Original Article

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A Multicenter Study of Genotype Variation/Demographic Patterns in 2475 Individuals Including 1444 Cases With Breast Cancer in Turkey

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ABSTRACT

Objective: Breast cancer (BC) is the most common cancer type in women and may be inherited, mostly in an autosomal dominant pattern. The clinical diagnosis of BC relies on the published diagnostic criteria, and analysis of two genes, *BRCA1* and *BRCA2*, which are strongly associated with BC, are included in these criteria. The aim of this study was to compare BC index cases with non-BC individuals in terms of genotype and diagnostic features to investigate the genotype/demographic information association.

Materials and Methods: Mutational analyses for the *BRCA1/BRCA2* genes was performed in 2475 individuals between 2013-2022 from collaborative centers across Turkey, of whom 1444 with BC were designated as index cases.

Results: Overall, mutations were identified in 17% (421/2475), while the percentage of mutation carriers in cases of BC was similar, 16.6% (239/1444). *BRCA1*/*BRCA2* gene mutations were detected in 17.8% (131/737) of familial cases and 12% (78/549) of sporadic cases. Mutations in *BRCA1* were found in 4.9%, whereas 12% were in *BRCA2* ($p<0.05$). Meta-analyses were performed to compare these results with other studies of Mediterranean-region populations.

Conclusion: Patients with *BRCA2* mutations were significantly more common than those with *BRCA1* mutations. In sporadic cases, there was a lower proportion with *BRCA1/BRCA2* variants, as expected, and these results were consistent with the data of Mediterranean-region populations. However, the present study, because of the large sample size, revealed more robust findings than previous studies. These findings may be helpful in facilitating the clinical management of BC for both familial and non-familial cases.

Keywords: Breast cancer; *BRCA1*; *BRCA2*; genomic profiling; population study

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Key Points

- Breast cancer
- *BRCA1*
- *BRCA2*
- Genomic profiling
- Population study

Introduction

Breast cancer (BC) is a condition affecting approximately two million people per year, globally. The incidence is estimated as 1:8 in women and 1:833 in men (1). The clinical diagnosis of BC relies on the published diagnostic criteria (2). Two genes have been identified as being strongly associated with BC but not all cases are due to inherited factors. These two genes are breast cancer (*BRCA*) 1 and *BRCA2*. The *BRCA1* gene, located on chromosome 17, codes for breast cancer type 1 susceptibility protein. This gene has 22 exons distributed over approximately 110 kb of genomic DNA. In contrast with the *BRCA1* gene, the *BRCA2* gene has 27 exons over approximately 84.2 kb of genomic DNA on chromosome 13 (3). To date, more than 3242 disease-causing mutations have been identified in either *BRCA1* or *BRCA2* (4). It has been suggested that patients with BC without detected variants in *BRCA1* or *BRCA2* probably have mutations on other cancer related genes or large gene deletions, somatic mosaic mutations, and mutations in un-analysed gene noncoding regions of *BRCA1* and/or *BRCA2* (1, 2).

There is clinical interest in whether the phenotypic presentation of BC differs depending on disease-causing variants in *BRCA1* or *BRCA2*. Early studies from Mediterranean countries, even the population-based studies, which have reported genotype/phenotype correlations have not found any evidence for phenotypic differences between patients with *BRCA1* mutations vs. patients with no identified mutation or between patients with *BRCA1 vs. BRCA2* mutations (4-8). These studies, however, tend to have relatively small sample sizes. The largest and most recent studies showed *BRCA2* was found more frequently in individuals with BC in the region. The main studies included patients without family history but are also limited by the low number of index cases in the study group. On the other hand, *BRCA2* positivity reported with relatively higher frequencies in the Mediterranean region of Turkey when compared with other international studies (9, 10).

In this study, mutational analysis for the *BRCA1* and *BRCA2* genes was performed in 2475 individuals, of whom 1444 had been diagnosed with BC and were considered index cases. Comparisons were then made between BC patients and those without BC and between patients with by *BRCA1* or *BRCA2* variants in terms of diagnostic and demographic features to describe the genotype/demographic association in BC in this population. Mutation type, either protein truncation or missense, was also compared in terms of phenotypic features, as well as with the probands with positive family histroy. These latter comparisons were made to determine whether there was additional prognostic information that can be provided to families, based on genetic test results or mode of inheritance.

Materials and Methods

Patient Characteristics

Patients with a diagnosis of BC and healthy individuals with family history of BC were enrolled between 2013 and 2020 with informed written consents. The study was approved by the institutional review boards of all participating universities and the ethics board at Cukurova University. All the cases were diagnosed with invasive ductal BC with no other types of cancers or any other precancerous conditions. Similarly, individuals that were studied for screening were not affected with any other malignancies. For the familial studies, individuals who had family history of invasive ductal BC were included. Patient selection was made according to the American Society of Clinical Oncology (ASCO) and National Comprehensive Cancer Network (NCCN) guidelines (11, 12). Enrolled patients were evaluated by all our collaborators from Turkey, including from the Mediterranean, Aegean, Black Sea, Central Anatolia, Marmara, Eastern Anatolia, and Southeastern Anatolia Regions, and also from Northern Cyprus. As this study was conducted retrospectively, patient selection criteria were re-evaluated according to the up-to-date ASCO and NCCN guidelines prior to genetic analyses. The goal was to identify if variants were present in the *BRCA1* and *BRCA2* genes in these patients with invasive ductal BC. For familial BC cases that were enrolled, we included only the index patients for phenotypic analyses.

Subjects were enrolled in our research protocol through six different centers across Turkey and Cyprus. Clinical information was not available for every feature of BC on every participant. Some patients were referred and enrolled in the mutation screening process without sending sufficient clinical information to determine diagnostic status. Some of other demographic data, such as ethnicity, were not included due to the heterogeneity of the Turkish population, and lack of the consent of the majority of patient cohort further information. Patients who had no information, such as family history, were not included in the demographic analysis. We have, however, included them in the description of the mutations. Patients who were under 18 years of age, who were all index cases, were included. Moreover, patients who were under 30 years of age and carried *TP53* mutations were excluded, due to the purpose of our study.

Screening and Classification of Genetic Variations

DNA was extracted from peripheral blood lymphocytes of both healthy individuals and BC cases. Next generation sequencing was performed for all coding exons and exon-intron junctions of the *BRCA1* and *BRCA2* genes. In addition, Multiplex Ligation-dependent Probe Amplification (MLPA) was performed for 591 AGENTEM's primary index patients, as this is the national reference center for *BRCA1*/*BRCA2*. MLPA assay was not performed in the other collaborative centers. Nucleotide change was considered as pathogenic, a polymorphism or a variant of unknown significance (or unclassifiable variant) when it was novel and parents were unavailable for study. American College of Medical Genetics and Genomics (ACMG) criteria were followed for variant classification. The variations that were not identified in the Human Gene Mutation Database (HGMD) and The Single Nucleotide Polymorphism Database (dbSNP) or any other clinical databases (ClinVar and VarSome) were assessed as novel changes. Novel variants were then investigated through *in silico* analysis for variant classification. *In silico* analysis tools, including PolyPhen, Mutation Taster, CADD, SIFT, BLOSUM, PhyloP, GeneSplicer, B-SIFT, MaxEntScan, QCI Inferred Activation, BayesDel, DANN, SpliceAI, GenoCanyon, fitCons, MUT Assesor, Varity, FATHMM-XF, FATHMM-MKL, EIGEN PC, LRT were used, based on the genomic location, population frequencies, type and possible impacts on protein of the variations.

Statistical Analysis

The BC disease features for the following groups were compared using student's t test: (1) gene loci mutated *BRCA1* versus *BRCA2* and (2) familial versus sporadic using Graph Pad Prism (8.0.1.) Patient clinical findings were analyzed after grouping by gender, familial or sporadic, and location of mutation in *BRCA1* or *BRCA2*. As patients came from different sources and may not have all demographic criteria assessed, the numbers for each analysis varied. Only information from patients with a definite diagnosis was used for statistical analyses.

