Identification of ten variants associated with risk of estrogen receptor negative breast cancer

Roger L. Milne[‡,1,2,*], Karoline B. Kuchenbaecker[‡,3,4], Kyriaki Michailidou[‡,3,5], Jonathan Beesley[6], Siddhartha Kar[7], Sara Lindström[8,9], Shirley Hui[10], Audrey Lemaçon[11], Penny Soucy[11], Joe Dennis[3], Xia Jiang[9], Asha Rostamianfar[10], Hilary Finucane[9,12], Manjeet K. Bolla[3], Lesley McGuffog[3], Qin Wang[3], Cora M. Aalfs[13], ABCTB Investigators[14], Marcia Adams[15], Julian Adlard[16], Simona Agata[17], Shahana Ahmed[7], Kristiina Aittomäki[18], Fares Al-Ejeh[19], Jamie Allen[3], Christine B. Ambrosone[20], Christopher I. Amos[21], Irene L. Andrulis[22,23], Hoda Anton-Culver[24], Natalia N. Antonenkova[25], Volker Arndt[26], Norbert Arnold[27], Kristan J. Aronson[28], Bernd Auber[29], Paul L. Auer[30,31], Margreet G.E.M. Ausems[32], Jacopo Azzollini[33], François Bacot[34], Judith Balmaña[35], Monica Barile[36], Laure Barjhoux[37], Rosa B. Barkardottir[38,39], Myrto Barrdahl[40], Daniel Barnes[3], Daniel Barrowdale[3], Caroline Baynes[7], Matthias W. Beckmann[41], Javier Benitez[42-44], Marina Bermisheva[45], Leslie Bernstein[46], Yves-Jean Bignon[47], Kathleen R. Blazer[48], Marinus J. Blok[49], Carl Blomqvist[50], William Blot[51,52], Kristie Bobolis[53], Bram Boeckx[54,55], Natalia V. Bogdanova[25,56,57], Anders Bojesen[58], Stig E. Bojesen[59-61], Bernardo Bonanni[36], Anne-Lise Børresen-Dale[62], Aniko Bozsik[63], Angela R. Bradbury[64], Judith S. Brand[65], Hiltrud Brauch[66-68], Hermann Brenner[26,68,69], Brigitte Bressac-de Paillerets[70], Carole Brewer[71], Louise Brinton[72], Per Broberg[73], Angela Brooks-Wilson[74,75], Joan Brunet[76], Thomas Brüning[77], Barbara Burwinkel[78,79], Saundra S. Buys[80], Jinyoung Byun[21], Qiuyin Cai[51], Trinidad Caldés[81], Maria A. Caligo[82], Ian Campbell[83,84], Federico Canzian[85], Olivier Caron[70], Angel Carracedo[86,87], Brian D. Carter[88], J. Esteban Castelao[89], Laurent Castera[90], Virginie Caux-Moncoutier[91], Salina B. Chan[92], Jenny Chang-Claude[40,93], Stephen J. Chanock[72], Xiaoqing Chen[6], Ting-Yuan David Cheng[94], Jocelyne Chiquette[95], Hans Christiansen[56], Kathleen B.M. Claes[96], Christine L. Clarke[97], Thomas Conner[98], Don M. Conroy[7], Jackie Cook[99], Emilie Cordina-Duverger[100], Sten Cornelissen[101], Isabelle Coupier[102], Angela Cox[103], David Cox[104,105], Simon S. Cross[106], Katarina Cuk[26], Julie M. Cunningham[107], Kamila Czene[65], Mary B. Daly[108], Francesca Damiola[37], Hatef Darabi[65], Rosemarie Davidson[109], Kim De Leeneer[96], Peter Devilee[110,111], Ed Dicks[7], Orland Diez[112], Yuan Chun Ding[46], Nina Ditsch[113], Kimberly F. Doheny[15], Susan M. Domchek[64], Cecilia M. Dorfling[114], Thilo Dörk[57], Isabel dos-Santos-Silva[115], Stéphane Dubois[11], Pierre-Antoine Dugué[1,2], Martine Dumont[11], Alison M. Dunning[7], Lorraine Durcan[116,117], Miriam Dwek[118], Bernd Dworniczak[119], Diana Eccles[117], Ros Eeles[120], Hans Ehrencrona[121], Ursula Eilber[40], Bent Ejlertsen[122], Arif B. Ekici[123], A. Heather Eliassen[124,125], EMBRACE[14], Christoph Engel[126,127], Mikael Eriksson[65], Laura Fachal[7], Laurence Faivre[128,129], Peter A. Fasching[41,130], Ulrike Faust[131], Jonine Figueroa[72,132], Dieter Flesch-Janys[133,134], Olivia Fletcher[135], Henrik Flyger[136], William D. Foulkes[137], Eitan Friedman[138,139], Lin Fritschi[140], Debra Frost[3], Marike Gabrielson[65], Pragna Gaddam[141], Patricia A. Ganz[142], Susan M. Gapstur[88], Judy Garber[143], Vanesa Garcia-Barberan[81], José A. García-Sáenz[81], Mia M. Gaudet[88], Marion Gauthier-Villars[91], Andrea Gehrig[144], GEMO Study Collaborators[14], Vassilios

Georgoulias[145], Anne-Marie Gerdes[146], Graham G. Giles[1,2], Gord Glendon[22], Andrew K Godwin[147], Mark S. Goldberg[148,149], David E. Goldgar[150], Anna González-Neira[42], Paul Goodfellow[151], Mark H. Greene[152], Grethe I. Grenaker Alnæs[62], Mervi Grip[153], Jacek Gronwald[154], Anne Grundy[155], Daphne Gschwantler-Kaulich[156], Pascal Guénel[100], Qi Guo[7], Lothar Haeberle[41], Eric Hahnen[157-159], Christopher A. Haiman[160], Niclas Håkansson[161], Emily Hallberg[162], Ute Hamann[163], Natalie Hammell[34], Susan Hankinson[164], Thomas V.O. Hansen[165], Patricia Harrington[7], Steven N. Hart[162], Jaana M. Hartikainen[166-168], Catherine S. Healey[7], HEBON[14], Alexander Hein[41], Sonja Helbig[57], Alex Henderson[169], Jane Heyworth[170], Belynda Hicks[171], Peter Hillemanns[57], Shirley Hodgson[172], Frans B. Hogervorst[173], Antoinette Hollestelle[174], Maartje J. Hooning[174], Bob Hoover[72], John L. Hopper[2], Chunling Hu[107], Guanmengqian Huang[163], Peter J. Hulick[175,176], Keith Humphreys[65], David J. Hunter[9,125], Evgeny N. Imyanitov[177], Claudine Isaacs[178], Motoki Iwasaki[179], Louise Izatt[180], Anna Jakubowska[154], Paul James[84,181], Ramunas Janavicius[181,182], Wolfgang Janni[183], Uffe Birk Jensen[184], Esther M. John[185,186], Nichola Johnson[135], Kristine Jones[171], Michael Jones[187], Arja Jukkola-Vuorinen[188], Rudolf Kaaks[40], Maria Kabisch[163], Katarzyna Kaczmarek[154], Daehee Kang[189-191], Karin Kast[192], kConFab/AOCS Investigators[14], Renske Keeman[101], Michael J. Kerin[193], Carolien M. Kets[194], Machteld Keupers[195], Sofia Khan[196], Elza Khusnutdinova[45,197], Johanna I. Kiiski[196], Sung-Won Kim[156], Julia A. Knight[198,199], Irene Konstantopoulou[200], Veli-Matti Kosma[166-168], Vessela N. Kristensen[62,201,202], Torben A. Kruse[203], Ava Kwong[204-206], Anne-Vibeke Lænkholm[207], Yael Laitman[138], Fiona Lalloo[208], Diether Lambrechts[54,55], Keren Landsman[209], Christine Lasset[210], Conxi Lazaro[211], Loic Le Marchand[212], Julie Lecarpentier[3], Andrew Lee[3], Eunjung Lee[160], Jong Won Lee[213], Min Hyuk Lee[214], Flavio Lejbkowicz[209], Fabienne Lesueur[215-218], Jingmei Li[65], Jenna Lilyquist[219], Anne Lincoln[220], Annika Lindblom[221], Jolanta Lissowska[222], Wing-Yee Lo[66,67], Sibylle Loibl[223], Jirong Long[51], Jennifer T. Loud[152], Jan Lubinski[154], Craig Luccarini[7], Michael Lush[3], Robert J. MacInnis[1,2], Tom Maishman[116,117], Enes Makalic[2], Ivana Maleva Kostovska[224], Siranoush Manoukian[33], JoAnn E. Manson[225], Sara Margolin[226], John W.M. Martens[174], Maria Elena Martinez[227,228], Keitaro Matsuo[229,230], Dimitrios Mavroudis[145], Sylvie Mazoyer[231], Catriona McLean[232], Hanne Meijers-Heijboer[233], Primitiva Menéndez[234], Jeffery Meyer[107], Hui Miao[235], Austin Miller[236], Nicola Miller[193], Gillian Mitchell[84,181], Marco Montagna[17], Kenneth Muir[237,238], Anna Marie Mulligan[239,240], Claire Mulot[241], Sue Nadesan[53], Katherine L. Nathanson[64], NBSC Collaborators[14], Susan L. Neuhausen[46], Heli Nevanlinna[196], Ines Nevelsteen[195], Dieter Niederacher[242], Sune F. Nielsen[59,60], Børge G. Nordestgaard[59-61], Aaron Norman[162], Robert L. Nussbaum[243], Edith Olah[63], Olufunmilayo I. Olopade[244], Janet E. Olson[162], Curtis Olswold[162], Kai-ren Ong[245], Jan C. Oosterwijk[246], Nick Orr[135], Ana Osorio[43,44], V. Shane Pankratz[247], Laura Papi[248], Tjoung-Won Park-Simon[57], Ylva Paulsson-Karlsson[249], Rachel Peake[250], Inge Søkilde Pedersen[251], Bernard Peissel[33], Ana Peixoto[252], Jose I.A. Perez[253], Paolo Peterlongo[254], Julian Peto[115], Georg Pfeiler[156], Catherine M. Phelan[255], Mila Pinchev[209], Dijana Plaseska-Karanfilska[224], Bruce Poppe[96], Mary E Porteous[256], Ross Prentice[30], Nadege Presneau[118], Darya Prokofieva[197], Elizabth Pugh[15], Miquel

Angel Pujana[257], Katri Pylkäs[258,259], Brigitte Rack[113], Paolo Radice[260], Nazneen Rahman[261], Johanna Rantala[262], Christine Rappaport-Fuerhauser[156], Gad Rennert[209,263], Hedy S. Rennert[209], Valerie Rhenius[7], Kerstin Rhiem[157-159], Andrea Richardson[264], Gustavo C. Rodriguez[265], Atocha Romero[81,266], Jane Romm[15], Matti A. Rookus[267], Anja Rudolph[40], Thomas Ruediger[268], Emmanouil Saloustros[269], Joyce Sanders[270], Dale P. Sandler[271], Suleeporn Sangrajrang[272], Elinor J. Sawyer[273], Daniel F. Schmidt[2], Minouk J. Schoemaker[187], Fredrick Schumacher[160], Peter Schürmann[57], Lukas Schwentner[183], Christopher Scott[162], Rodney J. Scott[274,275], Sheila Seal[261], Leigha Senter[276], Caroline Seynaeve[174], Mitul Shah[7], Priyanka Sharma[277], Chen-Yang Shen[278,279], Xin Sheng[160], Hermela Shimelis[107], Martha J. Shrubsole[51], Xiao-Ou Shu[51], Lucy E Side[280], Christian F. Singer[156], Christof Sohn[281], Melissa C. Southey[282], John J. Spinelli[283,284], Amanda B. Spurdle[6], Christa Stegmaier[285], Dominique Stoppa-Lyonnet[91], Grzegorz Sukiennicki[154], Harald Surowy[78,79], Christian Sutter[286], Anthony Swerdlow[187,287], Csilla I. Szabo[288], Rulla M. Tamimi[9,124,125], Yen Y. Tan[289], Jack A. Taylor[271,290], Maria-Isabel Tejada[291], Maria Tengström[166,292,293], Soo H. Teo[294,295], Mary B. Terry[296], Daniel C. Tessier[34], Alex Teulé[297], Kathrin Thöne[134], Darcy L. Thull[298], Maria Grazia Tibiletti[299], Laima Tihomirova[300], Marc Tischkowitz[137,301], Amanda E. Toland[302], Rob A.E.M. Tollenaar[303], Ian Tomlinson[304], Diana Torres[163,305], Martine Tranchant[11], Thérèse Truong[100], Jonathan Tryer[7], Kathy Tucker[306], Nadine Tung[307], Hans-Ulrich Ulmer[308], Celine Vachon[162], Christi J. van Asperen[309], David Van Den Berg[160], Ans M.W. van den Ouweland[310], Elizabeth J. van Rensburg[114], Liliana Varesco[311], Raymonda Varon-Mateeva[312], Ana Vega[313,314], Alessandra Viel[315], Joseph Vijai[220], Daniel Vincent[34], Jason Vollenweider[107], Lisa Walker[316], Zhaoming Wang[72,317], Shan Wang-Gohrke[183], Barbara Wappenschmidt[157-159], Clarice R. Weinberg[318], Jeffrey N. Weitzel[48], Camilla Wendt[226], Jelle Wesseling[101,270], Alice S. Whittemore[186], Juul T. Wijnen[111,309], Walter Willett[125,319], Robert Winqvist[258,259], Alicja Wolk[161], Anna H. Wu[160], Lucy Xia[160], Xiaohong R. Yang[72], Drakoulis Yannoukakos[200], Daniela Zaffaroni[33], Wei Zheng[51], Bin Zhu[171], Argyrios Ziogas[24], Elad Ziv[320], Kristin K. Zorn[298], Manuela Gago-Dominguez[86,227], Arto Mannermaa[166-168], Håkan Olsson[73], Manuel R. Teixeira[252,321], Jennifer Stone[250,322], Kenneth Offit[323,324], Laura Ottini[325], Sue K. Park[189-191], Mads Thomassen[203], Per Hall[65,326], Alfons Meindl[327], Rita K. Schmutzler[157-159], Arnaud Droit[11], Gary D. Bader[#,10], Paul D.P. Pharoah[#,3,7], Fergus J. Couch[#,107], Douglas F. Easton[#,3,7], Peter Kraft[#,9,125], Georgia Chenevix-Trench[#,6], Montserrat García-Closas[#,72], Marjanka K. Schmidt[#,101,328], Antonis C. Antoniou[#,3], Jacques Simard[#,11]

1. Cancer Epidemiology Centre, Cancer Council Victoria, Melbourne, Australia.
2. Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global health, The University of Melbourne, Melbourne, Australia.
3. Centre for Cancer Genetic Epidemiology, Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK.
4. The Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, UK.

5.	Department of Electron Microscopy/Molecular Pathology, The Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus.
6.	Cancer Division, QIMR Berghofer Medical Research Institute, Brisbane, Australia.
7.	Centre for Cancer Genetic Epidemiology, Department of Oncology, University of Cambridge, Cambridge, UK.
8.	Department of Epidemiology, University of Washington School of Public Health, Seattle, WA, USA.
9.	Program in Genetic Epidemiology and Statistical Genetics, Harvard T.H. Chan School of Public Health, Boston, MA, USA.
10.	The Donnelly Centre, University of Toronto, Toronto, Canada.
11.	Genomics Center, Centre Hospitalier Universitaire de Québec Research Center, Laval University, Québec City, Canada.
12.	Department of Mathematics, Massachusetts Institute of Technology, Cambridge, MA, USA.
13.	Department of Clinical Genetics, Academic Medical Center, Amsterdam, The Netherlands.
14.	A list of members and affiliations appears in the Supplementary Note.
15.	Center for Inherited Disease Research (CIDR), Institute ot Genetic Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA.
16.	Yorkshire Regional Genetics Service, Chapel Allerton Hospital, Leeds, UK.
17.	Istituto Oncologico Veneto IOV - IRCCS, Immunology and Molecular Oncology Unit, Padua, Italy.
18.	Department of Clinical Genetics, Helsinki University Hospital, University of Helsinki, Helsinki, Finland.
19.	Personalised Medicine Team, QIMR Berghofer Medical Research Institute, Brisbane, Australia.
20.	Roswell Park Cancer Institute, Buffalo, NY, USA.
21.	Center for Genomic Medicine, Department of Biomedical Data Science, Geisel School of Medicine, Dartmouth College, Lebanon, NH, USA.
22.	Fred A. Litwin Center for Cancer Genetics, Lunenfeld-Tanenbaum Research Institute of Mount Sinai Hospital, Toronto, Canada.
23.	Department of Molecular Genetics, University of Toronto, Toronto, Canada.
24.	Department of Epidemiology, University of California Irvine, Irvine, CA, USA.
25.	N.N. Alexandrov Research Institute of Oncology and Medical Radiology, Minsk, Belarus.
26.	Division of Clinical Epidemiology and Aging Research, German Cancer Research Center (DKFZ), Heidelberg, Germany.
27.	Department of Gynaecology and Obstetrics, University Hospital of Schleswig-Holstein, Campus Kiel, Christian-Albrechts University Kiel, Kiel, Germany.
28.	Department of Public Health Sciences, and Cancer Research Institute, Queen's University, Kingston, ON, Canada.
29.	Institute of Human Genetics, Hannover Medical School, Hannover, Germany.
30.	Cancer Prevention Program, Fred Hutchinson Cancer Research Center, Seattle, WA, USA.
31.	Zilber School of Public Health, University of Wisconsin-Milwaukee, Milwaukee, WI, USA.
32.	Department of Medical Genetics, University Medical Center Utrecht, Utrecht, The Netherlands.

33. Unit of Medical Genetics, Department of Preventive and Predictive Medicine, Fondazione IRCCS (Istituto Di Ricovero e Cura a Carattere Scientifico) Istituto Nazionale dei Tumori (INT), Milan, Italy.
34. McGill University and Génome Québec Innovation Centre, Montréal, Canada.
35. Department of Medical Oncology. University Hospital, Vall d'Hebron, Barcelona, Spain.
36. Division of Cancer Prevention and Genetics, Istituto Europeo di Oncologia, Milan, Italy.
37. Bâtiment Cheney D, Centre Léon Bérard, Lyon, France.
38. Laboratory of Cell Biology, Department of Pathology, Landspitali-LSH v/Hringbraut, Reykjavik, Iceland.
39. BMC (Biomedical Centre), Faculty of Medicine, University of Iceland, Reykjavik, Iceland.
40. Division of Cancer Epidemiology, German Cancer Research Center (DKFZ), Heidelberg, Germany.
41. Department of Gynaecology and Obstetrics, University Hospital Erlangen, Friedrich-Alexander University Erlangen-Nuremberg, Comprehensive Cancer Center Erlangen-EMN, Erlangen, Germany.
42. Genotyping Unit, Human Cancer Genetics Programme, Spanish National Cancer Research Centre, Madrid, Spain.
43. Human Genetics Group, Human Cancer Genetics Programme, Spanish National Cancer Centre (CNIO), Madrid, Spain.
44. Spanish Network on Rare Diseases (CIBERER), Madrid, Spain.
45. Institute of Biochemistry and Genetics, Ufa Scientific Center of Russian Academy of Sciences, Ufa, Russia.
46. Department of Population Sciences, Beckman Research Institute of City of Hope, Duarte, CA, USA.
47. Department of Oncogenetics, Centre Jean Perrin, BP 392, Clermont-Ferrand, France.
48. Clinical Cancer Genetics, City of Hope, Duarte, California, USA.
49. Department of Clinical Genetics, Maastricht University Medical Center, Maastricht, The Netherlands.
50. Department of Oncology, Helsinki University Hospital, University of Helsinki, Helsinki, Finland.
51. Division of Epidemiology, Department of Medicine, Vanderbilt Epidemiology Center, Vanderbilt-Ingram Cancer Center, Vanderbilt University School of Medicine, Nashville, TN, USA.
52. International Epidemiology Institute, Rockville, MD, USA.
53. City of Hope Clinical Cancer Genomics Community Research Network, Duarte, CA, USA.
54. Vesalius Research Center, VIB, Leuven, Belgium.
55. Laboratory for Translational Genetics, Department of Oncology, University of Leuven, Leuven, Belgium.
56. Department of Radiation Oncology, Hannover Medical School, Hannover, Germany.
57. Gynaecology Research Unit, Hannover Medical School, Hannover, Germany.
58. Department of Clinical Genetics, Vejle Hospital, Vejle, Denmark.
59. Copenhagen General Population Study, Herlev and Gentofte Hospital, Copenhagen University Hospital, Herlev, Denmark.

60. Department of Clinical Biochemistry, Herlev and Gentofte Hospital, Copenhagen University Hospital, Herlev, Denmark.
61. Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark.
62. Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway.
63. Department of Molecular Genetics, National Institute of Oncology, Budapest, Hungary.
64. Department of Medicine, Abramson Cancer Center, Perelman School of Medicine at the University of Pennsylvania, hiladelphia, PA, USA.
65. Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden.
66. Dr. Margarete Fischer-Bosch-Institute of Clinical Pharmacology, Stuttgart, Germany.
67. University of Tübingen, Tübingen, Germany.
68. German Cancer Consortium (DKTK), German Cancer Research Center (DKFZ), Heidelberg, Germany.
69. Division of Preventive Oncology, German Cancer Research Center (DKFZ) and National Center for Tumor Diseases (NCT), Heidelberg, Germany.
70. Gustave Roussy, Biopathology Department, Villejuif, F-94805, France.
71. Department of Clinical Genetics, Royal Devon & Exeter Hospital, Exeter, UK.
72. Division of Cancer Epidemiology and Genetics, National Cancer Institute, Rockville, MD, USA.
73. Department of Cancer Epidemiology, Clinical Sciences, Lund University, Lund, Sweden.
74. Genome Sciences Centre, BC Cancer Agency, Vancouver, BC, Canada.
75. Department of Biomedical Physiology and Kinesiology, Simon Fraser University, Burnaby, BC, Canada.
76. Genetic Counseling Unit, Hereditary Cancer Program, IDIBGI (Institut d'Investigació Biomèdica de Girona), Catalan Institute of Oncology, Girona, Spain.
77. Institute for Prevention and Occupational Medicine of the German Social Accident Insurance, Institute of the Ruhr University Bochum, Bochum, Germany.
78. Department of Obstetrics and Gynecology, University of Heidelberg, Heidelberg, Germany.
79. Molecular Epidemiology Group, C080, German Cancer Research Center (DKFZ), Heidelberg, Germany.
80. Department of Medicine, Huntsman Cancer Institute, 2000 Circle of Hope, Salt Lake City, UT, USA.
81. Medical Oncology Department, Hospital Clínico San Carlos, Madrid, Spain.
82. Section of Genetic Oncology, Dept. of Laboratory Medicine, University and University Hospital of Pisa, Pisa, Italy.
83. Research Department, Peter MacCallum Cancer Centre, East Melbourne, Australia.
84. Sir Peter MacCallum, Department of Oncology, The University of Melbourne, Melbourne, Australia.
85. Genomic Epidemiology Group, German Cancer Research Center (DKFZ), Heidelberg, Germany.

86. Genomic Medicine Group, Galician Foundation of Genomic Medicine, Instituto de Investigación Sanitaria de Santiago de Compostela (IDIS), Complejo Hospitalario Universitario de Santiago, Servicio Galego de Saúde SERGAS, Santiago De Compostela, Spain.

87. Centro de Investigación en Red de Enfermedades Raras (CIBERER) y Centro Nacional de Genotipado (CEGEN-PRB2), Universidad de Santiago de Compostela, Spain.

88. Epidemiology Research Program, American Cancer Society, Atlanta, GA, USA.

89. Oncology and Genetics Unit, Instituto de Investigacion Biomedica (IBI) Orense-Pontevedra-Vigo, Xerencia de Xestion Integrada de Vigo-SERGAS, Vigo, Spain.

90. Centre François Baclesse, 3 avenue Général Harris, Caen, France.

91. Service de Génétique Oncologique, Institut Curie, Paris, France.

92. 1600 Divisadero Street, C415, San Francisco, CA, USA.

93. University Cancer Center Hamburg (UCCH), University Medical Center Hamburg-Eppendorf, Hamburg, Germany.

94. Division of Cancer Prevention and Population Sciences, Roswell Park Cancer Institute, Buffalo, NY, USA.

95. Unité de recherche en santé des populations, Centre des maladies du sein Deschênes-Fabia, Hôpital du Saint-Sacrement, Québec, Canada.

96. Center for Medical Genetics, Ghent University, Gent, Belgium.

97. Westmead Institute for Medical Research, University of Sydney, Sydney, Australia.

98. Huntsman Cancer Institute, 2000 Circle of Hope, Salt Lake City, UT, USA.

99. Sheffield Clinical Genetics Service, Sheffield Children's Hospital, Sheffield, UK.

100. Cancer & Environment Group, Center for Research in Epidemiology and Population Health (CESP), INSERM, University Paris-Sud, University Paris-Saclay, Villejuif, France.

101. Division of Molecular Pathology, The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands.

102. Unité d'Oncogénétique, CHU Arnaud de Villeneuve, Montpellier, France.

103. Academic Unit of Molecular Oncology, Department of Oncology and Metabolism, University of Sheffield, Sheffield, UK.

104. Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, UK.

105. INSERM U1052, Cancer Research Center of Lyon, Lyon, France.

106. Academic Unit of Pathology, Department of Neuroscience, University of Sheffield, Sheffield, UK.

107. Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN, USA.

108. Department of Clinical Genetics, Timothy R. Talbot Jr. Chair for Cancer Research, Fox Chase Cancer Center, Philadelphia, PA, USA.

109. Department of Clinical Genetics, South Glasgow University Hospitals, Glasgow, UK.

110. Department of Pathology, Leiden University Medical Center, Leiden, The Netherlands.

111. Department of Human Genetics, Leiden University Medical Center, Leiden, The Netherlands.

112. Oncogenetics Group, Vall d'Hebron Institute of Oncology (VHIO), Clinical and Molecular Genetics Area, Vall d'Hebron University Hospital, Barcelona, Spain.
113. Department of Gynecology and Obstetrics, Ludwig-Maximilians University of Munich, Munich, Germany.
114. Cancer Genetics Laboratory, Department of Genetics, University of Pretoria, Arcadia, South Africa.
115. Department of Non-Communicable Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, UK.
116. Southampton Clinical Trials Unit, Faculty of Medicine, University of Southampton, Southampton, UK.
117. Cancer Sciences Academic Unit, Faculty of Medicine, University of Southampton, Southampton, UK.
118. Department of Biomedical Sciences, Faculty of Science and Technology, University of Westminster, London, UK.
119. Institute of Human Genetics, University of Münster, Münster, Germany.
120. Oncogenetics Team, The Institute of Cancer Research and Royal Marsden NHS Foundation Trust, London, UK.
121. Department of Clinical Genetics, Lund University Hospital, Lund, Sweden.
122. Department of Oncology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark.
123. Institute of Human Genetics, University Hospital Erlangen, Friedrich-Alexander University Erlangen-Nuremberg, Comprehensive Cancer Center Erlangen-EMN, Erlangen, Germany.
124. Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA.
125. Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, USA.
126. Institute for Medical Informatics, Statistics and Epidemiology, University of Leipzig, Leipzig, Germany.
127. LIFE - Leipzig Research Centre for Civilization Diseases, University of Leipzig, Leipzig, Germany
128. Genetics Department, Dijon University Hospital, Dijon, France
129. Oncogenetics, Centre Georges-François Leclerc, Dijon, France.
130. David Geffen School of Medicine, Department of Medicine Division of Hematology and Oncology, University of California at Los Angeles, Los Angeles, CA, USA.
131. Institute of Medical Genetics and Applied Genomics, University of Tuebingen, Germany.
132. Usher Institute of Population Health Sciences and Informatics, The University of Edinburgh Medical School, Edinburgh, UK.
133. Institute for Medical Biometrics and Epidemiology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany.
134. Department of Cancer Epidemiology, Clinical Cancer Registry, University Medical Center Hamburg-Eppendorf, Hamburg, Germany.
135. Breast Cancer Now Toby Robins Research Centre, The Institute of Cancer Research, London, UK.
136. Department of Breast Surgery, Herlev and Gentofte Hospital, Copenhagen University Hospital, Herlev, Denmark.
137. Program in Cancer Genetics, Departments of Human Genetics and Oncology, McGill University, Montreal, Quebec, Canada.

138. The Susanne Levy Gertner Oncogenetics Unit, Institute of Human Genetics, Chaim Sheba Medical Center, Ramat Gan, Israel.
139. Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel.
140. School of Public Health, Curtin University, Perth, Australia.
141. Clinical Cancer Genetics Laboratory, Memorial Sloane Kettering Cancer Center, New York, NY, USA.
142. UCLA Schools of Medicine and Public Health, Division of Cancer Prevention & Control Research, Jonsson Comprehensive Cancer Center, Los Angeles, CA, USA.
143. Cancer Risk and Prevention Clinic, Dana-Farber Cancer Institute, Boston, MA, USA.
144. Centre of Familial Breast and Ovarian Cancer, Department of Medical Genetics, Institute of Human Genetics, University Würzburg, Würzburg, Germany.
145. Department of Medical Oncology, University Hospital of Heraklion, Heraklion, Greece.
146. Department of Clincial Genetics, Rigshospitalet 4062, København Ø, Denmark.
147. Department of Pathology and Laboratory Medicine, University of Kansas Medical Center, Kansas City, KS, USA.
148. Department of Medicine, McGill University, Montreal, Canada.
149. Division of Clinical Epidemiology, Royal Victoria Hospital, McGill University, Montreal, Canada.
150. Department of Dermatology, Huntsman Cancer Institute, University of Utah School of Medicine, Salt Lake City, UT, USA.
151. Department of Obstetrics and Gynecology, The Ohio State University James Comprehensive Cancer Center, Columbus, OH, USA.
152. Clinical Genetics Branch, DCEG, NCI, NIH, Bethesda, MD, USA.
153. Department of Surgery, Oulu University Hospital, University of Oulu, Oulu, Finland.
154. Department of Genetics and Pathology, Pomeranian Medical University, Szczecin, Poland.
155. Centre de Recherche du Centre Hospitalier de Université de Montréal (CHUM), Montréal, Québec, Canada.
156. Department of OB/GYN and Comprehensive Cancer Centre, Medical University of Vienna, Vienna, Austria.
157. Center for Familial Breast and Ovarian Cancer, University Hospital of Cologne, Cologne, Germany.
158. Center for Integrated Oncology (CIO), University Hospital of Cologne, Cologne, Germany.
159. Center for Molecular Medicine Cologne (CMMC), University of Cologne, Cologne, Germany.
160. Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA.
161. Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden.
162. Department of Health Sciences Research, Mayo Clinic, Rochester, MN, USA.
163. Molecular Genetics of Breast Cancer, German Cancer Research Center (DKFZ), Heidelberg, Germany.
164. Department of Biostatistics & Epidemiology, University of Massachusetts, Amherst, Amherst, MA, USA.

165. Center for Genomic Medicine, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark.
166. Translational Cancer Research Area, University of Eastern Finland, Kuopio, Finland.
167. Institute of Clinical Medicine, Pathology and Forensic Medicine, University of Eastern Finland, Kuopio, Finland.
168. Imaging Center, Department of Clinical Pathology, Kuopio University Hospital, Kuopio, Finland.
169. Institute of Genetic Medicine, Centre for Life, Newcastle Upon Tyne Hospitals NHS Trust, Newcastle upon Tyne, UK.
170. School of Population Health, University of Western Australia, Perth, Australia.
171. Cancer Genomics Research Laboratory (CGR), Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD, USA.
172. Medical Genetics Unit, St George's, University of London, UK.
173. Family Cancer Clinic, The Netherlands Cancer Institute - Antoni van Leeuwenhoek hospital, Amsterdam, The Netherlands.
174. Department of Medical Oncology, Family Cancer Clinic, Erasmus MC Cancer Institute, Rotterdam, The Netherlands.
175. Center for Medical Genetics, NorthShore University HealthSystem, Evanston, IL, USA.
176. Pritzker School of Medicine, University of Chicago, Evanston, IL, USA.
177. N.N. Petrov Institute of Oncology, St.-Petersburg, Russia.
178. Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC, USA.
179. Division of Epidemiology, Center for Public Health Sciences, National Cancer Center, Tokyo, Japan.
180. Clinical Genetics, Guy's and St. Thomas' NHS Foundation Trust, London, UK.
181. Familial Cancer Centre, Peter MacCallum Cancer Centre, Melbourne, Australia.
182. State Research Institute Centre for Innovative medicine, Vilnius, Lithuania.
183. Department of Gynaecology and Obstetrics, University of Ulm, Ulm, Germany.
184. Department of Clinical Genetics, Aarhus University Hospital, Aarhus N, Denmark.
185. Department of Epidemiology, Cancer Prevention Institute of California, Fremont, CA, USA.
186. Departments of Health Research and Policy and Biomedical Data Sciences, Stanford University School of Medicine, Stanford, CA, USA.
187. Division of Genetics and Epidemiology, The Institute of Cancer Research, London, UK.
188. Department of Oncology, Oulu University Hospital, University of Oulu, Oulu, Finland.
189. Department of Preventive Medicine, Seoul National University College of Medicine, Seoul, Korea.
190. Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul, Korea.
191. Cancer Research Institute, Seoul National University, Seoul, Korea.
192. Department of Gynecology and Obstetrics, University Hospital Carl Gustav Carus, TU Dresden, Dresden, Germany.
193. School of Medicine, National University of Ireland, Galway, Ireland.

194. Department of Human Genetics, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands.
195. Leuven Multidisciplinary Breast Center, Department of Oncology, Leuven Cancer Institute, University Hospitals Leuven, Leuven, Belgium.
196. Department of Obstetrics and Gynecology, Helsinki University Hospital, University of Helsinki, Helsinki, Finland.
197. Department of Genetics and Fundamental Medicine, Bashkir State University, Ufa, Russia.
198. Prosserman Centre for Health Research, Lunenfeld-Tanenbaum Research Institute of Mount Sinai Hospital, Toronto, Canada.
199. Division of Epidemiology, Dalla Lana School of Public Health, University of Toronto, Toronto, Canada.
200. Molecular Diagnostics Laboratory, INRASTES, National Centre for Scientific Research "Demokritos", Athens, Greece.
201. Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway.
202. Department of Clinical Molecular Biology, Oslo University Hospital, University of Oslo, Oslo, Norway.
203. Department of Clinical Genetics, Odense University Hospital, Odense C, Denmark.
204. Hong Kong Hereditary Breast Cancer Family Registry, Hong Kong.
205. Department of Surgery, The University of Hong Kong, Hong Kong.
206. Department of Surgery, Hong Kong Sanatorium and Hospital, Hong Kong.
207. Department of Pathology, University Hospital of Region Zealand, division Slagelse, Slagelse, Denmark.
208. Genetic Medicine, Manchester Academic Health Sciences Centre, Central Manchester University Hospitals NHS Foundation Trust, Manchester, UK.
209. Clalit National Cancer Control Center, Haifa, Israel.
210. Unité de Prévention et d'Epidémiologie Génétique, Centre Léon Bérard, Lyon, France.
211. Molecular Diagnostic Unit, Hereditary Cancer Program, IDIBELL (Bellvitge Biomedical Research Institute),Catalan Institute of Oncology, Barcelona, Spain.
212. University of Hawaii Cancer Center, Honolulu, HI, USA.
213. Department of Surgery, University of Ulsan College of Medicine and Asan Medical Center, Seoul, Korea.
214. Department of Surgery, Soonchunhyang University and Hospital, Seoul, Korea.
215. Institut Curie, Paris, France.
216. PSL Research Unviersity, Paris, France.
217. Inserm, U900, Paris, France.
218. Mines Paris Tech, Fontainebleau, France.
219. Department of Health Sciences Research, Mayo Clinic, Scottsdale, AZ, USA.
220. Clinical Genetics Research Laboratory, Dept. of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA.
221. Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden.
222. Department of Cancer Epidemiology and Prevention, M. Sklodowska-Curie Memorial Cancer Center & Institute of Oncology, Warsaw, Poland.
223. German Breast Group, Neu Isenburg, Germany.

224. Research Centre for Genetic Engineering and Biotechnology "Georgi D. Efremov" , Macedonian Academy of Sciences and Arts, Skopje, Republic of Macedonia.
225. Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA.
226. Department of Oncology - Pathology, Karolinska Institutet, Stockholm, Sweden.
227. Moores Cancer Center, University of California San Diego, La Jolla, CA, USA.
228. Department of Family Medicine and Public Health, University of California San Diego, La Jolla, CA, USA.
229. Division of Molecular Medicine, Aichi Cancer Center Research Institute, Nagoya, Japan.
230. Department of Epidemiology, Nagoya University Graduate School of Medicine, Nagoya, Japan.
231. Lyon Neuroscience Research Center - CRNL, INSERM U1028, CNRS UMR5292, University of Lyon, Lyon, France.
232. Anatomical Pathology, The Alfred Hospital, Melbourne, Australia.
233. Department of Clinical Genetics, VU University Medical Centre, Amsterdam, the Netherlands.
234. Servicio de Anatomía Patológica, Hospital Monte Naranco, Oviedo, Spain.
235. Saw Swee Hock School of Public Health, National University of Singapore, Singapore, Singapore.
236. NRG Oncology, Statistics and Data Management Center, Roswell Park Cancer Institute, Buffalo, NY, USA.
237. Institute of Population Health, University of Manchester, Manchester, UK.
238. Division of Health Sciences, Warwick Medical School, Warwick University, Coventry, UK.
239. Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada.
240. Laboratory Medicine Program, University Health Network, Toronto, Canada.
241. Université Paris Sorbonne Cité, INSERM UMR-S1147, Paris, France.
242. Department of Gynecology and Obstetrics, University Hospital Düsseldorf, Heinrich-Heine University Düsseldorf, Düsseldorf, Germany.
243. 513 Parnassus Ave., HSE 901E, San Francisco, CA, USA.
244. Center for Clinical Cancer Genetics and Global Health, The University of Chicago, Chicago, IL, USA.
245. West Midlands Regional Genetics Service, Birmingham Women's Hospital Healthcare NHS Trust, Edgbaston, Birmingham, UK.
246. Department of Genetics, University Medical Center, Groningen University, Groningen, The Netherlands.
247. University of New Mexico Health Sciences Center, University of New Mexico, Albuquerque, NM, USA.
248. Unit of Medical Genetics, Department of Biomedical, Experimental and Clinical Sciences, University of Florence, Florence, Italy.
249. Department of Immunology, Genetics and Pathology, Uppsala University,Uppsala, Sweden.
250. The Curtin UWA Centre for Genetic Origins of Health and Disease, Curtin University and University of Western Australia, Perth, Australia.
251. Section of Molecular Diagnostics, Clinical Biochemistry, Aalborg University Hospital, Aalborg, Denmark.

252. Department of Genetics, Portuguese Oncology Institute, Porto, Portugal.
253. Servicio de Cirugía General y Especialidades, Hospital Monte Naranco, Oviedo, Spain.
254. IFOM, The FIRC (Italian Foundation for Cancer Research) Institute of Molecular Oncology, Milan, Italy.
255. Department of Cancer Epidemiology, Moffitt Cancer Center, Tampa, FL, USA.
256. South East of Scotland Regional Genetics Service, Western General Hospital, Edinburgh, UK.
257. ProCURE, Catalan Institute of Oncology, IDIBELL (Bellvitge Biomedical Research Institute), Barcelona, Spain.
258. Laboratory of Cancer Genetics and Tumor Biology, Cancer and Translational Medicine Research Unit, Biocenter Oulu, University of Oulu, Oulu, Finland.
259. Laboratory of Cancer Genetics and Tumor Biology, Northern Finland Laboratory Centre Oulu, Oulu, Finland.
260. Unit of Molecular Bases of Genetic Risk and Genetic Testing, Department of Preventive and Predictive Medicine, Fondazione IRCCS (Istituto Di Ricovero e Cura a Carattere Scientifico) Istituto Nazionale dei Tumori (INT), Milan, Italy.
261. Section of Cancer Genetics, The Institute of Cancer Research, London, UK.
262. Department of Clinical Genetics, Karolinska University Hospital, Stockholm, Sweden.
263. Carmel Medical Center and B. Rappaport Faculty Of Medicine-Technion, Haifa, Israel.
264. Brigham and Women's Hospital, Dana-Farber Cancer Institute, Boston, MA USA.
265. Division of Gynecologic Oncology, NorthShore University HealthSystem, University of Chicago, Evanston, IL, USA.
266. Medical Oncology Department, Hospital Universitario Puerta de Hierro, Madrid, Spain.
267. Department of Epidemiology. Netherlands Cancer Institute, Amsterdam, The Netherlands.
268. Institute of Pathology, Staedtisches Klinikum Karlsruhe, Karlsruhe, Germany.
269. Hereditary Cancer Clinic, University Hospital of Heraklion, Heraklion, Greece.
270. Department of Pathology, The Netherlands Cancer Institute - Antoni van Leeuwenhoek hospital, Amsterdam, The Netherlands.
271. Epidemiology Branch, National Institute of Environmental Health Sciences, NIH, Research Triangle Park, NC, USA.
272. National Cancer Institute, Bangkok, Thailand.
273. Research Oncology, Guy's Hospital, King's College London, London, UK.
274. Division of Molecular Medicine, Pathology North, John Hunter Hospital, Newcastle, Australia.
275. Discipline of Medical Genetics, School of Biomedical Sciences and Pharmacy, Faculty of Health, University of Newcastle, Callaghan, Australia.
276. Clinical Cancer Genetics Program, Division of Human Genetics, Department of Internal Medicine, The Comprehensive Cancer Center, The Ohio State University, Columbus, USA.
277. Department of Medicine, Kansas Medicial Center, Kansas City, KS, USA.
278. School of Public Health, China Medical University, Taichung, Taiwan.
279. Taiwan Biobank, Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan.

280. North East Thames Regional Genetics Service, Great Ormond Street Hospital for Children NHS Trust, London, UK.
281. National Center for Tumor Diseases, University of Heidelberg, Heidelberg, Germany.
282. Department of Pathology, The University of Melbourne, Melbourne, Australia.
283. Cancer Control Research, BC Cancer Agency, Vancouver, BC, Canada.
284. School of Population and Public Health, University of British Columbia, Vancouver, BC, Canada.
285. Saarland Cancer Registry, Saarbrücken, Germany.
286. Institute of Human Genetics, University Hospital Heidelberg, Heidelberg, Germany.
287. Division of Breast Cancer Research, The Institute of Cancer Research, London, UK.
288. National Human Genome Research Institute ,National Institutes of Health, Bethesda, MD, USA.
289. Dept of OB/GYN and Comprehensive Cancer Center, Medical University of Vienna, Vienna, Austria.
290. Epigenetic and Stem Cell Biology Laboratory, National Institute of Environmental Health Sciences, NIH, Research Triangle Park, NC, USA.
291. Molecular Genetics Laboratory, Clinical Genetics Service, Cruces University Hospital. BioCruces Health Research Institute, Barakaldo, Spain.
292. Cancer Center, Kuopio University Hospital, Kuopio, Finland.
293. Institute of Clinical Medicine, Oncology, University of Eastern Finland, Kuopio, Finland.
294. Cancer Research Malaysia, Subang Jaya, Selangor, Malaysia.
295. Breast Cancer Research Unit, Cancer Research Institute, University Malaya Medical Centre, Kuala Lumpur, Malaysia.
296. Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, USA.
297. Genetic Counseling Unit, Hereditary Cancer Program, IDIBELL (Bellvitge Biomedical Research Institute), Catalan Institute of Oncology, Barcelona, Spain.
298. Magee-Womens Hospital, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA.
299. Ospedale di Circolo ASST Settelaghi, Varese, Italy.
300. Latvian Biomedical Research and Study Centre, Riga, Latvia.
301. Department of Medical Genetics, Addenbrooke's Treatment Centre, Addenbrooke's Hosptital, Cambridge, UK.
302. Department of Molecular Virology, Immunology and Medical Genetics, Comprehensive Cancer Center, The Ohio State University, Columbus, OH, USA.
303. Department of Surgery, Leiden University Medical Center, Leiden, The Netherlands.
304. Wellcome Trust Centre for Human Genetics and Oxford NIHR Biomedical Research Centre, University of Oxford, Oxford, UK.
305. Institute of Human Genetics, Pontificia Universidad Javeriana, Bogota, Colombia.
306. Hereditary Cancer Clinic, Department of Medical Oncology, Prince of Wales Hospital, Randwick, Australia.

307. Department of Medical Oncology, Beth Israel Deaconess Medical Center, MA, USA.
308. Frauenklinik der Stadtklinik Baden-Baden, Baden-Baden, Germany.
309. Department of Clinical Genetics, Leiden University Medical Center, Leiden, The Netherlands.
310. Department of Clinical Genetics, Erasmus University Medical Center, Rotterdam, The Netherlands.
311. Unit of Hereditary Cancer, Department of Epidemiology, Prevention and Special Functions, IRCCS (Istituto Di Ricovero e Cura a Carattere Scientifico) AOU San Martino - IST Istituto Nazionale per la Ricerca sul Cancro, largo Rosanna Benzi 10, 16132 Genoa, Italy.
312. Institute of Human Genetics, Campus Virchov Klinikum, Charite Berlin, Germany.
313. Fundación Pública Galega de Medicina Xenómica, Servizo Galego de Saúde (SERGAS), Instituto de Investigaciones Sanitarias (IDIS), Santiago de Compostela, Spain.
314. Grupo de Medicina Xenómica, Centro de Investigación Biomédica en Red de Enfermedades Raras (CIBERER), Universidade de Santiago de Compostela (USC), Santiago de Compostela, Spain.
315. Unit of Functional onco-genomics and genetics, CRO Aviano, National Cancer Institute, Via Franco Gallini 2, 33081 Aviano (PN), Italy.
316. Oxford Regional Genetics Service, Churchill Hospital, Oxford, UK.
317. Department of Computational Biology, St. Jude Children's Research Hospital, Memphis, TN, USA.
318. Biostatistics and Computational Biology Branch, National Institute of Environmental Health Sciences, NIH, Research Triangle Park, NC, USA.
319. Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA, USA.
320. Department of Medicine, Institute for Human Genetics, UCSF Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA, USA.
321. Biomedical Sciences Institute (ICBAS), University of Porto, Porto, Portugal.
322. Department of Obstetrics and Gynaecology, University of Melbourne and the Royal Women's Hospital, Melbourne, Australia.
323. Clinical Genetics Research Lab, Cancer Biology and Genetics Program, Sloan Kettering Institute, New York, NY, USA
324. Clinical Genetics Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA.
325. Department of Molecular Medicine, University La Sapienza, c/oPoliclinico Umberto I, Rome, Italy.
326. Department of Oncology, South General Hospital, Stockholm, Sweden
327. Division of Gynaecology and Obstetrics, Technische Universität München, Munich, Germany.
328. Division of Psychosocial Research and Epidemiology, The Netherlands Cancer Institute - Antoni van Leeuwenhoek hospital, Amsterdam, The Netherlands.

[†]Co-first authorship
[#]Co-senior authorship

*Correspondence to: Roger L. Milne, Cancer Epidemiology Centre, Cancer Council Victoria, Melbourne, Australia; E-mail: roger.milne@cancervic.org.au.

Most common breast cancer susceptibility variants have been identified through genome-wide association studies (GWASs) of predominantly estrogen receptor (ER)-positive disease[1]. We conducted a GWAS using 21,468 ER-negative cases and 100,594 controls combined with 18,908 *BRCA1* mutation carriers (9,414 with breast cancer), all of European origin. We identified independent associations at P<5x10^{-8} with 10 variants at nine novel loci. At P<0.05, we replicated associations with 10 of 11 variants previously reported in ER-negative or *BRCA1* mutation carrier GWASs, and observed consistent associations with ER-negative disease for 105 susceptibility variants identified by other breast cancer GWASs. These 125 variants explain approximately 16% of the familial risk of this breast cancer subtype. There was high genetic correlation (0.72) between risk of ER-negative breast cancer and breast cancer risk for *BRCA1* carriers. These findings will likely lead to improved risk prediction and inform further fine-mapping and functional work to better understand the biological basis of ER-negative breast cancer.

GWASs have identified 107 single nucleotide polymorphisms (SNPs) that are independently associated with breast cancer risk[2-32]. Association studies focused on ER-negative disease, or *BRCA1* mutation carriers, who are more likely to develop ER-negative disease (70-80% of cases)[33], have identified 11 of these SNPs[3,9,12,19,29,30]. We aimed to discover additional ER-negative breast cancer susceptibility variants by performing a GWAS in women of European origin.

New genotyping data were generated for 9,655 ER-negative cases and 45,494 controls from 68 Breast Cancer Association Consortium (BCAC) studies and 15,566 *BRCA1* mutation carriers (7,784 with breast cancer) from 58 Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA) studies (Supplementary Tables 1 and 2) using the Illumina OncoArray beadchip, a 570K SNP custom array with genome-wide coverage[34]. Imputation was used to derive estimated genotypes for ~21M SNPs, using the 1000 Genomes Project (Phase 3) as reference; ~11.5M of those with imputation $r^2>0.3$ and minor allele frequency (MAF)>0.005 were included in further analyses. For BCAC data, we estimated per-allele odds ratios (ORs) using logistic regression, adjusting for country and principal components. For CIMBA data, we estimated per-allele hazard ratios (HR) using a retrospective cohort analysis framework, modelling time to breast cancer and stratifying on country, Ashkenazi Jewish origin and birth cohort[35,36] (see Online Methods). These analyses were also applied to an independent set of previously generated data from other genome-wide genotyping of additional European participants in 44 BCAC studies (11,813 ER-negative cases and 55,100 controls)[9,12,16,20,37,38] and 54 CIMBA studies (3,342 *BRCA1* mutation carriers, 1,630 with breast cancer) (Supplementary Tables 1 and 2). Fixed-effects meta-analysis was used to combine results across genotyping initiatives within consortia and, assuming that the OR and HR estimates approximate the same underlying relative risk, across consortia[39].

Results from the combined meta-analysis are summarised in Supplementary Figures 1 and 2. There was minimal inflation of test statistics (lambda1000=1.004;

Supplementary Figure 3). We identified 10 variants at nine novel loci that were independently associated with risk of ER-negative breast cancer at P<5x10^{-8} (Table 1; Supplementary Table 3; Supplementary Figures 4-11). Two independent signals were observed within 12kb at 11q22.3, for rs74911261 (MAF=0.02) and rs11374964 (MAF=0.42); OR estimates and statistical significance were largely unchanged when each variant was adjusted for the other (Supplementary Table 4). The association with 8p23.3-rs66823261 was not observed for *BRCA1* mutation carriers (P=0.32, P-heterogeneity=0.030).

For each of these 10 novel signals, we identified candidate causal SNPs analytically[40,41] (see Online Methods) and combined multiple sources of *in silico* functional annotation from public databases[42-52] to identify likely functional variants and target genes. Results are summarised in Supplementary Table 5 (including UCSC Genome Browser links; see also Supplementary Note), Figure 1 and Supplementary Figures 4-11 (data sources in Supplementary Table 6). Many candidate causal SNPs lie in predicted regulatory regions and are associated with expression of nearby genes in blood or other tissues. At 2p23, the predicted target genes include *ADCY3* and *NCOA1* (Supplementary Figure 4). At 6q23.1 (Supplementary Figure 5), the most plausible target gene is *L3MBTL3*[53]. A predicted target at 8q24.13 is *FBXO32*, which is expressed in ER-negative HMECs but not ER-positive MCF7 breast cancer cells (Supplementary Figure 7) and has a known role in cancer cachexia[54]. At 11q22.3 (Figure 1), a predicted target gene of common risk-associated variants is *NPAT*[55]. The rarer SNPs underlying the other 11q22.3 signal are predicted to target *ATM*, a known breast cancer susceptibility gene[56]. Three rare coding variants (MAF≤0.03) in *ATM, NPAT* and *KDELC2*, are also among the candidate causal SNPs at this locus. At 16p13, predicted target genes include *ADCY9* and *CREBBP* (Supplementary Figure 8). At 19q12 (Supplementary Figure 11), a potential target gene encodes cyclin E1 which is involved in cell cycle control and phosphorylation of NPAT[57].

Expression QTL associations were assessed between each candidate causal variant and genes within 1Mb using 79 ER-negative breast tumours from TCGA and 135 normal breast tissue samples from METABRIC[58-60]. The strongest associations identified were 6q23.1-rs6569648-*L3MBTL3* (P=4.3x10^{-6}) and 18q12.1-rs12965632-*CDH2* (P=1.0x10^{-4}), both in METABRIC (Supplementary Table 5). SNP rs6569648 was the top *cis*-eQTL (of all imputed variants within 1 Mb) for *L3MBTL3* while the p-value for the rs12965632-*CDH2* eQTL was within two orders of magnitude of the top *cis*-eQTLs for this gene (Supplementary Figures 12-13).

For 10 of the 11 variants previously identified through GWASs of ER-negative disease or overall disease in *BRCA1* mutation carriers[3,9,12,18,19,30,31], or reported as more strongly associated with ER-negative breast cancer[29], associations with ER-negative disease were replicated (P<0.05) using OncoArray data from BCAC, which does not overlap with any of the discovery studies (Table 2). Effect sizes were generally similar to those originally reported. Using all available CIMBA data, six of these 11 variants were associated with breast cancer risk (P<0.05) for *BRCA1* mutation carriers (Table 2). No evidence of association was observed for 20q11-rs2284378[12] in either BCAC or CIMBA (P≥0.46).

Based on estimated ORs using BCAC data for all cases with known ER status (16,988 ER-negative; 65,275 ER-positive), all 10 new and 10 previously reported

and replicated ER-negative disease susceptibility SNPs were more strongly associated with risk of ER-negative than ER-positive subtype (P-heterogeneity<0.05, except for novel hit 19p13.2-rs322144; Supplementary Table 7). Two variants (1q32.1-rs4245739 and 19p13.11-rs67397200) were not associated with ER-positive disease. For four variants (11q22.3- rs11374964, 11q22.3-rs74911261, 1q32.1-rs6678914 and 2p23.2-rs4577244), the risk-associated allele for ER-negative disease was associated with reduced risk of ER-positive disease (P<0.05).

For these 20 ER-negative breast cancer susceptibility SNPs, we also assessed associations by triple-negative (TN) status (negative for ER, progesterone receptor and HER2; Table 3), tumour grade (Table 4) and age at diagnosis (Supplementary Table 8) using BCAC data only. Five, including the novel susceptibility variants 11q22.3-rs11374964 and 11q22.3-rs74911261, were more strongly associated with risk of both TN and higher-grade disease (P<0.05), although after adjustment for TN status, heterogeneity by grade was observed only for 11q22.3-rs74911261 and 1q32.1-rs4245739 (P<0.05). For 2p23.3-rs4577244, heterogeneity was observed for grade only, while 6q25.2-rs2747652 was more strongly associated with risk of other (non-TN) ER-negative breast cancer subtypes (P<0.05). At younger ages, associations appeared to be stronger for two variants (5p15.33-rs10069690 and 19p13.11-rs67397200), and weaker for one (6q25.2-rs2747652) (P<0.05).

Elsewhere we report 65 novel susceptibility loci for overall breast cancer[1]. Three of these overlap within 500kb with the novel ER-negative disease-associated loci reported here (variants 2p23.3-rs200648189, 6q23.1-rs6569648 and 8q24.13-rs17350191). We assessed associations with risk of ER-negative disease, and with risk of overall breast cancer for *BRCA1* mutation carriers, for SNPs at the remaining 62 loci, as well as for the 96 previously reported breast cancer susceptibility variants that were not ER-negative specific. Of these 158 SNPs, 105 were associated (P<0.05) with risk of ER-negative breast cancer, and 24 with risk for *BRCA1* mutation carriers (Supplementary Tables 9-10). Results for *BRCA2* mutation carriers are presented in Supplementary Table 11.

Pathway analysis based on mapping each SNP to the nearest gene was performed using summary association statistics from the meta-analysis of BCAC and CIMBA data combined[61-64] (see Online Methods). This identified several pathways implicated in ER-negative disease (enrichment score [ES]≥0.41; Supplementary Figure 14; Supplementary Tables 12-13), including a subset that was not enriched in susceptibility to ER-positive disease (ES<0; Supplementary Table 14). One of the latter subsets was the adenylate cyclase (AC) activating pathway (ES=0.62; Supplementary Figure 15). Two of the predicted target genes for the 10 novel ER-negative breast cancer susceptibility variants, based on the eQTL analysis (Supplementary Table 5), *ADCY3* (P[TCGA]=6.7×10^{-3}] and *ADCY9* (P[METABRIC]=1.3×10^{-4}), are part of this pathway, and their association signals were critical to the elevated ES observed (Supplementary Figure 14). ADCY9 is stimulated by β2 adrenergic receptor (β2AR) signalling[65] in ER-negative breast cancer[66], which in turn drives AC-cAMP signalling, including for example mitogenic signalling through β-arrestin-Src-ERK[67].

To further explore the functional properties of the genome that contribute to ER-negative breast cancer heritability, we conducted a partitioned heritability analysis using linkage disequilibrium (LD) score regression[68]. Considering 52 "baseline"

genomic features, we observed the greatest enrichment for super-enhancers (2.5-fold, $p=2 \times 10^{-7}$) and the H3K4me3 histone mark (2.4-fold, p=0.0005), with 33% depletion (p=0.0002) observed for repressed regions (Supplementary Table 15). No differences in enrichment for these features were observed between susceptibility to ER-negative and ER-positive breast cancer, but baseline genomic features are not specific to cell type[68]. The estimated correlation between ER-negative and ER-positive breast cancer based on ~1M common genetic variants[69,70] was 0.60 (standard error [SE], 0.03) indicating that, although these two breast cancer subtypes have a shared genetic component, a substantial proportion is distinct. The estimated correlation between ER-negative disease in the general population and overall breast cancer for *BRCA1* mutation carriers was 0.72 (SE, 0.11).

In summary, in this study of women of European origin, we have identified 10 novel susceptibility variants for ER-negative breast cancer and replicated associations with ER-negative disease for 10 SNPs identified by previous GWASs. Most of these were not associated, or more weakly associated, with ER-positive disease, consistent with the findings from pathway and partitioned heritability analyses showing that ER-negative breast cancer has a partly distinct genetic aetiology. We also observed consistent associations with ER-negative disease for a further 105 overall breast cancer susceptibility SNPs. Together, these 125 variants explain ~14% of an assumed 2-fold increased risk of developing ER-negative disease for the first degree female relatives of women affected with this subtype (the newly identified SNPs explain ~1.5%); Supplementary Table 16) and ~40% of the estimated familial risk that is attributable to all variants imputable from the Oncoarray (see Online Methods). We have also identified nine novel breast cancer susceptibility variants for *BRCA1* mutation carriers and confirmed associations for a further 30 previously reported SNPs; these 39 variants explain ~8% of the variance in polygenic risk for carriers of these mutations (Supplementary Table 17). However, the lower number of *BRCA1* risk-associated variants may merely be a consequence of the smaller sample size, since the genetic correlation with ER-negative breast cancer is high. These findings will likely inform improved risk prediction, both for the general population and for *BRCA1* mutation carriers[30,71,72]. Further investigation is required for other populations of non-European origin. Fine-mapping and functional studies should lead to a better understanding of the biological basis of ER-negative breast cancer, and perhaps inform the design of more effective preventive interventions, early detection and treatments for this disease.

Data availability

A subset of the data that support the findings of this study is publically available via dbGaP (see URLs section; accession number phs001265.v1.p1). The complete dataset will not be made publically available due to restraints imposed by the ethics committees of individual studies; requests for data can be made to the corresponding author or the Data Access Coordination Committees (DACCs) of BCAC (see URLs section) and CIMBA (see URLs section). BCAC DACC approval is required to access data from studies ABCFS, ABCS, ABCTB, BBCC, BBCS, BCEES, BCFR-NY, BCFR-PA, BCFR-UT, BCINIS, BSUCH, CBCS, CECILE, CGPS, CTS, DIETCOMPLYF, ESTHER, GC-HBOC, GENICA, GEPARSIXTO, GESBC, HABCS, HCSC, HEBCS, HMBCS, HUBCS, KARBAC, KBCP, LMBC, MABCS,

MARIE, MBCSG, MCBCS, MISS, MMHS, MTLGEBCS, NC-BCFR, OFBCR, ORIGO, pKARMA, POSH, PREFACE, RBCS, SKKDKFZS, SUCCESSB, SUCCESSC, SZBCS, TNBCC, UCIBCS, UKBGS and UKOPS (see Supplementary Table 1). CIMBA DACC approval is required to access data from studies BCFR-ON, CONSIT TEAM, DKFZ, EMBRACE, FPGMX, GC-HBOC, GEMO, G-FAST, HEBCS, HEBON, IHCC, INHERIT, IOVHBOCS, IPOBCS, MCGILL, MODSQUAD, NAROD, OCGN, OUH and UKGRFOCR (see Supplementary Table 2).

URLs

Acknowledgements

Author Contributions

Writing group: R.L.M., K.B.K, K.Michailidou, J.Beesley, S.Kar, S.Lindström, S.Hui., G.D.B., P.D.P.P., F.J.C., D.F.E., P.K., G.CT., M.GC., M.K.S., A.C.A., J.Simard.

Conceived and coordinated the synthesis of the Oncoarray: D.F.E., A.C.A., J. Simard, C.I.A., J.Byun, S.J.C., E.D., D.J.H., A.Lee, P.D.P.P., J.T., Z.W.

OncoArray genotyping: M.A., A.C.A., S.E.B., M.K.B., F.B., G.CT., J.M.C., K.F.D., D.F.E., N.Hammell, B.Hicks, K.J., C.Luccarini, L.M, J.M., E.P., J.Romm, M.K.S., X.S., J.Simard., P.Soucy, D.C.T., D.V., J.Vollenweider, L.X., B.Z.

Oncoarray genotype calling and quality control: X.C., J.D., E.D., D.F.E., K.B.K, J.Lecarpentier, A.Lee, M.Lush.

Database management: D.Barrowdale., M.K.B., M.L., L.McG., Q.W., R.Keeman, M.K.S.

Statistical analysis: K.B.K, K.Michailidou, S.Hui, S.Kar, X.J., A.Rostamianfar, H.Finucane, S.Lindström, D.Barnes, P.K., P.D.P.P., G.D.B., R.L.M., A.C.A., D.F.E.

Bioinformatic analysis: J.Beesley, P.Soucy, A.Lemaçon, D.Barnes, F.AE. A.D., J. Simard, G.CT.

Provided DNA samples and/or phenotypic data: ABCTB.I., C.M.A., J.Adlard, S.Agata, S.Ahmed, J.Allen, K.A., C.B.A., I.L.A., H.AC., N.N.A., A.C.A., V.A., N.A., K.J.A., B.A., P.L.A., M.G.E.M.A., J.Azzollini, J.Balmaña, M.Barile, L.Barjhoux, R.B.B., M.Barrdahl, D.Barnes, D. Barrowdale, C.Baynes, M.W.B., J.Beesley, J.Benitez, M.Bermisheva, L.Bernstein, YJ.B., K.R.B., M.J.B., C.Blomqvist, W.B., K.B., B.Boeckx, N.V.B., A.Bojesen, S.E.B., M.K.B., B.Bonanni, A.Bozsik, A.R.B., J.S.B., H.Brauch, H.Brenner, B.BdP., C.Brewer, L.Brinton, P.B., A.BW., J.Brunet, T.B., B.Burwinkel, S.S.B., AL.BW., Q.C., T.Caldés, M.A.C., I.Campbell, F.C., O.C., A.Carracedo, B.D.C., J.E.C., L.C., V.CM., S.B.C., J.CC., S.J.C., X.C., G.CT., TYD.C., J.Chiquette, H.C., K.B.M.C., C.L.C., NBCS.C., T.Conner, D.M.C., J.Cook, E.CD., S.C., F.J.C., I.Coupier, D.C., A.Cox, S.S.C., K.Cuk, K.Czene, M.B.D., F.D., H.D., R.D., K.D., J.D., P.D., O.D., YC.D., N.D., S.M.D., C.M.D., S.D., PA.D.,

M.Dumont, A.M.D., L.D., M.Dwek, B.D., T.D., EMBRACE, D.F.E., D.E., R.E., H.Ehrencrona, U.E., B.E., A.B.E., A.H.E., C.E., M.E., L.Fachal, L.Faivre, P.A.F., U.F., J.F., D.FJ., O.F., H.Flyger, W.D.F., E.F., L.Fritschi, D.F., GEMO.S.C., M.Gabrielson, P.Gaddam, M.GD., P.A.G., S.M.G., J.Garber, V.GB., M.GC., J.A.GS., M.M.G., M.GV., A.Gehrig, V.G., AM.G., G.G.G., G.G., A.KG., M.S.G., D.E.G., A.GN., P.Goodfellow, M.H.G., G.I.GA., M.Grip, J.Gronwald, A.Grundy, D.GK., Q.G., P.Guénel, HEBON, L.H., E.Hahnen, C.A.H., P.Hall, E.Hallberg, U.H., S.Hankinson, T.V.O.H., P.Harrington, S.N.H., J.M.H., C.S.H., A.Hein, S.Helbig, A.Henderson, J.H., P.Hillemanns, S.Hodgson, F.B.H., A.Hollestelle, M.J.H., B.Hoover, J.L.H., C.H., G.H., P.J.H., K.H., D.J.H., N.Håkansson, E.N.I., C.I., M.I., L.I., A.J., P.J., R.J., W.J., UB.J., E.M.J., N.J., M.J., A.JV., R.Kaaks, M.Kabisch, K.Kaczmarek, D.K., K.Kast, R.Keeman, M.J.K., C.M.K., M.Keupers, S.Khan, E.K., J.I.K., J.A.K., I.K., V.K., P.K., V.N.K., T.A.K., K.B.K., A.K., Y.L., F.Lalloo, K.L., D.L., C.Lasset, C.Lazaro, L.IM., J.Lecarpentier, M.Lee, A.Lee, E.L., J.Lee, F.Lejbkowicz, F.Lesueur, J.Li, J.Lilyquist, A.Lincoln, A.Lindblom, S.Lindström, J.Lissowska, WY.L., S.Loibl, J.Long, J.T.L., J.Lubinski, C.Luccarini, M.Lush, AV.L., R.J.M., T.M., E.M., I.MK., A.Mannermaa, S.Manoukian, J.E.M., S.Margolin, J.W.M.M., ME.M., K.Matsuo, D.M., S.Mazoyer, L.M., C.McLean, H.MH., A.Meindl, P.M., H.M., K.Michailidou, A.Miller, N.M., R.L.M., G.M., M.M., K.Muir, A.M.M., C.Mulot, S.N., K.L.N., S.L.N., H.N., I.N., D.N., S.F.N., B.G.N., A.N., R.L.N., K.Offit, E.O., O.I.O., J.E.O., H.O., C.O., K.Ong, J.C.O., N.O., A.O., L.O., VS.P., L.P., S.K.P., TW.PS., Y.PK., R.Peake, IS.P., B.Peissel, A.P., J.I.A.P., P.P., J.P., G.P., P.D.P.P., C.M.P., M.P., D.PK., B.Poppe, M.EP., R.Prentice, N.P., D.P., MA.P., K.P., B.R., P.R., N.R., J.Rantala, C.RF., H.S.R., G.R., V.R., K.R., A.Richardson, G.C.R., A.Romero, M.A.R., A.Rudolph, T.R., E.S., J.Sanders, D.P.S., S.Sangrajrang, E.J.S., D.F.S., M.K.S., R.K.S., M.J.Schoemaker, F.S., L.Schwentner, P.Schürmann, C.Scott, R.J.S., S.Seal, L.Senter, C.Seynaeve, M.S., P.Sharma, CY.S., H.Shimelis, M.J.Shrubsole, XO.S., L.E.S., J.Simard, C.F.S., C.Sohn, P.Soucy, M.C.S., J.J.S., A.B.S., C.Stegmaier, J.Stone, D.SL., G.S., H.Surowy, C.Sutter, A.S., C.I.S., R.M.T., Y.Y.T., J.A.T., M.R.T., MI.T., M.Tengström, S.H.T., M.B.T., A.T., M.Thomassen, D.L.T., K.Thöne, MG.T., L.T., M.Tischkowitz, A.E.T., R.A.E.M.T., I.T., D.T., M.Tranchant, T.T., K.Tucker, N.T., HU.U., C.V., D.vdB., L.V., R.VM., A.Vega, A.Viel, J.Vijai, L.W., Q.W., S.WG., B.W., C.R.W., J.N.W., C.W., J.W., A.S.W., J.T.W., W.W., R.W., A.W., A.H.W., X.R.Y., D.Y., D.Z., W.Z., A.Z., E.Z., K.K.Z., I.dSS., kConFab.AOCS.I., C.J.v.A., E.vR., A.M.W.vdO.

All authors read and approved the final version of the manuscript.

Competing Financial Interests

The authors confirm that they have no competing financial interests

References

1.	Michailidou, K. *et al.* Identification of more than 70 new breast cancer susceptibility loci for breast cancer and definition of risk-associated genomic features *Nature* (under review).
2.	Ahmed, S. *et al.* Newly discovered breast cancer susceptibility loci on 3p24 and 17q23.2. *Nat Genet* **41**, 585-90 (2009).
3.	Antoniou, A.C. *et al.* A locus on 19p13 modifies risk of breast cancer in BRCA1 mutation carriers and is associated with hormone receptor-negative breast cancer in the general population. *Nat Genet* **42**, 885-92 (2010).
4.	Cai, Q. *et al.* Genome-wide association study identifies breast cancer risk variant at 10q21.2: results from the Asia Breast Cancer Consortium. *Hum Mol Genet* **20**, 4991-9 (2011).
5.	Cox, A. *et al.* A common coding variant in CASP8 is associated with breast cancer risk. *Nat Genet* **39**, 352-8 (2007).
6.	Easton, D.F. *et al.* Genome-wide association study identifies novel breast cancer susceptibility loci. *Nature* **447**, 1087-93 (2007).
7.	Fletcher, O. *et al.* Novel breast cancer susceptibility locus at 9q31.2: results of a genome-wide association study. *J Natl Cancer Inst* **103**, 425-35 (2011).
8.	Ghoussaini, M. *et al.* Genome-wide association analysis identifies three new breast cancer susceptibility loci. *Nat Genet* **44**, 312-8 (2012).
9.	Haiman, C.A. *et al.* A common variant at the TERT-CLPTM1L locus is associated with estrogen receptor-negative breast cancer. *Nat Genet* **43**, 1210-4 (2011).
10.	Hein, R. *et al.* Comparison of 6q25 breast cancer hits from Asian and European Genome Wide Association Studies in the Breast Cancer Association Consortium (BCAC). *PLoS One* **7**, e42380 (2012).
11.	Hunter, D.J. *et al.* A genome-wide association study identifies alleles in FGFR2 associated with risk of sporadic postmenopausal breast cancer. *Nat Genet* **39**, 870-4 (2007).
12.	Siddiq, A. *et al.* A meta-analysis of genome-wide association studies of breast cancer identifies two novel susceptibility loci at 6q14 and 20q11. *Hum Mol Genet* **21**, 5373-84 (2012).
13.	Stacey, S.N. *et al.* Common variants on chromosomes 2q35 and 16q12 confer susceptibility to estrogen receptor-positive breast cancer. *Nat Genet* **39**, 865-9 (2007).
14.	Stacey, S.N. *et al.* Common variants on chromosome 5p12 confer susceptibility to estrogen receptor-positive breast cancer. *Nat Genet* **40**, 703-6 (2008).
15.	Thomas, G. *et al.* A multistage genome-wide association study in breast cancer identifies two new risk alleles at 1p11.2 and 14q24.1 (RAD51L1). *Nat Genet* **41**, 579-84 (2009).
16.	Turnbull, C. *et al.* Genome-wide association study identifies five new breast cancer susceptibility loci. *Nat Genet* **42**, 504-7 (2010).
17.	Zheng, W. *et al.* Genome-wide association study identifies a new breast cancer susceptibility locus at 6q25.1. *Nat Genet* **41**, 324-8 (2009).
18.	Bojesen, S.E. *et al.* Multiple independent variants at the TERT locus are associated with telomere length and risks of breast and ovarian cancer. *Nat Genet* **45**, 371-84 (2013).
19.	Garcia-Closas, M. *et al.* Genome-wide association studies identify four ER negative-specific breast cancer risk loci. *Nat Genet* **45**, 392-8 (2013).

