Letter

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

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Abstract

Most common breast cancer susceptibility variants have been identified through genome-wide association studies (GWAS) 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 $P < 5 \times 10^{-8}$ with ten variants at nine new loci. At $P < 0.05$, we replicated associations with 10 of 11 variants previously reported in ER-negative disease or *BRCA1* mutation carrier GWAS and observed consistent associations with ER-negative disease for 105 susceptibility variants identified by other studies. 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 c[illegible]er risk for *BRCA1* mutation carriers. These findings may lead to improved risk p[illegible]apping and functional work to better u[illegible]-negative breast cancer.

References

1. Michailidou, K. *et al.* Association analysis identifies 65 new breast cancer risk loci. *Nature* (in press).

2. Ahmed, S. *et al.* Newly discovered breast cancer susceptibility loci on 3p24 and 17q23.2. *Nat. Genet.* **41**, 585–590 (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**, 885–892 (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**, 4991–4999 (2011).

5. Cox, A. *et al.* A common coding variant in CASP8 is associated with breast cancer risk. *Nat. Genet.* **39**, 352–358 (2007).

6. Easton, D.F. *et al.* Genome-wide association study identifies novel breast cancer susceptibility loci. *Nature* **447**, 1087–1093 (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**, 425–435 (2011).

8. Ghoussaini, M. *et al.* Genome-wide association analysis identifies three new breast cancer susceptibility loci. *Nat. Genet.* **44**, 312–318 (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**, 1210–1214 (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**, 870–874 (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**, 5373–5384 (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**, 865–869 (2007).

14. Stacey, S.N. *et al.* Common variants on chromosome 5p12 confer

susceptibility to estrogen receptor–positive breast cancer. *Nat. Genet.* **40**, 703–706 (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**, 579–584 (2009).

16. Turnbull, C. *et al.* Genome-wide association study identifies five new breast cancer susceptibility loci. *Nat. Genet.* **42**, 504–507 (2010).

17. Zheng, W. *et al.* Genome-wide association study identifies a new breast cancer susceptibility locus at 6q25.1. *Nat. Genet.* **41**, 324–328 (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**, 371–384, e1–e2 (2013).

19. Garcia-Closas, M. *et al.* Genome-wide association studies identify four ER negative–specific breast cancer risk loci. *Nat. Genet.* **45**, 392–398, e1–e2 (2013).

20. Michailidou, K. *et al.* Large-scale genotyping identifies 41 new loci associated with breast cancer risk. *Nat. Genet.* **45**, 353–361, e1–e2 (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**, 886–890 (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, 373–380 (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**, 6096–6111 (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**, 1046–1060 (2013).

27. Orr, N. *et al.* Fine-mapping identifies two additional breast cancer susceptibility loci at 9q31.2. *Hum. Mol. Genet.* **24**, 2966–2984 (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**, 374–386 (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. **25**, 3863–3876 (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**, 134–147 (2012).

34. Amos, C.I. *et al.* The OncoArray Consortium: a network for understanding the genetic architecture of common cancers. *Cancer Epidemiol. Biomarkers Prev.* **26**, 126–135 (2017).

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**, 274–291 (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**, 658–669 (2014).

38. Stevens, K.N. *et al.* 19p13.1 is a triple-negative-specific breast cancer susceptibility locus. *Cancer Res.* **72**, 1795–1803 (2012).

39. Willer, C.J., Li, Y. & Abecasis, G.R. METAL: fast and efficient meta-analysis of genomewide association scans. *Bioinformatics* **26**, 2190–2191 (2010).

40. Maller, J.B. *et al.* Bayesian refinement of association signals for 14 loci in 3 common diseases. *Nat. Genet.* **44**, 1294–1301 (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**, 463–468 (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**, 2976–2987 (2014).

44. Kundaje, A. *et al.* Integrative analysis of 111 reference human epigenomes. *Nature* **518**, 317–330 (2015).

45. Boyle, A.P. *et al.* Annotation of functional variation in personal genomes using RegulomeDB. *Genome Res.* **22**, 1790–1797 (2012).

46. He, B., Chen, C., Teng, L. & Tan, K. Global view of enhancer–promoter interactome in human cells. *Proc. Natl. Acad. Sci. USA* **111**, E2191–E2199 (2014).

47. Rao, S.S. *et al.* A 3D map of the human genome at kilobase resolution reveals principles of chromatin looping. *Cell* **159**, 1665–1680 (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**, 462–470 (2014).

50. GTEx Consortium. The Genotype-Tissue Expression (GTEx) pilot analysis: multitissue gene regulation in humans. *Science* **348**, 648–660 (2015).

51. Hnisz, D. *et al.* Super-enhancers in the control of cell identity and disease.

Cell **155**, 934–947 (2013).

52. Westra, H.J. *et al.* Systematic identification of *trans* eQTLs as putative drivers of known disease associations. *Nat. Genet.* **45**, 1238–1243 (2013).

53. James, L.I. *et al.* Small-molecule ligands of methyl-lysine binding proteins: optimization of selectivity for L3MBTL3. *J. Med. Chem.* **56**, 7358–7371 (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**, 29290–29300 (2015).

56. Easton, D.F. *et al.* Gene-panel sequencing and the prediction of breast-cancer risk. *N. Engl. J. Med.* **372**, 2243–2257 (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**, 633–641 (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**, 346–352 (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**, 1278–1283 (2007).

