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Supplemental Data

Large-Scale Gene-Centric Meta-Analysis across 39 Studies Identifies Type 2 Diabetes Loci

Richa Saxena, Clara C. Elbers, Yiran Guo, Inga Peter, Tom R. Gaunt, Jessica L. Mega, Matthew B. Lanktree, Archana Tare, Berta Almoguera Castillo, Yun R. Li, Toby Johnson, Marcel Bruinenberg, Diane Gilbert-Diamond, Ramakrishnan Rajagopalan, Benjamin F. Voight, Ashok Balasubramanyam, John Barnard, Florianne Bauer, Jens Baumert, Tushar Bhangale, Bernhard O. Böhm, Peter S. Braund, Paul R. Burton, Hareesh R. Chandrupatla, Robert Clarke, Rhonda M. Cooper-DeHoff, Errol D. Crook, George Davey-Smith, Ian N. Day, Anthonius de Boer, Mark C.H. de Groot, Fotios Drenos, Jane Ferguson, Caroline S. Fox, Clement E. Furlong, Quince Gibson, Christian Gieger, Lisa A. Gilhuijs-Pederson, Joseph T. Glessner, Anuj Goel, Yan Gong, Struan F.A. Grant, Diederick E. Grobbee, Claire Hastie, Steve E. Humphries, Cecilia E. Kim, Mika Kivimaki, Marcus Kleber, Christa Meisinger, Meena Kumari, Taimour Y Langaee, Debbie A. Lawlor, Mingyao Li, Maximilian T. Lobmeyer, Anke-Hilse Maitland-van der Zee, Matthijs F.L. Meijs, Cliona M. Molony, David A. Morrow, Gurunathan Murugesan, Solomon K. Musani, Christopher P. Nelson, Stephen J. Newhouse, Jeffery R. O'Connell, Sandosh Padmanabhan, Jutta Palmen, Sanjey R. Patel, Carl J. Pepine, Mary Pettinger, Thomas S. Price, Suzanne Rafelt, Jane Ranchalis, Asif Rasheed, Elisabeth Rosenthal, Ingo Ruczinski, Sonia Shah, Haiqing Shen, Günther Silbernagel, Erin N. Smith, Annemieke W.M. Spijkerman, Alice Stanton, Michael W. Steffes, Barbara Thorand, Mieke Trip, Pim van der Harst, Daphne L. van der A, Erik P.A. van Iperen, Jessica van Setten, Jana V. van Vliet-Ostaptchouk, Niek Verweij, Bruce H.R. Wolffenbuttel, Taylor Young, M. Hadi Zafarmand, Joseph M. Zmuda, the Look AHEAD Research Group, DIAGRAM consortium, Michael Boehnke, David Altshuler, Mark McCarthy, W.H. Linda Kao, James S. Pankow, Thomas P. Cappola, Peter Sever, Neil Poulter, Mark Caulfield, Anna Dominiczak, Denis C. Shields, Deepak L. Bhatt, Li Zhang, Sean P. Curtis, John Danesh, Juan P. Casas Yvonne T. van der Schouw, N. Charlotte Onland-Moret, Pieter A. Doevendans, Gerald W. Dorn II, Martin Farrall, Garret A. FitzGerald, Anders Hamsten Robert Hegele, Aroon D. Hingorani, Marten H. Hofker, Gordon S. Huggins, Thomas Illig, Gail P. Jarvik, Julie A. Johnson, Olaf H. Klungel, William C. Knowler, Wolfgang Koenig, Winfried März, James B. Meigs, Olle Melander, Patricia B. Munroe, Braxton D. Mitchell, Susan J. Bielinski, Daniel J. Rader, Muredach P. Reilly, Stephen S. Rich, Jerome I. Rotter, Danish Saleheen, Nilesh J. Samani, Eric E. Schadt, Alan R. Shuldiner, Roy Silverstein, Kandice Kottke-Marchant, Philippa J. Talmud, Hugh Watkins, Folkert W. Asselbergs, Paul IW de Bakker, Jeanne McCaffery, Cisca Wijmenga, Marc S. Sabatine, James G. Wilson, Alex Reiner, Donald W. Bowden, Hakon Hakonarson, David S. Siscovick, and Brendan J. Keating

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DIAGRAM CONSORTIUM

Benjamin F Voight[1,2,3], Laura J Scott[4], Valgerdur Steinthorsdottir[5], Andrew P Morris[6], Christian Dina[7,8], Ryan P Welch[9], Eleftheria Zeggini[6,10], Cornelia Huth[11a,12], Yurii S Aulchenko[13], Gudmar Thorleifsson[5], Laura J McCulloch[14], Teresa Ferreira[6], Harald Grallert[11b,12], Najaf Amin[13], Guanming Wu[15], Cristen J Willer[4], Soumya Raychaudhuri[1,2,16], Steve A McCarroll[1,17], Claudia Langenberg[18], Oliver M Hofmann[19], Josée Dupuis[20,21], Lu Qi[22-24], Ayellet V Segrè[1,2,17], Mandy van Hoek[25], Pau Navarro[26], Kristin Ardlie[1], Beverley Balkau[27,28], Rafn Benediktsson[29,30], Amanda J Bennett[14], Roza Blagieva[31], Eric Boerwinkle[32], Lori L Bonnycastle[33], Kristina Bengtsson Boström[34], Bert Bravenboer[35], Suzannah Bumpstead[10], Noël P Burtt[1], Guillaume Charpentier[36], Peter S Chines[33], Marilyn Cornelis[24], David J Couper[37], Gabe Crawford[1], Alex SF Doney[38,39], Katherine S Elliott[6], Amanda L Elliott[1,17,40], Michael R Erdos[33], Caroline S Fox[21,41], Christopher S Franklin[42], Martha Ganser[4], Christian Gieger[11c], Niels Grarup[43], Todd Green[1,2], Simon Griffin[18], Christopher J Groves[14], Candace Guiducci[1], Samy Hadjadj[44], Neelam Hassanali[14], Christian Herder[45], Bo Isomaa[46,47], Anne U Jackson[4], Paul RV Johnson[48], Torben Jørgensen[49,50], Wen HL Kao[51,52], Norman Klopp[11b], Augustine Kong[5], Peter Kraft[22,23], Johanna Kuusisto[53], Torsten Lauritzen[54], Man Li[51], Aloysius Lieverse[55], Cecilia M Lindgren[6], Valeriya Lyssenko[56], Michel Marre[57,58], Thomas Meitinger[59,60], Kristian Midthjell[61], Mario A Morken[33], Narisu Narisu[33], Peter Nilsson[56], Katharine R Owen[14], Felicity Payne[10], John RB Perry[62,63], Ann-Kristin Petersen[11c], Carl Platou[61], Christine Proença[7], Inga Prokopenko[6,14], Wolfgang Rathmann[64], N William Rayner[6,14], Neil R Robertson[6,14], Ghislain Rocheleau[65-67], Michael Roden[45,68], Michael J Sampson[69], Richa Saxena[1,2,40], Beverley M Shields[62,63], Peter Shrader[3,70], Gunnar Sigurdsson[29,30], Thomas Sparsø[43], Klaus Strassburger[64], Heather M Stringham[4], Qi Sun[22,23], Amy J Swift[33], Barbara Thorand[11a], Jean Tichet[71], Tiinamaija Tuomi[46,72], Rob M van Dam[24], Timon W van Haeften[73], Thijs van Herpt[25,55], Jana V van Vliet-Ostaptchouk[74], G Bragi Walters[5], Michael N Weedon[62,63], Cisca Wijmenga[75], Jacqueline Witteman[13], Richard N Bergman[76], Stephane Cauchi[7], Francis S Collins[77], Anna L Gloyn[14], Ulf Gyllensten[78], Torben Hansen[43,79], Winston A Hide[19], Graham A Hitman[80], Albert Hofman[13], David J Hunter[22,23], Kristian Hveem[61,81], Markku Laakso[53], Karen L Mohlke[82], Andrew D Morris[38,39], Colin NA Palmer[38,39], Peter P Pramstaller[83], Igor Rudan[42,84,85], Eric Sijbrands[25], Lincoln D Stein[15], Jaakko Tuomilehto[86], Andre Uitterlinden[25], Mark Walker[87], Nicholas J Wareham[18], Richard M Watanabe[76,88], Goncalo R Abecasis[4], Bernhard O Boehm[31], Harry Campbell[42], Mark J Daly[1,2], Andrew T Hattersley[62,63], Frank B Hu[22-24], James B Meigs[3,70], James S Pankow[89], Oluf Pedersen[43,90,91], H.-Erich Wichmann[11d,12,,92], Inês Barroso[10], Jose C Florez[1,2,3,93], Timothy M Frayling[62,63], Leif Groop[56,72], Rob Sladek[65-67], Unnur Thorsteinsdottir[5,94], James F Wilson[42], Thomas Illig[11b,,11e], Philippe Froguel[7,95], Cornelia M van Duijn[13], Kari Stefansson[5,94], David Altshuler[1,2,3,17,40,93], Michael Boehnke[4], Mark I McCarthy[6,14,96].

Affiliations

1. Broad Institute of Harvard and Massachusetts Institute of Technology (MIT), Cambridge, Massachusetts 02142, USA
2. Center for Human Genetic Research, Massachusetts General Hospital, 185 Cambridge Street, Boston, Massachusetts 02114, USA
3. Department of Medicine, Harvard Medical School, Boston, Massachusetts 02115, USA
4. Department of Biostatistics, University of Michigan, Ann Arbor, Michigan 48109-2029, USA
5. deCODE Genetics, 101 Reykjavik, Iceland
6. Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, OX3 7BN, UK
7. CNRS-UMR-8090, Institute of Biology and Lille 2 University, Pasteur Institute, F-59019 Lille, France
8. INSERM UMR915 CNRS ERL3147 F-44007 Nantes, France
9. Bioinformatics Program, University of Michigan, Ann Arbor MI USA 48109
10. Wellcome Trust Sanger Institute, Hinxton, CB10 1HH, UK

