Supplementary Table S1. The roles of involved genes in breast cancer.

|  |  |  |
| --- | --- | --- |
| Gene | Involved pathway/roles | References |
| *TP53*  | p53 signaling , Hereditary signaling, DNA damage response | [1-3] |
| *HER2/ERBB2* | HER-2 Signaling | [4] |
| *CCND1* | Estrogen signaling, p53 signaling | [5,6] |
| *FGFR1* | PTEN signaling, Epithelial-Mesenchymal Transition | [7,8] |
| *BRCA1* | Hereditary signaling, DNA damage response, p53 signaling | [9-11] |
| *BRCA2* | Hereditary signaling, DNA damage response | [10,11] |
| *BRCA3* | Hereditary signaling | [9,12] |
| *PTEN* | Hereditary signaling, p53 signaling, PTEN signaling | [3] |
| *ATM* | DNA damage response, Epithelial-Mesenchymal Transition | [13] |
| *MSH2* | DNA damage repair | [14,15] |
| *MLH1* | DNA damage response  | [16] |
| *PMS1* | DNA mismatch repair | [15] |
| *MSH3* | DNA mismatch repair | [15] |
| *CDH1* | Epithelial-Mesenchymal Transition | [3] |
| *HRAS* | mTOR Signaling, Epithelial-Mesenchymal Transition | [17,18] |
| *NRAS* | Epithelial-Mesenchymal Transition | [17,18] |
| *KRAS* | mTOR Signaling, Epithelial-Mesenchymal Transition | [17,18] |
| *BIRC5* | p53 signaling | [19] |
| *EGFR* | Estrogen signaling, HER-2 Signaling, Epithelial-Mesenchymal Transition, | [20,21] |
| *EMSY* | BRCA2 impairment | [22] |
| *ESR1* | Estrogen signaling | [23] |
| *HIF1A* | mTOR Signaling, Epithelial-Mesenchymal Transition | [24,25] |
| *IGF1R* | Estrogen signaling | [26] |
| *MYC* | Estrogen-mediated S-phase Entry | [27] |
| *NOTCH1* | Epithelial-Mesenchymal Transition | [17] |
| *PIK3CA* | Estrogen signaling, HER-2 Signaling, p53 signaling, mTOR Signaling | [28,29] |
| *RARB* | Epithelial-Mesenchymal Transition, Wnt/β-catenin signaling | [17,30] |
| *RASSF1* | Tumorigenesis signaling | [31] |
| *SRC* | Estrogen signaling | [32] |
| *TOP2A* | Cell Cycle G2/M DNA Damage Checkpoint Regulation | [33] |
| *TWIST1* | Epithelial-Mesenchymal Transition | [17] |
| *BARD1* | DNA damage response | [34] |
| *BRIP1* | DNA damage response | [35] |
| *CHEK2* | DNA damage response, p53 signaling | [36,37] |
| *NBN* | DNA damage response | [38] |
| *NF1* | DNA damage response | [39] |
| *PALB2* | DNA damage response | [40] |
| *RAD51C* | DNA homologous recombination, DNA damage repair | [41] |
| *RAD51D* | DNA homologous recombination, DNA damage repair | [41] |
| *STK11* | mTOR Signaling | [3,42] |

References

1 Børresen‐Dale AL: TP53 and breast cancer. Human mutation 2003;21:292-300.

2 Walsh T, Casadei S, Coats KH, Swisher E, Stray SM, Higgins J, Roach KC, Mandell J, Lee MK, Ciernikova S: Spectrum of mutations in BRCA1, BRCA2, CHEK2, and TP53 in families at high risk of breast cancer. Jama 2006;295:1379-1388.

3 Campeau PM, Foulkes WD, Tischkowitz MD: Hereditary breast cancer: new genetic developments, new therapeutic avenues. Human genetics 2008;124:31-42.

4 Olayioye MA: Intracellular signaling pathways of ErbB2/HER-2 and family members. Breast Cancer Research 2001;3:1-5.

5 Lin S-Y, Xia W, Wang JC, Kwong KY, Spohn B, Wen Y, Pestell RG, Hung M-C: β-catenin, a novel prognostic marker for breast cancer: its roles in cyclin D1 expression and cancer progression. Proceedings of the National Academy of Sciences 2000;97:4262-4266.

