK
2003	Post-doctoral Researcher, Department of Physiology, University of Wyoming, Laramie, WY
2003-2006	Post-doctoral Researcher, Department of Molecular Physiology and Biological Physics, University of Virginia, Charlottesville, VA
2006-2007	Instructor of Research, Department of Molecular Physiology and Biological Physics, University of Virginia
2007	Assistant Professor of Research, Department of Molecular Physiology and Biological Physics, University of Virginia
2007-2012	Assistant Professor, Department of Molecular Physiology and Biological Physics, University of Virginia
2007-present	Resident Faculty Member, Robert M. Berne Cardiovascular Research Center, University of Virginia
2012-present	Associate Professor, Department of Molecular Physiology and Biological Physics, University of Virginia
2015-present	*Tenure*, Department of Molecular Physiology and Biological Physics, University of Virginia

Other Experience

2007	Chairperson, Experimental Biology 2007 Featured Topic: “Gap Junctions Mediating Cell-Cell Communication in the Vasculature”
2007	Chairperson, Experimental Biology 2007 Featured Topic: “Gap Junctions Mediating Cell-Cell Communication in the Vasculature”

2008	Co-chair, International Symposium on Resistance arteries Topic Session: "Cellular communication within and across the vascular wall"
2008	Chairperson, Experimental Biology 2008 Featured Topic: "Intercellular calcium communication in the vasculature"
2009	Chairperson, Gap Junction Conference Session: Vascular Connexins
2009	Co-chairperson, Experimental Biology 2009 NAVBO/AAA Joint Symposium: "Smooth Muscle Cells"
2011	Scientific Oversight Committee, European Microcirculation Society Meeting
2011	Chairperson, Experimental Biology 2011 Featured Topic: "Signaling microdomains in the vasculature"
2013	Chairperson, Conference Committee, Microcirculatory Society, Joint MCS/NAVBO Meeting
2013	Co-Organizer, 2013 International Gap Junction Conference, Charleston South Carolina
2014	Chairperson, Conference Committee, Microcirculatory Society, Joint MCS/NAVBO Meeting
2015	Co-Organizer, Vasculata, NAVBO
2017	Chair, Experimental Biology 2017 Featured Topic: "New perspectives on vascular Diseases"

Society Membership

2008-present	North American Vascular Biology Organization
2006-present	American Heart Association
2006-present	Microcirculatory Society

1. Chair, Publication Committee, 2011-present
2. Chair, Communications Committee, 2009-2011
3. Elected, Councilor Microcirculatory Society, 2011-2015

2000-present	American Physiological Society

4. Fellowship Committee, 2010-2014

Study Sections

2008-2011	Study Section; American Heart Association; Cardiac Biology/Regulation
2008-2009	Reviewer, British Diabetes Association
2009-2010	Reviewer, Diabetes Australia
2011	NIH, Ad-hoc, Study Section: *Atherosclerosis and Inflammation in the CV System*
2012-present	Reviewer, British Heart Foundation
2012-present	Chair; American Heart Association; *Blood Pressure Regulation*
2014	NIH, Ad-hoc, Study Section: *Sepsis and the Vasculature*
2014-present	IH, Ad-hoc, *Microcirculation and Hypertension* Study Section

Editorial Boards

2011-2016	Editorial Consultant, *Biochemical Journal*
2012-2017	Editorial Board, *Journal of Biological Chemistry*
2013-2017	Associate Editor, *Microcirculation*
2014	Guest Editor, *FEBS Letters*
2016	Guest Editor, *Antioxidant and Redox Signaling*
Ad Hocs	*Nature; Science; Journal of Clinical Investigation; Nature Cell Biology; Circulation Research; Hypertension; ATVB; American Journal of Physiology; Nature Communications; Science Advances; Nature Medicine*

Honors

1998	Sigma Xi, Gustavus Adolphus College
2005	Norton B. Gilula Award, International Gap Junction Committee
2007	Bristol Meyer-Squibb Young Investigator Award
2017	Bowditch Lecture from the American Physiological Society

Patents/Licensed Products

---U.S. Patent Serial No. 14,437,548; "Compositions and Methods for Regulating Arterial Tone"
---U.S. Provisional Patent Serial No. 62/115,685 "Compositions and Methods for Regulating Blood Pressure"
---Millipore Corp. license (ABN1681) for "Panx1-Tyr198 Antibody"

