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*Supplementary material*

# Role of Genetic Variation in ABC Transporters in Breast Cancer Prognosis and Therapy Response

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**Supplementary Table S1**. Clinical data of patient in the testing set.

| **Characteristics** | **Patients, N (%)[1]** |
|---|---|
| Age at diagnosis, mean ± S.D.[2] (years) | 51.7 ± 9.4 |
| *Menopausal status* | |
| Premenopausal | 46 (46) |
| Postmenopausal | 55 (55) |
| Missing data | 4 |
| *Tumor size (pT)* | |
| pTis | 8 (8) |
| pT1 | 50 (48) |
| pT2 | 40 (39) |
| pT3 | 5 (5) |
| pTX | 2 |
| *Lymph node metastasis (pN)* | |
| Absent (pN0) | 68 (65) |
| Present (pN1-3) | 37 (35) |
| *Pathological stage* | |
| SI | 46 (44) |
| SII | 47 (45) |
| SIII | 12 (11) |
| *Histological type* | |
| Invasive ductal carcinoma | 88 (84) |
| Other type | 17 (16)[4] |
| *Pathological grade* | |
| G1 | 11 (11) |
| G2 | 35 (35) |
| G3 | 54 (54) |
| GX | 5 |
| *Estrogen receptor status* | |
| Positive | 38 (38) |
| Negative | 61 (62) |
| Missing data | 6 |
| *Progesterone receptor status* | |
| Positive | 39 (39) |
| Negative | 60 (61) |
| Missing data | 6 |
| *Expression of HER2* | |
| Positive | 2 (2) |
| Negative | 97 (97) |
| Missing data | 6 |
| *Expression of Ki-67, mean ± S.D.[2] (%)* | 32.9 ± 20.3 |

**Supplementary Table S1.** Clinical data of patient in the testing set. (Cont.).

| Characteristics | Patients, N (%)[1] |
|---|---|
| *Molecular subtype* | |
| Luminal A | 11 (11) |
| Luminal B | 30 (30) |
| Triple negative | 58 (59) |
| Missing data | 6 |
| *Response to neoadjuvant cytotoxic therapy* | |
| Complete or partial response | 47 (69) |
| Stable disease or progression | 21 (31) |
| Not applicable[3] | 37 |

Footnotes:
[1] Number of patients with % in parentheses
[2] S.D.=standard deviation
[3] Patients treated with adjuvant therapy without neoadjuvant cytotoxic therapy
[4] Six lobular, six medullary, two metaplastic, one mucinous, one papillary, and one neuroendocrine invasive carcinomas

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**Supplementary Table S2.** Prioritized variants for the validation phase.