20. Michailidou, K. *et al.* Large-scale genotyping identifies 41 new loci associated with breast cancer risk. *Nat Genet* **45**, 353-61 (2013).
21. Cai, Q. *et al.* Genome-wide association analysis in East Asians identifies breast cancer susceptibility loci at 1q32.1, 5q14.3 and 15q26.1. *Nat Genet* **46**, 886-90 (2014).
22. Long, J. *et al.* Genome-wide association study in east Asians identifies novel susceptibility loci for breast cancer. *PLoS Genet* **8**, e1002532 (2012).
23. Michailidou, K. *et al.* Genome-wide association analysis of more than 120,000 individuals identifies 15 new susceptibility loci for breast cancer. *Nat Genet* **47**, 373-80 (2015).
24. Milne, R.L. *et al.* Common non-synonymous SNPs associated with breast cancer susceptibility: findings from the Breast Cancer Association Consortium. *Hum Mol Genet* **23**, 6096-111 (2014).
25. Gaudet, M.M. *et al.* Identification of a BRCA2-specific modifier locus at 6p24 related to breast cancer risk. *PLoS Genet* **9**, e1003173 (2013).
26. Meyer, K.B. *et al.* Fine-scale mapping of the FGFR2 breast cancer risk locus: putative functional variants differentially bind FOXA1 and E2F1. *Am J Hum Genet* **93**, 1046-60 (2013).
27. Orr, N. *et al.* Fine-mapping identifies two additional breast cancer susceptibility loci at 9q31.2. *Hum Mol Genet* **24**, 2966-84 (2015).
28. French, J.D. *et al.* Functional variants at the 11q13 risk locus for breast cancer regulate cyclin D1 expression through long-range enhancers. *Am J Hum Genet* **92**, 489-503 (2013).
29. Dunning, A.M. *et al.* Breast cancer risk variants at 6q25 display different phenotype associations and regulate ESR1, RMND1 and CCDC170. *Nat Genet* **48**, 374-86 (2016).
30. Couch, F.J. *et al.* Identification of four novel susceptibility loci for oestrogen receptor negative breast cancer. *Nat Commun* **7**, 11375 (2016).
31. Lawrenson, K. *et al.* Functional mechanisms underlying pleiotropic risk alleles at the 19p13.1 breast-ovarian cancer susceptibility locus. *Nat Commun* **7**, 12675 (2016).
32. Wyszynski, A. *et al.* An intergenic risk locus containing an enhancer deletion in 2q35 modulates breast cancer risk by deregulating IGFBP5 expression. *Hum Mol Genet* (2016).
33. Mavaddat, N. *et al.* Pathology of breast and ovarian cancers among BRCA1 and BRCA2 mutation carriers: results from the Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA). *Cancer Epidemiol Biomarkers Prev* **21**, 134-47 (2012).
34. Amos, C.I. *et al.* The OncoArray Consortium: a Network for Understanding the Genetic Architecture of Common Cancers. *Cancer Epidemiol Biomarkers Prev* (2016).
35. Antoniou, A.C. *et al.* A weighted cohort approach for analysing factors modifying disease risks in carriers of high-risk susceptibility genes. *Genet Epidemiol* **29**, 1-11 (2005).
36. Barnes, D.R., Lee, A., Easton, D.F. & Antoniou, A.C. Evaluation of association methods for analysing modifiers of disease risk in carriers of high-risk mutations. *Genet Epidemiol* **36**, 274-91 (2012).
37. Ahsan, H. *et al.* A genome-wide association study of early-onset breast cancer identifies PFKM as a novel breast cancer gene and supports a

common genetic spectrum for breast cancer at any age. *Cancer Epidemiol Biomarkers Prev* **23**, 658-69 (2014).

38.   Stevens, K.N. *et al.* 19p13.1 is a triple-negative-specific breast cancer susceptibility locus. *Cancer Res* **72**, 1795-803 (2012).

39.   Willer, C.J., Li, Y. & Abecasis, G.R. METAL: fast and efficient meta-analysis of genomewide association scans. *Bioinformatics* **26**, 2190-1 (2010).

40.   Maller, J.B. *et al.* Bayesian refinement of association signals for 14 loci in 3 common diseases. *Nat Genet* **44**, 1294-301 (2012).

41.   Udler, M.S., Tyrer, J. & Easton, D.F. Evaluating the power to discriminate between highly correlated SNPs in genetic association studies. *Genet Epidemiol* **34**, 463-8 (2010).

42.   ENCODE Project Consortium. A user's guide to the encyclopedia of DNA elements (ENCODE). *PLoS Biol* **9**, e1001046 (2011).

43.   Kheradpour, P. & Kellis, M. Systematic discovery and characterization of regulatory motifs in ENCODE TF binding experiments. *Nucleic Acids Res* **42**, 2976-87 (2014).

44.   Kundaje, A. *et al.* Integrative analysis of 111 reference human epigenomes. *Nature* **518**, 317-30 (2015).

45.   Boyle, A.P. *et al.* Annotation of functional variation in personal genomes using RegulomeDB. *Genome Res* **22**, 1790-7 (2012).

46.   He, B., Chen, C., Teng, L. & Tan, K. Global view of enhancer-promoter interactome in human cells. *Proc Natl Acad Sci U S A* **111**, E2191-9 (2014).

47.   Rao, S.S. *et al.* A 3D map of the human genome at kilobase resolution reveals principles of chromatin looping. *Cell* **159**, 1665-80 (2014).

48.   Corradin, O. *et al.* Combinatorial effects of multiple enhancer variants in linkage disequilibrium dictate levels of gene expression to confer susceptibility to common traits. *Genome Res* **24**, 1-13 (2014).

49.   Forrest, A.R. *et al.* A promoter-level mammalian expression atlas. *Nature* **507**, 462-70 (2014).

50.   GTEx Consortium. Human genomics. The Genotype-Tissue Expression (GTEx) pilot analysis: multitissue gene regulation in humans. *Science* **348**, 648-60 (2015).

51.   Hnisz, D. *et al.* Super-enhancers in the control of cell identity and disease. *Cell* **155**, 934-47 (2013).

52.   Westra, H.J. *et al.* Systematic identification of trans eQTLs as putative drivers of known disease associations. *Nat Genet* **45**, 1238-43 (2013).

53.   James, L.I. *et al.* Small-molecule ligands of methyl-lysine binding proteins: optimization of selectivity for L3MBTL3. *J Med Chem* **56**, 7358-71 (2013).

54.   Sukari, A., Muqbil, I., Mohammad, R.M., Philip, P.A. & Azmi, A.S. F-BOX proteins in cancer cachexia and muscle wasting: Emerging regulators and therapeutic opportunities. *Semin Cancer Biol* **36**, 95-104 (2016).

55.   Ling Zheng, L. *et al.* Interaction of Heat Shock Protein Cpn10 with the Cyclin E/Cdk2 Substrate Nuclear Protein Ataxia-Telangiectasia (NPAT) Is Involved in Regulating Histone Transcription. *J Biol Chem* **290**, 29290-300 (2015).

56.   Easton, D.F. *et al.* Gene-panel sequencing and the prediction of breast-cancer risk. *N Engl J Med* **372**, 2243-57 (2015).

57.   Rogers, S. *et al.* Cyclin E2 is the predominant E-cyclin associated with NPAT in breast cancer cells. *Cell Div* **10**, 1 (2015).

58.   Li, Q. *et al.* Integrative eQTL-based analyses reveal the biology of breast cancer risk loci. *Cell* **152**, 633-41 (2013).

59. Cancer Genome Atlas Network. Comprehensive molecular portraits of human breast tumours. *Nature* **490**, 61-70 (2012).
60. Curtis, C. *et al.* The genomic and transcriptomic architecture of 2,000 breast tumours reveals novel subgroups. *Nature* **486**, 346-52 (2012).
61. Merico, D., Isserlin, R., Stueker, O., Emili, A. & Bader, G.D. Enrichment map: a network-based method for gene-set enrichment visualization and interpretation. *PLoS One* **5**, e13984 (2010).
62. Wang, K., Li, M. & Bucan, M. Pathway-based approaches for analysis of genomewide association studies. *Am J Hum Genet* **81**, 1278-83 (2007).
63. Wang, K., Li, M. & Hakonarson, H. Analysing biological pathways in genome-wide association studies. *Nat Rev Genet* **11**, 843-54 (2010).
64. Wang, L., Jia, P., Wolfinger, R.D., Chen, X. & Zhao, Z. Gene set analysis of genome-wide association studies: methodological issues and perspectives. *Genomics* **98**, 1-8 (2011).
65. Hacker, B.M. *et al.* Cloning, chromosomal mapping, and regulatory properties of the human type 9 adenylyl cyclase (ADCY9). *Genomics* **50**, 97-104 (1998).
66. Melhem-Bertrandt, A. *et al.* Beta-blocker use is associated with improved relapse-free survival in patients with triple-negative breast cancer. *J Clin Oncol* **29**, 2645-52 (2011).
67. Pon, C.K., Lane, J.R., Sloan, E.K. & Halls, M.L. The beta2-adrenoceptor activates a positive cAMP-calcium feedforward loop to drive breast cancer cell invasion. *FASEB J* **30**, 1144-54 (2016).
68. Finucane, H.K. *et al.* Partitioning heritability by functional annotation using genome-wide association summary statistics. *Nat Genet* **47**, 1228-35 (2015).
69. Bulik-Sullivan, B. *et al.* An atlas of genetic correlations across human diseases and traits. *Nat Genet* **47**, 1236-41 (2015).
70. Bulik-Sullivan, B.K. *et al.* LD Score regression distinguishes confounding from polygenicity in genome-wide association studies. *Nat Genet* **47**, 291-5 (2015).
71. Milne, R.L. & Antoniou, A.C. Genetic modifiers of cancer risk for BRCA1 and BRCA2 mutation carriers. *Ann Oncol* **22 Suppl 1**, i11-7 (2011).
72. Mavaddat, N. *et al.* Prediction of breast cancer risk based on profiling with common genetic variants. *J Natl Cancer Inst* **107**(2015).

Figure legends

Figure 1. Genomic region around independent ER negative risk associated variants, 11_108345515_G_A (rs11374964) and 11_108357137_G_A (rs74911261). One Mb region showing statistical significance of all genotyped and imputed SNPs and positions of candidate causal variants for two independent signals (shown below as red or blue ticks) in relation to RefSeq genes. Missense variants are labelled with asterisks. Breast cell enhancers overlapping candidate SNPs predicted to target nearby genes by IM-PET[46] are depicted as black bars. Chromatin interactions from ENCODE ChIA-PET in MCF7 cells overlapping candidate variants are shaded to reflect interaction confidence scores. Epigenomic features (derived from publicly available ChIP-seq and DNase-seq) that overlap candidate variants are shown as red or blue segments, depending on the intersected signal. Density tracks show the summed occurrence of ChIP-seq and DNase-seq peak signals at each position. Roadmap Epigenomics Project chromatin state models for HMEC and myoepithelial cells grouped into enhancer, promoter or transcribed annotations are shown as yellow, red or green segments, respectively. Transcript levels in MCF7 and HMEC cells are represented by histograms depicting mean normalised RNA-seq expression. All MCF7 ChIA-PET (ENCODE) and HMEC Hi-C[47] chromatin interactions are represented by black and blue arcs, respectively. NHGRI catalog GWAS SNPs are shown as green ticks. All Oncoarray SNPs (genotyped or imputed) are shown as black ticks and uninterrogated, common SNPs (dbSNP138, EUR MAF > 1%) as red ticks. Features may be examined in detail via exploration of a custom UCSC Genome Browser session accessible via hyperlinks within Supplementary Table 5.

Table 1: Ten novel loci associated with risk of estrogen receptor (ER)-negative breast cancer using meta-analysis of BCAC and CIMBA data

Location	SNP	Chr	Position	Nearest gene	Alleles[#]	BCAC ER-negative[†]			CIMBA *BRCA1* mutation carriers[‡]			Meta-analysis P-value	Heterogeneity P-value[¥]
						MAF	OR (95%CI)	P-value	MAF	HR (95%CI)	P-value		
2p23.3	rs200648189	2	24739694	*NCOA1*	CT/C	0.19	0.94 (0.91-0.97)	4.7×10^{-4}	0.20	0.88 (0.84-0.92)	3.3×10^{-7}	9.7×10^{-9}	2.0×10^{-2}
6q23.1	rs6569648	6	130349119	*L3MBTL3*	T/C	0.23	0.93 (0.90-0.95)	4.3×10^{-8}	0.22	0.94 (0.90-0.98)	5.4×10^{-3}	8.3×10^{-10}	0.64
8p23.3	rs66823261	8	170692	*RPL23AP53*	T/C	0.23	1.09 (1.06-1.12)	5.6×10^{-9}	0.22	1.02 (0.98-1.07)	0.32	3.3×10^{-8}	3.0×10^{-2}
8q24.13	rs17350191	8	124757661	*ANXA13*	C/T	0.34	1.07 (1.04-1.09)	2.0×10^{-8}	0.34	1.08 (1.04-1.12)	1.9×10^{-4}	1.7×10^{-11}	0.81
11q22.3	rs11374964	11	108345515	*KDELC2*	G/GA	0.42	0.94 (0.92-0.96)	3.6×10^{-8}	0.43	0.91 (0.88-0.95)	1.3×10^{-6}	4.1×10^{-13}	0.26
11q22.3	rs74911261	11	108357137	*KDELC2*	G/A	0.02	0.82 (0.75-0.89)	2.3×10^{-6}	0.02	0.74 (0.65-0.84)	2.0×10^{-6}	5.4×10^{-11}	0.17
16p13.3	rs11076805	16	4106788	*ADCY9*	C/A	0.25	0.92 (0.90-0.95)	2.2×10^{-8}	0.25	0.96 (0.92-1.00)	0.073	1.4×10^{-8}	0.14
18q12.1	rs36194942	18	25401204	*CDH2*	A/AT	0.30	0.94 (0.91-0.96)	2.5×10^{-7}	0.31	0.95 (0.91-0.99)	1.4×10^{-2}	1.4×10^{-8}	0.50
19p13.2	rs322144	19	11423703	*TSPAN16*	C/G	0.47	0.95 (0.93-0.97)	2.4×10^{-5}	0.46	0.92 (0.89-0.96)	3.7×10^{-5}	7.4×10^{-9}	0.23
19q12	rs113701136	19	30277729	*CCNE1*	C/T	0.32	1.07 (1.04-1.09)	1.7×10^{-7}	0.32	1.05 (1.01-1.09)	1.2×10^{-2}	6.8×10^{-9}	0.57

[#]More common allele listed first, minor allele second; [†]Combined data from 21,468 ER-negative cases and 100,594 controls of European ancestry from the Breast Cancer Association Consortium (BCAC); [‡]Combined data from 18,908 *BRCA1* mutation carriers from the Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA), 9,414 of whom had developed breast cancer; [¥]Test for heterogeneity in effect size for ER-negative disease and overall disease for *BRCA1* mutation carriers

Chr, chromosome; MAF, minor allele frequency; OR, odds ratio per copy of the minor allele; CI, confidence interval; HR, hazard ratio per copy of the minor allele

Table 2: Previously reported estrogen receptor (ER)-negative hits: replication using independent data from BCAC and combined results using all BCAC and CIMBA data

Location	SNP	Chr	Position	Ref	Nearest gene	Alleles[#]	INDEPENDENT REPLICATION			ALL AVAILABLE DATA COMBINED			
							BCAC ER-negative (OncoArray)*			BCAC ER-negative[†]		CIMBA *BRCA1*[‡]	
							MAF	OR (95%CI)	P-value	OR (95%CI)	P-value	HR (95%CI)	P-value
1q32.1	rs6678914	1	202187176	19	*LGR6*	G/A	0.41	0.94 (0.91-0.97)	1.1×10^{-4}	0.92 (0.90-0.94)	2.6×10^{-12}	0.98 (0.95-1.02)	0.31
1q32.1	rs4245739	1	204518842	19	*MDM4*	A/C	0.26	1.12 (1.09-1.17)	9.2×10^{-11}	1.14 (1.11-1.16)	3.1×10^{-23}	1.09 (1.04-1.13)	7.3×10^{-5}
2p24.1	rs12710696	2	19320803	19	*MIR4757*	C/T	0.37	1.04 (1.00-1.07)	2.5×10^{-2}	1.06 (1.04-1.09)	6.5×10^{-8}	1.01 (0.98-1.05)	0.49
2p23.2	rs4577244[‡]	2	29120733	30	*WDR43*	C/T	0.34	0.93 (0.89-0.96)	9.6×10^{-5}	0.92 (0.90-0.95)	1.5×10^{-9}	0.92 (0.88-0.96)	1.3×10^{-4}
5p15.33	rs10069690	5	1279790	9,18	*TERT*	C/T	0.26	1.19 (1.14-1.23)	3.8×10^{-21}	1.18 (1.15-1.21)	1.5×10^{-35}	1.18 (1.14-1.23)	3.7×10^{-16}
6q25.1	rs3757322[‡]	6	151942194	29	*ESR1*	T/G	0.32	1.14 (1.10-1.18)	5.5×10^{-14}	1.15 (1.12-1.18)	2.8×10^{-31}	1.14 (1.10-1.19)	2.9×10^{-12}
6q25.2	rs2747652[‡]	6	152437016	29	*ESR1*	C/T	0.48	0.92 (0.89-0.95)	1.1×10^{-7}	0.91 (0.89-0.93)	1.9×10^{-18}	1.00 (0.97-1.04)	0.96
13q22.1	rs6562760[‡]	13	73957681	30	*KLF5*	G/A	0.24	0.92 (0.88-0.95)	5.0×10^{-6}	0.92 (0.90-0.95)	8.7×10^{-10}	0.89 (0.86-0.93)	3.5×10^{-7}
16q12.2	rs11075995	16	53855291	19	*FTO*	T/A	0.30	1.07 (1.03-1.11)	3.3×10^{-4}	1.09 (1.06-1.12)	1.0×10^{-10}	1.01 (0.97-1.06)	0.49
19p13.11	rs67397200	19	17401404	3,31	*ANKLE1*	C/G	0.32	1.17 (1.13-1.21)	7.0×10^{-20}	1.17 (1.14-1.19)	2.7×10^{-37}	1.18 (1.14-1.23)	2.7×10^{-17}
20q11.21	rs2284378	20	32588095	12	*RALY*	C/T	0.32	0.99 (0.95-1.02)	0.46	1.03 (1.01-1.06)	1.7×10^{-2}	1.00 (0.97-1.04)	0.81

[#]More common allele listed first, minor allele second; *Includes Breast Cancer Association Consortium (BCAC) OncoArray data from 9,655 ER-negative cases and 45,494 controls cases and controls not included in previously published studies; [†]Combined data from 21,468 ER-negative cases and 100,594 controls of European ancestry from BCAC, which includes overlapping samples with previous publications for all SNPs; [‡]Combined data from 18,908 *BRCA1* mutation carriers from the Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA), 9,414 of whom had developed breast cancer - includes overlapping samples with previous publications for SNPs rs4577244, rs3757322, rs2747652 and rs6562760

Chr, chromosome; Ref, publication(s) in reference list in which the association was identified; MAF, minor allele frequency; OR, odds ratio per copy of the minor allele; CI, confidence interval; HR, hazard ratio per copy of the minor allele

Table 3: Associations for 10 novel and 10 previously reported (and replicated) ER-negative breast cancer susceptibility loci, by triple-negative status (BCAC data only: ER-negative cases[‡], all controls))

Location	SNP	Triple-negative		Other ER-negative		Heterogeneity
		OR (95%CI)	P-value	OR (95%CI)	P-value	P-value*
Loci identified by the present study						
2p23.3	rs200648189	0.95 (0.90-1.00)	4.8×10^{-2}	0.96 (0.91-1.03)	0.24	0.36
6q23.1	rs6569648	0.93 (0.89-0.97)	1.4×10^{-3}	0.93 (0.88-0.98)	5.6×10^{-3}	0.91
8p23.3	rs66823261	1.11 (1.05-1.16)	3.3×10^{-5}	1.12 (1.07-1.19)	2.4×10^{-5}	0.91
8q24.13	rs17350191	1.07 (1.03-1.11)	7.9×10^{-4}	1.07 (1.02-1.12)	4.0×10^{-3}	0.67
11q22.3	rs11374964	0.88 (0.85-0.91)	1.9×10^{-11}	0.99 (0.95-1.04)	0.75	1.5×10^{-5}
11q22.3	rs74911261	0.76 (0.66-0.87)	1.1×10^{-4}	0.98 (0.84-1.13)	0.76	3.0×10^{-2}
16p13.3	rs11076805	0.91 (0.87-0.96)	1.5×10^{-4}	0.95 (0.90-1.00)	4.5×10^{-2}	0.20
18q12.1	rs36194942	0.93 (0.89-0.96)	2.4×10^{-4}	0.92 (0.88-0.97)	9.9×10^{-4}	0.94
19p13.2	rs322144	0.94 (0.91-0.98)	5.9×10^{-3}	0.94 (0.90-0.98)	9.7×10^{-3}	0.68
19q12	rs113701136	1.10 (1.06-1.15)	9.1×10^{-7}	1.07 (1.02-1.12)	4.4×10^{-3}	0.12
Previously reported loci (associations replicated by the present study)						
1q32.1	rs6678914	0.94 (0.91-0.98)	2.1×10^{-3}	0.91 (0.87-0.95)	2.0×10^{-5}	0.45
1q32.1	rs4245739	1.18 (1.13-1.23)	4.3×10^{-15}	1.04 (1.00-1.10)	7.5×10^{-2}	6.5×10^{-4}
2p24.1	rs12710696	1.07 (1.03-1.11)	1.1×10^{-3}	1.04 (1.00-1.09)	6.1×10^{-2}	0.52
2p23.2	rs4577244	0.90 (0.86-0.94)	5.3×10^{-6}	0.94 (0.89-0.99)	1.9×10^{-2}	0.15
5p15.33	rs10069690	1.28 (1.23-1.33)	2.4×10^{-33}	1.07 (1.02-1.12)	5.4×10^{-3}	5.6×10^{-8}
6q25.1	rs3757322	1.15(1.10-1.19)	4.3×10^{-12}	1.14(1.10-1.20)	4.8×10^{-9}	0.35
6q25.2	rs2747652	0.93(0.89-0.96)	5.7×10^{-5}	0.87(0.83-0.91)	2.9×10^{-10}	9.6×10^{-3}
13q22.1	rs6562760	0.94 (0.90-0.98)	2.8×10^{-3}	0.92 (0.87-0.96)	8.8×10^{-4}	0.46
16q12.2	rs11075995	1.06 (1.02-1.11)	6.5×10^{-3}	1.08 (1.03-1.13)	3.1×10^{-3}	0.81
19p13.11	rs67397200	1.27 (1.22-1.32)	2.0×10^{-32}	1.05 (1.01-1.10)	2.7×10^{-2}	4.7×10^{-10}

[‡]Combined Breast Cancer Association Consortium (BCAC) data from 6,877 triple-negative and 4,467 other ER-negative cases and 83,700 controls; *ER-negative case-only analysis, by triple-negative status; OR, odds ratio per copy of the minor allele; CI, confidence interval

Table 4: Associations for 10 novel and 10 previously reported (and replicated) ER-negative breast cancer susceptibility loci, by grade (BCAC data only: ER-negative cases[‡], all controls)

Location	SNP	Grade 1		Grade 2		Grade 3		Heterogeneity
		OR (95%CI)	P-value	OR (95%CI)	P-value	OR (95%CI)	P-value	P-value*
Loci identified by the present study								
2p23.3	rs200648189	1.11 (0.92-1.33)	0.28	0.95 (0.88-1.03)	0.23	0.96 (0.91-1.00)	6.8×10^{-2}	0.70
6q23.1	rs6569648	0.93 (0.79-1.09)	0.37	0.93 (0.87-0.99)	1.6×10^{-2}	0.94 (0.91-0.98)	3.8×10^{-3}	0.34
8p23.3	rs66823261	1.13 (0.96-1.34)	0.14	1.12 (1.04-1.19)	1.2×10^{-3}	1.10 (1.05-1.15)	1.3×10^{-5}	0.11
8q24.13	rs17350191	1.16 (1.01-1.34)	3.0×10^{-2}	1.05 (0.99-1.11)	0.10	1.09 (1.05-1.12)	4.1×10^{-6}	0.94
11q22.3	rs11374964	0.91 (0.79-1.04)	0.16	0.99 (0.94-1.05)	0.85	0.93 (0.90-0.96)	1.3×10^{-5}	3.0×10^{-2}
11q22.3	rs74911261	1.22 (0.81-1.84)	0.35	0.89 (0.73-1.07)	0.21	0.74 (0.65-0.85)	7.4×10^{-6}	6.7×10^{-4}
16p13.3	rs11076805	0.90 (0.76-1.06)	0.21	0.93 (0.87-0.99)	3.2×10^{-2}	0.92 (0.88-0.95)	4.5×10^{-5}	0.71
18q12.1	rs36194942	0.97 (0.84-1.13)	0.73	0.93 (0.88-0.99)	2.2×10^{-2}	0.96 (0.92-0.99)	2.3×10^{-2}	0.98
19p13.2	rs322144	0.94 (0.81-1.08)	0.38	0.95 (0.90-1.01)	0.11	0.96 (0.93-1.00)	6.4×10^{-2}	0.48
19q12	rs113701136	1.02 (0.89-1.18)	0.77	1.06 (1.01-1.13)	3.0×10^{-2}	1.10 (1.06-1.14)	2.5×10^{-7}	0.12
Previously reported loci (associations replicated by the present study)								
1q32.1	rs6678914	0.95 (0.83-1.09)	0.46	0.90 (0.85-0.95)	9.3×10^{-5}	0.92 (0.89-0.95)	1.2×10^{-6}	0.75
1q32.1	rs4245739	1.02 (0.88-1.19)	0.75	1.05 (0.99-1.12)	8.7×10^{-2}	1.18 (1.14-1.22)	2.5×10^{-18}	4.3×10^{-5}
2p24.1	rs12710696	1.08 (0.94-1.23)	0.28	1.10 (1.04-1.16)	9.6×10^{-4}	1.04 (1.01-1.08)	1.6×10^{-2}	0.28
2p23.2	rs4577244	1.02 (0.88-1.20)	0.77	0.95 (0.89-1.01)	9.4×10^{-2}	0.90 (0.86-0.93)	1.2×10^{-7}	4.0×10^{-2}
5p15.33	rs10069690	0.96 (0.83-1.12)	0.64	1.07 (1.01-1.14)	2.2×10^{-2}	1.21 (1.17-1.26)	1.5×10^{-24}	7.3×10^{-4}
6q25.1	rs3757322	1.16 (1.01-1.34)	0.04	1.13 (1.07-1.20)	7.5×10^{-6}	1.18 (1.14-1.22)	4.5×10^{-20}	0.16
6q25.2	rs2747652	0.86 (0.75-0.98)	0.02	0.92 (0.87-0.97)	1.9×10^{-3}	0.90 (0.87-0.93)	1.6×10^{-9}	0.61
13q22.1	rs6562760	0.98 (0.84-1.15)	0.82	0.92 (0.87-0.98)	1.4×10^{-2}	0.91 (0.88-0.95)	1.2×10^{-5}	0.52
16q12.2	rs11075995	1.16 (1.00-1.35)	4.7×10^{-2}	1.09 (1.02-1.15)	7.5×10^{-3}	1.08 (1.04-1.13)	5.2×10^{28}	0.42
19p13.11	rs67397200	1.01 (0.87-1.16)	0.91	1.08 (1.02-1.14)	9.8×10^{-3}	1.22 (1.18-1.26)	5.3×10^{-37}	1.3×10^{-3}

[‡]Combined Breast Cancer Association Consortium (BCAC) data from 492 grade 1, 3,243 grade 2 and 8,568 grade 3 cases and 82,347 controls; * ER-negative case-only analysis of BCAC data, by grade (trend test, 1df); OR, odds ratio per copy of the minor allele; CI, confidence interval

Online Methods

Study subjects
Supplementary Table 1 summarises the studies from the Breast Cancer Association Consortium (BCAC) that contributed data. The majority were case-control studies. Sixty-eight BCAC studies participated in the ER-negative breast cancer component of the OncoArray, contributing 9,655 cases and 45,494 controls. All studies provided core data on disease status and age at diagnosis/observation, and the majority provided information on clinico-pathological and lifestyle factors, which have been curated and incorporated into the BCAC database (version 6). Estrogen receptor status for most (~70%) cases was obtained from clinical records. After removal of overlapping participants, genotype data were also available from eight GWASs[9,12,16,37,38] (4,480 ER-negative cases and 12,632 controls) and 40 studies previously genotyped using the Illumina iCOGS custom array[20] (7,333 ER-negative cases and 42,468 controls).

A total of 21,468 ER-negative cases were included in the combined analyses. Of those 5,793 had tumours that were also negative for progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) and were defined as triple-negative (TN). PR and HER2 status was also obtained predominantly from clinical records. A further 4,217 were positive for PR or HER and were considered non-TN. The remainder had unknown PR or HER status. All participating studies were approved by their appropriate ethics review boards and all subjects provided informed consent.

Subjects included from the Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA) were women of European ancestry aged 18 years or older with a pathogenic variant in *BRCA1*. The majority of the participants were sampled through cancer genetics clinics. Multiple members of the same families were included in some instances. Fifty-eight studies from 24 countries contributed Oncoarray genotype data. After quality control (see below) and removal of overlapping participants with the BCAC OncoArray study, data were available on 15,566 *BRCA1* mutation carriers, of whom 7,784 were affected with breast cancer (Supplementary Table 2). We also obtained iCOGS genotype data on 3,342 *BRCA1* mutation carriers (1,630 with breast cancer) from 54 studies through CIMBA. All mutation carriers provided written informed consent and participated under ethically approved protocols.

OncoArray SNP selection
Approximately 50% of the SNPs for the OncoArray were selected as a "GWAS backbone" (Illumina HumanCore), which aimed to provide high coverage for the majority of common variants through imputation. The remaining allocation was selected from lists supplied by each of six disease-based consortia, together with a seventh lists of SNPs of interest to multiple disease groups. Approximately 72k SNPs were selected specifically for their relevance to breast cancer, based on prior evidence of association with overall or subtype-specific disease, with breast density or with breast tissue specific gene expression. Lists were merged, as described previously[34].

Genotype calling and quality control

Details of the genotype calling and quality control (QC) for the iCOGS and GWAS are described elsewhere[19,20,23,30], and those for OncoArray are described in the Supplementary Note.

Imputation
Genotypes for ~21M SNPs were imputed for all samples using the October 2014 (Phase 3) release of the 1000 Genomes Project data as the reference panel and Nhap=800. The iCOGS, OncoArray and six of the GWAS datasets were imputed using a two-stage imputation approach, using SHAPEIT[73] for phasing and IMPUTEv2[74] for imputation. The imputation was performed in 5Mb non-overlapping intervals. All subjects were split into subsets of ~10,000 samples, with subjects from the same grouped in the subset. The Breast and Prostate Cancer Cohort Consortium (BPC3) and Breast Cancer Family Registry (BCFR) GWAS performed the imputation separately using MACH and Minimac[75,76]. We imputed genotypes for all SNPs that were polymorphic (MAF>0.1%) in either European or Asian samples. For the BCAC GWAS, data were included in the analysis for all SNPs with MAF>0.01 and imputation r^2>0.3. For iCOGS and OncoArray we included data for all SNPs with imputation r^2>0.3 and MAF>0.005.

Statistical analyses of BCAC data
Per-allele odds ratios and standard errors were generated for the Oncoarray, iCOGS and each GWAS, adjusting for principal components using logistic regression. The Oncorray and iCOGS analyses were additionally adjusted for country and study, respectively. For the OncoArray dataset, principal components analysis was performed using data for 33,661 SNPs (which included the 2,318 markers of continental ancestry) with a MAF≥0.05 and maximum correlation of 0.1, using purpose-written software (PCcalc; see URLs section) to allow standard calculations to be performed sufficiently rapidly on a very large dataset. We used the first 10 principal components, as additional components did not further reduce inflation in the test statistics. We used nine principal components for the iCOGS and up to 10 principal components for the other GWAS, where this was found to reduce inflation.

OR estimates were derived using MACH for the BCFR GWAS, ProbABEL[77] for the BPC3 GWAS, SNPTEST (see URLs section) for the remaining GWAS and purpose written software for the iCOGS and Oncoarray datasets. OR estimates and standard errors were combined by a fixed effects inverse variance meta-analysis using METAL[39]. This was first done across the eight GWAS, applying genomic control, as described previously[20]. It was then applied (without genomic control) to combine findings from the three BCAC genotyping initiatives (GWAS, iCOGS, OncoArray).

The independence of signals from two variants at 11q22.3 was by fitting the logistic regression models described above with both variants as covariates. This was done separately for iCOGS and OncoArray data and results for each variant combined by meta-analysis.

For selected SNPs we estimated per-allele ORs by ER-status using all available BCAC data for 82,263 cases with known ER status and 87,962 controls from the iCOGS and OncoArray studies. We also estimated the per-allele ORs by TN status (TN versus other ER-negative subtypes) and tumour grade, using available BCAC data for ER-negative cases and corresponding controls. Tests for heterogeneity by

subtype were derived by applying logistic regression to cases only. This was done separately for the iCOGS and Oncoarray datasets, adjusted as before, and then combined in a fixed-effects meta-analysis. Multinomial regression was applied to cases only to test a linear trend for grade, with the model constrained so that the difference between grade 1 and 3 was double that for the difference between grade 2 and 3; this method was also used to test for a linear trend with age with ordinal values 1, 2, 3 and 4 representing ages <40, 40-49, 50-59 and ≥60, respectively.

Statistical analyses of CIMBA data
Associations between genotypes and breast cancer risk for *BRCA1* mutation carriers were evaluated using a 1*df* per allele trend-test (*P*-trend), based on modeling the retrospective likelihood of the observed genotypes conditional on breast cancer phenotypes[36]. This was done separately for iCOGS and OncoArray data. To allow for the non-independence among related individuals, an adjusted test statistic was used which took into account the correlation in genotypes[3]. All analyses were stratified by country of residence and, for countries where strata were sufficiently large (USA and Canada), by Ashkenazi Jewish ancestry. The results from the iCOGS and OncoArray datasets were then pooled using fixed effects meta-analysis. We repeated these analyses modelling ovarian cancer as a competing risk and observed no substantial difference in the results obtained.

The independence of signals from two variants at 11q22.3 was assessed using OncoArray data only, fitting a Cox regression model with per-allele effects for both variants, adjusting for birth cohort, stratified by country of residence and using robust standard errors and clustered observations for relatives. This approach provides valid significance tests of associations, although the HR estimates can be biased[35].

Meta-analysis of BCAC and CIMBA
A fixed effects meta-analysis of results from BCAC and CIMBA was conducted using an inverse variance approach assuming fixed effects, as implemented in METAL[39]. The effect estimates used were the logarithm of the per-allele hazard ratio (HR) estimate for the association with breast cancer risk in *BRCA1* mutation carriers from CIMBA and the logarithm of the per-allele OR estimate for the association with risk of ER-negative breast cancer based on BCAC data, both of which were assumed to approximate the same relative risk. We assessed genomic inflation using common (MAF>1%) GWAS backbone variants. As lambda is influenced by sample size, we calculated lambda1000 to be comparable with other studies.

All statistical tests conducted were two-sided.

Definition of known hits
We identified all associations previously reported from genome-wide or candidate analysis at a significance level $P<5\times10^{-8}$ for overall breast cancer, ER-negative or ER-positive breast cancer, in *BRCA1* or *BRCA2* carriers, or in meta-analyses of these categories. We included only one SNP in any 500kb interval, unless joint analysis provided genome-wide significant evidence (conditional $P<5\times10^{-8}$) of more than one independent signal. Where multiple studies reported associations in the same region, we considered the first reported association unless a later study identified a different variant in the same region that was more strongly associated with breast cancer risk. One hundred and seven previously reported hits were

identified, 11 of these through GWAS of ER-negative disease or of breast cancer in *BRCA1* mutation carriers, or reported as more strongly associated with ER-negative breast cancer. These are listed in Table 2. The other 96 previously reported hits are listed in Supplementary Table 10.

Definition of new hits

To search for novel loci, we assessed all SNPs excluding those within 500kb of a known hit. This identified 206 SNPs in nine regions that were associated with disease risk at $P < 5 \times 10^{-8}$ in the meta-analysis of BCAC ER-negative breast cancer and CIMBA *BRCA1* mutation carriers. The SNP with lowest p-value from this analysis was considered the lead SNP. No additional loci were detected from the analysis of BCAC data only. Imputation quality, as assessed by the IMPUTE2 imputation r^2 in the Oncoarray dataset, was ≥0.89 for the 10 lead SNPs reported (Supplementary Table 3).

Candidate causal SNPs

To define the set of potentially causal variants at each of the novel susceptibility loci, we selected all variants with p-values within two orders of magnitude of the most significant SNP at each of the 10 novel loci. This is approximately equivalent to selecting variants whose posterior probability of causality is within two orders of magnitude of the most significant SNP[40,41]. This approach was applied to identify potentially causal variants for the signal given by the more frequent lead SNP at 11q22.3 (rs11374964). A similar approach was applied for the rarer lead SNP at this locus (rs74911261), but based on p-values from analyses adjusted for rs11374964.

Proportion of familial risk explained

The relative risk of ER-negative breast cancer for the first degree female relative of a woman with ER-negative disease has not been estimated. We therefore assumed that the 2-fold risk observed for overall disease also applied to ER-negative disease. In order to estimate the proportion of this explained by the 125 variants associated with ER-negative disease, we used minor allele frequency and OR estimates from the OncoArray-based genotype data and applied the formula:
$\sum_i p_i (1 - p_i)(\beta_i^2 - \tau_i^2)/\ln(\lambda))$, where p_i is the minor allele frequency for variant *i*, β_i is the log(OR) estimate for variant *i*, τ_i is the standard error of β_i and $\lambda=2$ is the assumed overall familial relative risk.

The corresponding estimate for the FRR due to all variants is the *frailty scale* heritability, defined as $h_f^2 = \sum_i 2p_i(1 - p_i)\gamma_i^2$, where the sum over all variants and γ_i is the true relative risk conferred by variant *i*, assuming a log-additive model. We first obtained the estimated heritability based on the full set of summary estimates using LD Score Regression[68], which derives a heritability estimate on the observed scale. We then converted this to an estimate on the fraility scale using the formula $h_f^2 = h_{obs}^2 \Big/ P(1 - P)$, where *P* is the proportion of samples in the population that are cases.

Proportion of polygenic risk-modifying variance explained for *BRCA1* carriers.

The proportion of the variance in the polygenic frailty modifying risk in BRCA1 carriers explained by the set of associated SNPs was estimated by $\sum_i \ln c_i/\sigma^2$, where

c_i is the squared estimated coefficient of variation in incidences associated with SNP_i[78] and σ^2 is the total polygenic variance, estimated from segregation data[79].

<u>*In Silico* Annotation of Candidate Causal variants</u>
We combined multiple sources of *in silico* functional annotation from public databases to help identify potential functional SNPs and target genes, based on previous observations that breast cancer susceptibility alleles are enriched in *cis*-regulatory elements and alter transcriptional activity[28,80-82]. The influence of candidate causal variants on transcription factor binding sites was determined using the ENCODE-Motifs resource[43]. To investigate functional elements enriched across the region encompassing the strongest candidate causal SNPs, we analysed chromatin biofeatures data from the Encyclopedia of DNA Elements (ENCODE) Project[42], Roadmap Epigenomics Projects[44] and other data obtained through the National Center for Biotechnology Information (NCBI) Gene Expression Omnibus (GEO) namely: Chromatin State Segmentation by Hidden Markov Models (chromHMM), DNase I hypersensitive and histone modifications of epigenetic markers H3K4, H3K9, and H3K27 in Human Mammary Epithelial (HMEC) and myoepithelial (MYO) cells, T47D and MCF7 breast cancer cells and transcription factor ChIP-seq in a range of breast cell lines (Supplementary Table 6). To identify the SNPs most likely to be functional we used RegulomeDB[45], and to identify putative target genes, we examined potential functional chromatin interactions between distal and proximal regulatory transcription-factor binding sites and the promoters at the risk regions, using Hi-C data generated in HMECs[47] and Chromatin Interaction Analysis by Paired End Tag (ChIA-PET) in MCF7 cells. This detects genome-wide interactions brought about by, or associated with, CCCTC-binding factor (CTCF), DNA polymerase II (POL2), and Estrogen Receptor (ER), all involved in transcriptional regulation[47]. Annotation of putative *cis*-regulatory regions and predicted target genes used the Integrated Method for Predicting Enhancer Targets (IM-PET)[46], the "Predicting Specific Tissue Interactions of Genes and Enhancers" (PreSTIGE) algorithm[48], Hnisz[51] and FANTOM[49]. Intersections between candidate causal variants and regulatory elements were identified using Galaxy, BedTools v2.24 and HaploReg v4.1, and visualised in the UCSC Genome Browser. Publically available eQTL databases including Gene-Tissue Expression (GTEx;[50] version 6, multiple tissues) and Westra[52] (blood), were queried for candidate causal variants.

<u>eQTL analyses</u>
Expression quantitative trait loci (eQTL) analyses were performed using data from The Cancer Genome Atlas (TCGA) and Molecular Taxonomy of Breast Cancer International Consortium (METABRIC) projects[59,60].

The TCGA eQTL analysis was based on 79 ER-negative breast tumors that had matched gene expression, copy number, and methylation profiles together with the corresponding germline genotypes available. All 79 individuals were of European ancestry as ascertained using the genotype data and the Local Ancestry in adMixed Populations (LAMP) software package (LAMP estimate cut-off >95% European)[83]. Germline genotypes were imputed into the 1000 Genomes reference panel (October 2014 release) using IMPUTE2[75,84]. Gene expression had been measured on the Illumina HiSeq 2000 RNA-Seq platform (gene-level RSEM normalized counts[85]), copy number estimates were derived from the Affymetrix SNP 6.0 (somatic copy

number alteration minus germline copy number variation called using the GISTIC2 algorithm[86]), and methylation beta values measured on the Illumina Infinium HumanMethylation450, as previously described[59]. Primary TCGA eQTL analysis focused on all potentially causal variants in the 10 new regions associated with breast cancer risk in the meta-analysis of ER-negative cases and controls from BCAC and *BRCA1* mutation carriers from CIMBA. We considered all genes located up to 1 Mb on either side of each of these variants. The effects of tumor copy number and methylation on gene expression were first removed using a method described previously[58], and eQTL analysis was performed by linear regression as implemented in the R package Matrix eQTL[87].

The METABRIC eQTL analysis was based on 135 normal breast tissue samples resected from breast cancer patients of European ancestry. Germline genotyping for the METABRIC study was also done on the Affymetrix SNP 6.0, and ancestry estimation and imputation for this data set was conducted as described for TCGA. Gene expression in the METABRIC study had been measured using the Illumina HT12 microarray platform and we used probe-level estimates. As for TCGA, we considered all genes in 10 regions using Matrix eQTL.

We also performed additional eQTL analyses using the METABRIC data set for all variants within 1 Mb of *L3MBTL3* and *CDH2* and the expression of these specific genes.

Global Genomic Enrichment Analyses
We performed stratified LD score regression analyses[68] for ER- breast cancer using the summary statistics based on the meta-analyses of OncoArray, GWAS, iCOGS and CIMBA. We used all SNPs in the 1000 Genomes Project phase 1 v3 release that had a minor allele frequency > 1% and an imputation quality score $R^2 > 0.3$ in the OncoArray data. LD scores were calculated using the 1000 Genomes Project Phase 1 v3 EUR panel. Further details are provided in the Supplementary Note.

We tested the differences in functional enrichment between ER-positive and ER-negative subsets for individual features through a Wald test, using the regression coefficients and standard errors for the two subsets based on the models described above. Finally, we assessed the heritability due to genotyped and imputed SNPs[70] and estimated the genetic correlation between ER-positive and ER-negative breast cancer[69]. The genetic correlation analysis was restricted to the ~1M SNPs included in HapMap 3.

Pathway Enrichment Analyses (see also the Supplementary Note)
The pathway gene set database Human_GOBP_AllPathways_no_GO_iea_January_19_2016_symbol.gmt (GeneSets; see URLs section)[61], was used for all analyses. Pathway size was determined by the total number of genes in the pathway to which SNPs in the imputed GWAS dataset could be mapped. To provide more biologically meaningful results, and reduce false positives, only pathways that contained between 10 and 200 genes were considered.

SNPs were mapped to the nearest gene within 500kb; those that were further than 500 kb away from any gene were excluded. Gene significance was calculated by

assigning the lowest p-value observed across all SNPs assigned to a gene[63,64], based on the meta-analysis of BCAC and CIMBA data described above.

The gene set enrichment analysis (GSEA)[61] algorithm, as implemented in the GenGen package (see URLs section)[62,63] was used to perform pathway analysis. Briefly, the algorithm calculates an enrichment score (ES) for each pathway based on a weighted Kolmogorov-Smirnov statistic[62]. Pathways that have most of their genes at the top of the ranked list of genes obtain higher ES values.

We defined an ES threshold (ES≥0.41) to yield a true-positive rate (TPR) of 0.20 and a false-positive rate (FPR) of 0.14, with true-positive pathways defined as those observed with false discovery rate (FDR)<0.05 in a prior analysis carried out using the analytic approach defined above applied to iCOGS data for ER-negative disease.

To visualize the pathway enrichment analysis results, an enrichment map was created using the Enrichment Map (EM) v 2.1.0 app[61] in Cytoscape v3.30[88], applying an edge-weighted force directed layout. To measure the contribution of each gene to enriched pathways and annotate the map, we reran the pathway enrichment analysis multiple times, each time excluding one gene. A gene was considered to drive the enrichment if the ES dropped to zero or less (pathway enrichment driver) after it was excluded. Pathways were grouped in the map if they shared >70% of their genes or their enrichment was driven by a shared gene.

Online-only References

73. Delaneau, O., Marchini, J. & Zagury, J.F. A linear complexity phasing method for thousands of genomes. *Nat Methods* **9**, 179-81 (2012).
74. Howie, B.N., Donnelly, P. & Marchini, J. A flexible and accurate genotype imputation method for the next generation of genome-wide association studies. *PLoS Genet* **5**, e1000529 (2009).
75. Howie, B., Fuchsberger, C., Stephens, M., Marchini, J. & Abecasis, G.R. Fast and accurate genotype imputation in genome-wide association studies through pre-phasing. *Nat Genet* **44**, 955-9 (2012).
76. Li, Y., Willer, C.J., Ding, J., Scheet, P. & Abecasis, G.R. MaCH: using sequence and genotype data to estimate haplotypes and unobserved genotypes. *Genet Epidemiol* **34**, 816-34 (2010).
77. Aulchenko, Y.S., Struchalin, M.V. & van Duijn, C.M. ProbABEL package for genome-wide association analysis of imputed data. *BMC Bioinformatics* **11**, 134 (2010).
78. Antoniou, A.C. & Easton, D.F. Polygenic inheritance of breast cancer: Implications for design of association studies. *Genet Epidemiol* **25**, 190-202 (2003).
79. Antoniou, A.C. *et al.* The BOADICEA model of genetic susceptibility to breast and ovarian cancers: updates and extensions. *Br J Cancer* **98**, 1457-66 (2008).
80. Darabi, H. *et al.* Polymorphisms in a Putative Enhancer at the 10q21.2 Breast Cancer Risk Locus Regulate NRBF2 Expression. *Am J Hum Genet* **97**, 22-34 (2015).
81. Glubb, D.M. *et al.* Fine-scale mapping of the 5q11.2 breast cancer locus reveals at least three independent risk variants regulating MAP3K1. *Am J Hum Genet* **96**, 5-20 (2015).

82. Ghoussaini, M. *et al.* Evidence that breast cancer risk at the 2q35 locus is mediated through IGFBP5 regulation. *Nat Commun* **4**, 4999 (2014).
83. Baran, Y. *et al.* Fast and accurate inference of local ancestry in Latino populations. *Bioinformatics* **28**, 1359-67 (2012).
84. Abecasis, G.R. *et al.* An integrated map of genetic variation from 1,092 human genomes. *Nature* **491**, 56-65 (2012).
85. Li, B. & Dewey, C.N. RSEM: accurate transcript quantification from RNA-Seq data with or without a reference genome. *BMC Bioinformatics* **12**, 323 (2011).
86. Mermel, C.H. *et al.* GISTIC2.0 facilitates sensitive and confident localization of the targets of focal somatic copy-number alteration in human cancers. *Genome Biol* **12**, R41 (2011).
87. Shabalin, A.A. Matrix eQTL: ultra fast eQTL analysis via large matrix operations. *Bioinformatics* **28**, 1353-8 (2012).
88. Shannon, P. *et al.* Cytoscape: a software environment for integrated models of biomolecular interaction networks. *Genome Res* **13**, 2498-504 (2003).

Supplementary Table 5: Summary information from Bioinformatic and eQTL analyses

browser	variant	chrom	position	locus	rsID	TF_motifs(delta TF-ChIP)	Histone_modific ChromHMM_enh ChromHMM_pro Open_chromatin RegulomeDB scGWAS_traits	Overlapping_Ref K RefGene TSS dist Functional_anno eQTL_target_all eQTL_GTEx breast eQTL_TCGA	eQTL_METABRIC	Predicted_target_gene

:Hnis
A-PE
:Hnis
:Hnis

ICF7:ChIA-PET
ICF7:ChIA-PET
ICF7:ChIA-PET
ICF7:ChIA-PET
ICF7:ChIA-PET
ICF7:ChIA-PET

I.1:MCF7:ChIA-PET

I.1:MCF7:ChIA-PET

:hIA-PET
iiA-PET,,,FAM91A1:MCF7:ChIA-PET
iiA-PET

:hIA-PET
:hIA-PET
:hIA-PET
:hIA-PET

T

35

IM-PET,,,KDELC2:HMEC:IM-PET,,,C11orf65:MCF7:ChIA-PET,,,KDELC2:MCF7:ChIA-PET,,,C11orf65:HCC1954:IM-PET

,,LOC643923:GA:-:0.0405219
,,LOC643923:GA:-:0.0405219

f:ChIA-PET

ι-:0.0410264

⊃-:0.0320156,CLUAP1:C-:0.0477839,IL32:C+:0.048916
ι-:0.0293509
⊃+:0.0418819

2:4:MCF7:ChIA-PET

A-+:0.0297273

Supplementary Table 4: Results for the two novel ER-negative susceptibility loci on 11q22.3

SNP	Chr	Position	Alleles[#]	BCAC ER-negative[†]			CIMBA *BRCA1* mutation carriers[‡]		
				MAF	OR (95%CI)	P-value	MAF	HR (95%CI)	P-value
Each SNP modelled individually									
rs11374964	11	108345515	G/GA	0.42	0.94 (0.92-0.96)	3.6×10^{-7}	0.43	0.92 (0.89-0.95)	1.6×10^{-7}
rs74911261	11	108357137	G/A	0.02	0.81 (0.74-0.89)	3.7×10^{-6}	0.02	0.78 (0.70-0.87)	1.1×10^{-5}
Both SNPs modelled together									
rs11374964	11	108345515	G/GA	0.42	0.95 (0.93-0.97)	3.5×10^{-5}	0.43	0.93 (0.90-0.96)	5.1×10^{-6}
rs74911261	11	108357137	G/A	0.02	0.84 (0.76-0.91)	8.6×10^{-5}	0.02	0.81 (0.73-0.91)	3.3×10^{-4}

[#]More common allele listed first, minor allele second; [†]Combined data from 16,988 ER-negative cases and 87,962 controls of European ancestry from the Breast Cancer Association Consortium (BCAC) - results differ from those in Table 1 as GWAS data were excluded (unit record data was not available to run the models with both SNPs together); [‡]Combined OncoArray data from 15,566 *BRCA1* mutation carriers from the Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA), 7,784 of whom had developed breast cancer - estimates from multivariable Cox regression; Chr, chromosome; MAF, minor allele frequency; OR, odds ratio per copy of the minor allele; CI, confidence interval; HR, hazard ratio per copy of the minor allele

Supplementary Table 3: Ten novel loci associated with risk of estrogen receptor (ER)-negative breast cancer using meta-analysis of BCAC and CIMBA data, by genotyping initiative

Location	SNP	Chr	Position	Alleles¶	MAF	ER-negative breast cancer (BCAC) — GWAS OR(95%CI)	P-value	$I^2_{(s)}$	$P(het_s)$	$r^2(imp)$	iCOGS OR(95%CI)	P-value	$I^2_{(s)}$	$P(het_s)$	$r^2(imp)$	OncoArray OR(95%CI)	P-value	$I^2_{(s)}$	$P(het_s)$	$I^2_{(IG)}$	$P(het_G)$	$r^2(imp)$	CIMBA iCOGS HR(95%CI)	P-value	$r^2(imp)$	OncoArray HR(95%CI)	P-value	$I^2_{(c)}$	$P(het_c)$
2p23.3	rs200648189	2	24739694	CT/C	0.19	0.96 (0.88-1.06)	4.1×10^{-1}	0	0.93	0.57	0.93 (0.87-0.99)	2.3×10^{-2}	0	0.58	0.90	0.94 (0.90-0.99)	9.3×10^{-3}	0	0.95	0	0.83	0.52	0.93 (0.81-1.08)	3.5×10^{-1}	0.89	0.87 (0.83-0.92)	3.5×10^{-7}	0.09	0.34
6q23.1	rs6569648	6	130349119	T/C	0.23	0.88 (0.83-0.94)	1.4×10^{-4}	0	0.96	1.00	0.94 (0.89-0.98)	3.3×10^{-3}	0	0.79	1.00	0.94 (0.91-0.98)	1.8×10^{-3}	0	0.88	0.31	0.24	1.00	0.96 (0.86-1.06)	4.2×10^{-1}	1.00	0.94 (0.89-0.98)	7.0×10^{-1}	0	0.61
8p23.3	rs66823261	8	170692	T/C	0.23	1.02 (0.96-1.09)	4.7×10^{-1}	0	0.49	0.74	1.13 (1.08-1.19)	1.0×10^{-6}	0	0.71	0.92	1.08 (1.04-1.13)	8.2×10^{-5}	0	0.85	0.66	0.05	0.72	1.14 (1.01-1.29)	4.0×10^{-2}	0.92	1.01 (0.96-1.06)	8.2×10^{-1}	0.33	0.06
8q24.13	rs17350191	8	124757661	C/T	0.34	1.07 (1.01-1.13)	3.1×10^{-2}	0.43	0.09	1.00	1.06 (1.02-1.11)	1.9×10^{-3}	0.12	0.27	1.00	1.07 (1.04-1.11)	3.2×10^{-5}	0	0.71	0	0.94	1.00	1.03 (0.95-1.13)	4.6×10^{-1}	1.00	1.08 (1.04-1.13)	1.6×10^{-4}	0.22	0.16
11q22.3	rs11374964	11	108345515	G/GA	0.42	0.94 (0.88-1.00)	6.0×10^{-2}	0	0.69	1.00	0.97 (0.94-1.01)	1.4×10^{-1}	0.26	0.07	1.00	0.91 (0.88-0.94)	2.7×10^{-4}	0	0.66	0.68	0.04	1.00	0.96 (0.88-1.05)	4.1×10^{-1}	1.00	0.90 (0.87-0.94)	7.8×10^{-7}	0.18	0.24
11q22.3	rs74911261	11	108357137	G/A	0.02	0.88 (0.70-1.10)	2.6×10^{-1}	0	0.88	0.90	0.79 (0.68-0.92)	2.6×10^{-3}	0	0.86	1.00	0.82 (0.73-0.91)	4.0×10^{-4}	0.01	0.44	0	0.75	0.87	0.82 (0.58-1.15)	2.5×10^{-1}	1.00	0.73 (0.63-0.83)	3.3×10^{-6}	0	0.74
16p13.3	rs11076805	16	4106788	C/A	0.25	0.91 (0.86-0.97)	2.8×10^{-3}	0.40	0.11	0.72	0.94 (0.89-0.99)	1.9×10^{-2}	0	0.80	0.97	0.92 (0.89-0.96)	2.9×10^{-5}	0.18	0.24	0	0.76	0.72	1.02 (0.90-1.16)	7.3×10^{-1}	0.97	0.95 (0.91-1.00)	4.1×10^{-2}	0.09	0.34
18q12.1	rs36194942	18	25401204	A/AT	0.30	0.92 (0.85-0.99)	1.9×10^{-2}	0	0.52	0.95	0.96 (0.92-1.00)	5.1×10^{-2}	0	0.48	0.95	0.92 (0.89-0.96)	9.6×10^{-6}	0	0.99	0.15	0.31	0.94	0.96 (0.87-1.06)	4.5×10^{-1}	0.94	0.95 (0.91-0.99)	1.8×10^{-2}	0	0.65
19p13.2	rs322144	19	11423703	C/G	0.47	0.94 (0.89-0.99)	2.1×10^{-2}	0	0.73	0.51	0.96 (0.91-1.01)	1.0×10^{-1}	0	0.92	0.99	0.95 (0.92-0.98)	1.5×10^{-3}	0.29	0.11	0	0.86	0.50	0.89 (0.79-1.01)	7.2×10^{-2}	0.99	0.93 (0.89-0.96)	1.7×10^{-4}	0	0.48
19q12	rs113701136	19	30277729	C/T	0.32	1.04 (0.98-1.10)	1.6×10^{-1}	0	0.89	0.97	1.06 (1.02-1.10)	4.0×10^{-3}	0.26	0.07	0.98	1.08 (1.04-1.12)	2.1×10^{-5}	0	0.48	0	0.61	0.96	1.11 (1.01-1.22)	3.0×10^{-2}	0.98	1.04 (1.00-1.09)	7.7×10^{-2}	0.21	0.18

Chr, chromosome; ¶More common allele listed first, minor allele second; MAF, minor allele frequency; $I^2_{(s)}$, I^2 for between-study heterogeneity in the OR; $P(het_s)$, P-value for between-study heterogeneity in the OR; $I^2_{(IG)}$, I^2 for heterogeneity in the OR between genotyping initiatives (GWAS/iCOGS/OncoArray); $P(het_G)$, P-value for heterogeneity in the OR between genotyping initiative
$I^2_{(c)}$, I^2 for between-country heterogeneity in the HR; $P(het_c)$, P-value for between-country heterogeneity in the HR; $r^2(imp)$, imputation r^2; BCAC (Breast Cancer Association Consortium) results were based on GWAS data for 4,480 cases and 12,632 controls, iCOGS data for 7,333 cases and 42,468 controls and OncoArray data 9,655 cases and 45,494 controls
CIMBA (Consortium of Investigators of Modifiers of BRCA1/2) results were based on iCOGS data for 3,342 BRCA1 mutation carriers (1,630 with breast cancer) and OncoArray data for 15,566 BRCA1 mutation carriers (7,784 with breast cancer)

Supplementary Table 2: CIMBA studies contributing data on *BRCA1* mutation carriers, by genotyping intiative

Acronym	Study Name	Country	OncoArray Unaffected	OncoArray Breast cancer	iCOGS Unaffected	iCOGS Breast cancer
BCFR-AU	Australian site of the Breast Cancer Family Registry	AUSTRALIA	13	25	0	2
BCFR-NC	Northern California site of the Breast Cancer Family Registry	USA	3	12	1	1
BCFR-NY	New York site of the Breast Cancer Family Registry	USA	24	37	4	5
BCFR-ON	Ontario site of the Breast Cancer Family Registry	CANADA	34	86	2	7
BCFR-PA	Philadelphia site of the Breast Cancer Family Registry	USA	26	17	14	16
BCFR-UT	Utah site of the Breast Cancer Family Registry	USA	135	64	1	0
BFBOCC	Baltic Familial Breast Ovarian Cancer Consortium	LITHUANIA/LATVIA	133	111	16	8
BIDMC	Beth Israel Deaconess Medical Center	USA	41	44	1	1
BMBSA	BRCA-gene mutations and breast cancer in South African women	SOUTH AFRICA	21	37	2	1
BRICOH	Beckman Research Institute of the City of Hope	USA	96	50	11	9
CBCS	Rigshospitalet	DENMARK	110	75	80	57
CNIO	Spanish National Cancer Centre	SPAIN	32	31	49	44
COH	City of Hope Cancer Center	USA	84	141	6	8
CONSIT TEAM	CONsorzio Studi ITaliani sui Tumori Ereditari Alla Mammella	ITALY	265	271	217	234
DEMOKRITOS	National Centre for Scientific Research Demokritos	GREECE	85	132	12	20
DFCI	Dana-Farber Cancer Institute	USA	82	65	3	4
DKFZ	German Cancer Research Center	GERMANY	19	36	0	2
EMBRACE	Epidemiological Study of Familial Breast Cancer	UK/IRELAND	907	785	14	13
FCCC	Fox Chase Cancer Center	USA	49	26	20	19
FPGMX	Fundación Pública Galega de Medicina Xenómica	SPAIN	40	61		
GC-HBOC	German Familial Breast Group	GERMANY	673	1145	54	111
GEMO	Genetic Modifiers of cancer risk in BRCA1/2 mutation carriers	FRANCE/USA	630	842	114	111
GEORGETOWN	Georgetown University	USA	6	5	1	2
G-FAST	Ghent University Hospital	BELGIUM	69	121	91	42
HCSC	Hospital Clinico San Carlos	SPAIN	85	55	5	6
HEBCS	Helsinki Breast Cancer Study	FINLAND	67	53	3	5
HEBON	Genen Omgeving studie van de werkgroep Hereditiair Borstkanker Onderzoek Nederland	NETHERLANDS	500	372	220	202
HUNBOCS	Molecular Genetic Studies of Breast- and Ovarian Cancer in Hungary	HUNGARY	101	179		
HVH	University Hospital Vall d'Hebron	SPAIN	56	62	0	1
ICO	Institut Català d'Oncologia	SPAIN	150	130	5	1
IHCC	International Hereditary Cancer Centre	POLAND	121	77	279	223
INHERIT	INterdisciplinary HEalth Research Internal Team BReast CAncer susceptibility	CANADA (QUEBEC)	52	37	6	2
IOVHBOCS	Istituto Oncologico Veneto	ITALY	93	111	5	4
IPOBCS	Portuguese Oncology Institute-Porto Breast Cancer Study	PORTUGAL	79	36	1	2
KCONFAB	Kathleen Cuningham Consortium for Research into Familial Breast Cancer	AUSTRALIA	355	366	24	26
KUMC	University of Kansas Medical Center	USA	3	11		
MAYO	Mayo Clinic	USA	126	121	12	10
MCGILL	McGill University	CANADA (QUEBEC)	30	24		
MODSQUAD	Modifier Study of Quantitative Effects on Disease	CZECH REPUBLIC			68	106
MSKCC	Memorial Sloane Kettering Cancer Center	USA	193	185	32	59
MUV	General Hospital Vienna	AUSTRIA	266	268	11	11
NAROD	Women's College Research Institute Hereditary Breast and Ovarian Cancer Study	CANADA			100	46
NCI	National Cancer Institute	USA	108	42	6	1
NNPIO	N.N. Petrov Institute of Oncology	RUSSIA	22	44	1	4
NORTHSHORE	NorthShore University HealthSystem	USA	40	40		
NRG_ONCOLOGY	NRG Oncology	USA/AUSTRALIA	153	166	4	7
OCGN	Ontario Cancer Genetics Network	CANADA	133	71	6	4
OSU CCG	The Ohio State University Comprehensive Cancer Center	USA	34	39	8	10
OUH	Odense University Hospital	DENMARK	358	192	10	10
PBCS	Università di Pisa	ITALY	39	49	6	5
SMC	Sheba Medical Centre	ISRAEL	99	65	57	41
SWE-BRCA	Swedish Breast Cancer Study	SWEDEN	237	188	52	38
UCHICAGO	University of Chicago	USA	51	43	7	0
UCSF	University of California San Francisco	USA	60	32	16	15
UKGRFOCR	UK and Gilda Radner Familial Ovarian Cancer Registries	UK	40	13	5	0
UPENN	University of Pennsylvania	USA	218	239	11	22
UPITT	Cancer Family Registry University of Pittsburg	USA	77	77		
UTMDACC	University of Texas MD Anderson Cancer Center	USA	18	25	27	45
VFCTG	Victorian Familial Cancer Trials Group	AUSTRALIA	104	103	2	1
WCP	Women's Cancer Program at Cedars-Sinai Medical Center	USA	137	50	10	6

Supplementary Table 1: BCAC studies contributing data on estrogen receptor negative cases and controls, by genotyping intiative†

Acronym	Study Name	Country	Study design	OncoArray		iCOGS		GWASs	
				Controls	Cases	Controls	Cases	Controls	Cases
ABCFS	Australian Breast Cancer Family Study	Australia	Case-control study	188	62	551	204	285	72
ABCS	Amsterdam Breast Cancer Study	Netherlands	Case-control study	4	27	1815	154		
ABCTB	Australian Breast Cancer Tissue Bank	Australia	Case-control study	374	290				
BBCC	Bavarian Breast Cancer Cases and Controls	Germany	Case-control study	248	354	458	67		
BBCS	British Breast Cancer Study	UK	Case-control study	442	18	1397	108		
BCEES	Breast Cancer Employment and Environment Study	Australia	Case-control study	834	115				
BCFR	Breast Cancer Family Registry	USA, Canada, Australia	Case-control study					2251	922
BCFR-NY	New York site of the Breast Cancer Family Registry	USA	Case-control study	27	60				
BCFR-PA	Philadelphia site of the Breast Cancer Family Registry	USA	Case-control study	0	27				
BCFR-UT	Utah site of the Breast Cancer Family Registry	USA	Case-control study	0	13				
BCINIS	Breast Cancer in Northern Israel Study	Israel	Case-control study	723	262				
BIGGS	Breast Cancer in Galway Genetic Study	Ireland	Case-control study			719	154		
BPC3	Breast and Prostate Cancer Cohort Consortium	International	Prospective cohorts: nested case-control studies					2305	1998
BREOGAN	Breast Oncology Galicia Network	Spain	Case-control study	725	246				
BSUCH	Breast Cancer Study of the University of Heidelberg	Germany	Case-control study	167	42	954	157		
CBCS	Canadian Breast Cancer Study	Canada	Case-control study	817	119				
CCGP	Crete Cancer Genetics Program	Greece	Case-control study	332	177				
CECILE	CECILE Breast Cancer Study	France	Case-control study	3	5	999	144		
CGPS	Copenhagen General Population Study	Denmark	Case-control study	712	160	4534	357		
CNIO-BCS	Spanish National Cancer Centre Breast Cancer Study	Spain	Case-control study			876	88		
CPSII	Cancer Prevention Study-II Nutrition Cohort	USA	Prospective cohort: nested case-control study	3025	99				
CTS	California Teachers Study	USA	Prospective cohort: nested case-control study	577	126	71	68		
DEMOKRITOS	Demokritos	Greece	Case-control study			95	413		
DIETCOMPLYF	DietCompLyf Breast Cancer Survival Study	UK	Prospective cohort: nested case-control study	0	104				
EPIC	European Prospective Investigation Into Cancer and Nutrition	International (Europe)	Prospective cohort: nested case-control study	3522	179				
ESTHER	ESTHER Breast Cancer Study	Germany	Case-control study	3	1	502	98		
GC-HBOC*	German Consortium for Hereditary Breast & Ovarian Cancer	Germany	Case-control study	1593	358	168			
GENICA	Gene Environment Interaction and Breast Cancer in Germany	Germany	Case-control study	284	78	427	104		
GEPARSIXTO	Randomized phase II trial	Germany	Case-only study	0	273				
GESBC	Genetic Epidemiology Study of Breast Cancer by Age 50	Germany	Case-control study	180	122				
HABCS	Hannover Breast Cancer Study	Germany	Case-control study	865	147				
HCSC	Hospital Clinico San Carlos	Spain	Case-control study	0	109				
HEBCS	Helsinki Breast Cancer Study	Finland	Case-control study	2	14	1233	235	1012	145
HMBCS	Hannover-Minsk Breast Cancer Study	Belarus	Case-control study	214	7	130	8		
HUBCS	Hannover-Ufa Breast Cancer Study	Russia	Case-control study	131	18				
KARBAC	Karolinska Breast Cancer Study	Sweden	Case-control study	0	3	662	63		
KBCP	Kuopio Breast Cancer Project	Finland	Case-control study	182	23	250	97		
KConFab/AOCS	Kathleen Cuningham Foundation Consortium for research into Familial Breast Cancer/Australian Ovarian Cancer Study	Australia and New Zeland	Case-control study			897	55		
LMBC	Leuven Multidisciplinary Breast Centre	Belgium	Case-control study	435	145	1388	378		
MABCS	Macedonian Breast Cancer Study	Macedonia	Case-control study	93	17				
MARIE	Mammary Carcinoma Risk Factor Investigation	Germany	Case-control study	288	8	1778	346	470	76
MBCSG	Milan Breast Cancer Study Group	Italy	Case-control study	366	75	400	42		
MCBCS	Mayo Clinic Breast Cancer Study	USA	Case-control study	179	84	1931	269		
MCCS	Melbourne Collaborative Cohort Study	Australia	Prospective cohort: nested case-control study	712	77	511	110		
MEC	Multiethnic Cohort	USA	Prospective cohort: nested case-control study	127	3	741	87		
MISS	Melanoma Inquiry of Southern Sweden	Sweden	Prospective cohort: nested case-control study	1523	79				
MMHS	Mayo Mammography Health Study	USA	Prospective cohort: nested case-control study	1605	50				
MTLGEBCS	Montreal Gene-Environment Breast Cancer Study	Canada	Case-control study	29	2	436	64		
NBCS	Norwegian Breast Cancer Study	Norway	Case-control study			217	200		
NBHS	Nashville Breast Health Study	USA	Case-control study	613	163	118	125		
NC-BCFR	Northern California Breast Cancer Family Registry	USA	Case-control study	149	261				
NHS	Nurses Health Study	USA	Prospective cohort: nested case-control study	1804	203				
NHS2	Nurses Health Study 2	USA	Prospective cohort: nested case-control study	1905	224				
OBCS	Oulu Breast Cancer Study	Finland	Case-control study			414	100		
OFBCR	Ontario Familial Breast Cancer Registry	Canada	Case-control study	217	259	511	269		
ORIGO	Leiden University Medical Centre Breast Cancer Study	Netherlands	Prospective cohort: nested case-control study	660	230	327	70		
OSU	Ohio State University	USA	Case-control study			203	207		
PBCS	NCI Polish Breast Cancer Study	Poland	Case-control study	1658	547				
pKARMA	Karolinska Mammography Project for Risk Prediction of Breast Cancer - Case-Control Study	Sweden	Case-control study	6042	166	5568	701		
PLCO	The Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial	USA	Prospective cohort: nested case-control study	858	184				
POSH	Prospective Study of Outcomes in Sporadic Versus Hereditary Breast Cancer	UK	Case-only study	0	207				
PREFACE	Evaluation of Predictive Factors regarding the Effectivity of Aromatase Inhibitor Therapy	Germany	Case-only study	0	15				
RBCS	Rotterdam Breast Cancer Study	Netherlands	Case-control study	231	87	699	124		
RPCI	Roswell Park Cancer Institute	USA	Case-control study			126	136		
SASBAC	Singapore and Sweden Breast Cancer Study	Sweden	Case-control study			661	43	756	109
SBCS	Sheffield Breast Cancer Study	UK	Case-control study			848	98		
SEARCH	Study of Epidemiology and Risk factors in Cancer Heredity	UK	Case-control study	989	420	8068	1173		
SISTER	The Sister Study	USA	Prospective cohort: nested case-control study	1560	282				
2SISTER	The Two Sister Study	USA	Case-only study	0	204				
SKKDKFZS*	Städtisches Klinikum Karlsruhe Deutsches Krebsforschungszentrum Study	Germany	Case-only study	0	298	0	135		
SMC	Swedish Mammography Cohort	Sweden	Prospective cohort: nested case-control study	708	195				
SUCCESSB	Simultaneous Study of Gemcitabine-Docetaxel Combination adjuvant treatment	Germany	Case-only study	0	159				
SUCCESSC	Simultaneous Study of Docetaxel Based Anthracycline Free Adjuvant Treatment Evaluation	Germany	Case-only study	0	204				
SZBCS	IHCC-Szczecin Breast Cancer Study	Poland	Case-control study	157	72	315	60		
TNBCC	Triple-Negative Breast Cancer Consortium	International	Case-control studies	0	288			2890	998
UCIBCS	UCI Breast Cancer Study	USA	Case-control study	258	73				
UK2	UK2 GWAS	UK	Case-control study					2663	160
UKBGS	UK Breakthrough Generations Study	UK	Prospective cohort: nested case-control study	567	78	470	22		
UKOPS	UK Ovarian Cancer Population Study	UK	Case-control study	974	0				
WHI	Women's Health Initiative	USA	Prospective cohort: nested case-control study	4613	658				

†Studies participated in one or more of the following genotyping initiatives: OncoArray, iCOGS or one of eight genome-wide association studies (GWASs)
*For the analysis of iCOGS data, cases from SKKDKFZS and controls from GC-HBOC included as one study

Members of consortia listed as authors

ABCTB Investigators

Christine Clarke (Westmead Institute for Medical Research, University of Sydney, NSW, Australia); Rosemary Balleine (Pathology West ICPMR, Westmead, NSW, Australia); Robert Baxter (Kolling Institute of Medical Research, University of Sydney, Royal North Shore Hospital, NSW, Australia); Stephen Braye (Pathology North, John Hunter Hospital, Newcastle, NSW, 2305, Australia); Jane Carpenter (Westmead Institute for Medical Research, University of Sydney); Jane Dahlstrom (Department of Anatomical Pathology, ACT Pathology, Canberra Hospital, ACT, Australia; ANU Medical School, Australian National University, ACT, Australia); John Forbes (Department of Surgical Oncology, Calvary Mater Newcastle Hospital, Australian New Zealand Breast Cancer Trials Group, and School of Medicine and Public Health, University of Newcastle, NSW, Australia); C Soon Lee (School of Science and Health, The University of Western Sydney, Sydney, Australia); Deborah Marsh (Hormones and Cancer Group, Kolling Institute of Medical Research, Royal North Shore Hospital, University of Sydney, NSW, Australia); Adrienne Morey (SydPath St Vincent's Hospital, Sydney, NSW, Australia); Nirmala Pathmanathan (Department of Tissue Pathology and Diagnostic Oncology, Pathology West; Westmead Breast Cancer Institute, Westmead Hospital, NSW, Australia); Rodney Scott (Centre for Information Based Medicine, Hunter Medical Research Institute, NSW, 2305, Australia; Priority Research Centre for Cancer, School of Biomedical Sciences and Pharmacy, Faculty of Health, University of Newcastle, NSW, Australia); Peter Simpson (The University of Queensland: UQ Centre for Clinical Research and School of Medicine, QLD, Australia); Allan Spigelman (Hereditary Cancer Clinic, St Vincent's Hospital, The Kinghorn Cancer Centre, Sydney, New South Wales, 2010, Australia); Nicholas Wilcken (Crown Princess Mary Cancer Centre, Westmead Hospital, Westmead, Australia; Sydney Medical School - Westmead, University of Sydney, NSW, Australia); Desmond Yip (Department of Medical Oncology, The Canberra Hospital, ACT, Australia; ANU Medical School, Australian National University, ACT, Australia); Nikolajs Zeps (St John of God Perth Northern Hospitals, Perth, WA, Australia)

EMBRACE

Helen Gregory (North of Scotland Regional Genetics Service, NHS Grampian & University of Aberdeen, Foresterhill, Aberdeen, UK); Zosia Miedzybrodzka (North of Scotland Regional Genetics Service, NHS Grampian & University of Aberdeen, Foresterhill, Aberdeen, UK); Patrick J. Morrison (Northern Ireland Regional Genetics Centre, Belfast Health and Social Care Trust, and Department of Medical Genetics, Queens University Belfast, Belfast, UK); Kai-ren Ong (West Midlands Regional Genetics Service, Birmingham Women's Hospital Healthcare NHS Trust, Edgbaston, Birmingham, UK); Alan Donaldson (Clinical Genetics Department, St Michael's Hospital, Bristol, UK); Marc Tischkowitz (Department of Medical Genetics, University of Cambridge, UK); Mark T. Rogers (All Wales Medical Genetics Services, University Hospital of Wales, Cardiff, UK); M. John Kennedy (Academic Unit of Clinical and Molecular Oncology, Trinity College Dublin and St James's Hospital, Dublin, Eire); Mary E. Porteous (South East of Scotland Regional Genetics Service, Western General Hospital, Edinburgh, UK); Carole Brewer (Department of Clinical Genetics, Royal Devon & Exeter Hospital, Exeter, UK); Rosemarie Davidson (Clinical Genetics, Southern General Hospital, Glasgow, UK); Louise Izatt (Clinical Genetics, Guy's and St. Thomas' NHS Foundation Trust, London, UK); Angela Brady (North West Thames Regional

Genetics Service, Kennedy-Galton Centre, Harrow, UK); Julian Barwell (Leicestershire Clinical Genetics Service, University Hospitals of Leicester NHS Trust, UK); Julian Adlard (Yorkshire Regional Genetics Service, Leeds, UK); Claire Foo (Department of Clinical Genetics, Alder Hey Hospital, Eaton Road, Liverpool, UK); D. Gareth Evans (Genetic Medicine, Manchester Academic Health Sciences Centre, Central Manchester University Hospitals NHS Foundation Trust, Manchester, UK); Fiona Lalloo (Genetic Medicine, Manchester Academic Health Sciences Centre, Central Manchester University Hospitals NHS Foundation Trust, Manchester, UK); Lucy E. Side (North East Thames Regional Genetics Service, Great Ormond Street Hospital for Children NHS Trust, London, UK); Jacqueline Eason (Nottingham Clinical Genetics Service, Nottingham University Hospitals NHS Trust, UK); Alex Henderson (Institute of Genetic Medicine, Centre for Life, Newcastle Upon Tyne Hospitals NHS Trust, Newcastle upon Tyne, UK); Lisa Walker (Oxford Regional Genetics Service, Churchill Hospital, Oxford, UK); Rosalind A. Eeles (Oncogenetics Team, The Institute of Cancer Research and Royal Marsden NHS Foundation Trust, UK); Jackie Cook (Sheffield Clinical Genetics Service, Sheffield Children's Hospital, Sheffield, UK); Katie Snape (South West Thames Regional Genetics Service, St.Georges Hospital, Cranmer Terrace, Tooting, London, UK); Diana Eccles (University of Southampton Faculty of Medicine, Southampton University Hospitals NHS Trust, Southampton, UK); Alex Murray (All Wales Medical Genetics Services, Singleton Hospital, Swansea, UK); Emma McCann (All Wales Medical Genetics Service, Glan Clwyd Hospital, Rhyl, UK).