6 Arnold A, Papanikolaou A: Cyclin D1 in breast cancer pathogenesis. Journal of clinical oncology 2005;23:4215-4224.

7 Chioni A-M, Grose R: FGFR1 cleavage and nuclear translocation regulates breast cancer cell behavior. Journal of Cell Biology 2012;197:801-817.

8 Wang K, Ji W, Yu Y, Li Z, Niu X, Xia W, Lu S: FGFR1-ERK1/2-SOX2 axis promotes cell proliferation, epithelial–mesenchymal transition, and metastasis in FGFR1-amplified lung cancer. Oncogene 2018;37:5340-5354.

9 Rosen EM, Fan S, Pestell RG, Goldberg ID: BRCA1 gene in breast cancer. Journal of cellular physiology 2003;196:19-41.

10 Rennert G, Bisland-Naggan S, Barnett-Griness O, Bar-Joseph N, Zhang S, Rennert HS, Narod SA: Clinical outcomes of breast cancer in carriers of BRCA1 and BRCA2 mutations. New England Journal of Medicine 2007;357:115-123.

11 Venkitaraman AR: Functions of BRCA1 and BRCA2 in the biological response to DNA damage. Journal of cell science 2001;114:3591-3598.

12 Thompson D, Szabo CI, Mangion J, Oldenburg RA, Odefrey F, Seal S, Barfoot R, Kroeze-Jansema K, Teare D, Rahman N: Evaluation of linkage of breast cancer to the putative BRCA3 locus on chromosome 13q21 in 128 multiple case families from the Breast Cancer Linkage Consortium. Proceedings of the National Academy of Sciences 2002;99:827-831.

13 Sun M, Guo X, Qian X, Wang H, Yang C, Brinkman KL, Serrano-Gonzalez M, Jope RS, Zhou B, Engler DA: Activation of the ATM-Snail pathway promotes breast cancer metastasis. Journal of molecular cell biology 2012;4:304-315.

14 Lin DP, Wang Y, Scherer SJ, Clark AB, Yang K, Avdievich E, Jin B, Werling U, Parris T, Kurihara N: An Msh2 point mutation uncouples DNA mismatch repair and apoptosis. Cancer Research 2004;64:517-522.

15 Peltomäki P: DNA mismatch repair and cancer. Mutation Research/Reviews in Mutation Research 2001;488:77-85.

16 Stojic L, Brun R, Jiricny J: Mismatch repair and DNA damage signalling. DNA repair 2004;3:1091-1101.

17 Foroni C, Broggini M, Generali D, Damia G: Epithelial–mesenchymal transition and breast cancer: Role, molecular mechanisms and clinical impact. Cancer treatment reviews 2012;38:689-697.

18 Kodaz H, Kostek O, Hacioglu MB, Erdogan B, Kodaz CE, Hacibekiroglu I, Turkmen E, Uzunoglu S, Cicin I: Frequency of RAS mutations (KRAS, NRAS, HRAS) in human solid cancer. Breast cancer 2017;7

19 Vegran F, Boidot R, Oudin C, Defrain C, Rebucci M, Lizard-Nacol S: Association of p53 gene alterations with the expression of antiapoptotic survivin splice variants in breast cancer. Oncogene 2007;26:290-297.

20 Pan M, Schinke H, Luxenburger E, Kranz G, Shakhtour J, Libl D, Huang Y, Gaber A, Pavšič M, Lenarčič B: EpCAM ectodomain EpEX is a ligand of EGFR that counteracts EGF-mediated epithelial-mesenchymal transition through modulation of phospho-ERK1/2 in head and neck cancers. PLoS biology 2018;16:e2006624.

21 Huang F, Shi Q, Li Y, Xu L, Xu C, Chen F, Wang H, Liao H, Chang Z, Liu F: HER2/EGFR–AKT signaling switches TGFβ from inhibiting cell proliferation to promoting cell migration in breast cancer. Cancer research 2018;78:6073-6085.

22 Jelinic P, Eccles LA, Tseng J, Cybulska P, Wielgos M, Powell SN, Levine DA: The EMSY threonine 207 phospho-site is required for EMSY-driven suppression of DNA damage repair. Oncotarget 2017;8:13792.

23 Zhuang T, Yu S, Zhang L, Yang H, Li X, Hou Y, Liu Z, Shi Y, Wang W, Yu N: SHARPIN stabilizes estrogen receptor α and promotes breast cancer cell proliferation. Oncotarget 2017;8:77137.