Population Comparison

GnomAD v2.1.1 data set (GRCh37/hg19) was used for the population comparison, which spans 125,748 exome sequences and 15,708 whole-genome sequences from unrelated individuals. The highest frequency of specific genetic alteration in gnomAD data set from various populations was used in order to compare our results with global data.

GnomAD v2.1.1 data set is the largest publicly available population data to date, and categorizes the populations as follows; African/African-American, Amish, Latino/Admixed American, Ashkenazi Jewish, East Asian, South Asian, Middle Eastern, European (Finnish), European (non-Finnish) and other. However, the proportion of the gnomAD population did not cluster with any of the Mediterranean populations. Therefore, it is more likely that Mediterranean populations were classified as "other", which includes individuals of mixed background, as in Turkey.

The MAF cut-off of 0.001 that is recommended for variant discovery in dominant inherited Mendelian diseases was used to classify variants as rare frequency (MAF ≤0.001) supporting variants' pathogenic effect, and common frequency (MAF ≥0.001) which are unlikely to be causative.

Results

Patient Characteristics

BRCA1 and *BRCA2* mutational analyses were performed in 2475 subjects. However, we were unable to curate all data for phenotypic features and not all subjects were interviewed for family history. Therefore we include 1444 (58.3%) cases contributing to results. Among 1444 BC patients, 737 (51%) of them had positive family history while 549 (49%) cases had no invasive ductal BC in their family. In the remaining patients (n = 158), family history of BC was unknown. Among *BRCA1*/*BRCA2* positive patients with a definite diagnosis, identification of a genetic alteration for familial patients was higher (54.8%; 131/239) than for patients with sporadic BC (32.6%; 78/239), and this was significant. The remaining variant positive patients (n = 30) were the individuals with unknown familial history of BC.

The median (range) age for all index patients (n = 1444) was 51.5 (15-88) years, and the average age was 48.6 years. Figure 1 details the demographic characteristics of our study population.

Mutation Analysis

Pathogenic mutations were identified in 218 individuals and variants of unknown significance for 139; in affected BC cases 114 of them had pathogenic variants and 85 cases had VUSs. Total variants, their pathogenicity, and internal frequencies are given in supplementary data (Supplementary Table 1). No genetic change could be identified for 2054 patients (82.9%) in total, and for 1205 (83.5%) of the BC cases. Among 737 BC cases with positive family history, 36 cases (4.9%) had variations in *BRCA1* and 95 cases (12.89 %) had variations in *BRCA2*, while 6 (4.6%) patients had genetic alterations in both genes resulting in a *BRCA1*:*BRCA2* ratio of 1/2.6. Twenty-seven of 549 patients

Table 1. Overall distribution of variant classification in *BRCA1* and *BRCA2* genes for both healthy individuals with BC diagnosed cases (n = 2475) and affected BC cases (n = 1444)

		Pathogenic	Likely Pathogenic	VUS
Both healthy individuals and BC diagnosed cases	***BRCA1***	70.1% (103/147)	11.5% (17/147)	18.4% (27/147)
	BRCA2	41.6% (118/283)	17.6% (50/283)	40.6% (115/283)
	Total	221 (51.3%)	67 (15.5%)	142 (33%)
Affected BC cases	***BRCA1***	71.4% (50/71)	11.3% (8/71)	18.3% (13/71)
	BRCA2	37.9% (66/174)	19.5% (34/174)	42.5% (74/174)
	Total	116	42	87

VUS: variant of uncertain significance; BC: breast cancer

(4.9%) without family history had variants in *BRCA1* and 51 patients (9.2%) had variants in *BRCA2*, resulting in a *BRCA1*:*BRCA2* ratio of approximately 1/2.

The mutations identified in *BRCA1* and *BRCA2* genes in all 2475 individuals were distributed as follows: 51.3% pathogenic, 15.5% likely pathogenic and 33% VUS (Table 1). Variant classifications for affected BC cases are also shown separately in Table 1.

The most frequent variants that were detected in both *BRCA1* and *BRCA2* are listed in Table 2. The most frequent variants were distributed equally across both genes. From the perspective of pathogenicity, pathogenic variants were present relatively more frequently, with nine variants. Novel genetic variations in both *BRCA*s are listed in Table 3. In contrast with the frequent variant list, *BRCA2* was more commonly found to be the site of novel variants with 14 versus one novel variant in *BRCA1*.

Clinical Features and Demographic Comparisons

The distribution of family history and the gender of cases for BC patients in this study are listed in Table 4. Phenotypes of these patients were compared by gender and mutation. Observed frequencies of clinical features listed in Table 5 for BC patients in this study. A proportion of cases were male, 20 of 1444 (1.39%) and pathogenic

Table 2. The most frequent detected variants in *BRCA1* and *BRCA2* genes

Gene	Variant	Impact	Class.[1]	Freq.[2] (%)
BRCA2	c.7689delC p.H2563Qfs*85	Frameshift	P[3]	3.92 (n = 17)
BRCA1	c.1444_1447delATTA p.I482*	Frameshift	P	3.46 (n = 15)
BRCA1	c.2800C>T p.Q934*	Nonsense	P	3 (n = 13)
BRCA1	c.4327C>T p.R1443*	Nonsense	P	3 (n = 13)
BRCA1	c.5266dupC p.Q1756Pfs*74	Frameshift	P	3 (n = 13)
BRCA2	c.1909+22delT	Inframe del	VUS[4]	2.07 (n = 9)
BRCA2	c.3836A>G p.N1279S	Missense	LP[5]	2.07 (n = 9)
BRCA2	c.9097dupA p.T3033fs*11	Frameshift	P	2.07 (n = 9)
BRCA2	c.3318C>G p.S1106R	Missense	LP	1.61 (n = 7)
BRCA2	c.3751dupA p.T1251fs*14	Frameshift	P	1.38 (n = 6)
BRCA2	c.4169delT p.L1390fs*20	Frameshift	P	1.38 (n = 6)
BRCA2	c.67+1G>A	Intronic	P	1.38 (n = 6)
BRCA2	c.8881G>A p.G2961S	Missense	VUS	1.38 (n = 6)

[1]Class.: classification; [2]Freq.: frequency; [3]P: pathogenic; [5]LP: likely pathogenic; [4]VUS: variant of uncertain significance

Table 3. Detected novel variants in *BRCA1* and *BRCA2* genes

Gene	Variant	Impact	Class.[1]
BRCA1	c.5152+23C>T	Intronic	VUS[3]
BRCA2	c.1519delA p.R507fs*2	Frameshift	LP[2]
BRCA2	c.1854C>A p.A618A	Synonymous	VUS
BRCA2	c.5647A>T p.K1883*	Nonsense	LP
BRCA2	c.5697T>A p.D1899E	Missense	VUS
BRCA2	c.6609T>A p.V2203V	Synonymous	VUS
BRCA2	c.6934G>C p.D2312H	Missense	LP
BRCA2	c.7645T>G p.C2549G	Missense	LP
BRCA2	c.7700A>G p.Y2567C	Missense	VUS
BRCA2	c.8020_8021dupAA p.I2675fs*2	Frameshift	LP
BRCA2	c.8021A>G p.K2674R	Missense	LP
BRCA2	c.8487+39T>C	Intronic	VUS
BRCA2	c.9370_9381delAACCTCCAGTGG p.N3124_W3127del	Inframe del	LP
BRCA2	c.9370_9383delAACCTCCAGTGGCGinsCT p.R3128delinsL	Missense	LP
BRCA2	c.9772G>A p.E3258K	Missense	VUS

[1]Class.: classification; [2]LP: likely pathogenic; [3]VUS: variant of uncertain significance

variations in *BRCA2* were present in two of the male BC patients. In this multicenter study, other demographic data, such as ethnicity, were not included due to the heterogeneity of the Turkish population and other legal issues in terms of the law on protection of personal data.

Subjects With A Positive Family History Versus Sporadic BC Cases

The phenotypic effects of mutation between the *BRCA1* gene and the *BRCA2* gene and BC features were investigated in 737 familial index patients and 549 sporadic BC patients. The median age was 52 years for familial index patients and 48.5 years for sporadic BC patients with average ages of 43.3 and 43.5 years, respectively. Comparison of the disease features of these two groups did not show any significant difference. However, patients with a positive family history were more likely to harbor *BRCA1/2* gene mutations than sporadic BC patients.