GEMO Study Collaborators
Dominique Stoppa-Lyonnet, Muriel Belotti, Anne-Marie Birot, Bruno Buecher, Emmanuelle Fourme, Marion Gauthier-Villars, Lisa Golmard, Claude Houdayer, Virginie Moncoutier, Antoine de Pauw, Claire Saule (Service de Génétique, Institut Curie, Paris, France); Fabienne Lesueur, Noura Mebirouk (Inserm U900, Institut Curie, Paris, France); Olga Sinilnikova†, Sylvie Mazoyer, Francesca Damiola, Laure Barjhoux, Carole Verny-Pierre, Mélanie Léone, Nadia Boutry-Kryza, Alain Calender, Sophie Giraud (Unité Mixte de Génétique Constitutionnelle des Cancers Fréquents, Hospices Civils de Lyon - Centre Léon Bérard, Lyon, France); Olivier Caron, Marine Guillaud-Bataille (Institut Gustave Roussy, Villejuif, France: Brigitte Bressac-de-Paillerets); Yves-Jean Bignon, Nancy Uhrhammer (Centre Jean Perrin, Clermont–Ferrand, France); Christine Lasset, Valérie Bonadona (Centre Léon Bérard, Lyon, France); Pascaline Berthet, Dominique Vaur, Laurent Castera (Centre François Baclesse, Caen, France); Hagay Sobol, Violaine Bourdon, Tetsuro Noguchi, Audrey Remenieras, François Eisinger, Catherine Noguès (Institut Paoli Calmettes, Marseille, France); Isabelle Coupier, Pascal Pujol (CHU Arnaud-de-Villeneuve, Montpellier, France); Jean-Philippe Peyrat, Joëlle Fournier, Françoise Révillion, Claude Adenis (Centre Oscar Lambret, Lille, France); Danièle Muller, Jean-Pierre Fricker (Centre Paul Strauss, Strasbourg, France); Emmanuelle Barouk-Simonet, Françoise Bonnet, Virginie Bubien, Nicolas Sevenet, Michel Longy (Institut Bergonié, Bordeaux, France); Christine Toulas, Rosine Guimbaud, Laurence Gladieff, Viviane Feillel (Institut Claudius Regaud, Toulouse, France); Dominique Leroux, Hélène Dreyfus, Christine Rebischung, Magalie Peysselon (CHU Grenoble, France); Fanny Coron, Laurence Faivre, Amandine Baurand, Caroline Jacquot, Geoffrey, Bertolone, Sarab Lizard (CHU Dijon, France); Fabienne Prieur, Marine Lebrun, Caroline Kientz (CHU St-Etienne, France); Sandra Fert Ferrer (Hôtel Dieu Centre Hospitalier, Chambéry, France); Véronique Mari (Centre Antoine Lacassagne, Nice, France); Laurence Vénat-Bouvet (CHU Limoges, France); Capucine Delnatte, Stéphane Bézieau (CHU Nantes, France); Isabelle Mortemousque (CHU

Bretonneau, Tours and Centre Hospitalier de Bourges France); Florence Coulet, Chrystelle Colas, Florent Soubrier, Mathilde Warcoin (Groupe Hospitalier Pitié-Salpétrière, Paris, France); Johanna Sokolowska, Myriam Bronner (CHU Vandoeuvre-les-Nancy, France); Marie-Agnès Collonge-Rame, Alexandre Damette (CHU Besançon, France); Paul Gesta (CHU Poitiers, Centre Hospitalier d'Angoulême and Centre Hospitalier de Niort, France); Hakima Lallaoui (Centre Hospitalier de La Rochelle); Jean Chiesa (CHU Nîmes Carémeau, France); Denise Molina-Gomes (CHI Poissy, France); Olivier Ingster (CHU Angers, France).

HEBON
Annemieke H. van der Hout (Department of Genetics, University Medical Center Groningen, Groningen, The Netherlands); Ans M.W. van den Ouweland (Department of Clinical Genetics, Family Cancer Clinic, Erasmus University Medical Center, Rotterdam, The Netherlands); Arjen R. Mensenkamp (Department of Human Genetics, Radboud University Medical Center, Nijmegen, The Netherlands); Carolien H.M. van Deurzen (Department of Pathology, Family Cancer Clinic, Erasmus University Medical Center, Rotterdam, The Netherlands); Carolien M. Kets (Department of Human Genetics, Radboud University Medical Center, Nijmegen, The Netherlands); Caroline Seynaeve (Department of Medical Oncology, Family Cancer Clinic, Erasmus MC Cancer Institute, Rotterdam, The Netherlands); Christi J. van Asperen (Department of Clinical Genetics, Leiden University Medical Center, Leiden, The Netherlands); Cora M. Aalfs (Department of Clinical Genetics, Academic Medical Center, Amsterdam, The Netherlands); Encarna B. Gómez Garcia (Department of Clinical Genetics , MUMC, Maastricht, The Netherlands); Flora E. van Leeuwen (Department of Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands); Frans B.L. Hogervorst (Family Cancer Clinic, Netherlands Cancer Institute, Amsterdam, The Netherlands); G.H. de Bock (Department of Oncological Epidemiology, University Medical Center, Groningen University, Groningen, The Netherlands); Hanne E.J. Meijers-Heijboer (Department of Clinical Genetics, VU University Medical Centre, Amsterdam, The Netherlands); Inge M. Obdeijn (Department of Radiology, Family Cancer Clinic, Erasmus University Medical Center, Rotterdam, The Netherlands); J. Margriet Collée (Department of Clinical Genetics, Family Cancer Clinic, Erasmus University Medical Center, Rotterdam, The Netherlands); J.J.P. Gille (Department of Clinical Genetics, VU University Medical Center, Amsterdam, The Netherlands); Jan C. Oosterwijk (Department of Genetics, University Medical Center Groningen, Groningen, The Netherlands); Juul T. Wijnen (Department of Human Genetics & Department of Clinical Genetics, Leiden University Medical Center, Leiden, The Netherlands); Lizet E. van der Kolk (Family Cancer Clinic, Netherlands Cancer Institute, Amsterdam, The Netherlands); Maartje J. Hooning (Department of Medical Oncology, Family Cancer Clinic, Erasmus MC Cancer Institute, Rotterdam, The Netherlands); Margreet G.E.M. Ausems (Department of Medical Genetics, University Medical Center Utrecht, Utrecht, The Netherlands); Marian J.E. Mourits (Department of Gynaecological Oncology, University Medical Center, Groningen University, Groningen, The Netherlands); Marinus J. Blok (Department of Clinical Genetics, Maastricht University Medical Center, Maastricht, The Netherlands); Marjanka K. Schmidt (Division of Psychosocial Research and Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands); Matti A. Rookus (Department of Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands); Muriel A. Adank (Department of Clinical Genetics, VU University Medical Centre, Amsterdam, The Netherlands); Peter Devilee (Department of Human Genetics & Department of Pathology, Leiden University Medical Center, Leiden, The

Netherlands); Rob B. van der Luijt (Department of Medical Genetics, University Medical Center Utrecht, Utrecht, The Netherlands); T.C.T.E.F. van Cronenburg (Department of Clinical Genetics Leiden University Medical Center Leiden, The Netherlands); Carmen C. van der Pol (Department of Oncological and Endocrine Surgery, University Medical Center Utrecht, Utrecht, The Netherlands):Nicola S. Russell (Department of Radiotherapy, Netherlands Cancer Institute, Amsterdam, The Netherlands); Sabine Siesling (The Netherlands Comprehensive Cancer Organization (IKNL), Utrecht, The Netherlands); Lucy Overbeek (The nationwide network and registry of histo- and cytopathology in The Netherlands [PALGA]); R. Wijnands (Department of Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands); Judith L. de Lange (Department of Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands).

kConFab/AOCS Investigators
Stephen Fox, Ian Campbell (Peter MacCallum Cancer Centre, Melbourne, Australia); Georgia Chenevix-Trench, Amanda Spurdle, Penny Webb (QIMR Berghofer Medical Research Institute, Brisbane, Australia); Anna de Fazio (Westmead Millenium Institute, Sydney, Australia); Margaret Tassell (BCNA delegate, Community Representative); Judy Kirk (Westmead Hospital, Sydney, Australia); Geoff Lindeman (Walter and Eliza Hall Institute, Melbourne, Australia); Melanie Price (University of Sydney, Sydney, Australia); Melissa Southey (University of Melbourne, Melbourne, Australia); Roger Milne (Cancer Council Victoria, Melbourne, Australia); Sid Deb (Melbourne Health, Melbourne, Australia); David Bowtell (Garvan Institute of Medical Research, Sydney, Australia).

NBSC Collaborators
Kristine K. Sahlberg (Department of Research, Vestre Viken Hospital, Drammen, Norway; Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Lars Ottestad (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Rolf Kåresen (Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway; Department of Breast- and Endocrine Surgery, Division of Surgery, Cancer and Transplantation Medicine, Oslo University Hospital Ullevål, Oslo, Norway); Anita Langerød (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Ellen Schlichting (Department of Breast- and Endocrine Surgery, Division of Surgery, Cancer and Transplantation Medicine, Oslo University Hospital Ullevål, Oslo, Norway); Marit Muri Holmen (Department of Radiology and Nuclear Medicine, Oslo University Hospital, Oslo, Norway); Toril Sauer (Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway; Department of Pathology at Akershus University hospital, Lørenskog, Norway); Vilde Haakensen (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Olav Engebråten (Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway; Department of Tumor Biology, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway; Department of Oncology, Division of Surgery and Cancer and Transplantation Medicine, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Bjørn Naume (Department of Oncology, Division of Surgery and Cancer and Transplantation Medicine, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Cecile E. Kiserud (National Advisory Unit on Late Effects after

Cancer Treatment, Department of Oncology, Oslo University Hospital, Oslo, Norway; Department of Oncology, Oslo University Hospital Ullevål, Oslo, Norway); Kristin V. Reinertsen (National Advisory Unit on Late Effects after Cancer Treatment, Department of Oncology, Oslo University Hospital, Oslo, Norway; Department of Oncology, Oslo University Hospital Ullevål, Oslo, Norway); Åslaug Helland (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway; Department of Oncology, Division of Surgery and Cancer and Transplantation Medicine, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Margit Riis (Department of Breast- and Endocrine Surgery, Division of Surgery, Cancer and Transplantation Medicine, Oslo University Hospital Ullevål, Oslo, Norway); Jürgen Geisler (Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway; Department of Breast-Endocrine Surgery, Akershus University Hospital, Oslo, Norway); Per Eystein Lønning (Section of Oncology, Institute of Medicine, University of Bergen and Department of Oncology, Haukeland University Hospital, Bergen, Norway); Solveig Hofvind (Cancer Registry of Norway, Oslo, Norway, Oslo; Akershus University College of Applied Sciences, Faculty of Health Science, Oslo, Norway); Tone F. Bathen (Department of Circulation and Medical Imaging, Norwegian University of Science and Technology (NTNU), Trondheim, Norway); Elin Borgen (Department of Pathology, Division of Diagnostics and Intervention, Oslo University Hospital, Oslo, Norway); Øystein Fodstad (Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway; Department of Tumor Biology, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Øystein Garred (Department of Pathology, Oslo University Hospital, Oslo, Norway); Gry Aarum Geitvik (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Gunhild Mari Mælandsmo (Department of Tumor Biology, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway; Department of Pharmacy, Faculty of Health Sciences, University of Tromsø, Tromsø, Norway); Hege G. Russnes (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway; Department of Pathology, Oslo University Hospital, Oslo, Norway); Therese Sørlie (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Ole Christian Lingjærde (Department of Computer Science, University of Oslo, Oslo, Norway); Helle Kristine Skjerven (Breast and Endocrine Surgery, Department of Breast and Endocrine Surgery, Vestre Viken Hospital, Drammen, Norway); Britt Fritzman (Østfold Hospital, Østfold, Norway).

In Silico Annotation of Candidate Causal Variants

Guide to results table (Supplementary Table 5) and UCSC Genome Browser session
Each candidate causal SNP has been annotated with publicly available genomic data in order to highlight potentially functional variants, prioritise experimental validation, and predict target genes. Annotations fall into categories relating to putative effects on transcription factors, regulatory element activities, expression quantitative trait loci (eQTL) and target gene prediction. For each variant, a link to the UCSC Genome Browser is provided that shows a 1 Mb region with relevant genomic data.

Transcription factors
Information regarding potential effects on transcription factor recognition sequences was obtained from the ENCODE-Motifs resource (http://compbio.mit.edu/encode-motifs)[1] using VCFtools v0.1.11 to access the downloaded HaploReg v4.0 database[2]. The impact each variant has on the position weight matrix for specific transcription factors is expressed as '+' or '-' for strengthened or weakened motifs relative to elements carrying the reference allele, respectively. Processed transcription factor ChIP-seq peak data for breast cell types were downloaded from ENCODE and other publications via NCBI GEO, in BED or NarrowPeak format, converted to the hg19 assembly using LiftOver if required, and given a standardised naming system (format = "_celltype;target_" in Supplementary Table 5). More details about the overlapping binding sites may be found within browser session track "TF-chip peaks overlapping candidate SNP" where TF-ChIP-seq peaks are named in the format "_Biosample_term_name, Experiment_target, Biosample_treatments, Biological_replicate(s), File_accession_". All ChIP-seq datasets are listed in Supplementary Table 6. Variants were assessed for overlap with ChIP-seq peaks using BedTools v2.25.0[3].

Regulatory features
Histone signatures derived from histone modification ChIP-seq experiments on breast cell types carried out by ENCODE, NIH Roadmap Epigenomics, and other published studies were obtained and formatted as for ChIP-seq data. Histone modification peaks overlapping candidate causal variants are represented as "_celltype;histone_mark_" in Supplementary Table 5 and "_Biosample_term_name, Experiment_target, Biosample_treatments, Biological_replicate(s), File_accession_" in the browser track "Histone modification ChIP-seq peaks overlapping candidate SNP". BedTools was used to intersect variants with histone signatures including commonly used marks associated with enhancers (H3K4me1, H3K4me2 and H3K27ac) and promoters (H3K4me3 and H3K9ac). Chromatin Hidden Markov Modelling (ChromHMM) states were obtained for breast cells from Roadmap (HMEC and myoepithelial cells) and published MCF7 data[4] and filtered for states corresponding to 'enhancers' (Roadmap 25-state E13, E14, E15, E16, E17, E18) or 'promoters' (Roadmap 25-state E1, E2, E3, E4, E22, E23). Chromatin state features containing candidate variants are represented as "_celltype;chromatin_state_". Chromatin accessibility data obtained from ENCODE, Roadmap and other published sources via NCBI GEO measured using DNase-seq and FAIRE-seq for relevant breast cell types were also tested for overlap with candidate causal variants. Intersected regions are reported in the format "_celltype;method_". Scores based on RegulomeDB[5] are presented for available SNPs (based on dbSNP141), where lower scores are increasingly likely to be functional (http://regulomedb.org/help#score).

eQTL

Genes showing expression levels correlated with query SNPs are shown in the column headed 'eQTL_target_all'. All genes reported to be associated with genotype in studies including GTEx version 6[6] (expression is any GTEx tissue, P value cutoff 10^{-6}) and Westra et al.,[7] (expression in whole blood). Genes associated with genotype in GTEx breast samples (N=186) are listed in the column "eQTL_GTEx.breast". eQTL data from TCGA and METABRIC studies for relevant variants are also presented (format "*Associated_gene:EffectAllele:EffectDirection:P_value*").

Other genomic features

Chromosomal position, the lead variant for the associated locus, and potentially conflicting rsIDs (assessed as overlapping at the query position) are given for each variant. GWAS tagSNPs were downloaded from the UCSC Table Browser (December 2015) and associated traits are listed if the tagSNP is within a 10 kb window of the candidate causal variant. NCBI RefSeq gene annotations were downloaded from the UCSC Table Browser and BedTools was used to determine overlapping genes ("Overlapping_RefGene"). The nearest RefGene transcription start site is also presented, given in the format "RefGeneTSS|distance". Basic genomic annotations such as intergenic, intronic, exonic, and untranslated regions based on RefSeq gene annotations were determined for each variant.

Target Gene Prediction

The column headed "Predicted_target_gene" lists genes predicted by various methods to be targets of, or the expression of which is associated with, regulatory elements in which the candidate causal variant lies. The reported gene is listed with cell type and method in the format "target:cell:method". A database was created comprising publicly available data based on various methods aiming to link enhancers with target genes (Annex to Supplementary Table 5). Laboratory based experimental approaches include genome-wide Chromatin Interaction Analysis with Paired-End-Tag sequencing (ChIA-PET)[8], Hi-C[9], and other Chromosome conformation capture (3C)-based techniques. Computational resources designed to predict target promoters by correlation of gene expression with ChIP-seq signals at specific regulatory elements including IM-PET[10], PreSTIGE[11] and data from Hnisz et al.[12] are also included. These methods associate enhancers defined by histone modification ChIP-seq for H3K4me1 (PreSTIGE), H3K27ac (Hnisz), H3K4me1, H3K4me3 and H3K27ac (IM-PET) with gene expression signals measured by RNA-seq. FANTOM5[13] data representing enhancer-promoter cap analysis of gene expression (CAGE) expression correlation from all cell types were downloaded from http://enhancer.binf.ku.dk/. Target genes have been predicted for multiple cell types and all data were included in the database, and filtered for breast derived cell types for this analysis (see Key to Supplementary Table 5).

The following strategy was used to assign potential target genes to regulatory elements. The published computational methods (Hnisz, PreSTIGE and IM-PET) included target gene annotation in the reported data. For ChIA-PET and Hi-C data, interaction peaks were mapped to promoters defined as -1.0 kb to +0.1 kb around GENCODE (v19) transcription start sites. Enhancer definitions were used as reported for computational methods while for ChIA-PET and Hi-C were interpreted as any region interacting with a promoter (regardless of other enhancer annotation information such as histone modification or open chromatin). FANTOM5 target promoters were predefined and

tissue specificity was determined by intersecting "TSS associated enhancers" with tissue-specific sets of enhancers.

All data were formatted to enable intersection of test variants with "enhancers" as defined by each method using the Galaxy "intersect" tool[14]. Each enhancer-promoter assignment or interaction was represented as a single record along with details about potential target promoter, cell type, method, scoring and confidence statistics from the original publication. A set of query SNPs (or any loci with genomic positional information in BED format) could be queried into a custom Galaxy workflow leading to generation of a table of predicted gene targets and a link to the UCSC Genome Browser for visualisation.

UCSC Genome Browser session
A custom session has been uploaded to UCSC Genome Browser[15] to facilitate exploration of breast cancer risk associated variation and implicated regulatory features. This can be accessed via the hyperlink (ie. "browser") in the functional annotation *xlsx* file. All standard Genome Browser data and functions are then available, including track display options (eg. right click on a particular track to activate visualisation options), highlighting regions (shift and mouse over region of interest), and the table browser (eg. to intersect or export data).

Within the session, Oncoarray candidate causal variants are shown in red, and names can be shown by activating "pack" mode (as for all tracks). Target gene prediction data from Hnisz, PreSTIGE and IM-PET shows enhancers depicted as black bars. The segment name revealed in 'pack' mode lists predicted target gene and cell-type (eg "WNT7B.MCF7"). ChIA-PET interactions, represented in BED12 format, have been filtered to remove duplicates and *trans*-chromosomal interactions. The interactions are shaded to reflect statistical confidence based on enrichment in the original experiment. ChIA-PET interaction names show the genomic co-ordinates of either-end of the interaction, the cell type (restricted to MCF7 for this analysis), the immunoprecipitation target, and the experimental replicate. Depicted interactions are restricted to those for which a candidate variant lies within an interaction "end" with the opposite end overlapping a TSS. All other interactions may be visualised by activating the standard ENCODE ChIA-PET track (\Regulation\ENCODE Chromatin Interactions Tracks\ChIA-PET from ENCODE/GIS-Ruan).

Chromatin interactions based on *in situ* Hi-C data from HMEC cells were downloaded from NCBI GEO (accession GSE63525)[9]. Annotated loops (representing potential enhancer-promoter interactions) processed by HiCCUPS were reformatted as BED files and tested for overlap with RefSeq promoters to assign potential target genes. Opposing ends of TSS-overlap loops were then annotated as 'potential enhancers'. Specific loop regions which overlap BC risk candidate causal variants are depicted as black segments and named "*TSS_target.Celltype*".

Various classes of genomic data representing regulatory features which harbour candidate variants are shown as separate tracks:
● *Histone modification ChIP-seq peaks overlapping candidate SNP*
● *DNase HS and FAIRE-seq peaks overlapping candidate SNP*
● *TF-chip peaks overlapping candidate SNP*

As mentioned above, changing the track display to 'pack' mode will show details of the overlapping peak in the format:
"*Biosample_term_name, Experiment_target, Biosample_treatments, Biological_replicate(s), File_accession*".

A representation of all TF and histone ChIP-seq, DNase-seq, and FAIRE-seq data tested for overlap with candidate variants is shown in three histogram tracks (computed with BedTools genomeCoverageBed). These show the summed peak density at each genomic position and allow simple visualisation of loci with relative abundance of regulatory features.

Tracks for Roadmap Epigenomics Chromatin state models (based on imputed data - 25 state, 12 marks, 127 epigenomes) were generated for breast Myoepithelial and HMEC cells. Chromatin states were separated and colour coded for states related to enhancers, promoters, and transcribed regions.

The bottom track ("Oncoarray SNPs") shows all directly genotyped and imputed SNPs passing quality control (imputation r^2>0.3) as black ticks. SNPs from dbSNP build 138 with a MAF > 0.01 in European samples which were not informative are shown in red.

Funding

Acknowledgements

(Germany), Ewa Putresza, Irene Masunaka, the WHI investigators, Maggie Angelakos, Judi Maskiell, Gillian Dite, Helen Tsimiklis, Vilius Rudaitis, Laimonas Griškevičius, Janis Eglitis, Anna Krilova, Aivars Stengrevics, Yuan Chun Ding, Linda Steele, Irene Feroce, Daniela Furlan, Viviana Gismondi Riccardo Dolcetti, Gabriele Capone, Anna Laura Putignano, Giuseppe Guannini, Antonella Savarese, Aline Martayan, Stefania Tommasi, Brunella Pilato, the Cogentech Cancer Genetic Test Laboratory (Italy), Riccardo Dolcetti, Barbara Pasini, Francesca Vignolo-Lutati, Sue Healey, JoEllen Weaver, Betsy Bove, Marta Santamariña, Ana Blanco, Miguel Aguado, Uxía Esperón, Belinda Rodríguez, GEMO Collaborating Centers (Unité Mixte de Génétique Constitutionnelle des Cancers Fréquents, Hospices Civils de Lyon & Centre Léon Bérard ; Service de Génétique Oncologique, Institut Curie, Paris; Service de Génétique & BB-0033-00074, Gustave Roussy, Villejuif; Centre Léon Bérard, Lyon; Centre François Baclesse, Caen; Institut Paoli Calmettes, Marseille; CHU Arnaud-de-Villeneuve, Montpellier; Centre Oscar Lambret, Lille; Centre Paul Strauss, Strasbourg; . Institut Bergonié, Bordeaux; Institut Claudius Regaud, Toulouse; CHU Grenoble; CHU Dijon; CHU St-Etienne; Hôtel Dieu Centre Hospitalier, Chambéry; Centre Antoine Lacassagne, Nice; CHU Limoges; CHU Nantes; CHU Bretonneau, Tours; Groupe Hospitalier Pitié-Salpétrière, Paris; CHU Vandoeuvre-les-Nancy; CHU Besançon; Creighton University, Omaha, USA), GEMO Investigators (Olga Sinilnikova†, Carole Verny-Pierre, Mélanie Léone, Nadia Boutry-Kryza, Alain Calender, Sophie Giraud, Bruno Buecher, Claude Houdayer, Etienne Rouleau, Lisa Golmard, Agnès Collet, Virginie Moncoutier, Muriel Belotti, Antoine de Pauw, Camille Elan, Catherine Nogues, Emmanuelle Fourme, Anne-Marie Birot, Marine Guillaud-Bataille. Centre Jean Perrin, Clermont–Ferrand, Nancy Uhrhammer, Valérie Bonadona, Sandrine Handallou, Agnès Hardouin, Pascaline Berthet, Dominique Vaur, Hagay Sobol, Violaine Bourdon, Tetsuro Noguchi, Audrey Remenieras, François Eisinger, Pascal Pujol, Jean-Philippe Peyrat, Joëlle Fournier, Françoise Révillion, Philippe Vennin†, Claude Adenis, Danièle Muller, Jean-Pierre Fricker, Emmanuelle Barouk-Simonet, Françoise Bonnet, Virginie Bubien, Nicolas Sevenet, Michel Longy, Christine Toulas, Rosine Guimbaud, Laurence Gladieff, Viviane Feillel, Dominique Leroux, Hélène Dreyfus, Christine Rebischung, Magalie Peysselon, Fanny Coron, Fabienne Prieur, Marine Lebrun, Caroline Kientz, Sandra Fert Ferrer, Marc Frénay, Laurence Vénat-Bouvet, Capucine Delnatte, Isabelle Mortemousque, Florence Coulet, Chrystelle Colas, Florent Soubrier, Mathilde Warcoin, Johanna Sokolowska, Myriam Bronner, Marie-Agnès Collonge-Rame, Alexandre Damette, Henry T. Lynch, Carrie L. Snyder, Ilse Coene, Brecht Crombez, Alicia Tosar, Paula Diaque, Kristiina Aittomäki, Taru A. Muranen, Kirsimari Aaltonen, Irja Erkkilä, Virpi Palola, Comprehensive Cancer Centre Netherlands, Comprehensive Centre South, Netherlands Cancer Registry, Dutch Pathology Registry, HEBON Collaborating Centers (Netherlands Cancer Institute, Erasmus Medical Center - Rotterdam, Leiden University Medical Center, Radboud University Nijmegen Medical Center, University Medical Center Utrecht, Amsterdam Medical Center, VU University Medical Center - Amsterdam, University Hospital Maastricht, The Netherlands Foundation for the detection of hereditary tumours, The Netherlands Comprehensive Cancer Organization [IKNL], the Dutch Pathology Registry [PALGA], Groningen University Medical Center - Groningen), HEBON Investigators (F.E. van Leeuwen, S. Verhoef, N.S. Russell, J.L. de Lange, R. Wijnands, J.M. Collée, C.H.M. van Deurzen, I.M. Obdeijn, T.C.T.E.F. van Cronenburg, A.R. Mensenkamp, R.B. van der Luijt, C.C. van der Pol, J.J.P. Gille, Q. Waisfisz, H.F. Vasen, S. Siesling, J.Verloop, L.I.H. Overbeek. E.B. Gómez-Garcia, A.H. van der Hout, M.J. Mourits, G.H. de Bock) Janos Papp, Tibor Vaszko, Aniko Bozsik, Judit Franko, Maria Balogh, Gabriella Domokos, Judit Ferenczi, the Oncogenetics

OncoArray genotype calling and quality control

Of the 568,712 variants selected for genotyping on OncoArray, 533,631 were successfully manufactured on the array (including 778 duplicate probes). OncoArray genotyping of BCAC and CIMBA samples was conducted at six sites. Details of the genotyping calling for the OncoArray are described in more detail elsewhere[16]. Briefly, we developed a single calling pipeline that was applied to more than 500,000 samples. An initial cluster file was generated using from 56,284 samples, selected over all the major genotyping centres and ethnicities, using the Gentrain2 algorithm. Variants likely to have problematic clusters were selected for manual inspection using the following criteria: call rate below 99%, minor allele frequency (MAF) <0.001, poor Illumina intensity and clustering metrics, deviation from the MAF observed in the 1000 Genomes Project using the criterion: $\frac{(|p_1 - p_0| - 0.01)^2}{((p_1 + p_0)(2 - p_1 - p_0))} > C$, where p_0 and p_1 are the minor frequencies in the 1000 Genome Project and Oncoarray datasets, respectively, and C=0.008. (This latter criterion is approximately equivalent to excluding SNPs on the basis of a Chi-square statistic of 16 for the difference in allele frequencies, assuming 1,000 samples in each group). This resulted in manual adjustment of the cluster file for 3,964 variants, and the exclusion of 16,526 variants. The final cluster file was then applied to the full dataset.

We excluded SNPs with a call rate <95% in any consortium, not in Hardy-Weinberg equilibrium ($P<10^{-7}$ in controls, or $P<10^{-12}$ in cases) or with concordance <98% among 5,280 duplicate pairs. For the imputation, we additionally excluded SNPs with a MAF<1% and a call rate <98% in any consortium, SNPs that could not be linked to the 1000 Genomes Project reference, those with MAF for Europeans that differed from that for the 1000 Genomes Project and a further 1,128 SNPs where the cluster plot was judged to be not ideal. Of the 533,631 SNPs which were manufactured on the array, 494,763 passed the initial QC and 469,364 were used in the imputation (see below).

For BCAC, we excluded probable duplicate samples and close relatives within each study, and probable duplicates between studies. These were identified by identity by state (IBS) analysis using a set of approximately 38,000 uncorrelated ($r^2<0.1$) SNPs for OncoArray and iCOGS and 16,000 SNPs for GWAS. Based on inspection of the distribution of IBS values, we identified first-degree relative pairs using the criterion 0.82<IBS<0.90 for OncoArray and 0.85<IBS<0.90 for iCOGS; similar criteria were used for each GWAS (with limits depending on the IBS distribution in that study).

We applied LD score regression to the summary results from GWAS, iCOGS and OncoArray to assess the evidence of overlap in individuals between the three datasets. We conducted three pair-wise cross-trait regression analyses (GWAS-iCOGS, GWAS-OncoArray and iCOGS-OncoArray) and used the intercept from the regression analysis to estimate the amount of overlap[17]. Assuming that the phenotypic correlation is 1 (that is, a case is a case in all datasets and a control is a control in all datasets), we found that for GWAS-iCOGS, the estimated overlap was 1.5% of individuals, for GWAS-OncoArray, the estimated overlap was 3.8% of individuals, and for iCOGS-OncoArray, the estimated overlap was 0.2% of individuals. It is unlikely that this degree of overlap would have influenced the results obtained from our analyses.

We also excluded samples with a call rate <95% and samples with extreme heterozygosity (>4.9 standard deviations from the mean for the reported ethnicity). Ancestry analysis was performed using a standardized approach in which 2,318 ancestry informative markers with minor allele frequencies of 0.05 on a subset of ~66,000 samples including 505 Hapmap 2 samples. The contribution of each of the three major continental ancestry groups (European, Asian and African) was estimated by mapping each individual to regions of a triangle based on the first two principal components, as implemented in the software package FastPop (http://sourceforge.net/projects/fastpop/)[18]. Individuals were thus classified into 4 groups: European (defined as >80% European ancestry), East Asian (>40% Asian ancestry), African (>20% African ancestry) and other (not fulfilling any of the above criteria)[16]. Of the 152,492 samples genotyped, the final dataset consisted of 142,072 samples, of which 9,655 ER-negative cases and 45,494 controls of European origin had not been included in a previous GWAS and had not been genotyped using iCOGS and were included in this analysis.

For the CIMBA samples we excluded individuals of non-European ancestry using multi-dimensional scaling. For this purpose we selected 30,733 uncorrelated autosomal SNPs (pair-wise $r^2< 0.10$) to compute the genomic kinship between all pairs of *BRCA1* and *BRCA2* carriers, along with 267 HapMap samples (CHB, JPT,

YRI and CEU). These were converted to distances and subjected to multidimensional scaling. Using the first two components, we calculated the proportion of European ancestry for each individual and excluded samples with >27% non-European ancestry to ensure that samples of Ashkenazi Jewish ancestry were included in the final sample.

Global Genomic Enrichment Analyses (further details)

We created a "full baseline model" as previously described[19] that included 52 "baseline" genomic features (24 non-cell-type specific publicly available annotations, a 500-bp window around each of the 24 annotations and a 100-bp window around each of four ChIP-seq peaks) and one category containing all SNPs. We estimated the enrichment for these 53 functional categories in a single multivariable LD score regression analysis.

We subsequently performed analyses using cell-type specific annotations for the four histone marks H3K4me1, H3K4me3, H3K9ac and H3K27ac across 27-81 cell types, depending on histone mark, giving a total of 220 cell-type specific marks[19]. We estimated the enrichment for each of these marks after adjusting for the baseline annotations by running 220 LD score regressions, each adding a different histone mark to the baseline model. We observed no associations after adjusting for 220 tests

Pathway Enrichment Analyses (further details)

Pathway enrichment analysis was performed to identify pathways associated with ER-negative breast cancer risk, pointing to biological hypotheses that can be further tested experimentally.

The pathway gene set database used contains pathway gene sets from Reactome[20], NCI Pathway Interaction Database[21], GO (Gene Ontology) biological process[22], HumanCyc[23], MSigdb[24], NetPath[25] and Panther[26]. GO pathways inferred from electronic annotation terms were excluded. Some manual annotation was performed on the pathway gene set database where annotation errors from public data were discovered. In particular, in several pathways, the PDPK1 gene was mistakenly entered as PDK1 gene and was manually corrected. The same pathway (e.g. apoptosis) may be defined in two or more databases with potentially different sets of genes, and all versions of these duplicate/overlapping pathways were included.

Gene information (hg19) was downloaded from the ANNOVAR[27] website (http://www.openbioinformatics.org/annovar/). Some pathways include genes that are also grouped closely together in the genome and are thus are likely to share the significance of a single SNP, which would artificially increase the pathway significance in our analysis. This was the case for pathways including histone genes. Thus, we selected representative SNP-gene associations to control for this effect (chr6:26055031 for HIST1, chr1:120904839, 149864043 for HIST2, chr1: 228615251 for HIST3 and chr12: 14919727 for HIST4).

Although there are several methods for pathway enrichment analysis, we chose the GSEA approach as it is one of the most established methods that is threshold free; many other methods such as SRT, ALIGATOR and Plink set-based test require an arbitrary p-value threshold to be defined for SNPs and applied before pathway analysis.

To focus on pathway enrichment analysis results about which we were most confident, we implemented a number of filters. First, only pathways with positive ES and containing at least one gene linked to a significant SNP ($P<5\times10^{-8}$) were retained for subsequent analysis. Second, we defined an ES threshold (ES≥0.41) based on a comparison with a gold standard pathway enrichment analysis we previously performed on the iCOGS data alone and where we were able to analytically compute FDR values by shuffling case/control labels (this was not computationally feasible with the more complex meta-analysis scheme used in this paper).

We chose the true positive rate (TPR) threshold by varying the TPR in steps of 0.1 and observing how the FPR changed. A TPR of 0.1 resulted in a very low FPR (0.02), but we considered this to be unduly conservative as it resulted in a small number of pathways (37, clustered into 8 themes) and excluded many pathways known to be involved in breast cancer. A TPR of 0.20 (FPR = 0.14) gave a reasonable balance between the true and false positive rates, while including pathways known to be involved in breast cancer. Thus this threshold was chosen for this study. A TPR of 0.3 gave an FPR of 0.30, which we considered high; further, the resulting additional pathways included (in addition to those included at TPR=0.2) were weaker (i.e. they had worse enrichment scores [ES<0.41] and had relatively very few genes included) than pathways appearing at lower FPRs (and TPRs). We rejected TPR thresholds >0.3 because each gave an FPR that was larger than the TPR.

Finally, we performed an in depth literature search on all resulting pathways to confirm their relevance to breast cancer biology, applying the following criteria: 1) reported in at least one of five published breast cancer pathway analyses[28-32]; or 2) reported elsewhere in the literature to be involved in breast cancer. We also removed pathways that were significant due to incorrect gene function annotation.

References

1. Kheradpour, P. & Kellis, M. Systematic discovery and characterization of regulatory motifs in ENCODE TF binding experiments. *Nucleic Acids Res* **42**, 2976-87 (2014).
2. Ward, L.D. & Kellis, M. HaploReg: a resource for exploring chromatin states, conservation, and regulatory motif alterations within sets of genetically linked variants. *Nucleic Acids Res* **40**, D930-4 (2012).
3. Quinlan, A.R. BEDTools: The Swiss-Army Tool for Genome Feature Analysis. *Curr Protoc Bioinformatics* **47**, 11 12 1-34 (2014).
4. Taberlay, P.C., Statham, A.L., Kelly, T.K., Clark, S.J. & Jones, P.A. Reconfiguration of nucleosome-depleted regions at distal regulatory elements

accompanies DNA methylation of enhancers and insulators in cancer. *Genome Res* **24**, 1421-32 (2014).

5. Boyle, A.P. *et al.* Annotation of functional variation in personal genomes using RegulomeDB. *Genome Res* **22**, 1790-7 (2012).

6. GTEx Consortium. Human genomics. The Genotype-Tissue Expression (GTEx) pilot analysis: multitissue gene regulation in humans. *Science* **348**, 648-60 (2015).

7. Westra, H.J. *et al.* Systematic identification of trans eQTLs as putative drivers of known disease associations. *Nat Genet* **45**, 1238-43 (2013).

8. Li, G. *et al.* Extensive promoter-centered chromatin interactions provide a topological basis for transcription regulation. *Cell* **148**, 84-98 (2012).

9. Rao, S.S. *et al.* A 3D map of the human genome at kilobase resolution reveals principles of chromatin looping. *Cell* **159**, 1665-80 (2014).

10. He, B., Chen, C., Teng, L. & Tan, K. Global view of enhancer-promoter interactome in human cells. *Proc Natl Acad Sci U S A* **111**, E2191-9 (2014).

11. Corradin, O. *et al.* Combinatorial effects of multiple enhancer variants in linkage disequilibrium dictate levels of gene expression to confer susceptibility to common traits. *Genome Res* **24**, 1-13 (2014).

12. Hnisz, D. *et al.* Super-enhancers in the control of cell identity and disease. *Cell* **155**, 934-47 (2013).

13. Andersson, R. *et al.* An atlas of active enhancers across human cell types and tissues. *Nature* **507**, 455-61 (2014).

14. Blankenberg, D. *et al.* Galaxy: a web-based genome analysis tool for experimentalists. *Curr Protoc Mol Biol* **Chapter 19**, Unit 19 10 1-21 (2010).

15. Kent, W.J. *et al.* The human genome browser at UCSC. *Genome Res* **12**, 996-1006 (2002).

16. Amos, C.I. *et al.* The OncoArray Consortium: a Network for Understanding the Genetic Architecture of Common Cancers. *Cancer Epidemiol Biomarkers Prev* (in press).

17. Bulik-Sullivan, B. *et al.* An atlas of genetic correlations across human diseases and traits. *Nat Genet* **47**, 1236-41 (2015).

18. Li, Y. *et al.* FastPop: a rapid principal component derived method to infer intercontinental ancestry using genetic data. *BMC Bioinformatics* **17**, 122 (2016).

19. Finucane, H.K. *et al.* Partitioning heritability by functional annotation using genome-wide association summary statistics. *Nat Genet* **47**, 1228-35 (2015).

20. Joshi-Tope, G. *et al.* Reactome: a knowledgebase of biological pathways. *Nucleic Acids Res* **33**, D428-32 (2005).

21. Schaefer, C.F. *et al.* PID: the Pathway Interaction Database. *Nucleic Acids Res* **37**, D674-9 (2009).

22. Ashburner, M. *et al.* Gene ontology: tool for the unification of biology. The Gene Ontology Consortium. *Nat Genet* **25**, 25-9 (2000).

23. Romero, P. *et al.* Computational prediction of human metabolic pathways from the complete human genome. *Genome Biol* **6**, R2 (2005).

24. Subramanian, A. *et al.* Gene set enrichment analysis: a knowledge-based approach for interpreting genome-wide expression profiles. *Proc Natl Acad Sci U S A* **102**, 15545-50 (2005).

25. Kandasamy, K. *et al.* NetPath: a public resource of curated signal transduction pathways. *Genome Biol* **11**, R3 (2010).

26.   Thomas, P.D. *et al.* PANTHER: a library of protein families and subfamilies indexed by function. *Genome Res* **13**, 2129-41 (2003).
27.   Wang, K., Li, M. & Hakonarson, H. ANNOVAR: functional annotation of genetic variants from high-throughput sequencing data. *Nucleic Acids Res* **38**, e164 (2010).
28.   Kar, S.P. *et al.* Genome-Wide Meta-Analyses of Breast, Ovarian, and Prostate Cancer Association Studies Identify Multiple New Susceptibility Loci Shared by at Least Two Cancer Types. *Cancer Discov* **6**, 1052-67 (2016).
29.   Braun, R. & Buetow, K. Pathways of distinction analysis: a new technique for multi-SNP analysis of GWAS data. *PLoS Genet* **7**, e1002101 (2011).
30.   Jia, P., Zheng, S., Long, J., Zheng, W. & Zhao, Z. dmGWAS: dense module searching for genome-wide association studies in protein-protein interaction networks. *Bioinformatics* **27**, 95-102 (2011).
31.   Mogushi, K. & Tanaka, H. PathAct: a novel method for pathway analysis using gene expression profiles. *Bioinformation* **9**, 394-400 (2013).
32.   Medina, I. *et al.* Gene set-based analysis of polymorphisms: finding pathways or biological processes associated to traits in genome-wide association studies. *Nucleic Acids Res* **37**, W340-4 (2009).

Members of consortia listed as authors

ABCTB Investigators
Christine Clarke (Westmead Institute for Medical Research, University of Sydney, NSW, Australia); Rosemary Balleine (Pathology West ICPMR, Westmead, NSW, Australia); Robert Baxter (Kolling Institute of Medical Research, University of Sydney, Royal North Shore Hospital, NSW, Australia); Stephen Braye (Pathology North, John Hunter Hospital, Newcastle, NSW, 2305, Australia); Jane Carpenter (Westmead Institute for Medical Research, University of Sydney); Jane Dahlstrom (Department of Anatomical Pathology, ACT Pathology, Canberra Hospital, ACT, Australia; ANU Medical School, Australian National University, ACT, Australia); John Forbes (Department of Surgical Oncology, Calvary Mater Newcastle Hospital, Australian New Zealand Breast Cancer Trials Group, and School of Medicine and Public Health, University of Newcastle, NSW, Australia); C Soon Lee (School of Science and Health, The University of Western Sydney, Sydney, Australia); Deborah Marsh (Hormones and Cancer Group, Kolling Institute of Medical Research, Royal North Shore Hospital, University of Sydney, NSW, Australia); Adrienne Morey (SydPath St Vincent's Hospital, Sydney, NSW, Australia); Nirmala Pathmanathan (Department of Tissue Pathology and Diagnostic Oncology, Pathology West; Westmead Breast Cancer Institute, Westmead Hospital, NSW, Australia); Rodney Scott (Centre for Information Based Medicine, Hunter Medical Research Institute, NSW, 2305, Australia; Priority Research Centre for Cancer, School of Biomedical Sciences and Pharmacy, Faculty of Health, University of Newcastle, NSW, Australia); Peter Simpson (The University of Queensland: UQ Centre for Clinical Research and School of Medicine, QLD, Australia); Allan Spigelman (Hereditary Cancer Clinic, St Vincent's Hospital, The Kinghorn Cancer Centre, Sydney, New South Wales, 2010, Australia); Nicholas Wilcken (Crown Princess Mary Cancer Centre, Westmead Hospital, Westmead, Australia; Sydney Medical School - Westmead, University of Sydney, NSW, Australia); Desmond Yip (Department of Medical Oncology, The Canberra Hospital, ACT, Australia; ANU Medical School, Australian National University, ACT, Australia); Nikolajs Zeps (St John of God Perth Northern Hospitals, Perth, WA, Australia)

EMBRACE
Helen Gregory (North of Scotland Regional Genetics Service, NHS Grampian & University of Aberdeen, Foresterhill, Aberdeen, UK); Zosia Miedzybrodzka (North of Scotland Regional Genetics Service, NHS Grampian & University of Aberdeen, Foresterhill, Aberdeen, UK); Patrick J. Morrison (Northern Ireland Regional Genetics Centre, Belfast Health and Social Care Trust, and Department of Medical Genetics, Queens University Belfast, Belfast, UK); Kai-ren Ong (West Midlands Regional Genetics Service, Birmingham Women's Hospital Healthcare NHS Trust, Edgbaston, Birmingham, UK); Alan Donaldson (Clinical Genetics Department, St Michael's Hospital, Bristol, UK); Marc Tischkowitz (Department of Medical Genetics, University of Cambridge, UK); Mark T. Rogers (All Wales Medical Genetics Services, University Hospital of Wales, Cardiff, UK); M. John Kennedy (Academic Unit of Clinical and Molecular Oncology, Trinity College Dublin and St James's Hospital, Dublin, Eire); Mary E. Porteous (South East of Scotland Regional Genetics Service, Western General Hospital, Edinburgh, UK); Carole Brewer (Department of Clinical Genetics, Royal Devon & Exeter Hospital, Exeter, UK); Rosemarie Davidson (Clinical Genetics, Southern General Hospital, Glasgow, UK); Louise Izatt (Clinical Genetics, Guy's and St. Thomas' NHS Foundation Trust, London, UK); Angela Brady (North West Thames Regional

Genetics Service, Kennedy-Galton Centre, Harrow, UK); Julian Barwell (Leicestershire Clinical Genetics Service, University Hospitals of Leicester NHS Trust, UK); Julian Adlard (Yorkshire Regional Genetics Service, Leeds, UK); Claire Foo (Department of Clinical Genetics, Alder Hey Hospital, Eaton Road, Liverpool, UK); D. Gareth Evans (Genetic Medicine, Manchester Academic Health Sciences Centre, Central Manchester University Hospitals NHS Foundation Trust, Manchester, UK); Fiona Lalloo (Genetic Medicine, Manchester Academic Health Sciences Centre, Central Manchester University Hospitals NHS Foundation Trust, Manchester, UK); Lucy E. Side (North East Thames Regional Genetics Service, Great Ormond Street Hospital for Children NHS Trust, London, UK); Jacqueline Eason (Nottingham Clinical Genetics Service, Nottingham University Hospitals NHS Trust, UK); Alex Henderson (Institute of Genetic Medicine, Centre for Life, Newcastle Upon Tyne Hospitals NHS Trust, Newcastle upon Tyne, UK); Lisa Walker (Oxford Regional Genetics Service, Churchill Hospital, Oxford, UK); Rosalind A. Eeles (Oncogenetics Team, The Institute of Cancer Research and Royal Marsden NHS Foundation Trust, UK); Jackie Cook (Sheffield Clinical Genetics Service, Sheffield Children's Hospital, Sheffield, UK); Katie Snape (South West Thames Regional Genetics Service, St.Georges Hospital, Cranmer Terrace, Tooting, London, UK); Diana Eccles (University of Southampton Faculty of Medicine, Southampton University Hospitals NHS Trust, Southampton, UK); Alex Murray (All Wales Medical Genetics Services, Singleton Hospital, Swansea, UK); Emma McCann (All Wales Medical Genetics Service, Glan Clwyd Hospital, Rhyl, UK).

GEMO Study Collaborators
Dominique Stoppa-Lyonnet, Muriel Belotti, Anne-Marie Birot, Bruno Buecher, Emmanuelle Fourme, Marion Gauthier-Villars, Lisa Golmard, Claude Houdayer, Virginie Moncoutier, Antoine de Pauw, Claire Saule (Service de Génétique, Institut Curie, Paris, France); Fabienne Lesueur, Noura Mebirouk (Inserm U900, Institut Curie, Paris, France); Olga Sinilnikova†, Sylvie Mazoyer, Francesca Damiola, Laure Barjhoux, Carole Verny-Pierre, Mélanie Léone, Nadia Boutry-Kryza, Alain Calender, Sophie Giraud (Unité Mixte de Génétique Constitutionnelle des Cancers Fréquents, Hospices Civils de Lyon - Centre Léon Bérard, Lyon, France); Olivier Caron, Marine Guillaud-Bataille (Institut Gustave Roussy, Villejuif, France: Brigitte Bressac-de-Paillerets); Yves-Jean Bignon, Nancy Uhrhammer (Centre Jean Perrin, Clermont–Ferrand, France); Christine Lasset, Valérie Bonadona (Centre Léon Bérard, Lyon, France); Pascaline Berthet, Dominique Vaur, Laurent Castera (Centre François Baclesse, Caen, France); Hagay Sobol, Violaine Bourdon, Tetsuro Noguchi, Audrey Remenieras, François Eisinger, Catherine Noguès (Institut Paoli Calmettes, Marseille, France); Isabelle Coupier, Pascal Pujol (CHU Arnaud-de-Villeneuve, Montpellier, France); Jean-Philippe Peyrat, Joëlle Fournier, Françoise Révillion, Claude Adenis (Centre Oscar Lambret, Lille, France); Danièle Muller, Jean-Pierre Fricker (Centre Paul Strauss, Strasbourg, France); Emmanuelle Barouk-Simonet, Françoise Bonnet, Virginie Bubien, Nicolas Sevenet, Michel Longy (Institut Bergonié, Bordeaux, France); Christine Toulas, Rosine Guimbaud, Laurence Gladieff, Viviane Feillel (Institut Claudius Regaud, Toulouse, France); Dominique Leroux, Hélène Dreyfus, Christine Rebischung, Magalie Peysselon (CHU Grenoble, France); Fanny Coron, Laurence Faivre, Amandine Baurand, Caroline Jacquot, Geoffrey, Bertolone, Sarab Lizard (CHU Dijon, France); Fabienne Prieur, Marine Lebrun, Caroline Kientz (CHU St-Etienne, France); Sandra Fert Ferrer (Hôtel Dieu Centre Hospitalier, Chambéry, France); Véronique Mari (Centre Antoine Lacassagne, Nice, France); Laurence Vénat-Bouvet (CHU Limoges, France); Capucine Delnatte, Stéphane Bézieau (CHU Nantes, France); Isabelle Mortemousque (CHU

Bretonneau, Tours and Centre Hospitalier de Bourges France); Florence Coulet, Chrystelle Colas, Florent Soubrier, Mathilde Warcoin (Groupe Hospitalier Pitié-Salpétrière, Paris, France); Johanna Sokolowska, Myriam Bronner (CHU Vandoeuvre-les-Nancy, France); Marie-Agnès Collonge-Rame, Alexandre Damette (CHU Besançon, France); Paul Gesta (CHU Poitiers, Centre Hospitalier d'Angoulême and Centre Hospitalier de Niort, France); Hakima Lallaoui (Centre Hospitalier de La Rochelle); Jean Chiesa (CHU Nîmes Carémeau, France); Denise Molina-Gomes (CHI Poissy, France); Olivier Ingster (CHU Angers, France).

HEBON
Annemieke H. van der Hout (Department of Genetics, University Medical Center Groningen, Groningen, The Netherlands); Ans M.W. van den Ouweland (Department of Clinical Genetics, Family Cancer Clinic, Erasmus University Medical Center, Rotterdam, The Netherlands); Arjen R. Mensenkamp (Department of Human Genetics, Radboud University Medical Center, Nijmegen, The Netherlands); Carolien H.M. van Deurzen (Department of Pathology, Family Cancer Clinic, Erasmus University Medical Center, Rotterdam, The Netherlands); Carolien M. Kets (Department of Human Genetics, Radboud University Medical Center, Nijmegen, The Netherlands); Caroline Seynaeve (Department of Medical Oncology, Family Cancer Clinic, Erasmus MC Cancer Institute, Rotterdam, The Netherlands); Christi J. van Asperen (Department of Clinical Genetics, Leiden University Medical Center, Leiden, The Netherlands); Cora M. Aalfs (Department of Clinical Genetics, Academic Medical Center, Amsterdam, The Netherlands); Encarna B. Gómez Garcia (Department of Clinical Genetics , MUMC, Maastricht, The Netherlands); Flora E. van Leeuwen (Department of Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands); Frans B.L. Hogervorst (Family Cancer Clinic, Netherlands Cancer Institute, Amsterdam, The Netherlands); G.H. de Bock (Department of Oncological Epidemiology, University Medical Center, Groningen University, Groningen, The Netherlands); Hanne E.J. Meijers-Heijboer (Department of Clinical Genetics, VU University Medical Centre, Amsterdam, The Netherlands); Inge M. Obdeijn (Department of Radiology, Family Cancer Clinic, Erasmus University Medical Center, Rotterdam, The Netherlands); J. Margriet Collée (Department of Clinical Genetics, Family Cancer Clinic, Erasmus University Medical Center, Rotterdam, The Netherlands); J.J.P. Gille (Department of Clinical Genetics, VU University Medical Center, Amsterdam, The Netherlands); Jan C. Oosterwijk (Department of Genetics, University Medical Center Groningen, Groningen, The Netherlands); Juul T. Wijnen (Department of Human Genetics & Department of Clinical Genetics, Leiden University Medical Center, Leiden, The Netherlands); Lizet E. van der Kolk (Family Cancer Clinic, Netherlands Cancer Institute, Amsterdam, The Netherlands); Maartje J. Hooning (Department of Medical Oncology, Family Cancer Clinic, Erasmus MC Cancer Institute, Rotterdam, The Netherlands); Margreet G.E.M. Ausems (Department of Medical Genetics, University Medical Center Utrecht, Utrecht, The Netherlands); Marian J.E. Mourits (Department of Gynaecological Oncology, University Medical Center, Groningen University, Groningen, The Netherlands); Marinus J. Blok (Department of Clinical Genetics, Maastricht University Medical Center, Maastricht, The Netherlands); Marjanka K. Schmidt (Division of Psychosocial Research and Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands); Matti A. Rookus (Department of Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands); Muriel A. Adank (Department of Clinical Genetics, VU University Medical Centre, Amsterdam, The Netherlands); Peter Devilee (Department of Human Genetics & Department of Pathology, Leiden University Medical Center, Leiden, The

Netherlands); Rob B. van der Luijt (Department of Medical Genetics, University Medical Center Utrecht, Utrecht, The Netherlands); T.C.T.E.F. van Cronenburg (Department of Clinical Genetics Leiden University Medical Center Leiden, The Netherlands); Carmen C. van der Pol (Department of Oncological and Endocrine Surgery, University Medical Center Utrecht, Utrecht, The Netherlands):Nicola S. Russell (Department of Radiotherapy, Netherlands Cancer Institute, Amsterdam, The Netherlands); Sabine Siesling (The Netherlands Comprehensive Cancer Organization (IKNL), Utrecht, The Netherlands); Lucy Overbeek (The nationwide network and registry of histo- and cytopathology in The Netherlands [PALGA]); R. Wijnands (Department of Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands); Judith L. de Lange (Department of Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands).

kConFab/AOCS Investigators
Stephen Fox, Ian Campbell (Peter MacCallum Cancer Centre, Melbourne, Australia); Georgia Chenevix-Trench, Amanda Spurdle, Penny Webb (QIMR Berghofer Medical Research Institute, Brisbane, Australia); Anna de Fazio (Westmead Millenium Institute, Sydney, Australia); Margaret Tassell (BCNA delegate, Community Representative); Judy Kirk (Westmead Hospital, Sydney, Australia); Geoff Lindeman (Walter and Eliza Hall Institute, Melbourne, Australia); Melanie Price (University of Sydney, Sydney, Australia); Melissa Southey (University of Melbourne, Melbourne, Australia); Roger Milne (Cancer Council Victoria, Melbourne, Australia); Sid Deb (Melbourne Health, Melbourne, Australia); David Bowtell (Garvan Institute of Medical Research, Sydney, Australia).

NBSC Collaborators
Kristine K. Sahlberg (Department of Research, Vestre Viken Hospital, Drammen, Norway; Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Lars Ottestad (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Rolf Kåresen (Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway; Department of Breast- and Endocrine Surgery, Division of Surgery, Cancer and Transplantation Medicine, Oslo University Hospital Ullevål, Oslo, Norway); Anita Langerød (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Ellen Schlichting (Department of Breast- and Endocrine Surgery, Division of Surgery, Cancer and Transplantation Medicine, Oslo University Hospital Ullevål, Oslo, Norway); Marit Muri Holmen (Department of Radiology and Nuclear Medicine, Oslo University Hospital, Oslo, Norway); Toril Sauer (Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway; Department of Pathology at Akershus University hospital, Lørenskog, Norway); Vilde Haakensen (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Olav Engebråten (Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway; Department of Tumor Biology, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway; Department of Oncology, Division of Surgery and Cancer and Transplantation Medicine, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Bjørn Naume (Department of Oncology, Division of Surgery and Cancer and Transplantation Medicine, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Cecile E. Kiserud (National Advisory Unit on Late Effects after

Cancer Treatment, Department of Oncology, Oslo University Hospital, Oslo, Norway; Department of Oncology, Oslo University Hospital Ullevål, Oslo, Norway); Kristin V. Reinertsen (National Advisory Unit on Late Effects after Cancer Treatment, Department of Oncology, Oslo University Hospital, Oslo, Norway; Department of Oncology, Oslo University Hospital Ullevål, Oslo, Norway); Åslaug Helland (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway; Department of Oncology, Division of Surgery and Cancer and Transplantation Medicine, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Margit Riis (Department of Breast- and Endocrine Surgery, Division of Surgery, Cancer and Transplantation Medicine, Oslo University Hospital Ullevål, Oslo, Norway); Jürgen Geisler (Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway; Department of Breast-Endocrine Surgery, Akershus University Hospital, Oslo, Norway); Per Eystein Lønning (Section of Oncology, Institute of Medicine, University of Bergen and Department of Oncology, Haukeland University Hospital, Bergen, Norway); Solveig Hofvind (Cancer Registry of Norway, Oslo, Norway, Oslo; Akershus University College of Applied Sciences, Faculty of Health Science, Oslo, Norway); Tone F. Bathen (Department of Circulation and Medical Imaging, Norwegian University of Science and Technology (NTNU), Trondheim, Norway); Elin Borgen (Department of Pathology, Division of Diagnostics and Intervention, Oslo University Hospital, Oslo, Norway); Øystein Fodstad (Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway; Department of Tumor Biology, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Øystein Garred (Department of Pathology, Oslo University Hospital, Oslo, Norway); Gry Aarum Geitvik (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Gunhild Mari Mælandsmo (Department of Tumor Biology, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway; Department of Pharmacy, Faculty of Health Sciences, University of Tromsø, Tromsø, Norway); Hege G. Russnes (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway; Department of Pathology, Oslo University Hospital, Oslo, Norway); Therese Sørlie (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Ole Christian Lingjærde (Department of Computer Science, University of Oslo, Oslo, Norway); Helle Kristine Skjerven (Breast and Endocrine Surgery, Department of Breast and Endocrine Surgery, Vestre Viken Hospital, Drammen, Norway); Britt Fritzman (Østfold Hospital, Østfold, Norway).

***In Silico* Annotation of Candidate Causal Variants**

Guide to results table (Supplementary Table 5) and UCSC Genome Browser session
Each candidate causal SNP has been annotated with publicly available genomic data in order to highlight potentially functional variants, prioritise experimental validation, and predict target genes. Annotations fall into categories relating to putative effects on transcription factors, regulatory element activities, expression quantitative trait loci (eQTL) and target gene prediction. For each variant, a link to the UCSC Genome Browser is provided that shows a 1 Mb region with relevant genomic data.

Transcription factors
Information regarding potential effects on transcription factor recognition sequences was obtained from the ENCODE-Motifs resource (http://compbio.mit.edu/encode-motifs)[1] using VCFtools v0.1.11 to access the downloaded HaploReg v4.0 database[2]. The impact each variant has on the position weight matrix for specific transcription factors is expressed as '+' or '-' for strengthened or weakened motifs relative to elements carrying the reference allele, respectively. Processed transcription factor ChIP-seq peak data for breast cell types were downloaded from ENCODE and other publications via NCBI GEO, in BED or NarrowPeak format, converted to the hg19 assembly using LiftOver if required, and given a standardised naming system (format = "*celltype;target*" in Supplementary Table 5). More details about the overlapping binding sites may be found within browser session track "TF-chip peaks overlapping candidate SNP" where TF-ChIP-seq peaks are named in the format "*Biosample_term_name, Experiment_target, Biosample_treatments, Biological_replicate(s), File_accession*". All ChIP-seq datasets are listed in Supplementary Table 6. Variants were assessed for overlap with ChIP-seq peaks using BedTools v2.25.0[3].

Regulatory features
Histone signatures derived from histone modification ChIP-seq experiments on breast cell types carried out by ENCODE, NIH Roadmap Epigenomics, and other published studies were obtained and formatted as for ChIP-seq data. Histone modification peaks overlapping candidate causal variants are represented as "*celltype;histone_mark*" in Supplementary Table 5 and "*Biosample_term_name, Experiment_target, Biosample_treatments, Biological_replicate(s), File_accession*" in the browser track "Histone modification ChIP-seq peaks overlapping candidate SNP". BedTools was used to intersect variants with histone signatures including commonly used marks associated with enhancers (H3K4me1, H3K4me2 and H3K27ac) and promoters (H3K4me3 and H3K9ac). Chromatin Hidden Markov Modelling (ChromHMM) states were obtained for breast cells from Roadmap (HMEC and myoepithelial cells) and published MCF7 data[4] and filtered for states corresponding to 'enhancers' (Roadmap 25-state E13, E14, E15, E16, E17, E18) or 'promoters' (Roadmap 25-state E1, E2, E3, E4, E22, E23). Chromatin state features containing candidate variants are represented as "*celltype;chromatin_state*". Chromatin accessibility data obtained from ENCODE, Roadmap and other published sources via NCBI GEO measured using DNase-seq and FAIRE-seq for relevant breast cell types were also tested for overlap with candidate causal variants. Intersected regions are reported in the format "*celltype;method*". Scores based on RegulomeDB[5] are presented for available SNPs (based on dbSNP141), where lower scores are increasingly likely to be functional (http://regulomedb.org/help#score).

eQTL

Genes showing expression levels correlated with query SNPs are shown in the column headed 'eQTL_target_all'. All genes reported to be associated with genotype in studies including GTEx version 6[6] (expression is any GTEx tissue, *P* value cutoff 10^{-6}) and Westra *et al.*,[7] (expression in whole blood). Genes associated with genotype in GTEx breast samples (N=186) are listed in the column "eQTL_GTEx.breast". eQTL data from TCGA and METABRIC studies for relevant variants are also presented (format "*Associated_gene:EffectAllele:EffectDirection:P_value*").

Other genomic features

Chromosomal position, the lead variant for the associated locus, and potentially conflicting rsIDs (assessed as overlapping at the query position) are given for each variant. GWAS tagSNPs were downloaded from the UCSC Table Browser (December 2015) and associated traits are listed if the tagSNP is within a 10 kb window of the candidate causal variant. NCBI RefSeq gene annotations were downloaded from the UCSC Table Browser and BedTools was used to determine overlapping genes ("Overlapping_RefGene"). The nearest RefGene transcription start site is also presented, given in the format "RefGeneTSS|distance". Basic genomic annotations such as intergenic, intronic, exonic, and untranslated regions based on RefSeq gene annotations were determined for each variant.

Target Gene Prediction

The column headed "Predicted_target_gene" lists genes predicted by various methods to be targets of, or the expression of which is associated with, regulatory elements in which the candidate causal variant lies. The reported gene is listed with cell type and method in the format "target:cell:method". A database was created comprising publicly available data based on various methods aiming to link enhancers with target genes (Annex to Supplementary Table 5). Laboratory based experimental approaches include genome-wide Chromatin Interaction Analysis with Paired-End-Tag sequencing (ChIA-PET)[8], Hi-C[9], and other Chromosome conformation capture (3C)-based techniques. Computational resources designed to predict target promoters by correlation of gene expression with ChIP-seq signals at specific regulatory elements including IM-PET[10], PreSTIGE[11] and data from Hnisz *et al.*[12] are also included. These methods associate enhancers defined by histone modification ChIP-seq for H3K4me1 (PreSTIGE), H3K27ac (Hnisz), H3K4me1, H3K4me3 and H3K27ac (IM-PET) with gene expression signals measured by RNA-seq. FANTOM5[13] data representing enhancer-promoter cap analysis of gene expression (CAGE) expression correlation from all cell types were downloaded from http://enhancer.binf.ku.dk/. Target genes have been predicted for multiple cell types and all data were included in the database, and filtered for breast derived cell types for this analysis (see Key to Supplementary Table 5).

The following strategy was used to assign potential target genes to regulatory elements. The published computational methods (Hnisz, PreSTIGE and IM-PET) included target gene annotation in the reported data. For ChIA-PET and Hi-C data, interaction peaks were mapped to promoters defined as -1.0 kb to +0.1 kb around GENCODE (v19) transcription start sites. Enhancer definitions were used as reported for computational methods while for ChIA-PET and Hi-C were interpreted as any region interacting with a promoter (regardless of other enhancer annotation information such as histone modification or open chromatin). FANTOM5 target promoters were predefined and

tissue specificity was determined by intersecting "TSS associated enhancers" with tissue-specific sets of enhancers.

All data were formatted to enable intersection of test variants with "enhancers" as defined by each method using the Galaxy "intersect" tool[14]. Each enhancer-promoter assignment or interaction was represented as a single record along with details about potential target promoter, cell type, method, scoring and confidence statistics from the original publication. A set of query SNPs (or any loci with genomic positional information in BED format) could be queried into a custom Galaxy workflow leading to generation of a table of predicted gene targets and a link to the UCSC Genome Browser for visualisation.

<u>UCSC Genome Browser session</u>
A custom session has been uploaded to UCSC Genome Browser[15] to facilitate exploration of breast cancer risk associated variation and implicated regulatory features. This can be accessed via the hyperlink (ie. "browser") in the functional annotation *xlsx* file. All standard Genome Browser data and functions are then available, including track display options (eg. right click on a particular track to activate visualisation options), highlighting regions (shift and mouse over region of interest), and the table browser (eg. to intersect or export data).

Within the session, Oncoarray candidate causal variants are shown in red, and names can be shown by activating "pack" mode (as for all tracks). Target gene prediction data from Hnisz, PreSTIGE and IM-PET shows enhancers depicted as black bars. The segment name revealed in 'pack' mode lists predicted target gene and cell-type (eg "WNT7B.MCF7"). ChIA-PET interactions, represented in BED12 format, have been filtered to remove duplicates and *trans*-chromosomal interactions. The interactions are shaded to reflect statistical confidence based on enrichment in the original experiment. ChIA-PET interaction names show the genomic co-ordinates of either-end of the interaction, the cell type (restricted to MCF7 for this analysis), the immunoprecipitation target, and the experimental replicate. Depicted interactions are restricted to those for which a candidate variant lies within an interaction "end" with the opposite end overlapping a TSS. All other interactions may be visualised by activating the standard ENCODE ChIA-PET track (\Regulation\ENCODE Chromatin Interactions Tracks\ChIA-PET from ENCODE/GIS-Ruan).

Chromatin interactions based on *in situ* Hi-C data from HMEC cells were downloaded from NCBI GEO (accession GSE63525)[9]. Annotated loops (representing potential enhancer-promoter interactions) processed by HiCCUPS were reformatted as BED files and tested for overlap with RefSeq promoters to assign potential target genes. Opposing ends of TSS-overlap loops were then annotated as 'potential enhancers'. Specific loop regions which overlap BC risk candidate causal variants are depicted as black segments and named "*TSS_target.Celltype*".

Various classes of genomic data representing regulatory features which harbour candidate variants are shown as separate tracks:
● *Histone modification ChIP-seq peaks overlapping candidate SNP*
● *DNase HS and FAIRE-seq peaks overlapping candidate SNP*
● *TF-chip peaks overlapping candidate SNP*

As mentioned above, changing the track display to 'pack' mode will show details of the overlapping peak in the format:
"*Biosample_term_name, Experiment_target, Biosample_treatments, Biological_replicate(s), File_accession*".

A representation of all TF and histone ChIP-seq, DNase-seq, and FAIRE-seq data tested for overlap with candidate variants is shown in three histogram tracks (computed with BedTools genomeCoverageBed). These show the summed peak density at each genomic position and allow simple visualisation of loci with relative abundance of regulatory features.

Tracks for Roadmap Epigenomics Chromatin state models (based on imputed data - 25 state, 12 marks, 127 epigenomes) were generated for breast Myoepithelial and HMEC cells. Chromatin states were separated and colour coded for states related to enhancers, promoters, and transcribed regions.

The bottom track ("Oncoarray SNPs") shows all directly genotyped and imputed SNPs passing quality control (imputation $r^2 > 0.3$) as black ticks. SNPs from dbSNP build 138 with a MAF > 0.01 in European samples which were not informative are shown in red.