24 Tam SY, Wu VW, Law HK: Hypoxia-induced epithelial-mesenchymal transition in cancers: HIF-1α and beyond. Frontiers in oncology 2020;10:486.

25 Guo X, Lee S, Cao P: The inhibitive effect of sh-HIF1A-AS2 on the proliferation, invasion, and pathological damage of breast cancer via targeting miR-548c-3p through regulating HIF-1α/VEGF pathway in vitro and vivo. OncoTargets and therapy 2019;12:825.

26 Rigiracciolo DC, Nohata N, Lappano R, Cirillo F, Talia M, Scordamaglia D, Gutkind JS, Maggiolini M: IGF-1/IGF-1R/FAK/YAP Transduction Signaling Prompts Growth Effects in Triple-Negative Breast Cancer (TNBC) Cells. Cells 2020;9:1010.

27 Bellat V, Verchère A, Ashe SA, Law B: Transcriptomic insight into salinomycin mechanisms in breast cancer cell lines: synergistic effects with dasatinib and induction of estrogen receptor β. BMC cancer 2020;20:1-21.

28 Li SY, Rong M, Grieu F, Iacopetta B: PIK3CA mutations in breast cancer are associated with poor outcome. Breast cancer research and treatment 2006;96:91-95.

29 Esteva FJ, Guo H, Zhang S, Santa-Maria C, Stone S, Lanchbury JS, Sahin AA, Hortobagyi GN, Yu D: PTEN, PIK3CA, p-AKT, and p-p70S6K status: association with trastuzumab response and survival in patients with HER2-positive metastatic breast cancer. The American journal of pathology 2010;177:1647-1656.

30 Wang Y, Zhou BP: Epithelial-mesenchymal transition in breast cancer progression and metastasis. Chinese journal of cancer 2011;30:603.

31 Dammann R, Schagdarsurengin U, Seidel C, Strunnikova M, Rastetter M, Baier K, Pfeifer G: The tumor suppressor RASSF1A in human carcinogenesis: an update. Histology and histopathology 2005

32 Finn R: Targeting Src in breast cancer. Annals of oncology 2008;19:1379-1386.

33 Weigelt B, Kreike B, Reis-Filho JS: Metaplastic breast carcinomas are basal-like breast cancers: a genomic profiling analysis. Breast cancer research and treatment 2009;117:273-280.

34 Schulz E, Valentin A, Ulz P, Beham-Schmid C, Lind K, Rupp V, Lackner H, Wölfler A, Zebisch A, Olipitz W: Germline mutations in the DNA damage response genes BRCA1, BRCA2, BARD1 and TP53 in patients with therapy related myeloid neoplasms. Journal of medical genetics 2012;49:422-428.

35 Cantor SB, Guillemette S: Hereditary breast cancer and the BRCA1-associated FANCJ/BACH1/BRIP1. Future oncology 2011;7:253-261.

36 Roeb W, Higgins J, King M-C: Response to DNA damage of CHEK2 missense mutations in familial breast cancer. Human molecular genetics 2012;21:2738-2744.

37 Nevanlinna H, Bartek J: The CHEK2 gene and inherited breast cancer susceptibility. Oncogene 2006;25:5912-5919.

38 Uzunoglu H, Korak T, Ergul E, Uren N, Sazci A, Utkan NZ, Kargi E, Triyaki Ç, Yirmibesoglu O: Association of the nibrin gene (NBN) variants with breast cancer. Biomedical reports 2016;4:369-373.

39 Kretova M, Sabova L, Hodny Z, Bartek J, Kollarovic G, Nelson BD, Hubackova S, Luciakova K: TGF-β/NF1/Smad4-mediated suppression of ANT2 contributes to oxidative stress in cellular senescence. Cellular signalling 2014;26:2903-2911.

40 Zhang F, Ma J, Wu J, Ye L, Cai H, Xia B, Yu X: PALB2 links BRCA1 and BRCA2 in the DNA-damage response. Current Biology 2009;19:524-529.

41 Polak P, Kim J, Braunstein LZ, Karlic R, Haradhavala NJ, Tiao G, Rosebrock D, Livitz D, Kübler K, Mouw KW: A mutational signature reveals alterations underlying deficient homologous recombination repair in breast cancer. Nature genetics 2017;49:1476.

42 Dancey J: mTOR signaling and drug development in cancer. Nature reviews Clinical oncology 2010;7:209.