Biographical and Bibliographic Information

JOSHUA W. KNOWLES

A. Academic history:

Colleges and universities attended, degrees received, dates.

8/91-5/95	BA	History, Biology (w/*honors*) University of North Carolina-Chapel Hill, NC
8/95-5/03	MD	Medicine University of North Carolina -Chapel Hill, NC
6/97-8/01	PhD	Genetics University of North Carolina-Chapel Hill, NC

Scholarships and honors (pre-MD degree)

1991-1993	Freshman and Sophomore Honors Program, UNC-Chapel Hill, NC
1991-1995	Dean's List several semesters, UNC-Chapel Hill, NC

Post-doctoral and residency training

7/1/03-6/30/05	Internship and Residency, Internal Medicine Stanford University School of Medicine, Stanford, CA
7/1/05-6/30/10	Cardiology Fellow, Division of Cardiovascular Medicine Stanford University School of Medicine, Stanford, CA

Other study and research opportunities

Research Grants (*current*):

10/1/10-9/30/15 Leducq Foundation Network Grant
Molecular mechanisms of novel genes associated with plasma lipids and cardiovascular disease
Contributor PI: Thomas Quertermous, MD
Overall PI: Dan Rader, MD (Penn)

7/1/10-6/30/15 American Heart Association SPO # 48273
National Fellow to Faculty Award
Identification and Characterization of Genetic Determinants of Insulin Resistance
PI

4/1/11-3/30/15 NIH, RFA HL11-006, 'Next Generation Genetic Association Studies (U01)
1 U01 HL107388-01
Identifying the gene networks of insulin resistance: the GENESIPS study
Co-Investigator PI: Thomas Quertermous, MD

Research Grants (*pending*)

Research Grants (*past*)

6/5/08- 6/4/09 Rosetta Inpharmatics LLC
Genome Wide Association Study for Determinants of Insulin Sensitivity
Co-Investigator PI: Thomas Quertermous, MD

9/25/06-7/31/09 NIH R01 HL087647
Whole genome association for early coronary artery disease and related phenotypes
Co-investigator PI: Thomas Quertermous, MD

4/1/08-4//109 Cardiovascular Institute Seed Grant, 2008
Genome Wide Association Study for Determinants of Insulin Sensitivity
Co-investigator PI: Thomas Quertermous, MD

9/1/06-9/1/08 American Heart Association Postdoctoral Grant 0625154Y
Replication and functional studies of a polymorphism in the LOX-1 gene that alters susceptibility to coronary disease
PI

1/1/06-1/1/07 Dean's Post-Doctoral Fellowship Award, Stanford
Identification of genetic polymorphisms that alter susceptibility to coronary artery disease
PI

4/1/06-4/1/07 Cardiovascular Institute Seed Grant CVI Award EAFGS
Genetic determinants of coronary artery disease
Co-Investigator PI: Thomas Quertermous, MD

9/1/06-9/1/07 LCIC Grant, Private Foundation Fellowship Grant SPO # 37759
Replication and functional characterization of a polymorphism in the LOX-1 gene that alters susceptibility to coronary disease
PI

10/1/03-9/31/08 NIH RO1 HL075774
Genetic Determinants of Peripheral Arterial Disease
Co-Investigator PI: John Cooke, MD, PhD
Co-PI: Thomas Quertermous, MD

Medical Board eligibility or boards passed, with date(s) (include licensure)

8/2006	A.B.I.M. Certification, Internal Medicine
10/2010	A.B.I.M. Certification, Cardiovascular Disease

Licensure

7/2004	California Medical License	# A87974
10/2007	Drug Enforcement Agency License	# FK0548175

B. Employment history. List all academic and non-academic positions.

Academic positions:

8/16/10-pres. Instructor, Division of Cardiovascular Medicine
Stanford University School of Medicine, Stanford, CA

Non-Academic positions:

8/16/10-pres. Attending Physician, Preventive Cardiology Clinic
Stanford Hospital and Clinics, Stanford, CA

C. Public and professional service.

International committees and task forces:

National committees and task forces:

Local committees and task forces:

2008-2009 Stanford Initiative in Human Genetics and Genomics
Organizer, campus-wide seminar series on human genetics topics

9/10/10 Panelist, Speed Science
Stanford Cardiovascular Institute Member Retreat, Stanford, CA

Community Service:

11/06-current Arbor Clinic, free clinic operated by Stanford Medical Students:
Attending Physician ~ one-half day per 1-2 mos. (volunteer)

3/10, 3/11 Healthy Heart Week (volunteer): Presentation to local elementary school about the importance of a healthy lifestyle for heart health.