11. a: Institute of Epidemiology II, Helmholtz Zentrum Muenchen, 85764 Neuherberg, Germany, b: Research Unit of Molecular Epidemiology, Helmholtz Zentrum Muenchen, 85764 Neuherberg, Germany, c: Institute of Genetic Epidemiology, Helmholtz Zentrum Muenchen, 85764 Neuherberg, Germany, d: Institute of Epidemiology I, Helmholtz Zentrum Muenchen, 85764 Neuherberg, Germany, b: Research Unit of Molecular Epidemiology, Helmholtz Zentrum Muenchen, 85764 Neuherberg, Germany, e: Hannover Unified Biobank, Hannover Medical School, 30625 Hannover, Germany
12. Institute of Medical Informatics, Biometry and Epidemiology, Ludwig-Maximilians-Universität München, 81377 Munich, Germany
13. Department of Epidemiology, Erasmus University Medical Center, P.O. Box 2040, 3000 CA Rotterdam, The Netherlands.
14. Oxford Centre for Diabetes, Endocrinology and Metabolism, University of Oxford, OX3 7LJ, UK
15. Ontario Institute for Cancer Research, 101 College Street, Suite 800, Toronto, Ontario M5G 0A3, Canada
16. Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115, USA
17. Department of Molecular Biology, Harvard Medical School, Boston, Massachusetts 02115, USA
18. MRC Epidemiology Unit, Institute of Metabolic Science, Addenbrooke's Hospital, Cambridge CB2 0QQ, UK
19. Department of Biostatistics, Harvard School of Public Health, Boston, Massachusetts 02115, USA
20. Department of Biostatistics, Boston University School of Public Health, Boston, Massachusetts 02118, USA
21. National Heart, Lung, and Blood Institute’s Framingham Heart Study, Framingham, Massachusetts 01702, USA
22. Department of Nutrition, Harvard School of Public Health, 665 Huntington Ave, Boston, MA 02115, USA
23. Department of Epidemiology, Harvard School of Public Health, 665 Huntington Ave, Boston, MA 02115, USA
24. Channing Laboratory, Dept. of Medicine, Brigham and Women's Hospital and Harvard Medical School, 181 Longwood Ave, Boston, MA 02115, USA
25. Department of Internal Medicine, Erasmus University Medical Centre, PO-Box 2040, 3000 CA Rotterdam, The Netherlands
26. MRC Human Genetics Unit, Institute of Genetics and Molecular Medicine, Western General Hospital, Edinburgh, EH4 2XU, UK
27. INSERM U780, F-94807 Villejuif. France
28. University Paris-Sud, F-91405 Orsay, France
29. Landspitali University Hospital, 101 Reykjavik, Iceland
30. Icelandic Heart Association, 201 Kopavogur, Iceland
31. Division of Endocrinology, Diabetes and Metabolism, Ulm University, 89081 Ulm, Germany
32. The Human Genetics Center and Institute of Molecular Medicine, University of Texas Health Science Center, Houston, Texas 77030, USA
33. National Human Genome Research Institute, National Institute of Health, Bethesda, Maryland 20892, USA
34. R&D Centre, Skaraborg Primary Care, 541 30 Skövde, Sweden
35. Department of Internal Medicine, Catharina Hospital, PO-Box 1350, 5602 ZA Eindhoven, The Netherlands
36. Endocrinology-Diabetology Unit, Corbeil-Essonnes Hospital, F-91100 Corbeil-Essonnes, France
37. Department of Biostatistics and Collaborative Studies Coordinating Center, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, 27599, USA
38. Diabetes Research Centre, Biomedical Research Institute, University of Dundee, Ninewells Hospital, Dundee DD1 9SY, UK
39. Pharmacogenomics Centre, Biomedical Research Institute, University of Dundee, Ninewells Hospital, Dundee DD1 9SY, UK
40. Department of Genetics, Harvard Medical School, Boston, Massachusetts 02115, USA
41. Division of Endocrinology, Diabetes, and Hypertension, Brigham and Women’s Hospital, Harvard Medical School, Boston, Massachusetts 02115, USA
42. Centre for Population Health Sciences, University of Edinburgh, Teviot Place, Edinburgh, EH8 9AG, UK
43. Hagedorn Research Institute, DK-2820 Gentofte, Denmark
44. Centre Hospitalier Universitaire de Poitiers, Endocrinologie Diabetologie, CIC INSERM 0801, INSERM U927, Université de Poitiers, UFR, Médecine Pharmacie, 86021 Poitiers Cedex, France

45. Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf, 40225 Düsseldorf, Germany
46. Folkhälsan Research Center, FIN-00014 Helsinki, Finland
47. Malmska Municipal Health Center and Hospital, 68601 Jakobstad, Finland
48. Diabetes Research and Wellness Foundation Human Islet Isolation Facility and Oxford Islet Transplant Programme, University of Oxford, Old Road, Headington, Oxford, OX3 7LJ, UK
49. Research Centre for Prevention and Health, Glostrup University Hospital, DK-2600 Glostrup, Denmark
50. Faculty of Health Science, University of Copenhagen, 2200 Copenhagen, Denmark
51. Department of Epidemiology, Johns Hopkins University, Baltimore, Maryland 21287, USA
52. Department of Medicine, and Welch Center for Prevention, Epidemiology, and Clinical Research, Johns Hopkins University, Baltimore, Maryland 21287, USA
53. Department of Medicine, University of Kuopio and Kuopio University Hospital, FIN-70211 Kuopio, Finland
54. Department of General Medical Practice, University of Aarhus, DK-8000 Aarhus, Denmark
55. Department of Internal Medicine, Maxima MC, PO-Box 90052, 5600 PD Eindhoven, The Netherlands
56. Department of Clinical Sciences, Diabetes and Endocrinology Research Unit, University Hospital Malmö, Lund University, 205 02 Malmö, Sweden
57. Department of Endocrinology, Diabetology and Nutrition, Bichat-Claude Bernard University Hospital, Assistance Publique des Hôpitaux de Paris, 75870 Paris Cedex 18, France
58. INSERM U695, Université Paris 7, 75018 Paris , France
59. Institute of Human Genetics, Helmholtz Zentrum Muenchen, 85764 Neuherberg, Germany
60. Institute of Human Genetics, Klinikum rechts der Isar, Technische Universität München, 81675 Muenchen, Germany
61. Nord-Trøndelag Health Study (HUNT) Research Center, Department of Community Medicine and General Practice, Norwegian University of Science and Technology, NO-7491 Trondheim, Norway
62. Genetics of Complex Traits, Institute of Biomedical and Clinical Science, Peninsula Medical School, University of Exeter, Magdalen Road, Exeter EX1 2LU, UK
63. Diabetes Genetics, Institute of Biomedical and Clinical Science, Peninsula Medical School, University of Exeter, Barrack Road, Exeter EX2 5DW, UK
64. Institute of Biometrics and Epidemiology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf, 40225 Düsseldorf, Germany
65. Department of Human Genetics, McGill University, Montreal H3H 1P3, Canada
66. Department of Medicine, Faculty of Medicine, McGill University, Montreal, H3A 1A4, Canada
67. McGill University and Genome Quebec Innovation Centre, Montreal, H3A 1A4. Canada
68. Department of Metabolic Diseases, Heinrich Heine University Düsseldorf, 40225 Düsseldorf, Germany
69. Department of Endocrinology and Diabetes, Norfolk and Norwich University Hospital NHS Trust , Norwich, NR1 7UY, UK.
70. General Medicine Division, Massachusetts General Hospital, Boston, Massachusetts, USA
71. Institut interrégional pour la Santé (IRSA), F-37521 La Riche, France
72. Department of Medicine, Helsinki University Hospital, University of Helsinki, FIN-00290 Helsinki, Finland
73. Department of Internal Medicine, University Medical Center Utrecht, 3584 CG Utrecht,The Netherlands
74. Molecular Genetics, Medical Biology Section, Department of Pathology and Medical Biology, University Medical Center Groningen and University of Groningen, 9700 RB Groningen, The Netherlands
75. Department of Genetics, University Medical Center Groningen and University of Groningen, 9713 EX Groningen, The Netherlands
76. Department of Physiology and Biophysics, University of Southern California School of Medicine, Los Angeles, California 90033, USA
77. National Institute of Health, Bethesda, Maryland 20892, USA
78. Department of Genetics and Pathology, Rudbeck Laboratory, Uppsala University, S-751 85 Uppsala, Sweden.
79. University of Southern Denmark, DK-5230 Odense, Denmark
80. Centre for Diabetes, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London E1 2AT, UK
81. Department of Medicine, The Hospital of Levanger, N-7600 Levanger, Norway

82. Department of Genetics, University of North Carolina, Chapel Hill, North Carolina 27599, USA
83. Institute of Genetic Medicine, European Academy Bozen/Bolzano (EURAC), Viale Druso 1, 39100 Bolzano, Italy
84. Croatian Centre for Global Health, Faculty of Medicine, University of Split, Soltanska 2, 21000 Split, Croatia
85. Institute for Clinical Medical Research, University Hospital "Sestre Milosrdnice", Vinogradska 29, 10000 Zagreb, Croatia
86. Department of Chronic Disease Prevention, National Institute for Health and Welfare, Helsinki FIN-00300, Finland,
87. Diabetes Research Group, Institute of Cellular Medicine, Newcastle University, Framlington Place, Newcastle upon Tyne NE2 4HH, UK
88. Department of Preventitive Medicine, Keck Medical School, University of Southern California, Los Angeles, CA, 90089-9001, USA
89. Division of Epidemiology and Community Health, University of Minnesota, Minneapolis, Minnesota 55454, USA
90. Department of Biomedical Science, Panum, Faculty of Health Science, University of Copenhagen, 2200 Copenhagen, Denmark
91. Faculty of Health Science, University of Aarhus, DK–8000 Aarhus, Denmark
92. Klinikum Grosshadern, 81377 Munich, Germany
93. Diabetes Unit, Massachusetts General Hospital, Boston, Massachusetts 02144, USA
94. Faculty of Medicine, University of Iceland, 101 Reykjavík, Iceland
95. Genomic Medicine, Imperial College London, Hammersmith Hospital, W12 0NN, London, UK
96. Oxford National Institute for Health Research Biomedical Research Centre, Churchill Hospital, Old Road Headington, Oxford, OX3 7LJ, UK

Look AHEAD RESEARCH GROUP AT BASELINE

Clinical Sites

The Johns Hopkins Medical Institutions Frederick Brancati, MD, MHS; Debi Celnik, MS, RD, LD; Jeff Honas, MS; Jeanne Clark, MD, MPH; Jeanne Charleston, RN; Lawrence Cheskin, MD; Kerry Stewart, EdD; Richard Rubin, PhD; Kathy Horak, RD

Pennington Biomedical Research Center George A. Bray, MD; Kristi Rau; Allison Strate, RN; Frank L. Greenway, MD; Donna H. Ryan, MD; Donald Williamson, PhD; Elizabeth Tucker; Brandi Armand, LPN; Mandy Shipp, RD; Kim Landry; Jennifer Perault

The University of Alabama at Birmingham Cora E. Lewis, MD, MSPH; Sheikilya Thomas MPH; Vicki DiLillo, PhD; Monika Safford, MD; Stephen Glasser, MD; Clara Smith, MPH; Cathy Roche, RN; Charlotte Bragg, MS, RD, LD; Nita Webb, MA; Staci Gilbert, MPH; Amy Dobelstein; L. Christie Oden; Trena Johnsey

Harvard Center

Massachusetts General Hospital: David M. Nathan, MD; Heather Turgeon, RN; Kristina P. Schumann, BA; Enrico Cagliero, MD; Kathryn Hayward, MD; Linda Delahanty, MS, RD; Barbara Steiner, EdM; Valerie Goldman, MS, RD; Ellen Anderson, MS, RD; Laurie Bissett, MS, RD; Alan McNamara, BS; Richard Ginsburg, PhD; Virginia Harlan, MSW; Theresa Michel, MS

Joslin Diabetes Center: Edward S. Horton, MD; Sharon D. Jackson, MS, RD, CDE; Osama Hamdy, MD, PhD; A. Enrique Caballero, MD; Sarah Ledbury, MEd, RD; Maureen Malloy, BS; Ann Goebel-Fabbri, PhD; Kerry Ovalle, MS, RCEP, CDE; Sarah Bain, BS; Elizabeth Bovaird, BSN,RN; Lori Lambert, MS, RD

Beth Israel Deaconess Medical Center: George Blackburn, MD, PhD; Christos Mantzoros, MD, DSc; Ann McNamara, RN; Heather McCormick, RD

University of Colorado Anschutz Medical Campus James O. Hill, PhD; Marsha Miller, MS, RD; Brent Van Dorsten, PhD; Judith Regensteiner, PhD; Holly R. Wyatt, M.D., Ligia Coelho, BS; Paulette Cohrs, RN, BSN; Susan Green; April Hamilton, BS, CCRC; Jere Hamilton, BA; Eugene Leshchinskiy; Michael McDermott, MD; Loretta Rome, TRS; Kristin Wallace, MPH; Terra Worley, BA

