BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Joseph D. Raffetto	Assistant Professor in Surgery
eRA COMMONS USER NAME (credential, e.g., agency login) JRAFFETTO	

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
California State University Northridge	BA	06/1987	Biology & Chemistry
California State University Northridge	MS	06/1989	Chemistry
Boston University School of Medicine	MD	06/1993	Medicine

A. Personal Statement

I am a vascular surgeon with research interest in understanding the cellular mechanisms of vascular disease, particularly chronic venous insufficiency disease. As a vascular surgeon, I have considerable experience in delicate surgical techniques in humans and in animal models of vascular disease. My vascular surgery expertise will be very critical for the studies with the vein segments and in the animal models of venous hypertension that are proposed in this grant application. Also, as a vascular surgeon I will have access to venous reflux data and discarded human greater saphenous vein collected from patients undergoing lower extremity bypass for peripheral vascular disease. I will also have access to venous reflux data, varicose saphenous vein and varix segments from patients undergoing varicose vein stripping, which constitute an important translational component of the project. As a vascular surgeon I understand the venous anatomy and how venous pathology affects the patient's clinical well-being. Although surgical approaches such as ablation and sclerotherapy are being used for treatment of varicose veins, many patients have high incidence of recurrent varicose veins and symptoms. This is because the pathophysiological mechanisms of varicose veins and the causes of their recurrence are not well understood. Studying the biomolecular events that lead to varicose veins is of great interest to me and I feel that my research in this under-investigated area would provide a better understanding of the mechanisms involved, and provide new treatment strategies to reduce the morbidity associated with varicose veins.

In addition to my clinical and surgical experience, I have considerable bench research experience on handling and performing experiments on isolated veins from experimental animals and humans. I am one of few clinician/scientists with interest and experience in characterization of the cellular and molecular mechanisms underlying the vein wall dysfunction and venous insufficiency disorders. Some of my research work is highlighted in 13 peer reviewed publications on the topic of vein function and venous disease in the last three years. The present proposal is an extension of my long-term interest in understanding the venous tissue mechanisms. The proposal highlights a novel link between hypoxia-inducible factor, matrix metalloproteinases, and the vein dysfunction associated with venous insufficiency disease.

In summary, I have a track record of successful and productive vascular research projects highly relevant to this application, and my clinical experience and basic research expertise have prepared me to be the principal investigator on this important translational research project.

B. Positions and Honors

Positions and Employment

6/93-6/94	Intern, General Surgery, SUNY at Buffalo
6/94-6/96	Jr. Resident, General Surgery, SUNY at Buffalo
6/96-6/97	Sr. Resident, General Surgery, SUNY at Buffalo
6/97-6/98	Chief Resident, General Surgery, SUNY at Buffalo
7/98-6/00	General Vascular Surgery Fellowship, Boston University School of Medicine
7/00-7/04	Boston Medical Center, Department of Surgery Section of Vascular Surgery

6/01-5/04	VA Medical Center Jamaica Plain and West Roxbury, Department of Surgery
5/04-present	VA Medical Center West Roxbury, Department of Surgery Section of Vascular Surgery
7/00-9/09	Assistant Professor of Surgery, Boston University School of Medicine
6/05-present	Research Scientist, Brigham & Women' s Hospital, Boston, MA
9/08-9/09	Instructor, Harvard Medical School, Brigham & Women' s Hospital, Boston, MA
9/09-present	Assistant Professor, Harvard Medical School, Brigham & Women' s Hospital, Boston, MA