C. Contributions to Science

1) **Vascular heterocellular communication:** My work on heterocellular communication initially began in the epithelium of the lung, where I studied how two different cell types, the alveolar type 1 and alveolar type 2 cells coordinated calcium communication via gap junction and ATP (*Am J Respir Cell Mol Biol*, 2003). I followed this theme to my post-doctoral work with Dr. Brian Duling by moving to the vasculature so as to identify how endothelium and smooth muscle cells of the microcirculation utilize the anatomical structure termed the myoendothelial junction to regulate calcium signaling (e.g., *Circ Res* 2005; 2007). It soon became evident that in order to fully appreciate the myoendothelial junction as a unique signaling domain, we had to be able to isolate and perform biochemical analysis using complex proteomic arrays, such as 2D gel electrophoresis (*Circ Res* 2010). One of the key discoveries that was made based on this analysis was that eNOS was consistently enriched at myoendothelial junctions, regardless of vascular bed (*ATV*B, 2011). This was functionally a logical outcome considering that after stimulation of a resistance artery with a smooth muscle cell-specific vasoconstrictor, the artery spontaneously relaxes by a process dependent on NO release from endothelium (*J Cell Sci* 2008; *ATVB*, 2011). Thus, the localization of the eNOS served to provide a rapid negative feedback. However, regardless of NO increases at the MEJ and increases of cGMP in smooth muscle cells after application of a vasoconstrictor, we noted that there was no detectable NO diffusing out into the endothelial monolayer or lumen, indicating possible consumption or trap of NO. In this way, NO was being produced and used locally in the vessel wall. We found that alpha globint was dramatically enriched in endothelium (*Nature*, 2012). In the same paper, we demonstrated that the alpha globin at the endothelial myoendothelial junction formed a macromolecular complex with eNOS (*Nature*, 2012). We have taken advantage of this unique interaction to design interfering peptides that we show can increase NO in isolated arterioles and lower system-wide blood pressure (HbαX; *ATVB*, 2014).

   a) **Isakson BE**, Ramos SI, Duling BR. Ca^{2+} and inositol 1,4,5-trisphosphate mediated signaling across the myoendothelial junction. *Circ Res*. 2007 Feb 2;100(2):246-54. PMID: 17218602
   b) Heberlein KR, Straub AC, Best AK, Greyson MA, Looft-Wilson RC, Sharma PR, Meher A, Leitinger N, **Isakson BE**. Plasminogen activator inhibitor-1 regulates myoendothelial junction formation. *Circ Res*. 2010 Apr 2;106(6):1092-102. doi: 10.1161/CIRCRESAHA.109.215723. PMID: 20133900;PMCID: PMC2848897
      -Editorial: Segal SS, Bagher P. Regulation of myoendothelial junction formation: bridging the gap. *Circ Res*. 2010 Apr2;106(6):1014-6. doi: 10.1161/CIRCRESAHA.110.217786. PMID: 20360262; PMCID: PMC2865428
   c) Straub AC, Lohman AW, Billaud M, Johnstone SR, Dwyer ST, Lee MY, Bortz PS, Best AK, Columbus L, Gaston B, **Isakson BE**. Endothelial cell expression of haemoglobin α regulates nitric oxide signaling. *Nature*. 2012 Nov 15;491(7424):473-7. doi: 10.1038/nature11626. PMID: 23123858; PMCID: PMC3531883
      -News and Views Commentary: Gladwin MT, Kim-Shapiro DB. Vascular biology: Nitric oxide caught in traffic. *Nature*. 2012 Nov 15;491(7424):344-5. doi: 10.1038/nature11640. PMID: 23123855
      -Faculty of 1000 "Must Read"
      -Science Signaling Editors' Choice
   d) Billaud M, Lohman AW, Johnstone SR, Biwer LA, Mutchler S, **Isakson BE**. Regulation of cellular communication by signaling microdomains in the blood vessel wall. *Pharmacol Review.* 2014 Mar 26;66(2):513-69. doi: 10.1124/pr.112.007351. PMID: 24671377; PMCID: PMC3973613
   e) Straub AC, Butcher JT, Billaud M, Mutchler SM, Artamonov MV, Nguyen AT, Johnson T, Best AK, Miller MP, Palmer LA, Columbus L, Somlyo AV, Le TH, **Isakson BE**. Hemoglobin α/eNOS coupling at myoendothelial junction is required for nitric oxide scavenging during vasoconstriction. *Arterioscler Thromb Vasc Biol.*2014 Dec;34(12):2594-600. doi: 10.1161/ATVBAHA.114.303974. PMID: 25278292; PMCID: PMC4239174
      -Editors Choice, December 2014

