BIOGRAPHICAL SKETCH

NAME: Kari E North

eRA COMMONS USER NAME (credential, e.g., agency login): KARI_NORTH

POSITION TITLE: Professor

EDUCATION/TRAINING			
INSTITUTION AND LOCATION	DEGREE	MM/YY	FIELD OF STUDY
University of South Florida, Tampa, FL	BA	1992	Anthropology
University of Kansas, Lawrence, KS	MA	1995	Anthropology
University of Kansas, Lawrence, KS	PhD	2000	Anthropological Genetics
Southwest Foundation for Biomedical Research, San Antonio, TX	Post-Doc	2001	Genetic Epidemiology

A. Personal Statement

I am an expert in the genetic epidemiology of complex traits and lead multiple large-scale genetic studies in collaboration with multiple international genetic consortia. I am the Principal Investigator (PI) of the Genetic Epidemiology of Causal Variants across the Life Course study (CaLiCo), a consortium of population based studies that have entered a partnership with the Population Architecture and Genomics in Epidemiology (PAGE) study. I am also a PI on a grant exploring the genetic epidemiology of obesity in large cohort studies (R01 DK075681), on a grant evaluating the impact of exome variants influencing adolescent weight gain in the ancestrally diverse National Longitudinal Study of Adolescent to Adult Health (R01 HD057194), and on a grant leveraging ancestry to map genes for adiposity in Hispanic descent individuals (R01 DK101855). At the University of North Carolina, I lead the Cardiovascular Disease (CVD) Genetic Epidemiology group whose research takes place at the intersection of human genetics, epidemiologic methodology, statistical techniques, and interdisciplinary translational research. The environment and infrastructure that I have built at UNC-CH has provided a fertile ground for innovation and the rapid development of my lab's research agenda. We are performing genome wide association studies and whole genome sequencing studies, as well as methylation and gene expression studies, primarily in populations most burdened by CVD. This comprehensive systems biology approach will lead to novel and more complete understanding of the pathogenesis of cardiovascular disease and its risk factors.

Peer reviewed publications that highlight relevant experience and qualifications

**Indicates equal contribution to the project as the Senior Author. All Authors jointly led this project.*

1.*Locke AE, Kahali B, Berndt SI, Justice AE, Pers TH, Day FR, Powell C, Vedantam S, … **North KE*,** Ingelsson E*, Hirschhorn JN*, Loos R*, Speliotes EK* Large-Scale Genetic Studies of Body Mass Index Provide Insight Into the Biological Basis of Obesity. *Nature*. 2015 Feb 12;518(7538):197-206. doi: 10.1038/nature14177. PMID: 25673413 PMCID: PMC4382211.

2. Wu Y, Waite LL, Jackson AU, Sheu WH, Buyske S, Absher D, Arnett DK, … Haiman CA, Chen YD, Kooperberg C, Assimes TL, Crawford DC, Hsiung CA, **North KE***, Mohlke KL*. Trans-ethnic fine-mapping of lipid Loci identifies population-specific signals and allelic heterogeneity that increases the trait variance explained. PLoS Genet. 2013 Mar;9(3):e1003379. PMCID: PMC3605054.

3. Randall JC, Winkler TW, Kutalik Z, Berndt SI, Jackson AU, Monda KL, Kilpeläinen TO, … Abecasis G, McCarthy MI, Hirschhorn JN, Qi L, Loos RJF*, Lindgren CM*, **North KE***, Heid IM*. Sex-stratified genome-wide association studies in 270,000 individuals 2 show evidence for sexual dimorphism in genetic loci for anthropometric traits. *Plos Genetics* 2013. Jun;9(6):e1003500. PMCID: PMC3674993.

4. Monda KL, Chen GK, Taylor KC, Palmer C, Edwards TL, Lange LA, Ng MC, … Zonderman AB; NABEC Consortium; UKBEC Consortium; BioBank Japan Project; AGEN Consortium, Kooperberg C, Papanicolaou GJ, Henderson BE, Reiner AP, Hirschhorn JN*, Loos RJ*, **North KE***, Haiman CA*. A meta-analysis identifies new loci associated with body mass index in individuals of African ancestry. Nat Genet. 2013 Jun;45(6):690-6. PMCID: PMC3694490.

