BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Cooke, John P	Professor of Medicine (Cardiovascular Medicine)
eRA COMMONS USER NAME (credential, e.g., agency login) COOKE.JOHN	

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
Cornell University, Ithaca, NY	BA	1976	Biology
Wayne State University, Detroit, MI	MD	1980	Medicine
Mayo Graduate School of Medicine, Rochester, MN	PhD	1985	Physiology
Mayo Graduate School of Medicine, Rochester, MN	Res/Fellow	1980-87	Cardiovascular Medicine

A. Personal Statement

I have 25 years of experience in fundamental and translational research in endothelial biology, with a record of developing therapeutic molecules to address atherosclerosis and angiogenesis, including 29 patents granted or pending, licensed to companies including Lumen, CoMentis and Vermillion. Building on our discovery that nicotine accelerates pathological neovascularization (in atherosclerosis, cancer and AMD), we defined the role of the endothelial nicotinic acetylcholine receptor (nAChR), and developed an antagonist of the nAChR that is now in clinical trials to treat age-related macular degeneration. We defined the role of ADMA (the endogenous NO synthase inhibitor) in models of atherosclerosis and angiogenesis, and extended this work into man. We have developed small molecule allosteric agonists, as well as antagonists, of this pathway. More recently, the lab has focused on elucidating, synthesizing, and delivering, modulators of endothelial phenotype and regenerative function. We have refined methodology to derive endothelial cells (ECs) from pluripotential cells, and demonstrated their therapeutic benefit in a pre-clinical model. We have generated new insights regarding innate immunity and epigenetic activation for cellular reprogramming, toward vascular regeneration.

B. Positions and Honors

Employment

1987-90 Assistant Professor of Medicine, Harvard Medical School, Boston, MA
1990-95 Assistant Professor of Medicine, Stanford University School of Medicine, Stanford, CA
1995-2004 Associate Professor of Medicine, Stanford University School of Medicine
2004-present Professor of Medicine, Stanford University School of Medicine
2009-present Associate Director, Stanford Cardiovascular Institute, Stanford University School of Medicine

Other Experience and Professional Memberships

2005-07 President, Society for Vascular Medicine
2006-2009 Director, American Board of Vascular Medicine
2006-2010 Chair, Young Investigator Award, Accreditation Coordinating Committee
2006-2010 Chair, Zipes Distinguished Young Scientist Award, Accreditation Coordinating Committee

Honors

1988 Milton Award, Harvard Medical School
1990 First Place, Young Investigator Competition, American College of Cardiology
1990 Henry Christian Award, American Federation for Clinical Research
1991 Vascular Academic Award, National Institutes of Health
1996 Established Investigator Award, American Heart Association
2001 Departmental Teaching Award, Stanford University School of Medicine
2008 "2008 Best PAD Research Award", Peripheral Arterial Disease Coalition
2009 Master of the Society for Vascular Medicine
2010 Election to the Association of American Physicians

C. Selected Peer-reviewed Publications - (from over 450 papers with over 19,500 citations; h index = 75 ISI Web of Knowledge, 01-09-13).

