BIOGRAPHICAL SKETCH

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NAME: Ingelsson, Erik

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

POSITION TITLE: Professor of Medicine (Cardiovascular Medicine) and, by courtesy, of Health Research and Policy (Epidemiology)

EDUCATION/TRAINING*:*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Uppsala University, Uppsala, Sweden	M.D.	06/2000	Medicine
Uppsala University, Uppsala, Sweden	Ph.D.	10/2005	Epidemiology
Framingham Heart Study, Boston University School of Medicine, Boston	Post-doc	06/2007	Cardiovascular medicine

A. Personal Statement

For the past fifteen years, I have been doing cardiovascular research with a special focus on the role of obesity and insulin resistance in development of subclinical and clinical cardiovascular disease. My research is translational and interdisciplinary, combining big data approaches, such as -omics in population-based samples, with gene editing in functional model systems to reach new insights into the pathophysiology of cardiovascular disease and related conditions, identification of new biomarkers for improved risk prediction, and discovery of novel targets for drug development. I have had a leading role in many of the large efforts identifying new loci associated with cardiovascular and metabolic traits, and have extensive experience from research on biomarkers and -omics methods, including development and application of prediction metrics and Mendelian randomization. I have served as PI of numerous –omics efforts in several Swedish cohort studies, including ULSAM, PIVUS, TwinGene and EpiHealth. I have published over 290 peer-reviewed original articles, of which >50 in journals with impact factor over 30. Before relocating to the U.S, I received many European research grants, and after joining the Stanford faculty in May 2016, I have received several NIH grants. I have won several prestigious awards and grants, such as the AHA Trudy Bush Fellowship for Cardiovascular Research in Women's Health, ERC starting grant, Wallenberg Academy Fellow and the Göran Gustafsson Prize in Medicine in 2015 (to the most successful medical researcher in Sweden under age 45).

1. **Ingelsson E**, Schaefer EJ, Contois JH, McNamara JR, Sullivan L, Keyes MJ, Pencina MJ, Schoonmaker C, Wilson PW, D'Agostino RB, Vasan RS. Clinical Utility of Different Lipid Measures for Prediction of Coronary Heart Disease in Men and Women. *JAMA*. 2007; 298(7):776-85.
2. Berndt SI, Gustafsson S, Mägi R, Ganna A, Wheeler E, [>300 authors], 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; 45(5):501-12.
3. Fall T, Xie W, Poon W, Yaghootkar H, Magi R, GENESIS consortium, Knowles JW, Lyssenko V, Weedon M, Frayling TM, **Ingelsson E**. Using Genetic Variants to Assess the Relationship between Circulating Lipids and Type 2 Diabetes. *Diabetes*. 2015; 64(7):2676-84.
4. Ganna A, **Ingelsson E**. 5 year mortality predictors in 498 103 UK Biobank participants: a prospective population-based study. *Lancet* 2015;386(9993):533-540.

B. Positions and Honors

Positions and Employment

2000-2002	Internship at Gävle County Hospital, Gävle, Sweden
2003-2006	Residency in general practice, Primary Health Care, Uppsala, Sweden combined with PhD studies at Uppsala University, Sweden

2006-2007	Postdoctoral Fellow, Framingham Heart Study, Boston University School of Medicine, USA
2007-2008	Junior Lecturer, Dept of Public Health and Caring Sciences, Uppsala University, Sweden
2008-2010	Associate Professor, Dept of Medical Epidemiology and Biostatistics, Karolinska Institutet
2010-2012	Professor of Cardiovascular Epidemiology, Dept. of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden
2012-2015	Visiting Professor of Cardiovascular Epidemiology, Wellcome Trust Center for Human Genetics, University of Oxford, UK
2013-2016	Professor of Molecular Epidemiology, Dept. of Medical Sciences, Uppsala University, Sweden
2016 and on	Professor of Medicine, Division of Cardiovascular Medicine, Department of Medicine, Stanford University School of Medicine