B. Positions and Honors

Positions and Employment

1995-1996 Instructor, Department of Anthropology, University of Kansas, Lawrence, KS
1996-1997 Teaching Assistant, Department of Anthropology, University of Kansas, Lawrence, KS

1997-2000 Senior Research Assistant, Department of Genetics, Southwest Foundation for Biomedical Research, San Antonio, TX
2000-2002 Post-doctoral Scientist, Department of Genetics, Southwest Foundation for Biomedical Research, San Antonio, TX
2002-2007 Assistant Professor, Department of Epidemiology, School of Public Health, University of North Carolina at Chapel Hill
2007-2014 Associate Professor, Department of Epidemiology, School of Public Health, University of North Carolina at Chapel Hill
2014-present Professor, Department of Epidemiology, School of Public Health, University of North Carolina at Chapel Hill

Other Experience and Professional Memberships

1998-Present Reviewer for JAMA, Nature Genetics, Plos Genetics, Neurology, Hypertension, International Journal of Obesity, American Journal of Hypertension, Atherosclerosis, BMC Genetics, Circulation, Diabetes Metabolism Research and Reviews, Epidemiology, Gastroenterology, Human Biology, Human Genetics, Obesity
2000-Present Member IGES, AHA, ADA, ASHG
2005-2010 Member *Gastroenterology* Editorial Board
2010-Present *Frontiers in Genetic Epidemiology* Editorial Board
2010-Present Guest Editor *Circulation*

Honors

1990-92 Pi Gamma Mu National Science Honors Society
2000 University of Kansas, Graduation with Honors
2004 Winner of Roger R Williams award for excellence in genetics research
2011 Review committee for the Helmholtz Institute, Munich Germany
2010-2012 First and Senior Author Abstract selected as among the top 10 percent of all accepted submitted to AHA Specialty Conferences in 2012

C. Contribution to Science

C.1. Genetic Influences on CVD Risk Factors in populations with American Indian ancestry. I have conducted research in American Indians throughout my career, first when collecting dissertation data at the Cheyenne River Indian Reservation in Eagle Butte, South Dakota. Obesity, diabetes, and CVD are highly prevalent among American Indians living on the reservation, imposing an alarming public health burden. I knew immediately that I had to do something to help fill the gaps in our understanding of the influence of genetics on obesity in American Indian communities. Specifically, I wanted to contribute by helping illuminate the molecular mechanisms underlying obesity and its clinical sequelae. My work at the Cheyenne River Indian Reservation began with the recruitment of families that now constitute the long running Strong Heart Family Study, which is still funded by NIH (partially funded by U01 HG007416). Since the late 1990s when this work was initiated, we have made significant discoveries with respect to the underpinnings of CVD in this unique population. At the start of the study, we were able to demonstrate a strong importance of genetic effects for CVD in this unique and understudied population. In our later work, as common GWAS identified variants were identified, we were able to demonstrate the generalization of lipid-, obesity, and CHD-related genetic effects in our American Indian populations. Ongoing work will consider the importance of population specific rare sequence variants for common complex diseases. We are also fortunate to be involved in the ancestrally diverse Hispanic Community Health Study (HCHS/SOL), which has study participants with high levels of American Indian ancestry. The objectives of HCHS/SOL include identifying the prevalence of and risk factors for diseases, disorders, and conditions in Hispanic populations and to determine the role of acculturation and disparities in the development of these conditions. Our most recent work has been conducting GWAS of CVD traits in HCHS/SOL, including for platelet counts (PLT) in 12,491 participants. We have discovered novel American Indian specific variants, for example a noncoding variant in *ACTN1* (rs117672662, MAF = 6%, β = 0.61), which codes for alpha-actinin, a multi-isoform actin-binding protein involved in cytoskeleton organization and platelet/megakaryocyte structural integrity. Missense mutations in *ACTN1* were recently implicated in the autosomal dominant Mendelian platelet disorder macrothrombocytopenia. Exome sequencing also associated this locus with PLT, which supports a potential functional role in PLT for this gene. The intronic *ACTN1 i*ndex SNP rs117672662 is a strong functional candidate, located within a putative cell-type specific enhancer in hematopoietic progenitor cells (CD34, CD8). Further, this SNP binds several transcription factors including GATA2, which is known to play a role in the development of specific hematopoietic lineages.