Funding

Acknowledgements

(Germany), Ewa Putresza, Irene Masunaka, the WHI investigators, Maggie Angelakos, Judi Maskiell, Gillian Dite, Helen Tsimiklis, Vilius Rudaitis, Laimonas Griškevičius, Janis Eglitis, Anna Krilova, Aivars Stengrevics, Yuan Chun Ding, Linda Steele, Irene Feroce, Daniela Furlan, Viviana Gismondi Riccardo Dolcetti, Gabriele Capone, Anna Laura Putignano, Giuseppe Guannini, Antonella Savarese, Aline Martayan, Stefania Tommasi, Brunella Pilato, the Cogentech Cancer Genetic Test Laboratory (Italy), Riccardo Dolcetti, Barbara Pasini, Francesca Vignolo-Lutati, Sue Healey, JoEllen Weaver, Betsy Bove, Marta Santamariña, Ana Blanco, Miguel Aguado, Uxía Esperón, Belinda Rodríguez, GEMO Collaborating Centers (Unité Mixte de Génétique Constitutionnelle des Cancers Fréquents, Hospices Civils de Lyon & Centre Léon Bérard ; Service de Génétique Oncologique, Institut Curie, Paris; Service de Génétique & BB-0033-00074, Gustave Roussy, Villejuif; Centre Léon Bérard, Lyon; Centre François Baclesse, Caen; Institut Paoli Calmettes, Marseille; CHU Arnaud-de-Villeneuve, Montpellier; Centre Oscar Lambret, Lille; Centre Paul Strauss, Strasbourg; . Institut Bergonié, Bordeaux; Institut Claudius Regaud, Toulouse; CHU Grenoble; CHU Dijon; CHU St-Etienne; Hôtel Dieu Centre Hospitalier, Chambéry; Centre Antoine Lacassagne, Nice; CHU Limoges; CHU Nantes; CHU Bretonneau, Tours; Groupe Hospitalier Pitié-Salpétrière, Paris; CHU Vandoeuvre-les-Nancy; CHU Besançon; Creighton University, Omaha, USA), GEMO Investigators (Olga Sinilnikova†, Carole Verny-Pierre, Mélanie Léone, Nadia Boutry-Kryza, Alain Calender, Sophie Giraud, Bruno Buecher, Claude Houdayer, Etienne Rouleau, Lisa Golmard, Agnès Collet, Virginie Moncoutier, Muriel Belotti, Antoine de Pauw, Camille Elan, Catherine Nogues, Emmanuelle Fourme, Anne-Marie Birot, Marine Guillaud-Bataille. Centre Jean Perrin, Clermont–Ferrand, Nancy Uhrhammer, Valérie Bonadona, Sandrine Handallou, Agnès Hardouin, Pascaline Berthet, Dominique Vaur, Hagay Sobol, Violaine Bourdon, Tetsuro Noguchi, Audrey Remenieras, François Eisinger, Pascal Pujol, Jean-Philippe Peyrat, Joëlle Fournier, Françoise Révillion, Philippe Vennin†, Claude Adenis, Danièle Muller, Jean-Pierre Fricker, Emmanuelle Barouk-Simonet, Françoise Bonnet, Virginie Bubien, Nicolas Sevenet, Michel Longy, Christine Toulas, Rosine Guimbaud, Laurence Gladieff, Viviane Feillel, Dominique Leroux, Hélène Dreyfus, Christine Rebischung, Magalie Peysselon, Fanny Coron, Fabienne Prieur, Marine Lebrun, Caroline Kientz, Sandra Fert Ferrer, Marc Frénay, Laurence Vénat-Bouvet, Capucine Delnatte, Isabelle Mortemousque, Florence Coulet, Chrystelle Colas, Florent Soubrier, Mathilde Warcoin, Johanna Sokolowska, Myriam Bronner, Marie-Agnès Collonge-Rame, Alexandre Damette, Henry T. Lynch, Carrie L. Snyder, Ilse Coene, Brecht Crombez, Alicia Tosar, Paula Diaque, Kristiina Aittomäki, Taru A. Muranen, Kirsimari Aaltonen, Irja Erkkilä, Virpi Palola, Comprehensive Cancer Centre Netherlands, Comprehensive Centre South, Netherlands Cancer Registry, Dutch Pathology Registry, HEBON Collaborating Centers (Netherlands Cancer Institute, Erasmus Medical Center - Rotterdam, Leiden University Medical Center, Radboud University Nijmegen Medical Center, University Medical Center Utrecht, Amsterdam Medical Center, VU University Medical Center - Amsterdam, University Hospital Maastricht, The Netherlands Foundation for the detection of hereditary tumours, The Netherlands Comprehensive Cancer Organization [IKNL], the Dutch Pathology Registry [PALGA], Groningen University Medical Center - Groningen), HEBON Investigators (F.E. van Leeuwen, S. Verhoef, N.S. Russell, J.L. de Lange, R. Wijnands, J.M. Collée, C.H.M. van Deurzen, I.M. Obdeijn, T.C.T.E.F. van Cronenburg, A.R. Mensenkamp, R.B. van der Luijt, C.C. van der Pol, J.J.P. Gille, Q. Waisfisz, H.F. Vasen, S. Siesling, J.Verloop, L.I.H. Overbeek. E.B. Gómez-Garcia, A.H. van der Hout, M.J. Mourits, G.H. de Bock) Janos Papp, Tibor Vaszko, Aniko Bozsik, Judit Franko, Maria Balogh, Gabriella Domokos, Judit Ferenczi, the Oncogenetics

OncoArray genotype calling and quality control

Of the 568,712 variants selected for genotyping on OncoArray, 533,631 were successfully manufactured on the array (including 778 duplicate probes). OncoArray genotyping of BCAC and CIMBA samples was conducted at six sites. Details of the genotyping calling for the OncoArray are described in more detail elsewhere[16]. Briefly, we developed a single calling pipeline that was applied to more than 500,000 samples. An initial cluster file was generated using from 56,284 samples, selected over all the major genotyping centres and ethnicities, using the Gentrain2 algorithm. Variants likely to have problematic clusters were selected for manual inspection using the following criteria: call rate below 99%, minor allele frequency (MAF) <0.001, poor Illumina intensity and clustering metrics, deviation from the MAF observed in the 1000 Genomes Project using the criterion: $\frac{(|p_1-p_0|-0.01)^2}{((p_1+p_0)(2-p_1-p_0))} > C$, where p_0 and p_1 are the minor frequencies in the 1000 Genome Project and Oncoarray datasets, respectively, and C=0.008. (This latter criterion is approximately equivalent to excluding SNPs on the basis of a Chi-square statistic of 16 for the difference in allele frequencies, assuming 1,000 samples in each group). This resulted in manual adjustment of the cluster file for 3,964 variants, and the exclusion of 16,526 variants. The final cluster file was then applied to the full dataset.

We excluded SNPs with a call rate <95% in any consortium, not in Hardy-Weinberg equilibrium ($P<10^{-7}$ in controls, or $P<10^{-12}$ in cases) or with concordance <98% among 5,280 duplicate pairs. For the imputation, we additionally excluded SNPs with a MAF<1% and a call rate <98% in any consortium, SNPs that could not be linked to the 1000 Genomes Project reference, those with MAF for Europeans that differed from that for the 1000 Genomes Project and a further 1,128 SNPs where the cluster plot was judged to be not ideal. Of the 533,631 SNPs which were manufactured on the array, 494,763 passed the initial QC and 469,364 were used in the imputation (see below).

For BCAC, we excluded probable duplicate samples and close relatives within each study, and probable duplicates between studies. These were identified by identity by state (IBS) analysis using a set of approximately 38,000 uncorrelated ($r^2<0.1$) SNPs for OncoArray and iCOGS and 16,000 SNPs for GWAS. Based on inspection of the distribution of IBS values, we identified first-degree relative pairs using the criterion 0.82<IBS<0.90 for OncoArray and 0.85<IBS<0.90 for iCOGS; similar criteria were used for each GWAS (with limits depending on the IBS distribution in that study).

We applied LD score regression to the summary results from GWAS, iCOGS and OncoArray to assess the evidence of overlap in individuals between the three datasets. We conducted three pair-wise cross-trait regression analyses (GWAS-iCOGS, GWAS-OncoArray and iCOGS-OncoArray) and used the intercept from the regression analysis to estimate the amount of overlap[17]. Assuming that the phenotypic correlation is 1 (that is, a case is a case in all datasets and a control is a control in all datasets), we found that for GWAS-iCOGS, the estimated overlap was 1.5% of individuals, for GWAS-OncoArray, the estimated overlap was 3.8% of individuals, and for iCOGS-OncoArray, the estimated overlap was 0.2% of individuals. It is unlikely that this degree of overlap would have influenced the results obtained from our analyses.

We also excluded samples with a call rate <95% and samples with extreme heterozygosity (>4.9 standard deviations from the mean for the reported ethnicity). Ancestry analysis was performed using a standardized approach in which 2,318 ancestry informative markers with minor allele frequencies of 0.05 on a subset of ~66,000 samples including 505 Hapmap 2 samples. The contribution of each of the three major continental ancestry groups (European, Asian and African) was estimated by mapping each individual to regions of a triangle based on the first two principal components, as implemented in the software package FastPop (http://sourceforge.net/projects/fastpop/)[18]. Individuals were thus classified into 4 groups: European (defined as >80% European ancestry), East Asian (>40% Asian ancestry), African (>20% African ancestry) and other (not fulfilling any of the above criteria)[16]. Of the 152,492 samples genotyped, the final dataset consisted of 142,072 samples, of which 9,655 ER-negative cases and 45,494 controls of European origin had not been included in a previous GWAS and had not been genotyped using iCOGS and were included in this analysis.

For the CIMBA samples we excluded individuals of non-European ancestry using multi-dimensional scaling. For this purpose we selected 30,733 uncorrelated autosomal SNPs (pair-wise $r^2< 0.10$) to compute the genomic kinship between all pairs of *BRCA1* and *BRCA2* carriers, along with 267 HapMap samples (CHB, JPT,

YRI and CEU). These were converted to distances and subjected to multidimensional scaling. Using the first two components, we calculated the proportion of European ancestry for each individual and excluded samples with >27% non-European ancestry to ensure that samples of Ashkenazi Jewish ancestry were included in the final sample.

Global Genomic Enrichment Analyses (further details)

We created a "full baseline model" as previously described[19] that included 52 "baseline" genomic features (24 non-cell-type specific publicly available annotations, a 500-bp window around each of the 24 annotations and a 100-bp window around each of four ChIP-seq peaks) and one category containing all SNPs. We estimated the enrichment for these 53 functional categories in a single multivariable LD score regression analysis.

We subsequently performed analyses using cell-type specific annotations for the four histone marks H3K4me1, H3K4me3, H3K9ac and H3K27ac across 27-81 cell types, depending on histone mark, giving a total of 220 cell-type specific marks[19]. We estimated the enrichment for each of these marks after adjusting for the baseline annotations by running 220 LD score regressions, each adding a different histone mark to the baseline model. We observed no associations after adjusting for 220 tests

Pathway Enrichment Analyses (further details)

Pathway enrichment analysis was performed to identify pathways associated with ER-negative breast cancer risk, pointing to biological hypotheses that can be further tested experimentally.

The pathway gene set database used contains pathway gene sets from Reactome[20], NCI Pathway Interaction Database[21], GO (Gene Ontology) biological process[22], HumanCyc[23], MSigdb[24], NetPath[25] and Panther[26]. GO pathways inferred from electronic annotation terms were excluded. Some manual annotation was performed on the pathway gene set database where annotation errors from public data were discovered. In particular, in several pathways, the PDPK1 gene was mistakenly entered as PDK1 gene and was manually corrected. The same pathway (e.g. apoptosis) may be defined in two or more databases with potentially different sets of genes, and all versions of these duplicate/overlapping pathways were included.

Gene information (hg19) was downloaded from the ANNOVAR[27] website (http://www.openbioinformatics.org/annovar/). Some pathways include genes that are also grouped closely together in the genome and are thus are likely to share the significance of a single SNP, which would artificially increase the pathway significance in our analysis. This was the case for pathways including histone genes. Thus, we selected representative SNP-gene associations to control for this effect (chr6:26055031 for HIST1, chr1:120904839, 149864043 for HIST2, chr1: 228615251 for HIST3 and chr12: 14919727 for HIST4).

Although there are several methods for pathway enrichment analysis, we chose the GSEA approach as it is one of the most established methods that is threshold free; many other methods such as SRT, ALIGATOR and Plink set-based test require an arbitrary p-value threshold to be defined for SNPs and applied before pathway analysis.

To focus on pathway enrichment analysis results about which we were most confident, we implemented a number of filters. First, only pathways with positive ES and containing at least one gene linked to a significant SNP ($P<5\times10^{-8}$) were retained for subsequent analysis. Second, we defined an ES threshold (ES≥0.41) based on a comparison with a gold standard pathway enrichment analysis we previously performed on the iCOGS data alone and where we were able to analytically compute FDR values by shuffling case/control labels (this was not computationally feasible with the more complex meta-analysis scheme used in this paper).

We chose the true positive rate (TPR) threshold by varying the TPR in steps of 0.1 and observing how the FPR changed. A TPR of 0.1 resulted in a very low FPR (0.02), but we considered this to be unduly conservative as it resulted in a small number of pathways (37, clustered into 8 themes) and excluded many pathways known to be involved in breast cancer. A TPR of 0.20 (FPR = 0.14) gave a reasonable balance between the true and false positive rates, while including pathways known to be involved in breast cancer. Thus this threshold was chosen for this study. A TPR of 0.3 gave an FPR of 0.30, which we considered high; further, the resulting additional pathways included (in addition to those included at TPR=0.2) were weaker (i.e. they had worse enrichment scores [ES<0.41] and had relatively very few genes included) than pathways appearing at lower FPRs (and TPRs). We rejected TPR thresholds >0.3 because each gave an FPR that was larger than the TPR.

Finally, we performed an in depth literature search on all resulting pathways to confirm their relevance to breast cancer biology, applying the following criteria:
1) reported in at least one of five published breast cancer pathway analyses[28-32]; or
2) reported elsewhere in the literature to be involved in breast cancer. We also removed pathways that were significant due to incorrect gene function annotation.

References

1. Kheradpour, P. & Kellis, M. Systematic discovery and characterization of regulatory motifs in ENCODE TF binding experiments. *Nucleic Acids Res* **42**, 2976-87 (2014).
2. Ward, L.D. & Kellis, M. HaploReg: a resource for exploring chromatin states, conservation, and regulatory motif alterations within sets of genetically linked variants. *Nucleic Acids Res* **40**, D930-4 (2012).
3. Quinlan, A.R. BEDTools: The Swiss-Army Tool for Genome Feature Analysis. *Curr Protoc Bioinformatics* **47**, 11 12 1-34 (2014).
4. Taberlay, P.C., Statham, A.L., Kelly, T.K., Clark, S.J. & Jones, P.A. Reconfiguration of nucleosome-depleted regions at distal regulatory elements

accompanies DNA methylation of enhancers and insulators in cancer. *Genome Res* **24**, 1421-32 (2014).

5. Boyle, A.P. *et al.* Annotation of functional variation in personal genomes using RegulomeDB. *Genome Res* **22**, 1790-7 (2012).

6. GTEx Consortium. Human genomics. The Genotype-Tissue Expression (GTEx) pilot analysis: multitissue gene regulation in humans. *Science* **348**, 648-60 (2015).

7. Westra, H.J. *et al.* Systematic identification of trans eQTLs as putative drivers of known disease associations. *Nat Genet* **45**, 1238-43 (2013).

8. Li, G. *et al.* Extensive promoter-centered chromatin interactions provide a topological basis for transcription regulation. *Cell* **148**, 84-98 (2012).

9. Rao, S.S. *et al.* A 3D map of the human genome at kilobase resolution reveals principles of chromatin looping. *Cell* **159**, 1665-80 (2014).

10. He, B., Chen, C., Teng, L. & Tan, K. Global view of enhancer-promoter interactome in human cells. *Proc Natl Acad Sci U S A* **111**, E2191-9 (2014).

11. Corradin, O. *et al.* Combinatorial effects of multiple enhancer variants in linkage disequilibrium dictate levels of gene expression to confer susceptibility to common traits. *Genome Res* **24**, 1-13 (2014).

12. Hnisz, D. *et al.* Super-enhancers in the control of cell identity and disease. *Cell* **155**, 934-47 (2013).

13. Andersson, R. *et al.* An atlas of active enhancers across human cell types and tissues. *Nature* **507**, 455-61 (2014).

14. Blankenberg, D. *et al.* Galaxy: a web-based genome analysis tool for experimentalists. *Curr Protoc Mol Biol* **Chapter 19**, Unit 19 10 1-21 (2010).

15. Kent, W.J. *et al.* The human genome browser at UCSC. *Genome Res* **12**, 996-1006 (2002).

16. Amos, C.I. *et al.* The OncoArray Consortium: a Network for Understanding the Genetic Architecture of Common Cancers. *Cancer Epidemiol Biomarkers Prev* (in press).

17. Bulik-Sullivan, B. *et al.* An atlas of genetic correlations across human diseases and traits. *Nat Genet* **47**, 1236-41 (2015).

18. Li, Y. *et al.* FastPop: a rapid principal component derived method to infer intercontinental ancestry using genetic data. *BMC Bioinformatics* **17**, 122 (2016).

19. Finucane, H.K. *et al.* Partitioning heritability by functional annotation using genome-wide association summary statistics. *Nat Genet* **47**, 1228-35 (2015).

20. Joshi-Tope, G. *et al.* Reactome: a knowledgebase of biological pathways. *Nucleic Acids Res* **33**, D428-32 (2005).

21. Schaefer, C.F. *et al.* PID: the Pathway Interaction Database. *Nucleic Acids Res* **37**, D674-9 (2009).

22. Ashburner, M. *et al.* Gene ontology: tool for the unification of biology. The Gene Ontology Consortium. *Nat Genet* **25**, 25-9 (2000).

23. Romero, P. *et al.* Computational prediction of human metabolic pathways from the complete human genome. *Genome Biol* **6**, R2 (2005).

24. Subramanian, A. *et al.* Gene set enrichment analysis: a knowledge-based approach for interpreting genome-wide expression profiles. *Proc Natl Acad Sci U S A* **102**, 15545-50 (2005).

25. Kandasamy, K. *et al.* NetPath: a public resource of curated signal transduction pathways. *Genome Biol* **11**, R3 (2010).

26. Thomas, P.D. *et al.* PANTHER: a library of protein families and subfamilies indexed by function. *Genome Res* **13**, 2129-41 (2003).
27. Wang, K., Li, M. & Hakonarson, H. ANNOVAR: functional annotation of genetic variants from high-throughput sequencing data. *Nucleic Acids Res* **38**, e164 (2010).
28. Kar, S.P. *et al.* Genome-Wide Meta-Analyses of Breast, Ovarian, and Prostate Cancer Association Studies Identify Multiple New Susceptibility Loci Shared by at Least Two Cancer Types. *Cancer Discov* **6**, 1052-67 (2016).
29. Braun, R. & Buetow, K. Pathways of distinction analysis: a new technique for multi-SNP analysis of GWAS data. *PLoS Genet* **7**, e1002101 (2011).
30. Jia, P., Zheng, S., Long, J., Zheng, W. & Zhao, Z. dmGWAS: dense module searching for genome-wide association studies in protein-protein interaction networks. *Bioinformatics* **27**, 95-102 (2011).
31. Mogushi, K. & Tanaka, H. PathAct: a novel method for pathway analysis using gene expression profiles. *Bioinformation* **9**, 394-400 (2013).
32. Medina, I. *et al.* Gene set-based analysis of polymorphisms: finding pathways or biological processes associated to traits in genome-wide association studies. *Nucleic Acids Res* **37**, W340-4 (2009).

Members of consortia listed as authors

ABCTB Investigators

Christine Clarke (Westmead Institute for Medical Research, University of Sydney, NSW, Australia); Rosemary Balleine (Pathology West ICPMR, Westmead, NSW, Australia); Robert Baxter (Kolling Institute of Medical Research, University of Sydney, Royal North Shore Hospital, NSW, Australia); Stephen Braye (Pathology North, John Hunter Hospital, Newcastle, NSW, 2305, Australia); Jane Carpenter (Westmead Institute for Medical Research, University of Sydney); Jane Dahlstrom (Department of Anatomical Pathology, ACT Pathology, Canberra Hospital, ACT, Australia; ANU Medical School, Australian National University, ACT, Australia); John Forbes (Department of Surgical Oncology, Calvary Mater Newcastle Hospital, Australian New Zealand Breast Cancer Trials Group, and School of Medicine and Public Health, University of Newcastle, NSW, Australia); C Soon Lee (School of Science and Health, The University of Western Sydney, Sydney, Australia); Deborah Marsh (Hormones and Cancer Group, Kolling Institute of Medical Research, Royal North Shore Hospital, University of Sydney, NSW, Australia); Adrienne Morey (SydPath St Vincent's Hospital, Sydney, NSW, Australia); Nirmala Pathmanathan (Department of Tissue Pathology and Diagnostic Oncology, Pathology West; Westmead Breast Cancer Institute, Westmead Hospital, NSW, Australia); Rodney Scott (Centre for Information Based Medicine, Hunter Medical Research Institute, NSW, 2305, Australia; Priority Research Centre for Cancer, School of Biomedical Sciences and Pharmacy, Faculty of Health, University of Newcastle, NSW, Australia); Peter Simpson (The University of Queensland: UQ Centre for Clinical Research and School of Medicine, QLD, Australia); Allan Spigelman (Hereditary Cancer Clinic, St Vincent's Hospital, The Kinghorn Cancer Centre, Sydney, New South Wales, 2010, Australia); Nicholas Wilcken (Crown Princess Mary Cancer Centre, Westmead Hospital, Westmead, Australia; Sydney Medical School - Westmead, University of Sydney, NSW, Australia); Desmond Yip (Department of Medical Oncology, The Canberra Hospital, ACT, Australia; ANU Medical School, Australian National University, ACT, Australia); Nikolajs Zeps (St John of God Perth Northern Hospitals, Perth, WA, Australia)

EMBRACE

Helen Gregory (North of Scotland Regional Genetics Service, NHS Grampian & University of Aberdeen, Foresterhill, Aberdeen, UK); Zosia Miedzybrodzka (North of Scotland Regional Genetics Service, NHS Grampian & University of Aberdeen, Foresterhill, Aberdeen, UK); Patrick J. Morrison (Northern Ireland Regional Genetics Centre, Belfast Health and Social Care Trust, and Department of Medical Genetics, Queens University Belfast, Belfast, UK); Kai-ren Ong (West Midlands Regional Genetics Service, Birmingham Women's Hospital Healthcare NHS Trust, Edgbaston, Birmingham, UK); Alan Donaldson (Clinical Genetics Department, St Michael's Hospital, Bristol, UK); Marc Tischkowitz (Department of Medical Genetics, University of Cambridge, UK); Mark T. Rogers (All Wales Medical Genetics Services, University Hospital of Wales, Cardiff, UK); M. John Kennedy (Academic Unit of Clinical and Molecular Oncology, Trinity College Dublin and St James's Hospital, Dublin, Eire); Mary E. Porteous (South East of Scotland Regional Genetics Service, Western General Hospital, Edinburgh, UK); Carole Brewer (Department of Clinical Genetics, Royal Devon & Exeter Hospital, Exeter, UK); Rosemarie Davidson (Clinical Genetics, Southern General Hospital, Glasgow, UK); Louise Izatt (Clinical Genetics, Guy's and St. Thomas' NHS Foundation Trust, London, UK); Angela Brady (North West Thames Regional

Genetics Service, Kennedy-Galton Centre, Harrow, UK); Julian Barwell (Leicestershire Clinical Genetics Service, University Hospitals of Leicester NHS Trust, UK); Julian Adlard (Yorkshire Regional Genetics Service, Leeds, UK); Claire Foo (Department of Clinical Genetics, Alder Hey Hospital, Eaton Road, Liverpool, UK); D. Gareth Evans (Genetic Medicine, Manchester Academic Health Sciences Centre, Central Manchester University Hospitals NHS Foundation Trust, Manchester, UK); Fiona Lalloo (Genetic Medicine, Manchester Academic Health Sciences Centre, Central Manchester University Hospitals NHS Foundation Trust, Manchester, UK); Lucy E. Side (North East Thames Regional Genetics Service, Great Ormond Street Hospital for Children NHS Trust, London, UK); Jacqueline Eason (Nottingham Clinical Genetics Service, Nottingham University Hospitals NHS Trust, UK); Alex Henderson (Institute of Genetic Medicine, Centre for Life, Newcastle Upon Tyne Hospitals NHS Trust, Newcastle upon Tyne, UK); Lisa Walker (Oxford Regional Genetics Service, Churchill Hospital, Oxford, UK); Rosalind A. Eeles (Oncogenetics Team, The Institute of Cancer Research and Royal Marsden NHS Foundation Trust, UK); Jackie Cook (Sheffield Clinical Genetics Service, Sheffield Children's Hospital, Sheffield, UK); Katie Snape (South West Thames Regional Genetics Service, St.Georges Hospital, Cranmer Terrace, Tooting, London, UK); Diana Eccles (University of Southampton Faculty of Medicine, Southampton University Hospitals NHS Trust, Southampton, UK); Alex Murray (All Wales Medical Genetics Services, Singleton Hospital, Swansea, UK); Emma McCann (All Wales Medical Genetics Service, Glan Clwyd Hospital, Rhyl, UK).

GEMO Study Collaborators
Dominique Stoppa-Lyonnet, Muriel Belotti, Anne-Marie Birot, Bruno Buecher, Emmanuelle Fourme, Marion Gauthier-Villars, Lisa Golmard, Claude Houdayer, Virginie Moncoutier, Antoine de Pauw, Claire Saule (Service de Génétique, Institut Curie, Paris, France); Fabienne Lesueur, Noura Mebirouk (Inserm U900, Institut Curie, Paris, France); Olga Sinilnikova†, Sylvie Mazoyer, Francesca Damiola, Laure Barjhoux, Carole Verny-Pierre, Mélanie Léone, Nadia Boutry-Kryza, Alain Calender, Sophie Giraud (Unité Mixte de Génétique Constitutionnelle des Cancers Fréquents, Hospices Civils de Lyon - Centre Léon Bérard, Lyon, France); Olivier Caron, Marine Guillaud-Bataille (Institut Gustave Roussy, Villejuif, France: Brigitte Bressac-de-Paillerets); Yves-Jean Bignon, Nancy Uhrhammer (Centre Jean Perrin, Clermont–Ferrand, France); Christine Lasset, Valérie Bonadona (Centre Léon Bérard, Lyon, France); Pascaline Berthet, Dominique Vaur, Laurent Castera (Centre François Baclesse, Caen, France); Hagay Sobol, Violaine Bourdon, Tetsuro Noguchi, Audrey Remenieras, François Eisinger, Catherine Noguès (Institut Paoli Calmettes, Marseille, France); Isabelle Coupier, Pascal Pujol (CHU Arnaud-de-Villeneuve, Montpellier, France); Jean-Philippe Peyrat, Joëlle Fournier, Françoise Révillion, Claude Adenis (Centre Oscar Lambret, Lille, France); Danièle Muller, Jean-Pierre Fricker (Centre Paul Strauss, Strasbourg, France); Emmanuelle Barouk-Simonet, Françoise Bonnet, Virginie Bubien, Nicolas Sevenet, Michel Longy (Institut Bergonié, Bordeaux, France); Christine Toulas, Rosine Guimbaud, Laurence Gladieff, Viviane Feillel (Institut Claudius Regaud, Toulouse, France); Dominique Leroux, Hélène Dreyfus, Christine Rebischung, Magalie Peysselon (CHU Grenoble, France); Fanny Coron, Laurence Faivre, Amandine Baurand, Caroline Jacquot, Geoffrey, Bertolone, Sarab Lizard (CHU Dijon, France); Fabienne Prieur, Marine Lebrun, Caroline Kientz (CHU St-Etienne, France); Sandra Fert Ferrer (Hôtel Dieu Centre Hospitalier, Chambéry, France); Véronique Mari (Centre Antoine Lacassagne, Nice, France); Laurence Vénat-Bouvet (CHU Limoges, France); Capucine Delnatte, Stéphane Bézieau (CHU Nantes, France); Isabelle Mortemousque (CHU

Bretonneau, Tours and Centre Hospitalier de Bourges France); Florence Coulet, Chrystelle Colas, Florent Soubrier, Mathilde Warcoin (Groupe Hospitalier Pitié-Salpétrière, Paris, France); Johanna Sokolowska, Myriam Bronner (CHU Vandoeuvre-les-Nancy, France); Marie-Agnès Collonge-Rame, Alexandre Damette (CHU Besançon, France); Paul Gesta (CHU Poitiers, Centre Hospitalier d'Angoulême and Centre Hospitalier de Niort, France); Hakima Lallaoui (Centre Hospitalier de La Rochelle); Jean Chiesa (CHU Nîmes Carémeau, France); Denise Molina-Gomes (CHI Poissy, France); Olivier Ingster (CHU Angers, France).

HEBON
Annemieke H. van der Hout (Department of Genetics, University Medical Center Groningen, Groningen, The Netherlands); Ans M.W. van den Ouweland (Department of Clinical Genetics, Family Cancer Clinic, Erasmus University Medical Center, Rotterdam, The Netherlands); Arjen R. Mensenkamp (Department of Human Genetics, Radboud University Medical Center, Nijmegen, The Netherlands); Carolien H.M. van Deurzen (Department of Pathology, Family Cancer Clinic, Erasmus University Medical Center, Rotterdam, The Netherlands); Carolien M. Kets (Department of Human Genetics, Radboud University Medical Center, Nijmegen, The Netherlands); Caroline Seynaeve (Department of Medical Oncology, Family Cancer Clinic, Erasmus MC Cancer Institute, Rotterdam, The Netherlands); Christi J. van Asperen (Department of Clinical Genetics, Leiden University Medical Center, Leiden, The Netherlands); Cora M. Aalfs (Department of Clinical Genetics, Academic Medical Center, Amsterdam, The Netherlands); Encarna B. Gómez Garcia (Department of Clinical Genetics , MUMC, Maastricht, The Netherlands); Flora E. van Leeuwen (Department of Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands); Frans B.L. Hogervorst (Family Cancer Clinic, Netherlands Cancer Institute, Amsterdam, The Netherlands); G.H. de Bock (Department of Oncological Epidemiology, University Medical Center, Groningen University, Groningen, The Netherlands); Hanne E.J. Meijers-Heijboer (Department of Clinical Genetics, VU University Medical Centre, Amsterdam, The Netherlands); Inge M. Obdeijn (Department of Radiology, Family Cancer Clinic, Erasmus University Medical Center, Rotterdam, The Netherlands); J. Margriet Collée (Department of Clinical Genetics, Family Cancer Clinic, Erasmus University Medical Center, Rotterdam, The Netherlands); J.J.P. Gille (Department of Clinical Genetics, VU University Medical Center, Amsterdam, The Netherlands); Jan C. Oosterwijk (Department of Genetics, University Medical Center Groningen, Groningen, The Netherlands); Juul T. Wijnen (Department of Human Genetics & Department of Clinical Genetics, Leiden University Medical Center, Leiden, The Netherlands); Lizet E. van der Kolk (Family Cancer Clinic, Netherlands Cancer Institute, Amsterdam, The Netherlands); Maartje J. Hooning (Department of Medical Oncology, Family Cancer Clinic, Erasmus MC Cancer Institute, Rotterdam, The Netherlands); Margreet G.E.M. Ausems (Department of Medical Genetics, University Medical Center Utrecht, Utrecht, The Netherlands); Marian J.E. Mourits (Department of Gynaecological Oncology, University Medical Center, Groningen University, Groningen, The Netherlands); Marinus J. Blok (Department of Clinical Genetics, Maastricht University Medical Center, Maastricht, The Netherlands); Marjanka K. Schmidt (Division of Psychosocial Research and Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands); Matti A. Rookus (Department of Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands); Muriel A. Adank (Department of Clinical Genetics, VU University Medical Centre, Amsterdam, The Netherlands); Peter Devilee (Department of Human Genetics & Department of Pathology, Leiden University Medical Center, Leiden, The

Netherlands); Rob B. van der Luijt (Department of Medical Genetics, University Medical Center Utrecht, Utrecht, The Netherlands); T.C.T.E.F. van Cronenburg (Department of Clinical Genetics Leiden University Medical Center Leiden, The Netherlands); Carmen C. van der Pol (Department of Oncological and Endocrine Surgery, University Medical Center Utrecht, Utrecht, The Netherlands):Nicola S. Russell (Department of Radiotherapy, Netherlands Cancer Institute, Amsterdam, The Netherlands); Sabine Siesling (The Netherlands Comprehensive Cancer Organization (IKNL), Utrecht, The Netherlands); Lucy Overbeek (The nationwide network and registry of histo- and cytopathology in The Netherlands [PALGA]); R. Wijnands (Department of Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands); Judith L. de Lange (Department of Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands).

kConFab/AOCS Investigators
Stephen Fox, Ian Campbell (Peter MacCallum Cancer Centre, Melbourne, Australia); Georgia Chenevix-Trench, Amanda Spurdle, Penny Webb (QIMR Berghofer Medical Research Institute, Brisbane, Australia); Anna de Fazio (Westmead Millenium Institute, Sydney, Australia); Margaret Tassell (BCNA delegate, Community Representative); Judy Kirk (Westmead Hospital, Sydney, Australia); Geoff Lindeman (Walter and Eliza Hall Institute, Melbourne, Australia); Melanie Price (University of Sydney, Sydney, Australia); Melissa Southey (University of Melbourne, Melbourne, Australia); Roger Milne (Cancer Council Victoria, Melbourne, Australia); Sid Deb (Melbourne Health, Melbourne, Australia); David Bowtell (Garvan Institute of Medical Research, Sydney, Australia).

NBSC Collaborators
Kristine K. Sahlberg (Department of Research, Vestre Viken Hospital, Drammen, Norway; Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Lars Ottestad (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Rolf Kåresen (Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway; Department of Breast- and Endocrine Surgery, Division of Surgery, Cancer and Transplantation Medicine, Oslo University Hospital Ullevål, Oslo, Norway); Anita Langerød (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Ellen Schlichting (Department of Breast- and Endocrine Surgery, Division of Surgery, Cancer and Transplantation Medicine, Oslo University Hospital Ullevål, Oslo, Norway); Marit Muri Holmen (Department of Radiology and Nuclear Medicine, Oslo University Hospital, Oslo, Norway); Toril Sauer (Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway; Department of Pathology at Akershus University hospital, Lørenskog, Norway); Vilde Haakensen (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Olav Engebråten (Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway; Department of Tumor Biology, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway; Department of Oncology, Division of Surgery and Cancer and Transplantation Medicine, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Bjørn Naume (Department of Oncology, Division of Surgery and Cancer and Transplantation Medicine, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Cecile E. Kiserud (National Advisory Unit on Late Effects after

Cancer Treatment, Department of Oncology, Oslo University Hospital, Oslo, Norway; Department of Oncology, Oslo University Hospital Ullevål, Oslo, Norway); Kristin V. Reinertsen (National Advisory Unit on Late Effects after Cancer Treatment, Department of Oncology, Oslo University Hospital, Oslo, Norway; Department of Oncology, Oslo University Hospital Ullevål, Oslo, Norway); Åslaug Helland (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway; Department of Oncology, Division of Surgery and Cancer and Transplantation Medicine, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Margit Riis (Department of Breast- and Endocrine Surgery, Division of Surgery, Cancer and Transplantation Medicine, Oslo University Hospital Ullevål, Oslo, Norway); Jürgen Geisler (Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway; Department of Breast-Endocrine Surgery, Akershus University Hospital, Oslo, Norway); Per Eystein Lønning (Section of Oncology, Institute of Medicine, University of Bergen and Department of Oncology, Haukeland University Hospital, Bergen, Norway); Solveig Hofvind (Cancer Registry of Norway, Oslo, Norway, Oslo; Akershus University College of Applied Sciences, Faculty of Health Science, Oslo, Norway); Tone F. Bathen (Department of Circulation and Medical Imaging, Norwegian University of Science and Technology (NTNU), Trondheim, Norway); Elin Borgen (Department of Pathology, Division of Diagnostics and Intervention, Oslo University Hospital, Oslo, Norway); Øystein Fodstad (Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway; Department of Tumor Biology, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Øystein Garred (Department of Pathology, Oslo University Hospital, Oslo, Norway); Gry Aarum Geitvik (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Gunhild Mari Mælandsmo (Department of Tumor Biology, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway; Department of Pharmacy, Faculty of Health Sciences, University of Tromsø, Tromsø, Norway); Hege G. Russnes (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway; Department of Pathology, Oslo University Hospital, Oslo, Norway); Therese Sørlie (Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Norway); Ole Christian Lingjærde (Department of Computer Science, University of Oslo, Oslo, Norway); Helle Kristine Skjerven (Breast and Endocrine Surgery, Department of Breast and Endocrine Surgery, Vestre Viken Hospital, Drammen, Norway); Britt Fritzman (Østfold Hospital, Østfold, Norway).

In Silico Annotation of Candidate Causal Variants

Guide to results table (Supplementary Table 5) and UCSC Genome Browser session
Each candidate causal SNP has been annotated with publicly available genomic data in order to highlight potentially functional variants, prioritise experimental validation, and predict target genes. Annotations fall into categories relating to putative effects on transcription factors, regulatory element activities, expression quantitative trait loci (eQTL) and target gene prediction. For each variant, a link to the UCSC Genome Browser is provided that shows a 1 Mb region with relevant genomic data.

Transcription factors
Information regarding potential effects on transcription factor recognition sequences was obtained from the ENCODE-Motifs resource (http://compbio.mit.edu/encode-motifs)[1] using VCFtools v0.1.11 to access the downloaded HaploReg v4.0 database[2]. The impact each variant has on the position weight matrix for specific transcription factors is expressed as '+' or '-' for strengthened or weakened motifs relative to elements carrying the reference allele, respectively. Processed transcription factor ChIP-seq peak data for breast cell types were downloaded from ENCODE and other publications via NCBI GEO, in BED or NarrowPeak format, converted to the hg19 assembly using LiftOver if required, and given a standardised naming system (format = "*celltype;target*" in Supplementary Table 5). More details about the overlapping binding sites may be found within browser session track "TF-chip peaks overlapping candidate SNP" where TF-ChIP-seq peaks are named in the format "*Biosample_term_name, Experiment_target, Biosample_treatments, Biological_replicate(s), File_accession*". All ChIP-seq datasets are listed in Supplementary Table 6. Variants were assessed for overlap with ChIP-seq peaks using BedTools v2.25.0[3].

Regulatory features
Histone signatures derived from histone modification ChIP-seq experiments on breast cell types carried out by ENCODE, NIH Roadmap Epigenomics, and other published studies were obtained and formatted as for ChIP-seq data. Histone modification peaks overlapping candidate causal variants are represented as "*celltype;histone_mark*" in Supplementary Table 5 and "*Biosample_term_name, Experiment_target, Biosample_treatments, Biological_replicate(s), File_accession*" in the browser track "Histone modification ChIP-seq peaks overlapping candidate SNP". BedTools was used to intersect variants with histone signatures including commonly used marks associated with enhancers (H3K4me1, H3K4me2 and H3K27ac) and promoters (H3K4me3 and H3K9ac). Chromatin Hidden Markov Modelling (ChromHMM) states were obtained for breast cells from Roadmap (HMEC and myoepithelial cells) and published MCF7 data[4] and filtered for states corresponding to 'enhancers' (Roadmap 25-state E13, E14, E15, E16, E17, E18) or 'promoters' (Roadmap 25-state E1, E2, E3, E4, E22, E23). Chromatin state features containing candidate variants are represented as "*celltype;chromatin_state*". Chromatin accessibility data obtained from ENCODE, Roadmap and other published sources via NCBI GEO measured using DNase-seq and FAIRE-seq for relevant breast cell types were also tested for overlap with candidate causal variants. Intersected regions are reported in the format "*celltype;method*". Scores based on RegulomeDB[5] are presented for available SNPs (based on dbSNP141), where lower scores are increasingly likely to be functional (http://regulomedb.org/help#score).

eQTL

Genes showing expression levels correlated with query SNPs are shown in the column headed 'eQTL_target_all'. All genes reported to be associated with genotype in studies including GTEx version 6[6] (expression is any GTEx tissue, P value cutoff 10^{-6}) and Westra et al.,[7] (expression in whole blood). Genes associated with genotype in GTEx breast samples (N=186) are listed in the column "eQTL_GTEx.breast". eQTL data from TCGA and METABRIC studies for relevant variants are also presented (format "*Associated_gene:EffectAllele:EffectDirection:P_value*").

Other genomic features

Chromosomal position, the lead variant for the associated locus, and potentially conflicting rsIDs (assessed as overlapping at the query position) are given for each variant. GWAS tagSNPs were downloaded from the UCSC Table Browser (December 2015) and associated traits are listed if the tagSNP is within a 10 kb window of the candidate causal variant. NCBI RefSeq gene annotations were downloaded from the UCSC Table Browser and BedTools was used to determine overlapping genes ("Overlapping_RefGene"). The nearest RefGene transcription start site is also presented, given in the format "RefGeneTSS|distance". Basic genomic annotations such as intergenic, intronic, exonic, and untranslated regions based on RefSeq gene annotations were determined for each variant.

Target Gene Prediction

The column headed "Predicted_target_gene" lists genes predicted by various methods to be targets of, or the expression of which is associated with, regulatory elements in which the candidate causal variant lies. The reported gene is listed with cell type and method in the format "target:cell:method". A database was created comprising publicly available data based on various methods aiming to link enhancers with target genes (Annex to Supplementary Table 5). Laboratory based experimental approaches include genome-wide Chromatin Interaction Analysis with Paired-End-Tag sequencing (ChIA-PET)[8], Hi-C[9], and other Chromosome conformation capture (3C)-based techniques. Computational resources designed to predict target promoters by correlation of gene expression with ChIP-seq signals at specific regulatory elements including IM-PET[10], PreSTIGE[11] and data from Hnisz et al.[12] are also included. These methods associate enhancers defined by histone modification ChIP-seq for H3K4me1 (PreSTIGE), H3K27ac (Hnisz), H3K4me1, H3K4me3 and H3K27ac (IM-PET) with gene expression signals measured by RNA-seq. FANTOM5[13] data representing enhancer-promoter cap analysis of gene expression (CAGE) expression correlation from all cell types were downloaded from http://enhancer.binf.ku.dk/. Target genes have been predicted for multiple cell types and all data were included in the database, and filtered for breast derived cell types for this analysis (see Key to Supplementary Table 5).

The following strategy was used to assign potential target genes to regulatory elements. The published computational methods (Hnisz, PreSTIGE and IM-PET) included target gene annotation in the reported data. For ChIA-PET and Hi-C data, interaction peaks were mapped to promoters defined as -1.0 kb to +0.1 kb around GENCODE (v19) transcription start sites. Enhancer definitions were used as reported for computational methods while for ChIA-PET and Hi-C were interpreted as any region interacting with a promoter (regardless of other enhancer annotation information such as histone modification or open chromatin). FANTOM5 target promoters were predefined and

tissue specificity was determined by intersecting "TSS associated enhancers" with tissue-specific sets of enhancers.

All data were formatted to enable intersection of test variants with "enhancers" as defined by each method using the Galaxy "intersect" tool[14]. Each enhancer-promoter assignment or interaction was represented as a single record along with details about potential target promoter, cell type, method, scoring and confidence statistics from the original publication. A set of query SNPs (or any loci with genomic positional information in BED format) could be queried into a custom Galaxy workflow leading to generation of a table of predicted gene targets and a link to the UCSC Genome Browser for visualisation.

UCSC Genome Browser session

A custom session has been uploaded to UCSC Genome Browser[15] to facilitate exploration of breast cancer risk associated variation and implicated regulatory features. This can be accessed via the hyperlink (ie. "browser") in the functional annotation *xlsx* file. All standard Genome Browser data and functions are then available, including track display options (eg. right click on a particular track to activate visualisation options), highlighting regions (shift and mouse over region of interest), and the table browser (eg. to intersect or export data).

Within the session, Oncoarray candidate causal variants are shown in red, and names can be shown by activating "pack" mode (as for all tracks). Target gene prediction data from Hnisz, PreSTIGE and IM-PET shows enhancers depicted as black bars. The segment name revealed in 'pack' mode lists predicted target gene and cell-type (eg "WNT7B.MCF7"). ChIA-PET interactions, represented in BED12 format, have been filtered to remove duplicates and *trans*-chromosomal interactions. The interactions are shaded to reflect statistical confidence based on enrichment in the original experiment. ChIA-PET interaction names show the genomic co-ordinates of either-end of the interaction, the cell type (restricted to MCF7 for this analysis), the immunoprecipitation target, and the experimental replicate. Depicted interactions are restricted to those for which a candidate variant lies within an interaction "end" with the opposite end overlapping a TSS. All other interactions may be visualised by activating the standard ENCODE ChIA-PET track (\Regulation\ENCODE Chromatin Interactions Tracks\ChIA-PET from ENCODE/GIS-Ruan).

Chromatin interactions based on *in situ* Hi-C data from HMEC cells were downloaded from NCBI GEO (accession GSE63525)[9]. Annotated loops (representing potential enhancer-promoter interactions) processed by HiCCUPS were reformatted as BED files and tested for overlap with RefSeq promoters to assign potential target genes. Opposing ends of TSS-overlap loops were then annotated as 'potential enhancers'. Specific loop regions which overlap BC risk candidate causal variants are depicted as black segments and named "*TSS_target.Celltype*".

Various classes of genomic data representing regulatory features which harbour candidate variants are shown as separate tracks:
- *Histone modification ChIP-seq peaks overlapping candidate SNP*
- *DNase HS and FAIRE-seq peaks overlapping candidate SNP*
- *TF-chip peaks overlapping candidate SNP*

As mentioned above, changing the track display to 'pack' mode will show details of the overlapping peak in the format:
"*Biosample_term_name, Experiment_target, Biosample_treatments, Biological_replicate(s), File_accession*".

A representation of all TF and histone ChIP-seq, DNase-seq, and FAIRE-seq data tested for overlap with candidate variants is shown in three histogram tracks (computed with BedTools genomeCoverageBed). These show the summed peak density at each genomic position and allow simple visualisation of loci with relative abundance of regulatory features.

Tracks for Roadmap Epigenomics Chromatin state models (based on imputed data - 25 state, 12 marks, 127 epigenomes) were generated for breast Myoepithelial and HMEC cells. Chromatin states were separated and colour coded for states related to enhancers, promoters, and transcribed regions.

The bottom track ("Oncoarray SNPs") shows all directly genotyped and imputed SNPs passing quality control (imputation $r^2>0.3$) as black ticks. SNPs from dbSNP build 138 with a MAF > 0.01 in European samples which were not informative are shown in red.

Funding

Acknowledgements

OncoArray genotype calling and quality control

Of the 568,712 variants selected for genotyping on OncoArray, 533,631 were successfully manufactured on the array (including 778 duplicate probes). OncoArray genotyping of BCAC and CIMBA samples was conducted at six sites. Details of the genotyping calling for the OncoArray are described in more detail elsewhere[16]. Briefly, we developed a single calling pipeline that was applied to more than 500,000 samples. An initial cluster file was generated using from 56,284 samples, selected over all the major genotyping centres and ethnicities, using the Gentrain2 algorithm. Variants likely to have problematic clusters were selected for manual inspection using the following criteria: call rate below 99%, minor allele frequency (MAF) <0.001, poor Illumina intensity and clustering metrics, deviation from the MAF observed in the 1000 Genomes Project using the criterion: $\frac{(|p_1-p_0|-0.01)^2}{((p_1+p_0)(2-p_1-p_0))} > C$, where p_0 and p_1 are the minor frequencies in the 1000 Genome Project and Oncoarray datasets, respectively, and C=0.008. (This latter criterion is approximately equivalent to excluding SNPs on the basis of a Chi-square statistic of 16 for the difference in allele frequencies, assuming 1,000 samples in each group). This resulted in manual adjustment of the cluster file for 3,964 variants, and the exclusion of 16,526 variants. The final cluster file was then applied to the full dataset.

We excluded SNPs with a call rate <95% in any consortium, not in Hardy-Weinberg equilibrium ($P<10^{-7}$ in controls, or $P<10^{-12}$ in cases) or with concordance <98% among 5,280 duplicate pairs. For the imputation, we additionally excluded SNPs with a MAF<1% and a call rate <98% in any consortium, SNPs that could not be linked to the 1000 Genomes Project reference, those with MAF for Europeans that differed from that for the 1000 Genomes Project and a further 1,128 SNPs where the cluster plot was judged to be not ideal. Of the 533,631 SNPs which were manufactured on the array, 494,763 passed the initial QC and 469,364 were used in the imputation (see below).

For BCAC, we excluded probable duplicate samples and close relatives within each study, and probable duplicates between studies. These were identified by identity by state (IBS) analysis using a set of approximately 38,000 uncorrelated ($r^2<0.1$) SNPs for OncoArray and iCOGS and 16,000 SNPs for GWAS. Based on inspection of the distribution of IBS values, we identified first-degree relative pairs using the criterion 0.82<IBS<0.90 for OncoArray and 0.85<IBS<0.90 for iCOGS; similar criteria were used for each GWAS (with limits depending on the IBS distribution in that study).

We applied LD score regression to the summary results from GWAS, iCOGS and OncoArray to assess the evidence of overlap in individuals between the three datasets. We conducted three pair-wise cross-trait regression analyses (GWAS-iCOGS, GWAS-OncoArray and iCOGS-OncoArray) and used the intercept from the regression analysis to estimate the amount of overlap[17]. Assuming that the phenotypic correlation is 1 (that is, a case is a case in all datasets and a control is a control in all datasets), we found that for GWAS-iCOGS, the estimated overlap was 1.5% of individuals, for GWAS-OncoArray, the estimated overlap was 3.8% of individuals, and for iCOGS-OncoArray, the estimated overlap was 0.2% of individuals. It is unlikely that this degree of overlap would have influenced the results obtained from our analyses.

We also excluded samples with a call rate <95% and samples with extreme heterozygosity (>4.9 standard deviations from the mean for the reported ethnicity). Ancestry analysis was performed using a standardized approach in which 2,318 ancestry informative markers with minor allele frequencies of 0.05 on a subset of ~66,000 samples including 505 Hapmap 2 samples. The contribution of each of the three major continental ancestry groups (European, Asian and African) was estimated by mapping each individual to regions of a triangle based on the first two principal components, as implemented in the software package FastPop (http://sourceforge.net/projects/fastpop/)[18]. Individuals were thus classified into 4 groups: European (defined as >80% European ancestry), East Asian (>40% Asian ancestry), African (>20% African ancestry) and other (not fulfilling any of the above criteria)[16]. Of the 152,492 samples genotyped, the final dataset consisted of 142,072 samples, of which 9,655 ER-negative cases and 45,494 controls of European origin had not been included in a previous GWAS and had not been genotyped using iCOGS and were included in this analysis.

For the CIMBA samples we excluded individuals of non-European ancestry using multi-dimensional scaling. For this purpose we selected 30,733 uncorrelated autosomal SNPs (pair-wise $r^2< 0.10$) to compute the genomic kinship between all pairs of *BRCA1* and *BRCA2* carriers, along with 267 HapMap samples (CHB, JPT,

YRI and CEU). These were converted to distances and subjected to multidimensional scaling. Using the first two components, we calculated the proportion of European ancestry for each individual and excluded samples with >27% non-European ancestry to ensure that samples of Ashkenazi Jewish ancestry were included in the final sample.

Global Genomic Enrichment Analyses (further details)

We created a "full baseline model" as previously described[19] that included 52 "baseline" genomic features (24 non-cell-type specific publicly available annotations, a 500-bp window around each of the 24 annotations and a 100-bp window around each of four ChIP-seq peaks) and one category containing all SNPs. We estimated the enrichment for these 53 functional categories in a single multivariable LD score regression analysis.

We subsequently performed analyses using cell-type specific annotations for the four histone marks H3K4me1, H3K4me3, H3K9ac and H3K27ac across 27-81 cell types, depending on histone mark, giving a total of 220 cell-type specific marks[19]. We estimated the enrichment for each of these marks after adjusting for the baseline annotations by running 220 LD score regressions, each adding a different histone mark to the baseline model. We observed no associations after adjusting for 220 tests

Pathway Enrichment Analyses (further details)

Pathway enrichment analysis was performed to identify pathways associated with ER-negative breast cancer risk, pointing to biological hypotheses that can be further tested experimentally.

The pathway gene set database used contains pathway gene sets from Reactome[20], NCI Pathway Interaction Database[21], GO (Gene Ontology) biological process[22], HumanCyc[23], MSigdb[24], NetPath[25] and Panther[26]. GO pathways inferred from electronic annotation terms were excluded. Some manual annotation was performed on the pathway gene set database where annotation errors from public data were discovered. In particular, in several pathways, the PDPK1 gene was mistakenly entered as PDK1 gene and was manually corrected. The same pathway (e.g. apoptosis) may be defined in two or more databases with potentially different sets of genes, and all versions of these duplicate/overlapping pathways were included.

Gene information (hg19) was downloaded from the ANNOVAR[27] website (http://www.openbioinformatics.org/annovar/). Some pathways include genes that are also grouped closely together in the genome and are thus are likely to share the significance of a single SNP, which would artificially increase the pathway significance in our analysis. This was the case for pathways including histone genes. Thus, we selected representative SNP-gene associations to control for this effect (chr6:26055031 for HIST1, chr1:120904839, 149864043 for HIST2, chr1: 228615251 for HIST3 and chr12: 14919727 for HIST4).

Although there are several methods for pathway enrichment analysis, we chose the GSEA approach as it is one of the most established methods that is threshold free; many other methods such as SRT, ALIGATOR and Plink set-based test require an arbitrary p-value threshold to be defined for SNPs and applied before pathway analysis.

To focus on pathway enrichment analysis results about which we were most confident, we implemented a number of filters. First, only pathways with positive ES and containing at least one gene linked to a significant SNP ($P<5x10^{-8}$) were retained for subsequent analysis. Second, we defined an ES threshold (ES≥0.41) based on a comparison with a gold standard pathway enrichment analysis we previously performed on the iCOGS data alone and where we were able to analytically compute FDR values by shuffling case/control labels (this was not computationally feasible with the more complex meta-analysis scheme used in this paper).

We chose the true positive rate (TPR) threshold by varying the TPR in steps of 0.1 and observing how the FPR changed. A TPR of 0.1 resulted in a very low FPR (0.02), but we considered this to be unduly conservative as it resulted in a small number of pathways (37, clustered into 8 themes) and excluded many pathways known to be involved in breast cancer. A TPR of 0.20 (FPR = 0.14) gave a reasonable balance between the true and false positive rates, while including pathways known to be involved in breast cancer. Thus this threshold was chosen for this study. A TPR of 0.3 gave an FPR of 0.30, which we considered high; further, the resulting additional pathways included (in addition to those included at TPR=0.2) were weaker (i.e. they had worse enrichment scores [ES<0.41] and had relatively very few genes included) than pathways appearing at lower FPRs (and TPRs). We rejected TPR thresholds >0.3 because each gave an FPR that was larger than the TPR.

Finally, we performed an in depth literature search on all resulting pathways to confirm their relevance to breast cancer biology, applying the following criteria:
1) reported in at least one of five published breast cancer pathway analyses[28-32]; or 2) reported elsewhere in the literature to be involved in breast cancer. We also removed pathways that were significant due to incorrect gene function annotation.

References

1. Kheradpour, P. & Kellis, M. Systematic discovery and characterization of regulatory motifs in ENCODE TF binding experiments. *Nucleic Acids Res* **42**, 2976-87 (2014).
2. Ward, L.D. & Kellis, M. HaploReg: a resource for exploring chromatin states, conservation, and regulatory motif alterations within sets of genetically linked variants. *Nucleic Acids Res* **40**, D930-4 (2012).
3. Quinlan, A.R. BEDTools: The Swiss-Army Tool for Genome Feature Analysis. *Curr Protoc Bioinformatics* **47**, 11 12 1-34 (2014).
4. Taberlay, P.C., Statham, A.L., Kelly, T.K., Clark, S.J. & Jones, P.A. Reconfiguration of nucleosome-depleted regions at distal regulatory elements

accompanies DNA methylation of enhancers and insulators in cancer. *Genome Res* **24**, 1421-32 (2014).

5. Boyle, A.P. *et al.* Annotation of functional variation in personal genomes using RegulomeDB. *Genome Res* **22**, 1790-7 (2012).

6. GTEx Consortium. Human genomics. The Genotype-Tissue Expression (GTEx) pilot analysis: multitissue gene regulation in humans. *Science* **348**, 648-60 (2015).

7. Westra, H.J. *et al.* Systematic identification of trans eQTLs as putative drivers of known disease associations. *Nat Genet* **45**, 1238-43 (2013).

8. Li, G. *et al.* Extensive promoter-centered chromatin interactions provide a topological basis for transcription regulation. *Cell* **148**, 84-98 (2012).

9. Rao, S.S. *et al.* A 3D map of the human genome at kilobase resolution reveals principles of chromatin looping. *Cell* **159**, 1665-80 (2014).

10. He, B., Chen, C., Teng, L. & Tan, K. Global view of enhancer-promoter interactome in human cells. *Proc Natl Acad Sci U S A* **111**, E2191-9 (2014).

11. Corradin, O. *et al.* Combinatorial effects of multiple enhancer variants in linkage disequilibrium dictate levels of gene expression to confer susceptibility to common traits. *Genome Res* **24**, 1-13 (2014).

12. Hnisz, D. *et al.* Super-enhancers in the control of cell identity and disease. *Cell* **155**, 934-47 (2013).

13. Andersson, R. *et al.* An atlas of active enhancers across human cell types and tissues. *Nature* **507**, 455-61 (2014).

14. Blankenberg, D. *et al.* Galaxy: a web-based genome analysis tool for experimentalists. *Curr Protoc Mol Biol* **Chapter 19**, Unit 19 10 1-21 (2010).

15. Kent, W.J. *et al.* The human genome browser at UCSC. *Genome Res* **12**, 996-1006 (2002).

16. Amos, C.I. *et al.* The OncoArray Consortium: a Network for Understanding the Genetic Architecture of Common Cancers. *Cancer Epidemiol Biomarkers Prev* (in press).

17. Bulik-Sullivan, B. *et al.* An atlas of genetic correlations across human diseases and traits. *Nat Genet* **47**, 1236-41 (2015).

18. Li, Y. *et al.* FastPop: a rapid principal component derived method to infer intercontinental ancestry using genetic data. *BMC Bioinformatics* **17**, 122 (2016).

19. Finucane, H.K. *et al.* Partitioning heritability by functional annotation using genome-wide association summary statistics. *Nat Genet* **47**, 1228-35 (2015).

20. Joshi-Tope, G. *et al.* Reactome: a knowledgebase of biological pathways. *Nucleic Acids Res* **33**, D428-32 (2005).

21. Schaefer, C.F. *et al.* PID: the Pathway Interaction Database. *Nucleic Acids Res* **37**, D674-9 (2009).

22. Ashburner, M. *et al.* Gene ontology: tool for the unification of biology. The Gene Ontology Consortium. *Nat Genet* **25**, 25-9 (2000).

23. Romero, P. *et al.* Computational prediction of human metabolic pathways from the complete human genome. *Genome Biol* **6**, R2 (2005).

24. Subramanian, A. *et al.* Gene set enrichment analysis: a knowledge-based approach for interpreting genome-wide expression profiles. *Proc Natl Acad Sci U S A* **102**, 15545-50 (2005).

25. Kandasamy, K. *et al.* NetPath: a public resource of curated signal transduction pathways. *Genome Biol* **11**, R3 (2010).

26. Thomas, P.D. *et al.* PANTHER: a library of protein families and subfamilies indexed by function. *Genome Res* **13**, 2129-41 (2003).
27. Wang, K., Li, M. & Hakonarson, H. ANNOVAR: functional annotation of genetic variants from high-throughput sequencing data. *Nucleic Acids Res* **38**, e164 (2010).
28. Kar, S.P. *et al.* Genome-Wide Meta-Analyses of Breast, Ovarian, and Prostate Cancer Association Studies Identify Multiple New Susceptibility Loci Shared by at Least Two Cancer Types. *Cancer Discov* **6**, 1052-67 (2016).
29. Braun, R. & Buetow, K. Pathways of distinction analysis: a new technique for multi-SNP analysis of GWAS data. *PLoS Genet* **7**, e1002101 (2011).
30. Jia, P., Zheng, S., Long, J., Zheng, W. & Zhao, Z. dmGWAS: dense module searching for genome-wide association studies in protein-protein interaction networks. *Bioinformatics* **27**, 95-102 (2011).
31. Mogushi, K. & Tanaka, H. PathAct: a novel method for pathway analysis using gene expression profiles. *Bioinformation* **9**, 394-400 (2013).
32. Medina, I. *et al.* Gene set-based analysis of polymorphisms: finding pathways or biological processes associated to traits in genome-wide association studies. *Nucleic Acids Res* **37**, W340-4 (2009).

Supplementary Table 1: BCAC studies contributing data on estrogen receptor negative cases and controls, by genotyping intiative†

Acronym	Study Name	Country	Study design	OncoArray		iCOGS		GWASs	
				Controls	Cases	Controls	Cases	Controls	Cases
ABCFS	Australian Breast Cancer Family Study	Australia	Case-control study	188	62	551	204	285	72
ABCS	Amsterdam Breast Cancer Study	Netherlands	Case-control study	4	27	1815	154		
ABCTB	Australian Breast Cancer Tissue Bank	Australia	Case-control study	374	290				
BBCC	Bavarian Breast Cancer Cases and Controls	Germany	Case-control study	248	354	458	67		
BBCS	British Breast Cancer Study	UK	Case-control study	442	18	1397	108		
BCEES	Breast Cancer Employment and Environment Study	Australia	Case-control study	834	115				
BCFR	Breast Cancer Family Registry	USA, Canada, Australia	Case-control study					2251	922
BCFR-NY	New York site of the Breast Cancer Family Registry	USA	Case-control study	27	60				
BCFR-PA	Philadelphia site of the Breast Cancer Family Registry	USA	Case-control study	0	27				
BCFR-UT	Utah site of the Breast Cancer Family Registry	USA	Case-control study	0	13				
BCINIS	Breast Cancer in Northern Israel Study	Israel	Case-control study	723	262				
BIGGS	Breast Cancer in Galway Genetic Study	Ireland	Case-control study			719	154		
BPC3	Breast and Prostate Cancer Cohort Consortium	International	Prospective cohorts: nested case-control studies					2305	1998
BREOGAN	Breast Oncology Galicia Network	Spain	Case-control study	725	246				
BSUCH	Breast Cancer Study of the University of Heidelberg	Germany	Case-control study	167	42	954	157		
CBCS	Canadian Breast Cancer Study	Canada	Case-control study	817	119				
CCGP	Crete Cancer Genetics Program	Greece	Case-control study	332	177				
CECILE	CECILE Breast Cancer Study	France	Case-control study	3	5	999	144		
CGPS	Copenhagen General Population Study	Denmark	Case-control study	712	160	4534	357		
CNIO-BCS	Spanish National Cancer Centre Breast Cancer Study	Spain	Case-control study			876	88		
CPSII	Cancer Prevention Study-II Nutrition Cohort	USA	Prospective cohort: nested case-control study	3025	99				
CTS	California Teachers Study	USA	Prospective cohort: nested case-control study	577	126	71	68		
DEMOKRITOS	Demokritos	Greece	Case-control study			95	413		
DIETCOMPLYF	DietCompLyf Breast Cancer Survival Study	UK	Prospective cohort: nested case-control study	0	104				
EPIC	European Prospective Investigation Into Cancer and Nutrition	International (Europe)	Prospective cohort: nested case-control study	3522	179				
ESTHER	ESTHER Breast Cancer Study	Germany	Case-control study	3	1	502	98		
GC-HBOC*	German Consortium for Hereditary Breast & Ovarian Cancer	Germany	Case-control study	1593	358	168			
GENICA	Gene Environment Interaction and Breast Cancer in Germany	Germany	Case-control study	284	78	427	104		
GEPARSIXTO	Randomized phase II trial	Germany	Case-only study	0	273				
GESBC	Genetic Epidemiology Study of Breast Cancer by Age 50	Germany	Case-control study	180	122				
HABCS	Hannover Breast Cancer Study	Germany	Case-control study	865	147				
HCSC	Hospital Clinico San Carlos	Spain	Case-control study	0	109				
HEBCS	Helsinki Breast Cancer Study	Finland	Case-control study	2	14	1233	235	1012	145
HMBCS	Hannover-Minsk Breast Cancer Study	Belarus	Case-control study	214	7	130	8		
HUBCS	Hannover-Ufa Breast Cancer Study	Russia	Case-control study	131	18				
KARBAC	Karolinska Breast Cancer Study	Sweden	Case-control study	0	3	662	63		
KBCP	Kuopio Breast Cancer Project	Finland	Case-control study	182	23	250	97		
KConFab/AOCS	Kathleen Cuningham Foundation Consortium for research into Familial Breast Cancer/Australian Ovarian Cancer Study	Australia and New Zeland	Case-control study			897	55		
LMBC	Leuven Multidisciplinary Breast Centre	Belgium	Case-control study	435	145	1388	378		
MABCS	Macedonian Breast Cancer Study	Macedonia	Case-control study	93	17				
MARIE	Mammary Carcinoma Risk Factor Investigation	Germany	Case-control study	288	8	1778	346	470	76
MBCSG	Milan Breast Cancer Study Group	Italy	Case-control study	366	75	400	42		
MCBCS	Mayo Clinic Breast Cancer Study	USA	Case-control study	179	84	1931	269		
MCCS	Melbourne Collaborative Cohort Study	Australia	Prospective cohort: nested case-control study	712	77	511	110		
MEC	Multiethnic Cohort	USA	Prospective cohort: nested case-control study	127	3	741	87		
MISS	Melanoma Inquiry of Southern Sweden	Sweden	Prospective cohort: nested case-control study	1523	79				
MMHS	Mayo Mammography Health Study	USA	Prospective cohort: nested case-control study	1605	50				
MTLGEBCS	Montreal Gene-Environment Breast Cancer Study	Canada	Case-control study	29	2	436	64		
NBCS	Norwegian Breast Cancer Study	Norway	Case-control study			217	200		
NBHS	Nashville Breast Health Study	USA	Case-control study	613	163	118	125		
NC-BCFR	Northern California Breast Cancer Family Registry	USA	Case-control study	149	261				
NHS	Nurses Health Study	USA	Prospective cohort: nested case-control study	1804	203				
NHS2	Nurses Health Study 2	USA	Prospective cohort: nested case-control study	1905	224				
OBCS	Oulu Breast Cancer Study	Finland	Case-control study			414	100		
OFBCR	Ontario Familial Breast Cancer Registry	Canada	Case-control study	217	259	511	269		
ORIGO	Leiden University Medical Centre Breast Cancer Study	Netherlands	Prospective cohort: nested case-control study	660	230	327	70		
OSU	Ohio State University	USA	Case-control study			203	207		
PBCS	NCI Polish Breast Cancer Study	Poland	Case-control study	1658	547				
pKARMA	Karolinska Mammography Project for Risk Prediction of Breast Cancer - Case-Control Study	Sweden	Case-control study	6042	166	5568	701		
PLCO	The Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial	USA	Prospective cohort: nested case-control study	858	184				
POSH	Prospective Study of Outcomes in Sporadic Versus Hereditary Breast Cancer	UK	Case-only study	0	207				
PREFACE	Evaluation of Predictive Factors regarding the Effectivity of Aromatase Inhibitor Therapy	Germany	Case-only study	0	15				
RBCS	Rotterdam Breast Cancer Study	Netherlands	Case-control study	231	87	699	124		
RPCI	Roswell Park Cancer Institute	USA	Case-control study			126	136		
SASBAC	Singapore and Sweden Breast Cancer Study	Sweden	Case-control study			661	43	756	109
SBCS	Sheffield Breast Cancer Study	UK	Case-control study			848	98		
SEARCH	Study of Epidemiology and Risk factors in Cancer Heredity	UK	Case-control study	989	420	8068	1173		
SISTER	The Sister Study	USA	Prospective cohort: nested case-control study	1560	282				
2SISTER	The Two Sister Study	USA	Case-only study	0	204				
SKKDKFZS*	Städtisches Klinikum Karlsruhe Deutsches Krebsforschungszentrum Study	Germany	Case-only study	0	298	0	135		
SMC	Swedish Mammography Cohort	Sweden	Prospective cohort: nested case-control study	708	195				
SUCCESSB	Simultaneous Study of Gemcitabine-Docetaxel Combination adjuvant treatment	Germany	Case-only study	0	159				
SUCCESSC	Simultaneous Study of Docetaxel Based Anthracycline Free Adjuvant Treatment Evaluation	Germany	Case-only study	0	204				
SZBCS	IHCC-Szczecin Breast Cancer Study	Poland	Case-control study	157	72	315	60		
TNBCC	Triple-Negative Breast Cancer Consortium	International	Case-control studies	0	288			2890	998
UCIBCS	UCI Breast Cancer Study	USA	Case-control study	258	73				
UK2	UK2 GWAS	UK	Case-control study					2663	160
UKBGS	UK Breakthrough Generations Study	UK	Prospective cohort: nested case-control study	567	78	470	22		
UKOPS	UK Ovarian Cancer Population Study	UK	Case-control study	974	0				
WHI	Women's Health Initiative	USA	Prospective cohort: nested case-control study	4613	658				

†Studies participated in one or more of the following genotyping initiatives: OncoArray, iCOGS or one of eight genome-wide association studies (GWASs)
*For the analysis of iCOGS data, cases from SKKDKFZS and controls from GC-HBOC included as one study

Supplementary Table 2: CIMBA studies contributing data on *BRCA1* mutation carriers, by genotyping intiative

Acronym	Study Name	Country	OncoArray		iCOGS	
			Unaffected	Breast cancer	Unaffected	Breast cancer
BCFR-AU	Australian site of the Breast Cancer Family Registry	AUSTRALIA	13	25	0	2
BCFR-NC	Northern California site of the Breast Cancer Family Registry	USA	3	12	1	1
BCFR-NY	New York site of the Breast Cancer Family Registry	USA	24	37	4	5
BCFR-ON	Ontario site of the Breast Cancer Family Registry	CANADA	34	86	2	7
BCFR-PA	Philadelphia site of the Breast Cancer Family Registry	USA	26	17	14	16
BCFR-UT	Utah site of the Breast Cancer Family Registry	USA	135	64	1	0
BFBOCC	Baltic Familial Breast Ovarian Cancer Consortium	LITHUANIA/LATVIA	133	111	16	8
BIDMC	Beth Israel Deaconess Medical Center	USA	41	44	1	1
BMBSA	BRCA-gene mutations and breast cancer in South African women	SOUTH AFRICA	21	37	2	1
BRICOH	Beckman Research Institute of the City of Hope	USA	96	50	11	9
CBCS	Rigshospitalet	DENMARK	110	75	80	57
CNIO	Spanish National Cancer Centre	SPAIN	32	31	49	44
COH	City of Hope Cancer Center	USA	84	141	6	8
CONSIT TEAM	CONsorzio Studi ITaliani sui Tumori Ereditari Alla Mammella	ITALY	265	271	217	234
DEMOKRITOS	National Centre for Scientific Research Demokritos	GREECE	85	132	12	20
DFCI	Dana-Farber Cancer Institute	USA	82	65	3	4
DKFZ	German Cancer Research Center	GERMANY	19	36	0	2
EMBRACE	Epidemiological Study of Familial Breast Cancer	UK/IRELAND	907	785	14	13
FCCC	Fox Chase Cancer Center	USA	49	26	20	19
FPGMX	Fundación Pública Galega de Medicina Xenómica	SPAIN	40	61		
GC-HBOC	German Familial Breast Group	GERMANY	673	1145	54	111
GEMO	Genetic Modifiers of cancer risk in BRCA1/2 mutation carriers	FRANCE/USA	630	842	114	111
GEORGETOWN	Georgetown University	USA	6	5	1	2
G-FAST	Ghent University Hospital	BELGIUM	69	121	91	42
HCSC	Hospital Clinico San Carlos	SPAIN	85	55	5	6
HEBCS	Helsinki Breast Cancer Study	FINLAND	67	53	3	5
HEBON	Genen Omgeving studie van de werkgroep Hereditiair Borstkanker Onderzoek Nederland	NETHERLANDS	500	372	220	202
HUNBOCS	Molecular Genetic Studies of Breast- and Ovarian Cancer in Hungary	HUNGARY	101	179		
HVH	University Hospital Vall d'Hebron	SPAIN	56	62	0	1
ICO	Institut Català d'Oncologia	SPAIN	150	130	5	1
IHCC	International Hereditary Cancer Centre	POLAND	121	77	279	223
INHERIT	INterdisciplinary HEalth Research Internal Team BReast CAncer susceptibility	CANADA (QUEBEC)	52	37	6	2
IOVHBOCS	Istituto Oncologico Veneto	ITALY	93	111	5	4
IPOBCS	Portuguese Oncology Institute-Porto Breast Cancer Study	PORTUGAL	79	36	1	2
KCONFAB	Kathleen Cuningham Consortium for Research into Familial Breast Cancer	AUSTRALIA	355	366	24	26
KUMC	University of Kansas Medical Center	USA	3	11		
MAYO	Mayo Clinic	USA	126	121	12	10
MCGILL	McGill University	CANADA (QUEBEC)	30	24		
MODSQUAD	Modifier Study of Quantitative Effects on Disease	CZECH REPUBLIC			68	106
MSKCC	Memorial Sloane Kettering Cancer Center	USA	193	185	32	59
MUV	General Hospital Vienna	AUSTRIA	266	268	11	11
NAROD	Women's College Research Institute Hereditary Breast and Ovarian Cancer Study	CANADA			100	46
NCI	National Cancer Institute	USA	108	42	6	1
NNPIO	N.N. Petrov Institute of Oncology	RUSSIA	22	44	1	4
NORTHSHORE	NorthShore University HealthSystem	USA	40	40		
NRG_ONCOLOGY	NRG Oncology	USA/AUSTRALIA	153	166	4	7
OCGN	Ontario Cancer Genetics Network	CANADA	133	71	6	4
OSU CCG	The Ohio State University Comprehensive Cancer Center	USA	34	39	8	10
OUH	Odense University Hospital	DENMARK	358	192	10	10
PBCS	Università di Pisa	ITALY	39	49	6	5
SMC	Sheba Medical Centre	ISRAEL	99	65	57	41
SWE-BRCA	Swedish Breast Cancer Study	SWEDEN	237	188	52	38
UCHICAGO	University of Chicago	USA	51	43	7	0
UCSF	University of California San Francisco	USA	60	32	16	15
UKGRFOCR	UK and Gilda Radner Familial Ovarian Cancer Registries	UK	40	13	5	0
UPENN	University of Pennsylvania	USA	218	239	11	22
UPITT	Cancer Family Registry University of Pittsburg	USA	77	77		
UTMDACC	University of Texas MD Anderson Cancer Center	USA	18	25	27	45
VFCTG	Victorian Familial Cancer Trials Group	AUSTRALIA	104	103	2	1
WCP	Women's Cancer Program at Cedars-Sinai Medical Center	USA	137	50	10	6