Baylor College of Medicine John P. Foreyt, PhD; Rebecca S. Reeves, DrPH, RD; Henry Pownall, PhD; Peter Jones, MD; Ashok Balasubramanyam, MD; Molly Gee, MEd, RD

University of California at Los Angeles School of Medicine Mohammed F. Saad, MD; Ken C. Chiu, MD; Siran Ghazarian, MD; Kati Szamos, RD; Magpuri Perpetua, RD; Michelle Chan, BS; Medhat Botrous

The University of Tennessee Health Science Center

University of Tennessee East. Karen C. Johnson, MD, MPH; Leeann Carmichael, RN; Lynne Lichtermann, RN, BSN

University of Tennessee Downtown. Abbas E. Kitabchi, PhD, MD; Jackie Day, RN; Helen Lambeth, RN, BSN; Debra Force, MS, RD, LDN; Debra Clark, LPN; Andrea Crisler, MT, Donna Green, RN; Gracie Cunningham; Maria Sun, MS, RD, LDN; Robert Kores, PhD; Renate Rosenthal, PhD; and Judith Soberman, MD

University of Minnesota Robert W. Jeffery, PhD; Carolyn Thorson, CCRP; John P. Bantle, MD; J. Bruce Redmon, MD; Richard S. Crow, MD; Jeanne Carls, MEd; Carolyne Campbell; La Donna James; T. Ockenden, RN; Kerrin Brelje, MPH, RD; M. Patricia Snyder, MA, RD; Amy Keranen, MS; Cara Walcheck, BS, RD; Emily Finch, MA; Birgitta I. Rice, MS, RPh, CHES; Vicki A. Maddy, BS, RD; Tricia Skarphol, BS

St. Luke's Roosevelt Hospital Center Xavier Pi-Sunyer, MD; Jennifer Patricio, MS; Jennifer Mayer, MS; Stanley Heshka, PhD; Carmen Pal, MD; Mary Anne Holowaty, MS, CN; Diane Hirsch, RNC, MS, CDE

University of Pennsylvania Thomas A. Wadden, PhD; Barbara J. Maschak-Carey, MSN, CDE; Gary D. Foster, PhD; Robert I. Berkowitz, MD; Stanley Schwartz, MD; Shiriki K. Kumanyika, PhD, RD, MPH; Monica Mullen, MS, RD; Louise Hesson, MSN; Patricia Lipschutz, MSN; Anthony Fabricatore, PhD; Canice Crerand, PhD; Robert Kuehnel, PhD; Ray Carvajal, MS; Renee Davenport; Helen Chomentowski

University of Pittsburgh David E. Kelley, MD; Jacqueline Wesche -Thobaben, RN,BSN,CDE; Lewis Kuller, MD, DrPH.; Andrea Kriska, PhD; Daniel Edmundowicz, MD; Mary L. Klem, PhD, MLIS; Janet Bonk, RN, MPH; Jennifer Rush, MPH; Rebecca Danchenko, BS; Barb Elnyczky, MA; Karen Vujevich, RN-BC, MSN, CRNP; Janet Krulia, RN ,BSN ,CDE; Donna Wolf, MS; Juliet Mancino, MS, RD, CDE, LDN; Pat Harper, MS, RD, LDN; Anne Mathews, MS, RD, LDN

Brown University Rena R. Wing, PhD; Vincent Pera, MD; John Jakicic, PhD; Deborah Tate, PhD; Amy Gorin, PhD; Renee Bright, MS; Pamela Coward, MS, RD; Natalie Robinson, MS, RD; Tammy Monk, MS; Kara Gallagher, PhD; Anna Bertorelli, MBA, RD; Maureen Daly, RN; Tatum Charron, BS; Rob Nicholson, PhD; Erin Patterson, BS; Julie Currin, MD; Linda Foss, MPH; Deborah Robles; Barbara Bancroft, RN, MS; Jennifer Gauvin, BS; Deborah Maier, MS; Caitlin Egan, MS; Suzanne Phelan, PhD; Hollie Raynor, PhD, RD; Don Kieffer, PhD; Douglas Raynor, PhD; Lauren Lessard, BS; Kimberley Chula-Maguire, MS; Erica Ferguson, BS, RD; Richard Carey, BS; Jane Tavares, BS; Heather Chenot, MS; JP Massaro, BS

The University of Texas Health Science Center at San Antonio Steve Haffner, MD; Maria Montez, RN, MSHP, CDE; Connie Mobley, PhD, RD; Carlos Lorenzo, MD
University of Washington / VA Puget Sound Health Care System Steven E. Kahn, MB, ChB; Brenda Montgomery, MS, RN, CDE; Robert H. Knopp, MD; Edward W. Lipkin, MD, PhD; Matthew L. Maciejewski, PhD; Dace L. Trence, MD; Roque M. Murillo, BS; S. Terry Barrett, BS

Southwestern American Indian Center, Phoenix, Arizona and Shiprock, New Mexico William C. Knowler, MD, DrPH; Paula Bolin, RN, MC; Tina Killean, BS; Carol Percy, RN; Rita Donaldson, BSN; Bernadette Todacheenie, EdD; Justin Glass, MD; Sarah Michaels, MD; Jonathan Krakoff, MD; Jeffrey Curtis, MD, MPH; Peter H. Bennett, MB, FRCP; Tina Morgan; Ruby Johnson; Cathy Manus; Janelia Smiley; Sandra Sangster; Shandiin Begay, MPH; Minnie Roanhorse; Didas Fallis, RN; Nancy Scurlock, MSN, ANP; Leigh Shovestull, RD

Coordinating Center

Wake Forest University School of Medicine Mark A. Espeland, PhD; Judy Bahnson, BA; Lynne Wagenknecht, DrPH; David Reboussin, PhD; W. Jack Rejeski, PhD; Wei Lang, PhD; Alain Bertoni, MD, MPH; Mara Vitolins, DrPH; Gary Miller, PhD; Paul Ribisl, PhD; Kathy Dotson, BA; Amelia Hodges, BS; Patricia Hogan, MS; Kathy Lane, BS; Carrie Williams, MA; Christian Speas, BS; Delia S. West, PhD; William Herman, MD, MPH

Central Resources Centers

DXA Reading Center, University of California at San Francisco Michael Nevitt, PhD; Ann Schwartz, PhD; John Shepherd, PhD; Jason Maeda, MPH; Cynthia Hayashi; Michaela Rahorst; Lisa Palermo, MS, MA

Central Laboratory, Northwest Lipid Research Laboratories Santica M. Marcovina, PhD, ScD; Greg Strylewicz, MS

ECG Reading Center, EPICARE, Wake Forest University School of Medicine

Ronald J. Prineas, MD, PhD; Zhu-Ming Zhang, MD; Charles Campbell, AAS, BS; Sharon Hall

Diet Assessment Center, University of South Carolina, Arnold School of Public Health, Center for Research in Nutrition and Health Disparities Elizabeth J Mayer-Davis, PhD; Cecilia Farach, DrPH

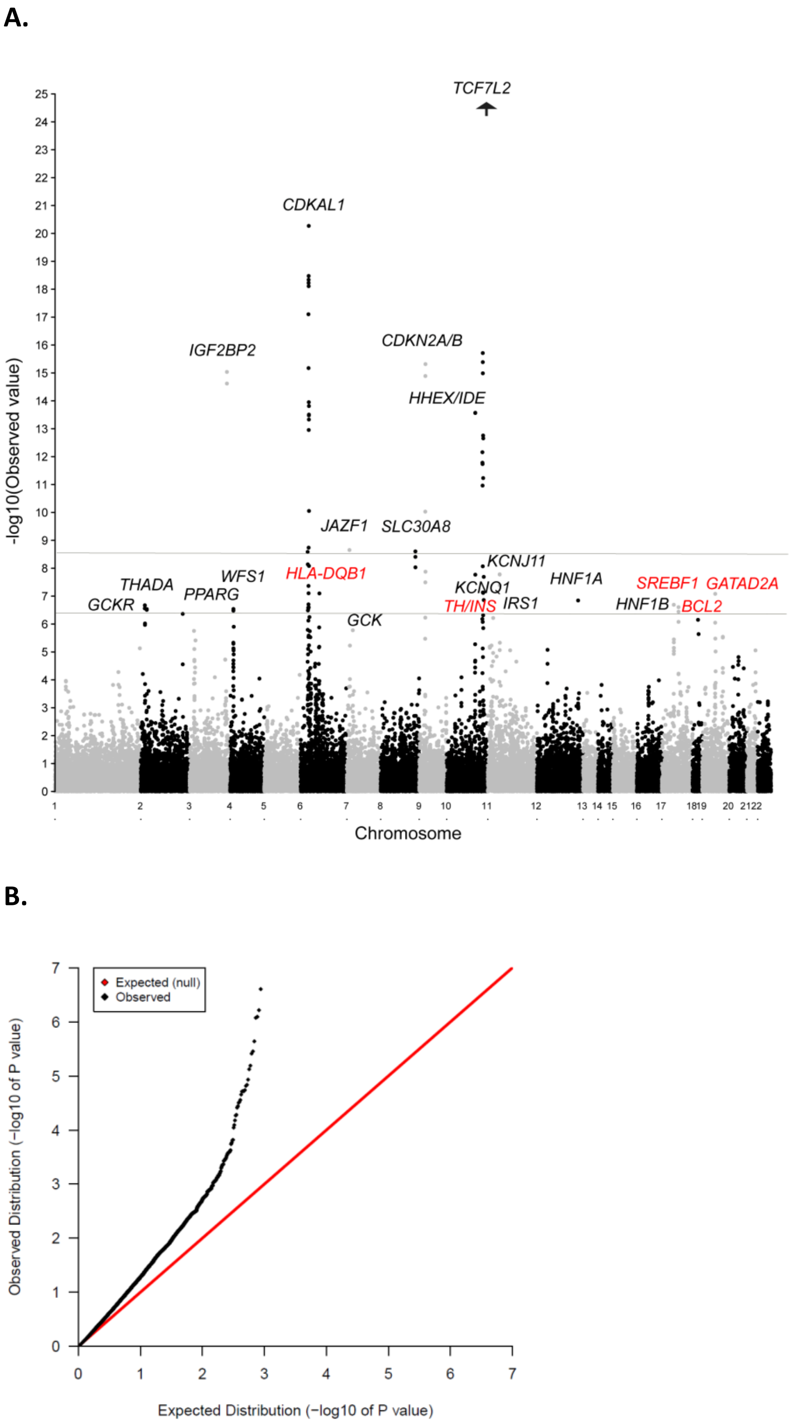
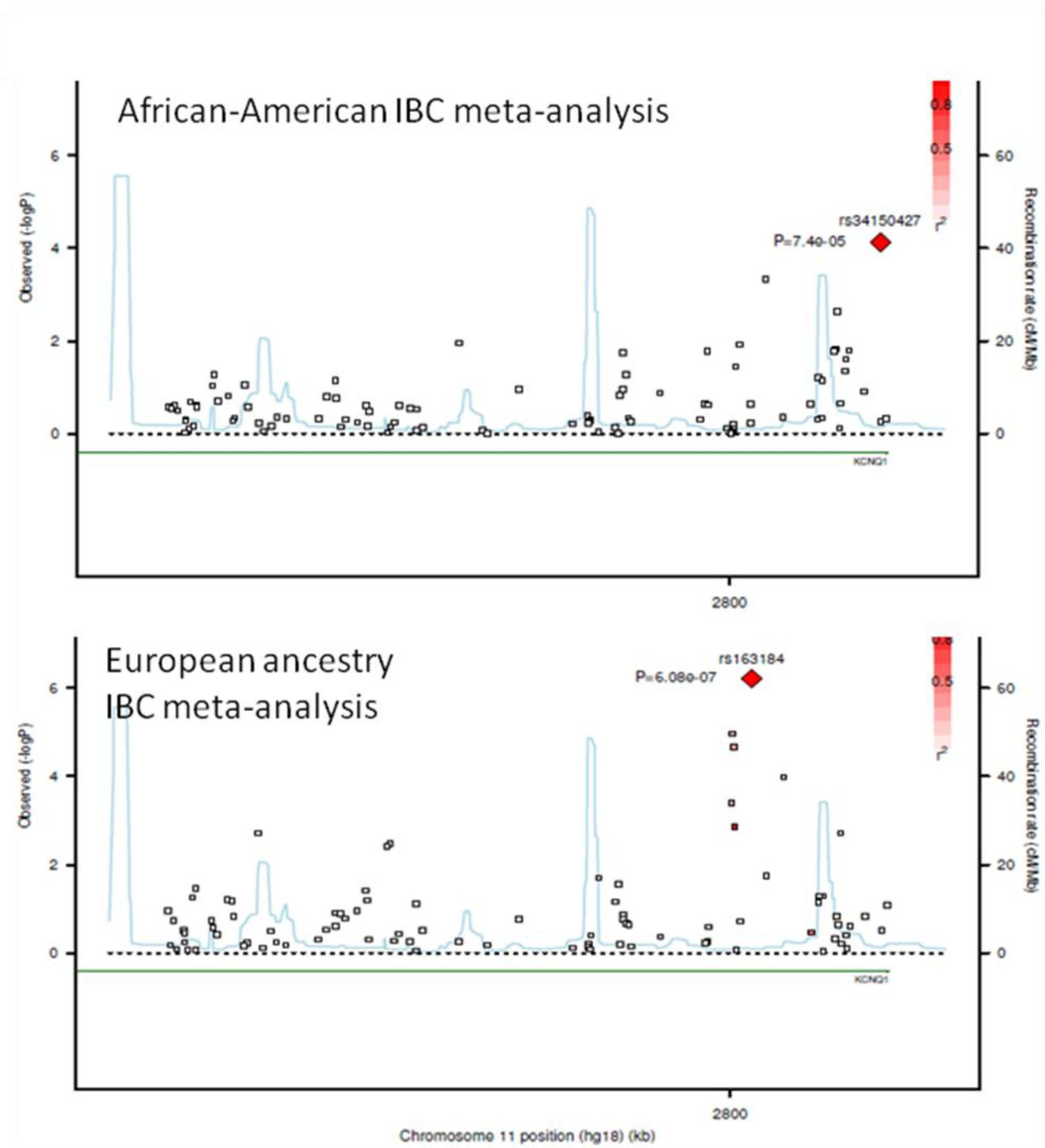