Other Experience and Professional Memberships

2002 and 2005	Faculty, Postgraduate Symposium, American Venous Forum
2003	Faculty, New Frontiers in Vascular Surgery, Massachusetts General Hospital Course
2005-2007	Program Meeting Co-Director, American Venous Forum
2005-present	Chief, Vascular Laboratory, VA Boston, West Roxbury, MA
2005-2007	Program Director, Vascular Fellows Basic Science, WL Gore sponsor
2006	Member of Proceeding Meeting, Diagnostics and Hemodynamics of Chronic Venous Disease Pacific Vascular Symposium 5
2006-2008	Moderator, Basic Science Session, American Venous Forum
2006	Moderator, Ask the Experts , American Venous Forum
2007-2008	Faculty, Postgraduate Symposium, American Venous Forum
2007	Faculty, Workshop Ultrasound, American Venous Forum
2007-2009	Moderator, Poster Session, American Venous Forum
2009-present	Director of Combined Vascular Fellowship, VA Boston, West Roxbury, MA
2009	Discussant, Invited Expert Multiple Sclerosis and Venous Disease
2009	Member of Proceeding Meeting, Ulcer Healing and Recurrence, Pacific Vascular Symposium 6
9/05-8/06	Member, Veterans Equitable Resource Administration Committee, VA Boston
7/08	Chair, Endovascular Standards in Vascular Interventional Radiology, VA Boston
5/09	Member, Search Committee, Cardiac Chief, VA Boston
6/04-present	Member, Committee on Applicants, American College of Surgeons, Massachusetts District #4
2/04-2/07	Member, Research Committee and Program Committee, American Venous Forum
2006	Member, Diagnostics Hemodynamics, Pacific Vascular Symposium V
2006-present	Member, Venous Guidelines, Society Vascular Surgery/American Venous Forum
2/07-2/08	Chairman, Program Committee, American Venous Forum
2007-present	Faculty, Vascular Education Self Assessment Program Writing Committee, American College Surgeons/Society Vascular Surgery
2007	Member, American Venous Forum Strategic Planning, American Venous Forum
2008-present	Chairman, Research Committee, American Venous Forum
2009-present	Councilor, Executive Committee, American Venous Forum
2009-present	Member, The Surgical Council on Resident Education, American College of Surgeons
2009	Member, Ulcer Healing and Recurrence, Pacific Vascular Symposium 6
2009-present	Faculty, Vascular Education Self Assessment Program-2 Writing Committee, American College Surgeons/Society Vascular Surgery
2000-present	Honorary Member, Colegio Argentino de Cirugia Venosa y Linfatica
2002-present	Fellow, American College of Surgeons
2002-present	Fellow, American College of Surgeons, Massachusetts Chapter
2002-present	Fellow, Society for Vascular Medicine and Biology
2002-present	Member, American Venous Forum
2002-present	Member, New England Society Vascular Surgery
2002-present	Member, Society Clinical Vascular Surgery
2003-present	Member, Boston Surgical Society
2009-present	Member, Society for Vascular Surgery
2/04-2/08	Member, Beiersdorf-Jobst Grant Review, American Venous Forum
2/08-2/09	Chairman, Beiersdorf-Jobst Grant Review, American Venous Forum

Honors and Awards

5/85-5/87	CSU-Northtidge, Dean's List Appointments

5/87	CSU-Northridge, Cum Laude Graduate
5/89	CSU-Northridge Graduate School, American Chemical Honor Society Phi Lambda Upsilon
5/93	Boston University School of Medicine Richard J Elkort Memorial Fund Award
6/98	SUNY at Buffalo Surgical Residency Program, Millard Fillmore Hospital Vogel Award
6/98	SUNY at Buffalo Surgical Residency Program, Best All Around Resident Award
2/99	Venous Research Award, The American Venous Forum
2/00	Venous Research Award, The American Venous Forum
2/03	American Venous Forum, Poster Contest 1st Place Winner
2003	Distinguished Reviewer, Journal of Vascular Surgery
2003-present	Key Reviewer, Journal of Vascular Surgery