| Gene | HGVS coding (GRCh38) | HGVS protein | Classification[1] | Rs ID[2] | Response[3] | DFS[3] | MAF[4] | GnomAD[5] |
|---|---|---|---|---|---|---|---|---|
| *ABCA1* | NC_000009.12:g.104781418_104781420del | — | 3'UTR | rs41474449 | NS | 0.049 | 0.07 | 0.08 |
| *ABCA4* | NC_000001.11:g.94011139C>T | — | intron | rs2065711 | 0.010 | NS | 0.20 | 0.25 |
| *ABCA4* | NC_000001.11:g.94008629A>C | — | intron | rs2275032 | 0.008 | NS | 0.14 | 0.18 |
| *ABCA4* | NC_000001.11:g.94014481C>T | — | intron | rs2275033 | NS | 0.040 | 0.40 | 0.43 |
| *ABCA4* | NC_000001.11:g.94045977G>A | — | intron | rs3789398 | 0.015 | NS | 0.35 | 0.33 |
| *ABCA4* | NC_000001.11:g.94010999G>A | — | intron | rs537831 | 0.018 | NS | 0.31 | 0.29 |
| *ABCA5* | NC_000017.11:g.69249800G>A | — | intron | rs1420904 | 0.047 | NS | 0.08 | 0.10 |
| *ABCA5* | NC_000017.11:g.69249759T>C | — | intron | rs2067851 | NS | 0.020 | 0.07 | 0.09 |
| *ABCA7* | NC_000019.10:g.1051139_1051140TG[1] | — | intron | rs9282562 | NS | 0.040 | 0.14 | 0.11 |
| *ABCA8* | NC_000017.11:g.68929782C>T | — | intron | rs4147976 | NS | 0.049 | 0.35 | 0.42 |
| *ABCA9* | NC_000017.11:g.69061147T>C | — | intron | rs11871944 | 0.021 | NS | 0.40 | 0.37 |
| *ABCA9* | NC_000017.11:g.68989851T>G | **p.Lys1306Thr** | **missense** | rs2302294 | NS | 0.030 | 0.34 | 0.35 |
| *ABCA12* | NC_000002.12:g.214989432C>T | — | synonymous | rs71428357 | 0.014 | NS | 0.08 | 0.05 |
| *ABCA13* | NC_000007.14:g.48389118A>T | **p.Tyr3851Phe** | **missense** | rs17132289 | NS | 0.030 | 0.08 | 0.07 |
| *ABCA13* | NC_000007.14:g.48410560T>C | — | synonymous | rs17548783 | NS | 0.040 | 0.49 | 0.48 |
| *ABCA13* | NC_000007.14:g.48198124G>C | — | intron | rs28637820 | 0.029 | NS | 0.13 | 0.13 |
| *ABCA13* | NC_000007.14:g.48276333G>C | **p.Ala2223Pro** | **missense** | rs74859514 | NS | <0.001 | 0.08 | 0.09 |
| *ABCA13* | NC_000007.14:g.48392165C>T | — | intron | rs7780299 | NS | 0.010 | 0.12 | 0.14 |
| *ABCB1* | NC_000007.14:g.87600124T>C | **p.Asn21Asp** | **missense** | rs9282564 | NS | 0.030 | 0.13 | 0.11 |
| *ABCB5* | NC_000007.14:g.20700049G>A | — | intron | rs12700230 | 0.008 | NS | 0.23 | 0.23 |
| *ABCB5* | NC_000007.14:g.20661065A>T | — | intron | rs2893007 [6] | NS | 0.03 [6] | 0.10 | 0.08 |
| *ABCB5* | NC_000007.14:g.20756864G>A | — | 3'UTR | rs3210441 | 0.037 | NS | 0.44 | 0.36 |
| *ABCB8* | NC_000007.14:g.151028635A>C | — | intron | rs2303922 | NS | 0.049 | 0.34 | 0.36 |
| *ABCB11* | NC_000002.12:g.168958145G>A | — | intron | rs853772 | 0.034 | NS | 0.25 | 0.48 |
| *ABCC1* | NC_000016.10:g.16138351del | — | intron | rs4148379 | NS | 0.049 | 0.20 | 0.22 |
| *ABCC2* | NC_000010.11:g.99804058G>A | **p.Val417Ile** | **missense** | rs2273697 | 0.031 | NS | 0.22 | 0.20 |

**Supplementary Table S2.** Prioritized variants for the validation phase. (Cont.)

| Gene | HGVS coding (GRCh38) | HGVS protein | Classification[1] | Rs ID[2] | Response[3] | DFS[3] | MAF[4] | GnomAD[5] |
|---|---|---|---|---|---|---|---|---|
| *ABCC3* | NC_000017.11:g.50635344G>A | — | intron | rs12604031 | 0.034 | NS | 0.44 | 0.40 |
| *ABCC3* | NC_000017.11:g.50676161C>T | — | intron | rs8077268 | NS | 0.020 | 0.10 | 0.11 |
| *ABCC4* | NC_000013.11:g.95206724T>C | — | synonymous | rs2274405 | NS | 0.030 | 0.37 | 0.34 |
| *ABCC4* | NC_000013.11:g.95209550A>G | — | synonymous | rs899494 | NS | 0.030 | 0.12 | 0.14 |
| *ABCC5* | NC_000003.12:g.184000591A>G | — | intron | rs12638017 | NS | 0.010 | 0.06 | 0.07 |
| *ABCC5* | NC_000003.12:g.183967461T>C | — | intron | rs4148579 | 0.044 | NS | 0.43 | 0.46 |
| *ABCC8* | NC_000011.10:g.17395957A>G | — | intron | rs739689 | 0.041 | NS | 0.40 | 0.35 |
| *ABCC10* | NC_000006.12:g.43427363G>A | — | upstream | rs75320251 | 0.045 | NS | 0.09 | 0.11 |
| *ABCC11* | NC_000016.10:g.48224287C>T | **p.Gly180Arg** | **missense** | rs17822931 | 0.047 | NS | 0.14 | 0.13 |
| *ABCC13* | NC_000021.9:g.14279748A>G | — | intron | rs2254297 | NS | 0.049 | 0.40 | 0.43 |
| *ABCC13* | NC_000021.9:g.14337293T>G | — | intron | rs2822582 | NS | 0.020 | 0.40 | 0.37 |
| *ABCD4* | NC_000014.9:g.74299377T>C | — | intron | rs2301346 | 0.012 | NS | 0.32 | 0.30 |
| *ABCD4* | NC_000014.9:g.74299190C>A | — | intron | rs2301347 | 0.003 | NS | 0.40 | 0.37 |
| *ABCF2* | NC_000007.14:g.151218016C>T | — | intron | rs79537035 | 0.032 | NS | 0.23 | 0.17 |
| *ABCG8* | NC_000002.12:g.43874090A>G | — | intron | rs34198326 | NS | 0.040 | 0.06 | 0.07 |
| *ABCG8* | NC_000002.12:g.43852262G>A | — | intron | rs56260466 | NS | 0.049 | 0.06 | 0.06 |
| *CFTR* | NC_000007.14:g.117559403A>G | — | intron | rs34855237 | NS | 0.03 | 0.08 | 0.21 |

