

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
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NAME Pepine, Carl J.	POSITION TITLE Professor of Medicine		
eRA COMMONS USER NAME (credential, e.g., agency login) PEPINCJ			
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
University of Pittsburgh, Pittsburgh, PA	B.S.	04/62	Premedical
New Jersey Medical School, Newark, NJ	M.D.	06/66	Medicine

A. Personal Statement

This application is to provide comprehensive research training to selected individuals electing to pursue an academic career in hypertension and related disorders. The aim is to train these individuals in pathophysiology of diseases leading to hypertension, as well as to improve our understanding of the consequences of CKD in terms of increased risk for cardiovascular disease. The program covers the spectrum from basic to clinical research. My expertise in hypertension and cardiovascular disease in unique at-risk populations, along with over 40 years of mentoring in clinical research, provides the background to support this training. I conduct clinical trials in areas related to this application (hypertension, vascular dysfunction, cardiac function, cell biology, etc), run several cores, and provide support for large databases dealing with hypertension and related clinical outcomes. These trials and their related activities (e.g., core labs, databases, etc.) will be available to mentees along with other opportunities for clinical investigation. Additionally, I direct the 12 Clinical Research Units in the *UF Clinical and Translational Science Institute*, and I will make all of these facilities available to the mentees. I have the time available to commit to mentoring one trainee/year.

B. Positions and Honors

Positions and Employment (selected)

1978-92 Chief Cardiology VA Medical Ctr Gainesville/ Co-Director UF Division Cardiovascular Medicine
1980-85 PI, UF Clinical Site, NHLBI-Percutaneous Transluminal Coronary Angioplasty Registry
1985-93 PI, UF Center, NHLBI-Studies in Left Ventricular Dysfunction (SOLVD).
1987-94 Co-I, UF Clinical Site, NHLBI Balloon Valvuloplasty Registry
1990-94 PI, UF Center, NHLBI-Asymptomatic Cardiac Ischemia (ACIP)
1991-96 PI, UF Center, NHLBI-Psychophysiologic Interventions in Myocardial Ischemia (PIMI)
1996- PI, UF Center, NHLBI-Women's Ischemia Syndrome Evaluation (WISE)
1998-08 Director, UF Division Cardiovascular Medicine
2000-08 PI, UF Center, NHLBI-Bypass Angioplasty Revascularization Investigation 2 Diabetes Trial (BARI2D)
2001-08 UF Eminent Scholar, American Heart Association-Suncoast Chapter Chair in CV Research.
2006-11 PI, UF Center, NHLBI-Cardiovascular Cell Therapy Research Network (CCTR N)
2007-11 PI, Training Core, UF Center, NHLBI- CCTR N
2008- PI, Ancillary Studies in Progenitor Cell Functions for CCTR N, NHLBI_5 R01 HL91005-02
2009- Director, Participant and Clinical Interaction Program (Clinical Research Units), UF CTSI
2009- MPI, UF Center, NHLBI-Women's Ischemia Syndrome Evaluation coronary vascular dysfunction
2012- PI, UF Regional Center, NHLBI-Cardiovascular Cell Therapy Research Network (CCTR N-2)
2012- PI, Training Core, UF Regional Center, NHLBI- CCTR N-2

Honors (selected): Alpha Omega Alpha; American Society for Clinical Investigation (1982); Young Investigator Award for Pioneering Contributions Employing Holter ECG Technology, ISHM (1990); Paul Dudley White Award, AMSUS (1991); Theodore Woodward Award, Am CL and Climatological Assoc (1998); Master, Am Coll of Cardiol (1999); Gifted Teacher Award, FL Chapter Am Coll of Cardiol (2001); UF Excellence Awards in research and education (1987-1986, 1989, 1990-1993, 1999-2001, 2005, 2008); UF Award for Excellence in Mentoring (2009); Gifted Scientist Award, FL Chapt. Am Coll of Cardiol (2009); Lifetime Achievement Award, UF Coll. of Medicine (2010), UF Dept. of Medicine Excellence in Teaching Award (2012).

Committees (selected): ACC President, 2003-04; Chair DSMB NHLBI-FREEDOM Trial, 2004-13; Co-Chair ACCF/AHA Expert Consensus Document on Hypertension in the Elderly, 2008-2010; Review Comm. for NHLBI Progenitor Cell Biology Consortium Planning Award RFA-HL-08-012, Oct 2008; Special Emphasis

Panel-NIH CV Sciences Small Business Activities: Cell Therapy ZRG1 CVS-K(10), Feb 2009; Review Comm. for NIH CV Sciences Small Business Activities: Cell Therapy ZRG1 CVS-K(10), February 2009; NHLBI Working Group on identifying patients at high risk of a cardiovascular event in the near future, 2009-2010; Review Panel for NHLBI Production Assistance for Cellular Therapies (PACT), March 2010-Feb 2011; Review Comm. NHLBI CV Clinical Trials, ad hoc member, June 2011 and June 2013.