C. Selected Peer-reviewed Publications (Selected from 51 peer-reviewed publications).

Most relevant to the current application

1. **Raffetto JD**, Ross RL, Khalil RA. Matrix metalloproteinase 2-induced venous dilation via hyperpolarization and activation of K^+ channels: Relevance to varicose vein formation. *J Vasc Surg*. 2007;45(2):373–80. (PMCID: PMC1794684)
2. **Raffetto JD**, Qiao X, Koledova VV, Khalil RA. Prolonged increases in vein wall tension increase matrix metalloproteinases and decrease constriction in rat vena cava. Potential implications in varicose veins. *J Vasc Surg.* 2008;48(2):447–56. (PMCID: PMC2575039)
4. **Raffetto JD**, Barros YV, Wells AK, Khalil RA. MMP-2 induced vein relaxation via inhibition of $[Ca^{2+}]_e$-dependent mechanisms of venous smooth muscle contraction. Role of RGD peptides. *J Surg Res. 2010*;159(2):755–764. (PMCID: PMC2844458)
5. **Raffetto JD**, Qiao X, Beauregard KG, Tanbe AF, Kumar A, Mam V, Khalil RA. Functional adaptation of venous smooth muscle response to vasoconstriction in proximal, distal, and varix segments of varicose veins. *J Vasc Surg*. 2010;51(4):962–71. (PMCID: PMC2847596)
5. Lim CS, Qiao X, Reslan OM, Xia Y, **Raffetto JD**, Paleolog E, Davies AH, Khalil RA. Prolonged mechanical stretch is associated with upregulation of hypoxia-inducible factors and reduced contraction in rat inferior vena cava. *J Vasc Surg*. 2010 Nov 22. [Epub ahead of print] PubMed PMID: 21106323. (PMCID: PMC in process)

Additional recent publications of importance to the field

1. **Raffetto JD**, Mendez VM, Marien BJ, Byers HR, Phillips TJ, Park HY, Menzoian JO. Changes in cellular motility and cytoskeletal actin in fibroblasts from patients with chronic venous disease and in newborn fibroblasts in the presence of chronic wound fluid. *J Vasc Surg* 2001;33:1233-1241.
2. **Raffetto JD**, Vasquez R, Goodwin DG, Menzoian JO. Mitogen-activated protein kinase pathway regulates cell proliferation in venous ulcer fibroblasts. *Vasc Endovascular Surg*. 2006;40(1):59-66.
3. **Raffetto JD**, Mendez VM, Phillips TJ, Park HY, Menzoian JO. The effect of passage number on fibroblast cellular senescence in patients with chronic venous insufficiency with and without ulcer. *Venous Digest* 2002;9:6-7.
4. Eberhardt RT, **Raffetto JD**. Contemporary review in cardiovascular medicine. Chronic venous insufficiency. *Circulation* 2005;111:2398-2409.
5. **Raffetto JD**, Gram CH, Overman KC, Menzoian JO. Mitogen-activated protein kinase p38 pathway in venous ulcer fibroblasts. *Vasc Endovascular Surg*. 2008;42(4):367-74.
6. **Raffetto JD**, Khalil RA. Mechanisms of varicose vein formation: valve dysfunction and wall dilation. *Phlebology*. 2008;23(2):85-98.
7. **Raffetto JD**, Khalil RA. Matrix metalloproteinases in venous tissue remodeling and varicose vein formation. *Curr Vasc Pharmacol.* 2008;6(3):158–72.
8. **Raffetto JD**, Khalil RA. Matrix metalloproteinases and their inhibitors in vascular remodeling and vascular disease. *Biochem Pharmacol*. 2008;75(2):346–59. (PMCID: PMC2254136)

9. **Raffetto JD**. Dermal pathology, cellular biology, and inflammation in chronic venous disease. *Thromb Res*. 2009;123 Suppl 4:S66-71.
10. **Raffetto JD**, Qiao X, Beauregard KG, Khalil RA. Estrogen receptor-mediated enhancement of venous relaxation in female rat: Implications in sex-related differences in varicose veins. *J Vasc Surg*. 2010;51(4):972–981. (PMCID: PMC2847594)

D. RESEARCH SUPPORT

ONGOING

Randomized Clinical Trial Raffetto (PI) 2008-2011
Beiersdorf-Jobst, Industry Funded Study
Compression versus anti-embolism stockings in patients with venous leg edema
The major goals of the study are to compare the clinical improvement and quality of life between wearing compression stockings versus anti-embolism stockings in patients with varicose veins and limb edema.

COMPLETED

Beiersdorf-Jobst Research Fellowship Raffetto (PI) 1999
The American Venous Forum Foundation

R01 HL-075771 Creager (PI) 2005-2010
NIH/NHLBI
Inflammation and insulin resistance in peripheral arterial disease
The major goals of this project are to test the hypothesis that inflammation and insulin resistance contribute to reduced walking distance in patients with intermittent claudication by impairing vascular reactivity and skeletal muscle metabolic function.