1. Tsai CW, **North KE**, Tin A, Haack K, Franceschini N, Saroja Voruganti V, Laston S, Zhang Y, Best LG, MacCluer JW, Beaty TH, Navas-Acien A, Linda Kao WH, Howard BV. Both rare and common variants in PCSK9 influence plasma low-density lipoprotein cholesterol level in American Indians.J Clin Endocrinol Metab. 2014 Nov 20:jc20143340. [Epub ahead of print] PMID: 25412415. PMCID: PMC4318886
2. Franceschini N, Tao R, Liu L, Rutherford S, Haack K, Almasy L, Göring HH, Laston S, Lee ET, Best LG, Fabsitz R, Cole SA, **North KE**. Mapping of a blood pressure QTL on chromosome 17 in American Indians of the strong heart family study. BMC Cardiovasc Disord. 2014 Nov 11;14:158. doi: 10.1186/1471-2261-14-158. PMID: 25387527.
3. Carlson CS, Matise TC, **North KE**, Haiman CA, Fesinmeyer MD, Buyske S, Schumacher FR, Peters U, Franceschini N, Ritchie MD, Duggan DG, Spencer KL, Dumitrescu L, Eaton CB, Thomas F, Young Carty C, Manolio TA, Heiss G, Le Marchand L, Crawford DC, Hindorff LA, and Kooperberg C, for the PAGE Study. Generalization and attenuation of association results from European GWAS in Populations of non-European Ancestry: the PAGE Study. *PLos Biology* 2013; 11 (9): e1001661
4. North KE, Howard BV, Welty TK, Best LG, Lee ET, Yeh JL, Fabsitz RR, Roman MJ, MacCluer JW. Genetic and environmental contributions to cardiovascular disease risk factors in American Indians: The Strong Heart Family Study. *American Journal of Epidemiology* 2003; 157 (4): 303-14

C.2. Genetic Epidemiology of Adiposity in Multiple Large Cohorts- My NIDDK (R01 DK075681) grant entitled "Adiposity in Multiple Large Cohorts" has enabled the large scale pursuit of obesity genes in several large cohort studies. In collaboration with Drs. Borecki and Cupples, we lead the Adiposity Working Group of the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) consortium and coordinate outside collaborations, with hundreds of epidemiological studies. Collectively, we have led and participated in a broad range of projects, including GWAS studies of adiposity traits in European and African descent populations, contrasting ancestry specific genetic architecture, generalization of adiposity-related common genetic variants among U.S. Hispanic women, and studies of gene by environment interaction. Overall, these large-scale collaborations have led to the discovery of hundreds of obesity susceptibility loci, as reported in high-impact journals like *Nature, Nature Genetics and Plos Genetics*. We have also been able to examine genetic effects across multiple genetic and environmental contexts so that we can better understand differences in obesity susceptibility and obesity-related morbidities. For example, we have demonstrated a strong importance in sex differences in the genetic underpinnings of body shape measures and of age in body size measures. Such information has the potential to identify important pathways for disease prediction, intervention, and treatment.

