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Place of Birth: [redacted]

Education

1986-1991	B.A.	English	Dartmouth College
1992-1996	M.D.		Columbia College of Physicians & Surgeons
2002-2004	M.P.H	Clinical Effectiveness	Harvard School of Public Health

Postdoctoral Training

07/96-06/99	Resident	Medicine	Massachusetts General Hospital
07/99-06/01, 07/02-06/03	Clinical Fellow	Cardiology	Massachusetts General Hospital
07/01-06/02	Chief Resident	Medicine	Massachusetts General Hospital
07/02-06/04	Postdoctoral Fellow	Epidemiology Christopher O'Donnell, mentor	Framingham Heart Study
07/02-06/07	Postdoctoral Fellow	Genomics Joel Hirschhorn, mentor	Broad Institute of Harvard and MIT

Faculty Academic Appointments

07/01-07/08	Instructor	Medicine	Harvard Medical School
08/08-	Assistant Professor	Medicine	Harvard Medical School

Appointments at Hospitals/Affiliated Institutions

11/98-09/03	Hospitalist	Medicine	Emerson Hospital
10/02-11/04	Intensivist	Medicine	Newton-Wellesley Hospital
07/03-06/04	Graduate Assistant	Cardiology	Massachusetts General Hospital
07/04-06/09	Assistant in Medicine	Cardiology	Massachusetts General Hospital
07/09-	Assistant Physician	Cardiology	Massachusetts General Hospital

Other Professional Positions

2004-	Affiliate Scientist	Framingham Heart Study
2007-	Faculty	Center for Human Genetic Research, MGH
2007-	Faculty	Cardiovascular Research Center, MGH
2007-2013	Affiliate Scientist	Broad Institute of Harvard and MIT
2009-	Faculty	Biological and Biomedical Sciences, Harvard University
2009-	Scientific Advisory Board	FDA Endocrinologic and Metabolic Drugs Committee
2012-	Scientific Advisory Board	Arrhythmogenic Potential of Drugs (ARITMO, Erasmus Medical Center, Rotterdam, Netherlands)
2013-	Associate Member	Broad Institute of Harvard and MIT

Major Administrative Leadership Positions

Local

2000-2001	Administrative Fellow	Cardiology, Massachusetts General Hospital
2001-2002	Chief Resident	Medicine, Massachusetts General Hospital
2005-	Course Director, Primer in Medical and Population Genetics	Broad Institute of Harvard and MIT
2007-	Medical Director, Electrocardiography Laboratory	Massachusetts General Hospital
2007-	Conference organizer, A Primer on Complex Trait Genetics: Basic Principles for the Beginning Investigator	Massachusetts General Hospital
2007-	Co-director, Human Cardiovascular Genetics Program	Cardiovascular Research Center, Massachusetts General Hospital
2008-	Co-course director, Genetics in Medicine: Bench to Bedside	Harvard Medical School

Committee Service

Local

2005-2006	Medical and Population Genetics Planning Committee	Broad Institute of Harvard and MIT Member

National

2009-	Cardiac Safety Research Consortium	FDA/Pharma/Academic roundtable Member
2013-	QT Drug Lists Advisory Board	Academic review of literature to guide clinicians (qtdrugs.org)

Professional Societies

1996-	American Medical Association	
1996-	Massachusetts Medical Society	
1999-	American College of Cardiology	
	2006-	Fellow
2003-	American Heart Association	
	2007-	Fellow, AHA Council on Epidemiology & Prevention; Council on Basic Cardiovascular Sciences; Council on Functional Genomics and Translational Biology

2006-	AHA Functional Genomics and Translational Biology Council	
	2006-	Leadership Committee Member
	2009-2011	Vice Chair, Program Committee
	2011-	Chair, Program Committee
2006-	Heart Rhythm Society	
	2010-	Member

Grant Review Activities

2005-	Subcommittee on Review of Research Proposals, Executive Committee on Research	Massachusetts General Hospital Reviewer
2009-	Endocrinologic & Metabolic Drugs Advisory Committee	Food and Drug Administration Ad Hoc Reviewer
2010-	Genomics & Translational Biology Epidemiology and Observational Epidemiology study section	American Heart Association Reviewer
2010-	Clinical and Integrative Cardiovascular Science study section	National Institutes of Health Ad Hoc Reviewer
2012-	Genetics of Health and Disease	National Institutes of Health Ad Hoc Reviewer

Editorial Activities

Ad hoc Reviewer

New England Journal of Medicine
Journal of the American Medical Association
Nature Genetics
Circulation
Circulation Research
Science
American Journal of Human Genetics
PLoS Genetics
Human Molecular Genetics
European Journal of Human Genetics
Journal of the American College of Cardiology
Nature Medicine

Other Editorial Roles

2007-2012	Section Editor	Genetics Section, Current Cardiovascular Risk Reports
2008-	Member, Editorial Board	Circulation: Cardiovascular Genetics