2) **Pannexin-based signaling in the vasculature.** As my lab developed, we began to examine role that smooth muscle cells were playing in regulating the cellular communication cross-talk with endothelium. In the process of these studies, we observed by electron microscopy that in resistance arteries on down the vascular tree, that smooth muscle cells had large gap between them, making any kind of gap junction based communication difficult. For this reason we began to explore the possibility that pannexin proteins, a closely related protein family member to connexin proteins that functions as an ATP release channel

(*Nature*, 2010), could fulfill the need for direct cellular contact between smooth muscle cells. Indeed, we found that only the pannexin isoform Pannexin1 was expressed throughout smooth muscle cells of the microcirculation (but not in smooth muscle of the large arteries; *Circ Res*, 2011) and that pannexin1 release of ATP was mediated only by activation of the α1D-adrenergic receptor (*Circ Res*, 2011) and could be regulated by S-nitrosylation of the channel (*J Biol Chem*, 2012). This work has been expanded to further show that the sympathetic stimulation and consequent vasoconstriction is unique to a pannexin1-α1-adrenergic receptor axis that can regulate blood pressure by activation of a unique tyrosine kinase reside on the channel (*Science Signaling*, 2015). We have recently pushed this work forward by examining the role of pannexin1 in the endothelium and found that the ATP released from veinous endothelium specifically is enough to completely regulate the acute inflammatory response (*Nature Communications*, 2015).

a) Chekeni FB, Elliott MR, Sandilos JK, Walk SF, Kinchen JM, Lazarowski ER, Armstrong AJ, Penuela S, Laird DW, Salvesen GS, **Isakson BE**, Bayliss DA, Ravichandran KS. Pannexin 1 channels mediate 'find-me' signal release and membrane permeability during apoptosis. *Nature.* 2010 Oct 14;467(7317):863-7. doi: 10.1038/nature09413. PMID: 20944749; PMCID: PMC3006164
b) Billaud, M, Lohman AW, Straub AC, Looft-Wilson R, Johnstone SR, Araj CA, Best AK, Chekeni FB, Ravichandran KS, Penuela S, Laird DW, **Isakson BE**. Pannexin1 regulates α1-adrenergic receptor-mediated vasoconstriction. *Circ Res.* 2011 Jun 24;109(1):80-5. doi: 10.1161/CIRCRESAHA.110.237594. PMID: 21546608; PMCID: PMC3135971
    -Journal cover art
    -Commentary: Williams R. Pannexin1 in the regulation of vasoconstriction. *Circ Res.* 2011;109:1.
    -Faculty of 1000 "Must Read"
c) Billaud M, Chiu YH, Lohman AW, Parpaite T, Butcher JT, Mutchler SM, DeLalio LJ, Artamonov MV, Sandilos JK, Best AK, Somlyo AV, Thompson RJ, Le TH, Ravichandran KS Bayliss DA, **Isakson BE**. A molecular signature in the pannexin 1 intracellular loop confers channel activation by the α1 adrenoreceptor in smooth muscle cells. *Sci Signal.* 2015 Feb 17;8(364):ra17. doi: 10.1126/scisignal.2005824. PMID: 25690012; PMCID: PMC4358815
    -Perspectives: Nielsen MS. Sympathetic vasoconstriction takes an unexpected pannexin detour. *Sci Signal.* 2015 Feb 17;8(364):fs4. doi: 10.1126/scisignal.aaa7312, 2015. PMID: 25690011
d) Lohman AW, Leskov IL, Butcher JT, Johnstone SR, Stokes TA, Begandt D, DeLalio LJ, Best AK, penuela S, Leitinger N, Ravichandran KS, Stokes KY, **Isakson BE**. Pannexin 1 channels regulate leukocyte emigration through the venous endothelium during acute inflammation*. Nat Comm.* 2015 Aug 5;6:7965. doi: 10.1038/ncomms8965, 2015. PMID: 26242575; PMCID: PMC4824045

Current complete list of articles (with two manuscripts currently *In Press*):
[redacted]

D. Research Support

Ivy Translation Fund (Isakson, B/Columbus, L; Co-PI) 03/01/2015 – 02/28/2017
Ivy Foundation
This grant attempts to move the patented HbαX peptide into a more clinical role by developing toxicity tests in mice, and further refinement of the HbαX structure by developing circular peptides. Modes of delivery are also being investigated.
Role: Co-PI

