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## BIOGRAPHICAL SKETCH

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NAME Breslin, Jerome W.	POSITION TITLE Assistant Professor of Physiology		
eRA COMMONS USER NAME (credential, e.g., agency login) jwbreslin			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
Rutgers University	B.A.	05/93	Biological Sciences
Seton Hall University	M.S.	05/98	Biology
University of Medicine and Dentistry of New Jersey	Ph.D.	12/02	Pharmacology and Physiology
Texas A&M University Health Sciences Center	Postdoctoral	12/04	Physiology
University of California, Davis	Postdoctoral	09/07	Surgery

### A. Personal Statement

The goal of the proposed research is to investigate the cellular and molecular mechanisms that lead to resolution of inflammation-induced microvascular hyperpermeability. Specifically, we plan to study how Rho family GTPases regulate the contraction and spreading behavior and intercellular adhesions of vascular endothelial cells in the context of endothelial barrier function. I have the training, experience, leadership, and motivation needed to successfully complete the proposed work. My background training has focused mainly on the microvascular function, however I have broad experience in pharmacology and physiology and view biological research questions from an integrative, holistic point of view. As a postdoctoral researcher at Texas A&M, I performed studies of endothelial barrier function using a combination of cell culture and isolated microvessel models, biochemical analyses of phosphorylation and activation of key signal transduction proteins, immunofluorescence confocal microscopy of cytoskeletal and junctional architecture, and measurement of cell-generated isometric tension. At U.C. Davis, I expanded my expertise to include development of fusion proteins, live cell imaging, and advanced training in intravital microscopy to study blood flow, leukocyte rolling and adhesion, extravasation of tracers from blood, and contractile behavior of lymphatics. As a PI on previous grants, I laid the foundation for the proposed research by establishing a cause-effect relationship between Rho-mediated endothelial cell contraction and neutrophil-induced microvascular hyperpermeability. In addition, I developed new fusion proteins to study the biochemical properties, cellular localization, and biological function of the atypical Rho family GTPase Rnd3, as well as optimized protocols to define its dynamic interactions with actin, tubulin, and VE-cadherin in live endothelial cells. In addition, I successfully administered these projects, collaborated with other investigators, and produced several peer-reviewed publications from each project. From my previous experience, I understand the importance of constructing a realistic research plan, budget, and timeline, utilizing frequent and effective communication between all people involved with the project, managing a laboratory team's intragroup dynamics, and successfully transitioning through the beginning, middle, and ending stages of a project. The current application builds logically upon my previous work, and I have chosen co-investigators and consultants (Dr. Worthylake, Dr. Chou, Dr. Tinsley) who provide additional expertise in cellular trafficking, protein chemistry, and cytoskeletal dynamics. In summary, I have demonstrated a record of successful and productive research projects that has high relevance to inflammation, trauma, and multiple disease conditions, as well as the expertise and experience to successfully lead the proposed project.

### B. Positions and Honors

#### Positions and Employment

1996-1997	Teaching Assistant, Dept. of Biology, Seton Hall University, South Orange, NJ
1997-1998	Study Monitor, Huntingdon Life Sciences, East Millstone, NJ
2000-2002	Teaching Assistant, School of Public Health, UMDNJ, Newark, NJ
2002	Instructor, Clinical Nutrition Program, UMDNJ Sch. of Health Related Professions, Newark, NJ
2002-2003	Postdoctoral Research Associate, Dept. of Surgery, Texas A&M University Health Science

Center, Temple, TX  
2003-2004 Postdoctoral Fellow, Dept. of Surgery, Scott & White Memorial Hospital, Temple, TX  
2004-2007 Postdoctoral Scholar - Fellow, Dept. of Surgery, UC Davis School of Medicine, Sacramento, CA  
2007- Assistant Professor (Tenure-Track), Dept. of Physiology, School of Medicine, Louisiana State University Health Sciences Center, New Orleans, LA

#### **Other Experience and Professional Membership**

2001 President, UMDNJ Graduate Student Association  
2005-2007 Chair, UC Davis Postdoctoral Scholars Association  
2006-2007 Chair, University of California Council of Postdoctoral Scholars  
2000- Member, The Microcirculatory Society, Inc.  
2001- Member, American Physiological Society  
2003- Member, American Society for Cell Biology  
2005- Member, American Association for the Advancement of Science  
2008- Member, American Heart Association

#### **Awards and Honors**

1989-1993 Garden State Scholarship, New Jersey Department of Education  
1998-2000 UMDNJ Graduate Fellowship  
2001 Caroline tum Suden/Frances A. Hellebrandt Professional Opportunity Award for Meritorious Research, American Physiological Society  
2003 Outstanding Student of the Year, New Jersey Medical School Faculty Organization  
2005 August Krogh Young Investigator Award, The Microcirculatory Society, Inc.  
2006 Lymphatic Research Foundation/Susan G. Komen Breast Cancer Foundation Young Investigator Scholarship