Honors and Prizes

1995	Alpha Omega Alpha	Columbia University College of Physicians & Surgeons	Medical Honor Society
2002, 2009	Partners in Excellence Award	Massachusetts General Hospital	
2008, 2011	Excellence in Tutoring Award	Harvard Medical School	Human Genetics, First Year Medical Students
2009	Best Translational	Massachusetts General	Selected from 256 abstracts

	Research Abstract, MGH Clinical Research Day	Hospital	
2009	Top Ten Cardiovascular Discoveries of 2009	American Heart Association	"GWAS identifies eight loci associated with blood pressure" (Newton-Cheh C et al *Nature Genetics* 2009)
2014	Top Original Paper of 2013 Award, Popular Science Category	Hypertension	"A Blood Pressure Genetic Risk Score Is a Significant Predictor of Incident Cardiovascular Events in 32 669 Individuals"

Funding Information

Past

2002-2005	Candidate gene association with QT interval (Young Investigator Award) GlaxoSmithKline Young Investigator Award PI ($150,000) Study focused on candidate genes involved in Long QT Syndrome
2002-2005	Training Program in the Epidemiology of Cardiovascular Disease NIH/T32 (HL07575) Trainee (PI: P. Ridker) Support for training in epidemiology and statistics
2005 (returned)	Candidate gene and genome-wide association of QT interval American Heart Association Scientist Development Grant PI ($236,364) Returned for overlap when K23 funded
2005-2010	Genetic determinants of cardiac repolarization NIH/K23 (HL080025) PI ($149,500/year) Candidate gene, genome-wide association and large-scale resequencing study of QT interval
2006-2010	Genetic determinants of QT interval, sudden death Doris Duke Clinical Scientist Development Award PI (NCE) Career development award supporting large-scale replication of QT interval genome-wide association studies
2009-2010	Effect of Moxifloxacin on the QT interval: Pilot NIH/CTSC PI ($50,000/year) Principal investigator on project examining the QT interval response to oral moxifloxacin as pilot for large-scale pharmacogenetic study.
2009-2012	Cardiology and Metabolic Patient Cohort Pfizer Co-I ($9,985/year) The goal of this project is to recruit 3000 patients from the MGH Heart Center, to store serum and plasma for future studies, and to genotype DNA for genes that confer susceptibility to T2D and cardiovascular disease.
2007-2012	Genome-wide association study of sudden cardiac arrest NIH/R01 (HL088456)

PI- subcontract (PI: N. Sotoodehnia)
PI of subcontract providing study design and analysis methods for study of genetics of sudden cardiac death

2007-2013 Genomic dissection of QT interval duration and sudden death
Burroughs Wellcome Career Award for Medical Scientists
PI ($151,000/year TDC)
Career development award supporting QT interval genome-wide association and extension to sudden cardiac death cohorts.

2010-2013 Physiologic effects of natriuretic peptide genetic variation
NIH/R01 (HL098283)
PI (PIs: Newton-Cheh, Wang) ($178,795/year TDC)
Study to fine map and identify novel genetic factors influencing plasma natriuretic peptide concentration through resequencing and to characterize the physiologic effects of genetic variants through chronic and acute sodium challenge.

Current

2013-2017 Physiologic profiling of sGC genetic variants
NIH/R01 (HL113933)
PI ($333,000/year TDC)
Study to characterize the role of soluble guanylate cyclase as the mediator of a blood pressure association at the locus using genotype-directed translational studies in humans and to elucidate the causal variant and its mechanism of action using cellular models of human genetic variants.

Teaching of Students in Courses

2001-2002	Core II, medical sub-internship	Massachusetts General Hospital
	HMS Fourth year students	2 hours per week (4 months)
2004-2006	Program in Clinical Effectiveness: Critique of the Literature seminar	Harvard School of Public Health
	MPH Students	2 hours
2004-2006	Core I Electrocardiography Series, Massachusetts General Hospital: Introduction to electrocardiography including leads, rates, intervals, determination of axis.	Harvard Medical School
	Medical Students	1 hour
2006-2010	First Year Human Genetics	Harvard Medical School
& 2012	Small group session of medical students	6 hours per week (3 weeks)
2007-	Genetics in Medicine: Bench to Bedside	Harvard Medical School
	PhD Students	3 hours
2008-	Program in Clinical Effectiveness: Genetic epidemiology	Harvard School of Public Health
	MPH Students	2 hours

Clinical Supervisory and Training Responsibilities

2001-2002	Chief Medical Resident Massachusetts General Hospital	Full-time, one year
2004-2006	Attending, Ellison general medicine service Massachusetts General Hospital	2-3 hours, twice weekly, one month
2004-2005,	Attending, Cardiology Consultation service	4 hours, 7 days per week, two weeks

2007	Massachusetts General Hospital	
2004-	Attend in outpatient fellow's clinic Massachusetts General Hospital	4 times per year
2005-2013	Attend on inpatient Heart Failure and Transplant service Massachusetts General Hospital	4 hours, 7 days per week, one half month; 3-4 times per year
2005	Attend on inpatient Cardiac Arrhythmia service Massachusetts General Hospital	4 hours, 7 days per week, one half month
2006-2013	Attend on inpatient Coronary Care Unit Massachusetts General Hospital	4 hours, 7 days per week, one half month
2008-2013	Attend on inpatient Heart Failure and Transplant service	4 hours, 7 days per week, one half month; 2 times per year