Impact of Mutation Types

The type of mutations in many genetic related disorders affects disease severity. To evaluate the effect of the type of mutations on the presence of BC features, we compared features of patients.

The proportions of mutations types detected are listed in Table 6.

Allele Frequency Comparison

Among a total of 220 different types of detected variations, 190 (86.4%) of them had higher allele frequencies than their aggregated gnomAD allele frequency. With a 0.001 MAF cut-off, 134 (60.9%) of the 220 variants were evaluated as rare and as all of them showed higher frequency in our study, they were considered as more likely to be pathogenic. In addition, 73.7% (56/76) of the globally common variants (MAF ≥0.001) were more frequent in our study while 20 (26.3%) showed lower frequencies than aggregated gnomAD. Distribution of common (MAF ≥0.001) and rare *BRCA1/2* variants (MAF ≤0.001) by gnomAD population and the aggregated gnomAD are given as supplementary data (Supplementary Table 2).

The frequencies of pathogenic variants and VUSs were compared across several ethnic groups and the local whole exome sequencing databases. The analysis showed that out of 28 pathogenic variants located in *BRCA1*, 31 occurred as a higher frequency than aggregated gnomAD data and distinctive populational gnomAD data. Details are given in supplementary data (Supplementary Table 2).

Table 4. Gender and family history distribution of cases

	Family history (+)	Family history (-)	Unknown family history
Female	729	537	158
Male	8	12	0
Total	737	549	158

Table 5. Phenotypic comparison of variant between genders in cases.

	Pathogenic	Likely Pathogenic	VUS
Female	113	43	87
Male	2	0	0
Total	115	43	87

VUS: variant of uncertain significance

Discussion and Conclusion

Mutations were sought in all coding exons and exon-intron junctions of the *BRCA1* and *BRCA2* genes in DNA from 2475 diagnosed and screening patients from Turkey and 221 (51.3%) previously reported pathogenic mutations, 142 (33%) VUS and 15 (3.7%) novel mutations were found, while the overall *BRCA1* and *BRCA2* mutation detection rate was 9.9%.

No mutation in *BRCA1/2* could be identified in 82.9% of all patients. Despite being one of the largest cohorts of *BRCA1/2* screening in the literature, as a limitation of our study, we were not able to examine gross deletion and duplication status of *BRCA1* and *BRCA2* genes in all mutation negative patients due to different infrastructures of collaborative centers. As noted in previous studies, the mutation detection rate varies from 2.7% to 19% for patients with positive family history but without clinical information in different populations (8, 9, 13).

One of the main focuses of this study was to pool a nationwide Mediterranean country dataset that will increase the power of further analysis for clinical interpretations, both in familial and non-familial cases and the cases with *BRCA1* and *BRCA2* mutations.

In multifactorial disorders such as cancers, correlation between genotype variation and demographic information is not as well understood as it is in Mendelian disorders. Analysis and interpretation of genetic test results should be considered with the patient's clinical and family history. This study also showed that a significant percentage of *BRCA1* and *BRCA2* variations are still classified as VUS. Thus, improvement of genetic variation databases is crucial for correct diagnosis. In the light of the fact that the genotype and phenotype correlation for BC is still controversial, these results can enhance our knowledge on this complicated, common and severe condition.

It was also observed that the most common mutations in the *BRCA1* and *BRCA2* genes in a representative Turkish population were not among the 10 most common mutations that were reported in a study that included all continents. *BRCA1* c.1444_1447delATTA p.I482* and *BRCA2* c.7689delC p.H2563Qfs*85 mutations can be considered

Table 6. Overall distribution of genetic variation types

	Frameshift	Missense	Nonsense	Intronic	In-frame dup	In-frame del
BRCA1	34	43	40	11	0	1
BRCA2	76	128	24	27	2	6
Total	110	171	64	38	2	7

to be founder mutations for Turkish population and a screening program can be planned for early diagnosis of BC (14).

We also demonstrated the importance of looking at the frequency of each variant per specific ethnic groups as opposed to the overall gnomAD frequency. Our analysis highlighted 56 pathogenic variants that had MAF ≤0.001 (Minor Allele Frequency) in the aggregated gnomAD population but were common in our population. Furthermore, when a more stringent MAF cut-off value (≤0.0001) was used, 123 pathogenic variants should be re-classified as more frequent and might be suggested as founder mutations for our population. In brief, these data also suggest that a number of variants still classified as pathogenic are not truly disease causing or the variants with the higher observed frequency are not truly benign.

The overall *BRCA1/2* mutation detection rate for patients with BC in Turkey was 9.9% in this study. The proportion of *BRCA1* to *BRCA2* mutations was approximately 2 to 2.5 for BC cases. Moreover, in patients with no family history of BC, *BRCA1* mutations accounted for 34.6% and *BRCA2* mutations accounted for 65.4% among mutation positive cases. Our study summarizes the interpretation process using the most important criteria as per ACMG guidelines, gene specific databases for analysis of the variant frequencies in the largest available population, together with local datasets and results of the computational predictions for a broadly representative but heterogeneous Turkish population.

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Ethics Committee Approval: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board (or Ethics Committee) of from Cukurova University Ethical Committee (102-2 and 07/08/2020).

Informed Consent: All participants were informed, and signed written consent

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.O.S., N.D., S.Y.O., M.C.E., K.D., C.K.P., O.Y., L.A., O.B., S.C., E.C., A.D., T.E., S.G., K.S., S.T., B.D., F.O., D.T., M.C., O.D., P.O., S.T.B., S.G.T.; Concept: A.B.; Design: K.D., M.D., A.B., S.G.T.; Data Collection or Processing: I.B., C.M., C.R., O.S., A.A., L.A., B.D., C.O.E., N.G., M.D.,; Analysis or Interpretation: I.B., C.M., C.R., O.S., A.A., B.D., C.O.E.; Literature Search: I.B., C.M., C.R., O.S., E.A., N.B., N.G., B.D.; Writing: M.C.E., M.D., A.B., S.G.T.

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Supplementary Table 1. The detected total variants list