Editorial Experience:

Reviewer: Scientific Journals

2008-pres. *Circulation Research, Journal of Molecular and Cellular Cardiology, Cardiovascular Drugs and Therapy, Diabetes*
Assisted with reviews for*: NEJM, Circulation*

D. Post-degree honors and awards if any. Include major invited papers and addresses, memberships in professional associations and learned societies, etc.

2003-2005 Stanford Clinical Investigator Pathway Program
Program designed to mentor candidates with outstanding credentials for research careers.

2006-2007 Stanford University Dean's Fellowship

2006-2007 The Future Leaders in CV Medical Research Program Fellowship Award

2007 Edwin Alderman Award for Excellence in Clinical Research
Awarded to the top research project by a Cardiology Fellow (*judged by faculty*)

2008 Edwin Alderman Award for Excellence in Clinical Research
Awarded to the top research project by a Cardiology Fellow (*judged by faculty*)

E. Publications

E.1. Peer-reviewed articles [33 total: 0 in press, 2 submitted]

E.1.A *Original research* contributions (26 total: 0 in press, 1 submitted)

1. Li Z, **Knowles JW**, Goyeau D, Prabhakar S, Short DB, Perkins AG, Goy MF. Low salt intake down-regulates the guanylin signaling pathway in rat distal colon. *Gastroenterology* 1996;111(6):1714-1721.

2. **Knowles JW**, Reddick RL, Jennette JC, Shesely EG, Smithies O, Maeda N. Enhanced atherosclerosis and kidney dysfunction in eNOS(-/-)Apoe(-/-) mice are ameliorated by enalapril treatment. *J Clin Invest* 2000;105(4):451-458.

3. **Knowles JW**, Esposito G, Mao L, Hagaman JR, Fox JE, Smithies O, Rockman HA, Maeda N. Pressure-independent enhancement of cardiac hypertrophy in natriuretic peptide receptor A-deficient mice. *J Clin Invest* 2001;107(8):975-984.

4. Goy MF, Oliver PM, Purdy KE, **Knowles JW**, Fox JE, Mohler PJ, Qian X, Smithies O, Maeda N. Evidence for a novel natriuretic peptide receptor that prefers brain natriuretic peptide over atrial natriuretic peptide. *Biochem J* 2001;358(Pt 2):379-387.

5. Ellmers LJ, **Knowles JW**, Kim HS, Smithies O, Maeda N, Cameron VA. Ventricular expression of natriuretic peptides in Npr1(-/-) mice with cardiac hypertrophy and fibrosis. *Am J Physiol Heart Circ Physiol* 2002;283(2):H707-714.

6. Hodgin JB, **Knowles JW***, Kim HS, Smithies O, Maeda N. Interactions between endothelial nitric oxide synthase and sex hormones in vascular protection in mice. *J Clin Invest* 2002;109(4):541-548.

7. **Knowles JW**, Erickson LM, Guy VK, Sigel CS, Wilder JC, Maeda N. Common variations in noncoding regions of the human natriuretic peptide receptor A gene have quantitative effects. *Hum Genet* 2003;112(1):62-70.

8. Alexander MR, **Knowles JW***, Nishikimi T, Maeda N. Increased atherosclerosis and smooth muscle cell hypertrophy in natriuretic peptide receptor A-/-apolipoprotein E-/- mice. *Arterioscler Thromb Vasc Biol* 2003;23(6):1077-1082.