Laboratory and Other Research Supervisory and Training Responsibilities

2006	Supervision of technician (Ripal Shah) who subsequently went into industry as a consultant	Weekly mentorship for 12 months
2006	Supervision of technician (Alim Hirji) as a medical student who subsequently completed pediatric residency at the Hospital for Sick Kids of Toronto	Weekly mentorship for 12 months
2006-2007	Supervision of technician (Sirisha Kovvali) who subsequently matriculated to the Oregon Health & Science University, MPH	Weekly mentorship for 24 months
2006-2007	Supervision of technician (Aarti Surti) who subsequently matriculated to the University of Michigan, MD	Weekly mentorship for 24 months
2007	Supervision of technician (Marie-Louise Meng) who subsequently matriculated to Harvard Medical School, MD	Weekly mentorship for 12 months
2007, 2008	Supervision of technician (Sara Tribune) who subsequently matriculated to Brown University, MD	Summer mentorship for 3 months each summer
2009-2012	Supervision of clinical research coordinator (Allicia Ryan) who subsequently matriculated to a school of osteopathy	Weekly mentorship for 36 months
2010	Supervision of technician (Kimberly Kummer), now a college student at Dartmouth	Summer mentorship for 3 months
2010-2012	Supervision of clinical research coordinator (Andrew Martinez)	Weekly mentorship for 24 months
2011, 2012	Supervision of technician (Samuel Kim) who subsequently matriculated to Harvard Medical School, MD	Summber mentorship for 3 months each summer
2011-2012	Supervision of research analyst (Sara Pulit) who subsequently matriculated to University of Utrecht, Netherlands, MS	Weekly mentorship for 12 months

2013	Supervision of clinical research coordinator (Jillian Pickett)	Summer mentorship for 3 months
2013-	Supervision of clinical research coordinator (Courtney Karol)	Weekly mentorship

Formally Supervised Trainees

2006- Peter Noseworthy, MD/ Electrophysiologist/Physician-scientist, Mayo Clinic
Supervision of postdoctoral fellow in studies of the genetic basis of cardiac arrhythmias and cardiotoxic drug responses. Peter authored a review of the genetics of sudden cardiac death published in Circulation, has participated in a genome-wide association study of QT interval published in Nature Genetics is conducting large-scale studies of association of genetic variants altering QT interval in the Finrisk study, and a physiologic study of QT interval response to exposure to moxifloxacin. Peter was awarded two post-doctoral fellowship grants on which I am the primary sponsor for this work from the American Heart Association (returned) and the Heart Rhythm Society (current).

2007-2012 J. Gustav Smith, Faculty, Lund University, Sweden

2014- Supervision of medical student (and subsequently PhD student) in genome-wide association studies of electrocardiographic measures and biomarkers of cardiovascular disease Gustav published 14 articles on which we were both co-authors, on 9 of which he was the first author. I was one of three thesis mentors on his PhD at Lund University, Sweden. He is currently completing a second post-doc in my laboratory for 2 years.

2008-2013 Pankaj Arora, MD/ Cardiology Fellow, University of Alabama
Supervision of postdoctoral fellow in resequencing and association studies of blood pressure genes in the Framingham Heart Study and in the Malmö Diet and Cancer Study. Pankaj worked on several studies of the genetic basis of blood pressure regulation. Pankaj authored a review of the genetic basis of hypertension at *Current Opinion in Cardiology* and an original research article in the *Journal of Clinical Investigation.*

2009-2010 Abigail Khan, MD/ Cardiology Fellow, University of Pennsylvania
Supervision of postdoc in characterizing the physiologic response in humans of genetic variation at the natriuretic peptide locus. Abigail was a postdoctoral fellow in my lab and worked on several studies of the genetic basis of blood pressure regulation.

2010-2011 Sandosh Padmanabhan, MD/ Faculty, University of Glasgow
Supervision of postdoctoral fellow, on one-year sabbatical from University of Glasgow where he is on the Genetics Faculty, using targeted exonic resequencing to characterize novel blood pressure loci. Sandosh is supported by an early faculty award from the British Heart Foundation on which I am the primary sponsor.

2010-2012 Erin Coglianese, MD/ Staff Cardiologist, Loyola University Medical Center
Supervision of postdoctoral research fellow initiating and completing a pilot study of the role of common genetic variation in the response to inhaled nitric oxide to examine the physiologic basis of an association with blood pressure.

2013- Gulum Kosova, PhD/ Postdoctoral fellow, Massachusetts General Hospital
Supervision of post-doctoral research fellow, focused on blood pressure genetics studies and computational biology. She is using next generation sequence data to identify novel genetic variation that influences blood pressure regulation.