Gene	Variant	Variant Type	Class.	Variant Freq. (%)	n
BRCA1	c.1444_1447delATTA p.I482*	Frameshift	P	3.46	15
BRCA1	c.2800C>T p.Q934*	Nonsense	P	3.00	13
BRCA1	c.4327C>T p.R1443*	Nonsense	P	3.00	13
BRCA1	c.5266dupC p.Q1756Pfs*74	Frameshift	P	3.00	13
BRCA1	c.181T>G p.C61G	Missense	P	1.15	5
BRCA1	c.5123C>A p.A1708E	Missense	P	1.15	5
BRCA1	c.135-2A>T	Intronic	LP	0.69	3
BRCA1	c.1881_1884del p.S628Efs*3	Frameshift	P	0.69	3
BRCA1	c.3211G>T p.E1071*	Nonsense	LP	0.69	3
BRCA1	c.3333del p.E1112Nfs*5	Frameshift	P	0.69	3
BRCA1	c.3607C>T p.R1203*	Nonsense	P	0.69	3
BRCA1	c.4391_4393delinsTT p.P1464Lfs*2	Frameshift	P	0.69	3
BRCA1	c.4956G>A p.M1652I	Missense	P	0.69	3
BRCA1	c.1895G>A p.S632N	Missense	LP	0.46	2
BRCA1	c.2019delA p.E673Dfs*28	Frameshift	P	0.46	2
BRCA1	c.2077G>A p.D693N	Missense	VUS	0.46	2
BRCA1	c.2599C>G p.Q867E	Missense	LP	0.46	2
BRCA1	c.3328_3330delAAG p.K1110del	Inframe del	VUS	0.46	2
BRCA1	c.4070_4071delAA p.E1357Gfs*10	Frameshift	LP	0.46	2
BRCA1	c.4936del p.V1646Sfs*12	Frameshift	P	0.46	2
BRCA1	c.5057dupA p.H1686Qfs*9	Frameshift	LP	0.46	2
BRCA1	c.509G>A p.R170Q	Missense	LP	0.46	2
BRCA1	c.5152+23C>T	Intronic	VUS	0.46	2
BRCA1	c.535T>C p.Y179H	Missense	VUS	0.46	2
BRCA1	c.53T>A p.M18K	Missense	VUS	0.46	2
BRCA1	c.788dupG p.S264*	Nonsense	P	0.46	2
BRCA1	c.979A>G p.T327A	Missense	VUS	0.46	2
BRCA1	c.1166_1169dup p.D390Efs*2	Frameshift	LP	0.23	1
BRCA1	c.134A>C p.K45T	Missense	VUS	0.23	1
BRCA1	c.1621C>T p.Q541*	Nonsense	P	0.23	1
BRCA1	c.1637_1685delinsGAAAG p.M546Ifs*5	Frameshift	LP	0.23	1
BRCA1	c.1644T>C p.I548I	Synonymous	VUS	0.23	1
BRCA1	c.1714G>T p.E572*	Nonsense	P	0.23	1
BRCA1	c.1772T>C p.I591T	Missense	VUS	0.23	1
BRCA1	c.1888G>T p.R629I	Missense	VUS	0.23	1
BRCA1	c.1938_1947delCAGTGAAGAG p.S646fs*2	Frameshift	P	0.23	1
BRCA1	c.2611_2612delCC p.P871Vfs*31	Frameshift	P	0.23	1
BRCA1	c.2666C>T p.S889F	Missense	VUS	0.23	1
BRCA1	c.2952del p.I986Sfs*14	Frameshift	P	0.23	1
BRCA1	c.3247A>G p.M1083V	Missense	LP	0.23	1
BRCA1	c.3700_3704del p.N1234Qfs*8	Frameshift	P	0.23	1
BRCA1	c.3756_3759delGTCT p.S1253fs*10	Frameshift	P	0.23	1
BRCA1	c.3770_3771delAG p.E1257Gfs*9	Frameshift	P	0.23	1
BRCA1	c.4033C>T p.L1335L	Nonsense	VUS	0.23	1

BRCA1	c.4035delA p.E1346fs*20	Frameshift	P	0.23	1
BRCA1	c.4063_4065delAAT p.N1355del	Inframe del	LP	0.23	1
BRCA1	c.4065_4068delTCAA p.N1355Kfs*10	Frameshift	P	0.23	1
BRCA1	c.4185+21_4185+22dupTG	Inframe dup	LP	0.23	1
BRCA1	c.4366A>G p.T1456A	Missense	VUS	0.23	1
BRCA1	c.4391_4393delCTAinsTT p.P1464Lfs*2	Frameshift	P	0.23	1
BRCA1	c.4443G>T p.E1478D	Missense	VUS	0.23	1
BRCA1	c.4487C>A p.S1496*	Nonsense	P	0.23	1
BRCA1	c.493_494delCT p.L165fs*16	Frameshift	P	0.23	1
BRCA1	c.4986+6 T>C	Intronic	LP	0.23	1
BRCA1	c.4986+6T>G	Intronic	VUS	0.23	1
BRCA1	c.4987A>T p.M1663L	Missense	LP	0.23	1
BRCA1	c.5102_5103delTG p.L1722Qfs*14	Frameshift	P	0.23	1
BRCA1	c.5194-2A>G	Intronic	P	0.23	1
BRCA1	c.692C>G p.T231R	Missense	VUS	0.23	1
BRCA1	c.734A>T p.D245V	Missense	VUS	0.23	1
BRCA1	c.81-4C>T	Intronic	VUS	0.23	1
BRCA2	c.7689delC p.H2563Qfs*85	Frameshift	P	3.92	17
BRCA2	c.1909+22delT	Inframe del	VUS	2.07	9
BRCA2	c.3836A>G p.N1279S	Missense	LP	2.07	9
BRCA2	c.9097dupA p.T3033fs*11	Frameshift	P	2.07	9
BRCA2	c.3318C>G p.S1106R	Missense	LP	1.61	7
BRCA2	c.3751dupA p.T1251fs*14	Frameshift	P	1.38	6
BRCA2	c.4169delT p.L1390fs*20	Frameshift	P	1.38	6
BRCA2	c.67+1G>A	Intronic	P	1.38	6
BRCA2	c.8881G>A p.G2961S	Missense	VUS	1.38	6
BRCA2	c.1519delA p.R507fs*2	Frameshift	LP	1.15	5
BRCA2	c.7472A>T p.Q2491L	Missense	VUS	1.15	5
BRCA2	c.9317G>A p.W3106*	Nonsense	P	1.15	5
BRCA2	c.1411G>A p.E471K	Missense	VUS	0.92	4
BRCA2	c.4471_4474del p.L1491Kfs*12	Frameshift	P	0.92	4
BRCA2	c.5969delA p.D1990Vfs*14	Frameshift	P	0.92	4
BRCA2	c.8478C>A p.Y2826*	Nonsense	P	0.92	4
BRCA2	c.10095delCinsGAATTATATCT p.S3366Nfs*4	Frameshift	LP	0.69	3
BRCA2	c.1343G>A p.R448H	Missense	VUS	0.69	3
BRCA2	c.1414C>T p.Q472*	Nonsense	P	0.69	3
BRCA2	c.2808_2811delACAA p.A938fs*21	Frameshift	P	0.69	3
BRCA2	c.4081C>G p.Q1361E	Missense	VUS	0.69	3
BRCA2	c.4258G>T p.D1420Y	Missense	VUS	0.69	3
BRCA2	c.4751del p.E1584Gfs*33	Frameshift	LP	0.69	3
BRCA2	c.6550C>G p.Q2184E	Missense	VUS	0.69	3
BRCA2	c.6814delA p.R2272Efs*8	Frameshift	P	0.69	3
BRCA2	c.7007G>A p.R2336H	Missense	P	0.69	3
BRCA2	c.9052_9057delAGTAAA p.K3019_3020del	Inframe del	LP	0.69	3
BRCA2	c.9934A>G p.I3312V	Missense	VUS	0.69	3
BRCA2	c.1773_1776delTTAT p.I591Mfs*22	Frameshift	P	0.46	2
BRCA2	c.122C>T p.P41L	Missense	VUS	0.46	2