1. Speliotes, E.K., **North KE*** et al. Association analyses of 249,796 individuals reveal 18 new loci associated with body mass index. Nat Genet 42, 937-48 (2010).
2. Berndt SI, Gustafsson S, Mägi R, Ganna A, Wheeler E, Feitosa MF, Justice AE, … Morris AP, Meyre D, Scherag A, McCarthy MI, Speliotes EK, North KE*, Loos RJ*, Ingelsson E*. Genome-wide meta-analysis identifies 11 new loci for anthropometric traits and provides insights into genetic architecture. Nat Genet. 2013 May;45(5):501-12. PMCID: PMC3973018.
3. Graff, M., North KE* et al. Genome-wide analysis of BMI in adolescents and young adults reveals additional insight into the effects of genetic loci over the life course. Hum Mol Genet 22, 3597-607 (2013).
4. Yoneyama S, Guo Y, Lanktree MB, Barnes MR, Elbers CC, Karczewski KJ, Padmanabhan S, Bauer F, Baumert J, Beitelshees A, Berenson GS, Boer JM, Burke G, Cade B, Chen W, Cooper-Dehoff RM, Gaunt TR, Gieger C, Gong Y, Gorski M, Heard-Costa N, Johnson T,….. **North KE** Gene-centric meta-analyses for central adiposity traits in up to 57 412 individuals of European descent confirm known loci and reveal several novel associations.Hum Mol Genet. 2014 May 1;23(9):2498-510. doi: 10.1093/hmg/ddt626. Epub 2013 Dec 17. PubMed [citation] PMID: 24345515, PMCID: PMC3988452.

C.3. Genetic Epidemiology of Common Complex Traits in Minority Populations. The PAGE and HisLa consortium are well suited to fill gaps in our understanding of the main genetic effects influencing traits and diseases burdening minority populations. Early in these projects, we have reported strong evidence for allelic heterogeneity extending across multiple phenotypes. As an example, I co-led the trans-ethnic fine-mapping study of triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C), in individuals of African American (n=6,832), East Asian (n=9,452), and European (n=10,829) ancestry. We found that among the 58 lipid loci previously identified in European populations, 33 exhibited evidence of association in at least one ancestry group and many loci displayed evidence for population specific

variants. Finally, the leveraging of data from multiple ethnic groups allowed us to narrow the regions likely harboring the causal variants for consideration in future functional studies. As a Hispanic Community Health Study Investigator and contributor to HisLa, we have also been able to leverage ancestral diversity in Hispanic populations to map new susceptibility loci for blood cell- and anthropometric-traits. Through my multifaceted research, I am developing a rigorous, quantitative foundation for addressing fundamental questions about the genetics of common complex traits in minority populations and about the origins of human genetic diversity.

1. Wu Y, Waite LL, Jackson AU, Sheu WH, Buyske S, Absher D, Arnett DK, … Haiman CA, Chen YD, Kooperberg C, Assimes TL, Crawford DC, Hsiung CA, **North KE***, Mohlke KL*. Trans-ethnic fine-mapping of lipid Loci identifies population-specific signals and allelic heterogeneity that increases the trait variance explained. PLoS Genet. 2013 Mar;9(3):e1003379. PMCID: PMC3605054.

2. Liu EY, Buyske S, Aragaki AK, Peters U, Boerwinkle E, Carlson C, Carty C, … Kooperberg C, **North KE**, Li Y. Genotype imputation of Metabochip SNPs using a study-specific reference panel of ~4,000 haplotypes in African Americans from the Women's Health Initiative. Genet Epidemiol. 2012 Feb;36(2):107-17. PMCID: PMC3410659.

3. Peters U, **North KE**, Sethupathy P, Buyske S, Haessler J, Jiao S, et al. A systematic mapping approach of 16q12.2/FTO and BMI in more than 20,000 African Americans narrows in on the underlying functional variation: results from the Population Architecture using Genomics and Epidemiology (PAGE) study. PLoS Genet. 2013 Jan;9(1):e1003171. PMCID: PMC3547789.