Footnotes:

[1] Classification in Annovar

[2] SNV number in dbSNP (https://www.ncbi.nlm.nih.gov/snp/)

[3] p-value provided for clinical associations; NS = non-significant

[4] MAF = minor allele frequency in the testing set

[5] The Genome Aggregation Database (gnomAD), allelic frequencies in European non-Finnish population

[6] Variant replacing failed rs11764054 based on tagging analysis; rs11764054 associated with DFS (p = 0.030)

**Supplementary Table S3.** Clinical data of patients in the validation set.

| Characteristics | Patients, N (%)[1] |
|---|---|
| *Age at diagnosis, mean ± S.D.[2] (years)* | 58.9 ± 12.5 |
| *Menopausal status* | |
| Premenopausal | 196 (25) |
| Postmenopausal | 592 (75) |
| Missing data | 14 |
| *Tumor size (pT)* | |
| pTis | 65 (8) |
| pT1 | 488 (62) |
| pT2 | 206 (27) |
| pT3 | 18 (2) |
| pT4 | 10 (1) |
| pTX | 15 |
| *Lymph node metastasis (pN)* | |
| Absent (pN0) | 507 (67) |
| Present (pN1-3) | 252 (33) |
| pNX | 43 |
| *Pathological stage* | |
| S0 | 61 (8) |
| SI | 343 (46) |
| SII | 282 (38) |
| SIII | 64 (9) |
| SIV | 1 (0) |
| Not determined | 51 |
| *Histological type* | |
| Invasive ductal carcinoma | 596 (75) |
| Other type | 196 (25) |
| Missing data | 10 |
| *Pathological grade* | |
| G1 | 177 (23) |
| G2 | 382 (50) |
| G3 | 209 (27) |
| GX | 34 |
| *Estrogen receptor status* | |
| Positive | 615 (77) |
| Negative | 181 (23) |
| Missing data | 6 |
| *Progesterone receptor status* | |
| Positive | 577 (73) |
| Negative | 219 (27) |
| Missing data | 6 |

**Supplementary Table S3.** Clinical data of patients in the validation set. (Cont.)

| Characteristics | Patients, N (%)[1] |
|---|---|
| *Expression of HER2* | |
| Positive | 194 (24) |
| Negative | 600 (76) |
| Missing data | 8 |
| *Expression of Ki-67, mean ± S.D.[2] (%)* | 23.3 ± 22.6 |
| *Molecular subtype* | |
| Luminal A | 320 (40) |
| Luminal B | 315 (40) |
| Triple negative | 94 (12) |
| HER2 | 63 (8) |
| Missing data | 10 |
| *Response to neoadjuvant cytotoxic therapy* | |
| Complete or partial response | 127 (76) |
| Stable disease or progression | 41 (24) |
| Not applicable[3] | 634 |