R37 HL058091 (D Kim-Shapiro PI) 06/01/2008-05/31/2017
NIH/NHLBI
Effects of nitric oxide in sickle bell blood
This grant focuses on the role of nitric oxide and the potential clinical value of NO-derived metabolites during blood transfusions in normal and obese individuals in the case of sickle cell and without. Our portion of the grant focuses the detrimental effects on the vasculature, including changes in blood pressure and vasoreactivity.
Role: Investigator

1 R01 HL728665 (Epstein, F PI) 07/01/2013 – 06/30/2018

NIH/GM
MRI as an imaging module for coronary artery disease
In this grant application, we examine heart function in several different pathological states focused on new methods and techniques to diagnose with MRI technology. Experiments performed by Isakson will be focused on confirming imaging results with wire-myograph coronary arteries and consultation regarding microcirculatory blood flow dynamics.
Role: Co-I

2 R01 HL088554 (Isakson, B PI) 06/01/2014 – 01/31/2019
NIH/NHLBI
Mechanisms of Heterocellular Signaling at the Myoendothelial Junction
The methods by which vascular cells communicate is key for understanding vascular processes such as hypertension and control of blood flow. Our model and the experiments proposed offer the first opportunity to investigate the capabilities of the myoendothelial junction and to understand its role in the vessel wall. We propose to study the ways in which vascular cells utilize this structure to maintain vascular function.
Role: PI

1 P01 HL120840 (Ravichandran, K PI) 07/01/2014 – 05/31/2019
NIH/NHLBI
Pannexin channels in vascular physiology and inflammation
We hypothesize that regulation of pannexin channel function may be an important component to peripheral vascular resistance and by extension blood pressure. To test this hypothesis, we put forth three specific aims: 1) Panx1 is a selective purine pore in smooth muscle, 2) Panx1 is active after α1D-adrenegic receptor activation, and 3) Panx1 can regulate peripheral resistance in the circulation. Appropriate tests for each specific aim integrate novel pharmacological tools, molecular techniques and mouse models.
Role: PI on Project 2 ($250,000/year directs)

Completed Research Support (last 3 years)
Clinical Research Breakthrough Initiative (Isakson, B PI) 01/01/2014 – 03/31/2016
UVA Clinical Research Fund
This focus of this work will be determine if pannexin can be targeted for pharmacological interventions, especially as it relates to human patients with treatment-resistant hypertension. In all cases, human arterioles will be used exclusively for testing potential new small molecule inhibitors.
Role: PI

Current Academic Position

Assistant Professor, *Texas A&M Health Science Center*, Temple, TX, 2016- present

Previous Academic Position

MSc Course Director, *University of Oxford,* Oxford, UK, 2014-2016

Education

Cornell University, Ithaca, New York, 2003-2007
Ph.D. in Molecular and Integrative Physiology
Areas of Specialization: Systems Physiology and Physiological Genomics

University of Scranton, Scranton, PA, 2000-2003
BSc in Neuroscience
BSc in Biomathematics, concentration in Physiology
Minor: Biochemistry
summa cum laude

Texas Academy of Mathematics and Science (TAMS), Denton, TX, 1998-2000
Residential early admission program at the University of North Texas

Research Experience

Postdoctoral Research:
Department of Pharmacology, University of Oxford, 2011- 2014
Advisors: Christopher Garland, Ph.D. and Kim Dora, Ph.D.
Examine the role of intracellular calcium in the regulation of blood flow *in vitro* using pressure myography and freshly isolated endothelial cells coupled with confocal microscopy.

Department of Medical Pharmacology and Physiology, University of Missouri, 2007-11
Advisor: Steven Segal, Ph.D.
Examined arteriolar function *in vivo* using the exteriorized mouse cremaster preparation in a mouse model of human disease (Duchenne Muscular Dystrophy) as well as examine calcium dynamics and its role in blood flow regulation using a novel transgenic mouse expressing a genetically encoded calcium indicator molecule, GCaMP2.

Doctoral Research:
Department of Molecular and Integrative Physiology, Cornell University, 2003-07
Advisor: Teresa Gunn, Ph.D.
Examined the role of Mahogunin Ring Finger-1, an E3 ubiquitin ligase, in cardiac development and pigmentation using molecular biological techniques and mouse genetics.

Undergraduate Research:

Department of Biology, University of Scranton, Spring 2002-03
Advisor: Terrence Sweeney, Ph.D.
Examined the effect of estrous cycle dependent arterial remodeling in ovarian and uterine arteries of Golden hamsters *in vivo*.