2013- Michael Rosenberg, MD/ Postdoctoral fellow, Massachusetts General Hospital
Supervision of post-doctoral fellow (trained as an electrophysiologist) focused on studies of sudden cardiac death and arrhythmias in response to drug exposure. Mike is leading several

translational studies and runs a multi-center consortium of torsade and drug response to anti-arrhythmics.

Formal Teaching of Peers (e.g., CME and other continuing education courses)

2005	Cardiac Case Review Harvard Review of Internal Medicine, Massachusetts General Hospital	One Talk Cambridge, Massachusetts
2006, 2007, 2008, 2009, 2010	Heart Failure Management Harvard Primary Care Internal Medicine, Massachusetts General Hospital	One Talk Cambridge, Massachusetts
2011	EPI Lecture Harvard School of Public Health	One Talk Boston, Massachusetts
2011	Heart Failure/Transplant Services Lecture Massachusetts General Hospital	One Talk Boston, Massachusetts

Invited Presentations and Courses

Local

2002 The Long QT Syndrome: Implications for the General Population / Grand Rounds
Department of Medicine, Massachusetts General Hospital, Boston, MA

2003 Genetics of QT Interval Variation in the General Population / Research Conference
Division of Preventative Medicine, Brigham and Women's Hospital, Boston, MA

2004 Dissecting the Genetic Determinants of Variation in Cardiac Repolarization / Research Conference
Division of Preventive Medicine, Brigham and Women's Hospital, Boston, MA

2004 Genetic Determinants of Variation in Electrocardiographic Measures / Research Conference
Endocrine Program, Broad Institute of Harvard and MIT, Cambridge, MA

2004 Genetic Dissection of QT Interval Variation in the General Population / Research Conference
Program in Medical and Population Genetics, Broad Institute of Harvard and MIT, Cambridge, MA

2005 Approaches to the Genetic Dissection of Complex Traits / Epidemiology Core Curriculum
Cardiology Fellowship, Massachusetts General Hospital, Boston, MA

2005 Clinical and Genetic Correlates of the Aldosterone to Renin Ratio in the Framingham Heart Study / Research Conference
Altshuler Laboratory, Department of Molecular Biology, Massachusetts General Hospital, Boston, MA

2005 Common variation in CAPON is reproducibly associated with QT interval variation in 3 cohorts / Research Conference
Altshuler Laboratory, Department of Molecular Biology, Massachusetts General Hospital, Boston, MA

2006 Genetic Determinants of the Electrocardiographic QT Interval: Insights from Population Studies / Medicine Grand Rounds
Department of Medicine, Massachusetts General Hospital, Boston, MA

2006 Identifying Novel Repolarization Genes: Genetic Dissection of QT Interval in Population Studies / Cardiology Grand Rounds
Department of Medicine, Massachusetts General Hospital, Boston, MA

2006 Approaches to the Genetic Dissection of Complex Traits / Epidemiology Core Curriculum
Cardiology Fellowship, Massachusetts General Hospital, Boston, MA

2006 Genetic dissection of QT interval variation: defining the genetic determinants of sudden cardiac death & drug-induced arrhythmias / Lab Group Retreat
Altshuler, Burtt, Daly, Hirschhorn lab group, Harvard Medical School

2008 Defining the genetic basis of QT interval duration: implications for drug toxicity and sudden cardiac death / Anesthesia Grand Rounds
Anesthesiology Department, Massachusetts General Hospital, Boston, MA

2009 Harnessing genetics to understand blood pressure physiology / Medicine Grand Rounds
Department of Medicine, Massachusetts General Hospital, Boston, MA

2009 Harnessing genetics to understand blood pressure physiology / Cardiology Grand Rounds
Cardiology Division, Massachusetts General Hospital, Boston, MA

2010 Pharmacogenomics / One-Day Primer on Human Genetics Symposium
Clinical Research Program, Massachusetts General Hospital, Boston, MA

2010 Insights into the genetic determinants of blood pressure / Research Seminar
Center for Human Genetic Research, Massachusetts General Hospital, Boston, MA

2010 Harnessing human genetics to understand myocardial repolarization and cardiotoxic drug response / Research Conference
Center for Life Sciences, Beth Israel Deaconess Medical Center, Boston, MA

2010 Harnessing human genetics to identify novel physiologic determinants of hypertension / Renal Grand Rounds
Brigham and Women's Hospital, Boston, MA

2011 Translating Genetic Variants Influencing Blood Pressure to the Patient / Invited Speaker
Heart Failure Research Conference, Massachusetts General Hospital, Boston, MA

2011 Torsade de pointes and polymorphic ventricular tachycardia / Invited Speaker
ECG Session: TdP and PMVT, Massachusetts General Hospital, Boston, MA

2011 Lessons from the Study of Blood Pressure Genetics / Invited Speaker
A Primer on Complex Trait Genetics: Basic Principles for the Beginning Investigator, Massachusetts General Hospital, Boston, MA

2011 Harnessing human genetics to identify novel blood pressure pathways / Invited Speaker
Cardiology Translational Research Seminar, Massachusetts General Hospital, Boston, MA