C. Peer-reviewed Publications- relevant to current application (Selected from over 750)

1. **Pepine CJ**, Handberg EM, Cooper-DeHoff RM, et al.; INVEST investigators. A calcium antagonist vs a non-calcium antagonist hypertension treatment strategy for patients with coronary artery disease. *JAMA* 2003;290:2805-16. PMID: 14657064
2. Bakris GL, Gaxiola E, Messerli FH, et al., **Pepine CJ**. Clinical outcomes in the diabetes cohort of the International Verapamil SR-Trandolapril study. *Hypertension* 2004;44(5):637-42. PMID: 15381674
3. Messerli FH, Kupfer S, **Pepine CJ**. J curve in hypertension and coronary artery disease. *Am J Cardiol* 2005;95:160.
4. Nathan S, **Pepine CJ**, Bakris GL. Calcium antagonists: effects on cardio-renal risk in hypertensive patients. *Hypertension* 2005;46:637-42. PMID: 16172420
5. **Pepine CJ**, Kowey PR, Kupfer S, et al.; INVEST Investigators. Predictors of adverse outcome among patients with hypertension and coronary artery disease. *J Am Coll Cardiol* 2006;47:547-51.
6. Cooper-DeHoff RM, Aranda JM Jr, Gaxiola E, et al., **Pepine CJ**. Blood pressure control and cardiovascular outcomes in high-risk Hispanic patients—findings from the INVEST. *Am Heart J* 2006;151:1072-9.
7. Cooper-DeHoff R, Cohen JD, Bakris GL, et al., **Pepine CJ**; INVEST Investigators. Predictors of development of diabetes mellitus in patients with coronary artery disease taking antihypertensive medications. *Am J Cardiol* 2006;98:890-4.
8. Langaee TY, Gong Y, Yarandi HN, et al., **Pepine CJ**, Johnson JA. Association of CYP3A5 polymorphisms with hypertension and antihypertensive response to verapamil. *Clin Pharmacol Ther* 2007;81(3):386-91.
9. Brunner M, Cooper-DeHoff RM, Gong Y, et al., **Pepine CJ**, Johnson JA; INVEST investigators. Factors influencing blood pressure response to trandolapril add-on therapy in patients taking verapamil SR. *Am J Cardiol* 2007;99:1549-54. PMCID: PMC2720593
10. Mancia G, Messerli F, Bakris G, et al., **Pepine CJ**. Blood pressure control and improved cardiovascular outcomes in the INVEST. *Hypertension* 2007;50:299-305. PMID: 17606861
11. Beitelshes AL, Gong Y, Wang D, et al., **Pepine CJ**, Johnson JA; INVEST investigators. *KCNMB1* genotype influences response to verapamil SR and adverse outcomes in the International Verapamil SR/Trandolapril Study (INVEST). *Pharmacogenet Genomics* 2007;17:719-29. PMCID: PMC2713584
12. Uretsky S, Messerli FH, Bangalore S, et al., **Pepine CJ**. Obesity paradox in patients with hypertension and coronary artery disease. *Am J Med* 2007;120:863-70.
13. Coca A, Messerli FH, Benetos A, et al., **Pepine CJ**. Predicting stroke risk in hypertensive patients with coronary artery disease: a report from the INVEST. *Stroke* 2008;39:343-8. PMCID: PMC2805179
14. Kolloch R, Legler UF, Champion A, et al., **Pepine CJ**. Impact of resting heart rate on outcomes in hypertensive patients with coronary artery disease: findings from the INVEST. *Eur Heart J* 2008;29:1327-34. PMCID: PMC2805436
15. Bangalore S, Messerli FH, Cohen JD, et al., **Pepine CJ**; INVEST investigators. Verapamil-sustained release-based treatment strategy is equivalent to atenolol-based treatment strategy at reducing cardiovascular events in patients with prior myocardial infarction. *Am Heart J* 2008;156:241-7.
16. Pacanowski MA, Gong Y, Cooper-DeHoff RM, et al., **Pepine CJ**, Johnson JA. β -adrenergic receptor gene polymorphisms and β -blocker treatment outcomes in hypertension. *Clin Pharmacol Ther* 2008;84:715-21. PMCID: PMC2675574
17. Pacanowski MA, Zineh I, Li H, et al., **Pepine CJ**, Johnson JA. Adrenergic gene polymorphisms and cardiovascular risk in the NHLBI-sponsored Women's Ischemia Syndrome Evaluation. *J Transl Med* 2008;6:11. PMCID: PMC2329599.
18. Gerhard T, Gong Y, Beitelshes AL, et al., **Pepine CJ**, Johnson JA. Alpha-adducin polymorphism associated with increased risk of adverse cardiovascular outcomes: results from GENetic Substudy of the International Verapamil SR-trandolapril Study. *Am Heart J* 2008;156:397-404. PMCID: PMC2547143.