63. Wang, K., Li, M. & Hakonarson, H. Analysing biological pathways in genome-wide association studies. *Nat. Rev. Genet.* **11**, 843–854 (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.* β-blocker use is associated with improved relapse-free survival in patients with triple-negative breast cancer. *J. Clin. Oncol.* **29**, 2645–2652 (2011).

67. Pon, C.K., Lane, J.R., Sloan, E.K. & Halls, M.L. The β2-adrenoceptor activates a positive cAMP–calcium feedforward loop to drive breast cancer cell invasion. *FASEB J.* **30**, 1144–1154 (2016).

68. Finucane, H.K. *et al.* Partitioning heritability by functional annotation using genome-wide association summary statistics. *Nat. Genet.* **47**, 1228–1235 (2015).

69. Bulik-Sullivan, B. *et al.* An atlas of genetic correlations across human diseases and traits. *Nat. Genet.* **47**, 1236–1241 (2015).

70. Bulik-Sullivan, B.K. *et al.* LD Score regression distinguishes confounding from polygenicity in genome-wide association studies. *Nat. Genet.* **47**, 291–295 (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–i17 (2011).

72. Mavaddat, N. *et al.* Prediction of breast cancer risk based on profiling with common genetic variants. *J. Natl. Cancer Inst.* **107**, djv036 (2015).

73. Delaneau, O., Marchini, J. & Zagury, J.F. A linear complexity phasing method for thousands of genomes. *Nat. Methods* **9**, 179–181 (2011).

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**, 955–959 (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**, 816–834 (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**, 1457–1466 (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**, 1359–1367 (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**, 1353–1358 (2012).

88. Shannon, P. *et al.* Cytoscape: a software environment for integrated models of biomolecular interaction networks. *Genome Res.* **13**, 2498–2504 (2003).

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Competing interests

The authors declare no competing financial interests.

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Integrated supplementary information

Supplementary figures

1. Manhattan plot of associations with breast cancer risk for all imputed and genotyped SNPs using combined data from ER-negative cases and controls and BRCA1 mutation carriers, before excluding known breast cancer susceptibility loci.
2. Manhattan plot of associations with breast cancer risk for all imputed and genotyped SNPs using combined data from ER-negative cases and controls and BRCA1 mutation carriers, after excluding known breast cancer susceptibility loci.
3. Quantile–quantile plot of associations with breast cancer risk for all imputed and genotyped SNPs using combined data from ER-negative cases and controls and BRCA1 mutation carriers.
4. Genomic region around the ER-negative risk-associated variant 2_24739694_CT_T (rs200648189).
5. Genomic region around the ER-negative risk-associated variant 6_130349119_T_C (rs6569648).
6. Genomic region around the ER-negative risk-associated variant 8_170692_T_C (rs66823261).

7. Genomic region around the ER-negative risk-associated variant 8_124757661_C_T (rs17350191).
8. Genomic region around the ER-negative risk-associated variant 16_4106788_C_A (rs11076805).
9. Genomic region around the ER-negative risk-associated variant 18_25401204_A_AT (rs36194942).
10. Genomic region around the ER-negative risk-associated variant 19_11423703_C_G (rs322144).
11. Genomic region around the ER-negative risk-associated variant 19_30277729_C_T (rs113701136).
12. Regional eQTL association plot for all variants within 1 Mb of L3MTBL3 and expression of L3MTBL3.
13. Regional eQTL association plot for all variants within 1 Mb of CDH2 and expression of CDH2.
14. Enrichment map for pathways enriched in susceptibility to ER-negative breast cancer.
15. Enrichment map of the adenylate cyclase theme, enriched in susceptibility to ER-negative breast cancer.

Supplementary information

PDF files

1. Supplementary Text and Figures
   Supplementary Figures 1–15 and Supplementary Note

Excel files

1. Supplementary Table 1
   BCAC studies contributing data on estrogen-receptor-negative cases and controls, by genotyping initiative.

2. Supplementary Table 2
   CIMBA studies contributing data on BRCA1 mutation carriers, by genotyping initiative.

3. 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.

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

5. Supplementary Table 5
   Summary information from bioinformatic and eQTL analyses.

6. Supplementary Table 6
   Data sources for *in silico* analyses of the ten novel ER-negative breast cancer susceptibility loci.

7. Supplementary Table 7
   Associations for ten novel and ten previously reported (and replicated) loci.

8. Supplementary Table 8
   Associations for ten novel and ten previously reported (and replicated) loci.

9. Supplementary Table 9
   Novel overall breast cancer susceptibility loci from Michailidou *et al.* (2016): associations with risk of ER-negative breast cancer and breast cancer for *BRCA1* mutation carriers.

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

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

12. Supplementary Table 12
Detailed information about themes and pathways appearing in the enrichment maps (Supplementary Figs. 13 and 14).

13. Supplementary Table 13
Detailed information about themes and unique genes appearing in the enrichment maps (Supplementary Figs. 13 and 14).

14. Supplementary Table 14
Pathways enriched in susceptibility to ER-negative breast cancer (enrichment score (ES) ≥ 0.41) but not ER-positive breast cancer (ES < 0).

15. Supplementary Table 15
Enrichments for ER-negative breast cancer based on summary statistics for combined analysis of BCAC (ER-negative) and CIMBA (*BRCA1* mutation carriers) data.

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

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

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