2012 Harnessing genetics to improve our understanding of blood pressure regulation / Invited Speaker
Center for Human Genetic Research, Massachusetts General Hospital, Boston, MA

2012 Harnessing Genetics to Improve Our Understanding of Blood Pressure / Invited Speaker
Cardiovascular Research Center Retreat, American Academy of Arts & Sciences, Cambridge, MA

2013 Genetics establishes a significant role for cGMP pathways in human blood pressure regulation / Invited Speaker
Anesthesia Research Conference, Massachusetts General Hospital, Boston, MA

2013 Harnessing genetics to improve our understanding of blood pressure regulation / Invited Speaker
Center for Human Genetic Research Retreat, Broad Institute, Cambridge, MA

2013 Torsade de pointes and polymorphic ventricular tachycardia / Invited Speaker
Cardiology Fellows Seminar, Massachusetts General Hospital, Boston, MA

2014 Genetic studies of blood pressure regulation converge on cGMP-regulating pathways / Invited Speaker
Heart Failure/Transplant Seminar, Massachusetts General Hospital, Boston, MA

Regional

2003 Candidate Gene Association Study of Risk of Myocardial Infarction / Journal Club
Framingham Heart Study, Framingham, MA

2003 Genetics of QT Interval Variation in the General Population / Research Conference
Program in Medical and Population Genetics, Whitehead Institute Center for Genome Research, Cambridge, MA

2003 Heritability of Electrocardiographic and Echocardiographic Measures of Left Ventricular Hypertrophy / Research Conference
Framingham Heart Study, Framingham, MA

2004 The role of 5-Lipoxygenase Activating Protein and Risk of Myocardial Infarction and Stroke / Journal Club
Framingham Heart Study, Framingham, MA

2005 Association of Genetic Variation in KCNH2 with QT Interval Variation / Research Conference
Framingham Heart Study, Framingham, MA

2005 Conserved non-coding regions represent functional genetic sequence under negative selection / Research Conference
Boston University School of Public Health, Program in Statistical Genetics,

2010 Harnessing human genetics to understand cardiovascular physiology: QT interval duration / Research Conference
Cardiovascular Research Center Seminars, Brown University, Providence, RI

2012 GWAS of the Electrocardiogram: Implications for SCD Syndromes / Invited Speaker
Heart Rhythm Society Scientific Sessions, Boston, MA

2012 Harnessing genetics to improve our understanding of blood pressure regulation / Invited Speaker
Framingham Heart Study Research Conference, Framingham, MA

2013 The Genetic Basis of Drug-induced Arrhythmia / Invited Speaker
Beth Israel Deaconess Medical Center Electrophysiology Section Seminar, Boston, MA

2014 What have genome-wide association studies taught us about cGMP and blood pressure regulation? / Invited Speaker
Ironwood Pharmaceuticals, Cambridge, MA

2014 What has human genetics taught us about the fundamental mechanisms underlying heart failure? / Invited Speaker
Novartis Institutes for BioMedical Research, Cambridge, MA

National

2004 Genetic Determinants of Variation in Electrocardiographic Measures / Research Conference
Laboratory of Biochemical Genetics and Metabolism, Rockefeller University, New York, NY

2005 Genomic studies in the Framingham population / Research Seminar
Cardiovascular Division, Johns Hopkins School of Medicine/Reynolds Center, Baltimore, MD

2006 Genetic determinants of the QT interval / Research Seminar
Center for Human Genomics, Wake Forest University School of Medicine, Charlotte, NC

2007 Defining the genetic basis of electrocardiographic QT interval duration and sudden cardiac death / Research Conference

Seminars in Clinical Research, Rockefeller University, New York, NY

2007 Genetic dissection of QT interval variation and sudden cardiac death / Research Seminar
Jackson Heart Study, University of Mississippi Medical Center, Jackson, MI

2007 The genetic dissection of QT interval duration: implications for drug toxicity and sudden death risk assessment / Research Seminar
Seminars in Integrative Genomics, Vanderbilt University Medical Center, Nashville, TN

2007 The genetic dissection of myocardial repolarization and sudden cardiac death / Research Seminar
Department of Preventive Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL

2008 Genetic determinants of QT interval and sudden death / Grand Rounds
Cardiology Division, MD Anderson

2008 QTGEN: Meta-analysis of genome-wide association studies of QT interval duration in 13,109 individuals / Research Conference
CHARGE Consortium Conference, Department of Epidemiology, University of Washington, Seattle

2009 Late-Breaking Developments in the Genetics of Blood Pressure Regulation and Hypertension / Late-breaking Research Conference
American Society of Hypertension, San Francisco, CA

2009 The Genetic Determinants of QT-interval Variation / International Congress on Genetics/Genomics
American Heart Association

2009 Integrative Genomic Studies in Humans at the FHS / Scientific Sessions
American Heart Association, Orlando, FL

2010 What can we learn from common genetic variants about sudden cardiac death risk? / Scientific Sessions
Heart Rhythm Society, Denver, CO