Figure S1. Summary meta-analysis results for 25 European ancestry IBC array association studies. A. Manhattan plot highlighting known and novel T2D associated loci. **B.** QQ plot of observed vs. the expected distribution of P-values. Each association study was subjected to genomic-control before meta-analysis. SNPs with MAF < 0.005 were filtered and SNPs with r2>0.1 were pruned for the plot. Lambda after meta-analysis = 1.357, which scales to $\lambda_{1000cases/1000controls}$ of 1.07.

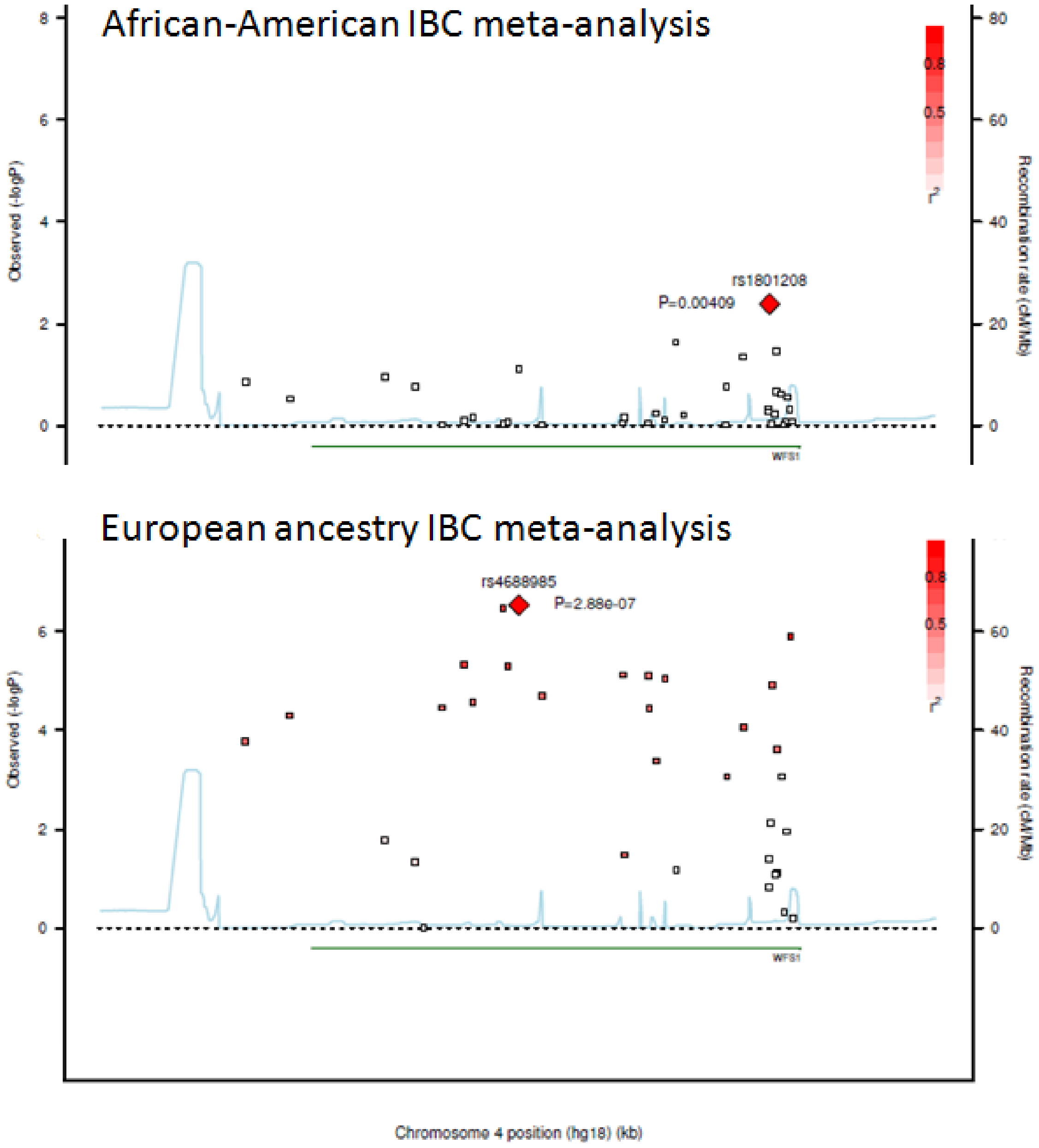
A.



African-American IBC meta-analysis

European ancestry IBC meta-analysis

B.


African-American IBC meta-analysis
rs1801208
P=0.00409
European ancestry IBC meta-analysis
rs4688985
P=2.88e-07
Observed (-logP)
Recombination rate (cM/Mb)
0.8
0.5
r2
WFS1
0
2
4
6
8
20
40
60
80
Chromosome 4 position (hg18) (kb)

C.

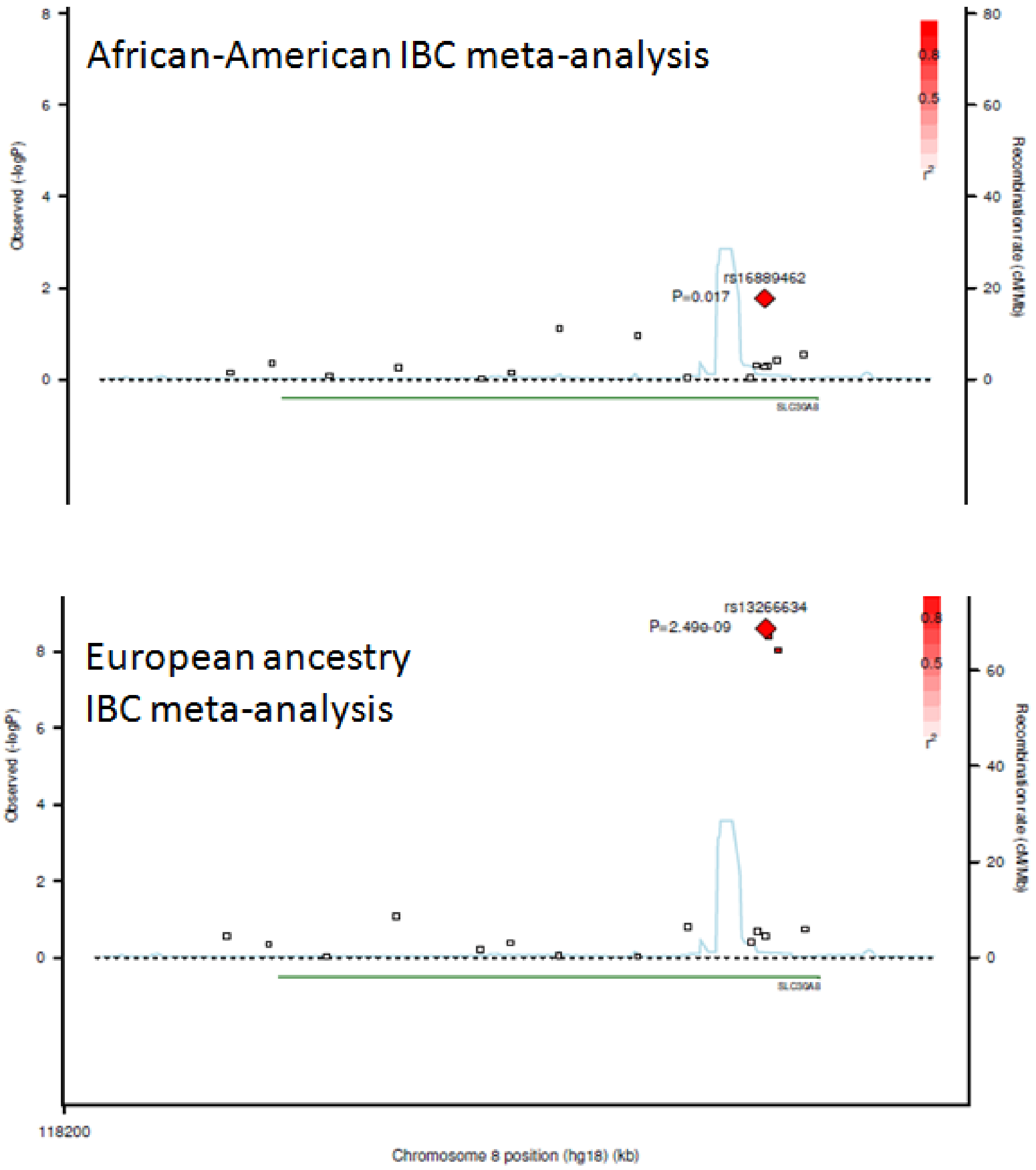


Figure S2. Regional plots of T2D association signals at missense SNPs observed in meta-analysis of African-American IBC studies that are not observed in European ancestry IBC meta-analysis. A. rs34150427 (V648I/ V521I) in *KCNQ1* ; **B.** rs1801208 (R456H) in *WFS1* and; **C.** rs16889462 (R324) in *SLC30A8* (adjacent to known SNP rs13266634).