St. Luke's Hospital Research Institute, Summer 2001
Advisor: James Reed, III, Ph.D.
Catalogued statistical techniques used in primary clinical literature.

Teaching Experience

MSc. in Pharmacology Course Director, Dept. of Pharmacology, *University of Oxford*, Michaelmas 2014-2016
Subject: Running, teaching and administrative organization of the MSc. in Pharmacology and admissions.

Lecturer, Magdalen College, *University of Oxford*, Hilary 2014-2016
Subject: Pharmacology and Physiology to first year biomedical and medical students. Topics include G-protein signaling, Starling's Law of the heart, mechanisms of local control of blood flow, renal physiology, and cholinergic and adrenergic signaling. Critical reading with third year biomedical and medical students. Areas of specialty are Cardiovascular, Renal and Respiratory Biology and Cellular Physiology, Signaling and Pharmacology.

Department of Pharmacology Seminar Teaching, *University of Oxford*, Trinity 2013
Subject: Receptor Pharmacology

Tutor, St. Peter's College, *University of Oxford*, Trinity Term 2012
Subject: Pharmacology and Physiology to first year medical students, tutorials covered local anesthetics, pharmacology of the neuromuscular junction, antidysrhythmics, pharmacokinetics, physiological actions of histamine, and receptor pharmacology

Department of Pharmacology Seminar Teaching, *University of Oxford*, Michaelmas 2011-12
Subject: Cholinergic signalling and the neuromuscular junction

Guest Lecturer, *University of Missouri*, Spring 2010
Subject: Skills in Biomedical Research including *in vivo* experimental techniques

Teaching Assistant, *Cornell University*, Autumn 2004
Subject: Introductory Animal Physiology for pre-medical students

Teaching Assistant, *University of Scranton*, Spring 2003
Subject: Drugs and Behavior for non-biology majors

Teaching Assistant, *University of Scranton*, Autumn 2002
Subject: Assisted in the set-up and running of the Behavioral Neuroscience Lab including the neuroanatomy

Publications (top 5 publications indicated with *)**

1) CJ Garland, SV Smirnov, **P Bagher**, CS Lim, CY Huang, R Mitchell, C Stanley, A Pinkney, KA Dora. (2015) The TRPM4 inhibitor 9-phenanthrol activates endothelial cell IK_{Ca} channels in rat isolated mesenteric artery. *British Journal of Pharmacology*. 172 (4): 1114-1123.

2) **P Bagher** and CJ Garland (2014) Scaffolding Builds to Reduce Blood Pressure. *Science Signalling*. 7 (333): 16.

3) KA Turlo, J Scapa, **P Bagher**, AW Jones, R Feil, RJ Korthuis, SS Segal and ML Iruela-Arispe (2013) Beta-1 Integrin is Essential for Vasoregulation and Smooth Muscle Cell Survival *in vivo*. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 33 (10): 2325-2335.

4) TM Gunn, D Silvius, **P Bagher**, K Sun, and KK Walker (2013) MGRN1-Dependent Pigment-Type Switching Requires its Ubiquitination Activity but not its Interaction with TSG101 or NEDD4. *Pigment Cell and Melanoma Research*. 26 (2), 263-268.

5) ***P Bagher**, T Beleznai, Y Kansui, R Mitchell, CJ Garland and KA Dora (2012) Low Intravascular Pressure Activates Endothelial Cell TRPV4 Channels, Local Ca^{2+} Events and IK_{Ca} Channels Reducing Arteriolar Tone. *Proceedings of the National Academy of Sciences*. 109 (44): 18174-18179.

6) **P Bagher**, MJ Davis and SS Segal (2011) Visualizing Calcium Responses to Acetylcholine Convection Along Endothelium of Arteriolar Networks in Cx40(BAC) GCaMP2 Transgenic Mice. *American Journal of Physiology- Heart and Circulatory Physiology*. 301 (3): H794-802.

   Selected as a featured article in the inaugural edition of 'Watch this @ AJP- Heart and Circ'- an online supplement highlighting noteworthy digital videos (January 17, 2011).

7) ***P Bagher** and SS Segal (2011) The Mouse Cremaster Muscle Preparation for Intravital Imaging of the Microcirculation. *Journal of Visualized Experiments*. 52.

8) **P Bagher**, L Polo-Parada and SS Segal (2011). Microiontophoresis and Micromanipulation for Intravital Fluorescence Imaging of the Microcirculation. *Journal of Visualized Experiments*. 52.

