Supplementary Table 1. Primers amplifying DNA including the identified SNP for identification of previously identified missense variants associated with anthracycline cardiotoxicity.

|  |  |  |  |
| --- | --- | --- | --- |
| **Gene** | **Variant location** | **Forward Primer** | **Reverse Primer** |
|  |  |  |  |
| *CELF4* | chr18:35077028 | TAGCAACTGTGACTGGGACG | TTCTCTCTTGGTGGGCTCTG |
| *HAS3* | chr16:69143577 | GCTACCAGTTCATCCACACG | AGGTCAGGGAAGGAGATGC |
| *ABCC1* | chr16:16235681 | CCTACTGCCTCGGATCTCTC | CTGGCCCAAAACGAGAAC |
| *ETFB* | Chr19: 51857738 | CAGGCTTCACTCGGATCTG | GAGGAGCAGTGACAACAGTAGG |
| *ABCC5* | chr3:183737356 | CCATTTCAGGTAGATCAAACGC | GAGTGGCTGCTCAAGTTTCC |
| *CAT* | chr11:34460231 | CTTCTGATTGGCTGCTCGG | ATTCCGTCTGCAAAACTGGC |
|  | chr11:34460704 | CTGCAGTGTTCTGCACAGC | CCCTCAATCTGTCCTCAAGC |
| *NOS3* | chr7:150696111 | CAGGAGACAGTGGATGGAGG | TGCAGGCCCTTCTTGAGAG |
| *RARG* | chr12:53605545 | GTGCCTCTGTCCTCCTGAGC | CTCATTGGAAGGGGTGGG |
| *GPR35* | chr2:241570127 | GGTCTTCTGCTCCCTGAAGG | GGAACTCCTTGGCCATGTAG |
| *SLC28A3* | chr9:86900926 | AAGGTGGGTGGGAAGTTGG | GCACCAATGGTGTCCATCC |
| *NCF4* | chr22:37256846 | GCCTGGGGAAGAGTTTGG | GGCCCACACTTCCTCTTACC |
| *RAC2* |  chr22:37632770 | CCCAATTCAGAAAGGCCCAC | CCATTGCCCTGAGAACCAAG |
| *CBR3* | chr21:37518706 | TGAGGTGCATGAGAGGGAAG | CCGAAGCAGACGTTTACCAG |
| *ABCC2* | chr10:101595996 | TTATGTGTCTACCTCCCGCC | CCCTCCCACCGCTAATATC |
|  | chr10:101611294 | AAATGCCTAGACTTGAGATGCTGC | CTAACCCATGGGGCCTTCTG |
| *CYBA* | chr16:88713236 | GGTGGAGCTTGGTTTCTCAC | GGACCCGAATTTTTGTTTGG |
| *UGT1A6* | chr2:234602277 | CTCTTTTCACAGACCCAGC | ACAGCCAAACAGAGACCTTC |

**Supplementary Table 2.** Sex, age at diagnosis and tumour type of study cohort\*.

|  |  |  |
| --- | --- | --- |
| **Sex** | **Age at Diagnosis** **(Years)** | **Tumour** |
| F | 0 | AML a |
| F | 1 | ALL b |
| F | 2 | NHL c |
| F | 3 | AML |
| F | 3 | WT d |
| M | 3 | ALL |
| F | 5 | ALL |
| F | 6 | ALL |
| M | 8 | AML |
| F | 8 | ESe |
| M | 8 | AML |
| M | 10 | WT |
| M | 12 | ALL d |
| F | 15 | ALL |
| F | 17 | ES |

a AML = Acute Myeloid Leukaemia; b ALL = Acute Lymphoblastic Leukaemia; c Non-Hodgkin’s Lymphoma;d Wilms’ Tumour; e Ewing’s Sarcoma.

\*Data for each individual in the study can be requested from the authors.

**Supplementary Table 3.** Published single nucleotide polymorphisms (SNPs) associated with anthracycline-induced cardiotoxicity

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Gene** | **Variant location** | **Variant Type** | **Amino acid change** | **rs ID** | **gnomAD****Variant****Frequency** | **Global Variant Frequency\*** | **Author/Year** |
| *ETFB* | chr19: 51857738 | Missense | p.Pro52Leu | rs79338777 | 0.07269 | 8% | Ruiz-Pinto et al. 2017 |
| *SOD2* | chr6:160113872 | Missense | p.Val16Ala | rs4880 | 0.4834 | 41% | Rajic et al. 2009 |
| *NOS3* | chr7:150696111 | Missense | p.Asp298Glu | rs1799983 | 0.7514 | 82% | Krajinovic et al. 2015 |
| *RARG* | chr12:53605545 | Missense | p.Ser427Leu | rs2229774 | 0.07327 | 9% | Aminkeng et al. 2005 |
| *GPR35* | chr2:241570127 | Missense | p.Thr253Met | rs12468485 | 0.06074 | 5% | Ruiz-Pinto et al. 2017 |
| *CBR3* | chr21:37518706 | Missense | p.Val244Met | rs1056892 | 0.3688 | 43% | Blanco et al. 2008 |
| *ABCC2* | chr10:101595996 | Missense | p.Val1188Glu | rs17222723 | 0.04541 | 4% | Wojnowski et al. 2005 |
|  | chr10:101611294 | Missense | p.Cys1515Tyr | rs8187710 | 0.05487 | 7% | Wojnowski et al. 2005 |
| *CYBA* | chr16:88713236 | Missense | p.Tyr72His | rs4673 | 0.694 | 66% | Visscher et al. 2012 |
| *HAS3* | chr16:69143577 | Synonymous | p.Ala93Ala | rs2232228 | 0.3942 | 34% | Wang et al. 2014 |
| *SLC28A3* | chr9:86900926 | Synonymous | p.Leu461Leu | rs7853758 | 0.156 | 20% | Visscher et al. 2012 |
| *UGT1A6* | chr2:234602277 | Synonymous | p.Val209Val | rs17863783 | 0.03966 | 7% | Visscher et al. 2013 |
| *CELF4* | chr18:35077028 | Intronic |  | rs1786814 | 0.1542 | 13% | Wang et al. 2016 |
| *CAT* | chr11:34460704 | Intronic |  | rs10836235 | 0.09973 | 13% | Rajic et al. 2009 |
| *RAC2* |  chr22:37632770 | Intronic |  | rs13058338 | 0.1957 | 16% | Wojnowski et al. 2005 |
| *ABCC5* | chr3:183737356 | Upstream |  | rs7627754 | 0.2009 | 26% | Krajinovic et al. 2015 |
| *CAT* | chr11:34460231 | Upstream |  | rs1001179 | 0.1631 | 13% | Rajic et al. 2009 |
| *NCF4* | chr22:37256846 | 5' Region |  | rs1883112 | 0.4149 | 41% | Wojnowski et al. 2005 |
| *ABCC1* | chr16:16235681 | 3' UTR variant | rs3743527 | 0.2268 | 29% | Semsei et al. 2012 |

\* Global Variant Frequency from 1000 Genomes.