Leadership Roles in Professional Organizations

2008-2010	Member of the Early Career Committee of the American Heart Association Council on Epidemiology and Prevention
2008-2010	Chair of the Connection Corner activity for American Heart Association's 49th and 50th Annual Conferences on Cardiovascular Disease, Epidemiology, and Prevention
2009-2010	Member of the Planning Committee for American Heart Association's 49th and 50th Annual Conferences on Cardiovascular Disease, Epidemiology, and Prevention
2011-2013	Member of the Leadership Committee of the EPI council in American Heart Association
2011-2013	Council leader of the International Mentoring Program of American Heart Association
2014 and on	Member of the Molecular Determinants of Cardiovascular Health Joint Committee of the FGTB and EPI councils, American Heart Association
2016-2017	Co-Chair of Scientific Statement from the American Heart Association: "The Expressed Genome in Cardiovascular Diseases and Stroke: Refinement, Diagnosis, and Prediction"
2017 and on	Deputy Editor for Circulation Cardiovascular Genetics, American Heart Association

Other Experience and Professional Memberships

2011-2016	Member of Sweden's Young Academy
2011-2015	Member of the Global Young Academy
2015-2016	National Director of EATRIS.se (Swedish node of the European Infrastructure for Translational Medicine)

Honors

2005	Finalist in the Jeremiah and Rose Stamler Research Award for New Investigators, American Heart Association, USA
2007	Award winner of the Linnéus Foundation for Medical Research, Uppsala, Sweden
2007	Recipient of Postdoctoral Stipend Award from the Swedish Society for Medical Research
2008	Winner of the Young Investigator Award, EuroPRevent 2008, European Association of Cardiovascular Prevention and Rehabilitation, Paris, France
2008	Recipient of Research Program Award from the Swedish Society of Medicine
2009	Winner of Trudy Bush Fellowship for Cardiovascular Research in Women's Health, American Heart Association, USA
2009	Winner of Ingvar Carlsson Award, Swedish Foundation for Strategic Research
2010	Fellow of the American Heart Association, FAHA
2011	Ranked #14 among "Sweden's 101 Super Talents 2010" by Veckans Affärer (largest weekly Swedish business journal)
2011	Young Scientist at the Annual Meeting of the New Champions 2011, World Economic Forum, Dalian, China
2013	Recipient of ERC Starting Grant 2013, European Research Council
2013	Wallenberg Academy Fellow, Knut och Alice Wallenberg Foundation
2015	Winner of the Göran Gustafsson Prize in Medicine
2015	Elected to The Royal Society of Arts and Sciences, Uppsala, Sweden

C. Contributions to Science

1. **Biomarkers and –omics.** Biomarkers and risk prediction belong to the very core of cardiovascular epidemiology, being key factors for improving health care and for achieving precision medicine. I have been working extensively with prediction of CVD by use of both traditional and more novel biomarkers and

by use of different statistical metrics for prediction. For example, the most influential paper from my post-doc at the Framingham Heart Study was a publication in *JAMA*, where we compared traditional lipids with apolipoproteins for risk prediction – a highly cited paper that had impact on guidelines for primary prevention of CVD from American Heart Association. This was also the first paper to apply net reclassification index (NRI), a risk prediction measure that has gained much popularity. I have also led development of new methods for risk prediction, such as application of various risk prediction metrics in a case-cohort setting. From 2011 and on, my group has changed focus going from analyses of one or a few biomarkers or variables at the time to analyses of hundreds to thousands of markers at once using -omics or other big data methods. A recent example is our study of thousands of metabolic features in relation to incident coronary heart disease where we identified four novel metabolites improving risk prediction. Another recent example of large-scale prediction is our paper in *Lancet* where we studied sex-specific associations of 655 measurements of demographics, health and lifestyle with all-cause mortality and six cause-specific mortality categories in 498,103 UK Biobank participants. Linked to this publication, we developed a hugely popular website, http://ubble.stanford.edu, disseminating our findings to researchers, policy-makers and the general public.