9. Caron KM, James LR, Kim HS, **Knowles J**, Uhlir R, Mao L, Hagaman JR, Cascio W, Rockman H, Smithies O. Cardiac hypertrophy and sudden death in mice with a genetically clamped renin transgene. *Proc Natl Acad Sci U S A* 2004;101(9):3106-3111.

10. **Knowles JW**, Wang H, Itakura H, Southwick A, Myers RM, Iribarren C, Fortmann SP, Go AS, Quertermous T, Hlatky MA. Association of polymorphisms in platelet and hemostatis system genes with acute myocardial infarction. *Am Heart J* 2007 154(6):1052-1058.

11. Assimes TL, **Knowles JW**, Priest JR, Basu A, Borchert A, Volcik KA, Grove ML, Tabor HK, Southwick A, Tabibiazar R, Sidney S, Boerwinkle E, Go AS, Iribarren C, Hlatky MA, Fortmann SP, Myers RM, Kuhn H, Risch N, Quertermous T. A near null variant of 12/15-LOX encoded by a novel SNP in ALOX15 and the risk of coronary artery disease. *Atherosclerosis* 2008;198(1):136-144.

12. **Knowles JW***, Assimes TL, Boerwinkle E, Fortmann SP, Go A, Grove ML, Hlatky M, Iribarren C, Li J, Myers R, Risch N, Sidney S, Southwick A, Volcik KA, Quertermous T. Failure to replicate an association of SNPs in the oxidized LDL receptor gene (OLR1) with CAD. *BMC Med Genet* 2008 Apr;9:23.

13. Assimes TL, **Knowles JW***, Priest JR, Basu A, Volcik KA, Southwick A, Tabor HK, Hartiala J, Allayee H, Grove ML, Tabibiazar R, Sidney S, Fortmann SP, Go A, Hlatky M, Iribarren C, Boerwinkle E, Myers R, Risch N, Quertermous T. Common polymorphisms of ALOX5 and ALOX5AP and risk of coronary artery disease. *Hum Genet* 2008;123(4): 399-408.

14. Assimes TL, **Knowles JW**, Basu A, Iribarren C, Southwick A, Tang H, Absher D, Li J, Fair JM, Rubin GD, Sidney S, Fortmann SP, Go AS, Hlatky MA, Myers RM, Risch N, Quertermous T. Susceptibility locus for clinical and subclinical coronary artery disease at chromosome 9p21 in the multi-ethnic ADVANCE Study. *Hum Mol Genet* 2008;17(15): 2320-2328.

15. Zakharia F, Basu A, Absher D, Assimes TL, Go AS, Hlatky MA, Iribarren C, **Knowles JW**, Li J, Narasimhan B, Sidney S, Southwick A, Myers RM, Quertermous T, Risch N, Tang H. Characterizing the admixed African ancestry of African Americans. *Genome Biol* 2009;10(12):R141.

16. Ingelsson E, [10 authors], **Knowles JW**, [54 authors], Florez JC; MAGIC Investigators [42 inst]. Detailed physiologic characterization reveals diverse mechanisms for novel genetic

Loci regulating glucose and insulin metabolism in humans. *Diabetes* 2010;59(5):1266-1275. [genotyping and data analysis]

17. Dackor J, Tobacco & Genetics Consortium; Franceschini N, ARIC; Bernardinelli L, ATVB Italian Study Group; **Knowles JW**, ADVANCE; [114 auth, 103 inst]. Genome-wide meta-analyses identify multiple loci associated with smoking behavior. *Nat Genet* 2010;42(5): 441-447

18. Ashley EA, Butte AJ, Wheeler MT, Chen R, Klein TE, Dewey FE, Dudley JT, Ormond KE, Pavlovic A, Morgan AA, Pushkarev D, Neff NF, Hudgins L, Gong L, Hodges LM, Berlin DS, Thorn CF, Sangkuhl K, Hebert JM, Woon M, Sagreiya H, Whaley R, **Knowles JW**, Chou MF, Thakuria JV, Rosenbaum AM, Zaranek AW, Church GM, Greely HT, Quake SR, Altman RB. Clinical assessment incorporating a personal genome. *Lancet* 2010;375(9725):1525-1535.