9) **P Bagher**, MJ Davis and SS Segal (2011) Intravital Macrozoom Imaging and Automated Analysis of Endothelial Cell Calcium Signals Coincident with Arteriolar Dilation in Cx40(BAC) GCaMP2 Transgenic Mice. *Microcirculation* 18 (4): 331-338.

10) ***P Bagher** and SS Segal (2011) Regulation of Blood Flow in the Microcirculation: Role of Conducted Vasodilation. *Acta Physiologica*. 202 (3): 271-284.

    Review of conducted vasodilation in the special issue "Homage to August Krogh celebrating the 90th anniversary of his Nobel Prize in physiology or medicine." Recognized as one of the top 5 most cited articles in *Acta Physiologica* in 2011.

11) *** **P Bagher**, D Duan and SS Segal (2011) Evidence for Impaired Neurovascular Transmission in a Mouse Model of Duchenne Muscular Dystrophy. *Journal of Applied Physiology* 110 (3): 601-9. * This article was chosen for an editorial

    *JH Lombard (2011) Microcirculation in a Mouse Model of Duchenne Muscular Dystrophy: Another Blow to the Vascular Hypothesis. *Journal of Applied Physiology* 110 (3): 587-588.

12) SS Segal and **P Bagher** (2010) Regulation of Myoendothelial Junction Formation: Bridging the Gap. *Circulation Research*. 106(6): 1014-1016.

13) J Jiao, K Sun, WP Walker, **P Bagher,** CD Cota and TM Gunn (2009) Abnormal regulation of TSG101 in mice with spongiform neurodegeneration. *Biochimica et Biophysica Acta (BBA)- Molecular Basis of Disease*. 1792 (10): 1027-1035.

14) Sweeney TE, **P Bagher**, J Bailey, S Cherra, FN Grisafi, EM Pauli, K Riley, and S Soares (2007) Intravascular pressure and diameter profile of the utero-ovarian resistance artery network: estrous cycle dependent modulation of resistance artery tone. *American Journal of Physiology- Heart and Circulatory*

Physiology. 293(5): H2937-44.

15) ***CD Cota *, **P Bagher***, P Pelc, CO Smith, CR Bodner and TM Gunn (2006) Mice with mutations in *Mahogunin Ring Finger-1* exhibit abnormal patterning of the left-right axis. *Developmental Dynamics*. 235(12):3438-47. *Authors contributed equally to work

16) **P Bagher**, J Jiao, CO Smith, CD Cota and TM Gunn (2006) Characterization of *Mahogunin Ring Finger-1* expression in mice. *Pigment Cell Research*. 19(6): 635-43.

17) J Reed, P Salen and **P Bagher** (2003) Methodological and Statistical Techniques: What do residents really need to know about statistics? *Journal of Medical Systems*. 27(3): 233-238.

International and National Conference Abstracts (First Author)

1) **P Bagher**, CJ Garland and KA Dora. Ca^{2+} Influx Through Vascular Smooth Muscle Cell Voltage-Gated Ca^{2+} Channels Increases Endothelial Cell Ca^{2+} to Evoke Vasodilation. Experimental Biology, March 28-April 1, 2015, Boston, MA. (Poster and Talk).

Invited Speaker- Gabor Kaley Lecture and Complementary Presentations

2) **P Bagher**, CJ Garland and KA Dora. Smooth Muscle Cell and Endothelial Cell Interactions are Required for Phenylephrine-Induced Endothelial Cell Calcium Activity. 64th Annual Meeting of the British Microcirculation Society: Microcirculation as an Interactive Network, April 10-11, 2014, Bristol, UK. (Talk)

Invited Speaker and Moor Instruments Technical Innovation Award Winner

3) **P Bagher**, TZ Beleznai, Y Kansui, R Mitchell, CJ Garland and KA Dora. Low Intravascular Pressure Activates Endothelial Cell TRPV4 Channels, Local Ca^{2+} Events and IK_{Ca} Channels Reducing Arteriolar Tone. Gordon Research Conference and Seminar: Calcium Signalling, June 15-21, 2013, Lucca, Italy. (Poster)

4) **P Bagher**, TZ Beleznai, Y Kansui, R Mitchell, CJ Garland and KA Dora. A Novel Role for Spontaneous Endothelial Cell Calcium Activity in the Vascular Myogenic Response. Experimental Biology, April 20-24, 2013, Boston, MA. (Poster and Talk)