a. **Ingelsson E**, Schaefer EJ, Contois JH, McNamara JR, Sullivan L, Keyes MJ, Pencina MJ, Schoonmaker C, Wilson PW, D'Agostino RB, Vasan RS. Clinical Utility of Different Lipid Measures for Prediction of Coronary Heart Disease in Men and Women. *JAMA*. 2007; 298(7):776-85. PMID: 17699011.
b. Ganna A, Reilly M, de Faire U, Pedersen N, Magnusson P, **Ingelsson E**. Risk Prediction Measures for Case-Cohort and Nested Case-Control Designs: An Application to Cardiovascular Disease. *Am J Epidemiol.* 2012; 175(7):715-24. PMCID: PMC3324433.
c. Ganna A, Salihovic S, Sundström J, Broeckling CD, Hedman ÅK, Magnusson PKE, Pedersen NL, Larsson A, Siegbahn A, Zilmer M, Prenni J, Ärnlöv J, Lind L, Fall T, **Ingelsson E**. Large-scale Metabolomic Profiling Identifies Novel Biomarkers for Incident Coronary Heart Disease. *PLoS Genet.* 2014;10(12):e1004801. PMCID: PMC4263376.
d. Ganna A, **Ingelsson E**. Five-year mortality predictors: A prospective study of ~500,000 UK Biobank participants. *Lancet* 2015;386(9993):533-540. PMID: 26049253.

2. **Genome-wide association studies.** The development in complex disease genetics has been remarkable in the past years starting off from the era of candidate gene-based studies with few consistently replicated genotype-phenotype associations to an exponentially increasing number of larger and larger genome-wide association study (GWAS) meta-analysis consortia, and now sequencing-based projects. My research group has led a number of projects having a large impact on the understanding of genetics of complex diseases. As a result of the work within GWAS consortia, we have published many papers in top-tier journals (e.g. 30 in *Nature Genetics*, nine in *Nature*, two in *Science*). I have had a leading role in many of these papers, as senior author, member of the writing group and/or steering committees. Most importantly, I was senior author of key papers identifying genetic loci associated with BMI, extreme obesity, circulating lipids, fasting glucose, insulin and 2-hour glucose. Our work has led to landmark papers dissecting the genetic architecture of complex traits - highlighting the very polygenetic nature of complex traits, the high degree of allelic heterogeneity, and that the genetics of extremes is similar to that of the full population - and discovering much new biology influencing these traits and giving leads to further in-depth characterization.

a. Speliotes EK, Willer CJ, Berndt SI, Monda KL, Thorleifsson G, Jackson AU, [>300 authors], Barroso I, Boehnke M*, Stefansson K*, North KE*, McCarthy MI*, Hirschhorn JN*, **Ingelsson E***, Loos RJ*. Association Analyses of 249,796 Individuals Reveal 18 New Loci Associated with Body Mass Index. *Nat Genet.* 2010; 42(11):937-48. PMCID: PMC3014648.
b. Scott RA, Lagou V, Welch RP, Wheeler E, [>200 authors], Teslovich TM, Florez JC*, Langenberg C*, **Ingelsson E***, Prokopenko I*, Barroso I*. Large-Scale Association Analyses Identify New Loci Influencing Glycemic Traits and Provide Insight into the Underlying Biological Pathways. *Nat Genet.* 2012; 44(9):991-1005. PMCID: PMC3433394.
c. Berndt SI, Gustafsson S, Mägi R, Ganna A, Wheeler E, [>300 authors], 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; 45(5):501-12. PMCID: PMC3973018.
d. Willer CJ, Schmidt EM, Sengupta S, Peloso GM, Gustafsson S, [>200 authors], Rich SS, Boehnke M*, Deloukas P*, Kathiresan S*, Mohlke KL*, **Ingelsson E***, Abecasis GR*. Discovery and

Refinement of Loci Associated with Lipid Levels. *Nat Genet.* 2013; 45(11):1274-83. PMCID: PMC3838666.