19. Assimes TL, Thorleifsson G, Kathiresan S, Voight BF, Holm H, Erdmann J, Willenborg C, König IR, Vaidya D, Xie C, McKeown PP, Morgan T, Reilly MP, Li M, et al. Lack of association between the Trp719Arg polymorphism in kinesin-like protein 6 and coronary artery disease in 19 case-control studies. *J Am Coll Cardiol* (*in press*, 9/2010).

20. Reilly MP*, Li M*, He J, Ferguson J, Qasim AN, Stylianou IM, Mehta NN, Burnett MS, Devaney JM, DerOhannessian S, Qu L, Thompson JR, Horne BD, Stewart AFR, Assimes TL, Barnard J, Wild P, Allayee H, Braund PS, Wright B, Schillert A, Ziegler A, Linsel-Nitschke P, Absher D, **Knowles J**, Iribarren C, Chen L, Carlquist JF, Hartiala J, Tang WHW, Wells GA, Nahrstaedt J, König IR, Pichard AD, Kent KM, Satler L, Lindsay JM, Waksman R, Peters A, Hengstenberg C, Schreiber S, Wichmann HR, Matthai W, Cappola T, Patel RS, Su S, Hlatky M, Willenborg C, Zafari AM, Vaccarino V, Balmforth AJ; †Wellcome Trust Case Control Consortium, Knouff CW, Waterworth DM, Walker MC, Martinelli N, Olivieri O, Girelli D, Quyyumi AA, Muhlestein JB, Anderson JL; †Myocardial Infarction Genetics Consortium, Erdmann J, Schunkert H, Hall AS, Quertermous T, Blankenberg S, Hazen SL, Roberts R, McPherson R, Kathiresan S, Samani NJ, Mooser V, Wilensky R, Hakonarson H, Epstein SE, Rader DJ. ADAMTS7 and ABO are novel coronary artery disease loci that have differential associations with coronary atherosclerosis and myocardial infarction. *Lancet* 2011; 377(9763):383-92

21. GIANT consortium. > 100 authors. Meta-analysis identifies 13 novel loci associated with waist-hip ratio and reveals sexual dimorphism in the genetic basis of fat distribution. *Nature Genetics* 2010; 42 (11): 949-60.

22. GIANT Consortium. > 100 authors. Hundreds of variants influence human height and cluster within genomic loci and biological pathways. *Nature Genetics* 2010; 467(7317): 832-8.

23. Witteles RM***, Knowles JW***, Perez M, Morris WM, Spettell CM, Brennan TA, Heidenreich PA. Overuse of left ventriculography. *J Am Coll Cardiol* (*submitted*, 7/2010).

24. STAMPEED Consortium. Kraja AT, Vaidya D, Pankow JS, Goodarzi MO, Assimes TL, Kullo I, Sovio U, Mathias R, Sun YV, Franceschini N, Absher D, Li G, Zhang Q, Feitosa M, Glazer NL, Haritunians T, **Knowles JW**, North KE, Iribarren C, Kral B, Yanek L, Jaquish C, Couper DJ, Chakravarti A, Psaty B, Becker LC, Province MA, Boerwinkle E,

Quertermous T, Jarvelin MR, Becker DM, Kardia SLR, Rotter J, Chen YDI, Borecki I. A bivariate genome-wide approach to metabolic syndrome. *Diabetes* 2011 Apr; 60: 1329-39.

25. GIANT consortium. > 100 authors. Association analyses of 249,796 individuals reveal 18 new loci associated with body mass index. *Nat Genet*. 2010 Nov;42(11):937-48. Epub 2010 Oct 10.