2011 Pharmacogenetics of QT Interval and Potential Clinical Applications to Reduce Off-Target Drug Toxicity / Invited Speaker
NHLBI and PMC New Frontiers in Personalized Medicine: Cardiovascular Research and Clinical Care Meeting, George Washington University, Washington, DC

2011 Genome Wide Association Studies - Hope or Hype / Invited Speaker
Heart Rhythm Society Scientific Sessions, San Francisco, CA

2011 Genetics establishes a significant role for cGMP pathways in human blood pressure regulation / Invited Speaker
Merck Research Laboratories Seminar, Rathway, NJ

2011 Whole exome sequencing of blood pressure extremes / Invited Speaker
American Heart Association Scientific Sessions, Orlando, FL

2011 Genetic markers of prognosis: What have we learned from studies of blood pressure? / Invited Speaker
American Heart Association Scientific Sessions, Orlando, FL

2012 Harnessing genetics to improve our understanding of blood pressure regulation / Invited Speaker
Northwestern University, Cardiology Grand Rounds, Chicago, IL

2012 The genetic basis of arrhythmias / Invited Speaker
University of Rochester, Cardiology Grand Rounds, Rochester, NY

2012 From Disease Variants to Disease Mechanism: Progress and Challenges / Invited Speaker
American Heart Association Scientific Sessions, Los Angeles, CA

2013 Harnessing genetics to identify novel therapeutic targets and cardiotoxic off-target effects/ Invited Speaker
Regeneron Pharmaceuticals, Tarrytown, NY

2013 Genomic Studies of the Electrocardiogram: New Insights into Arrhythmia Mechanisms / Invited Speaker
Heart Rhythm Society Scientific Sessions, Denver, CO

2013 Genomics of Sudden Cardiac Death / Invited Speaker
Heart Rhythm Society Scientific Sessions, Denver, CO

International

2006 Genetic dissection of the QT interval / Invited Seminar
Department of Epidemiology and Biostatistics Erasmus Medical Centre, Rotterdam, Netherlands

2006 Genetic dissection of QT interval variation / Invited Seminar
Folkhälsan-Östanlid Hospital, Jakobstad, Finland

2006 Genetic dissection of QT interval variation and sudden cardiac death / Invited Seminar
Diabetes and Endocrinology Research Unit, Lund University, Malmö, Sweden

2008 The genetic determinants of electrocardiographic QT interval variation and ventricular arrhythmias / Invited Seminar
Department of Epidemiology, Erasmus Medical Centre, Rotterdam, Netherlands

2009 The genetic dissection of complex cardiovascular traits: blood pressure and electrocardiographic QT interval / Invited Speaker
William Harvey Research Institute at Barts and the London School of Medicine and Dentistry, London, England

2009 The genetic basis of QT interval and blood pressure variation / Invited Seminar
University Medical Center, Groningen, Netherlands

2010 Genome-wide association of blood pressure and hypertension / Invited Talk
Toronto Heart Summit, University of Toronto, Canada

2010 Harnessing genetics to find determinants of sudden cardiac death and cardiotoxic drug response / Invited seminar
National Institute of Health and Welfare, Helsinki, Finland

2011 Genetics establishes a significant role for cGMP pathways in human blood pressure regulation/ Invited speaker
5th International Conference on cGMP, Halle, Germany

2012 Harnessing genetics to improve our understanding of blood pressure and arrhythmias / Invited Speaker
University of Glasgow, Glasgow, Scotland

2013 What have genome-wide association studies taught us about cGMP and blood pressure regulation? / Invited Speaker
6th International Conference on cGMP, Erfurt, Germany

2013 Harnessing genetics to identify novel therapeutic targets and cardiotoxic off-target effects / Invited Speaker
Nature Genetics/Wellcome Trust Genomics of Common Disease conference, Oxford, UK

Current Licensure and Certification

1998 Board of Registration in Medicine, Massachusetts (Full license)

2003 ABIM-Cardiovascular Disease (Certified)

2012 ABIM-Advanced Heart Failure/Transplant Cardiology (Certified)

Practice Activities

2004	Attending Physician, Cardiology	Heart Failure and Transplantation Section, Massachusetts General Hospital	Heart failure clinic and inpatient care of advanced heart failure patients

Technological and Other Scientific Innovations

MGH 3691: EP 08166038.3	Use of Adrenomedullin for Cardiovascular Risk Prediction, filed October 07, 2008; licensed to Brahms AG (now ThermoFischer) In this patent my colleagues and I are co-inventors described the use of adrenomedullin as a predictive biomarker of future cardiovascular events at the population level.
MGH 20275: EP 08268096.9	Arginine Vasopressin Pro-Hormone as Predictive Biomarker for Diabetes, filed October 31, 2008; licensed to Brahms AG (now ThermoFischer) In this patent, my colleagues and I are co-inventors of the use of Arginine vasopressin pro-hormone as a predictive biomarker of future diabetes status at the population level.
MGH provisional	INHIBITORS OF MICRORNAs THAT REGULATE PRODUCTION OF ATRIAL NATUERETIC PEPTIDE (ANP) AS THERAPEUTICS AND USES THEREOF In this patent, my colleagues and I are co-inventors of of the use of microRNA inhibitors to augment atrial natriuretic peptide activity in hypertension and heart failure.