Chr	**Gene Symbol**	**N SNPs (v1)**	**more SNPs (v2)**	**more SNPs (v3)**	**index SNP on IBC array for previously associated signal used for genetic risk score**
1	*HSD11B1*	12			
1	*IL6R*	42	1		
1	*LMNA*	7			
1	*PKLR(1q)*	5			
1	*PTGER3*	50			
1	*USF1*	27	1		
1	*NOTCH2*	1	11		rs10923931
1	*ADAM30*		7		
2	*GCKR*	13	1	6	rs780094
2	*IRS1*	31	2		rs2943634 (r^2=0.815 to rs7578326)
2	*LPIN1*	44	1		
2	*NEUROD1*	9			
2	*THADA*		27		rs7578597
2	*RBMS1*	1			rs6718526 (r^2=0.832 to rs7593730)
2	*ITGB6*	14			
3	*ADIPOQ*	21		1	
3	*PPARG*	100	2	3	rs1801282
3	*SLC2A2*	13			
3	*ADAMTS9*	1	5		rs4607103
3	*IGF2BP2*	2			rs1470579
4	*CPE*	65		12	
4	*WFS1*	36		1	rs1801214
6	*CDKAL1*	349	1	2	rs9368222
6	*ENPP1*	31	1		
6	*TNF*	17			
6	*VEGFA*	14	2		
7	*CDK5*	12			
7	*CDK6*	56	2		
7	*GCK*	28	1		
7	*JAZF1*		2		rs864745
7	*DGKB/TMEM195*	2			
8	*SLC30A8*	16			rs13266634
9	*CDKN2A/B*	128			rs10811661
9	*CDKN2B*	11	5		
10	*HHEX*	7			rs5015480
10	*IDE*	16			
10	*KIF11*	10			
10	*TCF7L2*	107	2		rs7903146
10	*CDC123/ CAMK1D*		2		
11	*ABCC8*	44		1	

11	*EXT2*	27	2		
11	*H19*	6	1		
11	*IGF2*	5			
11	*INS*	11			
11	*KCNJ11*	11			rs5219
11	*LOC387761*	179	6		
11	*TUB*	66			
11	*11p12 intergenic*	1			rs7107246 (r^2=0.917 to rs9300039)
11	*KCNQ1*	235	1	7	rs231362, rs163184
11	*CENTD2*	1			rs613937 (r^2=0.86 to rs1552224)
11	*MTNR1B*	8		9	rs10830963
12	*CDK4*	25			
12	*TCF1 (HNF1A)*	13	1	13	rs12427353 (r^2=0.882 to rs7957197)
12	*TSPAN8*		17		rs7961581
12	*LGR5*		22		
13	*PDX1*	10			
15	*ZFAND6*	1			rs2903265 (r^2=0.71 to rs11634397)
16	*FTO*	298	3		rs11642841
16	*HSD11B2*	4	1		
17	*CDK5R1*	12			
17	*HNF1B*	55			rs4430796
20	*CDK5RAP1*	18			
20	*HNF4A*	67		22	
20	*PCK1*	16	1		
22	*PPARA*	104		1	
X	*DUSP9*	9			

Table S1. List of Type 2 Diabetes candidate genes and 26 previously associated T2D variants on IBC Array.

Study	N Cases/ Controls (EA)	N Cases/ Controls (AA)	N Cases/ Controls (HN)	N Cases/ Controls (AN)	Age (mean, sd)	Gender (% male)	BMI (mean, sd)	Recruitment design	Year of collection	Age	Reference (PMID)
ARIC†	1278/2600	762/2256	---	---	62.3 (6.0)	46.0	28.2 (5.3)	Community-based	1985-2006	45-64	20400780
ASCOT	323/853	---	---	---	63.1(8.1)	81.8	29.1(6.7)	Clinical Trial	1998-2000	40-79	11403364
BWHHS	342/3101	---	---	---	68.9(5.5)	0.0	27.6 (4.9)	Population-based	1999-2001	60-79	16045529
CARDIA†	22/1366	84/1143	---	---	40.6 (3.5)	46.9	27.0 (1.8)	Community-based	1985-2003	18-30	20400780
CCCS	495/1091	---	---	---	64.0 (9.0)	70.7	30.6 (5.0)	Clinical Trial	2002-2003	45-92	16531616
CFS†	14/223	89/369	---	---	49.5 (14.3)	44.9	33.5 (9.0)	Community-based	1990-2008	20-90	20400780
CHS†	576/3375	180/569	---	---	72.77 (5.59)	44.0	26.38 (4.50)	Community-based	1988-2005	>65	20400780
CLEAR	317/1282	---	---	---	67.8, 9.6	85.4	28.0, 5.5	Case-control	2005	37-89	16474172
EPIC-NL	1033/1888	---	---	---	52.50 (11.00)	23.0	27.01 (4.59)	Nested case/control	1993-1997	20-70	19483199
FHS†	427/6272	---	---	---	49.57 (13.06)	45.2	27.52 (5.51)	Community-based	1948-present	20->80	20400780
INVEST	306/654	119/115	255/347	---	68.75 (9.45); 65.93 (10.32); 67.02 (10.13)	54.8; 37.1; 38.0	29.1 2(5.37); 30.98 (5.96); 28.92 (5.09)	Clinical trial	1997-2003	>50	14657064
JHS†	---	305/1689	---	---	50.4 (11.6)	39.4	32.2 (7.7)	Community-based	1999-2005	35-84	20400780
Look AHEAD cases; ARIC controls	2793/ 4124	---	---	---	59.6 (6.8); 61.9 (6.1)	49.6; 46.0	36.0 (5.9) 27.7 (5.2)	Clinical Trial	2001-2004	45-76; 45-64	17060218; 17363746
KORA	379/1224	---	---	---	52.6 (10.2)	56.9	27.6 (4.2)	Nested Case control	1984-2005	24-84	16032513 & 16032514
LURIC	868/1875	---	---	---	62.8 (10.6)	69.2	27.4 (4.1)	Population based	1997 to 2002	>18	19164808
MEDAL	465/4063	---	---	---	62.97 (14.00)	28.6	30.48 (6.30)	Clinical Trial	2002-2006	49-92	17113426
MERLIN	799/1131	---	---	---	63.57 (10.75)	66.3	29.00 (4.93)	Clinical Trial	2004-2006	>18	2029892
MESA†	239/2047	381/1227	297/874	109/529	67.13 (10.09)	47.8	27.86 (5.23)	Community-based	1999-2009	45-84	20400780

PennCAC	838/1274	---	---	---	55.61 (10.18)	65.3	32.60 (6.43)	Case-control	1998-2008	18-75	15289378
PennCATH	237/1092	---	---	---	60.01 (11.58)	67.2	29.14 (5.71)	Case-control	1998-2003	28-98	17258089
PHFS/CH Study	519/1617	---	---	---	56.64 (13.06)	68.8	29.28 (8.55)	Case-control	2002-2009 & 2003-2008	43-92	20124441
PROCARDIS	615/5835	---	---	---	61.0 (8.8)	59.1	27.7 (4.6)	Case Control	1998-2005	20-86	1808406
PROMIS	---	---	---	636/3022	53.3 (10.7)	82.5	25.2 (4.1)	Case-Control	2006-present	30-80	19404752
SMART	102/386	---	---	---	58.0 (12.0)	59.2	27.1 (4.0)	Patient recruitment	1996	18-80	10608355
UCP	479/643	---	---	---	64.17 (9.85)	73.5	27.6 (4.7)	Nested Case-Control	2000-2008	21-80	20712525
WHI	271/5259	66/327	40/189	22/153	67.9 (6.6)	0.0	28.4 (6.3)	Clinical trial and population-based observational study	1993-1998	50-79	9492970
WH-II	336/4214	---	---	---	60.9 (66.0)	73.6	26.7 (4.3)	Occupational	1985-1989	35-55	1674771
TOTAL	14,073/57,489	1,986/7,695	592/1,410	767/3,704							

Table S2. Characteristics of T2D case/control studies included in IBC Array meta-analyses. *Number of individuals >25years old with T2D and genotype information available for this study. EA denotes Europeans, AA denotes African Americans, HI denotes Hispanics and AN denotes Asians. Abbreviations: Atherosclerosis Risk In Communities (ARIC); British Heart Foundation Family Heart Study; British Women's Heart and Health Study (BWHHS); Coronary Artery Risk Development in Young Adults (CARDIA); Cleveland Clinic CHARISMA Study (CCCS); Cleveland Family Study (CFS); Cardiovascular Health Study (CHS); Carotid Lesion Epidemiology And Risk (CLEAR); European Prospective Investigation into Cancer and Nutrition in the Netherlands (EPIC-NL); Framingham Heart Study (FHS); INternational VErapamil SR Trandolapril Study (INVEST); Jackson Heart Study (JHS); Action for Health in Diabetes (Look AHEAD) Cooperative Health Research in the Region of Augsburg Study (KORA); Ludwigshafen Risk and Cardiovascular Health Study (LURIC); Multinational Etoricoxib and Diclofenac Arthritis Long-term (MEDAL) program; Metabolic Efficiency With Ranolazine for Less Ischemia in Non–ST-Elevation Acute Coronary Syndromes (MERLIN)-TIMI 36; Multi-Ethnic Study of Atherosclerosis (MESA); University of Pennsylvania Coronary Artery Calcification Study (PennCAC); University of Pennsylvania Catheterization study program (PennCATH); University of Pennsylvania Heart Failure Study (PHFS) and Cincinnati Heart Study (CH Study); Precocious Coronary Artery Disease (PROCARDIS); Pakistan Risk of Myocardial Infarction Study (PROMIS); Second Manifestations of ARTerial disease SMART) ; Utrecht Cardiovascular Pharmacogenetics (UCP); Women's Health Initiative (WHI); Whitehall II study (WH-II); †Members of the NHLBI Candidate gene Association Resource (CARe).