Supplementary Table 3: Ten novel loci associated with risk of estrogen receptor (ER)-negative breast cancer using meta-analysis of BCAC and CIMBA data, by genotyping initiative

Location	SNP	Chr	Position	Alleles‡	MAF	GWAS OR(95%CI)	P-value	$I^2_{(s)}$	P(het$_s$)	r²(imp)	iCOGS OR(95%CI)	P-value	$I^2_{(s)}$	P(het$_s$)	r²(imp)	OncoArray OR(95%CI)	P-value	$I^2_{(s)}$	P(het$_s$)	$I^2_{(g)}$	P(het$_g$)	r²(imp)	iCOGS HR(95%CI)	P-value	r²(imp)	OncoArray HR(95%CI)	P-value	$I^2_{(s)}$	P(het$_s$)
2p23.3	rs200648189	2	24739694	CT/C	0.19	0.96 (0.88-1.06)	4.1x10⁻¹	0	0.93	0.57	0.93 (0.87-0.99)	2.3x10⁻²	0	0.58	0.90	0.94 (0.90-0.99)	9.3x10⁻³	0	0.95	0	0.83	0.52	0.93 (0.81-1.08)	3.5x10⁻¹	0.89	0.87 (0.83-0.92)	3.5x10⁻⁷	0.09	0.34
6q23.1	rs6569648	6	130349119	T/C	0.23	0.88 (0.83-0.94)	1.4x10⁻⁴	0	0.96	1.00	0.94 (0.89-0.98)	3.3x10⁻³	0	0.79	1.00	0.94 (0.91-0.98)	1.8x10⁻³	0	0.88	0.31	0.24	1.00	0.96 (0.86-1.06)	4.2x10⁻¹	1.00	0.94 (0.89-0.98)	7.0x10⁻¹	0	0.61
8p23.3	rs66823261	8	170692	T/C	0.23	1.02 (0.96-1.09)	4.7x10⁻¹	0	0.49	0.74	1.13 (1.08-1.19)	1.0x10⁻⁶	0	0.71	0.92	1.08 (1.04-1.13)	8.2x10⁻⁵	0	0.85	0.66	0.05	0.72	1.14 (1.01-1.29)	4.0x10⁻²	0.92	1.01 (0.96-1.06)	8.2x10⁻¹	0.33	0.06
8q24.13	rs17350191	8	124757661	C/T	0.34	1.07 (1.01-1.13)	3.1x10⁻²	0.43	0.09	1.00	1.06 (1.02-1.11)	1.9x10⁻³	0.12	0.27	1.00	1.07 (1.04-1.11)	3.2x10⁻⁵	0	0.71	0	0.94	1.00	1.03 (0.95-1.13)	4.6x10⁻¹	1.00	1.08 (1.04-1.13)	1.6x10⁻⁴	0.22	0.16
11q22.3	rs11374964	11	108345515	G/GA	0.42	0.94 (0.88-1.00)	6.0x10⁻²	0	0.69	1.00	0.97 (0.94-1.01)	1.4x10⁻¹	0.26	0.07	1.00	0.91 (0.88-0.94)	2.7x10⁻⁴	0	0.66	0.68	0.04	1.00	0.96 (0.88-1.05)	4.1x10⁻¹	1.00	0.90 (0.87-0.94)	7.8x10⁻⁷	0.18	0.24
11q22.3	rs74911261	11	108357137	G/A	0.02	0.88 (0.70-1.10)	2.6x10⁻¹	0	0.88	0.90	0.79 (0.68-0.92)	2.6x10⁻³	0	0.86	1.00	0.82 (0.73-0.91)	4.0x10⁻⁴	0.01	0.44	0	0.75	0.87	0.82 (0.58-1.15)	2.5x10⁻¹	1.00	0.73 (0.63-0.83)	3.3x10⁻⁶	0	0.74
16p13.3	rs11076805	16	4106788	C/A	0.25	0.91 (0.86-0.97)	2.8x10⁻³	0.40	0.11	0.72	0.94 (0.89-0.99)	1.9x10⁻²	0	0.80	0.97	0.92 (0.89-0.96)	2.9x10⁻⁵	0.18	0.24	0	0.76	0.72	1.02 (0.90-1.16)	7.3x10⁻¹	0.97	0.95 (0.91-1.00)	4.1x10⁻²	0.09	0.34
18q12.1	rs36194942	18	25401204	A/AT	0.30	0.92 (0.85-0.99)	1.9x10⁻²	0	0.52	0.95	0.96 (0.92-1.00)	5.1x10⁻²	0	0.48	0.95	0.92 (0.89-0.96)	9.6x10⁻⁶	0	0.99	0.15	0.31	0.94	0.96 (0.87-1.06)	4.5x10⁻¹	0.94	0.95 (0.91-0.99)	1.8x10⁻²	0	0.65
19p13.2	rs322144	19	11423703	C/G	0.47	0.94 (0.89-0.99)	2.1x10⁻²	0	0.73	0.51	0.96 (0.91-1.01)	1.0x10⁻¹	0	0.92	0.99	0.95 (0.92-0.98)	1.5x10⁻³	0.29	0.11	0	0.86	0.50	0.89 (0.79-1.01)	7.2x10⁻²	0.99	0.93 (0.89-0.96)	1.7x10⁻⁴	0	0.48
19q12	rs113701136	19	30277729	C/T	0.32	1.04 (0.98-1.10)	1.6x10⁻¹	0	0.89	0.97	1.06 (1.02-1.10)	4.0x10⁻³	0.26	0.07	0.98	1.08 (1.04-1.12)	2.1x10⁻⁵	0	0.48	0	0.61	0.96	1.11 (1.01-1.22)	3.0x10⁻²	0.98	1.04 (1.00-1.09)	7.7x10⁻²	0.21	0.18

Chr, chromosome; ‡More common allele listed first, minor allele second; MAF, minor allele frequency; $I^2_{(s)}$, I^2 for between-study heterogeneity in the OR; P(het$_s$), P-value for between-study heterogeneity in the OR; $I^2_{(g)}$, I^2 for heterogeneity in the OR between genotyping initiatives (GWAS/iCOGS/OncoArray); P(het$_g$), P-value for heterogeneity in the OR between genotyping initiative
$I^2_{(c)}$, I^2 for between-country heterogeneity in the HR; P(het$_c$), P-value for between-country heterogeneity in the HR; r²(imp), imputation r²; BCAC (Breast Cancer Association Consortium) results were based on GWAS data for 4,480 cases and 12,632 controls, iCOGS data for 7,333 cases and 42,468 controls and OncoArray data 9,655 cases and 45,494 controls
CIMBA (Consortium of Investigators of Modifiers of BRCA1/2) results were based on iCOGS data for 3,342 BRCA1 mutation carriers (1,630 with breast cancer) and OncoArray data for 15,566 BRCA1 mutation carriers (7,784 with breast cancer)

Supplementary Table 4: Results for the two novel ER-negative susceptibility loci on 11q22.3

SNP	Chr	Position	Alleles[#]	BCAC ER-negative[†]			CIMBA *BRCA1* mutation carriers[‡]		
				MAF	OR (95%CI)	P-value	MAF	HR (95%CI)	P-value
Each SNP modelled individually									
rs11374964	11	108345515	G/GA	0.42	0.94 (0.92-0.96)	3.6×10^{-7}	0.43	0.92 (0.89-0.95)	1.6×10^{-7}
rs74911261	11	108357137	G/A	0.02	0.81 (0.74-0.89)	3.7×10^{-6}	0.02	0.78 (0.70-0.87)	1.1×10^{-5}
Both SNPs modelled together									
rs11374964	11	108345515	G/GA	0.42	0.95 (0.93-0.97)	3.5×10^{-5}	0.43	0.93 (0.90-0.96)	5.1×10^{-6}
rs74911261	11	108357137	G/A	0.02	0.84 (0.76-0.91)	8.6×10^{-5}	0.02	0.81 (0.73-0.91)	3.3×10^{-4}

[#]More common allele listed first, minor allele second; [†]Combined data from 16,988 ER-negative cases and 87,962 controls of European ancestry from the Breast Cancer Association Consortium (BCAC) - results differ from those in Table 1 as GWAS data were excluded (unit record data was not available to run the models with both SNPs together); [‡]Combined OncoArray data from 15,566 *BRCA1* mutation carriers from the Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA), 7,784 of whom had developed breast cancer - estimates from multivariable Cox regression; Chr, chromosome; MAF, minor allele frequency; OR, odds ratio per copy of the minor allele; CI, confidence interval; HR, hazard ratio per copy of the minor allele

Supplementary Table 5: Summary information from Bioinformatic and eQTL analyses

browser	variant	chrom	position	locus	rsID	TF_motifs(delta TF-ChIP	Histone_modific ChromHMM_enh ChromHMM_pro Open_chromatin RegulomeDB scGWAS_traits	Overlapping_Ref(RefGeneTSS)dist Functional_anno eQTL_target_all	eQTL_GTExbreueQTL_TCGA	eQTL_METABRIC	Predicted_target_gene

:Hnis
A-PE1
:Hnis
:Hnis

tCF7:ChIA-PET
tCF7:ChIA-PET
tCF7:ChIA-PET
tCF7:ChIA-PET
tCF7:ChIA-PET
tCF7:ChIA-PET

l.:1:MCF7:ChIA-PET

l.:1:MCF7:ChIA-PET

:ChIA-PET
iiA-PET,,,FAM91A1:MCF7:ChIA-PET
iiA-PET

:ChIA-PET
:ChIA-PET
:ChIA-PET
:ChIA-PET

T

35

IM-PET,,,KDELC2:HMEC:IM-PET,,,C11orf65:MCF7:ChIA-PET,,,KDELC2:MCF7:ChIA-PET,,,C11orf65:HCC1954:IM-PE1

,,LOC643923:GA:-:0.0405219
,,LOC643923:GA:-:0.0405219

f:ChIA-PET

ι-:0.0410264

⊃:-:0.0320156,CLUAP1:C:-:0.0477839,IL32:C:+:0.048916
ι-:0.0293509
`:+:0.0418819

2.4:MCF7:ChIA-PET

A:+:0.0297273

Field	Description
browser	hyperlink to UCSC Genome Browser showing 1 Mb around variant
variant	Oncoarray variant ID
chrom	Chromosome
position	Chromosome position, hg19/GRCh37 build
locus	Oncoarray variant ID for top snp at locus
rsID	dnSNP rsID: multiple IDs may be listed if several rsIDs (dbSNP 138) overlap the same position
rsID_at.same.pos	rsID(s) overlapping this position
TF_motifs|delta	ENCODE_PWM alteration. The delta shown as "+" (PWM strengthened) or "-" (weakened)
TF-ChIP	Transcription factor ChIP-seq from ENCODE and GEO datasets. Format = celltype;target,celltype;target,celltype;target,....
Histone_modifications	Histone modification ChIP-seq. Format = celltype;histonemark,celltype;histonemark,celltype;histonemark,....
ChromHMM_enhancer	Enhancers from 25-state chromatin state segmentation HMM modeling from Roadmap Epigenomics Project. Breast cell types = myoepithelial, HMEC, variant HMEC and MCF7
ChromHMM_promoter	Promoters from 25-state chromatin state segmentation HMM modeling from Roadmap Epigenomics Project. Breast cell types = myoepithelial, HMEC, variant HMEC and MCF7
Open_chromatin	Regions identified by DNase-seq and FAIRE-seq. Data from ENCODE, Roadmap, GEO
RegulomeDB_score	RegulomeDB score. Score (http://regulomedb.org/help#score). Scale: 1 is most ilkely to be functional, to 7 = least likely.
GWAS_traits	A GWAS signal within 5 kb either direction
Overlapping_RefGene	SNP falls within an annotated RefGene (within transcribed sequence)
RefGeneTSS|distance	Distance to nearest refseq transcription start site
Functional_annotation	RefGene functional annotation
eQTL_target_all	SNP reported to be associated with expression in studies including GTEx.v6, GEUVADIS, Westra Nat Genetics. All tissue types included.
eQTL_GTEx.breast	SNP is associated with expression in GTEx breast samples (N =186)
eQTL_TCGA	Significant eGene from TCGA. Format = Gene1:EffectAllele:Direction:Pvalue1,Gene2:EffectAllele:Direction:Pvalue2... ("+" denotes the effect allele is associated with increased expression)
eQTL_METABRIC	Significant eGene from METABRIC. Format = Gene1:EffectAllele:Direction:Pvalue1,Gene2:EffectAllele:Direction:Pvalue2... ("+" denotes the effect allele is associated with increased expression)
Predicted_target_gene	SNP lies in a putative regulatory element predicted to regulated the listed gene, reported by methods IM-PET, Hnisz, PreSTIGE, Chia-PET, Hi-C, 3C, 4C, 5C, FANTOM5. Format = target:cell:method,,,target:c

Summary of chromatin interaction and enhancer-promoter annotation methods

Method	PMID	Experimental basis	N cell types assayed	Data source	Breast cells	Target annotation
ChIA-PET	22265404	NGS of immunoprecipitated chromatin interactions	5	ENCODE, https://www.encodeproject.org/	MCF7	Intersection of TSS and chromatin interaction
Hi-C	25497547	Genome-wide chromatin interactions	6	NCBI GEO, http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE63525	HMEC	Intersection of TSS and chromatin interaction
Hnisz	24119843	Correlation of H3K27ac levels at enhancers and RNA-seq signals	82	Original publication	MCF7, HMEC, HCC1954	Reported in original publication
PreSTIGE	24196873	Correlation of cell type-specific H3K4me1 levels at enhancers and RNA-seq signals	14	PreSTIGE web resource, http://genetics.case.edu/prestige/	MCF7, HMEC	Reported in original publication
IM-PET	24821768	Correlation of combined H3K4me1, H3K4me3 and H3K27ac levels at enhancers and RNA-seq signals	31	4DGenome web resource, http://4dgenome.int-med.uiowa.edu/	MCF7, HMEC, HCC1954	Reported in original publication and 4DGenome web resource.
FANTOM5	24670763	Correlation of expression at enhancers and promoters by CAGE analysis	113	FANTOM5 web resource, http://enhancer.binf.ku.dk/presets/	Primary breast	TSS reported

ell:method,,,target:cell:method1,method2,,,......

Supplementary Table 6: Data Sources for *in silico* analyses of the 10 novel ER-negative breast cancer susceptibility loci

Filename	Class	Biosample_term	Experiment_targ	Biosample_treat	Biological_replic	Accession	BrowserName_(cell,target,treatment,note,accession)
GSE41995_AR.bed.gz	tf	MCF-7	AR	none	GFPtagged	GSE41995	MCF-7,AR,none,GFPtagged,GSE41995
GSE74069_AR_ChIP_DHT_4hrs_strigent_tf	MDA-MB-453	AR	DHT	x	GSE74069	MDA-MB-453,AR,DHT,x,GSE74069
GSE74069_AR_ChIP_MPA_4hrs_strigent_tf	MDA-MB-453	AR	MPA	x	GSE74069	MDA-MB-453,AR,MPA,x,GSE74069
GSE74069_AR_ChIP_Veh_4hrs_strigent_tf	MDA-MB-453	AR	Veh	x	GSE74069	MDA-MB-453,AR,Veh,x,GSE74069
GSM1099030_AR-peak.bed.gz	tf	MDA-MB-453	AR	none	x	GSM1099030	MDA-MB-453,AR,none,x,GSM1099030
GSE41995_ATF1.bed.gz	tf	MCF-7	ATF1	none	GFPtagged	GSE41995	MCF-7,ATF1,none,GFPtagged,GSE41995
ENCFF001UMJ.bed.gz	tf	MCF-7	CEBPB	none	rep1	ENCFF001UMJ	MCF-7,CEBPB,none,rep1,ENCFF001UMJ
ENCFF001UMK.bed.gz	tf	MCF-7	CEBPB	none	rep2	ENCFF001UMK	MCF-7,CEBPB,none,rep2,ENCFF001UMK
GSE57498_MCF7_ChromHMM.bed.gz	chromhmm	MCF-7	chromhmm	none	x	GSE57498	MCF-7,chromhmm,none,x,GSE57498
E027_25_imputed12marks_segments.bed.	chromhmm	BRST.MYOEP	chromhmm	none	x	RM_E027_25_im	BRST.MYOEP,chromhmm,none,x,RM_E027_25_imputed12marks
E028_25_imputed12marks_segments.bed.	chromhmm	BRST.HMEC	chromhmm	none	x	RM_E119_25_im	BRST.HMEC,chromhmm,none,x,RM_E119_25_imputed12marks
E119_25_imputed12marks_segments.bed.	chromhmm	BRST.vHMEC	chromhmm	none	x	RM_E028_25_im	BRST.vHMEC,chromhmm,none,x,RM_E028_25_imputed12marks
GSE46166_Peaks_cJun_reff_IgG_200.bec	tf	BT549	cJUN	IgG	x	GSE46166	BT549,cJUN,IgG,x,GSE46166
GSE46166_Peaks_cJun_reff_input_200.be	tf	BT549	cJUN	input	x	GSE46166	BT549,cJUN,input,x,GSE46166
GSE41995_CREB1.bed.gz	tf	MCF-7	CREB1	none	GFPtagged	GSE41995	MCF-7,CREB1,none,GFPtagged,GSE41995
ENCFF001UTR.bed.gz	tf	MCF-7	CTCF	none	rep1	ENCFF001UTR	MCF-7,CTCF,none,rep1,ENCFF001UTR
ENCFF002DBL.bed.gz	tf	MCF-7	CTCF	none	x	ENCFF002DBL	MCF-7,CTCF,none,x,ENCFF002DBL
ENCFF001UML.bed.gz	tf	MCF-7	CTCF	none	rep1	ENCFF001UML	MCF-7,CTCF,none,rep1,ENCFF001UML
ENCFF001UMN.bed.gz	tf	MCF-7	CTCF	none	rep2	ENCFF001UMN	MCF-7,CTCF,none,rep2,ENCFF001UMN
ENCFF001URB.bed.gz	tf	T47D	CTCF	dimethyl_sulfoxid	rep1	ENCFF001URB	T47D,CTCF,dimethyl_sulfoxide,rep1,ENCFF001URB
ENCFF001URC.bed.gz	tf	T47D	CTCF	dimethyl_sulfoxid	rep2	ENCFF001URC	T47D,CTCF,dimethyl_sulfoxide,rep2,ENCFF001URC
ENCFF002CNT.bed.gz	tf	T47D	CTCF	dimethyl_sulfoxid	x	ENCFF002CNT	T47D,CTCF,dimethyl_sulfoxide,x,ENCFF002CNT
ENCFF001SWS.bed.gz	tf	mammary_epithe	CTCF	none	x	ENCFF001SWS	mammary_epithelial_cell,CTCF,none,x,ENCFF001SWS
ENCFF002CEB.bed.gz	tf	mammary_epithe	CTCF	none	x	ENCFF002CEB	mammary_epithelial_cell,CTCF,none,x,ENCFF002CEB
ENCFF001UTQ.bed.gz	tf	MCF-7	CTCF	none	rep1	ENCFF001UTQ	MCF-7,CTCF,none,rep1,ENCFF001UTQ
ENCFF002DBK.bed.gz	tf	MCF-7	CTCF	none	x	ENCFF002DBK	MCF-7,CTCF,none,x,ENCFF002DBK
ENCFF001UTO.bed.gz	tf	MCF-7	CTCF	17b-estradiol	x	ENCFF001UTO	MCF-7,CTCF,17b-estradiol,x,ENCFF001UTO
ENCFF002DBJ.bed.gz	tf	MCF-7	CTCF	17b-estradiol	x	ENCFF002DBJ	MCF-7,CTCF,17b-estradiol,x,ENCFF002DBJ
ENCFF001UTP.bed.gz	tf	MCF-7	CTCF	none	x	ENCFF001UTP	MCF-7,CTCF,none,x,ENCFF001UTP
ENCFF002DBM.bed.gz	tf	MCF-7	CTCF	none	x	ENCFF002DBM	MCF-7,CTCF,none,x,ENCFF002DBM
ENCFF001UTS.bed.gz	tf	MCF-7	CTCF	none	x	ENCFF001UTS	MCF-7,CTCF,none,x,ENCFF001UTS
ENCFF002DBN.bed.gz	tf	MCF-7	CTCF	none	x	ENCFF002DBN	MCF-7,CTCF,none,x,ENCFF002DBN
ENCFF001XSV.bed.gz	tf	MCF-7	CTCF	none	rep1	ENCFF001XSV	MCF-7,CTCF,none,rep1,ENCFF001XSV
ENCFF001XSW.bed.gz	tf	MCF-7	CTCF	none	rep1	ENCFF001XSW	MCF-7,CTCF,none,rep1,ENCFF001XSW
ENCFF001XSX.bed.gz	tf	MCF-7	CTCF	none	rep2	ENCFF001XSX	MCF-7,CTCF,none,rep2,ENCFF001XSX
ENCFF001XSY.bed.gz	tf	MCF-7	CTCF	none	rep2	ENCFF001XSY	MCF-7,CTCF,none,rep2,ENCFF001XSY
ENCFF002DDK.bed.gz	tf	MCF-7	CTCF	none	x	ENCFF002DDK	MCF-7,CTCF,none,x,ENCFF002DDK
ENCFF001XRL.bed.gz	tf	mammary_epithe	CTCF	none	rep1	ENCFF001XRL	mammary_epithelial_cell,CTCF,none,rep1,ENCFF001XRL
ENCFF001XRM.bed.gz	tf	mammary_epithe	CTCF	none	rep2	ENCFF001XRM	mammary_epithelial_cell,CTCF,none,rep2,ENCFF001XRM
ENCFF001XRN.bed.gz	tf	mammary_epithe	CTCF	none	rep1	ENCFF001XRN	mammary_epithelial_cell,CTCF,none,rep1,ENCFF001XRN
ENCFF001XRO.bed.gz	tf	mammary_epithe	CTCF	none	rep2	ENCFF001XRO	mammary_epithelial_cell,CTCF,none,rep2,ENCFF001XRO
ENCFF002DDB.bed.gz	tf	mammary_epithe	CTCF	none	x	ENCFF002DDB	mammary_epithelial_cell,CTCF,none,x,ENCFF002DDB
GSM1122667_CTCF-SUM159-hg19-sd-q_	tf	SUM159	CTCF	none	x	GSM1122667	SUM159,CTCF,none,x,GSM1122667
ENCFF001VPX.bed.gz	tf	MCF_10A	E2F4	afimoxifene	x	ENCFF001VPX	MCF_10A,E2F4,afimoxifene,x,ENCFF001VPX
ENCFF002CZB.bed.gz	tf	MCF_10A	E2F4	afimoxifene	x	ENCFF002CZB	MCF_10A,E2F4,afimoxifene,x,ENCFF002CZB
GSM1462477_Egln2_peaks.bed.gz	tf	T47D	Egln2	hypoxia	x	GSM1462477	T47D,Egln2,hypoxia,x,GSM1462477
ENCFF001UMM.bed.gz	tf	MCF-7	EGR1	none	rep1	ENCFF001UMM	MCF-7,EGR1,none,rep1,ENCFF001UMM
ENCFF001UMO.bed.gz	tf	MCF-7	EGR1	none	rep2	ENCFF001UMO	MCF-7,EGR1,none,rep2,ENCFF001UMO
ENCFF001UMP.bed.gz	tf	MCF-7	ELF1	none	rep1	ENCFF001UMP	MCF-7,ELF1,none,rep1,ENCFF001UMP
ENCFF001UMQ.bed.gz	tf	MCF-7	ELF1	none	rep2	ENCFF001UMQ	MCF-7,ELF1,none,rep2,ENCFF001UMQ
GSE41995_ELK1.bed.gz	tf	MCF-7	ELK1	none	GFPtagged	GSE41995	MCF-7,ELK1,none,GFPtagged,GSE41995
ENCFF001URP.bed.gz	tf	T47D	EP300	dimethyl_sulfoxid	rep1	ENCFF001URP	T47D,EP300,dimethyl_sulfoxide,rep1,ENCFF001URP
ENCFF001URQ.bed.gz	tf	T47D	EP300	dimethyl_sulfoxid	rep2	ENCFF001URQ	T47D,EP300,dimethyl_sulfoxide,rep2,ENCFF001URQ
ENCFF002CNZ.bed.gz	tf	T47D	EP300	dimethyl_sulfoxid	x	ENCFF002CNZ	T47D,EP300,dimethyl_sulfoxide,x,ENCFF002CNZ
ENCFF001UNJ.bed.gz	tf	MCF-7	EP300	none	rep1	ENCFF001UNJ	MCF-7,EP300,none,rep1,ENCFF001UNJ
ENCFF001UNK.bed.gz	tf	MCF-7	EP300	none	rep2	ENCFF001UNK	MCF-7,EP300,none,rep2,ENCFF001UNK
GSM1187116_s01_MCF7_ER_rep1_macs	tf	MCF-7	ER	E2	rep1	GSM1187116	MCF-7,ER,E2,rep1,GSM1187116
GSM1187117_s02_MCF7_ER_rep2_macs	tf	MCF-7	ER	E2	rep2	GSM1187117	MCF-7,ER,E2,rep2,GSM1187117
GSM1187118_s03_MCF7_ER_rep3_macs	tf	MCF-7	ER	E2	rep3	GSM1187118	MCF-7,ER,E2,rep3,GSM1187118
GSM1669078_jc2334MCF7ERVehRep1.bv	tf	MCF-7	ER	vehicle	rep1	GSM1669078	MCF-7,ER,vehicle,rep1,GSM1669078
GSM1669079_jc2335MCF7ERE2Rep1.bw	tf	MCF-7	ER	E2	rep1	GSM1669079	MCF-7,ER,E2,rep1,GSM1669079
GSM1669080_jc2336MCF7ERPGRep1.bw	tf	MCF-7	ER	PG	rep1	GSM1669080	MCF-7,ER,PG,rep1,GSM1669080
GSM1669081_jc2337MCF7ERE2+PGRep	tf	MCF-7	ER	E2+PG	rep1	GSM1669081	MCF-7,ER,E2+PG,rep1,GSM1669081
GSM1669082_jc2338MCF7ERVehRep2.bw	tf	MCF-7	ER	vehicle	rep2	GSM1669082	MCF-7,ER,vehicle,rep2,GSM1669082
GSM1669083_jc2339MCF7ERE2Rep2.bw	tf	MCF-7	ER	E2	rep2	GSM1669083	MCF-7,ER,E2,rep2,GSM1669083
GSM1669084_jc2340MCF7ERPGRep2.bw	tf	MCF-7	ER	PG	rep2	GSM1669084	MCF-7,ER,PG,rep2,GSM1669084
GSM1669085_jc2341MCF7ERE2+PGRep;	tf	MCF-7	ER	E2+PG	rep2	GSM1669085	MCF-7,ER,E2+PG,rep2,GSM1669085
GSM1669086_jc2342MCF7ERVehRep3.bw	tf	MCF-7	ER	vehicle	rep3	GSM1669086	MCF-7,ER,vehicle,rep3,GSM1669086
GSM1669087_jc2343MCF7ERE2Rep3.bw	tf	MCF-7	ER	E2	rep3	GSM1669087	MCF-7,ER,E2,rep3,GSM1669087
GSM1669088_jc2344MCF7ERPGRep3.bw	tf	MCF-7	ER	PG	rep3	GSM1669088	MCF-7,ER,PG,rep3,GSM1669088
GSM1669089_jc2345MCF7ERE2+PGRep;	tf	MCF-7	ER	E2+PG	rep3	GSM1669089	MCF-7,ER,E2+PG,rep3,GSM1669089
GSM1669102_jc2358T47DERVehRep1.bw	tf	T47D	ER	vehicle	rep1	GSM1669102	T47D,ER,vehicle,rep1,GSM1669102
GSM1669103_jc2359T47DERE2Rep1.bwa	tf	T47D	ER	E2	rep1	GSM1669103	T47D,ER,E2,rep1,GSM1669103
GSM1669104_jc2360T47DERPGRep1.bw	tf	T47D	ER	PG	rep1	GSM1669104	T47D,ER,PG,rep1,GSM1669104
GSM1669105_jc2361T47DERE2+PGRep1	tf	T47D	ER	E2+PG	rep1	GSM1669105	T47D,ER,E2+PG,rep1,GSM1669105
GSM1669106_jc2362T47DERVehRep2.bw	tf	T47D	ER	vehicle	rep2	GSM1669106	T47D,ER,vehicle,rep2,GSM1669106
GSM1669107_jc2363T47DERE2Rep2.bw	tf	T47D	ER	E2	rep2	GSM1669107	T47D,ER,E2,rep2,GSM1669107
GSM1669108_jc2364T47DERPGRep2.bw	tf	T47D	ER	PG	rep2	GSM1669108	T47D,ER,PG,rep2,GSM1669108
GSM1669109_jc2365T47DERE2+PGRep2	tf	T47D	ER	E2+PG	rep2	GSM1669109	T47D,ER,E2+PG,rep2,GSM1669109
GSM1669110_jc2366T47DERVehRep3.bw	tf	T47D	ER	vehicle	rep3	GSM1669110	T47D,ER,vehicle,rep3,GSM1669110
GSM1669111_jc2367T47DERE2Rep3.bwa	tf	T47D	ER	E2	rep3	GSM1669111	T47D,ER,E2,rep3,GSM1669111
GSM1669112_jc2368T47DERPGRep3.bw	tf	T47D	ER	PG	rep3	GSM1669112	T47D,ER,PG,rep3,GSM1669112
GSM1669113_jc2369T47DERE2+PGRep3	tf	T47D	ER	E2+PG	rep3	GSM1669113	T47D,ER,E2+PG,rep3,GSM1669113
GSM986059_JC349_ER_siNT_E2_1_mac	tf	MCF-7	ER	E2	siNT	GSM986059	MCF-7,ER,E2,siNT,GSM986059
GSM986060_JC350_ER_siGATA_E2_1_rr	tf	MCF-7	ER	E2	siGATA	GSM986060	MCF-7,ER,E2,siGATA,GSM986060
GSM986061_JC406_ER_siNT_E2_2_mac	tf	MCF-7	ER	E2	siNT	GSM986061	MCF-7,ER,E2,siNT,GSM986061
GSM986062_JC407_ER_siGATA_E2_2_rr	tf	MCF-7	ER	E2	siGATA	GSM986062	MCF-7,ER,E2,siGATA,GSM986062
GSM986063_JC471_ER_siNT_E2_3_mac	tf	MCF-7	ER	E2	siNT	GSM986063	MCF-7,ER,E2,siNT,GSM986063
GSM986064_JC472_ER_siGATA_E2_3_rr	tf	MCF-7	ER	E2	siGATA	GSM986064	MCF-7,ER,E2,siGATA,GSM986064
GSM986089_JC589_ER_siNT_E2_1_mac	tf	ZR751	ER	E2	siNT	GSM986089	ZR751,ER,E2,siNT,GSM986089
GSM986090_JC590_ER_siGATA_E2_1_rr	tf	ZR751	ER	E2	siGATA	GSM986090	ZR751,ER,E2,siGATA,GSM986090
GSM1038222_ERalphainERacells.bed.gz	tf	MCF-7	ERalpha	E2	ERa.cells	GSM1038222	MCF-7,ERalpha,E2,ERa.cells,GSM1038222
GSM1038223_ERalphainERabcells.bed.gz	tf	MCF-7	ERalpha	E2	ERab.cells	GSM1038223	MCF-7,ERalpha,E2,ERab.cells,GSM1038223
GSM862178_t0_export.txt_unique.EE_W1	tf	MCF-7	ERalpha	t0	x	GSM862178	MCF-7,ERalpha,t0,x,GSM862178
GSM862179_t1_export.txt_unique.EE_W1	tf	MCF-7	ERalpha	t1	x	GSM862179	MCF-7,ERalpha,t1,x,GSM862179
GSM862180_t4_export.txt_unique.EE_W1	tf	MCF-7	ERalpha	t4	x	GSM862180	MCF-7,ERalpha,t4,x,GSM862180

File	Type	Cell	Target	Treatment	Condition	ID	Description
GSM862181_t24_export.txt_unique.EE_W	tf	MCF-7	ERalpha	t24	x	GSM862181	MCF-7,ERalpha,t24,x,GSM862181
GSM1038224_ERbetainERabcells.bed.gz	tf	MCF-7	ERbeta	E2	ERab.cells	GSM1038224	MCF-7,ERbeta,E2,ERab.cells,GSM1038224
GSM1038225_ERbetainERbCells.bed.gz	tf	MCF-7	ERbeta	E2	ERb.cells	GSM1038225	MCF-7,ERbeta,E2,ERb.cells,GSM1038225
ENCFF001URF.bed.gz	tf	T47D	ESR1	genistein	rep1	ENCFF001URF	T47D,ESR1,genistein,rep1,ENCFF001URF
ENCFF001URG.bed.gz	tf	T47D	ESR1	genistein	rep2	ENCFF001URG	T47D,ESR1,genistein,rep2,ENCFF001URG
ENCFF002CNV.bed.gz	tf	T47D	ESR1	genistein	x	ENCFF002CNV	T47D,ESR1,genistein,x,ENCFF002CNV
ENCFF001URD.bed.gz	tf	T47D	ESR1	bisphenol_A	rep1	ENCFF001URD	T47D,ESR1,bisphenol_A,rep1,ENCFF001URD
ENCFF001URE.bed.gz	tf	T47D	ESR1	bisphenol_A	rep2	ENCFF001URE	T47D,ESR1,bisphenol_A,rep2,ENCFF001URE
ENCFF002CNU.bed.gz	tf	T47D	ESR1	bisphenol_A	x	ENCFF002CNU	T47D,ESR1,bisphenol_A,x,ENCFF002CNU
ENCFF001URH.bed.gz	tf	T47D	ESR1	estradiol	rep1	ENCFF001URH	T47D,ESR1,estradiol,rep1,ENCFF001URH
ENCFF001URI.bed.gz	tf	T47D	ESR1	estradiol	rep2	ENCFF001URI	T47D,ESR1,estradiol,rep2,ENCFF001URI
ENCFF002CNW.bed.gz	tf	T47D	ESR1	estradiol	x	ENCFF002CNW	T47D,ESR1,estradiol,x,ENCFF002CNW
GSE41995_ESR1.bed.gz	tf	MCF-7	ESR1	none	GFPtagged	GSE41995	MCF-7,ESR1,none,GFPtagged,GSE41995
ENCFF001VPR.bed.gz	tf	MCF_10A	FOS	ethanol	x	ENCFF001VPR	MCF_10A,FOS,ethanol,x,ENCFF001VPR
ENCFF002CYV.bed.gz	tf	MCF_10A	FOS	ethanol	x	ENCFF002CYV	MCF_10A,FOS,ethanol,x,ENCFF002CYV
ENCFF001VPT.bed.gz	tf	MCF_10A	FOS	afimoxifene	x	ENCFF001VPT	MCF_10A,FOS,afimoxifene,x,ENCFF001VPT
ENCFF001SWW.bed.gz	histone	mammary_epithe	H3K27ac	none	x	ENCFF001SWW	mammary_epithelial_cell,H3K27ac,none,x,ENCFF001SWW
ENCFF001VCU.bed.gz	histone	MCF-7	H3K27ac	none	x	ENCFF001VCU	MCF-7,H3K27ac,none,x,ENCFF001VCU
GSE49651_MDAMB231.H3K27Ac.hg19.all	histone	MDA-MB-231	H3K27ac	none	x	GSE49651	MDA-MB-231,H3K27ac,none,x,GSE49651
ENCFF002CYX.bed.gz	tf	MCF_10A	FOS	afimoxifene	x	ENCFF002CYX	MCF_10A,FOS,afimoxifene,x,ENCFF002CYX
ENCFF001VPU.bed.gz	tf	MCF_10A	FOS	afimoxifene	x	ENCFF001VPU	MCF_10A,FOS,afimoxifene,x,ENCFF001VPU
ENCFF002CYY.bed.gz	tf	MCF_10A	FOS	afimoxifene	x	ENCFF002CYY	MCF_10A,FOS,afimoxifene,x,ENCFF002CYY
ENCFF001VPS.bed.gz	tf	MCF_10A	FOS	afimoxifene	x	ENCFF001VPS	MCF_10A,FOS,afimoxifene,x,ENCFF001VPS
GSM986077_JC622_H3K27ac_siNT_E2_M	histone	MCF-7	H3K27ac	E2	siNT	GSM986077	MCF-7,H3K27ac,E2,siNT,GSM986077
ENCFF002CYW.bed.gz	tf	MCF_10A	FOS	afimoxifene	x	ENCFF002CYW	MCF_10A,FOS,afimoxifene,x,ENCFF002CYW
GSE41995_FOS.bed.gz	tf	MCF-7	FOS	none	GFPtagged	GSE41995	MCF-7,FOS,none,GFPtagged,GSE41995
GSE41995_FOSB.bed.gz	tf	MCF-7	FOSB	none	GFPtagged	GSE41995	MCF-7,FOSB,none,GFPtagged,GSE41995
GSE41995_FOSL1.bed.gz	tf	MCF-7	FOSL1	none	GFPtagged	GSE41995	MCF-7,FOSL1,none,GFPtagged,GSE41995
ENCFF001UMR.bed.gz	tf	MCF-7	FOSL2	none	rep1	ENCFF001UMR	MCF-7,FOSL2,none,rep1,ENCFF001UMR
GSM986078_JC624_H3K27ac_siGATA_E	histone	MCF-7	H3K27ac	E2	siGATA	GSM986078	MCF-7,H3K27ac,E2,siGATA,GSM986078
ENCFF001UMS.bed.gz	tf	MCF-7	FOSL2	none	rep2	ENCFF001UMS	MCF-7,FOSL2,none,rep2,ENCFF001UMS
GSE41995_FOSL2.bed.gz	tf	MCF-7	FOSL2	none	GFPtagged	GSE41995	MCF-7,FOSL2,none,GFPtagged,GSE41995
ENCFF001URJ.bed.gz	tf	T47D	FOXA1	dimethyl_sulfoxid	rep1	ENCFF001URJ	T47D,FOXA1,dimethyl_sulfoxide,rep1,ENCFF001URJ
ENCFF001URK.bed.gz	tf	T47D	FOXA1	dimethyl_sulfoxid	rep2	ENCFF001URK	T47D,FOXA1,dimethyl_sulfoxide,rep2,ENCFF001URK
ENCFF002CNX.bed.gz	tf	T47D	FOXA1	dimethyl_sulfoxid	x	ENCFF002CNX	T47D,FOXA1,dimethyl_sulfoxide,x,ENCFF002CNX
GSM986079_JC621_H3K27ac_siNT_Veh_	histone	MCF-7	H3K27ac	Veh	siNT	GSM986079	MCF-7,H3K27ac,Veh,siNT,GSM986079
GSM986080_JC623_H3K27ac_siGATA_V	histone	MCF-7	H3K27ac	Veh	siGATA	GSM986080	MCF-7,H3K27ac,Veh,siGATA,GSM986080
GSE41995_FOXA1.bed.gz	tf	MCF-7	FOXA1	none	GFPtagged	GSE41995	MCF-7,FOXA1,none,GFPtagged,GSE41995
GSM1099031_FOXA1-peak.bed.gz	tf	MDA-MB-453	FOXA1	none	x	GSM1099031	MDA-MB-453,FOXA1,none,x,GSM1099031
GSM986065_JC731_FoxA1_siNT_Veh_N/	tf	MCF-7	FoxA1	Veh	siNT	GSM986065	MCF-7,FoxA1,Veh,siNT,GSM986065
GSM986066_JC732_FoxA1_siGATA_Veh_	tf	MCF-7	FoxA1	Veh	siGATA	GSM986066	MCF-7,FoxA1,Veh,siGATA,GSM986066
E119-H3K27ac.narrowPeak.gz	histone	BRST.vHMEC	H3K27ac	none	x	RM_E119-H3K27	BRST.vHMEC,H3K27ac,none,x,RM_E119-H3K27ac
ENCFF001UMT.bed.gz	tf	MCF-7	FOXM1	none	rep1	ENCFF001UMT	MCF-7,FOXM1,none,rep1,ENCFF001UMT
ENCFF001UMU.bed.gz	tf	MCF-7	FOXM1	none	rep2	ENCFF001UMU	MCF-7,FOXM1,none,rep2,ENCFF001UMU
GSM1000995_ds001_mcf7_dmso_macs_p	tf	MCF-7	FOXM1	dmso	x	GSM1000995	MCF-7,FOXM1,dmso,x,GSM1000995
GSM1000996_ds002_mcf7_ts.macs_peak	tf	MCF-7	FOXM1	ts	x	GSM1000996	MCF-7,FOXM1,ts,x,GSM1000996
GSM1000997_ds003_mcf7_dmso.macs_p	tf	MCF-7	FOXM1	dmso	x	GSM1000997	MCF-7,FOXM1,dmso,x,GSM1000997
GSM1000998_ds004_mcf7_ts.macs_peak	tf	MCF-7	FOXM1	ts	x	GSM1000998	MCF-7,FOXM1,ts,x,GSM1000998
GSM1000999_ds005_mda231_dmso.mact	tf	MDA-MB-231	FOXM1	dmso	x	GSM1000999	MDA-MB-231,FOXM1,dmso,x,GSM1000999
GSM1001000_ds006_mda231_ts.macs_pe	tf	MDA-MB-231	FOXM1	ts	x	GSM1001000	MDA-MB-231,FOXM1,ts,x,GSM1001000
GSM1001001_ds007_mda231_dmso.mact	tf	MDA-MB-231	FOXM1	dmso	x	GSM1001001	MDA-MB-231,FOXM1,dmso,x,GSM1001001
GSM1001002_ds008_mda231_ts.macs_pe	tf	MDA-MB-231	FOXM1	ts	x	GSM1001002	MDA-MB-231,FOXM1,ts,x,GSM1001002
GSM1001003_ds011_mcf7_dmso.macs_p	tf	MCF-7	FOXM1	dmso	x	GSM1001003	MCF-7,FOXM1,dmso,x,GSM1001003
GSM1001004_ds012_mcf7_ts.macs_peak	tf	MCF-7	FOXM1	ts	x	GSM1001004	MCF-7,FOXM1,ts,x,GSM1001004
GSM1001005_ds017_mcf7_dmso.macs_p	tf	MCF-7	FOXM1	dmso	x	GSM1001005	MCF-7,FOXM1,dmso,x,GSM1001005
GSM1001006_ds018_mcf7_ts.macs_peak	tf	MCF-7	FOXM1	ts	x	GSM1001006	MCF-7,FOXM1,ts,x,GSM1001006
GSE46166_Peaks_fra1_reff_IgG_200.bed.	tf	BT549	FRA1	IgG	x	GSE46166	BT549,FRA1,IgG,x,GSE46166
GSE46166_Peaks_fra1_reff_input_200.bec	tf	BT549	FRA1	input	x	GSE46166	BT549,FRA1,input,x,GSE46166
ENCFF001UMV.bed.gz	tf	MCF-7	GABPA	none	rep1	ENCFF001UMV	MCF-7,GABPA,none,rep1,ENCFF001UMV
ENCFF001UMW.bed.gz	tf	MCF-7	GABPA	none	rep2	ENCFF001UMW	MCF-7,GABPA,none,rep2,ENCFF001UMW
ENCFF001VQG.bed.gz	tf	MCF-7	GATA3	none	x	ENCFF001VQG	MCF-7,GATA3,none,x,ENCFF001VQG
ENCFF002CZK.bed.gz	tf	MCF-7	GATA3	none	x	ENCFF002CZK	MCF-7,GATA3,none,x,ENCFF002CZK
ENCFF001URL.bed.gz	tf	T47D	GATA3	dimethyl_sulfoxid	rep1	ENCFF001URL	T47D,GATA3,dimethyl_sulfoxide,rep1,ENCFF001URL
ENCFF001URM.bed.gz	tf	T47D	GATA3	dimethyl_sulfoxid	rep2	ENCFF001URM	T47D,GATA3,dimethyl_sulfoxide,rep2,ENCFF001URM
ENCFF002CNY.bed.gz	tf	T47D	GATA3	dimethyl_sulfoxid	x	ENCFF002CNY	T47D,GATA3,dimethyl_sulfoxide,x,ENCFF002CNY
ENCFF001UMX.bed.gz	tf	MCF-7	GATA3	none	rep1	ENCFF001UMX	MCF-7,GATA3,none,rep1,ENCFF001UMX
ENCFF001UMZ.bed.gz	tf	MCF-7	GATA3	none	rep2	ENCFF001UMZ	MCF-7,GATA3,none,rep2,ENCFF001UMZ
ENCFF001VQF.bed.gz	tf	MCF-7	GATA3	none	x	ENCFF001VQF	MCF-7,GATA3,none,x,ENCFF001VQF
ENCFF002CZJ.bed.gz	tf	MCF-7	GATA3	none	x	ENCFF002CZJ	MCF-7,GATA3,none,x,ENCFF002CZJ
GSE41995_GATA3.bed.gz	tf	MCF-7	GATA3	none	GFPtagged	GSE41995	MCF-7,GATA3,none,GFPtagged,GSE41995
GSM986067_JC315_GATA3_E2_1_macs.	tf	MCF-7	GATA3	E2	x	GSM986067	MCF-7,GATA3,E2,x,GSM986067
GSM986068_JC314_GATA3_Veh_1_mact	tf	MCF-7	GATA3	Veh	x	GSM986068	MCF-7,GATA3,Veh,x,GSM986068
GSM986069_JC427_GATA3_E2_2_macs.	tf	MCF-7	GATA3	E2	x	GSM986069	MCF-7,GATA3,E2,x,GSM986069
GSM986070_JC426_GATA3_Veh_2_mact	tf	MCF-7	GATA3	Veh	x	GSM986070	MCF-7,GATA3,Veh,x,GSM986070
GSM986071_JC485_GATA3_E2_3_macs.	tf	MCF-7	GATA3	E2	x	GSM986071	MCF-7,GATA3,E2,x,GSM986071
GSM986072_JC484_GATA3_Veh_3_mact	tf	MCF-7	GATA3	Veh	x	GSM986072	MCF-7,GATA3,Veh,x,GSM986072
GSM986073_JC556_GATA3_E2_4_macs.	tf	MCF-7	GATA3	E2	x	GSM986073	MCF-7,GATA3,E2,x,GSM986073
GSM986074_JC555_GATA3_Veh_4_mact	tf	MCF-7	GATA3	Veh	x	GSM986074	MCF-7,GATA3,Veh,x,GSM986074
GSM986075_JC633_GATA3_E2_5_macs.	tf	MCF-7	GATA3	E2	x	GSM986075	MCF-7,GATA3,E2,x,GSM986075
GSM986076_JC632_GATA3_Veh_5_mact	tf	MCF-7	GATA3	Veh	x	GSM986076	MCF-7,GATA3,Veh,x,GSM986076
ENCFF001SWZ.bed.gz	histone	mammary_epithe	H3K4me1	none	x	ENCFF001SWZ	mammary_epithelial_cell,H3K4me1,none,x,ENCFF001SWZ
GSE49651_MDAMB231.H3K4me1.hg19.al	histone	MDA-MB-231	H3K4me1	none	x	GSE49651	MDA-MB-231,H3K4me1,none,x,GSE49651
GSM986081_JC618_H3K4me1_siNT_E2_	histone	MCF-7	H3K4me1	E2	siNT	GSM986081	MCF-7,H3K4me1,E2,siNT,GSM986081
GSM986082_JC620_H3K4me1_siGATA_E	histone	MCF-7	H3K4me1	E2	siGATA	GSM986082	MCF-7,H3K4me1,E2,siGATA,GSM986082
GSM986083_JC617_H3K4me1_siNT_Veh	histone	MCF-7	H3K4me1	Veh	siNT	GSM986083	MCF-7,H3K4me1,Veh,siNT,GSM986083
GSM986084_JC619_H3K4me1_siGATA_V	histone	MCF-7	H3K4me1	Veh	siGATA	GSM986084	MCF-7,H3K4me1,Veh,siGATA,GSM986084
GSE42617_H3K4ME1.bed.gz	histone	MCF-7	H3K4me1	none	x	GSE42617	MCF-7,H3K4me1,none,x,GSE42617
E027-H3K4me1.narrowPeak.gz	histone	BRST.MYOEP	H3K4me1	none	x	RM_E027-H3K4	BRST.MYOEP,H3K4me1,none,x,RM_E027-H3K4me1
E028-H3K4me1.narrowPeak.gz	histone	BRST.HMEC	H3K4me1	none	x	RM_E028-H3K4	BRST.HMEC,H3K4me1,none,x,RM_E028-H3K4me1
E119-H3K4me1.narrowPeak.gz	histone	BRST.vHMEC	H3K4me1	none	x	RM_E119-H3K4	BRST.vHMEC,H3K4me1,none,x,RM_E119-H3K4me1
ENCFF001SXA.bed.gz	histone	mammary_epithe	H3K4me2	none	x	ENCFF001SXA	mammary_epithelial_cell,H3K4me2,none,x,ENCFF001SXA
ENCFF476WFI.bed.gz	histone	MCF-7	H3K4me2	none	rep1	ENCFF476WFI	MCF-7,H3K4me2,none,rep1,ENCFF476WFI
ENCFF696NQQ.bed.gz	histone	MCF-7	H3K4me2	none	rep2	ENCFF696NQQ	MCF-7,H3K4me2,none,rep2,ENCFF696NQQ
ENCFF258OSE.bed.gz	histone	MCF-7	H3K4me2	none	rep_1-2-2016	ENCFF258OSE	MCF-7,H3K4me2,none,rep_1-2-2016,ENCFF258OSE
ENCFF457GJC.bed.gz	histone	MCF-7	H3K4me2	none	rep_1-2-2016	ENCFF457GJC	MCF-7,H3K4me2,none,rep_1-2-2016,ENCFF457GJC
GSM1122654_H3K4me2-MCF7-hg19-sd-q	histone	MCF-7	H3K4me2	none	x	GSM1122654	MCF-7,H3K4me2,none,x,GSM1122654
GSM1122655_H3K4me2-siJarid1b-MCF7-I	histone	MCF-7	H3K4me2	siJarid1b	x	GSM1122655	MCF-7,H3K4me2,siJarid1b,x,GSM1122655
GSM1122665_H3K4me2-SUM159-hg19-sc	histone	SUM159	H3K4me2	none	x	GSM1122665	SUM159,H3K4me2,none,x,GSM1122665
GSM1402462_H3K4me2-HCC2157-hg19_	histone	HCC2157	H3K4me2	none	x	GSM1402462	HCC2157,H3K4me2,none,x,GSM1402462
GSM916108_H3K4me2_LTED_Hg19_Lupi	histone	MCF-7-LTED	H3K4me2	none	x	GSM916108	MCF-7-LTED,H3K4me2,none,x,GSM916108
E119-H3K4me2.narrowPeak.gz	histone	BRST.vHMEC	H3K4me2	none	x	RM_E119-H3K4	BRST.vHMEC,H3K4me2,none,x,RM_E119-H3K4me2

File	Type	Cell	Factor	Treatment	Condition	ID	Description
GSM2037450_HAUSP_MDA_MB_231_CH	tf	MDA-MB-231	HAUSP	none	x	GSM2037450	MDA-MB-231,HAUSP,none,x,GSM2037450
ENCFF001UMY.bed.gz	tf	MCF-7	HDAC2	none	rep1	ENCFF001UMY	MCF-7,HDAC2,none,rep1,ENCFF001UMY
ENCFF001UNA.bed.gz	tf	MCF-7	HDAC2	none	rep2	ENCFF001UNA	MCF-7,HDAC2,none,rep2,ENCFF001UNA
GSM1462475_HIF1alpha_peaks.bed.gz	tf	T47D	HIF1alpha	hypoxia	x	GSM1462475	T47D,HIF1alpha,hypoxia,x,GSM1462475
GSM1462476_HIF1beta_peaks.bed.gz	tf	T47D	HIF1beta	hypoxia	x	GSM1462476	T47D,HIF1beta,hypoxia,x,GSM1462476
GSE47164_AF1_HOXB7_MACS_peaks.be	tf	BT474	HOXB7	none	rep1	GSE47164	BT474,HOXB7,none,rep1,GSE47164
GSE47164_AF2_HOXB7_MACS_peaks.be	tf	BT474	HOXB7	none	rep1	GSE47164	BT474,HOXB7,none,rep1,GSE47164
GSM1122651_JARID1B-MCF7-hg19-sd-q	tf	MCF-7	JARID1B	none	x	GSM1122651	MCF-7,JARID1B,none,x,GSM1122651
GSM1122652_JARID1B-MCF7-siJARID1B	tf	MCF-7	JARID1B	siJARID1B	x	GSM1122652	MCF-7,JARID1B,siJARID1B,x,GSM1122652
GSM1122653_JARID1B-MCF7-siCTCF-hg	tf	MCF-7	JARID1B	siCTCF	x	GSM1122653	MCF-7,JARID1B,siCTCF,x,GSM1122653
GSM1122659_JARID1B-T47D-hg19-sd-q_	tf	T47D	JARID1B	none	x	GSM1122659	T47D,JARID1B,none,x,GSM1122659
GSM1122661_JARID1B-SUM185-hg19-sd	tf	SUM185	JARID1B	none	x	GSM1122661	SUM185,JARID1B,none,x,GSM1122661
GSM1122662_JARID1B-SUM185-siCTCF-tf	tf	SUM185	JARID1B	siCTCF	x	GSM1122662	SUM185,JARID1B,siCTCF,x,GSM1122662
GSM1122664_JARID1B-SUM159-hg19-sd	tf	SUM159	JARID1B	none	x	GSM1122664	SUM159,JARID1B,none,x,GSM1122664
GSM1122669_JARID1B-MDA231-hg19-sd	tf	MDA231	JARID1B	none	x	GSM1122669	MDA231,JARID1B,none,x,GSM1122669
GSM1122671_JARID1B-HCC2157-hg19-s	tf	HCC2157	JARID1B	none	x	GSM1122671	HCC2157,JARID1B,none,x,GSM1122671
GSE41995_JUN.bed.gz	tf	MCF-7	JUN	none	GFPtagged	GSE41995	MCF-7,JUN,none,GFPtagged,GSE41995
GSE66081_MDA-MB-231_JUN_IDR_0.01.	tf	MDA-MB-231	JUN	none	x	GSE66081	MDA-MB-231,JUN,none,x,GSE66081
GSM1848883_36noTNFJun_35IgG_peaks	tf	BT549	JUN	noTNF	IgG	GSM1848883	BT549,JUN,noTNF,IgG,GSM1848883
GSM1848883_noTNFJun36_Input38_peak	tf	BT549	JUN	noTNF	input	GSM1848883	BT549,JUN,noTNF,input,GSM1848883
GSM1848885_39TNFJun_35IgG_peaks.be	tf	BT549	JUN	TNF	IgG	GSM1848885	BT549,JUN,TNF,IgG,GSM1848885
GSM1848885_TNFJun39_Input38_peaks.t	tf	BT549	JUN	TNF	input	GSM1848885	BT549,JUN,TNF,input,GSM1848885
GSE41995_JUNB.bed.gz	tf	MCF-7	JUNB	none	GFPtagged	GSE41995	MCF-7,JUNB,none,GFPtagged,GSE41995
ENCFF001UNB.bed.gz	tf	MCF-7	JUND	none	rep1	ENCFF001UNB	MCF-7,JUND,none,rep1,ENCFF001UNB
ENCFF001UNC.bed.gz	tf	MCF-7	JUND	none	rep2	ENCFF001UNC	MCF-7,JUND,none,rep2,ENCFF001UNC
ENCFF001URN.bed.gz	tf	T47D	JUND	none	rep1	ENCFF001URN	T47D,JUND,none,rep1,ENCFF001URN
ENCFF001URO.bed.gz	tf	T47D	JUND	none	rep2	ENCFF001URO	T47D,JUND,none,rep2,ENCFF001URO
GSE41995_JUND.bed.gz	tf	MCF-7	JUND	none	GFPtagged	GSE41995	MCF-7,JUND,none,GFPtagged,GSE41995
ENCFF001UND.bed.gz	tf	MCF-7	MAX	none	rep1	ENCFF001UND	MCF-7,MAX,none,rep1,ENCFF001UND
ENCFF001UNE.bed.gz	tf	MCF-7	MAX	none	rep2	ENCFF001UNE	MCF-7,MAX,none,rep2,ENCFF001UNE
ENCFF001UTL.bed.gz	tf	MCF-7	MYC	none	rep1	ENCFF001UTL	MCF-7,MYC,none,rep1,ENCFF001UTL
ENCFF002DBG.bed.gz	tf	MCF-7	MYC	none	x	ENCFF002DBG	MCF-7,MYC,none,x,ENCFF002DBG
ENCFF001UTN.bed.gz	tf	MCF-7	MYC	none	x	ENCFF001UTN	MCF-7,MYC,none,x,ENCFF001UTN
ENCFF002DBI.bed.gz	tf	MCF-7	MYC	none	x	ENCFF002DBI	MCF-7,MYC,none,x,ENCFF002DBI
ENCFF001VPW.bed.gz	tf	MCF_10A	MYC	afimoxifene	x	ENCFF001VPW	MCF_10A,MYC,afimoxifene,x,ENCFF001VPW
ENCFF002CZA.bed.gz	tf	MCF_10A	MYC	afimoxifene	x	ENCFF002CZA	MCF_10A,MYC,afimoxifene,x,ENCFF002CZA
ENCFF001UTM.bed.gz	tf	MCF-7	MYC	none	rep1	ENCFF001UTM	MCF-7,MYC,none,rep1,ENCFF001UTM
ENCFF002DBH.bed.gz	tf	MCF-7	MYC	none	x	ENCFF002DBH	MCF-7,MYC,none,x,ENCFF002DBH
ENCFF001UTK.bed.gz	tf	MCF-7	MYC	17b-estradiol	rep1	ENCFF001UTK	MCF-7,MYC,17b-estradiol,rep1,ENCFF001UTK
ENCFF002DBF.bed.gz	tf	MCF-7	MYC	17b-estradiol	x	ENCFF002DBF	MCF-7,MYC,17b-estradiol,x,ENCFF002DBF
ENCFF001VPV.bed.gz	tf	MCF_10A	MYC	ethanol	x	ENCFF001VPV	MCF_10A,MYC,ethanol,x,ENCFF001VPV
ENCFF002CYZ.bed.gz	tf	MCF_10A	MYC	ethanol	x	ENCFF002CYZ	MCF_10A,MYC,ethanol,x,ENCFF002CYZ
GSM1099029_MYC-peak.bed.gz	tf	MDA-MB-453	MYC	none	x	GSM1099029	MDA-MB-453,MYC,none,x,GSM1099029
GSE41995_NR1D1.bed.gz	tf	MCF-7	NR1D1	none	GFPtagged	GSE41995	MCF-7,NR1D1,none,GFPtagged,GSE41995
GSE41995_NR1D2.bed.gz	tf	MCF-7	NR1D2	none	GFPtagged	GSE41995	MCF-7,NR1D2,none,GFPtagged,GSE41995
GSE41995_NR1H3.bed.gz	tf	MCF-7	NR1H3	none	GFPtagged	GSE41995	MCF-7,NR1H3,none,GFPtagged,GSE41995
GSE41995_NR2C1-L.bed.gz	tf	MCF-7	NR2C1-L	none	GFPtagged	GSE41995	MCF-7,NR2C1-L,none,GFPtagged,GSE41995
GSE41995_NR2C1-S.bed.gz	tf	MCF-7	NR2C1-S	none	GFPtagged	GSE41995	MCF-7,NR2C1-S,none,GFPtagged,GSE41995
GSE41995_NR2C2.bed.gz	tf	MCF-7	NR2C2	none	GFPtagged	GSE41995	MCF-7,NR2C2,none,GFPtagged,GSE41995
GSE41995_NR2F1.bed.gz	tf	MCF-7	NR2F1	none	GFPtagged	GSE41995	MCF-7,NR2F1,none,GFPtagged,GSE41995
ENCFF001UNF.bed.gz	tf	MCF-7	NR2F2	none	rep1	ENCFF001UNF	MCF-7,NR2F2,none,rep1,ENCFF001UNF
ENCFF001UNG.bed.gz	tf	MCF-7	NR2F2	none	rep2	ENCFF001UNG	MCF-7,NR2F2,none,rep2,ENCFF001UNG
GSE41995_NR2F2.bed.gz	tf	MCF-7	NR2F2	none	GFPtagged	GSE41995	MCF-7,NR2F2,none,GFPtagged,GSE41995
GSE41995_NR3C1.bed.gz	tf	MCF-7	NR3C1	none	GFPtagged	GSE41995	MCF-7,NR3C1,none,GFPtagged,GSE41995
GSE41995_NR4A1.bed.gz	tf	MCF-7	NR4A1	none	GFPtagged	GSE41995	MCF-7,NR4A1,none,GFPtagged,GSE41995
GSE41995_NR4A2.bed.gz	tf	MCF-7	NR4A2	none	GFPtagged	GSE41995	MCF-7,NR4A2,none,GFPtagged,GSE41995
GSM1462478_NRF1_peaks.bed.gz	tf	T47D	NRF1	hypoxia	x	GSM1462478	T47D,NRF1,hypoxia,x,GSM1462478
wgEncodeAwgDnaseDukeMcf7hypoxiaUni	dnase	MCF-7	open-chrom	hypoxia	x	ENC_dnase	MCF-7,open-chrom,hypoxia,x,ENC_dnase
wgEncodeAwgDnaseDukeT47dUniPk.narr	dnase	T47D	open-chrom	none	x	ENC_dnase	T47D,open-chrom,none,x,ENC_dnase
wgEncodeAwgDnaseUwdukeHmecUniPk.r	dnase	HMEC	open-chrom	none	x	ENC_dnase	HMEC,open-chrom,none,x,ENC_dnase
wgEncodeAwgDnaseUwdukeMcf7UniPk.na	dnase	MCF-7	open-chrom	none	x	ENC_dnase	MCF-7,open-chrom,none,x,ENC_dnase
GSE42617_FAIRE.bed.gz	faire	MCF-7	open-chrom	none	x	GSE42617	MCF-7,open-chrom,none,x,GSE42617
GSM1122847_HMEC_FAIRE_1.peaksMos	faire	HMEC	open-chrom	none	x	GSM1122847	HMEC,open-chrom,none,x,GSM1122847
GSM1122848_HMEC_FAIRE_2.peaksMos	faire	HMEC	open-chrom	none	x	GSM1122848	HMEC,open-chrom,none,x,GSM1122848
GSM925735_FAIRE_H19_LTED_rep1.bed	faire	MCF-7-LTED	open-chrom	none	rep1	GSM925735	MCF-7-LTED,open-chrom,none,rep1,GSM925735
GSM925736_FAIRE_H19_LTED_rep2.bed	faire	MCF-7-LTED	open-chrom	none	rep2	GSM925736	MCF-7-LTED,open-chrom,none,rep2,GSM925736
E028-DNase.hotspot.all.peaks.bed.gz	dnase	BRST.HMEC	open-chrom	none	all	RM_E028-DNase	BRST.HMEC,open-chrom,none,all,RM_E028-DNase
E028-DNase.hotspot.fdr0.01.peaks.bed.gz	dnase	BRST.HMEC	open-chrom	none	fdr0.01	RM_E028-DNase	BRST.HMEC,open-chrom,none,fdr0.01,RM_E028-DNase
E028-DNase.macs2.narrowPeak.gz	dnase	BRST.HMEC	open-chrom	none	x	RM_E028-DNase	BRST.HMEC,open-chrom,none,x,RM_E028-DNase
E119-DNase.macs2.narrowPeak.gz	dnase	BRST.vHMEC	open-chrom	none	x	RM_E119-DNase	BRST.vHMEC,open-chrom,none,x,RM_E119-DNase
GSM986085_JC476_p300_siNT_E2_2_ma	tf	MCF-7	p300	E2	siNT	GSM986085	MCF-7,p300,E2,siNT,GSM986085
GSM986086_JC478_p300_siGATA_E2_2_	tf	MCF-7	p300	E2	siGATA	GSM986086	MCF-7,p300,E2,siGATA,GSM986086
GSM986087_JC475_p300_siNT_Veh_2_m	tf	MCF-7	p300	Veh	siNT	GSM986087	MCF-7,p300,Veh,siNT,GSM986087
GSM986088_JC477_p300_siGATA_Veh_2	tf	MCF-7	p300	Veh	siGATA	GSM986088	MCF-7,p300,Veh,siGATA,GSM986088
GSM692743_PBX1_MCF7_red_m16_10_t	tf	MCF-7	PBX1	none	x	GSM692743	MCF-7,PBX1,none,x,GSM692743
GSM989353_PBX1_H19_LTED_rep4_win	tf	MCF-7-LTED	PBX1	none	x	GSM989353	MCF-7-LTED,PBX1,none,x,GSM989353
GSE41995_PGR.bed.gz	tf	MCF-7	PGR	none	GFPtagged	GSE41995	MCF-7,PGR,none,GFPtagged,GSE41995
ENCFF001UNL.bed.gz	tf	MCF-7	PML	none	rep1	ENCFF001UNL	MCF-7,PML,none,rep1,ENCFF001UNL
ENCFF001UNM.bed.gz	tf	MCF-7	PML	none	rep2	ENCFF001UNM	MCF-7,PML,none,rep2,ENCFF001UNM
ENCFF001VPZ.bed.gz	tf	MCF_10A	POLR2A	afimoxifene	x	ENCFF001VPZ	MCF_10A,POLR2A,afimoxifene,x,ENCFF001VPZ
ENCFF002CZD.bed.gz	tf	MCF_10A	POLR2A	afimoxifene	x	ENCFF002CZD	MCF_10A,POLR2A,afimoxifene,x,ENCFF002CZD
ENCFF001UTT.bed.gz	tf	MCF-7	POLR2A	none	x	ENCFF001UTT	MCF-7,POLR2A,none,x,ENCFF001UTT
ENCFF002DBQ.bed.gz	tf	MCF-7	POLR2A	none	x	ENCFF002DBQ	MCF-7,POLR2A,none,x,ENCFF002DBQ
ENCFF001UTU.bed.gz	tf	MCF-7	POLR2A	none	rep1	ENCFF001UTU	MCF-7,POLR2A,none,rep1,ENCFF001UTU
ENCFF002DBO.bed.gz	tf	MCF-7	POLR2A	none	x	ENCFF002DBO	MCF-7,POLR2A,none,x,ENCFF002DBO
ENCFF001VPY.bed.gz	tf	MCF_10A	POLR2A	ethanol	x	ENCFF001VPY	MCF_10A,POLR2A,ethanol,x,ENCFF001VPY
ENCFF002CZC.bed.gz	tf	MCF_10A	POLR2A	ethanol	x	ENCFF002CZC	MCF_10A,POLR2A,ethanol,x,ENCFF002CZC
ENCFF001UTV.bed.gz	tf	MCF-7	POLR2A	none	rep1	ENCFF001UTV	MCF-7,POLR2A,none,rep1,ENCFF001UTV
ENCFF002DBP.bed.gz	tf	MCF-7	POLR2A	none	x	ENCFF002DBP	MCF-7,POLR2A,none,x,ENCFF002DBP
GSE41995_PPARA.bed.gz	tf	MCF-7	PPARA	none	GFPtagged	GSE41995	MCF-7,PPARA,none,GFPtagged,GSE41995
GSE41995_PPARD.bed.gz	tf	MCF-7	PPARD	none	GFPtagged	GSE41995	MCF-7,PPARD,none,GFPtagged,GSE41995
GSE41995_PPARG.bed.gz	tf	MCF-7	PPARG	none	GFPtagged	GSE41995	MCF-7,PPARG,none,GFPtagged,GSE41995
GSM1669090_jc2346MCF7PRVehRep1.bw	tf	MCF-7	PR	vehicle	rep1	GSM1669090	MCF-7,PR,vehicle,rep1,GSM1669090
GSM1669091_jc2347MCF7PRE2Rep1.bw	tf	MCF-7	PR	E2	rep1	GSM1669091	MCF-7,PR,E2,rep1,GSM1669091
GSM1669092_jc2348MCF7PRPGRep1.bw	tf	MCF-7	PR	PG	rep1	GSM1669092	MCF-7,PR,PG,rep1,GSM1669092
GSM1669093_jc2349MCF7PRE2+PGRep1	tf	MCF-7	PR	E2+PG	rep1	GSM1669093	MCF-7,PR,E2+PG,rep1,GSM1669093
GSM1669094_jc2350MCF7PRVehRep2.bw	tf	MCF-7	PR	vehicle	rep2	GSM1669094	MCF-7,PR,vehicle,rep2,GSM1669094
GSM1669095_jc2351MCF7PRE2Rep2.bw	tf	MCF-7	PR	E2	rep2	GSM1669095	MCF-7,PR,E2,rep2,GSM1669095
GSM1669096_jc2352MCF7PRPGRep2.bw	tf	MCF-7	PR	PG	rep2	GSM1669096	MCF-7,PR,PG,rep2,GSM1669096
GSM1669097_jc2353MCF7PRE2+PGRep2	tf	MCF-7	PR	E2+PG	rep2	GSM1669097	MCF-7,PR,E2+PG,rep2,GSM1669097
GSM1669098_jc2354MCF7PRVehRep3.bw	tf	MCF-7	PR	vehicle	rep3	GSM1669098	MCF-7,PR,vehicle,rep3,GSM1669098

