## BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

| NAME | POSITION TITLE |
|---|---|
| Segal, Mark S. | Professor of Medicine |
| eRA COMMONS USER NAME (credential, e.g., agency login)<br>SEGALMS | |

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

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | YEAR(s) | FIELD OF STUDY |
|---|---|---|---|
| MIT, Cambridge, MA | B.S. | 1980-84 | Biology |
| Joint Degree Program: | | | |
| UT Southwestern, Dallas, TX | M.D./Ph.D. | 1984-92 | Cell & Molecular Biology |
| UT Southwestern, Dallas, TX | M.D./Ph.D. | 1984-92 | Medicine |

### A. Personal Statement

The goal of the proposed research is to understand at a mechanistic level whether relaxin by mobilizing BMDAC, can enhance bone repair. My primary research interest is in understanding BMDAC and how BMDAC defects lead to poor vascular function. As such we have been measuring BMDAC function and tracking them in rhodent models for over 10 years and have worked with Dr. Kirk Conrad studying the mechanism of relaxin mediated increases in BMDAC number and function for over 5 years. Specifically, we have been tracking whether BMDAC are recruited to femoral artery injury and venous intimal hyperplasia lesions using a chimeric mouse model for over 7 years. Last we have been enumerating mouse BMDAC by cell culture and flow cytometry for over 4 years. As such we have the expertise to carry-out the specific aims and to interpret the experiments. I currently meet weekly with Dr. Conrad where we discus data analysis and experiment planning. I am deeply committed to this project and see it as a wonderful advance in understanding the potential of BMDAC for repair of bone fractures and to fully understand the potential of BMDAC and/or relaxin to be used as a therapeutic to improve bone repair.

### B. Positions and Honors

**Positions and Employment**

| | |
|---|---|
| 1983-1984 | Undergraduate researcher, MIT. Mentor: Dr. Monty Krieger, Department of Biology at M.I.T. In the undergraduate research opportunities program, I spent two years researching the alterations in the glycosylation pattern of an LDL receptor mutant. |
| 1986-1990 | Graduate student, University of Texas Southwestern at Dallas. Mentors: Dr. Mary Jane Gething and Dr. Joseph Sambrook. I studied hemagglutinin protein's sites of interaction with and reliance on the heat shock protein 70, BiP, for proper folding. |
| 1992-1995 | Intern and Resident, Department of Internal Medicine, Parkland Memorial Hospital, University of Texas Southwestern at Dallas |
| 1995-1998 | Nephrology Research Fellow, Division of Nephrology, Beth Israel Deaconess Medical Center. Mentor: Dr. Vikas Sukhatme. Worked on a lentiviral expression vector as well as understanding the mechanism for the anti-angiogenic properties of endostatin. |
| 1998-1999 | Instructor of Medicine, Division of Nephrology, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School |
| 1999-2007 | Assistant Professor of Medicine, Division of Nephrology, Hypertension, and Renal Transplantation, University of Florida College of Medicine |
| 2007-2014 | Associate Professor of Medicine, Division of Nephrology, Hypertension, and Renal Transplantation, University of Florida College of Medicine |
| 2007-2014 | Associate Professor of Medicine, Division of Rheumatology & Clinical Immunology. Joint appointment. University of Florida College of Medicine |
| 2010-Present | Chief Division of Nephrology, Hypertension, and Renal Transplantation, University of Florida College of Medicine |
| 2010-Present | Vice-Chair of Research Department of Medicine, University of Florida College of Medicine |
| 2014-Present | Professor of Medicine, Division of Nephrology, Hypertension, and Renal Transplantation, University of Florida College of Medicine |

2014-Present Professor of Medicine, Division of Rheumatology & Clinical Immunology. Joint appointment. University of Florida College of Medicine

**Honors and Awards**

*1983-1984 Sigma XI Undergraduate Research Opportunity Program Award*
*1984 John L. Asinari Award. Awarded for outstanding biologic research to an MIT undergraduate*
*1998 K08 Award from the NIH NIDDK*
*2007 Awarded Fellowship status by the American Society of Nephrology*
*2007 Promoted to Associate Professor of Medicine at the University of Florida*
*2010 Awarded Fellowship status by the American Heart Association*
*2014 Named a UF Research Foundation Professor for 2014*
*2014 Promoted to Professor of Medicine at the University of Florida*