4. Graff M, Gordon-Larsen P, Lim U, Fowke JH, Love SA, Fesinmeyer M, Wilkens, … Buyske S, Buzková P, Hindorff LA, Matise T, Crawford D, Haiman C, Peters U**, North KE**. The Influence of obesity related single nucleotide polymorphisms on BMI across the Life Course: the PAGE Study. Diabetes. 2013 May; 62(5):1763-7. PMCID: PMC3636619.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/wayne.rosamond.1/bibliography/45413588/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

R01-DK089256 (formerly DK075681 (Multiple PIs: Baranski, Borecki, Cupples, **North**) 09/10/10-06/30/17 1.44 calendar
NIH NIDDK $576,812
Genetic Architecture of Adiposity in Multiple Large Cohorts
To extend the meta-analysis approach of multiple ongoing large cohorts to investigate adiposity traits.
Role: Multiple PI

N01HC65233 (Cai) 09/30/06- 05/31/20 0.48 Calendar
NHLBI $2,280,224
Hispanic Community Health Study
The objectives of this study are to identify the prevalence of and risk factors for diseases, disorders, and conditions in Hispanic populations and to determine the role of acculturation and disparities in their prevalence.
Role: Investigator

2R01HD057194-06 (Gordon-Larsen, North) 01/1/08-06/30/19 2.4 Calendar
NICHD $414,953
Exome Variants Underlying Weight Gain from Adolescence to Adulthood
This project will examine gene-by-environment interactions on trajectories of weight gain from adolescence to young adulthood.
Role: MPI

U01HG007416 (North) 09/01/13-05/31/17 3.24 Calendar
NIH $599,547
Population Architecture Using Genomics and Epidemiology (PAGE) Phase II – Study Investigators CALiCo II
The goal is to explore the associations of genetic variation with a broad range of phenotypes, including conditions that disproportionately burdens U.S. ethnic and racial minorities.

Role: Principal Investigator

13GRNT16490017 (North) 07/01/13-06/30/15 1.8 Calendar
AHA $70,000
Genetic Architecture of Adiposity in Individuals of Hispanic Descent
To perform GWAS of body mass index in populations of Hispanic-descent; and second, to investigate how common genetic variants interact with physical activity to influence adiposity risk in these populations.
Role: Principal Investigator

1R01DK101855-01 (North, Haiman, Loos) 08/15/14-07/31/17 1.44 Calendar
NIH NIDDK $ 599,687
Leveraging ancestral diversity to map adiposity loci in Hispanics
The proposed study plans to perform the first large-scale genomic study in search of obesity-susceptibility loci in HL populations.
Role: Contact Principal Investigator

Completed Research Support

R01 HD057194 (Gordon-Larsen) 07/01/08-06/30/14
NIH/NICHD
Gene-Environment Interactions and Weight Gain
Our goal is to examine gene-by-environment interactions on weight gain from adolescence to young adulthood in the multi-ethnic National Longitudinal Study of Adolescent Health.
Role: Co-Investigator

U01HG004803-04S1 (North) 07/17/08-05/31/14
NIH/NHGRI
Genetic Epidemiology of Casual Variants Across the Life Course
Genotyped well-replicated putative casual variants in well-characterized population-based studies and to determine the evidence for replication and generalization of these genetic effects.

R01HL089651 (North) 08/23/08 – 07/31/13
NIH/NHLBI
Comprehensive Mapping of a Blood Pressure QTL on Chromosome 17
The aims are to identify gene variants on chromosome 17 in American Indians of the Strong Heart Family Study that are associated with blood pressure variation.

R01 DE021418 (Offenbacher) 07/01/11-06/30/14
GWA Study of Periodontal Disease
The goal was to identify the underlying genetic determinants of periodontal disease and related dental phenotypes in the European-American and African-American participants of the ARIC study.
Role: Investigator

R01 DK075681 (Borecki) 04/01/08-04/31/13
NIH/NIDDK
Genetic Epidemiology of Metabolic Diseases of Obesity
Our goal was to investigate the genetic epidemiology of non-alcoholic fatty liver disease and abdominal fat in European American and African American study participants of the Family Heart Study.
Role: Subcontract PI

A10-0347-001 (North) 08/01/09-09/30/12
NHLBI SHARE
GWAS Analysis for the Women's Health Initiative Study
The goal was to detect, map, and identify genes that influence variation in complex traits in women.
Role: Subcontract PI

GO Grant (North) 09/30/09-07/31/12
NIH/NHLBI
Women's' Health Initiative Sequencing Project
Identified rare and common variants influencing NHLBI phenotypes using whole exomic sequencing.
Role: Subcontract PI