File	Type	Cell	Target	Treatment	Rep	Accession	Description
GSM1669099_jc2355MCF7PRE2Rep3.bw	tf	MCF-7	PR	E2	rep3	GSM1669099	MCF-7,PR,E2,rep3,GSM1669099
GSM1669100_jc2356MCF7PRPGRep3.bw	tf	MCF-7	PR	PG	rep3	GSM1669100	MCF-7,PR,PG,rep3,GSM1669100
GSM1669101_jc2357MCF7PRE2+PGRep	tf	MCF-7	PR	E2+PG	rep3	GSM1669101	MCF-7,PR,E2+PG,rep3,GSM1669101
GSM1669114_jc2370T47DPRVehRep1.bw	tf	T47D	PR	vehicle	rep1	GSM1669114	T47D,PR,vehicle,rep1,GSM1669114
GSM1669115_jc2371T47DPRE2Rep1.bw	tf	T47D	PR	E2	rep1	GSM1669115	T47D,PR,E2,rep1,GSM1669115
GSM1669116_jc2372T47DPRPGRep1.bw	tf	T47D	PR	PG	rep1	GSM1669116	T47D,PR,PG,rep1,GSM1669116
GSM1669117_jc2373T47DPRE2+PGRep1	tf	T47D	PR	E2+PG	rep1	GSM1669117	T47D,PR,E2+PG,rep1,GSM1669117
GSM1669118_jc2374T47DPRVehRep2.bw	tf	T47D	PR	vehicle	rep2	GSM1669118	T47D,PR,vehicle,rep2,GSM1669118
GSM1669119_jc2375T47DPRE2Rep2.bw	tf	T47D	PR	E2	rep2	GSM1669119	T47D,PR,E2,rep2,GSM1669119
GSM1669120_jc2376T47DPRPGRep2.bw	tf	T47D	PR	PG	rep2	GSM1669120	T47D,PR,PG,rep2,GSM1669120
GSM1669121_jc2377T47DPRE2+PGRep2	tf	T47D	PR	E2+PG	rep2	GSM1669121	T47D,PR,E2+PG,rep2,GSM1669121
GSM1669122_jc2378T47DPRVehRep3.bw	tf	T47D	PR	vehicle	rep3	GSM1669122	T47D,PR,vehicle,rep3,GSM1669122
GSM1669123_jc2379T47DPRE2Rep3.bw	tf	T47D	PR	E2	rep3	GSM1669123	T47D,PR,E2,rep3,GSM1669123
GSM1669124_jc2380T47DPRPGRep3.bw	tf	T47D	PR	PG	rep3	GSM1669124	T47D,PR,PG,rep3,GSM1669124
GSM1669125_jc2381T47DPRE2+PGRep3	tf	T47D	PR	E2+PG	rep3	GSM1669125	T47D,PR,E2+PG,rep3,GSM1669125
ENCFF001UNN.bed.gz	tf	MCF-7	RAD21	none	rep1	ENCFF001UNN	MCF-7,RAD21,none,rep1,ENCFF001UNN
ENCFF001UNO.bed.gz	tf	MCF-7	RAD21	none	rep2	ENCFF001UNO	MCF-7,RAD21,none,rep2,ENCFF001UNO
GSE41995_RARA.bed.gz	tf	MCF-7	RARA	none	GFPtagged	GSE41995	MCF-7,RARA,none,GFPtagged,GSE41995
GSE41995_RARG.bed.gz	tf	MCF-7	RARG	none	GFPtagged	GSE41995	MCF-7,RARG,none,GFPtagged,GSE41995
ENCFF001UNH.bed.gz	tf	MCF-7	REST	none	rep1	ENCFF001UNH	MCF-7,REST,none,rep1,ENCFF001UNH
ENCFF001UNI.bed.gz	tf	MCF-7	REST	none	rep2	ENCFF001UNI	MCF-7,REST,none,rep2,ENCFF001UNI
GSM1038229_RIP140inERacells.bed.gz	tf	MCF-7	RIP140	E2	ERa.cells	GSM1038229	MCF-7,RIP140,E2,ERa.cells,GSM1038229
GSM1038230_RIP140inERabcells.bed.gz	tf	MCF-7	RIP140	E2	ERab.cells	GSM1038230	MCF-7,RIP140,E2,ERab.cells,GSM1038230
GSM1038231_RIP140inERbcells.bed.gz	tf	MCF-7	RIP140	E2	ERb.cells	GSM1038231	MCF-7,RIP140,E2,ERb.cells,GSM1038231
GSE41995_RORA.bed.gz	tf	MCF-7	RORA	none	GFPtagged	GSE41995	MCF-7,RORA,none,GFPtagged,GSE41995
GSE41995_RORC.bed.gz	tf	MCF-7	RORC	none	GFPtagged	GSE41995	MCF-7,RORC,none,GFPtagged,GSE41995
GSE41995_RXRA.bed.gz	tf	MCF-7	RXRA	none	GFPtagged	GSE41995	MCF-7,RXRA,none,GFPtagged,GSE41995
GSE41995_RXRB.bed.gz	tf	MCF-7	RXRB	none	GFPtagged	GSE41995	MCF-7,RXRB,none,GFPtagged,GSE41995
ENCFF001UNP.bed.gz	tf	MCF-7	SIN3A	none	rep1	ENCFF001UNP	MCF-7,SIN3A,none,rep1,ENCFF001UNP
ENCFF001UNQ.bed.gz	tf	MCF-7	SIN3A	none	rep2	ENCFF001UNQ	MCF-7,SIN3A,none,rep2,ENCFF001UNQ
GSE41995_SPDEF.bed.gz	tf	MCF-7	SPDEF	none	GFPtagged	GSE41995	MCF-7,SPDEF,none,GFPtagged,GSE41995
GSM1187119_s04_MCF7_SPDEF_rep1_n	tf	MCF-7	SPDEF	none	rep1	GSM1187119	MCF-7,SPDEF,none,rep1,GSM1187119
GSM1187120_s05_MCF7_SPDEF_rep2_n	tf	MCF-7	SPDEF	none	rep2	GSM1187120	MCF-7,SPDEF,none,rep2,GSM1187120
GSM1187121_s06_MCF7_SPDEF_rep3_n	tf	MCF-7	SPDEF	none	rep3	GSM1187121	MCF-7,SPDEF,none,rep3,GSM1187121
GSM1038226_SRC3inERacells.bed.gz	tf	MCF-7	SRC3	E2	ERa.cells	GSM1038226	MCF-7,SRC3,E2,ERa.cells,GSM1038226
GSM1038227_SRC3inERabcells.bed.gz	tf	MCF-7	SRC3	E2	ERab.cells	GSM1038227	MCF-7,SRC3,E2,ERab.cells,GSM1038227
GSM1038228_SRC3inERbcells.bed.gz	tf	MCF-7	SRC3	E2	ERb.cells	GSM1038228	MCF-7,SRC3,E2,ERb.cells,GSM1038228
ENCFF001UNR.bed.gz	tf	MCF-7	SRF	none	rep1	ENCFF001UNR	MCF-7,SRF,none,rep1,ENCFF001UNR
ENCFF001UNS.bed.gz	tf	MCF-7	SRF	none	rep2	ENCFF001UNS	MCF-7,SRF,none,rep2,ENCFF001UNS
ENCFF001VQD.bed.gz	tf	MCF_10A	STAT3	afimoxifene	x	ENCFF001VQD	MCF_10A,STAT3,afimoxifene,x,ENCFF001VQD
ENCFF002CZH.bed.gz	tf	MCF_10A	STAT3	afimoxifene	x	ENCFF002CZH	MCF_10A,STAT3,afimoxifene,x,ENCFF002CZH
ENCFF001VQA.bed.gz	tf	MCF_10A	STAT3	ethanol	x	ENCFF001VQA	MCF_10A,STAT3,ethanol,x,ENCFF001VQA
ENCFF002CZE.bed.gz	tf	MCF_10A	STAT3	ethanol	x	ENCFF002CZE	MCF_10A,STAT3,ethanol,x,ENCFF002CZE
ENCFF002CZG.bed.gz	tf	MCF_10A	STAT3	ethanol	x	ENCFF002CZG	MCF_10A,STAT3,ethanol,x,ENCFF002CZG
ENCFF002CZF.bed.gz	tf	MCF_10A	STAT3	ethanol	x	ENCFF002CZF	MCF_10A,STAT3,ethanol,x,ENCFF002CZF
ENCFF001VQE.bed.gz	tf	MCF_10A	STAT3	afimoxifene	x	ENCFF001VQE	MCF_10A,STAT3,afimoxifene,x,ENCFF001VQE
ENCFF002CZI.bed.gz	tf	MCF_10A	STAT3	afimoxifene	x	ENCFF002CZI	MCF_10A,STAT3,afimoxifene,x,ENCFF002CZI
ENCFF001UNT.bed.gz	tf	MCF-7	TAF1	none	rep1	ENCFF001UNT	MCF-7,TAF1,none,rep1,ENCFF001UNT
ENCFF001UNU.bed.gz	tf	MCF-7	TAF1	none	rep2	ENCFF001UNU	MCF-7,TAF1,none,rep2,ENCFF001UNU
GSE66081_MDA-231_TAZ_IDR_0.01.	tf	MDA-MB-231	TAZ	none	x	GSE66081	MDA-MB-231,TAZ,none,x,GSE66081
ENCFF001UNV.bed.gz	tf	MCF-7	TCF12	none	rep1	ENCFF001UNV	MCF-7,TCF12,none,rep1,ENCFF001UNV
ENCFF001UNW.bed.gz	tf	MCF-7	TCF12	none	rep2	ENCFF001UNW	MCF-7,TCF12,none,rep2,ENCFF001UNW
ENCFF001VQI.bed.gz	tf	MCF-7	TCF7L2	none	x	ENCFF001VQI	MCF-7,TCF7L2,none,x,ENCFF001VQI
ENCFF002CZM.bed.gz	tf	MCF-7	TCF7L2	none	x	ENCFF002CZM	MCF-7,TCF7L2,none,x,ENCFF002CZM
GSM1099032_TCF7L2-DHT-peak.bed.gz	tf	MDA-MB-453	TCF7L2	DHT	x	GSM1099032	MDA-MB-453,TCF7L2,DHT,x,GSM1099032
GSM1099033_TCF7L2-vehicle-peak.bed.g	tf	MDA-MB-453	TCF7L2	vehicle	x	GSM1099033	MDA-MB-453,TCF7L2,vehicle,x,GSM1099033
ENCFF001UNX.bed.gz	tf	MCF-7	TEAD4	none	rep1	ENCFF001UNX	MCF-7,TEAD4,none,rep1,ENCFF001UNX
ENCFF001UNY.bed.gz	tf	MCF-7	TEAD4	none	rep2	ENCFF001UNY	MCF-7,TEAD4,none,rep2,ENCFF001UNY
GSE66081_MDA-MB-231_TEAD4_IDR_0.	tf	MDA-MB-231	TEAD4	none	x	GSE66081	MDA-MB-231,TEAD4,none,x,GSE66081
GSE41995_THRA.bed.gz	tf	MCF-7	THRA	none	GFPtagged	GSE41995	MCF-7,THRA,none,GFPtagged,GSE41995
GSE66753_MACS_peaks_minus_est.bed.	tf	MCF-7	TOP2B	minus_estrogen	x	GSE66753	MCF-7,TOP2B,minus_estrogen,x,GSE66753
GSE66753_MACS_peaks_plus_est.bed.gz	tf	MCF-7	TOP2B	plus_estrogen	x	GSE66753	MCF-7,TOP2B,plus_estrogen,x,GSE66753
GSE41995_VDR.bed.gz	tf	MCF-7	VDR	none	GFPtagged	GSE41995	MCF-7,VDR,none,GFPtagged,GSE41995
GSE41995_XBP1.bed.gz	tf	MCF-7	XBP1	none	GFPtagged	GSE41995	MCF-7,XBP1,none,GFPtagged,GSE41995
GSE66081_MDA-MB-231_YAP_IDR_0.01.	tf	MDA-MB-231	YAP	none	x	GSE66081	MDA-MB-231,YAP,none,x,GSE66081
ENCFF001VQJ.bed.gz	tf	MCF-7	ZNF217	none	x	ENCFF001VQJ	MCF-7,ZNF217,none,x,ENCFF001VQJ
ENCFF002CZN.bed.gz	tf	MCF-7	ZNF217	none	x	ENCFF002CZN	MCF-7,ZNF217,none,x,ENCFF002CZN
ENCFF001SXB.bed.gz	histone	mammary_epithe	H3K4me3	none	x	ENCFF001SXB	mammary_epithelial_cell,H3K4me3,none,x,ENCFF001SXB
ENCFF001XHB.bed.gz	histone	MCF-7	H3K4me3	none	rep2	ENCFF001XHB	MCF-7,H3K4me3,none,rep2,ENCFF001XHB
ENCFF001XHC.bed.gz	histone	MCF-7	H3K4me3	none	rep2	ENCFF001XHC	MCF-7,H3K4me3,none,rep2,ENCFF001XHC
ENCFF001XHD.bed.gz	histone	MCF-7	H3K4me3	none	rep1	ENCFF001XHD	MCF-7,H3K4me3,none,rep1,ENCFF001XHD
ENCFF001XHE.bed.gz	histone	MCF-7	H3K4me3	none	rep1	ENCFF001XHE	MCF-7,H3K4me3,none,rep1,ENCFF001XHE
ENCFF001XDR.bed.gz	histone	mammary_epithe	H3K4me3	none	rep1	ENCFF001XDR	mammary_epithelial_cell,H3K4me3,none,rep1,ENCFF001XDR
ENCFF001XDS.bed.gz	histone	mammary_epithe	H3K4me3	none	rep2	ENCFF001XDS	mammary_epithelial_cell,H3K4me3,none,rep2,ENCFF001XDS
ENCFF001XDT.bed.gz	histone	mammary_epithe	H3K4me3	none	rep1	ENCFF001XDT	mammary_epithelial_cell,H3K4me3,none,rep1,ENCFF001XDT
ENCFF001XDU.bed.gz	histone	mammary_epithe	H3K4me3	none	rep2	ENCFF001XDU	mammary_epithelial_cell,H3K4me3,none,rep2,ENCFF001XDU
GSE49651_MDAMB231.H3K4me3.hg19.A	histone	MDA-MB-231	H3K4me3	none	x	GSE49651	MDA-MB-231,H3K4me3,none,x,GSE49651
GSM1122656_H3K4me3-MCF7-hg19-sd-q	histone	MCF-7	H3K4me3	none	x	GSM1122656	MCF-7,H3K4me3,none,x,GSM1122656
GSM1122657_H3K4me3-siJarid1b-MCF7-l	histone	MCF-7	H3K4me3	siJarid1b	x	GSM1122657	MCF-7,H3K4me3,siJarid1b,x,GSM1122657
GSM1122666_H3K4me3-SUM159-hg19-sc	histone	SUM159	H3K4me3	none	x	GSM1122666	SUM159,H3K4me3,none,x,GSM1122666
GSM1402463_H3K4me3-HCC2157-hg19_	histone	HCC2157	H3K4me3	none	x	GSM1402463	HCC2157,H3K4me3,none,x,GSM1402463
GSE42617_H3K4ME3.bed.gz	histone	MCF-7	H3K4me3	none	x	GSE42617	MCF-7,H3K4me3,none,x,GSE42617
E027-H3K4me3.narrowPeak.gz	histone	BRST.MYOEP	H3K4me3	none	x	RM_E027-H3K4n	BRST.MYOEP,H3K4me3,none,x,RM_E027-H3K4me3
E028-H3K4me3.narrowPeak.gz	histone	BRST.HMEC	H3K4me3	none	x	RM_E028-H3K4n	BRST.HMEC,H3K4me3,none,x,RM_E028-H3K4me3
E119-H3K4me3.narrowPeak.gz	histone	BRST.vHMEC	H3K4me3	none	x	RM_E119-H3K4n	BRST.vHMEC,H3K4me3,none,x,RM_E119-H3K4me3
E027-H3K9ac.narrowPeak.gz	histone	BRST.MYOEP	H3K9ac	none	x	RM_E027-H3K9a	BRST.MYOEP,H3K9ac,none,x,RM_E027-H3K9ac
E119-H3K9ac.narrowPeak.gz	histone	BRST.vHMEC	H3K9ac	none	x	RM_E119-H3K9a	BRST.vHMEC,H3K9ac,none,x,RM_E119-H3K9ac
ENCFF001XRP.bed.gz	tf	fibroblast_of_mar	CTCF	none	rep1	ENCFF001XRP	fibroblast_of_mammary_gland,CTCF,none,rep1,ENCFF001XRP
ENCFF001XRQ.bed.gz	tf	fibroblast_of_mar	CTCF	none	rep2	ENCFF001XRQ	fibroblast_of_mammary_gland,CTCF,none,rep2,ENCFF001XRQ
ENCFF001XRR.bed.gz	tf	fibroblast_of_mar	CTCF	none	rep1	ENCFF001XRR	fibroblast_of_mammary_gland,CTCF,none,rep1,ENCFF001XRR
ENCFF001XRS.bed.gz	tf	fibroblast_of_mar	CTCF	none	rep2	ENCFF001XRS	fibroblast_of_mammary_gland,CTCF,none,rep2,ENCFF001XRS
ENCFF002DDC.bed.gz	tf	fibroblast_of_mar	CTCF	none	x	ENCFF002DDC	fibroblast_of_mammary_gland,CTCF,none,x,ENCFF002DDC
ENCFF001XDV.bed.gz	histone	fibroblast_of_mar	H3K4me3	none	rep1	ENCFF001XDV	fibroblast_of_mammary_gland,H3K4me3,none,rep1,ENCFF001XDV
ENCFF001XDW.bed.gz	histone	fibroblast_of_mar	H3K4me3	none	rep2	ENCFF001XDW	fibroblast_of_mammary_gland,H3K4me3,none,rep2,ENCFF001XDW
ENCFF001XDX.bed.gz	histone	fibroblast_of_mar	H3K4me3	none	rep1	ENCFF001XDX	fibroblast_of_mammary_gland,H3K4me3,none,rep1,ENCFF001XDX
ENCFF001XDY.bed.gz	histone	fibroblast_of_mar	H3K4me3	none	rep2	ENCFF001XDY	fibroblast_of_mammary_gland,H3K4me3,none,rep2,ENCFF001XDY
ENCFF001VQH.bed.gz	tf	MCF-7	HA-E2F1	none	x	ENCFF001VQH	MCF-7,HA-E2F1,none,x,ENCFF001VQH
ENCFF002CZL.bed.gz	tf	MCF-7	HA-E2F1	none	x	ENCFF002CZL	MCF-7,HA-E2F1,none,x,ENCFF002CZL
GSM2037451_HAUSP_H1299_CHIP_peal	tf	H1299	HAUSP	none	x	GSM2037451	H1299,HAUSP,none,x,GSM2037451
GSM2037452_H1299_HIF_hg19_rmdup_p	tf	H1299	HIF	none	x	GSM2037452	H1299,HIF,none,x,GSM2037452
wgEncodeAwgDnaseUwHmfUniPk.narrowf	dnase	HMF	open-chrom	none	x	ENC_dnase	HMF,open-chrom,none,x,ENC_dnase

Supplementary Table 7: Associations for ten novel and ten previously reported (and replicated) ER-negative breast cancer susceptibility loci, by ER status (BCAC data only)

SNP	Location	ER-negative[†]		ER-positive[‡]		Heterogeneity P-value*
		OR (95%CI)	P-value	OR (95%CI)	P-value	
Loci identified by the present study						
rs200648189	2p23.3	0.94 (0.91-0.97)	4.7×10^{-4}	0.99 (0.97-1.01)	0.49	4.7×10^{-3}
rs6569648	6q23.1	0.93 (0.90-0.95)	4.3×10^{-8}	0.96 (0.94-0.97)	2.0×10^{-7}	2.5×10^{-2}
rs66823261	8p23.3	1.09 (1.06-1.12)	5.6×10^{-9}	1.02 (1.01-1.04)	9.6×10^{-3}	1.3×10^{-5}
rs17350191	8q24.13	1.07 (1.04-1.09)	2.0×10^{-8}	1.03 (1.02-1.05)	6.3×10^{-5}	1.1×10^{-3}
rs11374964	11q22.3	0.94 (0.92-0.96)	3.6×10^{-8}	1.02 (1.01-1.04)	5.9×10^{-3}	2.8×10^{-12}
rs74911261	11q22.3	0.82 (0.75-0.89)	2.3×10^{-6}	1.05 (1.00-1.10)	5.0×10^{-2}	5.7×10^{-9}
rs11076805	16p13.3	0.92 (0.90-0.95)	2.2×10^{-8}	0.98 (0.97-1.00)	4.9×10^{-2}	1.2×10^{-4}
rs36194942	18q12.1	0.94 (0.91-0.96)	2.5×10^{-7}	0.98 (0.96-0.99)	2.9×10^{-3}	2.0×10^{-3}
rs322144	19p13.2	0.95 (0.93-0.97)	2.4×10^{-5}	0.98 (0.96-1.00)	1.2×10^{-2}	0.12
rs113701136	19q12	1.07 (1.04-1.09)	1.7×10^{-7}	1.02 (1.00-1.04)	1.6×10^{-2}	9.8×10^{-4}
Previously reported loci (associations replicated by the present study)						
rs6678914	1q32.1	0.92 (0.90-0.94)	2.6×10^{-12}	1.02 (1.00-1.03)	2.4×10^{-2}	8.1×10^{-16}
rs4245739	1q32.1	1.14 (1.11-1.16)	3.1×10^{-23}	1.00 (0.98-1.02)	0.87	5.0×10^{-19}
rs12710696	2p24.1	1.06 (1.04-1.09)	6.5×10^{-8}	1.01 (1.00-1.03)	7.7×10^{-2}	1.3×10^{-4}
rs4577244	2p23.2	0.92 (0.90-0.95)	1.5×10^{-9}	1.02 (1.01-1.04)	1.1×10^{-2}	2.8×10^{-14}
rs10069690	5p15.33	1.18 (1.15-1.21)	1.5×10^{-35}	1.03 (1.01-1.04)	1.1×10^{-3}	7.3×10^{-25}
rs3757322	6q25.1	1.15 (1.12-1.18)	2.8×10^{-31}	1.07 (1.05-1.08)	5.4×10^{-17}	1.1×10^{-9}
rs2747652	6q25.2	0.91 (0.89-0.93)	1.9×10^{-18}	0.95 (0.93-0.96)	1.5×10^{-13}	3.0×10^{-5}
rs6562760	13q22.1	0.92 (0.90-0.95)	8.7×10^{-10}	0.96 (0.94-0.98)	2.3×10^{-6}	2.7×10^{-3}
rs11075995	16q12.2	1.09 (1.06-1.12)	1.0×10^{-10}	1.02 (1.00-1.04)	2.2×10^{-2}	4.2×10^{-6}
rs67397200	19p13.11	1.17 (1.14-1.19)	2.7×10^{-37}	0.99 (0.98-1.01)	0.52	6.7×10^{-36}

[†]Combined Breast Cancer Association Consortium (BCAC) data from 16.988 cases and 87,962 controls
[‡]Combined BCAC data from 65,275 cases and 87,962 controls
*ER-negative case-only analysis of BCAC data (N=82,263), by ER status
OR, odds ratio per copy of the minor allele; CI, confidence interval

Supplementary Table 8: Associations for ten novel and ten previously reported (and replicated) ER-negative breast cancer susceptibility loci, by age in years (BCAC data only[†])

SNP	Location	OR (95%CI)				Heterogeneity P-value*
		< 40	40-49	50-59	≥ 60	
Loci identified by the present study						
rs200648189	2p23.3	0.98 (0.9-1.07)	0.96 (0.9-1.03)	0.94 (0.89-1.01)	0.93 (0.87-0.98)	0.060
rs6569648	6q23.1	0.93 (0.87-1.00)	0.91 (0.86-0.96)	0.95 (0.90-1.00)	0.95 (0.91-1.00)	0.16
rs66823261	8p23.3	1.16 (1.08-1.25)	1.15 (1.08-1.22)	1.11 (1.05-1.17)	1.06 (1.01-1.11)	0.15
rs17350191	8q24.13	1.09 (1.03-1.16)	1.08 (1.03-1.13)	1.05 (1.01-1.10)	1.09 (1.04-1.13)	0.84
rs11374964	11q22.3	0.89 (0.83-0.94)	0.93 (0.89-0.98)	0.95 (0.91-0.99)	0.95 (0.91-0.99)	0.16
rs74911261	11q22.3	0.72 (0.57-0.91)	0.78 (0.65-0.93)	0.86 (0.74-1.01)	0.83 (0.72-0.96)	0.12
rs11076805	16p13.3	0.92 (0.85-0.99)	0.95 (0.9-1.01)	0.92 (0.87-0.97)	0.93 (0.88-0.97)	0.68
rs36194942	18q12.1	0.95 (0.89-1.01)	0.92 (0.87-0.97)	0.94 (0.90-0.99)	0.93 (0.89-0.97)	0.95
rs322144	19p13.2	0.97 (0.91-1.04)	0.96 (0.91-1.02)	0.93 (0.89-0.98)	0.95 (0.91-1.00)	0.98
rs113701136	19q12	1.06 (1.00-1.13)	1.05 (1.00-1.11)	1.10 (1.05-1.15)	1.06 (1.02-1.11)	0.33
Previously reported loci (associations replicated by the present study)						
rs6678914	1q32.1	0.95 (0.89-1.00)	0.97 (0.92-1.01)	0.92 (0.88-0.96)	0.92 (0.88-0.96)	0.28
rs4245739	1q32.1	1.15 (1.08-1.23)	1.11 (1.06-1.17)	1.16 (1.11-1.21)	1.12 (1.07-1.17)	0.63
rs12710696	2p24.1	1.05 (0.99-1.12)	1.10 (1.05-1.16)	1.05 (1.01-1.10)	1.06 (1.02-1.11)	0.62
rs4577244	2p23.2	0.87 (0.81-0.94)	0.96 (0.90-1.01)	0.93 (0.89-0.98)	0.90 (0.86-0.95)	0.65
rs10069690	5p15.33	1.25 (1.17-1.34)	1.20 (1.14-1.27)	1.20 (1.15-1.26)	1.10 (1.06-1.15)	1.2×10^{-3}
rs3757322	6q25.1	1.21 (1.14-1.29)	1.18 (1.13-1.24)	1.16 (1.11-1.21)	1.12 (1.08-1.17)	0.065
rs2747652	6q25.2	0.97 (0.91-1.03)	0.91 (0.87-0.96)	0.87 (0.83-0.91)	0.90 (0.87-0.94)	1.0×10^{-2}
rs6562760	13q22.1	0.92 (0.86-0.99)	0.87 (0.82-0.92)	0.93 (0.89-0.98)	0.95 (0.91-1.00)	0.052
rs11075995	16q12.2	1.12 (1.04-1.20)	1.08 (1.02-1.14)	1.06 (1.01-1.11)	1.08 (1.04-1.13)	0.75
rs67397200	19p13.11	1.26 (1.18-1.34)	1.18 (1.13-1.25)	1.14 (1.09-1.19)	1.14 (1.10-1.19)	3.8×10^{-2}

[†]Combined Breast Cancer Association Consortium (BCAC) data from 1954, 3487, 4179 and 5116 cases aged <40, 40-49, 50-59 and ≥60 years, respectively, and 82,347 controls; *ER-negative case-only analysis, by age (trend test, 1df)

OR, odds ratio per copy of the minor allele; CI, confidence interval

Supplementary Table 9: Novel overall breast cancer suceptibility loci from Michailidou et al. (2017)*: asso

Location	SNP†	Chr	Position	Alleles⁊	MAF	GWAS	
						OR (95%CI)	*P*-value
1p36.13	rs2992756	1	18807339	C/T	0.49	0.99 (0.93-1.04)	5.8×10^{-01}
1p34.2	rs4233486	1	41380440	T/C	0.36	0.97 (0.92-1.03)	3.2×10^{-01}
1p34.2	rs79724016	1	42137311	T/G	0.03	0.95 (0.81-1.11)	5.2×10^{-01}
1p34.1	rs1707302	1	46600917	G/A	0.34	1.01 (0.96-1.07)	6.9×10^{-01}
1p32.3	rs140850326	1	50846032	I/D¥	0.49	0.93 (0.87-0.99)	3.4×10^{-02}
1p22.3	rs17426269	1	88156923	G/A	0.15	0.99 (0.92-1.07)	8.2×10^{-01}
1p12	rs7529522	1	118230221	T/C	0.23	1.04 (0.97-1.11)	2.9×10^{-01}
1q22	rs4971059	1	155148781	G/A	0.35	1.03 (0.97-1.09)	3.6×10^{-01}
1q32.1	rs35383942	1	201437832	C/T	0.06	1.00 (0.88-1.15)	9.8×10^{-01}
1q41	rs11117758	1	217220574	G/A	0.21	0.92 (0.86-0.99)	1.7×10^{-02}
2p25.1	rs113577745	2	10135681	C/G	0.10	1.07 (0.98-1.17)	1.3×10^{-01}
2q13	rs71801447	2	111925731	CTTATGTT/C	0.06	1.11 (0.97-1.26)	1.4×10^{-01}
2q36.3	rs12479355	2	227226952	A/G	0.21	0.93 (0.87-1.00)	3.8×10^{-02}
3p13	rs6805189	3	71532113	T/C	0.48	0.97 (0.92-1.03)	3.2×10^{-01}
3p12.1	rs13066793	3	87037543	A/G	0.09	0.93 (0.82-1.07)	3.2×10^{-01}
3p12.1	rs9833888	3	99723580	G/T	0.22	1.02 (0.96-1.09)	4.9×10^{-01}
3q23	rs34207738	3	141112859	CTT/C	0.41	0.99 (0.93-1.06)	8.7×10^{-01}
3q26.31	rs58058861	3	172285237	G/A	0.21	1.02 (0.96-1.09)	4.8×10^{-01}
4p14	rs6815814	4	38816338	A/C	0.26	1.03 (0.97-1.09)	3.9×10^{-01}
4q21.23	4:84370124	4	84370124	TA/TAA	0.47	1.06 (0.99-1.13)	1.1×10^{-01}
4q22.1	rs10022462	4	89243818	C/T	0.44	1.04 (0.99-1.10)	1.3×10^{-01}
4q28.1	rs77528541	4	126843504	G/T	0.13	0.91 (0.83-0.99)	2.3×10^{-02}
5p15.33	rs116095464	5	345109	T/C	0.05	1.13 (1.01-1.27)	3.5×10^{-02}
5q11.1	rs72749841	5	49641645	T/C	0.16	0.94 (0.84-1.06)	3.2×10^{-01}
5q11.1	rs35951924	5	50195093	A/AT	0.32	0.99 (0.92-1.07)	8.2×10^{-01}
5q22.1	rs6882649	5	111217786	T/G	0.34	0.93 (0.87-0.98)	8.1×10^{-03}
5q31.1	rs6596100	5	132407058	C/T	0.25	1.01 (0.95-1.07)	7.7×10^{-01}
5q35.1	rs4562056	5	169591487	G/T	0.33	1.03 (0.98-1.10)	2.6×10^{-01}
6p22.3	rs3819405	6	16399557	C/T	0.33	0.96 (0.90-1.02)	2.2×10^{-01}
6p22.3	rs2223621	6	20621238	C/T	0.38	1.04 (0.99-1.10)	1.5×10^{-01}
6p22.2	rs71557345	6	26680698	G/A	0.07	0.94 (0.85-1.05)	2.9×10^{-01}
6q14.1	rs12207986	6	81094287	A/G	0.47	0.94 (0.89-0.99)	1.7×10^{-02}
7p15.3	rs7971	7	21940960	A/G	0.35	1.03 (0.97-1.08)	3.8×10^{-01}
7p15.1	rs17156577	7	28356889	T/C	0.11	1.15 (1.04-1.27)	5.3×10^{-03}
7q21.3	rs17268829	7	94113799	T/C	0.28	1.05 (0.99-1.11)	1.2×10^{-01}
7q22.1	rs71559437	7	101552440	G/A	0.12	0.97 (0.90-1.06)	5.0×10^{-01}
8q22.3	rs514192	8	102478959	T/A	0.32	1.04 (0.98-1.10)	1.8×10^{-01}
8q23.1	rs12546444	8	106358620	A/T	0.10	0.97 (0.89-1.07)	5.9×10^{-01}
9q33.1	rs1895062	9	119313486	A/G	0.41	1.00 (0.94-1.05)	9.0×10^{-01}
9q33.3	rs10760444	9	129396434	A/G	0.43	1.07 (1.02-1.13)	1.3×10^{-02}
9q34.2	rs587745765	9	136151579	I/D‡	0.20	1.09 (1.00-1.18)	5.1×10^{-02}
10p14	rs67958007	10	9088113	TG/T	0.12	1.04 (0.94-1.15)	4.3×10^{-01}
10q23.33	rs140936696	10	95292187	C/CAA	0.18	1.02 (0.93-1.11)	7.2×10^{-01}
11p15	rs6597981	11	803017	G/A	0.48	0.96 (0.91-1.02)	1.7×10^{-01}

12q21.31	12:85009437:T:C	12	85009437	T/C	0.34	0.99 (0.93-1.05)	7.2×10^{-01}
12q24.31	12:120832146:C:T	12	120832146	C/T	0.16	1.06 (0.98-1.15)	1.6×10^{-01}
14q32.33	rs10623258	14	105212261	C/CTT	0.45	1.01 (0.93-1.10)	8.1×10^{-01}
16q12.2	rs28539243	16	54682064	G/A	0.49	1.06 (1.00-1.12)	3.4×10^{-02}
16q13	rs2432539	16	56420987	G/A	0.40	1.03 (0.97-1.08)	3.5×10^{-01}
16q24.2	rs4496150	16	87085237	C/A	0.25	0.93 (0.87-0.99)	1.7×10^{-02}
17q21.2	rs72826962	17	40836389	C/T	0.01	0.86 (0.58-1.26)	4.3×10^{-01}
17q21.31	17:44252468:G:A	17	44252468	G/A	0.19	0.94 (0.87-1.01)	1.1×10^{-01}
18q12.1	rs117618124	18	29977689	T/C	0.05	0.88 (0.77-1.01)	7.2×10^{-02}
19p13.13	rs78269692	19	13158277	T/C	0.05	1.08 (0.95-1.23)	2.3×10^{-01}
19p13.12	rs2594714	19	13954571	G/A	0.23	0.97 (0.91-1.03)	3.4×10^{-01}
19p13.11	rs2965183	19	19545696	G/A	0.35	1.03 (0.98-1.09)	2.4×10^{-01}
19q13.22	rs71338792	19	46183031	A/AT	0.23	1.02 (0.94-1.11)	6.0×10^{-01}
20p12.3	rs16991615	20	5948227	G/A	0.06	1.15 (1.03-1.29)	1.4×10^{-02}
20q13.13	rs6122906	20	48945911	A/G	0.18	1.07 (1.00-1.14)	6.8×10^{-02}
22q13.1	rs738321	22	38568833	C/G	0.38	0.97 (0.92-1.02)	2.8×10^{-01}
22q13.2	rs73161324	22	42038786	C/T	0.06	1.19 (1.03-1.36)	1.7×10^{-02}
22q13.31	rs28512361	22	46283297	G/A	0.11	1.01 (0.90-1.13)	9.2×10^{-01}

*Michailidou, K. et al. Identification of more than 70 new breast cancer susceptibility loci for breast cancer and definiti

†Results for 2p23.3-rs6725517, 6q23.1-rs6569648 and 8q24.13-rs58847541 are not reported because they represent the

Chr, chromosome; MAF, minor allele frequency; BCAC, Breast Cancer Association Consortium; CIMBA, Consortium of Inv

¥21 base-pair deletion; ‡36 base-pair deletion

BCAC results were based on GWAS data for 4,480 cases and 12,632 controls, iCOGS data for 7,333 cases and 42,468 con

CIMBA results were based on data for 18,908 *BRCA1* mutation carriers (9,414 with breast cancer)

Associations observed with ER-negative breast cancer based on P<0.05 in meta-analysis of all BCAC data

Associations observed with breast cancer for *BRCA1* mutation carriers based on P<0.05 in meta-analysis of

ciations with risk of ER-negative breast cancer and breast cancer for *BRCA1* mutation carriers

ER-negative breast cancer (BCAC)					*BRCA1* mutation
iCOGS		OncoArray		Combined	All CIMBA data co
OR (95%CI)	*P*-value	OR (95%CI)	*P*-value	*P*-value	HR (95%CI)
1.01 (0.97-1.06)	4.8×10^{-01}	1.03 (1.00-1.07)	4.2×10^{-02}	1.1×10^{-01}	1.01 (0.97-1.04)
0.95 (0.91-1.00)	4.7×10^{-02}	0.97 (0.94-1.00)	6.6×10^{-02}	4.4×10^{-03}	0.95 (0.92-0.99)
0.92 (0.83-1.03)	1.4×10^{-01}	0.89 (0.98-1.07)	6.2×10^{-01}	1.4×10^{-01}	0.96 (0.87-1.06)
1.00 (0.96-1.04)	8.8×10^{-01}	1.01 (0.98-1.04)	5.4×10^{-01}	5.7×10^{-01}	0.99 (0.95-1.03)
0.98 (0.94-1.02)	3.1×10^{-01}	0.96 (0.93-0.99)	2.3×10^{-02}	2.9×10^{-03}	1.03 (0.99-1.06)
1.00 (0.95-1.05)	9.6×10^{-01}	1.04 (0.99-1.08)	1.2×10^{-01}	3.4×10^{-01}	1.04 (0.99-1.09)
1.07 (1.02-1.11)	4.0×10^{-03}	1.05 (1.02-1.09)	5.8×10^{-03}	4.8×10^{-05}	1.03 (0.99-1.08)
0.97 (0.94-1.01)	1.6×10^{-01}	1.03 (1.00-1.07)	5.7×10^{-02}	4.2×10^{-01}	0.99 (0.96-1.03)
1.05 (0.96-1.14)	3.0×10^{-01}	1.15 (1.08-1.23)	3.2×10^{-05}	3.3×10^{-04}	1.02 (0.94-1.10)
1.03 (0.98-1.08)	1.9×10^{-01}	0.98 (0.95-1.02)	3.9×10^{-01}	3.7×10^{-01}	0.94 (0.90-0.98)
1.02 (0.96-1.09)	5.1×10^{-01}	1.06 (1.01-1.12)	1.8×10^{-02}	7.4×10^{-03}	0.99 (0.94-1.05)
1.04 (0.96-1.13)	3.0×10^{-01}	1.05 (0.99-1.12)	1.2×10^{-01}	3.2×10^{-02}	1.01 (0.94-1.09)
1.01 (0.96-1.05)	8.1×10^{-01}	1.00 (0.96-1.04)	9.8×10^{-01}	4.3×10^{-01}	0.96 (0.92-1.01)
0.94 (0.90-0.97)	8.9×10^{-04}	1.00 (0.97-1.03)	8.6×10^{-01}	9.9×10^{-03}	0.97 (0.93-1.00)
0.95 (0.89-1.01)	1.2×10^{-01}	0.96 (0.91-1.02)	1.8×10^{-01}	2.4×10^{-02}	0.96 (0.90-1.02)
1.01 (0.97-1.06)	6.2×10^{-01}	1.01 (0.98-1.05)	5.1×10^{-01}	2.5×10^{-01}	1.00 (0.96-1.04)
1.01 (0.97-1.05)	6.6×10^{-01}	1.03 (1.00-1.07)	5.5×10^{-02}	1.1×10^{-01}	1.03 (0.99-1.07)
0.99 (0.94-1.03)	5.3×10^{-01}	1.00 (0.96-1.04)	9.5×10^{-01}	8.5×10^{-01}	0.98 (0.94-1.03)
1.01 (0.97-1.06)	5.3×10^{-01}	1.06 (1.02-1.10)	2.9×10^{-03}	4.9×10^{-03}	0.99 (0.95-1.03)
1.08 (1.04-1.13)	3.9×10^{-05}	1.03 (1.00-1.06)	7.9×10^{-02}	2.9×10^{-05}	0.99 (0.96-1.03)
1.04 (1.00-1.08)	5.3×10^{-02}	1.01 (0.98-1.05)	4.2×10^{-01}	2.3×10^{-02}	0.98 (0.94-1.01)
0.92 (0.87-0.98)	6.9×10^{-03}	0.94 (0.90-0.99)	1.4×10^{-02}	1.3×10^{-05}	1.03 (0.97-1.09)
1.15 (1.06-1.25)	5.8×10^{-04}	1.03 (0.96-1.11)	3.5×10^{-01}	5.2×10^{-04}	1.01 (0.93-1.09)
0.91 (0.84-0.99)	2.1×10^{-02}	0.99 (0.94-1.04)	6.5×10^{-01}	5.2×10^{-02}	0.99 (0.93-1.05)
0.97 (0.93-1.02)	2.0×10^{-01}	0.96 (0.93-1.00)	4.4×10^{-02}	1.5×10^{-02}	1.00 (0.96-1.04)
0.98 (0.94-1.02)	3.0×10^{-01}	0.98 (0.94-1.01)	1.7×10^{-01}	7.9×10^{-03}	0.99 (0.95-1.03)
1.01 (0.96-1.06)	6.6×10^{-01}	0.95 (0.92-0.99)	8.4×10^{-03}	1.2×10^{-01}	0.97 (0.93-1.01)
1.03 (0.99-1.07)	2.1×10^{-01}	1.02 (0.99-1.05)	2.8×10^{-01}	5.9×10^{-02}	0.98 (0.95-1.02)
0.99 (0.95-1.04)	8.3×10^{-01}	0.97 (0.94-1.00)	5.4×10^{-02}	3.5×10^{-02}	0.98 (0.94-1.02)
1.00 (0.96-1.04)	8.9×10^{-01}	1.02 (0.99-1.05)	2.4×10^{-01}	2.1×10^{-01}	0.98 (0.95-1.02)
0.98 (0.91-1.06)	6.2×10^{-01}	0.91 (0.84-0.98)	1.0×10^{-02}	1.7×10^{-02}	1.07 (0.99-1.16)
0.97 (0.94-1.01)	1.5×10^{-01}	0.96 (0.93-0.99)	1.8×10^{-02}	6.1×10^{-04}	0.95 (0.92-0.98)
0.96 (0.92-0.99)	2.7×10^{-02}	0.96 (0.93-0.99)	2.0×10^{-02}	8.3×10^{-03}	1.02 (0.98-1.06)
1.07 (1.01-1.13)	2.5×10^{-02}	1.05 (1.00-1.10)	5.8×10^{-02}	3.3×10^{-04}	1.01 (0.95-1.07)
1.02 (0.98-1.06)	3.9×10^{-01}	1.02 (0.98-1.05)	4.0×10^{-01}	1.0×10^{-01}	1.02 (0.98-1.07)
0.96 (0.90-1.02)	2.0×10^{-01}	0.95 (0.90-1.00)	3.5×10^{-02}	1.7×10^{-02}	0.99 (0.93-1.05)
1.00 (0.97-1.05)	8.2×10^{-01}	1.01 (0.98-1.05)	4.2×10^{-01}	1.8×10^{-01}	1.02 (0.98-1.06)
0.95 (0.89-1.03)	2.0×10^{-01}	0.98 (0.93-1.03)	4.4×10^{-01}	1.3×10^{-01}	0.98 (0.92-1.05)
0.96 (0.92-1.00)	3.1×10^{-02}	0.93 (0.90-0.96)	7.8×10^{-06}	1.4×10^{-05}	0.95 (0.92-0.99)
1.04 (1.00-1.08)	2.8×10^{-02}	1.05 (1.02-1.08)	3.0×10^{-03}	1.4×10^{-05}	1.01 (0.97-1.05)
1.01 (0.96-1.06)	7.2×10^{-01}	1.05 (1.01-1.09)	1.3×10^{-02}	8.0×10^{-03}	1.02 (0.98-1.07)
1.03 (0.97-1.09)	3.0×10^{-01}	1.08 (1.03-1.14)	8.7×10^{-04}	8.4×10^{-04}	0.96 (0.90-1.01)
1.03 (0.98-1.09)	2.3×10^{-01}	1.04 (0.99-1.08)	9.7×10^{-02}	4.0×10^{-02}	1.00 (0.95-1.05)
0.95 (0.92-0.99)	1.4×10^{-02}	0.94 (0.91-0.97)	3.8×10^{-04}	9.9×10^{-06}	0.97 (0.94-1.01)

0.96 (0.92-1.01)	9.2x10^{-02}	0.93 (0.90-0.96)	6.1x10^{-05}	1.1x10^{-04}	1.02 (0.98-1.06)
1.06 (1.00-1.12)	5.1x10^{-02}	1.04 (1.00-1.09)	5.4x10^{-02}	2.5x10^{-03}	1.06 (1.00-1.11)
1.03 (0.99-1.07)	9.4x10^{-02}	1.03 (1.00-1.06)	6.8x10^{-02}	1.5x10^{-02}	1.00 (0.97-1.04)
1.01 (0.98-1.05)	4.8x10^{-01}	1.05 (1.01-1.08)	4.1x10^{-03}	1.1x10^{-03}	0.97 (0.94-1.01)
1.02 (0.98-1.06)	3.1x10^{-01}	1.02 (0.99-1.06)	1.9x10^{-01}	5.5x10^{-02}	0.98 (0.94-1.02)
0.98 (0.94-1.02)	3.8x10^{-01}	0.96 (0.92-0.99)	1.9x10^{-02}	1.7x10^{-03}	0.97 (0.93-1.01)
1.03 (0.85-1.25)	7.5x10^{-01}	1.13 (0.98-1.30)	9.0x10^{-02}	2.0x10^{-01}	1.06 (0.87-1.27)
0.96 (0.91-1.02)	1.6x10^{-01}	0.95 (0.91-0.99)	1.3x10^{-02}	1.7x10^{-03}	0.99 (0.94-1.04)
0.92 (0.83-1.01)	8.9x10^{-02}	0.84 (0.77-0.91)	2.7x10^{-05}	5.0x10^{-06}	0.89 (0.81-0.98)
1.05 (0.94-1.17)	4.2x10^{-01}	1.09 (1.02-1.17)	1.4x10^{-02}	6.2x10^{-03}	1.02 (0.94-1.12)
0.98 (0.93-1.02)	2.8x10^{-01}	1.00 (0.96-1.04)	8.7x10^{-01}	3.3x10^{-01}	1.00 (0.95-1.04)
1.05 (1.01-1.09)	9.3x10^{-03}	1.05 (1.02-1.09)	2.2x10^{-03}	2.3x10^{-05}	1.02 (0.98-1.05)
1.03 (0.98-1.09)	3.0x10^{-01}	1.03 (0.99-1.07)	1.0x10^{-01}	2.3x10^{-02}	0.99 (0.95-1.04)
1.08 (1.00-1.17)	3.7x10^{-02}	1.10 (1.04-1.18)	2.2x10^{-03}	1.7x10^{-05}	0.98 (0.91-1.05)
1.00 (0.95-1.05)	9.2x10^{-01}	1.08 (1.03-1.12)	4.5x10^{-04}	2.9x10^{-03}	0.98 (0.94-1.03)
0.98 (0.95-1.02)	3.7x10^{-01}	0.99 (0.96-1.02)	5.7x10^{-01}	1.9x10^{-01}	1.03 (0.99-1.06)
1.10 (1.01-1.19)	2.5x10^{-02}	1.10 (1.03-1.18)	2.8x10^{-03}	1.2x10^{-05}	1.04 (0.96-1.12)
1.12 (1.05-1.21)	1.3x10^{-03}	1.09 (1.04-1.14)	8.3x10^{-04}	1.5x10^{-05}	1.04 (0.98-1.10)

on of risk-associated genomic features, Reference 1 in the main text

e same signals as those reported for these regions for ER-negative disease

vestigators of Modifiers of BRCA1/2; [‡]More common allele listed first, minor allele second

trols and OncoArray data 9,655 cases and 45,494 controls

all CIMBA data

carriers combined *P*-value
7.5×10^{-01}
1.5×10^{-02}
4.4×10^{-01}
6.9×10^{-01}
1.8×10^{-01}
1.6×10^{-01}
1.6×10^{-01}
7.0×10^{-01}
7.0×10^{-01}
4.6×10^{-03}
8.0×10^{-01}
7.9×10^{-01}
1.1×10^{-01}
7.8×10^{-02}
1.7×10^{-01}
9.9×10^{-01}
1.5×10^{-01}
4.1×10^{-01}
7.5×10^{-01}
7.7×10^{-01}
2.0×10^{-01}
2.9×10^{-01}
8.9×10^{-01}
6.4×10^{-01}
9.7×10^{-01}
4.8×10^{-01}
1.7×10^{-01}
3.9×10^{-01}
3.3×10^{-01}
4.0×10^{-01}
8.4×10^{-02}
5.4×10^{-03}
2.6×10^{-01}
7.7×10^{-01}
2.8×10^{-01}
7.3×10^{-01}
4.2×10^{-01}
6.0×10^{-01}
8.0×10^{-03}
6.1×10^{-01}
3.0×10^{-01}
1.0×10^{-01}
9.3×10^{-01}
1.4×10^{-01}

3.4×10^{-01}
3.8×10^{-02}
9.3×10^{-01}
1.7×10^{-01}
2.8×10^{-01}
1.6×10^{-01}
5.7×10^{-01}
6.7×10^{-01}
1.5×10^{-02}
5.9×10^{-01}
8.4×10^{-01}
4.2×10^{-01}
7.3×10^{-01}
6.2×10^{-01}
4.5×10^{-01}
1.8×10^{-01}
3.2×10^{-01}
1.9×10^{-01}

Supplementary Table 10: Other previously reported (non ER-negative disease-specific) breast cancer suceptibility loci: associations with risk of ER-negative breast cancer* and breast cancer for*BRCA1* mutation carr

Location	SNP	Reference	Chr	Position	Alleles†	MAF	ER-negative breast cancer (BCAC)							*BRCA1* mutation
							GWAS		iCOGS		OncoArray		Combined	All CIMBA data co
							OR (95%CI)	P-value	OR (95%CI)	P-value	OR (95%CI)	P-value	P-value	HR (95%CI)
1p36.22	rs616488	[1]	1	10566215	A/G	0.33	0.91 (0.86-0.96)	7.3x10⁻⁰⁴	0.91 (0.87-0.95)	3.9x10⁻⁰⁶	0.89 (0.86-0.92)	4.8x10⁻¹¹	4.1x10⁻¹⁸	0.96 (0.92-1.00)
1p13.2	rs11552449	[1]	1	114448389	C/T	0.17	1.10 (1.02-1.18)	9.4x10⁻⁰²	1.04 (0.99-1.10)	8.3x10⁻⁰²	1.04 (1.00-1.08)	7.3x10⁻⁰²	8.4x10⁻⁰⁴	1.02 (0.97-1.07)
1p11.2	rs11249433	[2]	1	121280613	A/G	0.41	0.99 (0.93-1.06)	7.8x10⁻⁰¹	0.98 (0.96-1.04)	9.4x10⁻⁰¹	1.02 (0.99-1.06)	2.0x10⁻⁰¹	3.9x10⁻⁰¹	0.99 (0.95-1.03)
1q21.1	rs12405132	[3]	1	145644984	C/T	0.37	0.95 (0.90-1.01)	1.1x10⁻⁰¹	0.98 (0.95-1.02)	3.9x10⁻⁰¹	1.00 (0.96-1.03)	7.8x10⁻⁰¹	1.8x10⁻⁰¹	0.99 (0.96-1.03)
1q21.2	rs12048493	[3]	1	149927034	A/C	0.38	1.03 (0.96-1.11)	3.5x10⁻⁰¹	1.02 (0.98-1.07)	2.5x10⁻⁰¹	1.05 (1.02-1.09)	2.3x10⁻⁰³	1.3x10⁻⁰³	1.03 (1.00-1.07)
1q32.1	rs4951011	[4]	1	203766331	A/G	0.16	1.03 (0.96-1.11)	4.0x10⁻⁰¹	1.03 (0.98-1.09)	2.8x10⁻⁰¹	1.07 (1.02-1.11)	2.8x10⁻⁰³	1.9x10⁻⁰³	1.04 (0.99-1.09)
1q43	rs72755295	[3]	1	242034263	A/G	0.03	0.93 (0.70-1.23)	6.1x10⁻⁰¹	1.20 (1.08-1.33)	4.4x10⁻⁰⁴	1.09 (1.00-1.19)	5.6x10⁻⁰²	3.9x10⁻⁰⁴	1.13 (1.02-1.25)
2q14.1	rs4849887	[1]	2	121245122	C/T	0.10	0.98 (0.90-1.07)	6.7x10⁻⁰¹	0.90 (0.85-0.96)	2.2x10⁻⁰³	0.85 (0.81-0.90)	1.7x10⁻⁰⁸	4.1x10⁻⁰⁹	0.99 (0.93-1.05)
2q31.1	rs2016394	[1]	2	172972971	G/A	0.47	1.06 (1.00-1.11)	3.9x10⁻⁰²	1.00 (0.96-1.03)	8.2x10⁻⁰¹	1.00 (0.97-1.04)	9.8x10⁻⁰¹	4.5x10⁻⁰¹	1.03 (0.99-1.07)
2q31.1	rs1550623	[1]	2	174212894	A/G	0.15	0.99 (0.92-1.06)	7.6x10⁻⁰¹	0.95 (0.91-1.01)	7.8x10⁻⁰²	1.00 (0.95-1.04)	8.5x10⁻⁰¹	2.0x10⁻⁰¹	0.99 (0.94-1.04)
2q33.1	rs1830298	[5],[6]	2	202181247	T/C	0.28	1.09 (1.03-1.16)	3.3x10⁻⁰³	1.03 (0.99-1.07)	1.5x10⁻⁰¹	1.08 (1.04-1.12)	3.0x10⁻⁰⁵	7.4x10⁻⁰⁷	1.08 (1.04-1.13)
2q35	rs34005590	[7]	2	217963060	C/A	0.05	0.86 (0.72-1.02)	7.9x10⁻⁰²	0.93 (0.85-1.02)	1.3x10⁻⁰¹	0.98 (0.91-1.05)	5.4x10⁻⁰¹	5.5x10⁻⁰²	0.99 (0.91-1.08)
2q35	rs4442975	[8],[9]	2	217920769	G/T	0.50	0.96 (0.91-1.01)	8.9x10⁻⁰²	0.95 (0.92-0.99)	9.6x10⁻⁰³	0.94 (0.92-0.98)	4.9x10⁻⁰⁴	3.4x10⁻⁰⁶	0.99 (0.96-1.03)
2q35	rs16857609	[1]	2	218296508	C/T	0.26	1.07 (1.01-1.14)	2.6x10⁻⁰²	1.09 (1.04-1.13)	1.0x10⁻⁰⁴	1.07 (1.03-1.10)	5.2x10⁻⁰⁴	1.8x10⁻⁰⁸	1.04 (1.00-1.09)
3p26.1	rs6762644	[1]	3	4742276	A/G	0.38	0.97 (0.92-1.03)	3.0x10⁻⁰¹	1.02 (0.99-1.06)	2.8x10⁻⁰¹	1.04 (1.01-1.08)	1.2x10⁻⁰¹	5.3x10⁻⁰²	1.03 (0.99-1.07)
3p24.1	rs4973768	[10]	3	27416013	C/T	0.47	1.03 (0.98-1.08)	3.0x10⁻⁰¹	1.05 (1.01-1.09)	9.0x10⁻⁰³	1.04 (1.01-1.07)	1.4x10⁻⁰⁴	2.4x10⁻⁰⁴	1.01 (0.98-1.05)
3p.24.1	rs12493607	[1]	3	30682939	G/C	0.34	0.99 (0.93-1.04)	6.1x10⁻⁰¹	1.02 (0.98-1.06)	3.7x10⁻⁰¹	1.00 (0.96-1.03)	7.9x10⁻⁰¹	9.0x10⁻⁰¹	1.00 (0.96-1.04)
3p21.31	rs6796502	[3]	3	46866866	G/A	0.10	0.96 (0.87-1.05)	3.9x10⁻⁰¹	0.95 (0.89-1.01)	1.0x10⁻⁰¹	0.92 (0.87-0.97)	2.7x10⁻⁰³	6.5x10⁻⁰⁴	0.99 (0.94-1.05)
3p14.1	rs1053338	[11]	3	63967900	A/G	0.14	1.01 (0.93-1.09)	8.9x10⁻⁰¹	1.06 (1.00-1.12)	3.7x10⁻⁰²	1.03 (0.99-1.08)	1.8x10⁻⁰¹	2.5x10⁻⁰²	1.00 (0.95-1.05)
4q24	rs9790517	[1]	4	106084778	C/T	0.23	1.09 (1.02-1.16)	8.3x10⁻⁰³	1.03 (0.98-1.07)	2.8x10⁻⁰¹	0.98 (0.94-1.02)	2.3x10⁻⁰¹	3.5x10⁻⁰¹	1.01 (0.96-1.05)
4q34.1	rs6828523	[1]	4	175846426	C/A	0.12	0.94 (0.87-1.02)	1.6x10⁻⁰¹	1.02 (0.96-1.08)	4.8x10⁻⁰¹	1.00 (0.95-1.05)	9.3x10⁻⁰¹	9.3x10⁻⁰¹	1.04 (0.98-1.10)
5p15.33	rs3215401	[12]	5	1296255	A/AG	0.31	0.89 (0.81-0.98)	1.7x10⁻⁰²	0.89 (0.85-0.92)	8.4x10⁻⁰⁹	0.88 (0.85-0.91)	2.3x10⁻¹²	6.4x10⁻²¹	0.90 (0.87-0.94)
5p15.1	rs13162653	[3]	5	16187528	G/T	0.45	0.94 (0.89-1.00)	3.9x10⁻⁰²	0.96 (0.93-1.00)	6.8x10⁻⁰²	0.98 (0.95-1.01)	2.1x10⁻⁰¹	5.5x10⁻⁰³	0.99 (0.96-1.03)
5p13.3	rs2012709	[3]	5	32567732	C/T	0.48	1.00 (0.95-1.06)	9.2x10⁻⁰¹	1.03 (0.99-1.07)	9.8x10⁻⁰²	0.98 (0.95-1.01)	1.5x10⁻⁰¹	9.9x10⁻⁰¹	1.00 (0.96-1.03)
5p12	rs10941679	[13]	5	44706498	A/G	0.25	1.04 (0.98-1.11)	1.9x10⁻⁰¹	1.03 (0.99-1.08)	1.5x10⁻⁰¹	1.03 (1.00-1.07)	8.5x10⁻⁰²	9.4x10⁻⁰³	1.01 (0.96-1.05)
5q11.2	rs62355902	[14],[15]	5	56053723	A/T	0.16	1.06 (0.99-1.14)	1.0x10⁻⁰¹	1.10 (1.05-1.15)	2.3x10⁻⁰⁴	1.06 (1.02-1.11)	6.7x10⁻⁰³	2.1x10⁻⁰⁶	1.02 (0.97-1.07)
5q11.2	rs10472076	[1]	5	58184061	T/C	0.38	1.04 (0.99-1.10)	1.3x10⁻⁰¹	1.06 (1.02-1.10)	4.6x10⁻⁰³	1.03 (1.00-1.07)	4.0x10⁻⁰²	2.0x10⁻⁰⁴	1.02 (0.98-1.05)
5q11.2	rs1353747	[1]	5	58337481	T/G	0.09	0.97 (0.88-1.06)	4.8x10⁻⁰¹	0.92 (0.86-0.98)	8.4x10⁻⁰³	0.98 (0.92-1.03)	3.8x10⁻⁰¹	1.5x10⁻⁰²	0.97 (0.91-1.04)
5q14.2	rs7707921	[3]	5	81538046	A/T	0.25	0.97 (0.91-1.03)	3.3x10⁻⁰¹	0.97 (0.93-1.02)	2.0x10⁻⁰¹	0.97 (0.93-1.00)	7.6x10⁻⁰²	1.5x10⁻⁰²	1.02 (0.98-1.07)
5q14.3	rs10474352	[4]	5	90732225	C/T	0.16	0.96 (0.90-1.04)	3.4x10⁻⁰¹	1.00 (0.94-1.06)	9.8x10⁻⁰¹	0.98 (0.94-1.03)	4.1x10⁻⁰¹	3.1x10⁻⁰¹	0.99 (0.94-1.04)
5q33.3	rs1432679	[1]	5	158244083	T/C	0.43	1.05 (1.00-1.11)	6.3x10⁻⁰²	1.08 (1.04-1.13)	2.4x10⁻⁰⁵	1.08 (1.04-1.11)	4.0x10⁻⁰⁶	1.1x10⁻¹⁰	1.04 (1.01-1.08)
6p25.3	rs11242675	[1]	6	1318878	T/C	0.37	0.93 (0.88-0.98)	6.8x10⁻⁰³	0.96 (0.92-0.99)	2.2x10⁻⁰²	0.99 (0.96-1.02)	5.1x10⁻⁰¹	3.3x10⁻⁰³	0.96 (0.93-1.00)
6p24.3	rs9348512	[16]	6	10456706	C/A	0.33	1.02 (0.96-1.08)	5.3x10⁻⁰¹	0.99 (0.95-1.04)	6.7x10⁻⁰¹	1.01 (0.98-1.05)	5.1x10⁻⁰¹	6.5x10⁻⁰¹	1.01 (0.97-1.05)
6p23	rs204247	[1]	6	13722523	A/G	0.44	1.08 (1.03-1.14)	3.5x10⁻⁰³	1.01 (0.97-1.04)	7.4x10⁻⁰¹	1.00 (0.97-1.03)	9.9x10⁻⁰¹	1.6x10⁻⁰¹	1.01 (0.97-1.05)
6p22.1	rs9257408	[3].	6	28926220	G/C	0.41	1.07 (1.01-1.13)	2.0x10⁻⁰²	1.05 (1.01-1.09)	1.4x10⁻⁰²	1.03 (1.00-1.07)	5.9x10⁻⁰²	2.0x10⁻⁰⁴	1.03 (1.00-1.07)
6q14.1	rs17529111	[17]	6	82128386	T/C	0.22	1.12 (1.05-1.19)	5.9x10⁻⁰⁴	1.05 (1.00-1.09)	4.7x10⁻⁰²	1.06 (1.02-1.10)	1.5x10⁻⁰³	1.6x10⁻⁰⁶	1.01 (0.96-1.05)
6q25.1	rs9485372	[18]	6	149608874	G/A	0.19	1.02 (0.95-1.09)	5.9x10⁻⁰¹	0.95 (0.91-1.00)	6.4x10⁻⁰²	0.99 (0.95-1.03)	5.1x10⁻⁰¹	1.9x10⁻⁰¹	1.00 (0.95-1.04)
6q25	rs9397437	[19],[20]	6	151952332	G/A	0.07	1.35 (1.22-1.49)	7.4x10⁻⁰⁹	1.29 (1.20-1.38)	6.5x10⁻¹³	1.32 (1.25-1.40)	8.3x10⁻²²	2.8x10⁻⁴⁰	1.20 (1.12-1.28)
7q21.2	rs6964587	[11]	7	91630620	G/T	0.39	1.02 (0.96-1.07)	5.5x10⁻⁰¹	1.04 (1.00-1.08)	6.0x10⁻⁰²	1.02 (0.98-1.05)	3.5x10⁻⁰¹	4.5x10⁻⁰²	1.00 (0.97-1.04)
7q32.3	rs4593472	[3]	7	130667121	C/T	0.35	0.93 (0.87-0.98)	1.1x10⁻⁰²	0.99 (0.95-1.03)	6.8x10⁻⁰¹	0.97 (0.93-1.00)	5.3x10⁻⁰²	9.2x10⁻⁰³	0.98 (0.94-1.02)
7q34	rs11977670	[31]	7	139942304	G/A	0.43	1.03 (0.97-1.19)	3.4x10⁻⁰¹	0.98 (0.95-1.03)	5.9x10⁻⁰¹	1.02 (0.99-1.05)	5.5x10⁻⁰¹	2.1x10⁻⁰¹	1.06 (1.02-1.10)
7q35	rs720475	[1]	7	144074929	A/G	0.25	1.04 (0.97-1.11)	2.8x10⁻⁰¹	0.99 (0.95-1.03)	6.9x10⁻⁰¹	1.00 (0.96-1.03)	8.0x10⁻⁰¹	9.8x10⁻⁰¹	0.98 (0.94-1.02)
8p12	rs9693444	[1]	8	29509616	C/A	0.32	1.02 (0.96-1.08)	5.4x10⁻⁰¹	1.09 (1.04-1.13)	4.7x10⁻⁰⁵	1.02 (0.98-1.05)	2.9x10⁻⁰¹	6.4x10⁻⁰⁴	1.00 (0.96-1.04)
8p11.23	rs13365225	[3]	8	36858483	A/G	0.18	0.89 (0.83-0.96)	1.7x10⁻⁰³	0.93 (0.88-0.98)	3.5x10⁻⁰³	0.90 (0.86-0.94)	1.1x10⁻⁰⁶	1.4x10⁻¹⁰	0.95 (0.91-1.00)
8q21.11	rs6472903	[1]	8	76230301	T/G	0.17	0.98 (0.91-1.05)	5.8x10⁻⁰¹	0.94 (0.89-0.99)	1.3x10⁻⁰²	0.96 (0.92-1.00)	8.2x10⁻⁰²	3.7x10⁻⁰³	0.99 (0.95-1.04)
8q21.11	rs2943559	[1]	8	76417937	A/G	0.08	1.17 (1.06-1.29)	2.9x10⁻⁰³	1.07 (1.00-1.15)	5.5x10⁻⁰²	1.10 (1.04-1.16)	1.2x10⁻⁰³	3.1x10⁻⁰⁶	1.07 (1.00-1.14)
8q23.3	rs13267382	[3]	8	117209548	G/A	0.36	1.05 (1.00-1.12)	7.3x10⁻⁰²	1.06 (1.02-1.10)	4.8x10⁻⁰³	1.02 (0.98-1.05)	3.0x10⁻⁰¹	1.8x10⁻⁰²	0.97 (0.94-1.01)
8q24.21	rs13281615	[14]	8	128355618	A/G	0.41	1.07 (1.01-1.13)	1.9x10⁻⁰²	1.03 (0.99-1.07)	2.0x10⁻⁰¹	1.07 (1.03-1.10)	9.5x10⁻⁰⁵	8.8x10⁻⁰⁶	1.03 (0.99-1.07)
8q24.21	rs11780156	[1]	8	129194641	C/T	0.17	1.04 (0.97-1.11)	2.9x10⁻⁰¹	1.06 (1.00-1.11)	3.2x10⁻⁰²	1.05 (1.01-1.09)	1.8x10⁻⁰²	8.5x10⁻⁰⁴	0.95 (0.91-0.99)
9p21.3	rs1011970	[21]	9	22062134	G/T	0.16	1.09 (1.02-1.17)	1.5x10⁻⁰²	1.11 (1.06-1.17)	1.4x10⁻⁰⁵	1.05 (1.00-1.09)	3.7x10⁻⁰²	4.7x10⁻⁰⁷	1.05 (1.00-1.10)
9q31.2	rs10759243	[1]	9	110306115	C/A	0.29	1.09 (1.02-1.16)	9.0x10⁻⁰³	1.01 (0.97-1.05)	6.1x10⁻⁰¹	1.02 (0.99-1.06)	2.0x10⁻⁰¹	2.6x10⁻⁰²	1.00 (0.96-1.04)
9q31.2	rs676256	[22],[23]	9	110895353	T/C	0.38	0.98 (0.93-1.04)	5.1x10⁻⁰¹	0.98 (0.94-1.01)	2.3x10⁻⁰¹	0.98 (0.94-1.01)	1.5x10⁻⁰¹	4.6x10⁻⁰²	0.99 (0.95-1.02)
9q31.2	rs10816625	[23]	9	110837073	A/G	0.06	1.13 (0.99-1.29)	6.7x10⁻⁰²	1.05 (0.97-1.13)	2.3x10⁻⁰¹	1.07 (1.01-1.14)	2.8x10⁻⁰²	3.2x10⁻⁰³	0.99 (0.92-1.07)
9q31.2	rs13294895	[23]	9	110837176	C/T	0.18	1.00 (0.93-1.08)	9.9x10⁻⁰¹	1.04 (0.99-1.09)	1.3x10⁻⁰¹	0.99 (0.95-1.04)	7.5x10⁻⁰¹	4.9x10⁻⁰¹	1.03 (0.98-1.08)
10p15.1	rs2380205	[21]	10	5886734	C/T	0.44	0.98 (0.93-1.04)	5.6x10⁻⁰¹	1.01 (0.97-1.05)	7.2x10⁻⁰¹	0.97 (0.94-1.00)	8.6x10⁻⁰²	2.2x10⁻⁰¹	1.02 (0.99-1.06)
10p12.31	rs7072776	[1]	10	22032942	G/A	0.29	1.06 (1.00-1.14)	7.5x10⁻⁰²	0.94 (0.91-0.98)	7.1x10⁻⁰³	0.99 (0.95-1.02)	4.0x10⁻⁰¹	1.3x10⁻⁰¹	0.99 (0.95-1.03)
10p12.31	rs11814448	[1]	10	22315843	A/C	0.02	1.29 (1.02-1.63)	3.4x10⁻⁰²	1.20 (1.06-1.37)	4.0x10⁻⁰³	1.04 (0.94-1.16)	4.5x10⁻⁰¹	2.7x10⁻⁰³	1.13 (1.00-1.28)
10q21.2	rs10995201	[21],[24]	10	64299890	A/G	0.16	0.92 (0.85-1.00)	4.2x10⁻⁰²	0.87 (0.82-0.91)	1.0x10⁻⁰⁷	0.93 (0.89-0.98)	3.0x10⁻⁰³	1.6x10⁻⁰⁹	0.98 (0.94-1.03)
10q22.3	rs704010	[21]	10	80841148	C/T	0.38	1.07 (1.01-1.13)	1.6x10⁻⁰²	1.03 (0.99-1.07)	9.7x10⁻⁰²	1.06 (1.03-1.09)	5.8x10⁻⁰⁴	1.3x10⁻⁰⁵	1.01 (0.97-1.05)
10q25.2	rs7904519	[1]	10	114773927	A/G	0.46	1.12 (1.06-1.18)	5.3x10⁻⁰⁵	1.04 (1.01-1.08)	2.1x10⁻⁰²	1.08 (1.04-1.11)	7.4x10⁻⁰⁶	8.2x10⁻¹⁰	1.08 (1.04-1.12)
10q26.12	rs11199914	[1]	10	123093901	C/T	0.32	0.99 (0.93-1.04)	6.2x10⁻⁰¹	1.02 (0.98-1.06)	4.0x10⁻⁰¹	0.98 (0.95-1.02)	3.3x10⁻⁰¹	7.1x10⁻⁰¹	1.01 (0.97-1.05)
10q26.13	rs35054928	[14],[25]	10	123340431	G/GC	0.40	1.05 (0.98-1.12)	1.9x10⁻⁰¹	1.02 (0.98-1.06)	2.8x10⁻⁰¹	1.06 (1.03-1.10)	1.5x10⁻⁰⁴	1.4x10⁻⁰⁴	1.00 (0.96-1.04)
10q26.13	rs45631563	[25]	10	123349324	A/T	0.05	1.02 (0.89-1.17)	7.6x10⁻⁰¹	1.06 (0.97-1.15)	2.2x10⁻⁰¹	0.93 (0.86-1.00)	5.2x10⁻⁰²	6.2x10⁻⁰¹	1.04 (0.95-1.13)
10q26.13	rs2981578	[25]	10	123340311	T/C	0.47	1.04 (0.99-1.10)	1.1x10⁻⁰¹	1.04 (1.00-1.08)	4.7x10⁻⁰²	1.04 (1.00-1.07)	2.5x10⁻⁰²	7.1x10⁻⁰³	1.00 (0.97-1.04)
11p15.5	rs3817198	[14]	11	1909006	T/C	0.32	1.07 (1.01-1.13)	2.5x10⁻⁰²	1.06 (1.02-1.11)	2.8x10⁻⁰³	1.02 (0.99-1.06)	2.0x10⁻⁰¹	3.4x10⁻⁰⁴	1.06 (1.02-1.10)
11q13.1	rs3903072	[1]	11	65583066	G/T	0.47	0.93 (0.89-0.99)	1.2x10⁻⁰²	0.97 (0.94-1.01)	1.7x10⁻⁰¹	0.99 (0.96-1.02)	5.6x10⁻⁰¹	2.5x10⁻⁰²	0.99 (0.95-1.02)
11q13.3	rs554219	[21],[26]	11	69331642	C/G	0.13	-	-	-	-	0.98 (0.94-1.03)	4.8x10⁻⁰¹	4.8x10⁻⁰¹	1.02 (0.96-1.07)
11q13.3	rs75915166	[26]	11	69379161	C/A	0.06	1.04 (0.93-1.18)	4.8x10⁻⁰¹	1.06 (0.98-1.14)	1.6x10⁻⁰¹	0.99 (0.92-1.06)	7.6x10⁻⁰¹	3.6x10⁻⁰¹	1.02 (0.94-1.10)
11q24.3	rs11820646	[1]	11	129461171	C/T	0.40	0.92 (0.87-0.97)	1.6x10⁻⁰³	0.96 (0.92-1.00)	3.0x10⁻⁰²	0.94 (0.91-0.97)	2.0x10⁻⁰⁴	2.4x10⁻⁰⁷	0.94 (0.90-0.97)
12p13.1	rs12422552	[1]	12	14413931	G/C	0.26	1.12 (1.05-1.19)	3.4x10⁻⁰⁴	1.05 (1.00-1.09)	3.4x10⁻⁰²	1.04 (1.01-1.08)	1.8x10⁻⁰²	1.3x10⁻⁰⁵	1.00 (0.96-1.04)
12p11.22	rs7297051	[27],[28]	12	28174817	C/T	0.24	0.86 (0.81-0.92)	8.4x10⁻⁰⁶	0.87 (0.83-0.91)	1.3x10⁻⁰⁹	0.87 (0.84-0.91)	2.4x10⁻¹²	8.5x10⁻²⁵	0.88 (0.85-0.92)
12q22	rs17356907	[1]	12	96027759	A/G	0.30	0.88 (0.83-0.93)	2.4x10⁻⁰⁵	0.95 (0.91-0.99)	1.0x10⁻⁰²	0.94 (0.91-0.97)	7.5x10⁻⁰⁴	2.3x10⁻⁰⁸	0.97 (0.93-1.00)
12q24.21	rs1292011	[27]	12	115836522	A/G	0.42	0.98 (0.93-1.03)	4.1x10⁻⁰¹	0.98 (0.95-1.02)	4.2x10⁻⁰¹	0.98 (0.95-1.01)	1.5x10⁻⁰¹	6.8x10⁻⁰²	1.02 (0.99-1.06)
13q13.1	rs11571833	[1]	13	32972626	A/T	0.01	2.50 (0.92-6.79)	7.3x10⁻⁰²	1.48 (1.24-1.77)	1.6x10⁻⁰⁵	1.58 (1.35-1.84)	5.8x10⁻⁰⁹	1.5x10⁻¹³	1.07 (0.88-1.30)
14q13.3	rs2236007	[1]	14	37132769	G/A	0.21	1.01 (0.94-1.08)	8.1x10⁻⁰¹	0.96 (0.92-1.00)	7.8x10⁻⁰²	0.95 (0.91-0.99)	1.4x10⁻⁰²	8.0x10⁻⁰³	0.97 (0.93-1.01)
14q24.1	rs2588809	[1]	14	68660428	C/T	0.17	0.96 (0.89-1.05)	3.9x10⁻⁰¹	1.01 (0.96-1.07)	6.1x10⁻⁰¹	0.99 (0.95-1.03)	6.8x10⁻⁰¹	7.6x10⁻⁰¹	0.96 (0.92-1.01)
14q24.1	rs999737	[2]	14	69034682	C/T	0.23	0.91 (0.85-0.97)	3.4x10⁻⁰²	0.94 (0.90-0.98)	7.3x10⁻⁰³	0.92 (0.89-0.96)	7.2x10⁻⁰⁵	2.9x10⁻⁰⁸	0.96 (0.92-1.00)
14q32.11	rs941764	[1]	14	91841069	A/G	0.35	1.00 (0.95-1.06)	9.8x10⁻⁰¹	1.00 (1.00-1.08)	4.5x10⁻⁰²	1.01 (0.98-1.04)	5.9x10⁻⁰¹	1.2x10⁻⁰¹	1.02 (0.98-1.06)
14q32.12	rs11627032	[3]	14	93104072	T/C	0.25	0.92 (0.87-0.98)	1.1x10⁻⁰²	0.93 (0.89-0.97)	1.6x10⁻⁰³	0.95 (0.92-0.99)	8.5x10⁻⁰³	2.4x10⁻⁰⁶	0.96 (0.92-1.00)
15q26.1	rs2290203	[4]	15	91512067	G/A	0.21	0.94 (0.88-1.01)	9.5x10⁻⁰²	0.94 (0.90-0.99)	1.2x10⁻⁰²	0.96 (0.92-1.00)	5.5x10⁻⁰²	4.7x10⁻⁰⁴	0.98 (0.93-1.02)
16q12.1	rs4784227	[14],[29]	16	52599188	C/T	0.24	1.12 (1.06-1.19)	2.3x10⁻⁰⁴	1.16 (1.11-1.21)	6.3x10⁻¹²	1.14 (1.10-1.19)	2.8x10⁻¹³	1.7x10⁻²⁶	1.05 (1.00-1.09)
16q12.2	rs17817449	[1]	16	53813367	T/G	0.41	0.97 (0.92-1.02)	2.5x10⁻⁰¹	0.91 (0.87-0.94)	3.4x10⁻⁰⁷	0.93 (0.90-0.96)	3.0x10⁻⁰⁵	1.8x10⁻¹⁰	0.94 (0.91-0.98)
16q23.2	rs13329835	[1]	16	80650805	A/G	0.23	1.06 (0.99-1.13)	9.1x10⁻⁰²	1.02 (0.98-1.07)	4.0x10⁻⁰¹	1.06 (1.02-1.10)	3.7x10⁻⁰³	1.4x10⁻⁰³	1.06 (1.01-1.10)
17q11.2	chr17:29230520	[3]	17	29230520	GGT/G	0.27	0.99 (0.92-1.07)	8.5x10⁻⁰¹	0.95 (0.91-0.99)	1.3x10⁻⁰²	0.95 (0.92-0.99)	7.9x10⁻⁰³	4.9x10⁻⁰⁴	1.03 (0.99-1.07)
17q22	rs2787486	[10],[28]	17	53209774	A/C	0.30	0.96 (0.90-1.02)	1.8x10⁻⁰¹	0.96 (0.92-1.00)	6.6x10⁻⁰²	0.96 (0.93-1.00)	3.9x10⁻⁰²	2.2x10⁻⁰³	1.01 (0.97-1.05)
17q25.3	rs745570	[3]	17	77781725	G/A	0.50	1.08 (1.03-1.14)	4.0x10⁻⁰³	1.05 (1.01-1.09)	8.4x10⁻⁰³	1.04 (1.01-1.07)	1.6x10⁻⁰²	1.0x10⁻⁰⁵	1.03 (1.00-1.07)
18q11.2	rs527616	[1]	18	24337424	C/T	0.38	0.93 (0.88-0.99)	1.8x10⁻⁰²	0.98 (0.94-1.02)	3.3x10⁻⁰¹	1.00 (0.97-1.04)	9.7x10⁻⁰¹	1.3x10⁻⁰¹	0.99 (0.96-1.03)
18q11.2	rs1436904	[1]	18	24570667	T/G	0.40	0.96 (0.92-1.01)	3.7x10⁻⁰¹	1.00 (0.97-1.04)	8.2x10⁻⁰¹	0.99 (0.96-1.03)	7.1x10⁻⁰¹	6.2x10⁻⁰¹	0.99 (0.95-1.02)
18q12.3	rs6507583	[3]	18	42399590	A/G	0.07	0.96 (0.86-1.07)	4.5x10⁻⁰¹	0.97 (0.90-1.04)	3.9x10⁻⁰¹	0.97 (0.91-1.03)	3.2x10⁻⁰¹	1.3x10⁻⁰¹	0.99 (0.92-1.06)
19p13.11	rs4808801	[1]	19	18571141	A/G	0.34	0.97 (0.92-1.03)	3.0x10⁻⁰¹	0.92 (0.88-0.96)	2.8x10⁻⁰⁵	0.96 (0.93-0.99)	1.9x10⁻⁰²	5.7x10⁻⁰⁶	0.98 (0.94-1.02)
19q13.31	rs3760982	[1]	19	44286513	G/A	0.46	1.05 (1.00-1.11)	5.4x10⁻⁰²	1.04 (1.00-1.08)	4.9x10⁻⁰²	1.08 (1.05-1.12)	8.7x10⁻⁰⁷	5.3x10⁻⁰⁸	0.99 (0.96-1.03)
21q21.1	rs2823093	[27]	21	16520832	G/A	0.27	1.03 (0.97-1.09)	4.1x10⁻⁰¹	0.97 (0.93-1.02)	1.3x10⁻⁰¹	1.00 (0.96-1.04)	9.9x10⁻⁰¹	5.9x10⁻⁰¹	0.97 (0.93-1.01)
22q12.1	rs17879961	[1]	22	29121087	A/G	0.005	1.10 (0.73-1.66)	6.4x10⁻⁰¹	1.01 (0.78-1.31)	9.3x10⁻⁰¹	0.86 (0.68-1.09)	2.2x10⁻⁰¹	5.5x10⁻⁰¹	0.78 (0.59-1.05)
22q12.2	rs132390	[1]	22	29621477	T/C	0.10	1.12 (0.91-1.39)	2.8x10⁻⁰¹	1.10 (1.00-1.21)	5.1x10⁻⁰²	1.01 (0.92-1.09)	8.9x10⁻⁰¹	1.0x10⁻⁰¹	0.95 (0.86-1.05)

| 22q13.1 | chr22:39359355 | [30] | 22 | 39359355 | I/D§ | 0.04 | 1.01 (0.90-1.13) | 9.2x10⁻⁰¹ | 1.12 (1.05-1.21) | 1.3x10⁻⁰³ | 1.09 (1.04-1.14) | 8.3x10⁻⁰⁴ | 1.5x10⁻⁰⁵ | 1.01 (0.94-1.08) |
| 22q13.1 | rs6001930 | [1] | 22 | 40876234 | T/C | 0.10 | 1.15 (1.06-1.25) | 1.3x10⁻⁰³ | 1.10 (1.04-1.17) | 8.7x10⁻⁰⁴ | 1.14 (1.08-1.19) | 6.8x10⁻⁰⁷ | 1.6x10⁻¹¹ | 1.06 (1.00-1.13) |