**C. Selected Peer-reviewed Publications** (Selected from 64 peer-reviewed publications)

**Most relevant to the current application**


1. Segal, Mark S., Bihorac, Azra, and Koc, Mehmet. Circulating endothelial cells: tea leaves for renal disease. Invited Review. Am J Renal Physiol. 283(1):F11-9. PMID: 12060582
2. Koc, Mehmet, Bihorac, Azra, and Segal, Mark S. (2003). Circulating endothelial cells as potential markers of the state of the endothelium in hemodialysis patients. AJKD. 42(4):704-12. PMID: 14520620
3. Butler JM, Guthrie SM, Koc M, Afzal A, Caballero S, Brooks HL, Mames RN, Segal MS, Grant MB, Scott EW. (2005). SDF-1 is both necessary and sufficient to promote proliferative retinopathy. JCI. 115(1):86-93. PMID: 15630447
4. Koc, M., Bihorac, A., Ross, E., Schold, J. and Segal, Mark S. (2005). Circulating endothelial cells are associated with future vascular events in hemodialysis patients. Kidney Int. Mar;67(3):1078-83. PMID: 15698448
5. Diao, Yanpeng, Xue, Jing, Segal, Mark S. A novel mouse model of autologous venous graft intimal hyperplasia. Journal of Surgical Research. 2005. 126(1):106-13. PMID: 15916983
6. Segal, Mark S., Shah, Ronak, Afzal, Aqeela, Caballero, Sergio, Koc, Mehmet, Harrison, Jeffrey K., Grant, Maria B. Nitric oxide cytoskeletal-induced alterations reverse the endothelial progenitor cell migratory defect associated with diabetes. Diabetes. 2006. 55(1):102-9. PMID: 16380482
7. Lee, P., Li, Y., Richards, H.B., Chan, F.S., Zhuang, H., Narain, S., Butfiloski, E., Sobel, E.S., Reeves, W.H., Segal, M.S. Type I interferon: a novel risk factor for EPC depletion and endothelial dysfunction in SLE. Arthritis & Rheumatism. 2007. 56(11):3759-69. PMID: 20416954
8. Diao, Y., Guthrie, S., Xia, S.L., Ouyang, S., Zhang, L., Xue, J., Lee, P., Grant, M., Scott, E., Segal, M.S. Long-term Engraftment of Bone Marrow Derived-Cells in the Intimal Hyperplasia Lesion of Autologous Vein Grafts. American Journal of Physiology. 2008 Mar;172(3):839-48. Epub 2008 Feb 14. PMID: 18276778
9. Bihorac A, Yavas S, Subbiah S, Hobson CE, Schold JD, Gabrielli A, Layon AJ, Segal MS. Long-term risk of mortality and acute kidney injury during hospitalization after major surgery. Ann Surg. 2009 May;249(5):851-8. PMID: 19387314
10. Hobson CE, Yavas S, Segal MS, Schold JD, Tribble CG, Layon AJ, Bihorac A. Acute kidney injury is associated with increased long-term mortality after cardiothoracic surgery. Circulation. 2009 May 12;119(18):2444-53. PMID: 19398670
11. Busik JV, Tikhonenko M, Bhatwadekar A, Opreanu M, Yakubova N, Caballero S, Player D, Nakagawa T, Afzal A, Kielczewski J, Sochacki A, Hasty S, Li Calzi S, Kim S, Duclas SK, Segal MS, Guberski DL, Esselman WJ, Boulton ME, Grant MB. Diabetic retinopathy is associated with bone marrow neuropathy and a depressed peripheral clock. J Exp Med. 2009 Dec 21;206(13):2897-906. PMID: 19934019
12. Segal MS, Sautina L, Li S, Diao Y, Agoulnik AI, Kielczewski J, McGuane JT, Grant MB, Conrad KP. Relaxin increases human endothelial progenitor cell NO and migration and vasculogenesis in mice. Blood. 2012 Jan 12;119(2):629-36. PMID: 22028476
13. Mohandas R, Sautina L, Li S, Wen X, Huo T, Handberg E, Chi YY, Merz CN, Pepine CJ, Segal MS. Number and Function of Bone-Marrow Derived Angiogenic Cells and Coronary Flow Reserve in Women without Obstructive Coronary Artery Disease: A Substudy of the NHLBI-Sponsored Women's Ischemia Syndrome Evaluation (WISE). PLoS One. 2013 Dec 2;8(12):e81595. PMID: 24312563

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

1. Mohandas R, Segal MS. Endothelial progenitor cells and endothelial vesicles - what is the significance for patients with chronic kidney disease? Blood Purif. 2010;29(2):158-62. Epub 2010 Jan 8. PubMed PMID: 20093822
2. Beem E, Segal MS. Evaluation of stability and sensitivity of cell fluorescent labels when used for cell migration. J Fluoresc. 2013 Sep;23(5):975-87. PMID: 23722994