BRCA2	c.1310_1313delAAGA p.K437Ifs*22	Frameshift	P	0.46	2
BRCA2	c.1951G>T p.D651Y	Missense	VUS	0.46	2
BRCA2	c.2765dupT p.K923Qfs*13	Frameshift	P	0.46	2
BRCA2	c.3503T>C p.M1168T	Missense	P	0.46	2
BRCA2	c.4146_4148delAGA p.E1382del	Inframe del	LP	0.46	2
BRCA2	c.4243G>C p.E1415Q	Missense	VUS	0.46	2
BRCA2	c.4446_4451dupAACAGA p.E1482_T1483dup	Inframe dup	VUS	0.46	2
BRCA2	c.5312G>A p.G1771D	Missense	VUS	0.46	2
BRCA2	c.5351dupA p.N1784Tfs*3	Frameshift	P	0.46	2
BRCA2	c.5590G>A p.D1864N	Missense	VUS	0.46	2
BRCA2	c.5647A>T p.K1883*	Nonsense	LP	0.46	2
BRCA2	c.6008T>C p.I2003T	Missense	VUS	0.46	2
BRCA2	c.6080G>A p.R2027K	Missense	VUS	0.46	2
BRCA2	c.6935A>T p.D2312V	Missense	VUS	0.46	2
BRCA2	c.7544C>T p.T2515I	Missense	VUS	0.46	2
BRCA2	c.7976G>A p.R2659K	Missense	P	0.46	2
BRCA2	c.8092G>A p.A2698T	Missense	VUS	0.46	2
BRCA2	c.8452G>A p.V2818I	Missense	VUS	0.46	2
BRCA2	c.8649A>G p.P2883P	Synonymous	VUS	0.46	2
BRCA2	c.9501+4A>G	Intronic	VUS	0.46	2
BRCA2	c.9839C>A p.P3280H	Missense	P	0.46	2
BRCA2	c.9976A>T p.K3326*	Nonsense	LP	0.46	2
BRCA2	c.10037_10046delTGATAAATACinsATT p.L3346fs*35	Frameshift	LP	0.23	1
BRCA2	c.10078A>G p.K3360E	Missense	VUS	0.23	1
BRCA2	c.10089A>G p.I3363M	Missense	VUS	0.23	1
BRCA2	c.1055dupA p.Y352*	Nonsense	P	0.23	1
BRCA2	c.1114A>C p.N372H	Missense	P	0.23	1
BRCA2	c.1181A>C p.E394A	Missense	LP	0.23	1
BRCA2	c.1235C>G p.P412R	Missense	VUS	0.23	1
BRCA2	c.1570A>G p.M524V	Missense	VUS	0.23	1
BRCA2	c.1587_1590delTAAA p.F529fs*28	Frameshift	P	0.23	1
BRCA2	c.1605C>T p.A535A	Synonymous	P	0.23	1
BRCA2	c.1627C>A p.H543N	Missense	LP	0.23	1
BRCA2	c.1648G>A p.E550K	Missense	VUS	0.23	1
BRCA2	c.1773_1776delTTAT p.I591fs*22	Frameshift	P	0.23	1
BRCA2	c.1854C>A p.A618A	Synonymous	VUS	0.23	1
BRCA2	c.2264C>G p.S755C	Missense	VUS	0.23	1
BRCA2	c.2372C>A p.S791*	Nonsense	P	0.23	1
BRCA2	c.2706T>C p.A902A	Synonymous	VUS	0.23	1
BRCA2	c.2779A>G p.M927V	Missense	VUS	0.23	1
BRCA2	c.280C>T p.P94S	Missense	VUS	0.23	1
BRCA2	c.2892A>T p.K964N	Missense	LP	0.23	1
BRCA2	c.3073A>G p.K1025E	Missense	LP	0.23	1
BRCA2	c.3171_3172del p.K1058Tfs*8	Frameshift	P	0.23	1
BRCA2	c.3263dupC p.Q1089Sfs*10	Frameshift	P	0.23	1
BRCA2	c.6290C>T p.T2097M	Missense	LP	0.23	1
BRCA2	c.3302A>G p.H1101R	Missense	VUS	0.23	1

BRCA2	c.3465_3466delTT p.S1156*	Nonsense	VUS	0.23	1
BRCA2	c.349_350delCT p.L117fs*6	Frameshift	P	0.23	1
BRCA2	c.3545_3546delTT p.F1182*	Nonsense	P	0.23	1
BRCA2	c.375T>A p.D125E	Missense	VUS	0.23	1
BRCA2	c.4237A>G p.K1413E	Missense	VUS	0.23	1
BRCA2	c.426-1G>C	Intronic	P	0.23	1
BRCA2	c.4519delC p.Q1507Rfs*36	Frameshift	P	0.23	1
BRCA2	c.4531G>A p.E1511K	Missense	VUS	0.23	1
BRCA2	c.4631dupA p.N1544Kfs*4	Frameshift	P	0.23	1
BRCA2	c.4901T>C p.F1634S	Missense	VUS	0.23	1
BRCA2	c.5020delA p.S1674Vfs*8	Frameshift	P	0.23	1
BRCA2	c.5130_5133TGTA p.Y1710*	Nonsense	P	0.23	1
BRCA2	c.5153-26A>G	Intronic	VUS	0.23	1
BRCA2	c.518delG p.G173fs*12	Frameshift	P	0.23	1
BRCA2	c.5483A>G p.K1828R	Missense	VUS	0.23	1
BRCA2	c.5697T>A p.D1899E	Missense	VUS	0.23	1
BRCA2	c.5722_5723delCT p.L1908Rfs*2	Frameshift	P	0.23	1
BRCA2	c.575T>C p.M192T	Missense	VUS	0.23	1
BRCA2	c.5870T>C p.I1957T	Missense	VUS	0.23	1
BRCA2	c.5975C>T p.S1992L	Missense	VUS	0.23	1
BRCA2	c.6085_6089delGAAAA p.E2029Yfs*18	Frameshift	P	0.23	1
BRCA2	c.6231G>C p.K2077N	Missense	LP	0.23	1
BRCA2	c.6320delC p.P2107Lfs*12	Frameshift	P	0.23	1
BRCA2	c.6365T>C p.M2122T	Missense	VUS	0.23	1
BRCA2	c.6405_6409delCTTAA p.N2135fs*3	Frameshift	P	0.23	1
BRCA2	c.6468_6469delTC p.Q2157Ifs*18	Frameshift	P	0.23	1
BRCA2	c.6469C>T p.Q2157*	Nonsense	P	0.23	1
BRCA2	c.6609T>A p.V2203V	Synonymous	VUS	0.23	1
BRCA2	c.6613G>A p.V2205M	Missense	VUS	0.23	1
BRCA2	c.6614T>G p.V2205G	Missense	LP	0.23	1
BRCA2	c.6742C>A p.H2248N	Missense	VUS	0.23	1
BRCA2	c.6842G>A p.G2281E	Missense	LP	0.23	1
BRCA2	c.6934G>C p.D2312H	Missense	LP	0.23	1
BRCA2	c.7072T>C p.S2358P	Missense	VUS	0.23	1
BRCA2	c.7227T>C p.P2409P	Synonymous	VUS	0.23	1
BRCA2	c.7435+10G>A	Intronic	VUS	0.23	1
BRCA2	c.7436-1G>C	Intronic	P	0.23	1
BRCA2	c.7522G>A p.G2508S	Missense	VUS	0.23	1
BRCA2	c.7633G>A p.V2545I	Missense	P	0.23	1
BRCA2	c.7645T>G p.C2549G	Missense	LP	0.23	1
BRCA2	c.7700A>G p.Y2567C	Missense	VUS	0.23	1
BRCA2	c.771_775del p.N257Kfs*17	Frameshift	P	0.23	1
BRCA2	c.7766C>T p.P2589L	Missense	LP	0.23	1
BRCA2	c.7783G>T p.A2595S	Missense	VUS	0.23	1
BRCA2	c.7855T>C p.W2619R	Missense	VUS	0.23	1
BRCA2	c.8020_8021dupAA p.I2675fs*2	Frameshift	LP	0.23	1
BRCA2	c.8021A>G p.K2674R	Missense	LP	0.23	1

BRCA2	c.8117A>G p.N2706S	Missense	VUS	0.23	1
BRCA2	c.8155A>G p.I2719V	Missense	VUS	0.23	1
BRCA2	c.8322-47G>T	Intronic	VUS	0.23	1
BRCA2	c.8324T>G p.M2775R	Missense	VUS	0.23	1
BRCA2	c.8359C>T p.R2787C	Missense	VUS	0.23	1
BRCA2	c.8395delA p.R2799Dfs*22	Frameshift	P	0.23	1
BRCA2	c.8487+39T>C	Intronic	VUS	0.23	1
BRCA2	c.8878C>T p.Q2960*	Nonsense	P	0.23	1
BRCA2	c.8930delA p.Y2977Ffs*11	Frameshift	VUS	0.23	1
BRCA2	c.8940delA p.E2981Kfs*7	Frameshift	P	0.23	1
BRCA2	c.8953+80G>A	Intronic	VUS	0.23	1
BRCA2	c.9038C>T p.T3013I	Missense	VUS	0.23	1
BRCA2	c.9253del p.T3085Qfs*19	Frameshift	P	0.23	1
BRCA2	c.9370_9381delAACCTCCAGTGG p.N3124_W3127del	Inframe del	LP	0.23	1
BRCA2	c.9370_9383delAACCTCCAGTGGCGinsCT p.R3128delinsL	Missense	LP	0.23	1
BRCA2	c.9382C>T p.R3128*	Nonsense	P	0.23	1
BRCA2	c.9397_9398delTC p.S3133fs*16	Frameshift	LP	0.23	1
BRCA2	c.9502-12T>G	Intronic	VUS	0.23	1
BRCA2	c.9556G>C p.A3186P	Missense	VUS	0.23	1
BRCA2	c.9586A>G p.K3196E	Missense	P	0.23	1
BRCA2	c.9613_9614delGCinsCT p.A3205L	Missense	LP	0.23	1
BRCA2	c.9682delA p.S3228Vfs*21	Frameshift	P	0.23	1
BRCA2	c.9717G>A p.W3106*	Nonsense	P	0.23	1
BRCA2	c.9730G>T p.V3244F	Missense	VUS	0.23	1
BRCA2	c.9772G>A p.E3258K	Missense	VUS	0.23	1