*results for ER-negative disease also reported in Michailidou, K. et al. Identification of more than 70 new breast cancer susceptibility loci for breast cancer and definition of risk-associated genomic features, Reference 1 in the main text
Chr, chromosome; MAF, minor allele frequency; BCAC, Breast Cancer Association Consortium; CIMBA, Consortium of Investigators of Modifiers of BRCA1/2; †More common allele listed first, minor allele second; §31kb deletion
BCAC results were based on GWAS data for 4,480 cases and 12,632 controls, iCOGS data for 7,333 cases and 42,468 controls and OncoArray data 9,655 cases and 45,494 controls
CIMBA results were based on data for 18,908 BRCA1 mutation carriers (9,414 with breast cancer)

REFERENCES:
1. Michailidou, K. et al. Large-scale genotyping identifies 41 new loci associated with breast cancer risk. Nat Genet 45, 353-61 (2013).
2. Thomas, G. et al. A multistage genome-wide association study in breast cancer identifies two new risk alleles at 1p11.2 and 14q24.1 (RAD51L1). Nat Genet 41, 579-84 (2009).
3. Michailidou, K. et al. Genome-wide association analysis of more than 120,000 individuals identifies 15 new susceptibility loci for breast cancer. Nat Genet 47, 373-80 (2015).
4. Cai, Q. et al. Genome-wide association analysis in East Asians identifies breast cancer susceptibility loci at 1q32.1, 5q14.3 and 15q26.1. Nat Genet 46, 886-90 (2014).
5. Cox, A. et al. A common coding variant in CASP8 is associated with breast cancer risk. Nat Genet 39, 352-8 (2007).
6. Lin, W.Y. et al. Identification and characterization of novel associations in the CASP8/ALS2CR12 region on chromosome 2 with breast cancer risk. Hum Mol Genet 24, 285-98 (2015).
7. Wyszynski, A. et al. An intergenic enhancer deletion in 2q35 modulates breast cancer risk by deregulating IGFBP5 expression. Hum Mol Genet (in press).
8. Stacey, S.N. et al. Common variants on chromosomes 2q35 and 16q12 confer susceptibility to estrogen receptor-positive breast cancer. Nat Genet 39, 865-9 (2007).
9. Ghoussaini, M. et al. Evidence that breast cancer risk at the 2q35 locus is mediated through IGFBP5 regulation. Nat Commun 4, 4999 (2014).
10. Ahmed, S. et al. Newly discovered breast cancer susceptibility loci on 3p24 and 17q23.2. Nat Genet 41, 585-90 (2009).
11. Milne, R.L. et al. Common non-synonymous SNPs associated with breast cancer susceptibility: findings from the Breast Cancer Association Consortium. Hum Mol Genet 23, 6096-111 (2014).
12. Bojesen, S.E. et al. Multiple independent variants at the TERT locus are associated with telomere length and risks of breast and ovarian cancer. Nat Genet 45, 371-84 (2013).
13. Stacey, S.N. et al. Common variants on chromosome 5p12 confer susceptibility to estrogen receptor-positive breast cancer. Nat Genet 40, 703-6 (2008).
14. Easton, D.F. et al. Genome-wide association study identifies novel breast cancer susceptibility loci. Nature 447, 1087-93 (2007).
15. Glubb, D.M. et al. Fine-scale mapping of the 5q11.2 breast cancer locus reveals at least three independent risk variants regulating MAP3K1. Am J Hum Genet 96, 5-20 (2015).
16. Gaudet, M.M. et al. Identification of a BRCA2-specific modifier locus at 6p24 related to breast cancer risk. PLoS Genet 9, e1003173 (2013).
17. Siddiq, A. et al. A meta-analysis of genome-wide association studies of breast cancer identifies two novel susceptibility loci at 6q14 and 20q11. Hum Mol Genet 21, 5373-84 (2012).
18. Long, J. et al. Genome-wide association study in east Asians identifies novel susceptibility loci for breast cancer. PLoS Genet 8, e1002532 (2012).
19. Zheng, W. et al. Genome-wide association study identifies a new breast cancer susceptibility locus at 6q25.1. Nat Genet 41, 324-8 (2009).
20. Dunning, A.M. et al. Breast cancer risk variants at 6q25 display different phenotype associations and regulate ESR1, RMND1 and CCDC170. Nat Genet (in press).
21. Turnbull, C. et al. Genome-wide association study identifies five new breast cancer susceptibility loci. Nat Genet 42, 504-7 (2010).
22. Fletcher, O. et al. Novel breast cancer susceptibility locus at 9q31.2: results of a genome-wide association study. J Natl Cancer Inst 103, 425-35 (2011).
23. Orr, N. et al. Fine-mapping identifies two additional breast cancer susceptibility loci at 9q31.2. Hum Mol Genet 24, 2966-84 (2015).
24. Darabi, H. et al. Polymorphisms in a Putative Enhancer at the 10q21.2 Breast Cancer Risk Locus Regulate NRBF2 Expression. Am J Hum Genet 97, 22-34 (2015).
25. Meyer, K.B. et al. Fine-scale mapping of the FGFR2 breast cancer risk locus: putative functional variants differentially bind FOXA1 and E2F1. Am J Hum Genet 93, 1046-60 (2013).
26. French, J.D. et al. Functional variants at the 11q13 risk locus for breast cancer regulate cyclin D1 expression through long-range enhancers. Am J Hum Genet 92, 489-503 (2013).
27. Ghoussaini, M. et al. Genome-wide association analysis identifies three new breast cancer susceptibility loci. Nat Genet 44, 312-8 (2012).
28. Zheng, W. (unpublished data).
29. Udler, M.S. et al. Fine scale mapping of the breast cancer 16q12 locus. Hum Mol Genet 19, 2507-15 (2010).
30. Long, J. et al. A common deletion in the APOBEC3 genes and breast cancer risk. J Natl Cancer Inst 105, 573-9 (2013).
31. Sawyer, E. et al. Genetic predisposition to in situ and invasive lobular carcinoma of the breast. PLoS Genet 10, e1004285 (2014).

Associations observed with ER-negative breast cancer based on P<0.05 in meta-analysis of all BCAC data
Associations observed with breast cancer for *BRCA1* mutation carriers based on P<0.05 in meta-analysis of all CIMBA data

Supplementary Table 11: Associations of 179 breast cancer susceptibility loci with risk for *BRCA2* mutation carriers

How identified	Location	SNP	Alleles[†]	MAF	HR (95%CI)	P-value
Other previous hit for breast cancer	1p36.22	rs616488	A/G	0.32	0.95 (0.91-1.00)	6.3×10^{-2}
New hit for overall breast cancer	1p36.13	rs2992756	C/T	0.50	1.00 (0.96-1.05)	9.2×10^{-1}
New hit for overall breast cancer	1p34.2	rs4233486	T/C	0.36	0.95 (0.90-1.00)	3.6×10^{-2}
New hit for overall breast cancer	1p34.2	rs79724016	T/G	0.04	0.93 (0.82-1.06)	3.0×10^{-1}
New hit for overall breast cancer	1p34.1	rs1707302	G/A	0.32	1.03 (0.98-1.09)	1.9×10^{-1}
New hit for overall breast cancer	1p32.3	rs140850326	I/D[†]	0.46	0.99 (0.94-1.03)	5.5×10^{-1}
New hit for overall breast cancer	1p22.3	rs17426269	G/A	0.16	1.01 (0.94-1.07)	8.2×10^{-1}
Other previous hit for breast cancer	1p13.2	rs11552449	C/T	0.17	1.04 (0.98-1.11)	2.1×10^{-1}
New hit for overall breast cancer	1p12	rs7529522	T/C	0.24	1.01 (0.96-1.07)	6.0×10^{-1}
Other previous hit for breast cancer	1p11.2	rs11249433	A/G	0.41	1.04 (0.99-1.09)	9.6×10^{-2}
Other previous hit for breast cancer	1q21.1	rs12405132	C/T	0.35	1.02 (0.97-1.07)	4.9×10^{-1}
Other previous hit for breast cancer	1q21.2	rs12048493	A/C	0.38	1.00 (0.95-1.05)	8.6×10^{-1}
New hit for overall breast cancer	1q22	rs4971059	G/A	0.34	1.01 (0.96-1.06)	7.5×10^{-1}
New hit for overall breast cancer	1q32.1	rs35383942	C/T	0.06	1.13 (1.02-1.25)	1.7×10^{-2}
Previous hit for ER-negative disease	1q32.1	rs6678914	G/A	0.41	0.99 (0.94-1.04)	5.8×10^{-1}
Other previous hit for breast cancer	1q32.1	rs4951011	A/G	0.16	1.02 (0.95-1.08)	6.5×10^{-1}
Previous hit for ER-negative disease	1q32.1	rs4245739	A/C	0.28	0.96 (0.91-1.01)	1.2×10^{-1}
New hit for overall breast cancer	1q41	rs11117758	G/A	0.22	0.94 (0.89-1.00)	3.7×10^{-2}
Other previous hit for breast cancer	1q43	rs72755295	A/G	0.03	1.17 (1.02-1.34)	2.5×10^{-2}
New hit for overall breast cancer	2p25.1	rs113577745	C/G	0.10	1.01 (0.93-1.09)	8.7×10^{-1}
Previous hit for ER-negative disease	2p24.1	rs12710696	C/T	0.38	1.00 (0.95-1.05)	9.3×10^{-1}
New hit for ER-negative breast cancer	2p23.3	rs200648189	CT/C	0.19	1.00 (0.94-1.07)	9.2×10^{-1}
Previous hit for ER-negative disease	2p23.2	rs4577244‡	C/T	0.22	0.99 (0.93-1.04)	6.2×10^{-1}
New hit for overall breast cancer	2q13	rs71801447	CTTATGTT/C	0.07	1.09 (0.99-1.20)	6.8×10^{-2}
Other previous hit for breast cancer	2q14.1	rs4849887	C/T	0.11	1.00 (0.93-1.08)	9.9×10^{-1}
Other previous hit for breast cancer	2q31.1	rs2016394	G/A	0.46	0.99 (0.94-1.04)	6.0×10^{-1}
Other previous hit for breast cancer	2q31.1	rs1550623	A/G	0.15	1.00 (0.94-1.07)	9.7×10^{-1}
Other previous hit for breast cancer	2q33.1	rs1830298	T/C	0.30	1.02 (0.97-1.07)	4.9×10^{-1}
Other previous hit for breast cancer	2q35	rs4442975	G/T	0.49	0.98 (0.94-1.03)	4.7×10^{-1}
Other previous hit for breast cancer	2q35	rs34005590	C/A	0.04	0.98 (0.88-1.11)	7.9×10^{-1}
Other previous hit for breast cancer	2q35	rs16857609	C/T	0.27	0.97 (0.92-1.02)	1.9×10^{-1}
New hit for overall breast cancer	2q36.3	rs12479355	A/G	0.21	0.94 (0.89-1.00)	5.0×10^{-2}
Other previous hit for breast cancer	3p26.1	rs6762644	A/G	0.37	0.99 (0.94-1.04)	5.9×10^{-1}
Other previous hit for breast cancer	3p24.1	rs4973768	C/T	0.50	1.07 (1.02-1.12)	4.1×10^{-3}
Other previous hit for breast cancer	3p.24.1	rs12493607	G/C	0.33	1.01 (0.96-1.06)	7.5×10^{-1}
Other previous hit for breast cancer	3p21.31	rs6796502	G/A	0.10	1.03 (0.95-1.11)	4.8×10^{-1}
Other previous hit for breast cancer	3p14.1	rs1053338	A/G	0.14	1.02 (0.96-1.09)	4.9×10^{-1}
New hit for overall breast cancer	3p13	rs6805189	T/C	0.47	1.03 (0.98-1.08)	2.1×10^{-1}
New hit for overall breast cancer	3p12.1	rs13066793	A/G	0.09	0.91 (0.84-0.99)	3.6×10^{-2}
New hit for overall breast cancer	3p12.1	rs9833888	G/T	0.22	1.04 (0.98-1.10)	2.2×10^{-1}
New hit for overall breast cancer	3q23	rs34207738	CTT/C	0.40	0.98 (0.94-1.03)	4.4×10^{-1}
New hit for overall breast cancer	3q26.31	rs58058861	G/A	0.21	1.03 (0.97-1.09)	3.5×10^{-1}
New hit for overall breast cancer	4p14	rs6815814	A/C	0.28	0.96 (0.91-1.01)	1.3×10^{-1}
New hit for overall breast cancer	4q21.23	4:84370124	TA/TAA	0.49	0.98 (0.94-1.03)	4.8×10^{-1}
New hit for overall breast cancer	4q22.1	rs10022462	C/T	0.45	0.99 (0.94-1.04)	6.3×10^{-1}
Other previous hit for breast cancer	4q24	rs9790517	C/T	0.22	0.98 (0.93-1.04)	5.4×10^{-1}
New hit for overall breast cancer	4q28.1	rs77528541	G/T	0.12	0.94 (0.87-1.02)	1.3×10^{-1}
Other previous hit for breast cancer	4q34.1	rs6828523	C/A	0.11	0.97 (0.90-1.04)	4.0×10^{-1}
New hit for overall breast cancer	5p15.33	rs116095464	T/C	0.06	1.04 (0.93-1.15)	5.0×10^{-1}
Previous hit for ER-negative disease	5p15.33	rs10069690	C/T	0.27	1.06 (1.01-1.12)	2.7×10^{-2}
Other previous hit for breast cancer	5p15.33	rs3215401	A/AG	0.31	0.94 (0.89-0.98)	1.0×10^{-2}
Other previous hit for breast cancer	5p15.1	rs13162653	G/T	0.44	1.05 (1.00-1.10)	6.4×10^{-2}
Other previous hit for breast cancer	5p13.3	rs2012709	C/T	0.49	1.01 (0.96-1.05)	8.0×10^{-1}
Other previous hit for breast cancer	5p12	rs10941679	A/G	0.24	1.09 (1.03-1.15)	1.9×10^{-3}
New hit for overall breast cancer	5q11.1	rs72749841	T/C	0.16	0.98 (0.91-1.06)	6.5×10^{-1}
New hit for overall breast cancer	5q11.1	rs35951924	A/AT	0.32	0.96 (0.91-1.02)	1.9×10^{-1}
Other previous hit for breast cancer	5q11.2	rs62355902	A/T	0.16	1.10 (1.03-1.17)	4.0×10^{-3}
Other previous hit for breast cancer	5q11.2	rs10472076	T/C	0.38	1.02 (0.97-1.07)	4.9×10^{-1}
Other previous hit for breast cancer	5q11.2	rs1353747	T/G	0.09	0.94 (0.86-1.01)	1.0×10^{-1}
Other previous hit for breast cancer	5q14.2	rs7707921	A/T	0.25	1.00 (0.95-1.05)	9.4×10^{-1}
Other previous hit for breast cancer	5q14.3	rs10474352	C/T	0.15	0.98 (0.91-1.04)	4.6×10^{-1}

New hit for overall breast cancer	5q22.1	rs6882649	T/G	0.32	0.97 (0.92-1.02)	2.5×10^{-1}
New hit for overall breast cancer	5q31.1	rs6596100	C/T	0.23	0.97 (0.91-1.02)	2.4×10^{-1}
Other previous hit for breast cancer	5q33.3	rs1432679	T/C	0.45	1.03 (0.98-1.08)	2.0×10^{-1}
New hit for overall breast cancer	5q35.1	rs4562056	G/T	0.36	1.01 (0.96-1.06)	7.4×10^{-1}
Other previous hit for breast cancer	6p25.3	rs11242675	T/C	0.35	1.01 (0.96-1.06)	7.4×10^{-1}
Other previous hit for breast cancer	6p24.3	rs9348512	C/A	0.34	0.87 (0.83-0.91)	1.9×10^{-8}
Other previous hit for breast cancer	6p23	rs204247	A/G	0.45	1.08 (1.03-1.13)	1.1×10^{-3}
New hit for overall breast cancer	6p22.3	rs3819405	C/T	0.34	0.97 (0.92-1.02)	2.0×10^{-1}
New hit for overall breast cancer	6p22.3	rs2223621	C/T	0.37	1.03 (0.98-1.08)	2.8×10^{-1}
New hit for overall breast cancer	6p22.2	rs71557345	G/A	0.07	1.02 (0.93-1.13)	6.5×10^{-1}
Other previous hit for breast cancer	6p22.1	rs9257408	G/C	0.43	1.00 (0.95-1.05)	9.9×10^{-1}
New hit for overall breast cancer	6q14.1	rs12207986	A/G	0.46	0.97 (0.93-1.02)	2.3×10^{-1}
Other previous hit for breast cancer	6q14.1	rs17529111	T/C	0.22	1.06 (1.00-1.12)	3.9×10^{-2}
New hit for ER-negative breast cancer	6q23.1	rs6569648	T/C	0.23	0.97 (0.92-1.02)	2.6×10^{-1}
Other previous hit for breast cancer	6q25.1	rs9485372	G/A	0.19	0.92 (0.87-0.98)	8.0×10^{-3}
Previous hit for ER-negative disease	6q25.1	rs3757322‡	T/G	0.35	1.07 (1.02-1.12)	5.9×10^{-3}
Other previous hit for breast cancer	6q25	rs9397437	G/A	0.08	1.12 (1.03-1.22)	8.6×10^{-3}
Previous hit for ER-negative disease	6q25.2	rs2747652‡	C/T	0.48	0.98 (0.93-1.02)	3.3×10^{-1}
New hit for overall breast cancer	7p15.3	rs7971	A/G	0.35	0.96 (0.91-1.01)	9.4×10^{-2}
New hit for overall breast cancer	7p15.1	rs17156577	T/C	0.12	1.03 (0.95-1.10)	4.9×10^{-1}
Other previous hit for breast cancer	7q21.2	rs6964587	G/T	0.41	1.05 (1.00-1.10)	6.9×10^{-2}
New hit for overall breast cancer	7q21.3	rs17268829	T/C	0.28	1.00 (0.95-1.05)	8.8×10^{-1}
New hit for overall breast cancer	7q22.1	rs71559437	G/A	0.12	1.09 (1.01-1.18)	2.0×10^{-2}
Other previous hit for breast cancer	7q32.3	rs4593472	C/T	0.33	1.03 (0.98-1.08)	2.8×10^{-1}
Other previous hit for breast cancer	7q34	rs11977670	G/A	0.44	1.02 (0.98-1.07)	3.5×10^{-1}
Other previous hit for breast cancer	7q35	rs720475	G/A	0.26	0.99 (0.94-1.04)	6.2×10^{-1}
New hit for ER-negative breast cancer	8p23.3	rs66823261	T/C	0.22	1.02 (0.96-1.08)	5.5×10^{-1}
Other previous hit for breast cancer	8p12	rs9693444	C/A	0.33	0.99 (0.94-1.04)	6.0×10^{-1}
Other previous hit for breast cancer	8p11.23	rs13365225	A/G	0.18	0.98 (0.92-1.04)	4.6×10^{-1}
Other previous hit for breast cancer	8q21.11	rs6472903	T/G	0.17	0.95 (0.89-1.02)	1.3×10^{-1}
Other previous hit for breast cancer	8q21.11	rs2943559	A/G	0.09	1.08 (0.99-1.17)	7.0×10^{-2}
New hit for overall breast cancer	8q22.3	rs514192	T/A	0.33	1.01 (0.96-1.06)	6.4×10^{-1}
New hit for overall breast cancer	8q23.1	rs12546444	A/T	0.10	0.97 (0.90-1.05)	4.8×10^{-1}
Other previous hit for breast cancer	8q23.3	rs13267382	G/A	0.35	1.00 (0.96-1.05)	8.6×10^{-1}
New hit for ER-negative breast cancer	8q24.13	rs17350191	C/T	0.35	1.00 (0.95-1.05)	9.2×10^{-1}
Other previous hit for breast cancer	8q24.21	rs13281615	A/G	0.42	1.05 (1.00-1.10)	6.1×10^{-2}
Other previous hit for breast cancer	8q24.21	rs11780156	C/T	0.19	0.99 (0.93-1.05)	7.7×10^{-1}
Other previous hit for breast cancer	9p21.3	rs1011970	G/T	0.17	1.04 (0.98-1.11)	2.1×10^{-1}
Other previous hit for breast cancer	9q31.2	rs10759243	C/A	0.29	1.05 (1.00-1.10)	7.6×10^{-2}
Other previous hit for breast cancer	9q31.2	rs10816625	A/G	0.07	0.96 (0.88-1.06)	4.3×10^{-1}
Other previous hit for breast cancer	9q31.2	rs13294895	C/T	0.17	1.04 (0.98-1.11)	1.8×10^{-1}
Other previous hit for breast cancer	9q31.2	rs676256	T/C	0.36	1.00 (0.95-1.05)	9.3×10^{-1}
New hit for overall breast cancer	9q33.1	rs1895062	A/G	0.40	1.00 (0.95-1.05)	9.9×10^{-1}
New hit for overall breast cancer	9q33.3	rs10760444	A/G	0.44	0.98 (0.94-1.03)	4.9×10^{-1}
New hit for overall breast cancer	9q34.2	rs587745765	I/D‡	0.21	1.01 (0.95-1.07)	8.1×10^{-1}
Other previous hit for breast cancer	10p15.1	rs2380205	C/T	0.43	0.99 (0.95-1.04)	7.1×10^{-1}
New hit for overall breast cancer	10p14	rs67958007	TG/T	0.13	1.10 (1.03-1.18)	6.6×10^{-3}
Other previous hit for breast cancer	10p12.31	rs7072776	G/A	0.30	1.03 (0.98-1.08)	2.8×10^{-1}
Other previous hit for breast cancer	10p12.31	rs11814448	A/C	0.02	1.03 (0.88-1.21)	6.8×10^{-1}
Other previous hit for breast cancer	10q21.2	rs10995201	A/G	0.15	0.95 (0.89-1.01)	1.0×10^{-1}
Other previous hit for breast cancer	10q22.3	rs704010	C/T	0.38	1.02 (0.98-1.07)	3.3×10^{-1}
New hit for overall breast cancer	10q23.33	rs140936696	C/CAA	0.17	1.01 (0.94-1.07)	8.3×10^{-1}
Other previous hit for breast cancer	10q25.2	rs7904519	A/G	0.47	1.01 (0.96-1.06)	6.5×10^{-1}
Other previous hit for breast cancer	10q26.12	rs11199914	C/T	0.33	0.94 (0.89-0.98)	9.3×10^{-3}
Other previous hit for breast cancer	10q26.13	rs2981578	T/C	0.51	1.20 (1.14-1.25)	1.1×10^{-13}
Other previous hit for breast cancer	10q26.13	rs35054928	G/GC	0.44	1.23 (1.17-1.29)	5.8×10^{-18}
Other previous hit for breast cancer	10q26.13	rs45631563	A/T	0.05	0.84 (0.75-0.94)	1.9×10^{-3}
New hit for overall breast cancer	11p15	rs6597981	G/A	0.50	0.96 (0.92-1.01)	1.3×10^{-1}
Other previous hit for breast cancer	11p15.5	rs3817198	T/C	0.33	1.10 (1.04-1.15)	2.8×10^{-4}
Other previous hit for breast cancer	11q13.1	rs3903072	G/T	0.47	0.97 (0.92-1.02)	2.0×10^{-1}
Other previous hit for breast cancer	11q13.3	rs554219	C/G	0.13	1.07 (1.00-1.15)	4.4×10^{-2}
Other previous hit for breast cancer	11q13.3	rs75915166	C/A	0.06	1.04 (0.94-1.15)	4.1×10^{-1}
New hit for ER-negative breast cancer	11q22.3	rs11374964	G/GA	0.43	1.02 (0.97-1.07)	3.8×10^{-1}

New hit for ER-negative breast cancer	11q22.3	rs74911261	G/A	0.02	0.94 (0.80-1.09)	4.2×10^{-1}
Other previous hit for breast cancer	11q24.3	rs11820646	C/T	0.39	0.92 (0.88-0.97)	1.2×10^{-3}
Other previous hit for breast cancer	12p13.1	rs12422552	G/C	0.28	0.99 (0.94-1.04)	7.3×10^{-1}
Other previous hit for breast cancer	12p11.22	rs7297051	C/T	0.23	0.92 (0.87-0.97)	2.5×10^{-3}
New hit for overall breast cancer	12q21.31	12:85009437:T:C	T/C	0.32	1.04 (0.98-1.09)	2.0×10^{-1}
Other previous hit for breast cancer	12q22	rs17356907	A/G	0.30	1.01 (0.96-1.07)	6.0×10^{-1}
Other previous hit for breast cancer	12q24.21	rs1292011	A/G	0.41	0.95 (0.90-0.99)	3.0×10^{-2}
New hit for overall breast cancer	12q24.31	12:120832146:C:T	C/T	0.15	1.02 (0.95-1.09)	6.0×10^{-1}
Other previous hit for breast cancer	13q13.1	rs11571833	A/T	0.03	0.99 (0.85-1.14)	8.4×10^{-1}
Previous hit for ER-negative disease	13q22.1	rs6562760‡	G/A	0.25	0.96 (0.91-1.01)	1.1×10^{-1}
Other previous hit for breast cancer	14q13.3	rs2236007	G/A	0.21	0.97 (0.92-1.03)	3.9×10^{-1}
Other previous hit for breast cancer	14q24.1	rs2588809	C/T	0.20	1.05 (0.99-1.11)	1.1×10^{-1}
Other previous hit for breast cancer	14q24.1	rs999737	C/T	0.22	0.95 (0.90-1.00)	6.9×10^{-2}
Other previous hit for breast cancer	14q32.11	rs941764	A/G	0.34	1.02 (0.97-1.07)	5.1×10^{-1}
Other previous hit for breast cancer	14q32.12	rs11627032	T/C	0.26	1.01 (0.96-1.07)	7.5×10^{-1}
New hit for overall breast cancer	14q32.33	rs10623258	C/CTT	0.46	1.00 (0.95-1.05)	9.2×10^{-1}
Other previous hit for breast cancer	15q26.1	rs2290203	G/A	0.21	0.95 (0.90-1.01)	1.1×10^{-1}
New hit for ER-negative breast cancer	16p13.3	rs11076805	C/A	0.26	0.93 (0.88-0.99)	1.3×10^{-2}
Other previous hit for breast cancer	16q12.1	rs4784227	C/T	0.27	1.21 (1.15-1.28)	6.8×10^{-13}
Other previous hit for breast cancer	16q12.2	rs17817449	T/G	0.40	0.97 (0.93-1.02)	2.5×10^{-1}
Previous hit for ER-negative disease	16q12.2	rs11075995	T/A	0.23	1.03 (0.98-1.09)	2.6×10^{-1}
New hit for overall breast cancer	16q12.2	rs28539243	G/A	0.49	1.01 (0.96-1.06)	6.4×10^{-1}
New hit for overall breast cancer	16q13	rs2432539	G/A	0.40	1.04 (0.99-1.09)	1.1×10^{-1}
Other previous hit for breast cancer	16q23.2	rs13329835	A/G	0.24	1.05 (0.99-1.10)	1.2×10^{-1}
New hit for overall breast cancer	16q24.2	rs4496150	C/A	0.26	0.97 (0.92-1.02)	2.9×10^{-1}
Other previous hit for breast cancer	17q11.2	chr17:29230520	GGT/G	0.27	0.92 (0.87-0.97)	2.4×10^{-3}
New hit for overall breast cancer	17q21.2	rs72826962	C/T	0.01	1.21 (0.98-1.50)	7.3×10^{-2}
New hit for overall breast cancer	17q21.31	17:44252468:G:A	G/A	0.20	0.90 (0.85-0.96)	6.1×10^{-4}
Other previous hit for breast cancer	17q22	rs2787486	A/C	0.29	1.02 (0.97-1.07)	5.3×10^{-1}
Other previous hit for breast cancer	17q25.3	rs745570	G/A	0.50	1.03 (0.98-1.08)	2.2×10^{-1}
Other previous hit for breast cancer	18q11.2	rs527616	G/C	0.37	0.98 (0.93-1.03)	4.2×10^{-1}
Other previous hit for breast cancer	18q11.2	rs1436904	T/G	0.39	0.98 (0.93-1.02)	3.3×10^{-1}
New hit for ER-negative breast cancer	18q12.1	rs36194942	A/AT	0.31	0.99 (0.94-1.04)	6.2×10^{-1}
New hit for overall breast cancer	18q12.1	rs117618124	T/C	0.04	0.93 (0.83-1.06)	2.9×10^{-1}
Other previous hit for breast cancer	18q12.3	rs6507583	A/G	0.07	0.9 (0.82-0.99)	2.2×10^{-2}
New hit for ER-negative breast cancer	19p13.2	rs322144	C/G	0.45	0.98 (0.93-1.03)	4.2×10^{-1}
New hit for overall breast cancer	19p13.13	rs78269692	T/C	0.05	0.98 (0.87-1.10)	6.9×10^{-1}
New hit for overall breast cancer	19p13.12	rs2594714	G/A	0.22	0.99 (0.93-1.05)	7.3×10^{-1}
Previous hit for ER-negative disease	19p13.11	rs67397200	C/G	0.30	1.00 (0.95-1.05)	8.6×10^{-1}
Other previous hit for breast cancer	19p13.11	rs4808801	A/G	0.33	0.97 (0.92-1.02)	1.8×10^{-1}
New hit for overall breast cancer	19p13.11	rs2965183	G/A	0.36	1.06 (1.01-1.12)	1.6×10^{-2}
New hit for ER-negative breast cancer	19q12	rs113701136	C/T	0.32	1.06 (1.01-1.12)	1.7×10^{-2}
Other previous hit for breast cancer	19q13.31	rs3760982	G/A	0.46	1.02 (0.97-1.07)	3.7×10^{-1}
New hit for overall breast cancer	19q13.22	rs71338792	A/AT	0.23	1.04 (0.98-1.10)	2.3×10^{-1}
New hit for overall breast cancer	20p12.3	rs16991615	G/A	0.07	1.00 (0.92-1.10)	9.3×10^{-1}
Previous hit for ER-negative disease	20q11.21	rs2284378	C/T	0.31	1.02 (0.97-1.07)	4.9×10^{-1}
New hit for overall breast cancer	20q13.13	rs6122906	A/G	0.19	1.06 (1.00-1.12)	7.0×10^{-2}
Other previous hit for breast cancer	21q21.1	rs2823093	G/A	0.27	0.94 (0.89-0.99)	1.4×10^{-2}
Other previous hit for breast cancer	22q12.1	rs17879961	A/G	0.004	1.83 (1.23-2.71)	2.7×10^{-3}
Other previous hit for breast cancer	22q12.2	rs132390	T/C	0.03	1.09 (0.96-1.24)	1.9×10^{-1}
New hit for overall breast cancer	22q13.1	rs738321	C/G	0.38	0.97 (0.92-1.02)	2.1×10^{-1}
Other previous hit for breast cancer	22q13.1	chr22:39359355	I/D§	0.004	1.67 (0.97-2.88)	6.3×10^{-2}
Other previous hit for breast cancer	22q13.1	rs6001930	T/C	0.10	1.02 (0.95-1.11)	5.5×10^{-1}
New hit for overall breast cancer	22q13.2	rs73161324	C/T	0.05	1.01 (0.91-1.13)	7.8×10^{-1}
New hit for overall breast cancer	22q13.31	rs28512361	G/A	0.11	0.98 (0.91-1.06)	6.3×10^{-1}

Chr, chromosome; MAF, minor allele frequency; ‡More common allele listed first, minor allele second;
†21 base-pair deletion; ‡36 base-pair deletion; ¥14 base-pair insertion; §31 kb deletion
Results based on OncoArray data for 10,988 *BRCA2* mutation carriers (5,611 with breast cancer) and iCOGS data for 1,418 *BRCA2*
mutation carriers (755 with breast cancer), all from the Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA)

Supplementary Table 12: Detailed informat

Theme

ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE

ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADHERENS JUNCTION
ADHERENS JUNCTION
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS

APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
APOPTOSIS
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL AGING/TELOMERE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE

CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
DNA DEMETHYLATION/DEALKYLATION
DNA DEMETHYLATION/DEALKYLATION
DOUBLE STRAND BREAK REPAIR
DOUBLE STRAND BREAK REPAIR
DOUBLE STRAND BREAK REPAIR
DOUBLE STRAND BREAK REPAIR
DOUBLE STRAND BREAK REPAIR
DOUBLE STRAND BREAK REPAIR
DOUBLE STRAND BREAK REPAIR
DOUBLE STRAND BREAK REPAIR
DOUBLE STRAND BREAK REPAIR
DOUBLE STRAND BREAK REPAIR
DOUBLE STRAND BREAK REPAIR
DOUBLE STRAND BREAK REPAIR
DOUBLE STRAND BREAK REPAIR
DOUBLE STRAND BREAK REPAIR
DOUBLE STRAND BREAK REPAIR
DOUBLE STRAND BREAK REPAIR
DOUBLE STRAND BREAK REPAIR
EPITHELIAL-MESENCHYMAL INTERACTIONS
EPITHELIAL-MESENCHYMAL INTERACTIONS
EPITHELIAL-MESENCHYMAL INTERACTIONS
EPITHELIAL-MESENCHYMAL INTERACTIONS
ESTROGEN RECEPTOR SIGNALING
ESTROGEN RECEPTOR SIGNALING
ESTROGEN RECEPTOR SIGNALING
ESTROGEN RECEPTOR SIGNALING
ESTROGEN RECEPTOR SIGNALING
ESTROGEN RECEPTOR SIGNALING
ESTROGEN RECEPTOR SIGNALING
ESTROGEN RECEPTOR SIGNALING

ESTROGEN RECEPTOR SIGNALING
ESTROGEN RECEPTOR SIGNALING
ESTROGEN RECEPTOR SIGNALING
ESTROGEN RECEPTOR SIGNALING
ESTROGEN RECEPTOR SIGNALING
ESTROGEN RECEPTOR SIGNALING
ESTROGEN RECEPTOR SIGNALING
ESTROGEN RECEPTOR SIGNALING
ESTROGEN RECEPTOR SIGNALING
ESTROGEN RECEPTOR SIGNALING
ESTROGEN RECEPTOR SIGNALING
ESTROGEN RECEPTOR SIGNALING
ESTROGEN RECEPTOR SIGNALING
GENE SILENCING
GENE SILENCING
GENE SILENCING
GENE SILENCING
GENE SILENCING
GENE SILENCING
GENE SILENCING
GENE SILENCING
GENE SILENCING
GENE SILENCING
GENE SILENCING
GENE SILENCING
GENE SILENCING
GENE SILENCING
REGULATION OF NITRIC OXIDE METABOLISN
REGULATION OF NITRIC OXIDE METABOLISN
REGULATION OF NITRIC OXIDE METABOLISN
REGULATION OF NITRIC OXIDE METABOLISN
REGULATION OF NITRIC OXIDE METABOLISN
REGULATION OF NITRIC OXIDE METABOLISN
REGULATION OF NITRIC OXIDE METABOLISN
REGULATION OF NITRIC OXIDE METABOLISN
REGULATION OF NITRIC OXIDE METABOLISN
REGULATION OF NITRIC OXIDE METABOLISN
REGULATION OF NITRIC OXIDE METABOLISN
REGULATION OF NITRIC OXIDE METABOLISN
REGULATION OF NITRIC OXIDE METABOLISN
REPRODUCTIVE SYSTEM
REPRODUCTIVE SYSTEM
REPRODUCTIVE SYSTEM
REPRODUCTIVE SYSTEM
REPRODUCTIVE SYSTEM
REPRODUCTIVE SYSTEM
REPRODUCTIVE SYSTEM
REPRODUCTIVE SYSTEM
REPRODUCTIVE SYSTEM
REPRODUCTIVE SYSTEM
REPRODUCTIVE SYSTEM

REPRODUCTIVE SYSTEM
REPRODUCTIVE SYSTEM
RESPONSE TO CATECHOLAMINE
RESPONSE TO CATECHOLAMINE
RESPONSE TO CATECHOLAMINE
RESPONSE TO CATECHOLAMINE
WNT/BETA CATENIN
WNT/BETA CATENIN
WNT/BETA CATENIN
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED

OTHER-NOT CLUSTERED

OTHER-NOT CLUSTERED

†Standardized Enrichment Score is the actual val

tion about themes and pathways appearing in the enrichment maps (Supplementary Figure

Pathway

ACTIVATION OF NMDA RECEPTOR UPON GLUTAMATE BINDING AND POSTSYNAPTIC EVENT!
ACTIVATION OF PROTEIN KINASE A ACTIVITY
ACTIVATION OF PROTEIN KINASE A ACTIVITY
ADENYLATE CYCLASE ACTIVATING PATHWAY
ADENYLATE CYCLASE ACTIVATING PATHWAY
ADENYLATE CYCLASE INHIBITORY PATHWAY
ADENYLATE CYCLASE INHIBITORY PATHWAY
ADENYLATE CYCLASE-ACTIVATING ADRENERGIC RECEPTOR SIGNALING PATHWAY
ADENYLATE CYCLASE-ACTIVATING ADRENERGIC RECEPTOR SIGNALING PATHWAY
ADENYLATE CYCLASE-ACTIVATING G-PROTEIN COUPLED RECEPTOR SIGNALING PATHWAY
ADENYLATE CYCLASE-ACTIVATING G-PROTEIN COUPLED RECEPTOR SIGNALING PATHWAY
ADENYLATE CYCLASE-ACTIVATING G-PROTEIN COUPLED RECEPTOR SIGNALING PATHWAY
ADENYLATE CYCLASE-ACTIVATING G-PROTEIN COUPLED RECEPTOR SIGNALING PATHWAY
ADENYLATE CYCLASE-INHIBITING G-PROTEIN COUPLED RECEPTOR SIGNALING PATHWAY
ADENYLATE CYCLASE-INHIBITING G-PROTEIN COUPLED RECEPTOR SIGNALING PATHWAY
ADENYLATE CYCLASE-INHIBITING G-PROTEIN COUPLED RECEPTOR SIGNALING PATHWAY
ADENYLATE CYCLASE-INHIBITING G-PROTEIN COUPLED RECEPTOR SIGNALING PATHWAY
ADRENERGIC RECEPTOR SIGNALING PATHWAY
ADRENERGIC RECEPTOR SIGNALING PATHWAY
CA-DEPENDENT EVENTS
CA-DEPENDENT EVENTS
CALMODULIN INDUCED EVENTS
CALMODULIN INDUCED EVENTS
CAM PATHWAY
CAM PATHWAY
CAMP BIOSYNTHETIC PROCESS
CAMP BIOSYNTHETIC PROCESS
CAMP METABOLIC PROCESS
CAMP METABOLIC PROCESS
CAMP METABOLIC PROCESS
CAMP METABOLIC PROCESS
CAMP-MEDIATED SIGNALING
CAMP-MEDIATED SIGNALING
CAMP-MEDIATED SIGNALING
CYCLIC NUCLEOTIDE METABOLIC PROCESS
CYCLIC NUCLEOTIDE METABOLIC PROCESS
CYCLIC NUCLEOTIDE METABOLIC PROCESS
CYCLIC NUCLEOTIDE METABOLIC PROCESS
CYCLIC-NUCLEOTIDE-MEDIATED SIGNALING
CYCLIC-NUCLEOTIDE-MEDIATED SIGNALING
CYCLIC-NUCLEOTIDE-MEDIATED SIGNALING
DAG AND IP3 SIGNALING
DAG AND IP3 SIGNALING
EGFR INTERACTS WITH PHOSPHOLIPASE C-GAMMA
EGFR INTERACTS WITH PHOSPHOLIPASE C-GAMMA
ENDOTHELIN SIGNALING PATHWAY
ENDOTHELIN SIGNALING PATHWAY

G-PROTEIN MEDIATED EVENTS
G-PROTEIN MEDIATED EVENTS
INHIBITION OF ADENYLATE CYCLASE PATHWAY
INHIBITION OF ADENYLATE CYCLASE PATHWAY
LPA4-MEDIATED SIGNALING EVENTS
LPA4-MEDIATED SIGNALING EVENTS
NEGATIVE REGULATION OF BLOOD CIRCULATION
PHOSPHOLIPASE C-MEDIATED CASCADE: FGFR1
PHOSPHOLIPASE C-MEDIATED CASCADE: FGFR1
PHOSPHOLIPASE C-MEDIATED CASCADE; FGFR2
PHOSPHOLIPASE C-MEDIATED CASCADE; FGFR2
PHOSPHOLIPASE C-MEDIATED CASCADE; FGFR3
PHOSPHOLIPASE C-MEDIATED CASCADE; FGFR3
PHOSPHOLIPASE C-MEDIATED CASCADE; FGFR4
PHOSPHOLIPASE C-MEDIATED CASCADE; FGFR4
PKA ACTIVATION IN GLUCAGON SIGNALLING
PKA ACTIVATION IN GLUCAGON SIGNALLING
PKA ACTIVATION
PKA ACTIVATION
PKA-MEDIATED PHOSPHORYLATION OF CREB
PKA-MEDIATED PHOSPHORYLATION OF CREB
PLC BETA MEDIATED EVENTS
PLC BETA MEDIATED EVENTS
PLC-GAMMA1 SIGNALLING
PLC-GAMMA1 SIGNALLING
PLCG1 EVENTS IN ERBB2 SIGNALING
PLCG1 EVENTS IN ERBB2 SIGNALING
POSITIVE REGULATION OF INTERLEUKIN-2 PRODUCTION
POST NMDA RECEPTOR ACTIVATION EVENTS
PURINE RIBONUCLEOTIDE CATABOLIC PROCESS
PURINE-CONTAINING COMPOUND CATABOLIC PROCESS
PURINE-CONTAINING COMPOUND CATABOLIC PROCESS
REGULATION OF CARDIAC MUSCLE CELL CONTRACTION
REGULATION OF CELL COMMUNICATION BY ELECTRICAL COUPLING
REGULATION OF RELEASE OF SEQUESTERED CALCIUM ION INTO CYTOSOL BY SARCOPLASMI
RIBONUCLEOTIDE CATABOLIC PROCESS
ADHERENS JUNCTION ORGANIZATION
ADHERENS JUNCTIONS INTERACTIONS
ACTIVATION OF CYSTEINE-TYPE ENDOPEPTIDASE ACTIVITY INVOLVED IN APOPTOTIC SIGNAL
ACTIVATION OF CYSTEINE-TYPE ENDOPEPTIDASE ACTIVITY INVOLVED IN APOPTOTIC SIGNAL
APOPTOTIC DNA FRAGMENTATION
BIOCARTA_CASPASE_PATHWAY
BIOCARTA_CASPASE_PATHWAY
BIOCARTA_DEATH_PATHWAY
BIOCARTA_DEATH_PATHWAY
BIOCARTA_DEATH_PATHWAY
BIOCARTA_FAS_PATHWAY
BIOCARTA_FAS_PATHWAY
BIOCARTA_FAS_PATHWAY
BIOCARTA_SODD_PATHWAY
CASP8 ACTIVITY IS INHIBITED

DIMERIZATION OF PROCASPASE-8
IN UTERO EMBRYONIC DEVELOPMENT
MACROPHAGE DIFFERENTIATION
NEGATIVE REGULATION OF EXTRINSIC APOPTOTIC SIGNALING PATHWAY IN ABSENCE OF LIG
NEGATIVE REGULATION OF MYOTUBE DIFFERENTIATION
NEGATIVE REGULATION OF SIGNAL TRANSDUCTION IN ABSENCE OF LIGAND
NEGATIVE REGULATION OF STRIATED MUSCLE CELL DIFFERENTIATION
POSITIVE REGULATION OF CYSTEINE-TYPE ENDOPEPTIDASE ACTIVITY INVOLVED IN APOPTO
POSITIVE REGULATION OF CYSTEINE-TYPE ENDOPEPTIDASE ACTIVITY INVOLVED IN APOPTO
REGULATION BY C-FLIP
REGULATION OF EXECUTION PHASE OF APOPTOSIS
REGULATION OF EXECUTION PHASE OF APOPTOSIS
REGULATION OF EXTRINSIC APOPTOTIC SIGNALING PATHWAY IN ABSENCE OF LIGAND
REGULATION OF MACROPHAGE DIFFERENTIATION
SA_CASPASE_CASCADE
SA_CASPASE_CASCADE
TNFR1-INDUCED PROAPOPTOTIC SIGNALING
TRAIL SIGNALING PATHWAY
TRAIL SIGNALING PATHWAY
TRIF-MEDIATED PROGRAMMED CELL DEATH
BIOCARTA_ACH_PATHWAY
BIOCARTA_TEL_PATHWAY
CELL AGING
CELL AGING
CELL AGING
ESTABLISHMENT OF PROTEIN LOCALIZATION TO CHROMOSOME
ESTABLISHMENT OF PROTEIN LOCALIZATION TO CHROMOSOME
EXTENSION OF TELOMERES
HETEROCHROMATIN ORGANIZATION
NEGATIVE REGULATION OF CELL AGING
PROTEIN LOCALIZATION TO CHROMOSOME, TELOMERIC REGION
PROTEIN LOCALIZATION TO CHROMOSOME, TELOMERIC REGION
REGULATION OF CELL AGING
REGULATION OF CELL AGING
REGULATION OF CELLULAR SENESCENCE
REGULATION OF CELLULAR SENESCENCE
REGULATION OF PRI-MIRNA TRANSCRIPTION FROM RNA POLYMERASE II PROMOTER
REPLICATIVE SENESCENCE
REPLICATIVE SENESCENCE
REPLICATIVE SENESCENCE
RNA-DEPENDENT DNA REPLICATION
RNA-DEPENDENT DNA REPLICATION
TELOMERE MAINTENANCE VIA TELOMERASE
TELOMERE MAINTENANCE VIA TELOMERASE
TELOMERE MAINTENANCE
BIOCARTA_G1_PATHWAY
BIOCARTA_G1_PATHWAY
BIOCARTA_G1_PATHWAY
BIOCARTA_P53_PATHWAY
BIOCARTA_P53_PATHWAY
CELL CYCLE

FOXM1 TRANSCRIPTION FACTOR NETWORK
FOXM1 TRANSCRIPTION FACTOR NETWORK
FOXM1 TRANSCRIPTION FACTOR NETWORK
FOXM1 TRANSCRIPTION FACTOR NETWORK
G2 DNA DAMAGE CHECKPOINT
G2 DNA DAMAGE CHECKPOINT
MITOTIC G2/M TRANSITION CHECKPOINT
NEGATIVE REGULATION OF B CELL ACTIVATION
NEGATIVE REGULATION OF B CELL ACTIVATION
NEGATIVE REGULATION OF G2/M TRANSITION OF MITOTIC CELL CYCLE
POSITIVE REGULATION OF CELL CYCLE G2/M PHASE TRANSITION
POSITIVE REGULATION OF DNA DAMAGE RESPONSE, SIGNAL TRANSDUCTION BY P53 CLASS
POSITIVE REGULATION OF DNA DAMAGE RESPONSE, SIGNAL TRANSDUCTION BY P53 CLASS
POSITIVE REGULATION OF G2/M TRANSITION OF MITOTIC CELL CYCLE
POSITIVE REGULATION OF SIGNAL TRANSDUCTION BY P53 CLASS MEDIATOR
POSITIVE REGULATION OF SIGNAL TRANSDUCTION BY P53 CLASS MEDIATOR
SA_REG_CASCADE_OF_CYCLIN_EXPR
SA_REG_CASCADE_OF_CYCLIN_EXPR
SOMATIC STEM CELL DIVISION
DNA DEALKYLATION
DNA DEMETHYLATION
BIOCARTA_ATRBRCA_PATHWAY
BIOCARTA_ATRBRCA_PATHWAY
CELLULAR RESPONSE TO GAMMA RADIATION
DNA DOUBLE STRAND BREAK RESPONSE
DNA DOUBLE STRAND BREAK RESPONSE
DOUBLE-STRAND BREAK REPAIR VIA SYNTHESIS-DEPENDENT STRAND ANNEALING
DOUBLE-STRAND BREAK REPAIR VIA SYNTHESIS-DEPENDENT STRAND ANNEALING
DOUBLE-STRAND BREAK REPAIR VIA SYNTHESIS-DEPENDENT STRAND ANNEALING
G2 M DNA DAMAGE CHECKPOINT
G2 M DNA DAMAGE CHECKPOINT
NONHOMOLOGOUS END-JOINING (NHEJ)
NONHOMOLOGOUS END-JOINING (NHEJ)
POSITIVE REGULATION OF DNA REPAIR
RECRUITMENT AND ATM-MEDIATED PHOSPHORYLATION OF REPAIR AND SIGNALING PROT
RECRUITMENT AND ATM-MEDIATED PHOSPHORYLATION OF REPAIR AND SIGNALING PROT
RESOLUTION OF D-LOOP STRUCTURES THROUGH SYNTHESIS-DEPENDENT STRAND ANNEAL
RESOLUTION OF D-LOOP STRUCTURES THROUGH SYNTHESIS-DEPENDENT STRAND ANNEAL
RESOLUTION OF D-LOOP STRUCTURES THROUGH SYNTHESIS-DEPENDENT STRAND ANNEAL
NEGATIVE REGULATION OF CARTILAGE DEVELOPMENT
NEGATIVE REGULATION OF CHONDROCYTE DIFFERENTIATION
REGULATION OF CARTILAGE DEVELOPMENT
REGULATION OF CHONDROCYTE DIFFERENTIATION
BIOCARTA_CARM_ER_PATHWAY
BIOCARTA_HER2_PATHWAY
BIOCARTA_MTA3_PATHWAY
BMAL1:CLOCK,NPAS2 ACTIVATES CIRCADIAN GENE EXPRESSION
CELLULAR RESPONSE TO ALCOHOL
CELLULAR RESPONSE TO ESTRADIOL STIMULUS
CELLULAR RESPONSE TO ESTROGEN STIMULUS
CIRCADIAN CLOCK

CIRCADIAN CLOCK
INTRACELLULAR ESTROGEN RECEPTOR SIGNALING PATHWAY
INTRACELLULAR STEROID HORMONE RECEPTOR SIGNALING PATHWAY
INTRACELLULAR STEROID HORMONE RECEPTOR SIGNALING PATHWAY
INTRACELLULAR STEROID HORMONE RECEPTOR SIGNALING PATHWAY
NUCLEAR RECEPTOR TRANSCRIPTION PATHWAY
NUCLEAR RECEPTOR TRANSCRIPTION PATHWAY
NUCLEAR RECEPTOR TRANSCRIPTION PATHWAY
NUCLEAR SIGNALING BY ERBB4
RESPONSE TO ESTRADIOL
RORA ACTIVATES GENE EXPRESSION
SIGNALING EVENTS MEDIATED BY HDAC CLASS II
SIGNALING MEDIATED BY P38-ALPHA AND P38-BETA
CELLULAR RESPONSE TO DSRNA
CELLULAR RESPONSE TO DSRNA
CELLULAR RESPONSE TO EXOGENOUS DSRNA
DSRNA FRAGMENTATION
NEGATIVE REGULATION OF GENE SILENCING
POSTTRANSCRIPTIONAL GENE SILENCING BY RNA
POSTTRANSCRIPTIONAL GENE SILENCING BY RNA
POSTTRANSCRIPTIONAL GENE SILENCING
POSTTRANSCRIPTIONAL GENE SILENCING
PRODUCTION OF SMALL RNA INVOLVED IN GENE SILENCING BY RNA
REGULATION OF GENE SILENCING BY RNA
REGULATION OF GENE SILENCING
REGULATION OF POSTTRANSCRIPTIONAL GENE SILENCING
RNA INTERFERENCE
POSITIVE REGULATION OF MONOOXYGENASE ACTIVITY
POSITIVE REGULATION OF MONOOXYGENASE ACTIVITY
POSITIVE REGULATION OF NITRIC OXIDE BIOSYNTHETIC PROCESS
POSITIVE REGULATION OF NITRIC OXIDE METABOLIC PROCESS
POSITIVE REGULATION OF NITRIC-OXIDE SYNTHASE ACTIVITY
POSITIVE REGULATION OF NITRIC-OXIDE SYNTHASE ACTIVITY
POSITIVE REGULATION OF OXIDOREDUCTASE ACTIVITY
POSITIVE REGULATION OF OXIDOREDUCTASE ACTIVITY
POSITIVE REGULATION OF REACTIVE OXYGEN SPECIES BIOSYNTHETIC PROCESS
REGULATION OF MONOOXYGENASE ACTIVITY
REGULATION OF MONOOXYGENASE ACTIVITY
REGULATION OF NITRIC-OXIDE SYNTHASE ACTIVITY
REGULATION OF NITRIC-OXIDE SYNTHASE ACTIVITY
ACTIVIN RECEPTOR SIGNALING PATHWAY
DEVELOPMENT OF PRIMARY FEMALE SEXUAL CHARACTERISTICS
FEMALE GONAD DEVELOPMENT
NEGATIVE REGULATION OF CYTOKINE BIOSYNTHETIC PROCESS
NEGATIVE REGULATION OF INSULIN SECRETION
NEGATIVE REGULATION OF PEPTIDE HORMONE SECRETION
NEGATIVE REGULATION OF PEPTIDE SECRETION
OVARIAN FOLLICLE DEVELOPMENT
OVULATION CYCLE PROCESS
OVULATION CYCLE
POSITIVE REGULATION OF REPRODUCTIVE PROCESS

REGULATION OF ENDOCRINE PROCESS
SIGNALING BY ACTIVIN
CELLULAR RESPONSE TO CATECHOLAMINE STIMULUS
CELLULAR RESPONSE TO MONOAMINE STIMULUS
RESPONSE TO CATECHOLAMINE
RESPONSE TO MONOAMINE
FORMATION OF THE BETA-CATENIN:TCF TRANSACTIVATING COMPLEX
FORMATION OF THE BETA-CATENIN:TCF TRANSACTIVATING COMPLEX
REPRESSION OF WNT TARGET GENES
ACROSOME REACTION
ACTIN CYTOSKELETON REORGANIZATION
AMINO ACID AND OLIGOPEPTIDE SLC TRANSPORTERS
AMINO ACID TRANSPORT ACROSS THE PLASMA MEMBRANE
BIOCARTA_DNAFRAGMENT_PATHWAY
BIOCARTA_RARRXR_PATHWAY
BIOCARTA_SET_PATHWAY
BIOCARTA_VDR_PATHWAY
CELL RECOGNITION
CHROMOSOME SEPARATION
GLYCOPROTEIN HORMONES
INSULIN IGF PATHWAY-PROTEIN KINASE B SIGNALING CASCADE
MICROTUBULE ANCHORING
MITOCHONDRIAL RNA PROCESSING
MITOCHONDRIAL RNA PROCESSING
MYOBLAST DIFFERENTIATION
N-CADHERIN SIGNALING EVENTS
NEGATIVE REGULATION OF ESTABLISHMENT OF PROTEIN LOCALIZATION TO PLASMA MEMI
NEURONAL STEM CELL POPULATION MAINTENANCE
P38MAPK EVENTS
PEPTIDE HORMONE BIOSYNTHESIS
PHOSPHATIDYLINOSITOL 3-KINASE SIGNALING
PHOSPHATIDYLINOSITOL-3-PHOSPHATE BIOSYNTHETIC PROCESS
PHOSPHATIDYLINOSITOL-3-PHOSPHATE BIOSYNTHETIC PROCESS
POSITIVE REGULATION OF ANTIGEN RECEPTOR-MEDIATED SIGNALING PATHWAY
POSITIVE REGULATION OF GLYCOPROTEIN BIOSYNTHETIC PROCESS
POSITIVE REGULATION OF GLYCOPROTEIN METABOLIC PROCESS
POSITIVE REGULATION OF PROTEIN EXPORT FROM NUCLEUS
PROTEIN IMPORT INTO PEROXISOME MATRIX
PROTEIN K63-LINKED DEUBIQUITINATION
PROTEIN KINASE C SIGNALING
RAP PROTEIN SIGNAL TRANSDUCTION
REGULATION OF CELLULAR EXTRAVASATION
REGULATION OF HORMONE METABOLIC PROCESS
REGULATION OF MYOBLAST FUSION
REGULATION OF PROTEIN EXPORT FROM NUCLEUS
REGULATION OF PROTEIN EXPORT FROM NUCLEUS
REGULATION OF PROTEIN HOMOOLIGOMERIZATION
SIGNALING EVENTS MEDIATED BY THE HEDGEHOG FAMILY
SMOOTH MUSCLE CELL DIFFERENTIATION
TISSUE REGENERATION
TRNA THREONYLCARBAMOYLADENOSINE METABOLIC PROCESS

TRNA THREONYLCARBAMOYLADENOSINE METABOLIC PROCESS
YAP1- AND WWTR1 (TAZ)-STIMULATED GENE EXPRESSION

ue used to create the enrichment map in Supplementary Figure 14. This value is (ES-min(ES))/(max(ES

Database	Pathway ID	Enrichment Score (ES)	Standardized ES†	Gene
REACTOME DATABASE ID RELEASE 55	442755	0.4343	0.0554	ADCY3
GOBP	GO:0034199	0.5247	0.2721	ADCY3
GOBP	GO:0034199	0.5247	0.2721	ADCY9
REACTOME DATABASE ID RELEASE 55	170660	0.6199	0.5003	ADCY3
REACTOME DATABASE ID RELEASE 55	170660	0.6199	0.5003	ADCY9
REACTOME	R-HSA-170670.1	0.5521	0.3376	ADCY3
REACTOME	R-HSA-170670.1	0.5521	0.3376	ADCY9
GOBP	GO:0071880	0.4217	0.0252	ADCY9
GOBP	GO:0071880	0.4217	0.0252	PDE4D
GOBP	GO:0007189	0.4122	0.0024	PTHLH
GOBP	GO:0007189	0.4122	0.0024	ADCY3
GOBP	GO:0007189	0.4122	0.0024	ADCY9
GOBP	GO:0007189	0.4122	0.0024	PDE4D
GOBP	GO:0007193	0.4223	0.0266	MCHR1
GOBP	GO:0007193	0.4223	0.0266	ADCY3
GOBP	GO:0007193	0.4223	0.0266	ADCY9
GOBP	GO:0007193	0.4223	0.0266	CORT
GOBP	GO:0071875	0.4217	0.0252	ADCY9
GOBP	GO:0071875	0.4217	0.0252	PDE4D
REACTOME	R-HSA-111996.1	0.4310	0.0474	ADCY3
REACTOME	R-HSA-111996.1	0.4310	0.0474	ADCY9
REACTOME	R-HSA-111933.1	0.4216	0.0250	ADCY3
REACTOME	R-HSA-111933.1	0.4216	0.0250	ADCY9
REACTOME	R-HSA-111997.1	0.4216	0.0250	ADCY3
REACTOME	R-HSA-111997.1	0.4216	0.0250	ADCY9
GOBP	GO:0006171	0.4718	0.1453	ADCY3
GOBP	GO:0006171	0.4718	0.1453	ADCY9
GOBP	GO:0046058	0.5935	0.4371	PTHLH
GOBP	GO:0046058	0.5935	0.4371	ADCY3
GOBP	GO:0046058	0.5935	0.4371	ADCY9
GOBP	GO:0046058	0.5935	0.4371	PDE4D
GOBP	GO:0019933	0.4832	0.1726	ADCY3
GOBP	GO:0019933	0.4832	0.1726	ADCY9
GOBP	GO:0019933	0.4832	0.1726	PDE4D
GOBP	GO:0009187	0.4588	0.1141	PTHLH
GOBP	GO:0009187	0.4588	0.1141	ADCY3
GOBP	GO:0009187	0.4588	0.1141	ADCY9
GOBP	GO:0009187	0.4588	0.1141	PDE4D
GOBP	GO:0019935	0.4454	0.0819	ADCY3
GOBP	GO:0019935	0.4454	0.0819	ADCY9
GOBP	GO:0019935	0.4454	0.0819	PDE4D
REACTOME DATABASE ID RELEASE 55	1489509	0.4559	0.1072	ADCY3
REACTOME DATABASE ID RELEASE 55	1489509	0.4559	0.1072	ADCY9
REACTOME DATABASE ID RELEASE 55	212718	0.4683	0.1369	ADCY3
REACTOME DATABASE ID RELEASE 55	212718	0.4683	0.1369	ADCY9
PANTHER PATHWAY	P00019	0.4392	0.0670	ADCY3
PANTHER PATHWAY	P00019	0.4392	0.0670	ADCY9

REACTOME DATABASE ID RELEASE 55	112040	0.4310	0.0474	ADCY3
REACTOME DATABASE ID RELEASE 55	112040	0.4310	0.0474	ADCY9
REACTOME DATABASE ID RELEASE 55	997269	0.5521	0.3376	ADCY3
REACTOME DATABASE ID RELEASE 55	997269	0.5521	0.3376	ADCY9
PATHWAY INTERACTION DATABASE NCI-NA	LPA4-MEDIATED S	0.5537	0.3415	ADCY3
PATHWAY INTERACTION DATABASE NCI-NA	LPA4-MEDIATED S	0.5537	0.3415	ADCY9
GOBP	GO:1903523	0.4744	0.1515	PDE4D
REACTOME	R-HSA-5654219.1	0.4569	0.1094	ADCY3
REACTOME	R-HSA-5654219.1	0.4569	0.1094	ADCY9
REACTOME	R-HSA-5654221.1	0.4192	0.0193	ADCY3
REACTOME	R-HSA-5654221.1	0.4192	0.0193	ADCY9
REACTOME	R-HSA-5654227.1	0.4425	0.0750	ADCY3
REACTOME	R-HSA-5654227.1	0.4425	0.0750	ADCY9
REACTOME DATABASE ID RELEASE 55	5654228	0.4150	0.0091	ADCY3
REACTOME DATABASE ID RELEASE 55	5654228	0.4150	0.0091	ADCY9
REACTOME	R-HSA-164378.1	0.4943	0.1992	ADCY3
REACTOME	R-HSA-164378.1	0.4943	0.1992	ADCY9
REACTOME DATABASE ID RELEASE 55	163615	0.4478	0.0877	ADCY3
REACTOME DATABASE ID RELEASE 55	163615	0.4478	0.0877	ADCY9
REACTOME DATABASE ID RELEASE 55	111931	0.4419	0.0737	ADCY3
REACTOME DATABASE ID RELEASE 55	111931	0.4419	0.0737	ADCY9
REACTOME	R-HSA-112043.1	0.4219	0.0255	ADCY3
REACTOME	R-HSA-112043.1	0.4219	0.0255	ADCY9
REACTOME DATABASE ID RELEASE 55	167021	0.4450	0.0810	ADCY3
REACTOME DATABASE ID RELEASE 55	167021	0.4450	0.0810	ADCY9
REACTOME DATABASE ID RELEASE 55	1251932	0.4736	0.1496	ADCY3
REACTOME DATABASE ID RELEASE 55	1251932	0.4736	0.1496	ADCY9
GOBP	GO:0032743	0.4614	0.1202	PDE4D
REACTOME DATABASE ID RELEASE 55	438064	0.4256	0.0346	ADCY3
GOBP	GO:0009154	0.5344	0.2953	PDE4D
GOBP	GO:0072523	0.4459	0.0831	AOX1
GOBP	GO:0072523	0.4459	0.0831	PDE4D
GOBP	GO:0086004	0.4661	0.1315	PDE4D
GOBP	GO:0010649	0.4786	0.1615	PDE4D
GOBP	GO:0010880	0.4741	0.1507	PDE4D
GOBP	GO:0009261	0.5100	0.2368	PDE4D
GOBP	GO:0034332	0.4359	0.0593	CDH2
REACTOME	R-HSA-418990.2	0.5433	0.3166	CDH2
GOBP	GO:0097296	0.4650	0.1290	CASP8
GOBP	GO:0097296	0.4650	0.1290	CFLAR
GOBP	GO:0006309	0.4490	0.0906	DFFA
MSIGDB_C2	BIOCARTA_CASPA	0.4325	0.0510	DFFA
MSIGDB_C2	BIOCARTA_CASPA	0.4325	0.0510	CASP8
MSIGDB_C2	BIOCARTA_DEATH	0.4502	0.0934	DFFA
MSIGDB_C2	BIOCARTA_DEATH	0.4502	0.0934	CASP8
MSIGDB_C2	BIOCARTA_DEATH	0.4502	0.0934	CFLAR
MSIGDB_C2	BIOCARTA_FAS_P	0.4661	0.1315	DFFA
MSIGDB_C2	BIOCARTA_FAS_P	0.4661	0.1315	CASP8
MSIGDB_C2	BIOCARTA_FAS_P	0.4661	0.1315	CFLAR
MSIGDB_C2	BIOCARTA_SODD_	0.4379	0.0640	CASP8
REACTOME DATABASE ID RELEASE 55	5218900	0.4860	0.1793	CASP8