**D. Research Support**

**Ongoing Research Support**

1 P01 HD065647-01A1 (Conrad, PI) 7/01/2011 – 6/30/2016
NIH/NICHD
*Corpus Luteal Contribution to Maternal Pregnancy Physiology and Outcome in ART*
The proposed program project will investigate the corpus luteal contribution to maternal pregnancy physiology and outcomes in ART using fundamental, clinical, and epidemiological approaches.
Role: Principal Investigator Project 2

2 R01 EY012601-13 (Grant, PI) 9/30/1998 – 5/31/2015
NIH/NEI
*Dysfunction of Endothelial Precursor Subtypes Dictates the Outcomes of Diabetic Retinopathy*
This project investigates the role of endothelial progenitor cells in the development of diabetic retinopathy.
Role: Co-Investigator

1 R01 HL110170-01- (Grant, PI) 9/30/1998 – 5/31/2015 .
NIH/NEI
*Vascular Reparative Mechanism by ACE2/Ang-(1-7) in Diabetes*
This project tests the hypothesis that the ACE/ACE2 balance within EPCs dictates their reparative capability and can therefore predict progression of retinal MVC.
Role: Co-Investigator

5 R01 DK091443-02 (Moldawer, PI) 9/01/2011 – 8/30/2014
NIH/NIDDK
*Inflamation and Repari as Determinanats of Hemodialysis Fistual Maturation*
This project investigates the factors that determine whether a fistula will mature or not.
Role: Co-Investigator

3 U01 HL087366-04S1 (Pepine, PI) 1/01/2007 – 12/31/2018
NIH/NHLBI
*UFCC for Cardiovascular Cell Therapy Research Network (*includes *Skills Development Core)*
To establish a University of Florida Clinical Center for the Cardiovascular Cell Therapy Research Network. The central focus of this grant is to develop methods for and characterize the responses to autologous bone marrow cells as well as novel cell types using randomized, placebo-controlled trials in CAD patients.
Role: Co-Investigator

NIH P50 GM111152 (Moore, PI) 9/1/2014-8/30/2019
NIH/NIGMS
*PICS: A New Horizon for Surgical Critical Care*
To establish a sepsis center at UF focused on a studying a new phenotype for many surgical ICU sepsis survivors: chronic critical illness (CCI) manifested as a persistent inflammation, immunosuppression and catabolism syndrome (PICS)
Role: PI Project 3

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5 R01 HL091005-04 (Pepine, PI) 9/30/2008 – 7/31/2013
NIH/NHLBI

*Ancillary Functional Studies for the CCTRN*
To investigate pathophysiologically relevant alterations of circulating and bone marrow vascular progenitor cells and their relationship with LV function and outcomes after myocardial injury and cell therapy.
Role: PD/PI

5 U01 DK082189-03 (Huber, PI) 9/10/2000 – 5/31/2013
NIH/NIDDK
*Modulation of the Hemodynamic Factors Associated with AVF Maturation*
UF was selected to develop a multicenter observational cohort study to identify predictors of AVF maturation/non-maturation.
Role: Co-Investigator

1 T32 DK07518-24 (Segal, PI) 7/01/1985 – 6/30/12 (NCE)
NIH/NIDDK
*Pre and Postdoctoral Training in Nephrology and Hypertension*
The objective of this grant is to provide training of predoctoral and postdoctoral candidates into basic and clinical research related to nephrology with the purpose of providing the necessary training to become independent investigators

REGISTRAT (Segal, PI) 3/21/2011 – 5/12/2012 (NCE)
Otsuka
*An observational prospective registry to identify demographic and clinical characteristics of patients hospitalized with euvolemic and hypervolemic hyponatremia and assess the comparative effectiveness of available treatments.*

5 R01 HL 079352-04 (Segal, PI) 8/01/2005 - 4/30/2011
NIH/NHLBI
*Uric Acid and Hypertension in African Americans*
The objective of this grant is to evaluate the effect on blood pressure and endothelial function of simultaneously treating African Americans, stage I hypertensions with allopurinol along with a diuretic.

Alliance for Lupus Research (Segal, PI) 8/15/2007 - 8/15/2010
ALR
Alliance for Lupus Research “Accelerated Atherosclerosis in SLE: The type I interferon link”
This project investigates the role of IFN-α in the excess cardiovascular risk in patients with SLE.
There is no overlap between this grant and the submitted proposal.