3. **Mendelian randomization.** With the availability of hundreds of robust genotype-phenotype associations, Mendelian randomization (MR) methods provide epidemiologists with an approach to infer causality avoiding reverse causation and confounding that have riddled observational studies in the past. Knowledge about the causal roles of risk factors that have been suggested to be involved in the development of cardiovascular disease and type 2 diabetes provides crucial insights regarding the etiological understanding of these conditions, and can accelerate development of new prevention strategies and treatment regimens. I have led several large projects using these approaches, and further developing the methodology. Within the ENGAGE consortium, I led a large effort resulting in several papers in high-impact journals, studying obesity as a causal risk factor for various health outcomes. I was also the senior author on the first paper describing a causal link between low LDL cholesterol and metabolic disturbances, including development of type 2 diabetes, using MR methods.
    a. Fall T, Hägg S, Mägi R, Ploner A, [>100 authors], Stefansson K, Pedersen NL*, McCarthy MI*, **Ingelsson E***, Prokopenko I* for the European Network for Genetic and Genomic Epidemiology (ENGAGE) consortium. The Role of Adiposity in Cardiometabolic Traits: A Mendelian Randomization Analysis. *PLOS Med.* 2013; 10(6):e1001474. PMCID: PMC3692470.
    b. Fall T, Hägg S, Ploner A, Mägi R, Fischer K, Draisma HHM, [>100 authors], Pedersen NL, Prokopenko I, McCarthy MI, **Ingelsson E**. Age- and Sex-Specific Causal Effects of Adiposity on Cardiovascular Risk Factors. *Diabetes.* 2015; 64(5):1841-52. PMCID: PMC4407863.
    c. Hägg S, Fall T, Ploner A, Magi R, [>50 authors], Prokopenko I, McCarthy MI, Pedersen NL, **Ingelsson E**. Adiposity as a Cause of Cardiovascular Disease: A Mendelian Randomization Study. *Int J Epidemiol*. 2015;44(2):578-86. PMCID: PMC4553708.
    d. Fall T, Xie W, Poon W, Yaghootkar H, Magi R, GENESIS consortium, Knowles JW, Lyssenko V, Weedon M, Frayling TM*, **Ingelsson E***. Using Genetic Variants to Assess the Relationship between Circulating Lipids and Type 2 Diabetes. *Diabetes*. 2015; 64(7):2676-84. PMID: 25948681.

4. **Functional characterization of GWAS loci.** GWAS have provided us with hundreds of genetic loci robustly associated with metabolic and cardiovascular traits. However, for the majority of these, mechanisms are largely unknown. Understanding of the causal genes and their function is a crucial first step towards development of new drug therapies. Over the past three years, I have refocused much of my research efforts towards identification and characterization of genes discovered in GWAS using a combination of in-depth studies in human (including various -omics methods), *in vivo* (in mice and zebrafish) and *in vitro* studies (in adipocytes and myocytes). However, already in 2010, I published one of the first examples of a detailed characterization of GWAS signals (for fasting glucose and insulin), by use of refined physiological measures of glucose metabolism in humans, including intravenous measures of insulin sensitivity. We followed this up with similar study where we characterized all known loci associated with type 2 diabetes. Also, I am one of the senior authors of a recent paper in *JCI* where we have identified a novel insulin resistance locus via GWAS, and then performed *in vitro* studies in adipocytes giving a detailed characterization of the biology underlying the signal. These studies serve as examples of the power of combining population-based data with functional follow-up studies.
    a. **Ingelsson E**, Langenberg C, Hivert MF, Prokopenko I, [60 authors], Watanabe RM, Florez JC. Detailed Physiologic Characterization Reveals Diverse Mechanisms for Novel Genetic Loci Regulating Glucose and Insulin Metabolism in Humans. *Diabetes*. 2010; 59(5):1266-75. PMCID: PMC2857908.
    b. Dimas AS, Lagou V, Barker A, Knowles JW, Mägi R, [53 authors], Dupuis J, Watanabe RM*, Florez JC*, **Ingelsson E***, McCarthy MI*, Prokopenko I* on behalf of the Meta-Analyses of Glucose and Insulin-related traits Consortium (MAGIC) Investigators. Impact of Type 2 Diabetes Susceptibility Variants on Quantitative Glycemic Traits Reveals Mechanistic Heterogeneity. *Diabetes*. 2014; 63(6):2158-71. PMCID: PMC4030103.
    c. Knowles JW, Xie W, Zhang Z, Chennemsetty I, [31 authors], Laakso M, Hao K*, **Ingelsson E***, Frayling TM*, Weedon MN*, Walker M*, Quertermous T.* Identification and Validation of N-Acetyltransferase 2 as an Insulin Sensitivity Gene. *J Clin Invest*. 2015; 125(4):1739-51. PMCID: PMC4409020.