Education of Patients and Service to the Community

Activities

1996	Native Alaskan/Indian Health Service rotations / Medical Student Two month rotation in Indian Health Service hospital in rural Alaska
2007-	Lexington, MA Medical Reserve Corps, Department of Public Health / Executive Committee Contribute to disaster planning and resource allocation at town level

Publications - Peer reviewed publications in print or other media

Note: surname changed from Newton to Newton-Cheh in 1999

1. Polanczyk CA, **Newton C**, Dec GW, Di Salvo TG. Quality of care and hospital readmission in congestive heart failure: An explicit review process. *J Card Fail*. 2001 Dec; 7(4): 289-98.

2. **Newton-Cheh C**, Larson MG, Corey DC, Benjamin EJ, Herbert AG, Levy D, D'Agostino RB, O'Donnell CJ. QT interval is a heritable quantitative trait with evidence of linkage to chromosome 3 in a genome-wide linkage analysis: The Framingham Heart Study. *Heart Rhythm*. 2005 Mar; 2(3): 277-84.

3. Kathiresan S, Larson MG, Vasan RS, Guo CY, Vita JA, Mitchell GF, Keyes MJ, **Newton-Cheh C**, Musone SL, Lochner AL, Drake JA, Levy D, O'Donnell CJ, Hirschhorn JN, Benjamin EJ. Common genetic variation at the endothelial nitric oxide synthase locus and relations to brachial artery

vasodilator function in the community. *Circulation*. 2005 Sep 6; 112(10):1419-27.

4. Drake JA, Bird C, Nemesh J, Thomas DJ, **Newton-Cheh C**, Reymond A, Excoffier L, Attar H, Antonarakis SE, Dermitzakis ET, Hirschhorn JN. Conserved noncoding sequences are selectively constrained and not mutation cold spots. *Nature Genetics*. 2006 Feb; 38(2): 223-227.

5. Kathiresan S, Gona P, Larson MG, Vita JA, Mitchell GF, Tofler GH, Levy D, **Newton-Cheh C**, Wang TJ, Benjamin EJ, Vasan RS. Cross-sectional relations of multiple biomarkers from distinct biological pathways to brachial artery endothelial function. *Circulation*. 2006 Feb 21; 113(7): 938-45.

6. Kathiresan S, Larson MG, Vasan RS, Guo CY, Gona P, Keaney JF Jr, Wilson PW, **Newton-Cheh C**, Musone SL, Camargo AL, Drake JA, Levy D, O'Donnell CJ, Hirschhorn JN, Benjamin EJ. Contribution of Clinical Correlates and 13 C-reactive protein Gene Polymorphisms to Interindividual Variability in Serum C-Reactive Protein Level. *Circulation*. 2006 Mar 21; 113(11):1415-23.

7. Arking DE, Pfeufer A, Post W, Kao WH, **Newton-Cheh C**, Ikeda M, West K, Kashuk C, Akyol M, Perz S, Jalilzadeh S, Illig T, Gieger C, Guo CY, Larson MG, Wichmann HE, Marban E, O'Donnell CJ, Hirschhorn JN, Kaab S, Spooner PM, Meitinger T, Chakravarti A. A common genetic variant in the NOS1 regulator NOS1AP modulates cardiac repolarization. *Nature Genetics*. 2006 Jun; 38(6): 644-651.

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Narrative Report

My laboratory in the Massachusetts General Hospital Center for Human Genetic Research and Cardiovascular Research Center is focused on identification of the genetic factors that underlie variation in hypertension and arrhythmia risk by large population-based studies of blood pressure and QT interval duration, determination of the role of these factors in human physiology, elucidation of novel mechanisms of disease that highlight potential therapeutic targets, with the goal of improving human health at the population level. I spend 83% of my time on research, 10% on patient care, 5% on teaching and 2% on administration. Areas of excellence in the Newton-Cheh laboratory include the genetics of blood pressure and of myocardial repolarization. Elevated blood pressure is an important modifiable risk factor for stroke, heart failure, myocardial infarction and end-stage renal disease. Electrocardiographic QT interval prolongation at rest is a risk factor for sudden cardiac death and occurs as a potentially fatal cardiotoxic side effect of many medications, leading to loss of valuable compounds from the drug development pipeline.

I established that a common genetic variant in the 3' untranslated region of *NPPA* is associated with higher plasma atrial natriuretic peptide (ANP) concentration, and as a consequence lower blood pressure

and hypertension risk (Newton-Cheh, *Nature Genetics* 2009). This was the first *in vivo* demonstration of the role of inter-individual variability in the natriuretic peptide system in blood pressure regulation and was the first common variant for blood pressure reported. This work served as the basis of my R01, on which I am PI, to conduct translational studies using dietary sodium challenge and acute intravenous saline administration in individuals selected on the basis of natriuretic peptide genotype to define the impact of the natriuretic peptide system on acute and chronic responses to salt exposure. We have just published in the *Journal of Clinical Investigation* the results of this work in which we demonstrate that the genetic effect on ANP is as strong as the impact of a 20-fold reduction in sodium intake and identify that the variant acts by interrupting a previously unrecognized negative regulator of ANP, micro-RNA miR-425. We have filed a patent on the use of antagonists of miR-425 to treat hypertension.