1. Heeschen C, Jang J, Hoai-Ky V, Kaji S, Yang P, Hu RS, **Cooke JP**: Nicotine is an agent of angiogenesis. Nicotine stimulates angiogenesis and promotes tumor growth and atherosclerosis. *Nature Medicine.* 2001 Jul; 7(7):833-9.
2. Dayoub H, Achan V, Adimoolam S, Jacobi J, Stuehlinger M, Wang B, Tsao PS, Kimoto M, Vallance P, Patterson AJ, **Cooke JP**: DDAH Regulates NO Synthesis: Genetic and physiological evidence. *Circulation.* 2003; 108: 1043-1048.
3. Zhu B, Heeschen C, Sievers RE, Karliner JS, Parmley WW, Glantz SA and **Cooke JP**: Second Hand Smoke Stimulates Tumor Angiogenesis and Growth, *Cancer Cell.* 2003; 4(3):191-6.
4. Ho H-K V, Jang JJ, Kaji S, Spektor G, Fong A, Yang P, Hu RS, Schatzman R, Quertermous T, **Cooke JP**: Developmental Endothelial Locus-1 (Del-1): a Novel Angiogenic Protein. Its Role in Ischemia *Circulation.* 2004 Mar 16;109(10):1314-9.
5. Wilson A, Harada R, Nair N, Balasubramanian N, **Cooke JP**: L-arginine supplementation in peripheral arterial disease: No benefit and possible harm. *Circulation.* 2007 Jul 10;116(2):188-95.
6. Ng M, Wu J, Chang E, Wang B-Y, Katzenburg-Clark R, Ishii-Watabe A, Gerritsen ME, **Cooke JP**: A central role for nicotinic cholinergic regulation of growth factor-induced endothelial cell migration – Novel insights into angiogenesis. *Arterioscler Thromb Vasc Biol.* 2007 Jan;27(1):106-12.
7. Li Z, Wu JC, Sheikh AY, Kraft D, Cao F-, Xie X, Robbins RC, **Cooke JP**, Wu JC: Differentiation, survival, and function of embryonic stem cell-derived endothelial cells for ischemic heart disease. *Circulation.* 2007 Sep 11;116(11 Suppl):I46-54.
8. Wilson AM, Kimura E, Harada RK, Nair N, Narasimhan B, Meng X-Y, Zhang F, Beck KR, Olin JW, Fung ET, **Cooke JP**: Beta-2 microglobulin as a biomarker in peripheral arterial disease. Proteomic profiling and clinical studies. *Circulation.* 2007 Sep 18;116(12):1396-403.
9. Huang NF, Niiyama H, De A, Gambhir SS, **Cooke JP**. Embryonic stem cell-derived endothelial cells for treatment of hindlimb ischemia. *J Vis Exp*. 2009 Jan 23;(23). pii: 1034. doi: 10.3791/1034. PMCID: PMC2781824
10. Wu JC, Chruscinski A, de Jesus Perez VA, Singh H, Pitsiouni M, Rabinovitch M, Utz PJ, **Cooke JP** : Cholinergic modulation of angiogenesis : Role of the α7 nicotinic acetylcholine receptor. *J Cell Biochem*. 2009, Oct 1;108(2): 433-46. PMCID: PMC3140170
11. Huang NF, Fleissner F, Sun J, **Cooke JP**: Role of nitric oxide signaling in endothelial differentiation of embryonic stem cells. *Stem Cells and Development.* 2010 Oct;19(10):1617-26. PMCID: PMC3121801
12. Leeper NJ, Hunter AL, **Cooke JP**: Stem cell therapy for vascular regeneration: Adult, embryonic and induced pluripotent stem cells. *Circulation.* 2010;122:517-526. PMCID: PMC2920605
13. Huang NF, Niiyama H, Peter C, De A, Natkunam Y, Fleissner F, Li Z, Rollins MD, Wu JC, Gambhir SS, **Cooke JP**: Embryonic stem cell-derived endothelial cells incorporate into ischemic hindlimb and restore perfusion. *Arteriosclerosis, Thrombosis and Vascular Biology.* 2010 May;30(5):984-91. PMCID: PMC2874560
14. Rufaihah AJ, Huang NF, Jame S, Lee J, Nguyen HN, Byers B, De A, Okogbaa JN, Rollins M, Reijo-Pera R, Gambhir SS, **Cooke JP**: Endothelial cells derived from human IPSCs increase capillary density and improve perfusion in a mouse model of peripheral arterial disease. *Arteriosclerosis, Thrombosis and Vascular Biology*. 2011 Nov;31(11):e72-9. PMCID: PMC3210551
15. Wong WT, Huang NF, Botham CM, Sayed N and Cooke JP: Endothelial cells derived from nuclear reprogramming. *Circ Res.* 2012 Oct 26;111(10):1363-75. PMCID: PMC3526979
16. Lee J, Sayed N, Hunter A, Au KF, Wong WH, Mocarski E, Reijo Pera R, **Cooke JP**: Activation of innate immunity is required for efficient nuclear reprogramming. *Cell.* 2012 Oct 26;151(3):547-58. PMCID: pending
17. Hong G, Lee JC, Robinson JT, Raaz U, Xie L, Huang NF, **Cooke JP** and Dai H: Multi-functional in vivo vascular imaging using near-infrared II fluorescence. *Nature Medicine*. 2012 Dec 6;18(12):1841-6. PMCID: pending

D. Research Support

Ongoing Research Support

TORNIER04618 Cooke, PI 08/01/12 - 02/28/**13**

Tornier, Inc., Evaluation of the efficacy of Tornier Cell Transplantation in a mouse model of peripheral limb ischemia. The study is to determine if Tornier cell implantation can promote angiogenesis and restore blood flow in a murine model of peripheral limb ischemia.

SPO109490 Cooke, PI 10/01/12 - 04/30/**13**

NIH, RNAcore for the Progenitor Cell Biology Consortium. The goal of this project is to service the Progenitor Cell Biology Consortium by producing mRNA and modified mRNA as well as to be an innovator of RNA synthesis technology including *in vivo* application.

1K12 HL087746 Cooke, PI 04/01/07 - 03/31/**14**

NIH, Stanford Career Development In Vascular Medicine. The purpose of this project is to develop a K12 clinical research training program in vascular medicine.