						European Ancestry IBC					**DIAGRAM GWAS meta-analysis**		
						(14,073 cases, 57,489 controls)					**(8,130 cases, 38,987 controls)**		
Chr	**NCBI 36 position**	**Candidate gene**	**SNP**	**Effect Allele**	**Effect Allele Freq IBC**	**Odds Ratio**	**95% CI**	***P***	**I^2 (%)**		**Odds Ratio**	**95% CI**	***P***
1	198298703	*NR5A2*	rs3006246	A	0.261	0.93	0.89 - 0.96	5.26E-05	0		1.01	0.96 - 1.07	6.40E-01
1	240116272	*EXO1*	rs4408133	C	0.361	1.08	1.04 - 1.11	7.40E-06	0		1.02	0.96 - 1.08	6.10E-01
2	21087477	*APOB*	rs533617	C	0.039	1.17	1.08 - 1.26	6.18E-05	20.9		1.03	0.81 - 1.31	8.17E-01
3	127308749	*ALDH1L1*	rs1127717	C	0.209	1.08	1.04 - 1.12	8.08E-05	0		0.99	0.94 - 1.04	6.48E-01
3	172217793	*SLC2A2*	rs11924032	A	0.261	0.93	0.89 - 0.96	1.87E-05	0		0.95	0.91 - 1.00	3.31E-02
4	157954125	*PDGFC*	rs6822892	G	0.341	0.94	0.91 - 0.97	9.03E-05	24.6		0.95	0.90 - 0.99	2.56E-02
5	174809033	*DRD1*	rs6882300	T	0.017	1.27	1.13 - 1.43	6.63E-05	0		1.10	0.93 - 1.25	2.39E-01
6	32734250	*HLA-DQB1*	rs9273363	A	0.27	1.1	1.06 - 1.14	7.99E-08	16.8		1.06	1.01 - 1.10	1.64E-02
7	30678486	*CRHR2*	rs2284216	T	0.092	0.87	0.83 - 0.93	5.91E-06	0		0.98	0.91 - 1.06	6.28E-01
8	145607956	*SLC39A4*	rs4925820	G	0.456	1.06	1.03 - 1.10	8.88E-05	0		NA	NA	NA
10	75339196	*C10orf55*	rs2227551	G	0.262	0.93	0.90 - 0.97	8.13E-05	0		0.97	0.92 - 1.01	1.30E-01
11	2150416	*TH*	rs10770141	A	0.387	1.07	1.04 - 1.11	6.44E-06	0		1.05	1.00 - 1.10	7.08E-02
11	13364347	*ARNTL*	rs2290035	T	0.462	0.93	0.91 - 0.96	1.46E-05	14.9		1.03	0.99 - 1.07	1.66E-01
11	41535933	*NA*	rs7946270	T	0.459	0.93	0.90 - 0.96	4.98E-05	20.9		1.03	0.98 - 1.07	2.10E-01
11	49127350	*FOLH1*	rs16906158	C	0.09	1.13	1.07 - 1.19	8.75E-06	31.8		1.07	1.00 - 1.14	5.17E-02
12	12766184	*CDKN1B*	rs7330	C	0.396	1.07	1.04 - 1.11	8.40E-06	0		NA	NA	NA
17	17662182	*SREBF1*	rs4925115	A	0.375	1.09	1.05 - 1.20	2.04E-07	0		1.04	0.99 - 1.08	1.01E-01
18	58996864	*BCL2*	rs12454712	C	0.374	0.93	0.90 - 0.96	2.29E-06	20.6		NA	NA	NA
19	19471596	*GATAD2A*	rs3794991	T	0.083	1.14	1.08 - 1.20	8.95E-07	25		1.11	1.04 - 1.17	1.55E-03
19	50864118	*GIPR*	rs11671664	A	0.107	1.12	1.07 - 1.18	2.86E-06	0		1.06	0.98 - 1.14	1.71E-01
20	6707115	*BMP2*	rs235768	A	0.38	0.93	0.91 - 0.97	3.45E-05	0		0.99	0.94 - 1.03	4.81E-01
20	25141849	*ENTPD6*	rs6115089	A	0.052	1.15	1.07 - 1.23	9.04E-05	33.1		0.97	0.86 - 1.09	6.09E-01
20	42451674	*HNF4A*	rs4812831	A	0.104	1.11	1.06 - 1.16	2.12E-05	0		1.08	1.01 - 1.17	3.36E-02
20	51053708	*TSHZ2*	rs2252098	T	0.461	0.94	0.91 - 0.97	3.86E-05	0		1.01	0.97 - 1.05	6.28E-01
21	42548763	*ABCG1*	rs225378	A	0.459	0.93	0.91 - 0.96	8.78E-06	27		0.97	0.92 - 1.02	2.50E-01

Table S3. European Ancestry Index SNPs for top association signals in IBC and replication results in DIAGRAM Meta-analysis of T2D GWAS.

rs9273363 **(*HLA-DQB1*)**

Studies	Allele A freq	OR (95% CI)	*P*-value	Direction	$P_{\text{heterogeneity}}$
LADA excluded (DCDG, DGI, FUSION, WTCCC)	0.2768	1.02 (0.96 - 1.09)	0.49	+++-	0.3097
LADA not excluded (deCODE, EUROSPAN, ERGO, KORA)	0.2662	1.09 (1.02 - 1.16)	0.0074	++++	0.8537
ALL DIAGRAM studies	0.2714	1.06 (1.01 - 1.11)	0.016	+++-++++	0.5083

rs10770141 **(*TH/INS* region)**

Studies	Allele A freq	OR (95% CI)	*P*-value	Direction	$P_{\text{heterogeneity}}$
LADA excluded (DCDG, DGI, FUSION, WTCCC)	0.3417	1.16 (1.05 - 1.28)	0.003631	+?+?	0.1219
LADA not excluded (deCODE, EUROSPAN, ERGO, KORA)	0.3936	1.01 (0.95 - 1.07)	0.7241	+-?+	0.6424
ALL DIAGRAM studies	0.3797	1.05 (1.00 - 1.10)	0.07082	+?+?+-?+	0.07196

Table S4. Meta analysis of most significant HLA-DQB1 and TH/INS region SNPs in DIAGRAM subsamples including and excluding LADA.

Gene	**Allele**	**Chr**	**Position**	**Effect Allele**	**Freq IBC**	**OR (95% CI)**	***P***
HLA-DQA1	HLA_DQA1*03	6	32716285	G	0.18	1.14 (1.08 - 1.20)	2.80E-07
HLA-DQA1	HLA_DQA1*0301	6	32716285	G	0.18	1.14 (1.08 - 1.20)	2.80E-07
HLA-DQA1	CHR6_POS32717108	6	32717109	T	0.18	1.14 (1.08 - 1.20)	2.80E-07
HLA-DQA1	CHR6_POS32717120	6	32717121	G	0.18	1.14 (1.08 - 1.20)	2.80E-07
HLA-DQA1	CHR6_POS32717128	6	32717129	G	0.18	1.14 (1.08 - 1.20)	2.80E-07
HLA-DQA1	DQA1_AA49_E2_32717128	6	32717129	S	0.18	1.14 (1.08 - 1.20)	2.80E-07
HLA-DQA1	DQA1_AA70_E2_32717191_Q	6	32717192	G	0.18	1.14 (1.08 - 1.20)	2.80E-07
HLA-DQA1	CHR6_POS32717277_G	6	32717278	G	0.18	1.14 (1.08 - 1.20)	2.80E-07
HLA-DQA1	DQA1_AA99_E2_32717278_V	6	32717279	G	0.18	1.14 (1.08 - 1.20)	2.80E-07
HLA-DQA1	CHR6_POS32718379	6	32718380	A	0.18	1.14 (1.08 - 1.20)	2.80E-07
HLA-DQA1	DQA1_AA210_E4_32718380	6	32718381	T	0.18	1.14 (1.08 - 1.20)	2.80E-07
HLA-DRB1	HLA_DRB1*04	6	32660043	G	0.168	1.14 (1.08 - 1.20)	3.57E-07
HLA-DRB1	CHR6_POS32665482	6	32665483	A	0.168	1.14 (1.08 - 1.20)	3.93E-07
HLA-DRB1	DRB1_AA63_E2_32660049	6	32660050	H	0.168	1.14 (1.08 - 1.20)	4.01E-07
HLA-DRB1	CHR6_POS32660050	6	32660051	G	0.168	1.14 (1.08 - 1.20)	4.01E-07
HLA-DRB1	DRB1_AA7_E1_32665481	6	32665482	F	0.168	1.14 (1.08 - 1.20)	4.09E-07
HLA-DRB1	DRB1_AA43_E2_32660109_H	6	32660110	G	0.168	1.14 (1.08 - 1.20)	4.31E-07
HLA-DRB1	CHR6_POS32660110_G	6	32660111	G	0.168	1.14 (1.08 - 1.20)	4.31E-07
HLA-DRB1	CHR6_POS32660111	6	32660112	T	0.168	1.14 (1.08 - 1.20)	4.31E-07
HLA-DRB1	CHR6_POS32657591_A	6	32657592	G	0.168	1.14 (1.08 - 1.20)	4.77E-07
HLA-DRB1	DRB1_AA126_E3_32657590_Y	6	32657591	G	0.168	1.14 (1.08 - 1.20)	4.83E-07
HLA-DRB1	DRB1_AA210_E3_32657338	6	32657339	L	0.168	1.14 (1.08 - 1.20)	5.06E-07
HLA-DRB1	CHR6_POS32657339	6	32657340	G	0.168	1.14 (1.08 - 1.20)	5.06E-07
HLA-DRB1	HLA_DRB1*0401	6	32660043	G	0.102	1.17 (1.10 - 1.24)	5.70E-07
HLA-DRB1	DRB1_AA126_E3_32657590_YE	6	32657591	G	0.281	1.11 (1.07 - 1.16)	9.71E-07
HLA-DRB1	DRB1_AA126_E3_32657590_HQ	6	32657591	A	0.281	1.11 (1.07 - 1.16)	9.71E-07
HLA-DRB1	CHR6_POS32657591_G	6	32657592	A	0.281	1.11 (1.07 - 1.16)	9.71E-07
HLA-DRB1	CHR6_POS32656559	6	32656560	G	0.281	1.11 (1.07 - 1.16)	1.02E-06
HLA-DRB1	DRB1_AA41_E2_32660115_VD	6	32660116	G	0.189	1.13 (1.07 -1.18)	1.62E-06
HLA-DRB1	DRB1_AA101_E2_32659935_K	6	32659936	G	0.239	1.12 (1.07 - 1.17)	1.65E-06
HLA-DRB1	DRB1_AA43_E2_32660109_HF	6	32660110	G	0.302	1.11 (1.06 - 1.16)	1.66E-06
HLA-DRB1	CHR6_POS32660115_AT	6	32660116	G	0.302	1.11 (1.06 - 1.16)	1.66E-06
HLA-DRB1	CHR6_POS32660115_CG	6	32660116	A	0.302	1.11 (1.06 - 1.16)	1.66E-06
HLA-DRB1	DRB1_AA41_E2_32660115_VLD	6	32660116	G	0.302	1.11 (1.06 - 1.16)	1.66E-06
HLA-DRB1	DRB1_AA41_E2_32660115_GSP	6	32660116	A	0.302	1.11 (1.06 - 1.15)	1.66E-06
C6orf10	rs2395153	6	32453574	G	0.391	1.10 (1.06 - 1.15)	1.69E-06
BTNL2	rs4424066	6	32462407	G	0.419	1.10 (1.06 - 1.14)	3.09E-06
BTNL2	rs2076529	6	32471934	C	0.419	1.10 (1.06 - 1.14)	3.19E-06
HLA-DRB5	rs5020946	6	32558068	G	0.418	1.10 (1.06 - 1.14)	3.22E-06
BTNL2	rs2076530	6	32471795	C	0.428	1.10 (1.05 - 1.14)	3.28E-06
BTNL2	rs3817973	6	32469090	T	0.419	1.10 (1.06 - 1.14)	3.32E-06
HLA-DRB1	DRB1_AA41_E2_32660115_V	6	32660116	G	0.177	1.12 (1.07 - 1.18)	5.00E-06
HLA-DRB1	CHR6_POS32660115_A	6	32660116	G	0.29	1.10 (1.06 - 1.15)	5.28E-06
HLA-DRB1	DRB1_AA41_E2_32660115_VL	6	32660116	G	0.29	1.10 (1.06 - 1.15)	5.28E-06

Gene	**Allele**	**Chr**	**Position**	**Effect Allele**	**Freq IBC**	**OR (95% CI)**	***P***
HLA-DRB1	CHR6_POS32657518	6	32657519	T	0.177	1.12 (1.07 -1.18)	5.46E-06
HLA-DRB1	DRB1_AA150_E3_32657518	6	32657519	N	0.177	1.12 (1.07 -1.18)	5.46E-06
HLA-DRB1	rs2516049	6	32678379	C	0.304	1.10 (1.05 - 1.15)	8.98E-06
HLA-DRB1	DRB1_AA134_E3_32657566	6	32657567	A	0.305	1.10 (1.05 - 1.15)	1.02E-05

Table S5. Imputation of HLA-alleles in 10,636 cases and 38,063 controls from European ancestry IBC studies and association with T2D.