Supplementary Table 2. Distribution of common (MAF ≥0.001) and rare variants (MAF ≤0.001) in *BRCAs* by aggregated and population specific gnomAD data

No.	Gene	Variant	Mutation Type	ACMG Class.	n	Variant Frequency (n)	Observered Allel Frequency	gnomAD Aggregated Global Frequency	gnomAD Populational Freqency	Database/ Population	
1	*BRCA1*	c.1166_1169dup p.D390Efs*2	Frameshift	LP	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
2	*BRCA1*	c.134A>C p.K45T	Missense	VUS	1	0.23	0.020202%	0.079800%	0.001766%	gnomAD	European (non-Finnish)
3	*BRCA1*	c.135-2A>T	Intronic	LP	3	0.69	0.060606%	0.000000%	0.000000%	gnomAD	
4	*BRCA2*	c.7689delC p.H2563Qfs*85	Frameshift	P	17	3.92	0.343434%	0.000000%	0.000000%	gnomAD	
5	*BRCA1*	c.1621C>T p.Q541*	Nonsense	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
6	*BRCA1*	c.1637_1685delinsGA AAG p.M546Ifs*5	Frameshift	LP	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
7	*BRCA1*	c.1644T>C p.I548I	Synonymous	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
8	*BRCA1*	c.1714G>T p.E572*	Nonsense	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
9	*BRCA1*	c.1772T>C p.I591T	Missense	VUS	1	0.23	0.020202%	0.000797%	0.001762%	gnomAD	European
10	*BRCA1*	c.181T>G p.C61G	Missense	P	5	1.15	0.101010%	0.319000%	0.006168%	gnomAD	European (non-Finnish)
11	*BRCA1*	c.1881_1884del p.S628Efs*3	Frameshift	P	3	0.69	0.060606%	0.000398%	0.002893%	gnomAD	Latino/ Admixed American
12	*BRCA1*	c.1886G>T p.R629I	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
13	*BRCA1*	c.1895G>A p.S632N	Missense	LP	2	0.46	0.040404%	0.000398%	0.016360%	gnomAD	Other
14	*BRCA1*	c.1938_1947delCAG TGAAGAG p.S646fs*2	Frameshift	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
15	*BRCA1*	c.2019delA p.E673Dfs*28	Frameshift	P	2	0.46	0.040404%	0.000000%	0.000000%	gnomAD	
16	*BRCA1*	c.2077G>A p.D693N	Missense	VUS	2	0.46	0.040404%	5.840000%	9.370000%	gnomAD	Ashkenazi Jewish
17	*BRCA1*	c.2599C>G p.Q867E	Missense	LP	2	0.46	0.040404%	0.000000%	0.000000%	gnomAD	
18	*BRCA1*	c.2611_2612delCC p.P871Vfs*31	Frameshift	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
19	*BRCA1*	c.2666C>T p.S889F	Missense	VUS	1	0.23	0.020202%	0.001195%	0.002644%	gnomAD	European (non-Finnish)
20	*BRCA1*	c.1444_1447delATTA p.I482*	Frameshift	P	15	3.46	0.303030%	0.000000%	0.000000%	gnomAD	
21	*BRCA1*	c.2952del p.I986Sfs*14	Frameshift	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
22	*BRCA1*	c.3211G>T p.E1071*	Nonsense	LP	3	0.69	0.060606%	0.000000%	0.000000%	gnomAD	
23	*BRCA1*	c.3247A>G p.M1083V	Missense	LP	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
24	*BRCA1*	c.3328_3330delAAG p.K1110del	Inframe del	VUS	2	0.46	0.040404%	0.039560%	0.323600%	gnomAD	South Asian
25	*BRCA1*	c.3333del p.E1112Nfs*5	Frameshift	P	3	0.69	0.060606%	0.000000%	0.000000%	gnomAD	
26	*BRCA1*	c.3607C>T p.R1203*	Nonsense	P	3	0.69	0.060606%	0.001195%	0.005456%	gnomAD	East Asian
27	*BRCA1*	c.3700_3704del p.N1234Qfs*8	Frameshift	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
28	*BRCA1*	c.3756_3759delGTCT p.S1253fs*10	Frameshift	P	1	0.23	0.020202%	0.002388%	0.016320%	gnomAD	Other
29	*BRCA1*	c.3770_3771delAG p.E1257Gfs*9	Frameshift	P	1	0.23	0.020202%	0.000796%	0.003266%	gnomAD	South Asian

30	*BRCA1*	c.4033C>T p.L1335L	Nonsense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
31	*BRCA1*	c.4035delA p.E1346fs*20	Frameshift	P	1	0.23	0.020202%	0.004248%	0.009301%	gnomAD	European (non-Finnish)
32	*BRCA1*	c.4063_4065delAAT p.N1355del	Inframe del	LP	1	0.23	0.020202%	0.000399%	0.000881%	gnomAD	European (non-Finnish)
33	*BRCA1*	c.4065_4068delTCAA p.N1355Kfs*10	Frameshift	P	1	0.23	0.020202%	0.001190%	0.003280%	gnomAD	South Asian
34	*BRCA1*	c.4070_4071delAA p.E1357Gfs*10	Frameshift	LP	2	0.46	0.040404%	0.000000%	0.000000%	gnomAD	
35	*BRCA1*	c.4185+21_4185+22dupTG	Inframe dup	LP	1	0.23	0.020202%	0.006964%	0.018960%	gnomAD	South Asian
36	*BRCA1*	c.2800C>T p.Q934*	Nonsense	P	13	3.00	0.262626%	0.000000%	0.000000%	gnomAD	
37	*BRCA1*	c.4366A>G p.T1456A	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
38	*BRCA1*	c.4391_4393delCTAinsTT p.P1464Lfs*2	Frameshift	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
39	*BRCA1*	c.4391_4393delinsTT p.P1464Lfs*2	Frameshift	P	3	0.69	0.060606%	0.000000%	0.000000%	gnomAD	
40	*BRCA1*	c.4443G>T p.E1478D	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
41	*BRCA1*	c.4487C>A p.S1496*	Nonsense	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
42	*BRCA1*	c.493_494delCT p.L165fs*16	Frameshift	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
43	*BRCA1*	c.4936del p.V1646Sfs*12	Frameshift	P	2	0.46	0.040404%	0.000796%	0.009925%	gnomAD	Ashkenazi Jewish
44	*BRCA1*	c.4956G>A p.M1652I	Missense	P	3	0.69	0.060606%	1.818000%	3.799000%	gnomAD	South Asian
45	*BRCA1*	c.4986+6T>C	Intronic	LP	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
46	*BRCA1*	c.4986+6T>G	Intronic	VUS	1	0.23	0.020202%	0.000400%	0.000892%	gnomAD	European (non-Finnish)
47	*BRCA1*	c.4987A>T p.M1663L	Missense	LP	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
48	*BRCA1*	c.5057dupA p.H1686Qfs*9	Frameshift	LP	2	0.46	0.040404%	0.000000%	0.000000%	gnomAD	
49	*BRCA1*	c.509G>A p.R170Q	Missense	LP	2	0.46	0.040404%	0.003579%	0.007033%	gnomAD	European
50	*BRCA1*	c.5102_5103delTG p.L1722Qfs*14	Frameshift	P	1	0.23	0.020202%	0.000398%	0.005438%	gnomAD	East Asian
51	*BRCA1*	c.5123C>A p.A1708E	Missense	P	5	1.15	0.101010%	0.001990%	0.005784%	gnomAD	Latino/ Admixed American
52	*BRCA1*	c.5152+23C>T	Intronic	VUS	2	0.46	0.040404%	0.000000%	0.000000%	gnomAD	
53	*BRCA1*	c.5194-2A>G	Intronic	P	1	0.23	0.020202%	0.000398%	0.000879%	gnomAD	European (non-Finnish)
54	*BRCA1*	c.4327C>T p.R1443*	Nonsense	P	13	3.00	0.262626%	0.002476%	0.008468%	gnomAD	Latino/ Admixed American
55	*BRCA1*	c.535T>C p.Y179H	Missense	VUS	2	0.46	0.040404%	0.000795%	0.001758%	gnomAD	European (non-Finnish)
56	*BRCA1*	c.53T>A p.M18K	Missense	VUS	2	0.46	0.040404%	0.000000%	0.000000%	gnomAD	
57	*BRCA1*	c.692C>G p.T231R	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
58	*BRCA1*	c.734A>T p.D245V	Missense	VUS	1	0.23	0.020202%	0.001200%	0.002652%	gnomAD	European (non-Finnish)
59	*BRCA1*	c.788dupG p.S264*	Nonsense	P	2	0.46	0.040404%	0.000000%	0.000000%	gnomAD	
60	*BRCA1*	c.81-4C>T	Intronic	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
61	*BRCA1*	c.979A>G p.T327A	Missense	VUS	2	0.46	0.040404%	0.000000%	0.000000%	gnomAD	
62	*BRCA2*	c.1773_1776delTTAT p.I591Mfs*22	Frameshift	P	2	0.46	0.040404%	0.000000%	0.000000%	gnomAD	