26. CARDIoGRAM consortium. > 100 authors. Large-scale association analysis identifies 13 new susceptibility loci for coronary artery disease. Schunkert H, König IR, Kathiresan S, Reilly MP, Assimes TL, Holm H, Preuss M, Stewart AF, Barbalic M, Gieger C, Absher D, Aherrahrou Z, Allayee H, Altshuler D, Anand SS, Andersen K, Anderson JL, Ardissino D, Ball SG, Balmforth AJ, Barnes TA, Becker DM, Becker LC, Berger K, Bis JC, Boekholdt SM, Boerwinkle E, Braund PS, Brown MJ, Burnett MS, Buysschaert I; Cardiogenics, Carlquist JF, Chen L, Cichon S, Codd V, Davies RW, Dedoussis G, Dehghan A, Demissie S, Devaney JM, Diemert P, Do R, Doering A, Eifert S, Mokhtari NE, Ellis SG, Elosua R, Engert JC, Epstein SE, de Faire U, Fischer M, Folsom AR, Freyer J, Gigante B, Girelli D, Gretarsdottir S, Gudnason V, Gulcher JR, Halperin E, Hammond N, Hazen SL, Hofman A, Horne BD, Illig T, Iribarren C, Jones GT, Jukema JW, Kaiser MA, Kaplan LM, Kastelein JJ, Khaw KT, **Knowles JW,** Kolovou G, Kong A, Laaksonen R, Lambrechts D, Leander K, Lettre G, Li M, Lieb W, Loley C, Lotery AJ, Mannucci PM, Maouche S, Martinelli N, McKeown PP, Meisinger C, Meitinger T, Melander O, Merlini PA, Mooser V, Morgan T, Mühleisen TW, Muhlestein JB, Münzel T, Musunuru K, Nahrstaedt J, Nelson CP, Nöthen MM, Olivieri O, Patel RS, Patterson CC, Peters A, Peyvandi F, Qu L, Quyyumi AA, Rader DJ, Rallidis LS, Rice C, Rosendaal FR, Rubin D, Salomaa V, Sampietro ML, Sandhu MS, Schadt E, Schäfer A, Schillert A, Schreiber S, Schrezenmeir J, Schwartz SM, Siscovick DS, Sivananthan M, Sivapalaratnam S, Smith A, Smith TB, Snoep JD, Soranzo N, Spertus JA, Stark K, Stirrups K, Stoll M, Tang WH, Tennstedt S, Thorgeirsson G, Thorleifsson G, Tomaszewski M, Uitterlinden AG, van Rij AM, Voight BF, Wareham NJ, Wells GA, Wichmann HE, Wild PS, Willenborg C, Witteman JC, Wright BJ, Ye S, Zeller T, Ziegler A, Cambien F, Goodall AH, Cupples LA, Quertermous T, März W, Hengstenberg C, Blankenberg S, Ouwehand WH, Hall AS, Deloukas P, Thompson JR, Stefansson K, Roberts R, Thorsteinsdottir U, O'Donnell CJ, McPherson R, Erdmann J; the CARDIoGRAM Consortium, Samani NJ. *Nat Genet.* 2011 Mar 6.

* co-first authors

E.1.B *Reviews and case reports* (5 total: 0 in press, 1 submitted)

1. **Knowles JW**, Maeda N. Genetic modifiers of atherosclerosis in mice. *Arterioscler Thromb Vasc Biol* 2000;20(11):2336-2345. Review.

2. **Knowles JW**, Elliott AB, Brody J. A case of complete heart block reverting to normal sinus rhythm after treatment for cardiac invasive Burkitt's lymphoma. *Ann Hematol* 2007;86(9):687-690.

3. **Knowles JW**, Assimes TL, Li J, Quertermous T, Cooke JP. Genetic susceptibility to peripheral arterial disease: a dark corner in vascular biology. *Arterioscler Thromb Vasc Biol* 2007;27(10):2068-2078. Review.

4. Wheeler MT, Ho M, **Knowles JW**, Pavlovic A, Ashley EA. Pharmacogenetics of heart failure: evidence, opportunities, and challenges for cardiovascular pharmacogenomics. *J Cardiovasc Trans Res* 2008;1(1):25-36.

5. deGoma EM**, Knowles JW,** Angeli F, Budoff MJ, Rader DJ. The evolution of traditional risk factors. *Circulation* Submitted Dec 2010.