						Original Results			**Conditional Results**		
						(14,073 cases, 57,489 controls)			**(10,636 cases & 38,063 controls)**		
Gene	**SNP**	**Chr**	**Position**	**Effect Allele**	**Effect Allele Freq IBC**	**OR (95% CI)**	***P***		**OR (95% CI)**	***P***	**r^2 with lead SNP**
SLC39A4	rs4925820	8	145,607,956	G	0.456	1.06 (103 - 1.10)	8.88E-05				
	rs4977219	8	145,487,506	C	0.509	1.00 (0.97 - 1.03)	7.58E-01		1.08 (1.04 - 1.11)	2.53E-05	0.001
NA/LRRC4C	rs7946270	11	41,535,933	T	0.459	0.93 (0.90 - 0.96)	4.98E-05				
	rs7944293	11	41,547,494	C	0.001	1.68 (1.01 - 2.82)	4.78E-02		1.94 (1.81 - 1.98)	3.06E-06	
ENTPD6	rs6115089	20	25,141,849	A	0.052	1.15 (1.07 - 1.23)	9.04E-05				
	rs2073077	20	25,143,913	C	0.151	0.95 (0.91 - 0.99)	2.07E-02		0.90 (0.84 - 0.96)	3.75E-04	0.002
PDGFC	rs6822892	4	157,954,125		0.341	0.94 (0.91 - 0.97)	9.03E-05				
	rs7682653	4	157,914,308	A	0.001	4.32 (1.26 - 14.78)	1.72E-01		16.24 (3.62 - 72.94)	2.76E-04	
GIPR	rs11671664	19	50,864,118	A	0.107	1.12 (1.07 - 1.18)	2.86E-06				
	rs8109951	19	50,981,343	T	0.365	1.03 (1.00 - 1.07)	4.70E-02		1.07 (1.03 - 1.11)	5.09E-04	0.028
HNF1A/P2RX7	rs1800574	12	119,901,247	T	0.029	1.28 (1.17 - 1.40)	1.43E-07				
	rs208297	12	120,086,410	T	0.001	5.63 (1.62 - 19.59)	6.62E-03		27.11 (4.71 - 156.05)	2.20E-04	NA
CENTD2	rs613937	11	72,152,487	G	0.172	0.92 (0.88 - 0.95)	2.23E-05				
	rs615703	11	72,152,880	A	0.001	1.77 (1.03 - 3.02)	3.78E-02		3.44 (1.63 - 7.28)	1.21E-03	0.051

Table S6. Loci with P<1.0E-04 in IBC meta-analysis and significant locus-specific evidence of independent T2D association signals.

				Caucasian IBC (14,073 cases, 57,489 controls)		**African American IBC (1,986 cases & 7,695 controls)**		**Hispanic IBC (592 cases & 1,410 controls)**		**Asian IBC (767 cases & 3,704 controls)**		**Multi-ethnic IBC (17,418 cases & 70,298 controls)**		
Chr	**Candidate gene**	**Lead SNP on array**	**Effect Allele**	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**I^2**
10	*TCF7L2*	rs7903146	T	1.44 (1.40 - 1.49)	1.21E-109	1.37 (1.27 - 1.49)	5.06E-15	1.16 (0.98-1.36)	7.81E-02	1.31 (1.16 - 1.48)	1.10E-05	1.41 (1.37 - 1.45)	5.28E-125	41.3
6	*CDKAL1*	rs9368222	A	1.18 (1.14 - 1.22)	5.37E-21	1.03 (0.94 - 1.13)	5.43E-01	1.14 (0.96-1.35)	1.34E-01	1.18 (1.00 - 1.39)	4.38E-02	1.14 (1.11 - 1.18)	2.49E-17	24.9
9	*CDKN2A/B*	rs10811661	C	0.84 (0.81 - 0.88)	4.83E-16	0.92 (0.80 - 1.09)	3.10E-01	0.87 (0.70-1.07)	1.89E-01	0.85 (0.73 - 1.00)	5.25E-02	0.86 (0.82 - 0.89)	2.80E-15	16
3	*IGF2BP2*	rs1470579	C	1.14 (1.10 - 1.18)	9.19E-16	1.06 (0.98 - 1.16)	1.64E-01	1.06 (0.91-1.24)	4.62E-01	1.10 (0.98 - 1.23)	9.77E-02	1.12 (1.09 - 1.15)	4.55E-15	14.1
7	*JAZF1*	rs864745	C	0.90 (0.88 - 0.93)	2.22E-09	0.88 (0.81 - 0.97)	3.05E-03	0.97 (0.83-1.12)	6.54E-01	0.83 (0.66 - 1.04)	1.05E-01	0.90 (0.88 - 0.93)	1.42E-11	21.5
10	*HHEX/IDE*	rs5015480	T	0.89 (0.86 - 0.91)	2.68E-14	0.97 (0.90 - 1.04)	3.54E-01	0.98 (0.85-1.13)	7.83E-01	1.00 (0.89 - 1.12)	9.69E-01	0.91 (0.89 - 0.94)	4.47E-11	28.3
8	*SLC30A8*	rs13266634	T	0.90 (0.87 - 0.93)	2.49E-09	0.96 (0.84 - 1.10)	5.32E-01	0.87 (0.73-1.03)	1.05E-01	0.86 (0.75 - 0.98)	2.42E-02	0.90 (0.88 - 0.93)	2.71E-10	19.5
11	*KCNJ11*	rs5215	C	1.09 (1.06 - 1.13)	1.65E-08	1.10 (0.97 - 1.25)	1.25E-01	1.10 (0.94-1.28)	2.39E-01	1.16 (1.03 - 1.31)	1.21E-02	1.09 (1.06 - 1.13)	1.03E-09	0.4
18	***BCL2***	**rs12454712**	**C**	**0.93 (0.90 - 0.96)**	**2.29E-06**	**0.96 (0.88 - 1.05)**	**3.39E-01**	**0.91 (0.78-1.06)**	**2.32E-01**	**0.88 (0.79 - 0.99)**	**3.23E-02**	**0.92 (0.90 - 0.95)**	**2.14E-08**	**0**
12	*HNF1A*	rs1800574	T	1.28 (1.17 - 1.40)	1.43E-07	1.15 (0.72 - 1.86)	5.57E-01	1.58 (0.84-2.98)	1.57E-01	1.16 (0.91 - 1.48)	2.34E-01	1.27 (1.16 - 1.38)	3.57E-08	0
17	*HNF1B*	rs4430796	G	1.08 (1.05 - 1.12)	2.48E-07	1.02 (0.94 - 1.15)	6.06E-01	1.04 (0.90-1.21)	5.66E-01	1.11 (0.99 - 1.25)	6.84E-02	1.07 (1.04 - 1.10)	9.71E-07	14.2
17	***SREBF1***	**rs4925115**	**A**	**1.09 (1.05 - 1.20)**	**2.04E-07**	**1.05 (0.97 - 1.14)**	**2.17E-01**	**0.97 (0.84-1.12)**	**6.95E-01**	**1.06 (0.94 - 1.20)**	**3.00E-01**	**1.07 (1.04 - 1.10)**	**1.08E-06**	**0**
2	*GCKR*	rs780094	T	0.92 (0.89 - 0.95)	2.12E-07	0.98 (0.89 - 1.11)	6.92E-01	1.01 (0.87-1.17)	9.19E-01	0.98 (0.87 - 1.12)	8.02E-01	0.93 (0.91 - 0.96)	1.24E-06	33.5
11	*IRS1 region*	rs2943634	A	0.92 (0.89 - 0.95)	4.32E-07	0.96 (0.89 - 1.04)	3.25E-01	0.89 (0.75-1.05)	1.81E-01	1.01 (0.89 - 1.15)	8.86E-01	0.93 (0.91 - 0.96)	1.25E-06	20.5
11	*KCNQ1*	rs163184	G	1.08 (1.05 - 1.11)	6.08E-07	0.97 (0.89 - 1.08)	5.87E-01	1.08 (0.94-1.25)	2.71E-01	1.03 (0.92 - 1.16)	5.83E-01	1.07 (1.04 - 1.10)	3.53E-06	1.3
3	*PPARG*	rs7649970	T	0.9 (0.86 - 0.94)	7.87E-06	1.04 (0.94 - 1.14)	4.72E-01	0.78 (0.61-0.98)	3.47E-02	0.83 (0.70 - 0.99)	3.82E-02	0.91 (0.87 - 0.95)	4.54E-06	0