19. Anderson RD, Sizemore BC, Barrow GM, et al., **Pepine CJ**. Pulse pressure and adverse outcomes in women: a report from the Women's Ischemia Syndrome Evaluation (WISE). *Am J Hypertens* 2008;21:1224-30. PMID: PMC2586110.
20. Pacanowski M, Zineh I, Cooper-DeHoff RM, **Pepine CJ**, Johnson JA. Genetic and pharmacogenetic associations between NOS3 polymorphisms, blood pressure, and cardiovascular events in hypertension. *Am J Hypertens* 2009;22:748-53. PMID: PMC2803093.
21. Beitelshes AL, Navare H, Wang D, et al., **Pepine CJ**, Schork NJ, Johnson JA. CACNA1C gene polymorphisms, cardiovascular disease outcomes, and treatment response. *Circ Cardiovasc Genet* 2009;2:362-70. PMID: PMC2761685.
22. Denardo SJ, Messerli FH, Gaxiola E, et al., **Pepine CJ**. Characteristics and outcomes of revascularized patients with hypertension. *Hypertension* 2009;53:624-30. PMID: PMC2794408
23. Johnson AD, Gong Y, Wang D, et al., **Pepine CJ**, Johnson JA, Sadee W. Promoter polymorphisms in ACE (angiotensin I-converting enzyme) associated with clinical outcomes in hypertension. *Clin Pharmacol Ther* 2009;85:36-44. PMID: PMC2709290
24. Bangalore S, Messerli FH, Franklin SS, et al., **Pepine CJ**. Pulse pressure and risk of cardiovascular outcomes in patients with hypertension and coronary artery disease. *Eur Heart J* 2009;30:1395-1401. PMID: 19351690
25. Bavry AA, Anderson RD, Gong Y, et al., **Pepine CJ**. Outcomes among hypertensive patients with concomitant peripheral and coronary artery disease: findings from the INternational VErapamil-SR/Trandolapril Study. *Hypertension* 2010;55:48-53. PMID: PMC3000120
26. Denardo SJ, Gong Y, Nichols WW, et al., **Pepine CJ**. Blood pressure and outcomes in very old hypertensive coronary artery disease patients. *Am J Med* 2010;123:719-26. PMID: PMC3008373
27. **Pepine CJ**, Anderson RD, Sharaf BL, et al. Coronary microvascular reactivity to adenosine predicts adverse outcome in women evaluated for suspected ischemia: results from the NHLBI WISE (Women's Ischemia Syndrome Evaluation) Study. *J Am Coll Cardiol* 2010;55:2825-32. PMID: PMC2898523.
28. Cooper-DeHoff RM, Gong Y, Handberg EM, et al., **Pepine CJ**. Tight blood pressure control and cardiovascular outcomes among hypertensive patients with diabetes and coronary artery disease. *JAMA* 2010;304:61-8. PMID: PMC3008411
29. Park KE, **Pepine CJ**. Bone marrow-derived cells and hypertension. *Expert Rev Cardiovasc Ther* 2010;8:1139-48.
30. Denardo SJ, Messerli FH, Gaxiola E, et al., **Pepine CJ**. Coronary revascularization strategy and outcomes according to blood pressure (from the INVEST). *Am J Cardiol* 2010;106:498-503. PMID: PMC3005196
31. Aronow W, Fleg J, **Pepine CJ**, et al. ACCF/AHA 2011 expert consensus document on hypertension in the elderly: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. *Circulation* 2011;123:2434-506. PMID: 21518977
32. Cooper-DeHoff RM, Egelund EF, **Pepine CJ**. Blood pressure lowering in patients with diabetes—one level might not fit all. *Nat Rev Cardiol* 2011;8:42-9. PMID: PMC3016088
33. Bavry AA, Khaliq A, Gong Y, et al., **Pepine CJ**. Harmful effects of nonsteroidal anti-inflammatory drugs among patients with hypertension and coronary artery disease. *Am J Med* 2011;124:614-20.
34. Bavry AA, **Pepine CJ**. Treatment of hypertension: lower is better, or is it? *Hypertension*. 2012;60:281-2. PMID: PMC3832986
35. Gerhard T, Delaney JA, Cooper-Dehoff RM, et al., **Pepine CJ**, Winterstein AG. Comparing marginal structural models to standard methods for estimating treatment effects of antihypertensive combination therapy. *BMC Med Res Methodol*. 2012;12(1):119. PMID: PMC3573973
36. Karnes JH, Gong Y, Pacanowski MA, et al., **Pepine CJ**, Johnson JA, Cooper-DeHoff RM. Impact of TCF7L2 single nucleotide polymorphisms on hydrochlorothiazide-induced diabetes. *Pharmacogenet Genomics*. 2013;23(12):697-705. PMID: PMC3893755
37. Smith SM, Gong Y, Handberg EM, et al., **Pepine CJ**, Cooper-DeHoff RM. Predictors and outcomes of resistant hypertension among patients with coronary artery disease and hypertension. *J Hypertens*. 2014;32(3):635-43. PMID: PMC4118668
38. Smith SM, Huo T, Johnson BD, et al., **Pepine CJ**, Cooper-DeHoff RM. Cardiovascular and mortality risk of apparent resistant hypertension in women with suspected myocardial ischemia. *JAMA*. 2014;3(1):e000660. PMID: PMC3959684