I have led international consortia (Steering Committee co-chair) that have completed genome-wide association studies identifying 60 novel genetic loci that regulate blood pressure in humans, (Newton-Cheh, *Nature Genetics* 2009; Ehret, *Nature* 2011, manuscript in preparation). The first paper was recognized by the American Heart Association as one of the top ten discoveries of 2009. These unbiased surveys of the entire genome have focused attention on that natriuretic peptide/guanylate cyclase receptor A and nitric oxide/soluble guanylate cyclase (sGC) systems, both of which cause vasodilation and natriuresis via production of the intracellular second messenger cyclic guanosine monophosphate (cGMP). This work served as the basis for an R01 on which I am principal investigator, which has just been funded. Through this grant, we are recruiting individuals on the basis of their genotype at a SNP in sGC and administering inhaled nitric oxide and performing platelet assays to determine the role of the SNP in sGC-mediated cGMP response, as well as attempting to elucidate the molecular mechanism underlying the blood pressure association.

I have also led the QTGEN and QT-IGC consortia (Steering Committee chair) that have identified in total 68 independent genetic variants at 35 loci that influence QT interval variation (Newton-Cheh, *Nature Genetics* 2009; manuscript under review). While several loci harboring common QT variants are also known to harbor rare variants that cause congenital Long QT Syndrome, most of the loci are novel. Collectively, these studies highlight the role of myocardial calcium signaling as a mediator of repolarization. My laboratory is currently testing the hypothesis that these variants in aggregate mark individuals at risk of cardiotoxic side effects of marketed pharmaceutical agents through physiologic experiments in the GCRC setting.

In the area of teaching, I served as chief medical resident and administrative cardiology fellow at the Massachusetts General Hospital in part for my skills as a teacher. I have attended on the general medical wards at MGH (2004, 05, 06), in the coronary care unit (2006, 07, 08, 09, 10, 11, 12), on the transplant service (2004, 05, 06, 07, 08, 09, 10, 11, 12, 13) and cardiology consultation service (2004, 05, 06). I tutor in the HMS first year genetics course (2006, 07, 08, 09, 10, 12) and teach in (2008, 09, 10, 11, 12, 13) and co-direct since 2009 the Genetics 228 course in the Biological and Biomedical Sciences Program at Harvard Medical School, and direct the Primer on Medical and Population Genetics course at the Broad Institute of Harvard and MIT, now in its 8th year.

My clinical contributions include serving as a staff cardiologist in the Heart Failure and Transplantation Section, directing the care of inpatients and outpatients requiring advanced heart failure therapies including ventricular assist device therapy and transplantation. I carry a panel of 300 outpatients, with clinic every two weeks.

In summary, my laboratory is generating key insights into the genetic basis of blood pressure regulation and myocardial repolarization, which have implications for our understanding of the physiology of hypertension and cardiotoxic drug response. We are expanding our research efforts to translate these genetic findings with the use of high-resolution phenotyping of carriers of known genetic factors that operate at the population level, with the promise that we may improve both the efficacy and reduce the toxicity of therapies for the prevention of human disease.

Committee on Energy and Commerce
U.S. House of Representatives
Witness Disclosure Requirement - "Truth in Testimony"
Required by House Rule XI, Clause 2(g)

1. Your Name: Christopher Newton-Cheh, MD, MPH			
2. Are you testifying on behalf of the Federal, or a State or local government entity?		**Yes**	**No** X
3. Are you testifying on behalf of an entity that is not a government entity?		**Yes** X	**No**
4. Other than yourself, please list which entity or entities you are representing: American Heart Association			
5. Please list any Federal grants or contracts (including subgrants or subcontracts) that you or the entity you represent have received on or after October 1, 2011: HL088456, HL098283, HL113933			
6. If your answer to the question in item 3 in this form is "yes," please describe your position or representational capacity with the entity or entities you are representing: I am a volunteer for the American Heart Association, a non-profit organization focused on the prevention and treatment of cardiovascular disease and stroke			
7. If your answer to the question in item 3 is "yes," do any of the entities disclosed in item 4 have parent organizations, subsidiaries, or partnerships that you are not representing in your testimony?		**Yes**	**No** X
8. If the answer to the question in item 3 is "yes," please list any Federal grants or contracts (including subgrants or subcontracts) that were received by the entities listed under the question in item 4 on or after October 1, 2011, that exceed 10 percent of the revenue of the entities in the year received, including the source and amount of each grant or contract to be listed: NA			
9. Please attach your curriculum vitae to your completed disclosure form. see attached			

Signature: [redacted] **Date:** 9/8/14