				Caucasian IBC (14,073 cases, 57,489 controls)		African American IBC (1,986 cases & 7,695 controls)		Hispanic IBC (592 cases & 1,410 controls)		Asian IBC (767 cases & 3,704 controls)		Multi-ethnic IBC (17,418 cases & 70,298 controls)		
Chr	**Candidate gene**	**Lead SNP on array**	**Effect Allele**	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	I^2
11	***TH/INS***	**rs10770141**	**A**	**1.07 (1.04 - 1.11)**	**6.44E-06**	**1.04 (0.96 - 1.11)**	**3.55E-01**	**1.12 (0.97-1.30)**	**1.32E-01**	**1.07 (0.94 - 1.22)**	**3.03E-01**	**1.07 (1.04 - 1.09)**	**4.96E-06**	**8.3**
2	*THADA*	rs7578597	C	0.86 (0.82 - 0.91)	2.91E-07	0.98 (0.90 - 1.07)	5.80E-01	0.83 (0.64-1.07)	1.44E-01	1.16 (0.88 - 1.54)	2.98E-01	0.90 (0.86 - 0.95)	9.67E-06	40.2
19	***GIPR***	**rs11671664**	**A**	**1.12 (1.07 - 1.18)**	**2.86E-06**	**1.00 (0.89 - 1.12)**	**9.62E-01**	**1.21 (0.95-1.53)**	**1.26E-01**	**1.02 (0.87 - 1.21)**	**7.74E-01**	**1.10 (1.05 - 1.14)**	**1.13E-05**	**0**
19	***GATAD2A***	**rs3794991**	**T**	**1.14 (1.08 - 1.20)**	**8.95E-07**	**0.99 (0.85 - 1.14)**	**8.63E-01**	**1.27 (0.95-1.69)**	**1.06E-01**	**0.99 (0.82 - 1.20)**	**9.36E-01**	**1.11 (1.06 - 1.16)**	**1.68E-05**	**13.4**
11	*CENTD2*	rs613937	G	0.92 (0.88 - 0.95)	2.23E-05	0.97 (0.89 - 1.04)	3.67E-01	0.86 (0.70-1.07)	1.81E-01	0.91 (0.79 - 1.04)	1.67E-01	0.93 (0.90 - 0.96)	2.04E-05	9.5
11	***FOLH1***	**rs16906158**	**C**	**1.13 (1.07 - 1.19)**	**8.75E-06**	**0.99 (0.90 - 1.07)**	**7.31E-01**	**1.10 (0.89-1.35)**	**3.87E-01**	**1.12 (0.98 - 1.28)**	**9.16E-02**	**1.09 (1.05 - 1.14)**	**3.11E-05**	**26.8**
3	***SLC2A2***	**rs11924032**	**A**	**0.93 (0.89 - 0.96)**	**1.87E-05**	**1.01 (0.93 - 1.09)**	**8.55E-01**	**0.88 (0.75-1.03)**	**1.22E-01**	**0.98 (0.87 - 1.11)**	**7.77E-01**	**0.94 (0.91 - 0.97)**	**4.72E-05**	**0**
3	*PPARG*	rs1797912	A	1.06 (1.03 - 1.09)	5.48E-05	0.81 (0.65 - 1.01)	6.12E-02	1.15 (0.97-1.36)	1.04E-01	0.98 (0.85 - 1.14)	6.45E-01	1.06 (1.03 - 1.09)	7.08E-05	8.8
4	*WFS1*	rs4688985	A	0.91 (0.88 - 0.95)	2.88E-07	1.12 (0.99 - 1.26)	7.82E-02	0.95 (0.79-1.15)	6.03E-01	0.84 (0.71 - 1.00)	5.25E-02	0.94 (0.91 - 0.97)	1.31E-04	44.7
11	*KCNQ1*	rs231362	A	0.93 (0.90 - 0.96)	5.90E-06	0.96 (0.88 - 1.05)	3.53E-01	1.09 (0.93-1.26)	2.90E-01	0.98 (0.85 - 1.11)	7.11E-01	0.95 (0.92 - 0.97)	1.57E-04	18.7
12	***HMGA2***	**rs9668162**	**G**	**0.97 (0.90 - 1.06)**	**5.17E-01**	**1.26 (1.15 - 1.37)**	**2.41E-07**	**1.21 (0.97-1.51)**	**9.14E-02**	**1.04 (0.91 - 1.19)**	**5.40E-01**	**1.10 (1.05 - 1.16)**	**2.10E-04**	**16.9**
7	*GCK*	rs1990458	T	0.93 (0.90 - 0.96)	1.67E-06	0.96 (0.88 - 1.05)	4.21E-01	1.13 (0.97-1.31)	1.18E-01	1.07 (0.96 - 1.20)	2.36E-01	0.95 (0.92 - 0.98)	2.63E-04	0
2	*THADA*	rs10200833	C	0.94 (0.91 - 0.98)	2.63E-03	0.97 (0.89 - 1.06)	5.53E-01	0.93 (0.74-1.17)	5.61E-01	0.87 (0.69 - 1.10)	2.33E-01	0.95 (0.92 - 0.98)	1.42E-03	16.1
3	*ADAMTS9*	rs9860730	G	0.95 (0.92 - 0.98)	1.24E-03	0.97 (0.89 - 1.07)	5.67E-01	0.89 (0.77-1.03)	1.30E-01	1.00 (0.89 - 1.13)	9.38E-01	0.95 (0.93 - 0.98)	1.77E-03	0
1	*NOTCH2*	rs2641348	G	1.06 (1.01 -1.12)	1.95E-02	1.04 (0.96 - 1.12)	3.21E-01	1.04 (0.83-1.29)	7.44E-01	1.19 (0.92 - 1.54)	1.76E-01	1.06 (1.02 - 1.11)	6.18E-03	0
9	*CDKN2A/B*	rs10757282	C	1.04 (1.01 - 1.08)	2.23E-02	1.06 (0.97 - 1.15)	1.83E-01	1.02 (0.88-1.19)	7.91E-01	1.03 (0.84 - 1.27)	7.81E-01	1.04 (1.01 - 1.07)	6.71E-03	8.5
11	*MTNR1B*	rs10830963	G	1.05 (1.01 - 1.08)	8.07E-03	1.06 (0.92 - 1.22)	4.11E-01	1.12 (0.94-1.32)	2.13E-01	0.95 (0.84 - 1.06)	3.49E-01	1.04 (1.01 - 1.07)	9.88E-03	8.1

				Caucasian IBC (14,073 cases, 57,489 controls)		**African American IBC (1,986 cases & 7,695 controls)**		**Hispanic IBC (592 cases & 1,410 controls)**		**Asian IBC (767 cases & 3,704 controls)**		**Multi-ethnic IBC (17,418 cases & 70,298 controls)**		
Chr	**Candidate gene**	**Lead SNP on array**	**Effect Allele**	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**I^2**
7	*JAZF1*	rs12113122	G	1.55 (1.11 - 2.15)	5.13E-02	1.09 (0.98 - 1.22)	1.08E-01	1.25 (0.79-2.00)	3.41E-01	1.11 (0.75 - 1.64)	0.60	1.14 (1.03 - 1.25)	1.11E-02	0
12	*TSPAN8/LGR5*	rs7961581	C	1.06 (1.01 - 1.10)	1.57E-02	0.98 (0.90 - 1.08)	7.32E-01	0.97 (0.81-1.17)	7.61E-01	0.99 (0.78 - 1.25)	9.07E-01	1.04 (1.00 - 1.08)	3.05E-02	0
10	*CDC123/CAMK1D*	rs12779790	G	1.07 (0.99 - 1.15)	7.28E-02	1.02 (0.73 - 1.44)	9.00E-01	0.83 (0.41-1.68)	6.04E-01	1.02 (0.73 - 1.44)	9.00E-01	1.06 (0.99 - 1.14)	8.67E-02	0
11	*CENTD2*	rs615703	A	1.77 (1.03 - 3.02)	3.78E-02	0.94 (0.86 - 1.02)	1.52E-01	0.97 (0.66-1.41)	8.66E-01	0.92 (0.68 - 1.25)	6.06E-01	0.95 (0.87 - 1.03)	2.02E-01	0
15	*ZFAND6*	rs2903265	A	0.99 (0.95 - 1.02)	4.62E-01	1.01 (0.94 - 1.09)	6.96E-01	0.92 (0.78-1.09)	3.46E-01	0.93 (0.83 - 1.04)	2.10E-01	0.99 (0.96 - 1.02)	3.68E-01	0
7	*DGKB-TMEM195*	rs10244051	T	0.96 (0.88 - 1.05)	4.02E-01	1.00 (0.78 - 1.28)	9.86E-01	0.78 (0.46-1.31)	3.49E-01	1.00 (0.78 - 1.28)	9.86E-01	0.98 (0.90 - 1.06)	5.41E-01	12.1
12	*HNF1A*	rs208297	T	5.63 (1.62 - 19.6)	6.62E-03	0.96 (0.80 - 1.15)	6.36E-01	1.34 (0.56-3.19)	5.13E-01	0.88 (0.34 - 2.27)	0.78	1.00 (0.84 - 1.19)	9.72E-01	28

Table S7. Association results for T2D loci in European, African American, Hispanic and Asian populations. T2D risk variants with study-wide or borderline significance implicated by this study are highlighted in bold.

Study	**Effect/ other allele**	**Effect allele frequency**	**OR (95% CI)**	***P***	***n=T2D cases/ controls***
Look AHEAD (cases) /ARIC (controls)	T/C	0.31	1.59 (1.45 - 1.75)	4.86E-22	2793/4124
CCCS	T/C	0.29	1.75 (1.48 - 2.07)	9.36E-11	495/1091
ARIC	T/C	0.30	1.35 (1.23 - 1.48)	1.66E-10	1278/2600
EPIC-NL	T/C	0.31	1.50 (1.31 - 1.73)	5.62E-09	1033/1888
LURIC	T/C	0.30	1.47 (1.29 - 1.68)	7.19E-09	868/1875
CHS	T/C	0.30	1.46 (1.27 - 1.67)	4.67E-08	576/3375
Procardis	T/C	0.30	1.47 (1.28 - 1.69)	5.12E-08	615/5835
WHI	T/C	0.29	1.75 (1.43 - 2.13)	5.49E-08	271/5259
PennCAC	T/C	0.32	1.54 (1.31 - 1.82)	1.53E-07	838/1274
MERLIN	T/C	0.30	1.47 (1.27 - 1.70)	2.07E-07	799/1131
FHS	T/C	0.29	1.44 (1.24 - 1.67)	1.48E-06	427/6272
UCP	T/C	0.32	1.57 (1.30 - 1.89)	2.99E-06	479/643
ASCOT	T/C	0.29	1.59 (1.29 - 1.96)	1.22E-05	235/2426
BWHHS	T/C	0.28	1.41 (1.19 - 1.67)	8.08E-05	1508/1902
MEDAL	T/C	0.29	1.36 (1.16 - 1.59)	0.00014	465/4063
CLEAR	T/C	0.30	1.43 (1.18 - 1.73)	0.00025	317/1282
PennCATH	T/C	0.32	1.40 (1.13 - 1.73)	0.0022	237/1092
MESA	T/C	0.30	1.37 (1.11 - 1.69)	0.0030	239/2047
PHFS/CH Study	T/C	0.30	1.25 (1.06 - 1.47)	0.0072	519/1617
INVEST	T/C	0.30	1.25 (1.01 - 1.54)	0.040	306/654
WH-II	T/C	0.29	1.20 (1.00 - 1.43)	0.046	336/4214
SMART	T/C	0.30	1.47 (1.00 - 2.17)	0.052	102/386
CFS	T/C	0.26	1.59 (0.93 - 2.72)	0.089	14/223
KORA	T/C	0.29	1.11 (0.92 - 1.36)	0.28	379/1224
CARDIA	T/C	0.30	1.05 (0.58 - 1.88)	0.88	22/1366

Table S8. Association results for TCF7L2 rs7903146 in 25 studies included in the European ancestry IBC meta-analysis.

Chr	NCBI 36 position	Candidate gene	SNP	Effect Allele	Effect Allele Freq IBC	OR (95% CI)	*P*	I^2 (%)
1	114105331	*RSBN1*	rs6679677	A	0.095	1.06 (1.00-1.11)	0.04	14.4
1	114179091	*PTPN22*	rs2476601	A	0.096	1.05 (1.00-1.11)	0.04	17
1	205006527	*IL10*	rs3024505	A	0.16	0.97 (0.86-1.10)	0.67	1.2
2	162832297	*IFIH1*	rs1990760	C	0.396	1.00 (0.97-1.03)	0.81	2.1
2	204447164	*CTLA4*	rs3087243	A	0.448	1.01 (0.98-1.04)	0.51	0
4	123548812	*ADAD1*	rs17388568	A	0.275	1.01 (0.97-1.04)	0.73	12.8
5	35910332	*IL7R*	rs6897932	T	0.265	0.98 (0.94-1.02)	0.3	0
5	132656783	*FSTL4*	rs17166496	G	0.412	0.99 (0.96-1.02)	0.35	0
10	6512897	*PRKCQ*	rs11258747	T	0.221	0.98 (0.95-1.02)	0.29	2.6
11	2126350	*IGF2AS*	rs3741208	A	0.359	0.97 (0.94-1.01)	0.1	16
11	2126719	*INS-IGF2*	rs1004446	A	0.373	1.01 (0.98-1.04)	0.59	34.7
12	9724895	*CLEC2D*	rs3764021	T	0.469	1.00 (0.97-1.03)	0.91	37.3
12	54756892	*ERBB3*	rs11171739	C	0.417	0.98 (0.95-1.02)	0.3	22.4
12	110368991	*SH2B3*	rs3184504	T	0.497	1.04 (1.00-1.07)	0.03	32.5
12	110971201	*C12orf30*	rs17696736	G	0.451	1.02 (0.99-1.05)	0.17	29.1
16	11087374	*CLEC16A*	rs12708716	G	0.365	1.01 (0.97-1.04)	0.72	0
18	12769947	*PTPN2*	rs2542151	G	0.159	0.98 (0.94-1.03)	0.44	0
18	65682622	*CD226*	rs763361	T	0.478	1.02 (0.99-1.06)	0.2	15.1

Table S9. Association results for known T1D associated SNPs in the European Ancestry IBC T2D meta-analysis.