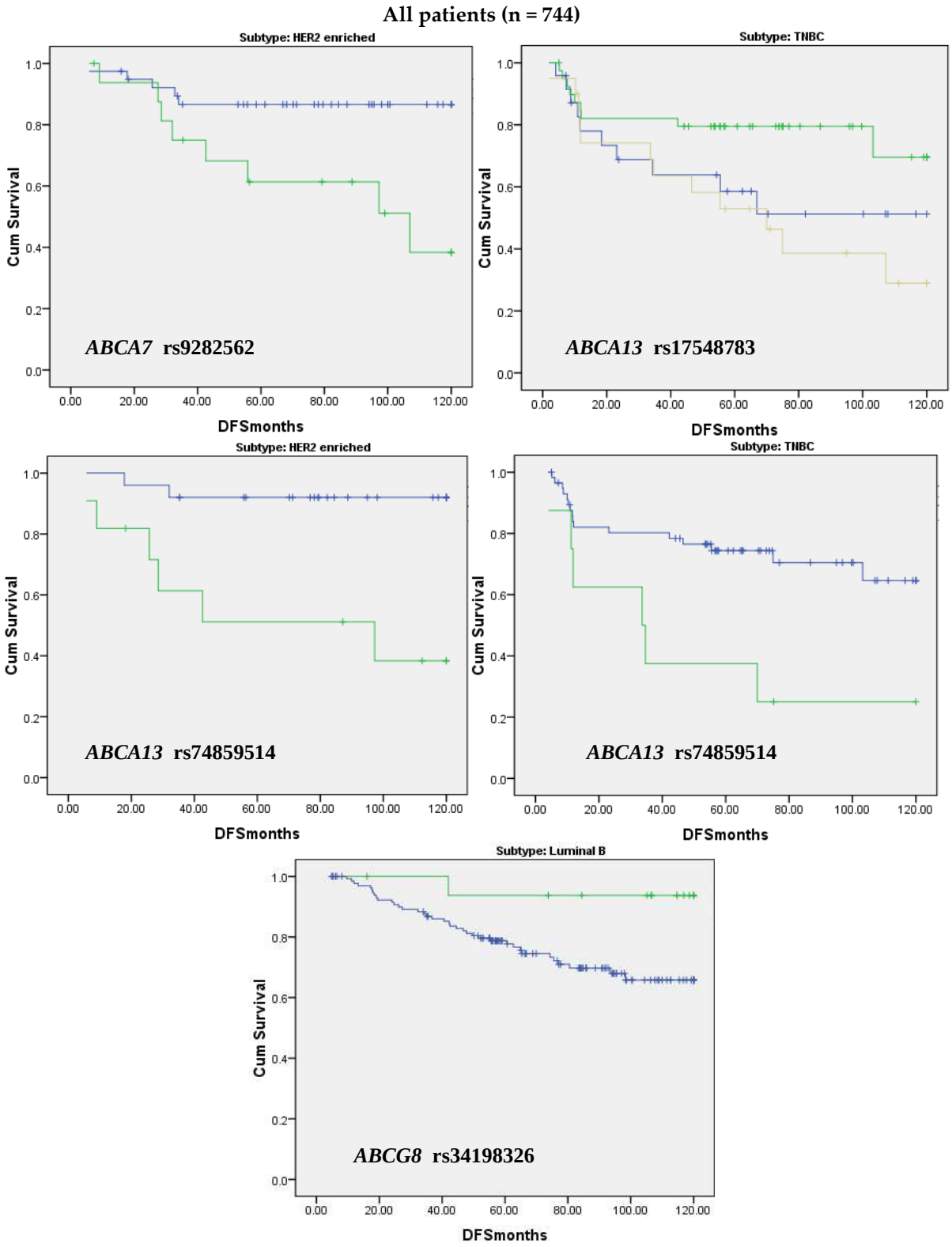
Footnotes:

[1] Number of patients with % in parentheses

[2] S.D.=standard deviation

[3] Patients treated with adjuvant therapy without neoadjuvant cytotoxic therapy

**Figure S1.** Kaplan-Meier survival plots showing significant associations of validated variants with DFS of breast patients stratified according to their molecular subtypes.




Blue line = common homozygotes; green line = heterozygotes or rare allele carriers; yellow line = rare homozygotes. For all SNPs except *ABCA13* rs17548783 recessive genetic model is displayed.

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**Figure S2.** Significant associations of gene expression in healthy tissues with variants significantly associated with survival or response to cytotoxic chemotherapy – plots are derived from an eQTL analysis at GTEx portal.