D. Research Support

Ongoing Research Support

- 5 UM1 HL087366-08 Pepine (PI) 01/07- 02/19
UFRCC for Cardiovascular Cell Therapy Research Network (includes Investigator Training Core)
One of seven regional centers in a collaborative network evaluating novel CV cellular therapies.
Role: Principal Investigator, UF Regional Center
- 5 UL1 TR000064-05 Nelson (PI) 07/09 - 03/14 NCE
UF Clinical and Translational Science Award
Create environment for individuals from diverse disciplines to interact and provide resources, services and technologies to address local and regional barriers to collaborative clinical research.
Role: Co-Investigator. Leadership Group and Director of UF Clinical Research Units
- 5 R01 HL090957-04S Bairey Merz (PI)/Pepine (MPI) 09/08 – 08/15
Women's Ischemia Syndrome Evaluation (WISE) Coronary Vascular Dysfunction
Study of microvascular diathesis underlying angina and/ischemia in women without flow-limiting stenoses.
Role: Principal Investigator for UF site and MPI for Project
- 5 U01 AG022376-09 Pahor (PI) 09/03 - 11/15
Physical Exercise to Prevent Disability
Data-basing and analysis of ECGs online from an RCT for active life style vs. usual care among older subjects.
Role: Principal Investigator for ECG Core
- 5 U01 GM074492-10 Johnson (PI) 08/05 - 07/15
Pharmacogenomic Evaluation of Antihypertensive Responses PEAR (Competitive Renewal)
To delineate the mechanistic basis for genetic determinants of BP lowering and adverse metabolic responses to thiazide diuretics and beta-blockers when used for antihypertensive treatment.
Role: Co-Investigator
- R01 HL033610-28 Raizada, PI 09/96 - 06/18
Angiotensin and Neuroimmune Activation in Hypertension
To understand why sympathetic nerves become permanently overactive by focusing on the role of the brain and peripheral immune system in causing this overactivity.
Role: Co-Investigator
- R01 HL056921-18 Raizada, PI 09/96 - 02/16
CVD Protection Mechanisms Involving ACE2/Ang-(1-7) Axis
This work tests whether imbalance in vasodeleterious axis (ACE/Ang II/AT1R) and vasoprotective axis (ACE2/Ang-(1-7)/MasR) of the RAS initiates signaling results in endothelial dysfunction leading to CVD.
Role: Consultant

Completed Research Support

- INVEST Project: 536-1996 Abbott Labs/
UF Opportunity Fund Pepine (Project PI) 03/98–03/10
INternational VErapamil-trandolapril SStudy (INVEST)
Study of treatment strategies for hypertension in CAD patients, extended to 2010 for long-term follow-up.
Role: Principal Investigator
- U01 HL64924 NIH/NHLBI Pepine (PI) 07/01 – 05/09
Altered Renin Angiotensin System as a Mechanism for Coronary Microvascular Dysfunction in Women
RAAS contribution to coronary macro/microvascular dysfunction in women with symptom/signs of cardiac ischemia without obstructive CAD.
Role: Principal Investigator
- R01 HL091005-04 Pepine (PI) 10/08 – 07/13
Ancillary Functional Studies for the CCTRN
Investigation of pathophysiologically relevant alterations of circulating/bone marrow vascular progenitor cells.
Role: Principal Investigator