REACTOME DATABASE ID RELEASE 55	69416	0.4860	0.1793	CASP8
GOBP	GO:0001701	0.4212	0.0239	CASP8
GOBP	GO:0030225	0.5281	0.2802	CASP8
GOBP	GO:2001240	0.5273	0.2784	TERT
GOBP	GO:0010832	0.4220	0.0260	CFLAR
GOBP	GO:1901099	0.5273	0.2784	TERT
GOBP	GO:0051154	0.4127	0.0035	CFLAR
GOBP	GO:2001269	0.4279	0.0401	CASP8
GOBP	GO:2001269	0.4279	0.0401	CFLAR
REACTOME	R-HSA-3371378.1	0.4860	0.1793	CASP8
GOBP	GO:1900117	0.4943	0.1993	DFFA
GOBP	GO:1900117	0.4943	0.1993	CDKN2A
GOBP	GO:2001239	0.4922	0.1941	TERT
GOBP	GO:0045649	0.4404	0.0701	CASP8
MSIGDB_C2	SA_CASPASE_CAS	0.5552	0.3451	DFFA
MSIGDB_C2	SA_CASPASE_CAS	0.5552	0.3451	CASP8
REACTOME	R-HSA-5357786.2	0.4783	0.1608	CASP8
PATHWAY INTERACTION DATABASE NCI-NA	TRAIL SIGNALING	0.4312	0.0480	CASP8
PATHWAY INTERACTION DATABASE NCI-NA	TRAIL SIGNALING	0.4312	0.0480	CFLAR
REACTOME DATABASE ID RELEASE 55	2562578	0.4260	0.0353	CASP8
MSIGDB_C2	BIOCARTA_ACH_F	0.5688	0.3778	TERT
MSIGDB_C2	BIOCARTA_TEL_P/	0.6706	0.6217	TERT
GOBP	GO:0007569	0.4542	0.1031	TERT
GOBP	GO:0007569	0.4542	0.1031	CDKN2A
GOBP	GO:0007569	0.4542	0.1031	ATM
GOBP	GO:0070199	0.6937	0.6773	TERT
GOBP	GO:0070199	0.6937	0.6773	BRCA2
REACTOME DATABASE ID RELEASE 55	180786	0.4875	0.1829	TERT
GOBP	GO:0070828	0.5417	0.3128	CDKN2A
GOBP	GO:0090344	0.6567	0.5885	TERT
GOBP	GO:0070198	0.6490	0.5701	TERT
GOBP	GO:0070198	0.6490	0.5701	BRCA2
GOBP	GO:0090342	0.5290	0.2824	TERT
GOBP	GO:0090342	0.5290	0.2824	CDKN2A
GOBP	GO:2000772	0.5862	0.4195	TERT
GOBP	GO:2000772	0.5862	0.4195	CDKN2A
GOBP	GO:1902893	0.6356	0.5379	TERT
GOBP	GO:0090399	0.8284	1.0000	TERT
GOBP	GO:0090399	0.8284	1.0000	CDKN2A
GOBP	GO:0090399	0.8284	1.0000	ATM
GOBP	GO:0006278	0.5843	0.4150	TERT
GOBP	GO:0006278	0.5843	0.4150	ATM
GOBP	GO:0007004	0.6456	0.5618	TERT
GOBP	GO:0007004	0.6456	0.5618	ATM
REACTOME DATABASE ID RELEASE 55	157579	0.4177	0.0155	TERT
MSIGDB_C2	BIOCARTA_G1_P/	0.4355	0.0581	CDKN2A
MSIGDB_C2	BIOCARTA_G1_P/	0.4355	0.0581	ATM
MSIGDB_C2	BIOCARTA_G1_P/	0.4355	0.0581	CCNE1
MSIGDB_C2	BIOCARTA_P53_P	0.4658	0.1309	ATM
MSIGDB_C2	BIOCARTA_P53_P	0.4658	0.1309	CCNE1
PANTHER PATHWAY	P00013	0.4198	0.0205	CCNE1

PATHWAY INTERACTION DATABASE NCI-NA	FOXM1 TRANSCRI	0.4407	0.0708	ESR1
PATHWAY INTERACTION DATABASE NCI-NA	FOXM1 TRANSCRI	0.4407	0.0708	CDKN2A
PATHWAY INTERACTION DATABASE NCI-NA	FOXM1 TRANSCRI	0.4407	0.0708	BRCA2
PATHWAY INTERACTION DATABASE NCI-NA	FOXM1 TRANSCRI	0.4407	0.0708	CCNE1
GOBP	GO:0031572	0.5234	0.2690	BABAM1
GOBP	GO:0031572	0.5234	0.2690	ATM
GOBP	GO:0044818	0.4708	0.1428	ATM
GOBP	GO:0050869	0.4305	0.0463	CDKN2A
GOBP	GO:0050869	0.4305	0.0463	ATM
GOBP	GO:0010972	0.4125	0.0031	ATM
GOBP	GO:1902751	0.4123	0.0026	RAD51B
GOBP	GO:0043517	0.5451	0.3210	CDKN2A
GOBP	GO:0043517	0.5451	0.3210	ATM
GOBP	GO:0010971	0.4602	0.1173	RAD51B
GOBP	GO:1901798	0.4790	0.1625	CDKN2A
GOBP	GO:1901798	0.4790	0.1625	ATM
MSIGDB_C2	SA_REG_CASCADI	0.5062	0.2278	CDKN2A
MSIGDB_C2	SA_REG_CASCADI	0.5062	0.2278	CCNE1
GOBP	GO:0048103	0.4686	0.1377	CDKN2A
GOBP	GO:0035510	0.4665	0.1324	FTO
GOBP	GO:0080111	0.4312	0.0478	FTO
MSIGDB_C2	BIOCARTA_ATRBF	0.4567	0.1090	ATM
MSIGDB_C2	BIOCARTA_ATRBF	0.4567	0.1090	BRCA2
GOBP	GO:0071480	0.4696	0.1401	ATM
REACTOME DATABASE ID RELEASE 55	5693606	0.4353	0.0577	BABAM1
REACTOME DATABASE ID RELEASE 55	5693606	0.4353	0.0577	ATM
GOBP	GO:0045003	0.4201	0.0214	ATM
GOBP	GO:0045003	0.4201	0.0214	BRCA2
GOBP	GO:0045003	0.4201	0.0214	RAD51B
REACTOME	R-HSA-69473.2	0.4241	0.0309	BABAM1
REACTOME	R-HSA-69473.2	0.4241	0.0309	ATM
REACTOME	R-HSA-5693571.1	0.4639	0.1264	BABAM1
REACTOME	R-HSA-5693571.1	0.4639	0.1264	ATM
GOBP	GO:0045739	0.4394	0.0675	BABAM1
REACTOME	R-HSA-5693565.1	0.4405	0.0703	BABAM1
REACTOME	R-HSA-5693565.1	0.4405	0.0703	ATM
REACTOME DATABASE ID RELEASE 55	5693554	0.4355	0.0583	ATM
REACTOME DATABASE ID RELEASE 55	5693554	0.4355	0.0583	BRCA2
REACTOME DATABASE ID RELEASE 55	5693554	0.4355	0.0583	RAD51B
GOBP	GO:0061037	0.5215	0.2643	PTHLH
GOBP	GO:0032331	0.5077	0.2314	PTHLH
GOBP	GO:0061035	0.4875	0.1829	PTHLH
GOBP	GO:0032330	0.4995	0.2117	PTHLH
MSIGDB_C2	BIOCARTA_CARM	0.4438	0.0781	ESR1
MSIGDB_C2	BIOCARTA_HER2_	0.4821	0.1698	ESR1
MSIGDB_C2	BIOCARTA_MTA3	0.4838	0.1741	ESR1
REACTOME	R-HSA-1368108.1	0.5209	0.2630	NCOA1
GOBP	GO:0097306	0.4181	0.0166	ESR1
GOBP	GO:0071392	0.5780	0.3998	ESR1
GOBP	GO:0071391	0.4833	0.1728	ESR1
REACTOME	R-HSA-400253.1	0.4437	0.0779	NCOA1

REACTOME	R-HSA-400253.1	0.4437	0.0779	PPP1CB
GOBP	GO:0030520	0.5593	0.3550	ESR1
GOBP	GO:0030518	0.4217	0.0251	ESR1
GOBP	GO:0030518	0.4217	0.0251	CCNE1
GOBP	GO:0030518	0.4217	0.0251	NCOA1
REACTOME	R-HSA-383280.1	0.4767	0.1569	ESR1
REACTOME	R-HSA-383280.1	0.4767	0.1569	NR2F6
REACTOME	R-HSA-383280.1	0.4767	0.1569	HNF4G
REACTOME DATABASE ID RELEASE 55	1251985	0.4518	0.0973	ESR1
GOBP	GO:0032355	0.4796	0.1640	ESR1
REACTOME	R-HSA-1368082.1	0.5497	0.3319	NCOA1
PATHWAY INTERACTION DATABASE NCI-NA	SIGNALING EVENT	0.5074	0.2305	ESR1
PATHWAY INTERACTION DATABASE NCI-NA	SIGNALING MEDI/	0.4406	0.0705	ESR1
GOBP	GO:0071359	0.4562	0.1079	TERT
GOBP	GO:0071359	0.4562	0.1079	RALB
GOBP	GO:0071360	0.4569	0.1096	RALB
GOBP	GO:0031050	0.5095	0.2356	TERT
GOBP	GO:0060969	0.6892	0.6664	TERT
GOBP	GO:0035194	0.4124	0.0028	TERT
GOBP	GO:0035194	0.4124	0.0028	TNRC6B
GOBP	GO:0016441	0.4112	0.0000	TERT
GOBP	GO:0016441	0.4112	0.0000	TNRC6B
GOBP	GO:0070918	0.5095	0.2356	TERT
GOBP	GO:0060966	0.6605	0.5975	TERT
GOBP	GO:0060968	0.5325	0.2909	TERT
GOBP	GO:0060147	0.6605	0.5975	TERT
GOBP	GO:0016246	0.6554	0.5855	TERT
GOBP	GO:0032770	0.6466	0.5642	TERT
GOBP	GO:0032770	0.6466	0.5642	ESR1
GOBP	GO:0045429	0.4481	0.0885	ESR1
GOBP	GO:1904407	0.4481	0.0885	ESR1
GOBP	GO:0051000	0.7346	0.7752	TERT
GOBP	GO:0051000	0.7346	0.7752	ESR1
GOBP	GO:0051353	0.5059	0.2270	TERT
GOBP	GO:0051353	0.5059	0.2270	ESR1
GOBP	GO:1903428	0.4215	0.0247	ESR1
GOBP	GO:0032768	0.4148	0.0086	TERT
GOBP	GO:0032768	0.4148	0.0086	ESR1
GOBP	GO:0050999	0.4699	0.1406	TERT
GOBP	GO:0050999	0.4699	0.1406	ESR1
GOBP	GO:0032924	0.5005	0.2140	INHBB
GOBP	GO:0046545	0.4333	0.0530	INHBB
GOBP	GO:0008585	0.4333	0.0530	INHBB
GOBP	GO:0042036	0.5133	0.2446	INHBB
GOBP	GO:0046676	0.4505	0.0941	INHBB
GOBP	GO:0090278	0.4322	0.0504	INHBB
GOBP	GO:0002792	0.4126	0.0034	INHBB
GOBP	GO:0001541	0.4579	0.1120	INHBB
GOBP	GO:0022602	0.4414	0.0724	INHBB
GOBP	GO:0042698	0.4182	0.0167	INHBB
GOBP	GO:2000243	0.4991	0.2106	INHBB

GOBP	GO:0044060	0.4149	0.0088	INHBB
REACTOME DATABASE ID RELEASE 55	1502540	0.5210	0.2631	INHBB
GOBP	GO:0071870	0.4291	0.0429	PDE4D
GOBP	GO:0071868	0.4291	0.0429	PDE4D
GOBP	GO:0071869	0.4291	0.0429	PDE4D
GOBP	GO:0071867	0.4291	0.0429	PDE4D
REACTOME	R-HSA-201722.2	0.4371	0.0620	TERT
REACTOME	R-HSA-201722.2	0.4371	0.0620	TCF7L2
REACTOME DATABASE ID RELEASE 55	4641265	0.4123	0.0027	TCF7L2
GOBP	GO:0007340	0.4709	0.1432	ADCY3
GOBP	GO:0031532	0.4347	0.0564	FRY
REACTOME	R-HSA-425374.1	0.4182	0.0167	SLC6A18
REACTOME DATABASE ID RELEASE 55	352230	0.5339	0.2940	SLC6A18
MSIGDB_C2	BIOCARTA_DNAFI	0.5028	0.2196	DFFA
MSIGDB_C2	BIOCARTA_RARRX	0.4764	0.1562	NCOA1
MSIGDB_C2	BIOCARTA_SET_P	0.4608	0.1188	DFFA
MSIGDB_C2	BIOCARTA_VDR_F	0.4843	0.1751	NCOA1
GOBP	GO:0008037	0.4248	0.0325	KCNU1
GOBP	GO:0051304	0.4932	0.1966	APITD1
REACTOME DATABASE ID RELEASE 55	209822	0.4456	0.0825	INHBB
PANTHER PATHWAY	P00033	0.4207	0.0227	MDM4
GOBP	GO:0034453	0.4252	0.0336	PEX14
GOBP	GO:0000963	0.5413	0.3119	GTPBP3
GOBP	GO:0000963	0.5413	0.3119	TRMT61B
GOBP	GO:0045445	0.5165	0.2523	TCF7L2
PATHWAY INTERACTION DATABASE NCI-NA	N-CADHERIN SIGN	0.4122	0.0024	CDH2
GOBP	GO:0090005	0.4264	0.0363	ANXA13
GOBP	GO:0097150	0.5715	0.3843	CDH2
REACTOME DATABASE ID RELEASE 55	171007	0.4664	0.1323	RALB
REACTOME DATABASE ID RELEASE 55	209952	0.4670	0.1338	INHBB
GOBP	GO:0014065	0.4647	0.1281	PIK3C2B
GOBP	GO:0036092	0.6415	0.5520	PIK3C2B
GOBP	GO:0036092	0.6415	0.5520	ATM
GOBP	GO:0050857	0.4366	0.0608	KCNN4
GOBP	GO:0010560	0.4915	0.1924	TCF7L2
GOBP	GO:1903020	0.4440	0.0786	TCF7L2
GOBP	GO:0046827	0.5167	0.2529	TCF7L2
GOBP	GO:0016558	0.4646	0.1280	PEX14
GOBP	GO:0070536	0.5459	0.3228	BABAM1
GOBP	GO:0070528	0.4710	0.1434	PLVAP
GOBP	GO:0032486	0.4819	0.1695	SGSM3
GOBP	GO:0002691	0.5444	0.3194	PLVAP
GOBP	GO:0032350	0.4184	0.0172	TCF7L2
GOBP	GO:1901739	0.4467	0.0852	CFLAR
GOBP	GO:0046825	0.5059	0.2271	CDKN2A
GOBP	GO:0046825	0.5059	0.2271	TCF7L2
GOBP	GO:0032462	0.5224	0.2666	PEX14
PATHWAY INTERACTION DATABASE NCI-NA	SIGNALING EVENT	0.4896	0.1880	PTHLH
GOBP	GO:0051145	0.4252	0.0336	MKL1
GOBP	GO:0042246	0.4795	0.1637	CFLAR
GOBP	GO:0070525	0.5931	0.4360	GTPBP3

GOBP	GO:0070525	0.5931	0.4360	TRMT61B
REACTOME DATABASE ID RELEASE 55	2032785	0.4338	0.0543	NCOA1

)-min(ES))

Number of SNPs in gene	SNP with lowest P-value	P-value	Distance to gene from SNP (bp)	Appears in Supplementary Figure 14
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
8,270	5_58429733_C_T	1.7×10^{-8}	0	Yes
1,366	12_28174817_C_T	2.3×10^{-31}	49901	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
8,270	5_58429733_C_T	1.7×10^{-8}	0	Yes
427	22_41059171_A_G	7.7×10^{-12}	16010	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
56	1_10506667_G_A	1.7×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
8,270	5_58429733_C_T	1.7×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
1,366	12_28174817_C_T	2.3×10^{-31}	49901	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
8,270	5_58429733_C_T	1.7×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
8,270	5_58429733_C_T	1.7×10^{-8}	0	Yes
1,366	12_28174817_C_T	2.3×10^{-31}	49901	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
8,270	5_58429733_C_T	1.7×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
8,270	5_58429733_C_T	1.7×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes

836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
8,270	5_58429733_C_T	1.7×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
1,630	16_4106788_C_A	1.4×10^{-8}	0	Yes
8,270	5_58429733_C_T	1.7×10^{-8}	0	Yes
836	2_25129473_A_G	1.3×10^{-8}	0	Yes
8,270	5_58429733_C_T	1.7×10^{-8}	0	Yes
570	2_201524267_A_C	5.4×10^{-10}	0	Yes
8,270	5_58429733_C_T	1.7×10^{-8}	0	Yes
8,270	5_58429733_C_T	1.7×10^{-8}	0	Yes
8,270	5_58429733_C_T	1.7×10^{-8}	0	Yes
8,270	5_58429733_C_T	1.7×10^{-8}	0	Yes
8,270	5_58429733_C_T	1.7×10^{-8}	0	Yes
5,742	18_25401204_AT_A	1.4×10^{-8}	129725	
5,742	18_25401204_AT_A	1.4×10^{-8}	129725	
321	2_202122995_A_G	3.2×10^{-11}	0	
323	2_202004837_G_C	3.1×10^{-9}	0	
112	1_10537437_C_G	2.0×10^{-20}	0	
112	1_10537437_C_G	2.0×10^{-20}	0	
321	2_202122995_A_G	3.2×10^{-11}	0	
112	1_10537437_C_G	2.0×10^{-20}	0	
321	2_202122995_A_G	3.2×10^{-11}	0	
323	2_202004837_G_C	3.1×10^{-9}	0	
112	1_10537437_C_G	2.0×10^{-20}	0	
321	2_202122995_A_G	3.2×10^{-11}	0	
323	2_202004837_G_C	3.1×10^{-9}	0	
321	2_202122995_A_G	3.2×10^{-11}	0	
321	2_202122995_A_G	3.2×10^{-11}	0	

321	2_202122995_A_G	3.2×10^{-11}	0
321	2_202122995_A_G	3.2×10^{-11}	0
321	2_202122995_A_G	3.2×10^{-11}	0
381	5_1279790_C_T	1.9×10^{-49}	0
323	2_202004837_G_C	3.1×10^{-9}	0
381	5_1279790_C_T	1.9×10^{-49}	0
323	2_202004837_G_C	3.1×10^{-9}	0
321	2_202122995_A_G	3.2×10^{-11}	0
323	2_202004837_G_C	3.1×10^{-9}	0
321	2_202122995_A_G	3.2×10^{-11}	0
112	1_10537437_C_G	2.0×10^{-20}	0
170	9_21963048_C_T	4.3×10^{-15}	0
381	5_1279790_C_T	1.9×10^{-49}	0
321	2_202122995_A_G	3.2×10^{-11}	0
112	1_10537437_C_G	2.0×10^{-20}	0
321	2_202122995_A_G	3.2×10^{-11}	0
321	2_202122995_A_G	3.2×10^{-11}	0
321	2_202122995_A_G	3.2×10^{-11}	0
323	2_202004837_G_C	3.1×10^{-9}	0
321	2_202122995_A_G	3.2×10^{-11}	0
381	5_1279790_C_T	1.9×10^{-49}	0
381	5_1279790_C_T	1.9×10^{-49}	0
381	5_1279790_C_T	1.9×10^{-49}	0
170	9_21963048_C_T	4.3×10^{-15}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
381	5_1279790_C_T	1.9×10^{-49}	0
485	13_32972626_A_T	2.5×10^{-11}	0
381	5_1279790_C_T	1.9×10^{-49}	0
170	9_21963048_C_T	4.3×10^{-15}	0
381	5_1279790_C_T	1.9×10^{-49}	0
381	5_1279790_C_T	1.9×10^{-49}	0
485	13_32972626_A_T	2.5×10^{-11}	0
381	5_1279790_C_T	1.9×10^{-49}	0
170	9_21963048_C_T	4.3×10^{-15}	0
381	5_1279790_C_T	1.9×10^{-49}	0
170	9_21963048_C_T	4.3×10^{-15}	0
381	5_1279790_C_T	1.9×10^{-49}	0
381	5_1279790_C_T	1.9×10^{-49}	0
170	9_21963048_C_T	4.3×10^{-15}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
381	5_1279790_C_T	1.9×10^{-49}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
381	5_1279790_C_T	1.9×10^{-49}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
381	5_1279790_C_T	1.9×10^{-49}	0
170	9_21963048_C_T	4.3×10^{-15}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
755	19_30277729_C_T	6.8×10^{-9}	25171
701	11_108098459_TAA_T	2.5×10^{-12}	0
755	19_30277729_C_T	6.8×10^{-9}	25171
755	19_30277729_C_T	6.8×10^{-9}	25171

2,783	6_151985574_T_C	8.9×10^{-39}	26056
170	9_21963048_C_T	4.3×10^{-15}	0
485	13_32972626_A_T	2.5×10^{-11}	0
755	19_30277729_C_T	6.8×10^{-9}	25171
141	19_17393925_C_A	4.7×10^{-53}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
170	9_21963048_C_T	4.3×10^{-15}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
4,358	14_69029203_C_T	1.1×10^{-10}	0
170	9_21963048_C_T	4.3×10^{-15}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
4,358	14_69029203_C_T	1.1×10^{-10}	0
170	9_21963048_C_T	4.3×10^{-15}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
170	9_21963048_C_T	4.3×10^{-15}	0
755	19_30277729_C_T	6.8×10^{-9}	25171
170	9_21963048_C_T	4.3×10^{-15}	0
3,106	16_53809123_C_T	6.0×10^{-14}	0
3,106	16_53809123_C_T	6.0×10^{-14}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
485	13_32972626_A_T	2.5×10^{-11}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
141	19_17393925_C_A	4.7×10^{-53}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
485	13_32972626_A_T	2.5×10^{-11}	0
4,358	14_69029203_C_T	1.1×10^{-10}	0
141	19_17393925_C_A	4.7×10^{-53}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
141	19_17393925_C_A	4.7×10^{-53}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
141	19_17393925_C_A	4.7×10^{-53}	0
141	19_17393925_C_A	4.7×10^{-53}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
485	13_32972626_A_T	2.5×10^{-11}	0
4,358	14_69029203_C_T	1.1×10^{-10}	0
1,366	12_28174817_C_T	2.3×10^{-31}	49901
1,366	12_28174817_C_T	2.3×10^{-31}	49901
1,366	12_28174817_C_T	2.3×10^{-31}	49901
1,366	12_28174817_C_T	2.3×10^{-31}	49901
2,783	6_151985574_T_C	8.9×10^{-39}	26056
2,783	6_151985574_T_C	8.9×10^{-39}	26056
2,783	6_151985574_T_C	8.9×10^{-39}	26056
1,426	2_24739694_C_CT	9.7×10^{-9}	67651
2,783	6_151985574_T_C	8.9×10^{-39}	26056
2,783	6_151985574_T_C	8.9×10^{-39}	26056
2,783	6_151985574_T_C	8.9×10^{-39}	26056
1,426	2_24739694_C_CT	9.7×10^{-9}	67651

575	2_28956786_G_A	1.2×10^{-8}	17827
2,783	6_151985574_T_C	8.9×10^{-39}	26056
2,783	6_151985574_T_C	8.9×10^{-39}	26056
755	19_30277729_C_T	6.8×10^{-9}	25171
1,426	2_24739694_C_CT	9.7×10^{-9}	67651
2,783	6_151985574_T_C	8.9×10^{-39}	26056
187	19_17359535_C_T	9.4×10^{-32}	0
3,619	8_76360637_A_G	1.2×10^{-8}	91565
2,783	6_151985574_T_C	8.9×10^{-39}	26056
2,783	6_151985574_T_C	8.9×10^{-39}	26056
1,426	2_24739694_C_CT	9.7×10^{-9}	67651
2,783	6_151985574_T_C	8.9×10^{-39}	26056
2,783	6_151985574_T_C	8.9×10^{-39}	26056
381	5_1279790_C_T	1.9×10^{-49}	0
447	2_121077184_A_G	1.2×10^{-13}	24898
447	2_121077184_A_G	1.2×10^{-13}	24898
381	5_1279790_C_T	1.9×10^{-49}	0
381	5_1279790_C_T	1.9×10^{-49}	0
381	5_1279790_C_T	1.9×10^{-49}	0
1,327	22_40734189_G_GA	8.3×10^{-11}	0
381	5_1279790_C_T	1.9×10^{-49}	0
1,327	22_40734189_G_GA	8.3×10^{-11}	0
381	5_1279790_C_T	1.9×10^{-49}	0
381	5_1279790_C_T	1.9×10^{-49}	0
381	5_1279790_C_T	1.9×10^{-49}	0
381	5_1279790_C_T	1.9×10^{-49}	0
381	5_1279790_C_T	1.9×10^{-49}	0
381	5_1279790_C_T	1.9×10^{-49}	0
2,783	6_151985574_T_C	8.9×10^{-39}	26056
2,783	6_151985574_T_C	8.9×10^{-39}	26056
2,783	6_151985574_T_C	8.9×10^{-39}	26056
381	5_1279790_C_T	1.9×10^{-49}	0
2,783	6_151985574_T_C	8.9×10^{-39}	26056
381	5_1279790_C_T	1.9×10^{-49}	0
2,783	6_151985574_T_C	8.9×10^{-39}	26056
2,783	6_151985574_T_C	8.9×10^{-39}	26056
381	5_1279790_C_T	1.9×10^{-49}	0
2,783	6_151985574_T_C	8.9×10^{-39}	26056
381	5_1279790_C_T	1.9×10^{-49}	0
2,783	6_151985574_T_C	8.9×10^{-39}	26056
605	2_121079515_A_C	9.3×10^{-18}	24203
605	2_121079515_A_C	9.3×10^{-18}	24203
605	2_121079515_A_C	9.3×10^{-18}	24203
605	2_121079515_A_C	9.3×10^{-18}	24203
605	2_121079515_A_C	9.3×10^{-18}	24203
605	2_121079515_A_C	9.3×10^{-18}	24203
605	2_121079515_A_C	9.3×10^{-18}	24203
605	2_121079515_A_C	9.3×10^{-18}	24203
605	2_121079515_A_C	9.3×10^{-18}	24203
605	2_121079515_A_C	9.3×10^{-18}	24203
605	2_121079515_A_C	9.3×10^{-18}	24203

605	2_121079515_A_C	9.3×10^{-18}	24203
605	2_121079515_A_C	9.3×10^{-18}	24203
8,270	5_58429733_C_T	1.7×10^{-8}	0
8,270	5_58429733_C_T	1.7×10^{-8}	0
8,270	5_58429733_C_T	1.7×10^{-8}	0
8,270	5_58429733_C_T	1.7×10^{-8}	0
381	5_1279790_C_T	1.9×10^{-49}	0
2,437	10_114782803_T_C	6.5×10^{-15}	0
2,437	10_114782803_T_C	6.5×10^{-15}	0
836	2_25129473_A_G	1.3×10^{-8}	0
1,573	927_CAATAAATAAATA_CA	2.0×10^{-12}	0
290	5_1241565_A_G	8.4×10^{-13}	0
290	5_1241565_A_G	8.4×10^{-13}	0
112	1_10537437_C_G	2.0×10^{-20}	0
1,426	2_24739694_C_CT	9.7×10^{-9}	67651
112	1_10537437_C_G	2.0×10^{-20}	0
1,426	2_24739694_C_CT	9.7×10^{-9}	67651
3,952	8_36849946_C_G	2.8×10^{-12}	56303
154	L0491895_A_AGCGAGACT	4.6×10^{-9}	0
605	2_121079515_A_C	9.3×10^{-18}	24203
527	1_204518842_C_A	7.0×10^{-26}	0
813	1_10566272_C_T	9.7×10^{-22}	0
118	19_17456375_TCTC_T	1.4×10^{-23}	0
217	2_29094032_C_A	8.6×10^{-9}	0
2,437	10_114782803_T_C	6.5×10^{-15}	0
5,742	18_25401204_AT_A	1.4×10^{-8}	129725
541	8_124757661_C_T	1.7×10^{-11}	8014
5,742	18_25401204_AT_A	1.4×10^{-8}	129725
447	2_121077184_A_G	1.2×10^{-13}	24898
605	2_121079515_A_C	9.3×10^{-18}	24203
533	1_204464181_C_T	1.0×10^{-24}	0
533	1_204464181_C_T	1.0×10^{-24}	0
701	11_108098459_TAA_T	2.5×10^{-12}	0
182	19_44281824_C_CTCTT	2.7×10^{-9}	0
2,437	10_114782803_T_C	6.5×10^{-15}	0
2,437	10_114782803_T_C	6.5×10^{-15}	0
2,437	10_114782803_T_C	6.5×10^{-15}	0
813	1_10566272_C_T	9.7×10^{-22}	0
141	19_17393925_C_A	4.7×10^{-53}	0
308	19_17462094_T_G	1.3×10^{-26}	0
196	22_40810946_T_C	1.6×10^{-11}	0
308	19_17462094_T_G	1.3×10^{-26}	0
2,437	10_114782803_T_C	6.5×10^{-15}	0
323	2_202004837_G_C	3.1×10^{-9}	0
170	9_21963048_C_T	4.3×10^{-15}	0
2,437	10_114782803_T_C	6.5×10^{-15}	0
813	1_10566272_C_T	9.7×10^{-22}	0
1,366	12_28174817_C_T	2.3×10^{-31}	49901
1,176	22_40904707_CT_C	4.0×10^{-13}	0
323	2_202004837_G_C	3.1×10^{-9}	0
118	19_17456375_TCTC_T	1.4×10^{-23}	0

| 217 | 2_29094032_C_A | 8.6×10^{-9} | 0 |
| 1,426 | 2_24739694_C_CT | 9.7×10^{-9} | 67651 |

Supplementary Table 13: Detailed information about themes and unique genes appearing in the enrichment maps (Supplementary Fig

Theme	Gene	Number of SNPs in gene	SNP with lowest P-value	P-value	Distance to gene from SNP (bp)
ADENYLATE CYCLASE	PTHLH	1,366	12_28174817_C_T	2.3×10^{-31}	49901
ADENYLATE CYCLASE	MCHR1	427	22_41059171_A_G	7.6×10^{-12}	16010
ADENYLATE CYCLASE	AOX1	570	2_201524267_A_C	5.4×10^{-10}	0
ADENYLATE CYCLASE	ADCY3	836	2_25129473_A_G	1.3×10^{-8}	0
ADENYLATE CYCLASE	ADCY9	1,630	16_4106788_C_A	1.4×10^{-8}	0
ADENYLATE CYCLASE	PDE4D	8,270	5_58429733_C_T	1.7×10^{-8}	0
ADENYLATE CYCLASE	CORT	56	1_10506667_G_A	1.7×10^{-8}	0
ADHERENS JUNCTION	CDH2	5,742	18_25401204_AT_A	1.4×10^{-8}	129725
APOPTOSIS	TERT	381	5_1279790_C_T	1.9×10^{-49}	0
APOPTOSIS	DFFA	112	1_10537437_C_G	2.0×10^{-20}	0
APOPTOSIS	CDKN2A	170	9_21963048_C_T	4.3×10^{-15}	0
APOPTOSIS	CASP8	321	2_202122995_A_G	3.2×10^{-11}	0
APOPTOSIS	CFLAR	323	2_202004837_G_C	3.1×10^{-9}	0
CELL AGING/TELOMERE	TERT	381	5_1279790_C_T	1.9×10^{-49}	0
CELL AGING/TELOMERE	CDKN2A	170	9_21963048_C_T	4.3×10^{-15}	0
CELL AGING/TELOMERE	ATM	701	11_108098459_TAA_T	2.5×10^{-12}	0
CELL AGING/TELOMERE	BRCA2	485	13_32972626_A_T	2.5×10^{-11}	0
CELL CYCLE/DNA DAMAGE RESPONSE	BABAM1	141	19_17393925_C_A	4.7×10^{-53}	0
CELL CYCLE/DNA DAMAGE RESPONSE	ESR1	2,783	6_151985574_T_C	8.9×10^{-39}	26056
CELL CYCLE/DNA DAMAGE RESPONSE	CDKN2A	170	9_21963048_C_T	4.3×10^{-15}	0
CELL CYCLE/DNA DAMAGE RESPONSE	ATM	701	11_108098459_TAA_T	2.5×10^{-12}	0
CELL CYCLE/DNA DAMAGE RESPONSE	BRCA2	485	13_32972626_A_T	2.5×10^{-11}	0
CELL CYCLE/DNA DAMAGE RESPONSE	RAD51B	4,358	14_69029203_C_T	1.1×10^{-10}	0
CELL CYCLE/DNA DAMAGE RESPONSE	CCNE1	755	19_30277729_C_T	6.8×10^{-9}	25171
DNA DEMETHYLATION/DEALKYLATION	FTO	3,106	16_53809123_C_T	6.0×10^{-14}	0
DOUBLE STRAND BREAK REPAIR	BABAM1	141	19_17393925_C_A	4.7×10^{-53}	0
DOUBLE STRAND BREAK REPAIR	ATM	701	11_108098459_TAA_T	2.5×10^{-12}	0
DOUBLE STRAND BREAK REPAIR	BRCA2	485	13_32972626_A_T	2.5×10^{-11}	0
DOUBLE STRAND BREAK REPAIR	RAD51B	4,358	14_69029203_C_T	1.1×10^{-10}	0
EPITHELIAL-MESENCHYMAL INTERACTIONS	PTHLH	1,366	12_28174817_C_T	2.3×10^{-31}	49901
ESTROGEN RECEPTOR SIGNALING	ESR1	2,783	6_151985574_T_C	8.9×10^{-39}	26056
ESTROGEN RECEPTOR SIGNALING	NR2F6	187	19_17359535_C_T	9.4×10^{-32}	0
ESTROGEN RECEPTOR SIGNALING	CCNE1	755	19_30277729_C_T	6.8×10^{-9}	25171
ESTROGEN RECEPTOR SIGNALING	NCOA1	1,426	2_24739694_C_CT	9.7×10^{-9}	67651
ESTROGEN RECEPTOR SIGNALING	HNF4G	3,619	8_76360637_A_G	1.2×10^{-8}	91565
ESTROGEN RECEPTOR SIGNALING	PPP1CB	575	2_28956786_G_A	1.2×10^{-8}	17827
GENE SILENCING	TERT	381	5_1279790_C_T	1.9×10^{-49}	0
GENE SILENCING	RALB	447	2_121077184_A_G	1.2×10^{-13}	24898
GENE SILENCING	TNRC6B	1,327	22_40734189_G_GA	8.3×10^{-11}	0
REGULATION OF NITRIC OXIDE METABOLISM	TERT	381	5_1279790_C_T	1.9×10^{-49}	0
REGULATION OF NITRIC OXIDE METABOLISM	ESR1	2,783	6_151985574_T_C	8.9×10^{-39}	26056
REPRODUCTIVE SYSTEM	INHBB	605	2_121079515_A_C	9.3×10^{-18}	24203
RESPONSE TO CATECHOLAMINE	PDE4D	8,270	5_58429733_C_T	1.7×10^{-8}	0
WNT/BETA CATENIN	TERT	381	5_1279790_C_T	1.9×10^{-49}	0
WNT/BETA CATENIN	TCF7L2	2,437	10_114782803_T_C	6.5×10^{-15}	0
OTHER-NOT CLUSTERED	BABAM1	141	19_17393925_C_A	4.7×10^{-53}	0
OTHER-NOT CLUSTERED	PTHLH	1,366	12_28174817_C_T	2.3×10^{-31}	49901
OTHER-NOT CLUSTERED	PLVAP	308	19_17462094_T_G	1.3×10^{-26}	0
OTHER-NOT CLUSTERED	MDM4	527	1_204518842_C_A	7.0×10^{-26}	0
OTHER-NOT CLUSTERED	PIK3C2B	533	1_204464181_C_T	1.0×10^{-24}	0
OTHER-NOT CLUSTERED	GTPBP3	118	19_17456375_TCTC_T	1.3×10^{-23}	0
OTHER-NOT CLUSTERED	PEX14	813	1_10566272_C_T	9.7×10^{-22}	0
OTHER-NOT CLUSTERED	DFFA	112	1_10537437_C_G	2.0×10^{-20}	0
OTHER-NOT CLUSTERED	INHBB	605	2_121079515_A_C	9.3×10^{-18}	24203
OTHER-NOT CLUSTERED	CDKN2A	170	9_21963048_C_T	4.3×10^{-15}	0
OTHER-NOT CLUSTERED	TCF7L2	2,437	10_114782803_T_C	6.5×10^{-15}	0
OTHER-NOT CLUSTERED	RALB	447	2_121077184_A_G	1.2×10^{-13}	24898

OTHER-NOT CLUSTERED	MKL1	1,176	22_40904707_CT_C	$4.0x10^{-13}$	0
OTHER-NOT CLUSTERED	SLC6A18	290	5_1241565_A_G	$8.4x10^{-13}$	0
OTHER-NOT CLUSTERED	FRY	1,573	)27_CAATAAATAAATA_C	$2.0x10^{-12}$	0
OTHER-NOT CLUSTERED	ATM	701	11_108098459_TAA_T	$2.5x10^{-12}$	0
OTHER-NOT CLUSTERED	KCNU1	3,952	8_36849946_C_G	$2.8x10^{-12}$	56303
OTHER-NOT CLUSTERED	ANXA13	541	8_124757661_C_T	$1.7x10^{-11}$	8014
OTHER-NOT CLUSTERED	KCNN4	182	19_44281824_C_CTCTT	$2.7x10^{-9}$	0
OTHER-NOT CLUSTERED	CFLAR	323	2_202004837_G_C	$3.1x10^{-9}$	0
OTHER-NOT CLUSTERED	APITD1	154	0491895_A_AGCGAGAC	$4.6x10^{-9}$	0
OTHER-NOT CLUSTERED	TRMT61B	217	2_29094032_C_A	$8.6x10^{-9}$	0
OTHER-NOT CLUSTERED	NCOA1	1,426	2_24739694_C_CT	$9.7x10^{-9}$	67651
OTHER-NOT CLUSTERED	ADCY3	836	2_25129473_A_G	$1.3x10^{-8}$	0
OTHER-NOT CLUSTERED	CDH2	5,742	18_25401204_AT_A	$1.4x10^{-8}$	129725

ures 14-15)

Supplementary Table 14: Pathways enri

Theme

ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADENYLATE CYCLASE
ADHERENS JUNCTION
ADHERENS JUNCTION
APOPTOSIS
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
CELL CYCLE/DNA DAMAGE RESPONSE
DOUBLE STRAND BREAK REPAIR
DOUBLE STRAND BREAK REPAIR
GENE SILENCING
WNT/BETA CATENIN
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED
OTHER-NOT CLUSTERED

ched in susceptibility to ER-negative breast cancer (enrichment score [ES]≥0.41) but

Pathway
ACTIVATION OF PROTEIN KINASE A ACTIVITY
ADENYLATE CYCLASE ACTIVATING PATHWAY
ADENYLATE CYCLASE INHIBITORY PATHWAY
CA-DEPENDENT EVENTS
CALMODULIN INDUCED EVENTS
CAM PATHWAY
CAMP BIOSYNTHETIC PROCESS
INHIBITION OF ADENYLATE CYCLASE PATHWAY
LPA4-MEDIATED SIGNALING EVENTS
PKA-MEDIATED PHOSPHORYLATION OF CREB
PKA ACTIVATION
PKA ACTIVATION IN GLUCAGON SIGNALLING
ADHERENS JUNCTION ORGANIZATION
ADHERENS JUNCTIONS INTERACTIONS
APOPTOTIC DNA FRAGMENTATION
CELL CYCLE
G2 DNA DAMAGE CHECKPOINT
MITOTIC G2/M TRANSITION CHECKPOINT
NEGATIVE REGULATION OF G2/M TRANSITION OF MITOTIC CELL CYCLE
CELLULAR RESPONSE TO GAMMA RADIATION
NONHOMOLOGOUS END-JOINING (NHEJ)
CELLULAR RESPONSE TO EXOGENOUS DSRNA
REPRESSION OF WNT TARGET GENES
ACROSOME REACTION
AMINO ACID TRANSPORT ACROSS THE PLASMA MEMBRANE
BIOCARTA_DNAFRAGMENT_PATHWAY
BIOCARTA_RARRXR_PATHWAY
BIOCARTA_SET_PATHWAY
BIOCARTA_VDR_PATHWAY
CHROMOSOME SEPARATION
INSULIN IGF PATHWAY-PROTEIN KINASE B SIGNALING CASCADE
MITOCHONDRIAL RNA PROCESSING
MYOBLAST DIFFERENTIATION
N-CADHERIN SIGNALING EVENTS
NEGATIVE REGULATION OF ESTABLISHMENT OF PROTEIN LOCALIZATION TO PLASMA
NEURONAL STEM CELL POPULATION MAINTENANCE
P38MAPK EVENTS
POSITIVE REGULATION OF GLYCOPROTEIN BIOSYNTHETIC PROCESS
POSITIVE REGULATION OF GLYCOPROTEIN METABOLIC PROCESS
PROTEIN KINASE C SIGNALING
REGULATION OF CELLULAR EXTRAVASATION
REGULATION OF HORMONE METABOLIC PROCESS
REGULATION OF MYOBLAST FUSION
TISSUE REGENERATION
TRNA THREONYLCARBAMOYLADENOSINE METABOLIC PROCESS
YAP1- AND WWTR1 (TAZ)-STIMULATED GENE EXPRESSION

not ER-positive breast cancer (ES<0)

Database

GOBP
REACTOME DATABASE ID RELEASE 55
REACTOME
REACTOME
REACTOME
REACTOME
GOBP
REACTOME DATABASE ID RELEASE 55
PATHWAY INTERACTION DATABASE NCI-NATURE CURATED DATA
REACTOME DATABASE ID RELEASE 55
REACTOME DATABASE ID RELEASE 55
REACTOME
GOBP
REACTOME
GOBP
PANTHER PATHWAY
GOBP
GOBP
GOBP
GOBP
REACTOME
GOBP
REACTOME DATABASE ID RELEASE 55
GOBP
REACTOME DATABASE ID RELEASE 55
MSIGDB_C2
MSIGDB_C2
MSIGDB_C2
MSIGDB_C2
GOBP
PANTHER PATHWAY
GOBP
GOBP
PATHWAY INTERACTION DATABASE NCI-NATURE CURATED DATA
GOBP
GOBP
REACTOME DATABASE ID RELEASE 55
GOBP
GOBP
GOBP
GOBP
GOBP
GOBP
GOBP
GOBP
REACTOME DATABASE ID RELEASE 55

Pathway ID	Enrichment Score	Number of Genes	Genes
GO:0034199	0.52	16	ADCY3,ADCY9,F
170660	0.62	10	ADCY3,ADCY9,C
R-HSA-170670.1	0.55	14	ADCY3,ADCY9,C
R-HSA-111996.1	0.43	30	ADCY3,ADCY9,F
R-HSA-111933.1	0.42	28	ADCY3,ADCY9,F
R-HSA-111997.1	0.42	28	ADCY3,ADCY9,F
GO:0006171	0.47	16	ADCY3,ADCY9,C
997269	0.55	14	ADCY3,ADCY9,C
LPA4-MEDIATED SIGNALING EVENTS	0.55	15	ADCY3,ADCY9,C
111931	0.44	20	ADCY3,ADCY9,F
163615	0.45	19	ADCY3,ADCY9,F
R-HSA-164378.1	0.49	17	ADCY3,ADCY9,F
GO:0034332	0.44	60	CDH2,SORBS1,C
R-HSA-418990.2	0.54	29	CDH2,CDH8,CA
GO:0006309	0.45	13	DFFA,CECR2,DIC
P00013	0.42	14	CCNE1,RPA3,PS
GO:0031572	0.52	29	BABAM1,ATM,E
GO:0044818	0.47	15	ATM,HUS1B,FA
GO:0010972	0.41	17	ATM,HUS1B,FA
GO:0071480	0.47	11	ATM,XRCC6,ATI
R-HSA-5693571.1	0.46	36	BABAM1,ATM,T
GO:0071360	0.46	10	RALB,COLEC12,
4641265	0.41	13	TCF7L2,AES,TLE
GO:0007340	0.47	10	ADCY3,STX2,SY
352230	0.53	30	SLC6A18,SLC6A
BIOCARTA_DNAFRAGMENT_PATHWAY	0.50	10	DFFA,CASP3,GZ
BIOCARTA_RARRXR_PATHWAY	0.48	15	NCOA1,NCOA3,
BIOCARTA_SET_PATHWAY	0.46	11	DFFA,CREBBP,A
BIOCARTA_VDR_PATHWAY	0.48	12	NCOA1,NCOA3,
GO:0051304	0.49	15	APITD1,SMARC,
P00033	0.42	22	MDM4,FOXO1,
GO:0000963	0.54	14	GTPBP3,TRMT6
GO:0045445	0.52	20	TCF7L2,MYOCD
N-CADHERIN SIGNALING EVENTS	0.41	36	CDH2,PTPN1,RI
GO:0090005	0.43	12	ANXA13,PID1,L
GO:0097150	0.57	10	CDH2,DLL1,HES
171007	0.47	12	RALB,MAPKAPK
GO:0010560	0.49	14	TCF7L2,PLCB1,F
GO:1903020	0.44	16	TCF7L2,PLCB1,F
GO:0070528	0.47	13	PLVAP,SLC26A6
GO:0002691	0.54	13	PLVAP,PLCB1,PT
GO:0032350	0.42	17	TCF7L2,GATA3,
GO:1901739	0.45	10	CFLAR,CD53,MY
GO:0042246	0.48	13	CFLAR,EYS,IGF1
GO:0070525	0.59	12	GTPBP3,TRMT6
2032785	0.43	29	NCOA1,HIPK1,T

PRKAR1A,PRKAR2B,ADCY1,PRKACB,ADCY2,ADCY8,PRKACA,PRKAR2A,PRKACG,PRKAR1B,ADCY5,ADCY7,ADCY4,A

GNAL,ADCY1,ADCY2,ADCY8,ADCY5,ADCY7,ADCY4,ADCY6

GNAL,ADCY1,ADCY2,GNAI3,ADCY8,GNAT3,GNAI1,GNAI2,ADCY5,ADCY7,ADCY4,ADCY6

PDE1C,PRKAR1A,PRKAR2B,ADCY1,PRKACB,PLA2G4A,CAMK4,ADCY2,ADCY8,PRKACA,PDE1A,PRKAR2A,CREB1,CA

PDE1C,PRKAR1A,PRKAR2B,ADCY1,PRKACB,CAMK4,ADCY2,ADCY8,PRKACA,PDE1A,PRKAR2A,CREB1,CALM3,PRKO

PDE1C,PRKAR1A,PRKAR2B,ADCY1,PRKACB,CAMK4,ADCY2,ADCY8,PRKACA,PDE1A,PRKAR2A,CREB1,CALM3,PRKO

CALCRL,ADCY1,ADCY2,RAMP2,ADCY10,ADM,NPR3,UCN2,GNAS,ADCY5,TAAR1,ADORA2A,ADCY4,ADCY6

GNAL,ADCY1,ADCY2,GNAI3,ADCY8,GNAT3,GNAI1,GNAI2,ADCY5,ADCY7,ADCY4,ADCY6

GNAL,ADCY1,RPS6KA5,ADCY2,ADCY8,PRKACA,PRKCE,CREB1,LPAR4,ADCY5,ADCY7,ADCY4,ADCY6

PRKAR1A,PRKAR2B,ADCY1,PRKACB,ADCY2,ADCY8,PRKACA,PRKAR2A,CREB1,CALM3,PRKACG,PRKAR1B,ADCY5,A

PRKAR1A,PRKAR2B,ADCY1,PRKACB,ADCY2,ADCY8,PRKACA,PRKAR2A,CALM3,PRKACG,PRKAR1B,ADCY5,ADCY7,C

PRKAR1A,PRKAR2B,ADCY1,PRKACB,ADCY2,ADCY8,PRKACA,PRKAR2A,PRKACG,PRKAR1B,GNAS,ADCY5,ADCY7,AI

CDH8,CADM2,ACTN2,PVR,CDH10,CDH11,CDH13,CDH4,TBCD,JUP,CTNND1,PVRL1,DLC1,CDH18,CDH12,RAMP2,C

DM2,PVR,CDH10,CDH11,CDH13,CDH4,JUP,CTNND1,PVRL1,CDH18,CDH12,CTNNA1,CDH6,CDH7,CADM1,CDH1,

CER1,KPNA1,CASP3,H1F0,DNASE1L3,HMGB2,KPNB1,HMGB1,DFFB,FOXL2,ENDOG

ME3,CCNE2,PSMD11,PSMD12,CCND2,CINP,PSMD14,PSMD7,PSMD3,PSMD13,PSMD4,CCND3

BRE,BRCA1,FANCI,FOXN3,DTL,FAM175A,PLK1,HMGA2,TAOK1,CHEK1,BRSK1,NBN,NEK6,TAOK2,MAPKAPK2,TAC

NCI,FOXN3,NAE1,HMGA2,NBN,TAOK3,CLSPN,BLM,TICRR,CDK5RAP3,CCNA2,HUS1,ZNF830

NCI,FOXN3,NAE1,HMGA2,NBN,TAOK3,FHL1,USP47,CLSPN,BLM,TICRR,CDK5RAP3,CCNA2,HUS1,ZNF830

R,XRCC5,WRN,TLK2,YAP1,TSPYL5,KDM1A,CRYAB,TMEM109

TP53BP1,XRCC6,BRE,BRCA1,FAM175A,XRCC5,SUMO1,LIG4,POLM,UBE2V2,BARD1,TDP2,RNF8,NHEJ1,HERC2,NI

IFNB1,MB21D1,TMEM173,CAV1,MAVS,MUL1,IFIT1,FLOT1

1,CTNNB1,CTBP2,HDAC1,TLE3,TLE4,LEF1,TCF7L1,TLE2,TCF7,CTBP1

T6,ZP4,ACR,ROPN1B,TNP2,PKDREJ,SPESP1,AKAP3

19,SLC38A1,SLC38A2,SLC43A1,SLC6A14,SLC3A2,SLC7A8,SLC43A2,SLC38A4,SLC7A6,SLC36A1,SLC7A9,SLC6A15,S

MB,HMGB2,TOP2A,HMGB1,DFFB,TOP2B,CASP7,ENDOG

POLR2A,NCOR2,GTF2E1,NCOA2,HDAC3,RXRA,KAT2B,GTF2F1,TBP,GTF2A1,GTF2B,RARA,ERCC3

NP32A,GZMA,GZMB,HMGB2,PRF1,DFFB,NME1,APEX1,SET

NCOA2,TSC2,RXRA,CREBBP,MED1,HDAC1,EP300,CARM1,KAT2B,NCOR1

AD1,ERCC4,M1AP,RECQL5,FANCM,TEX14,ESPL1,STRA13,NCAPD3,MEIOB,DIS3L2,TOP2A,TOP2B,NCAPD2

IGF1,IGF1R,INSRR,TSC2,IGF2,GSK3B,IRS2,TSC1,INSR,PTEN,IRS1,PIK3CA,IGF2R,FOXO3,GSK3A,INPPL1,PDPK1,MD

1B,TRNT1,PNPT1,ELAC2,KIAA0391,HSD17B10,MTO1,SUPV3L1,TRIT1,TRMU,PUS1,TRMT10C,FASTKD5

IGF1,NRG1,IFRD1,EPAS1,JAG1,GREM1,MBNL1,SDC1,RBPJ,SRF,NOTCH1,RB1,SOX15,T,REST,HINFP,MAPK12,TB

HOA,PTPN11,ROCK1,MYL2,JUP,CTNND1,GSN,AXIN1,GAP43,MAPK8,PIK3R1,FER,CTNNA1,CNR1,DCTN1,CTNNB1

RRC15,GOPC,PPP2R5A,PKDCC,RHOQ,BCL2L1,PPFIA1,TMEM59,CSK,TMBIM1

5,MMP24,JAG1,HES1,PROX1,NOTCH1,SOX2,SRRT

K3,KRAS,RALA,HRAS,MAPKAPK2,MAPK11,RALGDS,NRAS,MAPK14,MAPK13,MAPK12

PXYLP1,IGF1,CTNNB1,RAMP1,CCR7,ARFGEF1,CCL19,CCL21,SOAT1,CHP1,SLC51B,GOLGA2

PXYLP1,IGF1,RAB1A,CTNNB1,RAMP1,CCR7,ARFGEF1,CCL19,CCL21,SOAT1,CHP1,SLC51B,RAB1B,GOLGA2

AVP,MAS1,ZP4,PLEK,AZU1,DGKQ,ZP3,PDGFB,HTR2B,FLOT1,ADAM15

TGER4,CXCL12,OLFM4,CCL25,CCR2,RIPK3,FADD,ADAM8,CCL28,CCL21,ICAM1

BMP2,ARNT,DKK3,STC2,TRERF1,BMP6,HIF1A,BMP5,FFAR3,PAX8,WNT4,REST,STUB1,AKR1C3,HPN

YOD1,EHD1,MYF5,EHD2,MYOG,FLOT1,MYF6,MAPK14

,LARGE,ERBB4,TEC,CPQ,TXK,NOV,APOD,KLK6,NACA,APOA5

1B,HSD17B10,MTO1,OSGEPL1,TRIT1,TRMU,TP53RK,OSGEP,PUS1,TRMT10C,YRDC

EAD4,TBL1XR1,CHD9,TBL1X,NCOA6,HELZ2,NCOA2,SMARCD3,RXRA,CREBBP,MED1,TEAD1,HIPK2,GATA4,RUNX

ADCY6

ALM3,PRKCD,PRKCG,MAPK1,PRKCA,PRKACG,PRKAR1B,ADRBK1,ADCY5,ADCY7,CALM2,PDE1B,CALM1,ADCY4,AI
CD,PRKCG,PRKCA,PRKACG,PRKAR1B,ADRBK1,ADCY5,ADCY7,CALM2,PDE1B,CALM1,ADCY4,ADCY6
CD,PRKCG,PRKCA,PRKACG,PRKAR1B,ADRBK1,ADCY5,ADCY7,CALM2,PDE1B,CALM1,ADCY4,ADCY6

ADCY7,CALM2,CALM1,ADCY4,ADCY6
CALM2,CALM1,ADCY4,ADCY6
DCY4,ADCY6
CTNNA1,LAMA5,ACTN1,CDH6,CDH7,ACTB,CADM1,CDH1,RCC2,PVRL3,ZNF703,CTNNB1,PTPRK,RHOD,FERMT2,F
PVRL3,PVRL4,CDH3,CDH9,CDH17,CDH5,PVRL2,CADM3,CDH24,ANG,CDH15

DK3,FZR1,NEK11,RBBP8,PLK5,CDC14B,UIMC1,CLSPN,BLM,BRCC3,CDK5RAP3,CCNA2

3N,PIAS4,XRCC4,RIF1,WHSC1,KAT5,PAXIP1,RAD50,PRKDC,MRE11A,UIMC1,RNF168,H2AFX,DCLRE1C,UBE2N,MI

SLC16A10,SLC1A4,SLC7A11,SLC7A1,SLC38A5,SLC1A5,SLC7A3,SLC7A5,SLC7A10,SLC7A7,SLC6A20,SLC36A2,SLC3

M2,IRS4,INS

X2
,LRP5,CALM3,PIP5K1C,GJA1,GRIA2,CDC42,CTTN,FGFR1,PIK3CA,DAGLB,MAPRE1,CAMK2G,DAGLA,CALM2,RAC1

2,YAP1,CARM1,TBX5,WWTR1,CTGF,TGS1,KAT2B,TEAD2,NKX2-5,PPARA,TEAD3,NPPA

DCY6

RAB8B,PKP2,PVRL4,SMAD7,CDH3,PIP5K1C,CDH9,CDH17,CDH5,TAOK2,PIP5K1A,ARHGEF7,ACTG1,PVRL2,VCL,CT

DC1,BRCC3,TDP1,POLL

A1,SLC6A12,SLC6A6,SLC38A3

,KIF5B,CALM1,PLCG1

TN,MLLT4,WHAMM,ACTN3,CADM3,TRIP6,TESK2,CDH24,ANG,CSK,CDH15,THY1

Supplementary Table 15: Enrichments* for ER- breast cancer based on summary statistics for c[...]

Annotation[¥]	Proportion SNPs	Proportion heritability	Enrichment	P-value
SuperEnhancers, extended 500bp	0.17	0.43	2.48	2×10^{-7}
SuperEnhancers	0.17	0.40	2.36	1×10^{-5}
H3K4me3, extended 500 bp	0.26	0.60	2.35	5×10^{-4}
H3K4me1	0.43	1.00	2.35	3×10^{-4}
H3K27ac[†] extended 500 bp	0.42	0.98	2.31	1×10^{-12}
H3K27ac[†]	0.39	0.81	2.07	2×10^{-7}
H3K27ac[‡] extended 500 bp	0.34	0.67	1.98	5×10^{-4}
DGF, extended 500 bp	0.54	1.03	1.90	7×10^{-5}
H3K4me1, extended 500 bp	0.61	0.91	1.49	2×10^{-4}
Introns, extended 500 bp	0.40	0.57	1.43	9×10^{-4}
Repressed, extended 500 bp	0.72	0.48	0.67	2×10^{-4}

[¥]Of the 52 baseline genomic features described in Finucane, H.K. et al. Partitioning heritability by functiona[...]
*Statistically significant after Bonferroni correction for 52 tests
[†]Hnisz, D. et al. Super-enhancers in the control of cell identity and disease. Cell 155, 934-47 (2013)
[‡]Schizophrenia Working Group of the Psychiatric Genomics Consortium. Biological insights from 108 schizo[...]

Supplementary Table 15: Enrichments* for ER- breast cancer based on summary statistics for c[...]

Annotation[¥]	Proportion SNPs	Proportion heritability	Enrichment	P-value
SuperEnhancers, extended 500bp	0.17	0.43	2.48	2×10^{-7}
SuperEnhancers	0.17	0.40	2.36	1×10^{-5}
H3K4me3, extended 500 bp	0.26	0.60	2.35	5×10^{-4}
H3K4me1	0.43	1.00	2.35	3×10^{-4}
H3K27ac[†] extended 500 bp	0.42	0.98	2.31	1×10^{-12}
H3K27ac[†]	0.39	0.81	2.07	2×10^{-7}
H3K27ac[‡] extended 500 bp	0.34	0.67	1.98	5×10^{-4}
DGF, extended 500 bp	0.54	1.03	1.90	7×10^{-5}
H3K4me1, extended 500 bp	0.61	0.91	1.49	2×10^{-4}
Introns, extended 500 bp	0.40	0.57	1.43	9×10^{-4}

ombined analysis of BCAC (ER-negative) and CIMBA (BRCA1 mutation carrier

al annotation using genome-wide association summary statistics. Nat Genet 47, 1228

ophrenia-associated genetic loci. *Nature* **511**, 421-7 (2014).

rs) data

-35 (2015).

Supplementary Table 16: List of 125 SNPs associated with risk of ER-negative breast cancer

How identified	Location	SNP	MAF	OR	%FRR
Previous hit for breast cancer	1p36.22	rs616488	0.33	0.89	0.424
New hit for overall breast cancer	1p34.2	rs4233486	0.36	0.97	0.023
New hit for overall breast cancer	1p32.3	rs140850326	0.49	0.96	0.051
Previous hit for breast cancer	1p13.2	rs11552449	0.17	1.04	0.023
New hit for overall breast cancer	1p12	rs7529522	0.23	1.05	0.053
Previous hit for breast cancer	1q21.2	rs12048493	0.38	1.05	0.071
Previous hit for breast cancer	1q32.1	rs6678914	0.41	0.94	0.124
Previous hit for breast cancer	1q32.1	rs4245739	0.26	1.12	0.347
Previous hit for breast cancer	1q32.1	rs4951011	0.16	1.07	0.080
New hit for overall breast cancer	1q32.1	rs35383942	0.06	1.15	0.150
Previous hit for breast cancer	1q43	rs72755295	0.03	1.09	0.023
New hit for overall breast cancer	2p25.1	rs113577745	0.10	1.06	0.035
Previous hit for breast cancer	2p24.1	rs12710696	0.36	1.04	0.041
New hit for ER-negative breast cancer	2p23.3	rs200648189	0.19	0.94	0.072
Previous hit for breast cancer	2p23.2	rs4577244	0.23	0.93	0.125
New hit for overall breast cancer	2q13	rs71801447	0.06	1.05	0.011
Previous hit for breast cancer	2q14.1	rs4849887	0.10	0.85	0.334
Previous hit for breast cancer	2q33.1	rs1830298	0.28	1.08	0.162
Previous hit for breast cancer	2q35	rs4442975	0.50	0.94	0.129
Previous hit for breast cancer	2q35	rs16857609	0.26	1.07	0.119
Previous hit for breast cancer	3p24.1	rs4973768	0.47	1.04	0.047
Previous hit for breast cancer	3p21.31	rs6796502	0.10	0.92	0.080
Previous hit for breast cancer	3p14.1	rs1053338	0.14	1.03	0.007
New hit for overall breast cancer	3p13	rs6805189	0.48	1.00	0.008
New hit for overall breast cancer	3p12.1	rs13066793	0.09	0.96	0.010
New hit for overall breast cancer	4p14	rs6815814	0.26	1.06	0.084
New hit for overall breast cancer	4q21.23	4:84370124	0.47	1.03	0.023
New hit for overall breast cancer	4q22.1	rs10022462	0.44	1.01	0.007
New hit for overall breast cancer	4q28.1	rs77528541	0.13	0.94	0.053
Previous hit for breast cancer	5p15.33	rs10069690	0.26	1.19	0.830
Previous hit for breast cancer	5p15.33	rs3215401	0.31	0.88	0.495
New hit for overall breast cancer	5p15.33	rs116095464	0.05	1.03	0.003
Previous hit for breast cancer	5p15.1	rs13162653	0.45	0.98	0.006
Previous hit for breast cancer	5p12	rs10941679	0.25	1.03	0.016
New hit for overall breast cancer	5q11.1	rs35951924	0.32	0.96	0.042
Previous hit for breast cancer	5q11.2	rs62355902	0.16	1.06	0.057
Previous hit for breast cancer	5q11.2	rs10472076	0.38	1.03	0.020
Previous hit for breast cancer	5q11.2	rs1353747	0.09	0.98	0.005
Previous hit for breast cancer	5q14.2	rs7707921	0.25	0.97	0.016
New hit for overall breast cancer	5q22.1	rs6882649	0.34	0.98	0.002
Previous hit for breast cancer	5q33.3	rs1432679	0.43	1.08	0.200
Previous hit for breast cancer	6p25.3	rs11242675	0.37	0.99	0.005
New hit for overall breast cancer	6p22.3	rs3819405	0.33	0.97	0.022
New hit for overall breast cancer	6p22.2	rs71557345	0.07	0.91	0.069
Previous hit for breast cancer	6p22.1	rs9257408	0.41	1.03	0.020
Previous hit for breast cancer	6q14.1	rs17529111	0.22	1.06	0.075
New hit for overall breast cancer	6q14.1	rs12207986	0.47	0.96	0.051

New hit for ER-negative breast cancer	6q23.1	rs6569648	0.23	0.94	0.089
Previous hit for breast cancer	6q25	rs9397437	0.07	1.32	0.716
Previous hit for breast cancer	6q25.1	rs3757322	0.32	1.14	0.529
Previous hit for breast cancer	6q25.2	rs2747652	0.47	0.92	0.240
New hit for overall breast cancer	7p15.3	rs7971	0.35	0.96	0.046
New hit for overall breast cancer	7p15.1	rs17156577	0.11	1.05	0.025
Previous hit for breast cancer	7q21.2	rs6964587	0.39	1.02	0.003
New hit for overall breast cancer	7q22.1	rs71559437	0.12	0.95	0.029
Previous hit for breast cancer	7q32.3	rs4593472	0.35	0.97	0.019
New hit for ER-negative breast cancer	8p23.3	rs66823261	0.23	1.08	0.140
Previous hit for breast cancer	8p12	rs9693444	0.32	1.02	0.003
Previous hit for breast cancer	8p11.23	rs13365225	0.18	0.90	0.225
Previous hit for breast cancer	8q21.11	rs6472903	0.17	0.96	0.025
Previous hit for breast cancer	8q21.11	rs2943559	0.08	1.10	0.088
Previous hit for breast cancer	8q23.3	rs13267382	0.36	1.02	0.003
New hit for ER-negative breast cancer	8q24.13	rs17350191	0.34	1.07	0.139
Previous hit for breast cancer	8q24.21	rs13281615	0.41	1.07	0.150
Previous hit for breast cancer	8q24.21	rs11780156	0.17	1.05	0.039
Previous hit for breast cancer	9p21.3	rs1011970	0.16	1.05	0.037
Previous hit for breast cancer	9q31.2	rs10759243	0.29	1.02	0.003
Previous hit for breast cancer	9q31.2	rs676256	0.38	0.98	0.002
Previous hit for breast cancer	9q31.2	rs10816625	0.06	1.07	0.029
New hit for overall breast cancer	9q33.1	rs1895062	0.41	0.93	0.174
New hit for overall breast cancer	9q33.3	rs10760444	0.43	1.05	0.077
New hit for overall breast cancer	9q34.2	rs587745765	0.20	1.05	0.046
New hit for overall breast cancer	10p14	rs67958007	0.12	1.08	0.080
Previous hit for breast cancer	10p12.31	rs11814448	0.02	1.04	0.004
Previous hit for breast cancer	10q21.2	rs10995201	0.16	0.93	0.090
Previous hit for breast cancer	10q22.3	rs704010	0.38	1.06	0.108
New hit for overall breast cancer	10q23.33	rs140936696	0.18	1.04	0.022
Previous hit for breast cancer	10q25.2	rs7904519	0.46	1.08	0.202
Previous hit for breast cancer	10q26.13	rs35054928	0.40	1.06	0.108
Previous hit for breast cancer	10q26.13	rs2981578	0.47	1.04	0.045
Previous hit for breast cancer	11p15.5	rs3817198	0.32	1.02	0.003
New hit for overall breast cancer	11p15	rs6597981	0.48	0.94	0.128
Previous hit for breast cancer	11q13.1	rs3903072	0.47	0.99	0.005
New hit for ER-negative breast cancer	11q22.3	rs11374964	0.42	0.91	0.303
New hit for ER-negative breast cancer	11q22.3	rs74911261	0.02	0.82	0.102
Previous hit for breast cancer	11q24.3	rs11820646	0.40	0.94	0.123
Previous hit for breast cancer	12p13.1	rs12422552	0.26	1.04	0.035
Previous hit for breast cancer	12p11.22	rs7297051	0.24	0.87	0.499
New hit for overall breast cancer	12q21.31	12:85009437:T:C	0.34	0.93	0.162
Previous hit for breast cancer	12q22	rs17356907	0.30	0.94	0.108
New hit for overall breast cancer	12q24.31	12:120832146:C:T	0.16	1.04	0.020
Previous hit for breast cancer	13q13.1	rs11571833	0.01	1.58	0.290
Previous hit for breast cancer	13q22.1	rs6562760	0.23	0.92	0.168
Previous hit for breast cancer	14q13.3	rs2236007	0.21	0.95	0.052
Previous hit for breast cancer	14q24.1	rs999737	0.23	0.92	0.168
Previous hit for breast cancer	14q32.12	rs11627032	0.25	0.95	0.062
New hit for overall breast cancer	14q32.33	rs10623258	0.45	1.03	0.023

			MAF	OR	%FRR
Previous hit for breast cancer	15q26.1	rs2290203	0.21	0.96	0.029
New hit for ER-negative breast cancer	16p13.3	rs11076805	0.25	0.92	0.178
Previous hit for breast cancer	16q12.1	rs4784227	0.24	1.14	0.441
Previous hit for breast cancer	16q12.2	rs11075995	0.24	1.07	0.111
Previous hit for breast cancer	16q12.2	rs17817449	0.41	0.93	0.174
New hit for overall breast cancer	16q12.2	rs28539243	0.49	1.05	0.075
Previous hit for breast cancer	16q23.2	rs13329835	0.23	1.06	0.077
New hit for overall breast cancer	16q24.2	rs4496150	0.25	0.96	0.036
Previous hit for breast cancer	17q11.2	chr17:29230520	0.27	0.95	0.065
New hit for overall breast cancer	17q21.31	17:44252468:G:A	0.19	0.95	0.048
Previous hit for breast cancer	17q22	rs2787486	0.30	0.96	0.040
Previous hit for breast cancer	17q25.3	rs745570	0.50	1.04	0.048
New hit for ER-negative breast cancer	18q12.1	rs36194942	0.30	0.92	0.199
New hit for overall breast cancer	18q12.1	rs117618124	0.05	0.84	0.196
New hit for overall breast cancer	19p13.13	rs78269692	0.05	1.09	0.042
Previous hit for breast cancer	19p13.11	rs67397200	0.30	1.17	0.738
Previous hit for breast cancer	19p13.11	rs4808801	0.34	0.96	0.046
New hit for overall breast cancer	19p13.11	rs2965183	0.35	1.05	0.069
New hit for ER-negative breast cancer	19p13.2	rs322144	0.47	0.95	0.085
New hit for ER-negative breast cancer	19q12	rs113701136	0.32	1.08	0.175
New hit for overall breast cancer	19q13.22	rs71338792	0.23	1.03	0.012
Previous hit for breast cancer	19q13.31	rs3760982	0.46	1.08	0.203
New hit for overall breast cancer	20p12.3	rs16991615	0.06	1.10	0.065
New hit for overall breast cancer	20q13.13	rs6122906	0.18	1.08	0.116
Previous hit for breast cancer	22q13.1	chr22:39359355	0.04	1.09	0.038
Previous hit for breast cancer	22q13.1	rs6001930	0.10	1.14	0.215
New hit for overall breast cancer	22q13.2	rs73161324	0.06	1.10	0.064
New hit for overall breast cancer	22q13.31	rs28512361	0.11	1.09	0.097

MAF, minor allele frequency; OR, odds ratio pero copy of the minor allele, estimated based on OncoArray data
%FRR, percentage explained of an assumed 2-fold increased risk of ER-negative breast cancer to the first-degree
female relative of a woman with ER-negative breast cancer

Supplementary Table 17: List of 39 SNPs associated with breast cancer risk for *BRCA1* mutation ca

How identified	Location	SNP	MAF	HR
Previous hit for breast cancer	1p36.22	rs616488	0.33	0.96
New hit for overall breast cancer	1p34.2	rs4233486	0.36	0.95
Previous hit for breast cancer	1q32.1	rs4245739	0.26	1.09
New hit for overall breast cancer	1q41	rs11117758	0.21	0.94
Previous hit for breast cancer	1q43	rs72755295	0.03	1.13
New hit for ER-negative breast cancer	2p23.3	rs200648189	0.19	0.88
Previous hit for breast cancer	2p23.2	rs4577244	0.23	0.92
Previous hit for breast cancer	2q33.1	rs1830298	0.28	1.08
Previous hit for breast cancer	2q35	rs16857609	0.26	1.04
Previous hit for breast cancer	5p15.33	rs10069690	0.26	1.18
Previous hit for breast cancer	5p15.33	rs3215401	0.31	0.90
Previous hit for breast cancer	5q33.3	rs1432679	0.43	1.04
New hit for overall breast cancer	6q14.1	rs12207986	0.47	0.95
New hit for ER-negative breast cancer	6q23.1	rs6569648	0.23	0.94
Previous hit for breast cancer	6q25	rs9397437	0.07	1.20
Previous hit for breast cancer	6q25.1	rs3757322	0.32	1.14
New hit for overall breast cancer	7q34	rs11977670	0.43	1.06
Previous hit for breast cancer	8p11.23	rs13365225	0.18	0.95
Previous hit for breast cancer	8q21.11	rs2943559	0.08	1.07
New hit for ER-negative breast cancer	8q24.13	rs17350191	0.34	1.08
New hit for overall breast cancer	9q33.1	rs1895062	0.41	0.95
Previous hit for breast cancer	10q25.2	rs7904519	0.46	1.08
Previous hit for breast cancer	11p15.5	rs3817198	0.32	1.06
New hit for ER-negative breast cancer	11q22.3	rs11374964	0.42	0.91
New hit for ER-negative breast cancer	11q22.3	rs74911261	0.02	0.74
Previous hit for breast cancer	11q24.3	rs11820646	0.40	0.94
Previous hit for breast cancer	12p11.22	rs7297051	0.24	0.88
New hit for overall breast cancer	12q24.31	12:120832146:C:T	0.16	1.06
Previous hit for breast cancer	13q22.1	rs6562760	0.23	0.89
New hit for ER-negative breast cancer	16p13.3	rs11076805	0.25	0.96
Previous hit for breast cancer	16q12.1	rs4784227	0.24	1.05
Previous hit for breast cancer	16q12.2	rs17817449	0.41	0.94
Previous hit for breast cancer	16q23.2	rs13329835	0.23	1.06
New hit for ER-negative breast cancer	18q12.1	rs36194942	0.30	0.95
New hit for overall breast cancer	18q12.1	rs117618124	0.05	0.89
Previous hit for breast cancer	19p13.11	rs67397200	0.30	1.18
New hit for ER-negative breast cancer	19p13.2	rs322144	0.47	0.92
New hit for ER-negative breast cancer	19q12	rs113701136	0.32	1.05
Previous hit for breast cancer	22q13.1	rs6001930	0.10	1.06

MAF, minor allele frequency; HR, hazard ratio pero copy of the minor allele, estimated based on all available CI
%VPR, percentage explained of the variance in polygenic risk of breast cancer for *BRCA1* mutation carriers

rriers

%VPR
0.06
0.09
0.23
0.09
0.07
0.35
0.18
0.19
0.05
0.86
0.34
0.06
0.10
0.10
0.38
0.59
0.13
0.06
0.05
0.21
0.10
0.22
0.11
0.32
0.20
0.14
0.42
0.07
0.34
0.05
0.07
0.14
0.09
0.08
0.09
0.93
0.26
0.08
0.05