#### **C. Selected Peer-Reviewed Publications** (Selected from 16 peer-reviewed publications)

##### **Most relevant to the current application**

1. Breslin, J.W., Yuan, S.Y. Involvement of RhoA and Rho Kinase in Neutrophil-Stimulated Endothelial Hyperpermeability. *Am. J. Physiol. Heart Circ. Physiol.* 286: H1057-H1062, 2004.
2. Breslin, J.W., Sun, H., Xu, W, Rodarte, C, Moy, A.B., Wu, M.H., Yuan, S.Y. Involvement of ROCK-mediated endothelial tension development in neutrophil-stimulated microvascular leakage. *Am. J. Physiol. Heart Circ. Physiol.* 290: H741-H750, 2006.
3. Sun, H., Breslin, J.W., Zhu, J., Yuan, S.Y., Wu, M.H. Rho and ROCK Signaling in VEGF-induced coronary venular hyperpermeability. *Microcirculation* 13: 237-247, 2006.
4. Guo, M., Breslin, J.W., Wu, M.H., Gottardi, C.J., Yuan, S.Y. VE-cadherin and  $\beta$ -catenin binding dynamics during histamine-induced endothelial hyperpermeability. *Am J. Physiol Cell Physiol.* 294: C977-C984, 2008.
5. Breslin, J.W., Kurtz, K.M. Lymphatic endothelial cells adapt their barrier function in response to changes in shear stress. *Lymphat Res Biol*, In press. 2010.

##### **Additional recent publications of importance to the field (in chronological order)**

1. Varma, S., Breslin J.W., Lal, B.K., Hobson, R.W., Pappas, P.J., Durán, W.N. p42/44 MAP kinase regulates baseline permeability and cGMP-induced hyperpermeability in endothelial cells. *Microvasc. Res.* 63: 172-178, 2002.
2. Breslin, J.W., Pappas, P.J., Cerveira, J.J., Hobson, R.W., Durán, W.N. VEGF increases endothelial permeability by separate signaling pathways involving ERK-1/2 and nitric oxide. *Am. J. Physiol. Heart Circ. Physiol.* 284: H92-H100, 2003.

3. Aramoto, H., Breslin, J.W., Pappas, P.J., Hobson, R.W., Durán, W.N. Vascular endothelial growth factor stimulates differential signaling pathways in the *in vivo* microcirculation. *Am. J. Physiol. Heart Circ. Physiol.* 287: H1590-H1598, 2004.
4. Tinsley, J.H., Breslin, J.W., Teasdale, N.R., Yuan, S.Y. PKC-dependent, burn-induced adherens junction reorganization and barrier dysfunction in pulmonary microvascular endothelial cells. *Am. J. Physiol. Lung Cell Mol. Physiol.* 289: L217-L223, 2005.
5. Varma, S, Lal, B.K., Zheng R., Breslin, J.W., Saito, S., Pappas, P.J., Hobson, R. W., Durán, W. N. Hyperglycemia alters PI3K and Akt signaling and leads to endothelial proliferative dysfunction. *Am. J. Physiol. Heart Circ. Physiol.* 289: H1744-H1751, 2005.
6. Reynoso, R., Perrin, R.M., Breslin, J.W., Daines, D.A., Watson, K.D., Watterson, D.M., Wu, M.H., Yuan, S. A role for long chain myosin light chain kinase (MLCK-210) in microvascular hyperpermeability during severe burns. *Shock.* 28: 589-595, 2007.
7. Yuan, S.Y. Breslin, J.W., Perrin, R., Gaudreault, N., Guo, M., Kargozaran, H. Wu, M.H. Microvascular permeability in diabetes and insulin resistance. *Microcirculation.* 14: 363-373, 2007.
8. Breslin, J.W., Gaudreault, N., Watson, K.D., Reynoso, R., Yuan, S.Y., Wu, M.H. Vascular endothelial growth factor-C stimulates the lymphatic pump by a VEGF receptor-3-dependent mechanism. *Am J Physiol Heart Circ Physiol.* 293: H709-H718, 2007.
9. Kargozaran, H. Yuan, S.Y., Breslin, J.W., Watson, K.D., Gaudreault, N., Breen, A., Wu, M.H. A role for endothelial-derived matrix metalloproteinase-2 in breast cancer cell transmigration across the endothelial-basement membrane barrier. *Clin Exp Metastasis.* 24: 495-502, 2007.
10. Breslin, J.W., Yuan, S.Y., Wu, M.H. VEGF-C alters barrier function of cultured lymphatic endothelial cells through a VEGFR-3-dependent mechanism. *Lymphat. Res. Biol.* 5: 105-114, 2007.
11. Breslin, J.W., Wu, M.H., Guo, M., Reynoso, R. Yuan, S.Y. Toll-like receptor 4 contributes to microvascular inflammation and barrier dysfunction in thermal injury. *Shock,* 29: 349-355, 2008.

## **D. Research Support**

### **Ongoing Research Support**

0835388N Breslin (PI)

7/1/08 – 6/30/12

American Heart Association, National Affiliate Scientist Development Grant

“Cellular Signaling Mechanisms in Microvascular Permeability”

The goal of this project is to determine the cellular and molecular mechanisms by which the atypical Rho family member Rnd3 promotes enhanced endothelial barrier function.

Role: PI

P20 RR018766 Kapusta (PI)

7/1/08 – 5/31/13

“Mentoring in Cardiovascular Biology”

This NIH Center of Biomedical Research Excellence project provides mentoring, seed funding, and core facilities for junior faculty working toward attaining their first NIH R01 grant.

Role: PI on sub-project 5925 “Regulation of Endothelial Cell Permeability by Rho/ROCK Signaling.”

### **Completed Research Support**

F32 HL076079-02 Breslin (PI)

1/1/05 - 12/31/06

“Regulation of Endothelial Permeability via RhoA/ROCK”

In this project we characterized the role of the small GTPase RhoA and its downstream effector, Rho Kinase (ROCK), in neutrophil-induced changes in endothelial permeability.

Role: PI