Invited Speaker- Wiggers Award Featured Topic: Novel Pathways Regulating Microvascular Tone and Function

5) **P Bagher**, TZ Beleznai, Y Kansui, CJ Garland and KA Dora. The Role of Spontaneous Endothelial Cell Calcium Events and Intermediate-Conductance Calcium-Activated Potassium Channel Activity in Myogenic Tone Development in Rat Cremasteric Arterioles. Joint Meeting of the British and American Microcirculation Societies, July 4-6, 2012, Oxford, England. (Poster and Talk)

Invited Speaker- Myogenic Mechanisms in the Microcirculation Session

6) **P Bagher**, CJ Garland and KA Dora. A Novel Approach for Imaging Calcium Events Simultaneously in Arteriolar Vascular Smooth Muscle and Endothelial Cells. Experimental Biology, April 21-25, 2012, San Diego, CA. (Poster and Talk)

Invited Speaker- Microcirculatory Society President's Symposium II: Young Investigators Novel Trends

7) **P Bagher**, MJ Davis and SS Segal. Macrozoom Imaging of Endothelial Cell Calcium Signaling in Arteriolar Networks of Cx40BAC-GCaMP2 Transgenic Mice. World Congress of Microcirculation, September 26-28, 2010, Paris, France. (Poster)

8) **P Bagher**, D Duan and SS Segal. Impaired Neurovascular transmission in a mouse model of Duchenne Muscular Dystrophy. Microcirculatory Society Fall Meeting, October 16-17, 2009, Columbia, MO. (Poster)

9) **P Bagher**, MJ Davis and SS Segal, Fast calcium responses along endothelium of arteriolar networks during blood flow. Experimental Biology, April 18-22, 2009, New Orleans, LA. (Poster and Talk)

Invited Speaker- Microcirculatory Society's Young Investigator Symposium

10) **P Bagher**, CD Cota, CO Smith, P Pelc and TM Gunn. Congenital heart defects in *Mahogunin Ring Finger-1* (*Mgrn1*) mutant mice. The Weinstein Cardiovascular Development Conference, May 11-13, 2006, St. Petersburg, FL. (Poster)

Research Funding

Medical Research Fund Pump Priming
"*Neurovascular Transmission in a Mouse Model of Duchenne Muscular Dystrophy*"
Oxford Medical Research Fund
May 2015-May 2016
P Bagher, Principal Investigator
£8,750 (~$13,000)

British Heart Foundation Project Grant
"*Investigation of endothelial cell signalling in freshly isolated tubes"*
British Heart Foundation
January 2015-January 2018
K Dora, P Bagher, CJ Garland Co-Principal Investigators
£177,000 (~$270,000)

Ruth L. Kirschstein National Research Service Award (NRSA) Postdoctoral Fellow
"Fast Calcium Responses Along Arteriolar Endothelium In Vivo"
National Institute of Health
August 2009-February 2011
P Bagher, Principal Investigator

Northeastern Affiliate Predoctoral Fellow
"The Role of Mahogunin Proteins in Cardiac Development"
American Heart Association
June 2006- July 2007
P Bagher, Principal Investigator

Awards and Honors

Invited participant in the ADVANCE Center Roadmap Workshop at Texas A&M University, April 2016
International Judge: 6th International Postgraduate Symposium in Biomedical Sciences at the University of Queensland, Australia
Featured in "Women Physiologists: Centenary Celebrations and Beyond" published by the Physiological Society, which highlights the top 100 women physiologists
Moor Instruments Technical Innovation Award Winner 64th Annual Meeting of the British Microcirculation Society: Microcirculation as an Interactive Network, April 2014
Co-discussion Leader: New Insights into Calcium Signalling, Gordon Research Seminar 2013
Invited Speaker: Wiggers Award Featured Topic: Novel Pathways Regulating Microvascular Tone and Function, Experimental Biology 2013
International Early Career Physiologist Travel Award, Experimental Biology 2013
British Pharmacological Society Bain Memorial Travel Award, Experimental Biology 2013
The Physiological Society Travel Award, Experimental Biology 2013
Co-chair: President's Symposium II: Rapid Fire Discussion of Novel Trends, Experimental Biology