E.2. Non-peer-reviewed articles [1 total: 0 in press, 0 submitted]

1. **Knowles JW**, Maeda N. Dyslipidemia and hypertension: twin killers in renal vascular disease. *Am J Kidney Dis* 2001;37(6):1322-1323.

E.3. Books [0]

E.4. Book chapters [1]

1. **Knowles JW**. (2004). Genes that Modify Susceptibility to Atherosclerosis: Targets for Drug Action. In: M. Wilkins (ed.) Cardiovascular Pharmacogenetics. (pp. 79-106) Heidelberg, Germany: Springer-Verlag. ISBN: 978-3-540-40204-6

E.5. Book reviews [0]

E.6. Abstracts [6 of 9]

1. **Knowles J**, Li Z, Goy MF. Expression of a cGMP-stimulated phosphodiesterase in the rat gastrointestinal-tract, as detected by *in-situ* hybridization and functional assay. *Gastroenterology* 1994;106(4 Suppl A): A1032.

2. Enhanced atherosclerosis and kidney dysfunction in eNOS$^{-/-}$Apoe$^{-/-}$ mice are ameliorated by enalapril treatment. National MD/PhD Student Conference. Aspen, CO 2000

3. Enhanced atherosclerosis and kidney dysfunction in eNOS$^{-/-}$Apoe$^{-/-}$ mice are ameliorated by enalapril treatment. ATVB Meeting. Denver, CO 2000

4. Natriuretic peptide receptor A knockout mice have an enhanced response to hypertrophic stimuli in the heart. Keystone Meeting. Snowbird, UT 2000

5. **Knowles JW**, Assimes T, Priest JR, Tabor H, Southwick A, Volcik K, Boerwinkle E, Grove ML, Wang J, Tabibiazar R, Sidney S, Risch N, Iribarren C, Go A, Myers R, Hlatky M, Fortmann S, Quertermous T. Failure to replicate an association of a single nucleotide polymorphism in the oxidized LDL receptor gene (Orl1) with CAD. AHA Western States Affiliate - Young Investigators Forum, San Francisco, CA, Sept. 2006.

6. †Absher D, Assimes TL, Basu A, Fortmann SP, Go AS, Hlatky MA, Iribarren C, **Knowles JW**, Li J, Risch N, Sidney S, Southwick A, Tang H, Myers RM, Quertermous T. Genome-wide association study for early coronary disease and related phenotypes. Cold Spring

Harbor Laboratory Clinical Cardiovascular Genomics Meeting, Oct. 2007. † *alphabetical order*.

E.7. Invited presentations [8 of 10]

1. *Enhanced atherosclerosis and kidney dysfunction in eNOS$^{-/-}$Apoe$^{-/-}$ mice are ameliorated by enalapril treatment.*
National MD/PhD Student Conference
Aspen, CO 2000

2. *Natriuretic peptide receptor A knockout mice have an enhanced response to hypertrophic stimuli in the heart.*
Keystone Meeting
Snowbird, UY 2000

3. *Genome Wide Association Study for Early Onset Coronary Disease and Related Phenotypes*.
Cold Spring Harbor Meeting on Clinical Cardiovascular Genetics
Cold Spring Harbor, NY November, 2007

4. *Genome Wide Association Studies of Cardiovascular Disease*
Stanford Biostatistics Seminar
Stanford, CA January, 2008

5. *The Athlete's Heart*
Senior Games of California
Stanford, CA April, 2010

6. *Genetics of Cardiovascular Disease*
Stanford School of Medicine, Introductory Epidemiology Course [Instructor: Rita Popat]
Stanford, CA March, 2010

7. *Genome wide association study for determinants of insulin sensitivity*
Vanderbilt University, Cardiology Special Seminar
Nashville, TN December, 2010

8. *Genome wide association study for determinants of insulin sensitivity*
University of Pennsylvania, Cardiology Special Seminar
Philadelphia, PA December, 2010

E.8. Patents NA