* denotes shared last authorship

Complete List of Published Work in MyBibliography (>300 peer-reviewed publications):
http://www.ncbi.nlm.nih.gov/sites/myncbi/erik.ingelsson.1/bibliography/47532577/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

NIH/NIDDK (1R01 DK106236-01A1) Ingelsson (PI) 09/01/16-08/31/21
Beyond GWAS of insulin resistance: An integrated approach to translate genetic association to function
We will perform a series of studies in unique samples of up to 13,811 individuals from the general population, genetically modified zebrafish and cell-based model systems. Our work is anticipated to lead to new important insights to the development of insulin resistance, which in turn can lead to better treatment of this and related conditions.

NIH/NHLBI (1R01 HL135313-01) Ingelsson (PI) 02/01/17-01/31/20
Causal associations of circulating biomarkers with cardiovascular disease
We will assess the causal role of 36 biomarkers on the development of coronary heart disease, stroke, heart failure, atrial fibrillation and type 2 diabetes in 502,650 participants of the UK Biobank using Mendelian randomization. Our work is anticipated to give important insights regarding the etiological understanding of these diseases and accelerate development of new prevention strategies, including druggable targets.

NIH/NIDDK (1R01 DK114183-01A1) Assimes (Co-I) 04/01/18-03/31/23
Proteomic determinants of direct measures of insulin sensitivity
We will comprehensively examine the levels of ~1,000 proteins in the blood of individuals who underwent laborious 'gold standard' testing for the presence of insulin resistance. We will use this information to better understand the causes of insulin resistance and to improve our ability to identify individuals at risk of complications of insulin resistance.

Precision Wellness (SPO #134382) Ingelsson (PI) 12/01/17-11/30/18
Evaluation of the Precision Wellness cardiovascular analytics tool
We are using electronic health records from the STARR database at Stanford Medicine to further develop and validate a cardiovascular risk engine developed by a start-up company called Precision Wellness.

NIH/NIDDK (1P30 DK116074-01) Kim (Co-I) 09/15/17-06/30/22
Stanford Diabetes Research Center
I was a co-applicant for the Diabetes Research Center grant that was awarded to Stanford in 2017, and act as leader of the Metabolism and Signaling Affinity Group.

Knut och Alice Wallenberg Foundation (grant no. 2013.0126) Ingelsson (PI) 01/01/14-12/31/18
Cardiomics: Use of -omics methods for identification of novel drug targets and clinical biomarkers for coronary heart disease
The overall aims of this research program are to improve risk prediction and treatment of coronary heart disease through improved understanding of biology underlying disease development and identification of new biomarkers for improved risk stratification and individualized treatment. The work combines epidemiological studies with functional work in zebrafish.

Completed Research Support

Swedish Heart-Lung Foundation (grant no. 20140422) Ingelsson (PI) 01/01/15-12/31/17
Beyond GWAS of obesity: An integrated approach to translate genetic association to function Beyond GWAS of obesity: from genetic association to function
The aims of this proposal are to characterize genetic loci for obesity using a combination of epidemiological studies, *in vivo* models in zebrafish and *in vitro* models in adipocytes and hepatocytes.