63	*BRCA2*	c.10037_10046delTGATAAATACinsATT p.L3346fs*35	Frameshift	LP	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
64	*BRCA2*	c.10078A>G p.K3360E	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
65	*BRCA2*	c.10089A>G p.I3363M	Missense	VUS	1	0.23	0.020202%	0.008139%	0.065350%	gnomAD	South Asian
66	*BRCA2*	c.10095delCinsGAATTATATCT p.S3366Nfs*4	Frameshift	LP	3	0.69	0.060606%	0.000000%	0.000000%	gnomAD	
67	*BRCA2*	c.1055dupA p.Y352*	Nonsense	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
68	*BRCA2*	c.1114A>C p.N372H	Missense	P	1	0.23	0.020202%	27.330000%	35.660000%	gnomAD	Ashkenazi Jewish
69	*BRCA2*	c.1181A>C p.E394A	Missense	LP	1	0.23	0.020202%	0.002398%	0.005293%	gnomAD	European (non-Finnish)
70	*BRCA2*	c.122C>T p.P41L	Missense	VUS	2	0.46	0.040404%	0.000398%	0.000879%	gnomAD	European (non-Finnish)
71	*BRCA2*	c.1235C>G p.P412R	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
72	*BRCA2*	c.1310_1313delAAGA p.K437Ifs*22	Frameshift	P	2	0.46	0.040404%	0.000411%	0.006433%	gnomAD	African/ African-American
73	*BRCA2*	c.1343G>A p.R448H	Missense	VUS	3	0.69	0.060606%	0.000403%	0.002942%	gnomAD	Latino/ Admixed American
74	*BRCA2*	c.1411G>A p.E471K	Missense	VUS	4	0.92	0.080808%	0.000000%	0.000000%	gnomAD	
75	*BRCA2*	c.1414C>T p.Q472*	Nonsense	P	3	0.69	0.060606%	0.000000%	0.000000%	gnomAD	
76	*BRCA2*	c.1519delA p.R507fs*2	Frameshift	LP	5	1.15	0.101010%	0.000000%	0.000000%	gnomAD	
77	*BRCA2*	c.1570A>G p.M524V	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
78	*BRCA2*	c.1587_1590delTAAA p.F529fs*28	Frameshift	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
79	*BRCA2*	c.1605C>T p.A535A	Synonymous	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
80	*BRCA2*	c.1627C>A p.H543N	Missense	LP	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
81	*BRCA2*	c.1648G>A p.E550K	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
82	*BRCA2*	c.1773_1776delTTAT p.I591fs*22	Frameshift	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
83	*BRCA2*	c.1854C>A p.A618A	Synonymous	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
84	*BRCA2*	c.5266dupC p.Q1756Pfs*74	Frameshift	P	13	3.00	0.262626%	0.000000%	0.000000%	gnomAD	
85	*BRCA2*	c.1951G>T p.D651Y	Missense	VUS	2	0.46	0.040404%	0.000416%	0.000906%	gnomAD	European (non-Finnish)
86	*BRCA2*	c.2264C>G p.S755C	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
87	*BRCA2*	c.2372C>A p.S791*	Nonsense	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
88	*BRCA2*	c.2706T>C p.A902A	Synonymous	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
89	*BRCA2*	c.2765dupT p.K923Qfs*13	Frameshift	P	2	0.46	0.040404%	0.000000%	0.000000%	gnomAD	
90	*BRCA2*	c.2779A>G p.M927V	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
91	*BRCA2*	c.2808_2811delACAA p.A938fs*21	Frameshift	P	3	0.69	0.060606%	0.000797%	0.001764%	gnomAD	European (non-Finnish)
92	*BRCA2*	c.280C>T p.P94S	Missense	VUS	1	0.23	0.020202%	0.004779%	0.016350%	gnomAD	Other
93	*BRCA2*	c.2892A>T p.K964N	Missense	LP	1	0.23	0.020202%	0.004428%	0.036790%	gnomAD	South Asian
94	*BRCA2*	c.3073A>G p.K1025E	Missense	LP	1	0.23	0.020202%	0.004799%	0.009723%	gnomAD	European (non-Finnish)
95	*BRCA2*	c.3171_3172del p.K1058Tfs*8	Frameshift	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
96	*BRCA2*	c.3263dupC p.Q1089Sfs*10	Frameshift	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
97	*BRCA2*	c.6290C>T p.T2097M	Missense	LP	1	0.23	0.020202%	0.008314%	0.026390%	gnomAD	Latino/ Admixed American