2013
Invited Speaker: Myogenic Mechanisms in the Microcirculation Session, MicroCirc 2012
British Heart Foundation Travel Award, Experimental Biology, 2012
International Early Career Physiologist Travel Award, Experimental Biology, 2012
Invited Speaker: Microcirculatory Society's President's Symposium II: Young Investigators Novel Trends, Experimental Biology 2012
Ruth L. Kirschstein National Research Service Award (NRSA) Postdoctoral Fellow, 2009-2011
Pappenheimer Postdoctoral Travel Award Recipient, Experimental Biology, 2009
Invited Speaker: Microcirculatory Society's Young Investigator Symposium, Experimental Biology, 2009
NIH Training Grant Fellow, 2008-2009
American Heart Association Predoctoral Fellow, Northeast Affiliate, 2006-07
Invited Speaker: Third Annual Biological and Biomedical Sciences Graduate Program Symposium, Cornell University, 2005
Graduated *summa cum laude* from the University of Scranton, 2003
Steven Sawyer Memorial Research Fellow, Summer 2002
Xavier Grant, Merit Based Award, 2000-03
Arrupe Scholarship for Underrepresented Minorities, 2000-03
Deans' List, 2000-2003

Invited Seminar/Symposium/Webinar Speaker

Scientists Empowering Scientists
Webinar- Contributed as an Expert Panelist
Achieving the Impossible: Large Patch Pipettes, Large Tips, Long Tapers and Beveled or Polished Tips
Invited by: Jan Dolzer, Ph.D. and Adair Oesterle
May 5 and May 12, 2016

Celebration of 100 years of Women's Membership of The Physiological Society
The Physiological Society: Hodgkin Huxley House
Microcirculation: Small Vessels, Big Impact
Invited by: Susan Wray, Ph.D.
December 3, 2015

6th International Postgraduate Symposium in Biomedical Sciences
University of Queensland, Australia
Providing Postgraduate Students with Global Opportunities
Invited by: Conrad Sernia, Ph.D.
November 4, 2015

6th International Postgraduate Symposium in Biomedical Sciences
University of Queensland, Australia
Cross-Talk Between Cells of the Arteriolar Wall
Invited by: Conrad Sernia, Ph.D.
November 3, 2015

Department of Medical Physiology Seminar Series
Texas A&M Health Science Center College of Medicine
Pressure-Dependent Regulation of Endothelial Cell Calcium: A Role for TRPV4 Channels

Invited by: Xu Peng, Ph.D. and David Zawieja, Ph.D.
October 15, 2015

Department of Physiology, Development and Neuroscience Seminar
University of Cambridge, UK
Cross-Talk Between Cells of the Arteriolar Wall
Invited by: Bill Harris, Ph.D.
September 29, 2015

Department of Pharmacology Tea Club Seminar
University of Cambridge, UK
Illuminating the Lumen: Endothelial Cell Calcium in Both Vasoconstriction and Vasodilation
Invited by: Robin Irvine, Ph.D. and Robin Hiley, Ph.D.
February 13, 2015

Endocrinology, Nutrition & Metabolism and Cardiovascular Seminar
University of Southampton at Southampton General Hospital, UK
The Role of Calcium in the Microcirculation
Invited by: Professor Geraldine Clough, Ph.D.
November 26, 2013

Integrative Physiology Seminar Series
University of North Texas Health Science Center
The Role of Calcium in the Microcirculation
Invited By: Professor Steve Mifflin, Ph.D.
October 25, 2013

Center for Cell Death and Differentiation Seminar Series
Texas A&M Health Science Center College of Medicine
Pressure-Dependent Regulation of Endothelial Cell Calcium: A Role for TRPV4 Channels
Invited by: Binu Tharakan, Ph.D.
April 30, 2013

Cardiovascular Seminar Series
Robert M. Berne Cardiovascular Research Center at the University of Virginia
Low Intravascular Pressure Activates Endothelial Cell TRPV4 Channels, Local Ca^{2+} Events and IK_{Ca} Channels Reducing Arteriolar Tone
Invited by: Brant E. Isakson, Ph.D.
December 18, 2012

Medical Pharmacology and Physiology Spring Seminar Series
University of Missouri
A Role for Convection in Vasodilation
Invited by: Steven Segal, Ph.D.
May 11, 2010

Ad Hoc Reviewer for the Following Journals

American Journal of Physiology - Heart and Circulatory Physiology
Hypertension
Journal of Physiology
Journal of Vascular Research

Vascular Pharmacology
Nature Methods
Pharmacology Reviews
Circulation Research
Science Signaling
British Journal of Pharmacology

Memberships in Professional Societies

The American Physiological Society
British Pharmacological Society
The Microcirculatory Society, Inc.
The Physiological Society

References