1T32 HL098049 Cooke & Dalman, PI 02/01/10 - 01/31/**15**

NIH, Mechanisms and Innovation in Vascular Disease. This is a training program for postdoctoral fellows in translational vascular biology. The overarching goal for this program is to produce researchers who are well-schooled in the fundamental problems of vascular disease, and are driven to find innovative strategies to address those problems.

1R01 EY02060901 Cooke & Campochiaro, PI 09/30/11 - 08/31/**15**

NIH, The role of the Nicotinic Cholinergic Pathway in Retinopathy of Prematurity. These studies have the potential to provide new insights regarding the pathogenesis of ischemia-induced neovscularization in the retina and may provide the bases for new treatments for retinopathy of prematurity.

1R01 HL093172 Wu, PI 04/15/09 - 11/30/**15**

NIH. Molecular Imaging of Targeted Cardiac Gene Therapy. In this project, we seek to develop a smart vector system that incorporates high transfection efficiency, hypoxia sensing switch mechanism, tissue specificity, and a therapeutic gene based on short-hairpin inhibition of prolyl hydroxylase-2 (shPHD2). The overall goal is to improve myocardial neoangiogenesis following injury

1U01 HL100397 Cooke, PI 09/30/09 - 04/30/**16**

NIH. Basic and translational research of iPSC-based hematologic and vascular therapies. This U0-1 is designed to elucidate genetic determinants of nuclear reprogramming, as well as determinants of differentiation to hematopoietic and endothelial lineage. Induced pluripotential stem cells (iPSCs) will be differentiated to endothelial and hematopoietic cells and characterized in vitro and in pre-clinical models of hematopoiesis and angiogenesis.

1UM1 HL113456 Cooke, PI 04/01/12 - 03/31/**19**

NIH. Cell Characterization and Imaging for Regenerative Therapies in Ischemic Diseases. The major goal of this project is to contribute to the clinical effort of the Cardiovascular Cell Therapy Research Network (CCTRN) through our innovative in vivo imaging and cell characterization approaches for the treatment of cardiovascular disease with cell therapies.

1R01 AR063963 (NIH Director's Transformative Research Award) Blau, PI 09/30/12 - 08/31/**16**

Telomere extension using nucleoside-modified mRNA and exosomes as a novel therapy for DMD. The Cooke lab has developed mmRNA technology permitting telomere extension, and the Blau lab has shown the importance of telomere length in the pathobiology of Duchenne's muscular dystrophy. We will determine if

telomere extension improves replicative capacity of cardiac myocytes and/or cKit+ stem cells, and enhances myocyte contractility and left ventricular function.

Completed Research Support

No Identifying Number Cooke, PI 02/01/05 - 01/31/**10**
Genzyme Study. A Phase 2, Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter, Dose-selection Study of Ad2/Hypoxia Inducible Factor (HIF)-1α/VP16 in Patients with Intermittent Claudication.

No Identifying Number Cooke & Swartz, Co-PI 04/01/09 - 03/31/**10**
The Wallace H. Coulter Translational Research Grant Program at Stanford University. Efficient and Safe Methods for Nuclear Reprogramming

NIH, 1R01 CA098303 Cooke, PI 03/04/05 - 02/28/**10**
Signal-transduction of endothelial nAChR in angiogenesis.

No Identifying Number Cooke, PI 11/15/09 - 04/15/**10**
Johnson & Johnson
Evaluation of the efficacy of ATRM Cell Transplantation in a mouse model of peripheral arterial disease

4588SC Haskell, PI 07/01/09 - 06/30/**10**
University of California, San Francisco
Multifactor Risk Reduction for Optimal Management of PAD.

NIH, 1R01 HL075774 Cooke, PI 09/22/03 - 06/30/**10**
Genetic Determinants of Peripheral Arterial Disease.

NIH, 1P50HL083800 Dalman, PI 04/01/06 - 04/30/**11**
AAA Disease: Mechanism, Stratification and Treatment.

18XT-0098 Cooke, PI 07/01/09 - 06/30/**11**
University of California Office of the President. An atypical nicotine receptor: Target for anti-angiogenics Mechanisms.

1RC2 0D006604 Cooke, PI 09/30/09 - 08/31/**11**
NIH. NCE-based strategy for nuclear reprogramming regenerative medicine.

SPO #46914 Cooke, PI 02/11/10 - 02/10/**12**
Pluristem. Safety of Intramuscular Injection of Allogeneic PLX-PAD Cells for the Treatment of Critical Limb Ischemia.

Bio-X proposal 53 Cooke, PI 10/01/10 - 09/30/**12**
Matrix-induced alignment: effects on endothelial biology.

11IRG5180026 Cooke, PI 01/01/11 - 12/31/**12**
AHA. Toward a Novel Therapy for Hypertension in Insulin Resistant Patients**.**