98	*BRCA2*	c.3302A>G p.H1101R	Missense	VUS	1	0.23	0.020202%	0.000043%	0.000934%	gnomAD	European
99	*BRCA2*	c.1909+22delT	Inframe del	VUS	9	2.07	0.181818%	11.300000%	13.800000%	gnomAD	Ashkenazi Jewish
100	*BRCA2*	c.3465_3466delTT p.S1156*	Nonsense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
101	*BRCA2*	c.349_350delCT p.L117fs*6	Frameshift	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
102	*BRCA2*	c.3503T>C p.M1168T	Missense	P	2	0.46	0.040404%	0.000399%	0.002892%	gnomAD	Latino/ Admixed American
103	*BRCA2*	c.3545_3546delTT p.F1182*	Nonsense	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
104	*BRCA2*	c.3836A>G p.N1279S	Missense	LP	9	2.07	0.181818%	0.000000%	0.000000%	gnomAD	
105	*BRCA2*	c.375T>A p.D125E	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
106	*BRCA2*	c.9097dupA p.T3033fs*11	Frameshift	P	9	2.07	0.181818%	0.003185%	0.006483%	gnomAD	European (non-Finnish)
107	*BRCA2*	c.4081C>G p.Q1361E	Missense	VUS	3	0.69	0.060606%	0.000000%	0.000000%	gnomAD	
108	*BRCA2*	c.4146_4148delAGA p.E1382del	Inframe del	LP	2	0.46	0.040404%	0.007223%	0.024010%	gnomAD	European (Finnish)
109	*BRCA2*	c.3318C>G p.S1106R	Missense	LP	7	1.61	0.141414%	0.000420%	0.000914%	gnomAD	European (non-Finnish)
110	*BRCA2*	c.4237A>G p.K1413E	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
111	*BRCA2*	c.4243G>C p.E1415Q	Missense	VUS	2	0.46	0.040404%	0.000000%	0.000000%	gnomAD	
112	*BRCA2*	c.4258G>T p.D1420Y	Missense	VUS	3	0.69	0.060606%	0.666000%	1.880000%	gnomAD	European (Finnish)
113	*BRCA2*	c.426-1G>C	Intronic	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
114	*BRCA2*	c.4446_4451dupAACAGA p.E1482_T1483dup	Inframe dup	VUS	2	0.46	0.040404%	0.000400%	0.000885%	gnomAD	European (non-Finnish)
115	*BRCA2*	c.4471_4474del p.L1491Kfs*12	Frameshift	P	4	0.92	0.080808%	0.000399%	0.006187%	gnomAD	African/ African-American
116	*BRCA2*	c.4519delC p.Q1507Rfs*36	Frameshift	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
117	*BRCA2*	c.4531G>A p.E1511K	Missense	VUS	1	0.23	0.020202%	0.002840%	0.019620%	gnomAD	South Asian
118	*BRCA2*	c.4631dupA p.N1544Kfs*4	Frameshift	P	1	0.23	0.020202%	0.000710%	0.001554%	gnomAD	European (non-Finnish)
119	*BRCA2*	c.4751del p.E1584Gfs*33	Frameshift	LP	3	0.69	0.060606%	0.000000%	0.000000%	gnomAD	
120	*BRCA2*	c.4901T>C p.F1634S	Missense	VUS	1	0.23	0.020202%	0.001427%	0.003120%	gnomAD	European (non-Finnish)
121	*BRCA2*	c.5020delA p.S1674Vfs*8	Frameshift	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
122	*BRCA2*	c.5130_5133TGTA p.Y1710*	Nonsense	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
123	*BRCA1*	c.5153-26A>G	Intronic	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
124	*BRCA2*	c.518delG p.G173fs*12	Frameshift	P	1	0.23	0.020202%	0.003185%	0.011470%	gnomAD	African/ African-American
125	*BRCA2*	c.5312G>A p.G1771D	Missense	VUS	2	0.46	0.040404%	0.031580%	0.096690%	gnomAD	Ashkenazi Jewish
126	*BRCA2*	c.5351dupA p.N1784Tfs*3	Frameshift	P	2	0.46	0.040404%	0.000000%	0.000000%	gnomAD	
127	*BRCA2*	c.5483A>G p.K1828R	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
128	*BRCA2*	c.5590G>A p.D1864N	Missense	VUS	2	0.46	0.040404%	0.001220%	0.016760%	gnomAD	Other
129	*BRCA2*	c.5647A>T p.K1883*	Nonsense	LP	2	0.46	0.040404%	0.000000%	0.000000%	gnomAD	
130	*BRCA2*	c.5697T>A p.D1899E	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
131	*BRCA2*	c.5722_5723delCT p.L1908Rfs*2	Frameshift	P	1	0.23	0.020202%	0.000399%	0.003268%	gnomAD	South Asian

132	*BRCA2*	c.575T>C p.M192T	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
133	*BRCA2*	c.5870T>C p.I1957T	Missense	VUS	1	0.23	0.020202%	0.002391%	0.006535%	gnomAD	South Asian
134	*BRCA2*	c.5969delA p.D1990Vfs*14	Frameshift	P	4	0.92	0.080808%	0.000000%	0.000000%	gnomAD	
135	*BRCA2*	c.5975C>T p.S1992L	Missense	VUS	1	0.23	0.020202%	0.000709%	0.001553%	gnomAD	European (non-Finnish)
136	*BRCA2*	c.6008T>C p.I2003T	Missense	VUS	2	0.46	0.040404%	0.000000%	0.000000%	gnomAD	
137	*BRCA2*	c.6080G>A p.R2027K	Missense	VUS	2	0.46	0.040404%	0.000000%	0.000000%	gnomAD	
138	*BRCA2*	c.6085_6089delGAAAA p.E2029Yfs*18	Frameshift	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
139	*BRCA2*	c.6231G>C p.K2077N	Missense	LP	1	0.23	0.020202%	0.011660%	0.096250%	gnomAD	South Asian
140	*BRCA2*	c.6320delC p.P2107Lfs*12	Frameshift	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
141	*BRCA2*	c.6365T>C p.M2122T	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
142	*BRCA2*	c.6405_6409delCTTAA p.N2135fs*3	Frameshift	P	1	0.23	0.020202%	0.000416%	0.017240%	gnomAD	Other
143	*BRCA2*	c.6468_6469delTC p.Q2157Ifs*18	Frameshift	P	1	0.23	0.020202%	0.000436%	0.003910%	gnomAD	Other-South Asian
144	*BRCA2*	c.6469C>T p.Q2157*	Nonsense	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
145	*BRCA2*	c.6550C>G p.Q2184E	Missense	VUS	3	0.69	0.060606%	0.001220%	0.010160%	gnomAD	Ashkenazi Jewish
146	*BRCA2*	c.6609T>A p.V2203V	Synonymous	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
147	*BRCA2*	c.6613G>A p.V2205M	Missense	VUS	1	0.23	0.020202%	0.002446%	0.005358%	gnomAD	European (non-Finnish)
148	*BRCA2*	c.6614T>G p.V2205G	Missense	LP	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
149	*BRCA2*	c.3751dupA p.T1251fs*14	Frameshift	P	6	1.38	0.121212%	0.000407%	0.016740%	gnomAD	Other
150	*BRCA2*	c.6742C>A p.H2248N	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
151	*BRCA2*	c.6814delA p.R2272Efs*8	Frameshift	P	3	0.69	0.060606%	0.000000%	0.000000%	gnomAD	
152	*BRCA2*	c.6842G>A p.G2281E	Missense	LP	1	0.23	0.020202%	0.000408%	0.003397%	gnomAD	South Asian
153	*BRCA2*	c.6934G>C p.D2312H	Missense	LP	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
154	*BRCA2*	c.6935A>T p.D2312V	Missense	VUS	2	0.46	0.040404%	0.022050%	0.189900%	gnomAD	South Asian
155	*BRCA2*	c.7007G>A p.R2336H	Missense	P	3	0.69	0.060606%	0.000000%	0.000000%	gnomAD	
156	*BRCA2*	c.7072T>C p.S2358P	Missense	VUS	1	0.23	0.020202%	0.000797%	0.006550%	gnomAD	South Asian
157	*BRCA2*	c.7227T>C p.P2409P	Synonymous	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
158	*BRCA2*	c.7435+10G>A	Intronic	VUS	1	0.23	0.020202%	0.000400%	0.000887%	gnomAD	European (non-Finnish)
159	*BRCA2*	c.7436-1G>C	Intronic	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
160	*BRCA2*	c.7472A>T p.Q2491L	Missense	VUS	5	1.15	0.101010%	0.000000%	0.000000%	gnomAD	
161	*BRCA2*	c.7522G>A p.G2508S	Missense	VUS	1	0.23	0.020202%	0.015910%	0.225500%	gnomAD	East Asian
162	*BRCA2*	c.7544C>T p.T2515I	Missense	VUS	2	0.46	0.040404%	0.059780%	0.166200%	gnomAD	European
163	*BRCA2*	c.7633G>A p.V2545I	Missense	P	1	0.23	0.020202%	0.000709%	0.004020%	gnomAD	African/ African-American
164	*BRCA2*	c.7645T>G p.C2549G	Missense	LP	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
165	*BRCA2*	c.4169delT p.L1390fs*20	Frameshift	P	6	1.38	0.121212%	0.000000%	0.000000%	gnomAD	
166	*BRCA2*	c.7700A>G p.Y2567C	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
167	*BRCA2*	c.771_775del p.N257Kfs*17	Frameshift	P	1	0.23	0.020202%	0.000798%	0.009244%	gnomAD	European (Finnish)
168	*BRCA2*	c.7766C>T p.P2589L	Missense	LP	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
169	*BRCA2*	c.7783G>T p.A2595S	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
170	*BRCA2*	c.7855T>C p.W2619R	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	

171	*BRCA2*	c.7976G>A p.R2659K	Missense	P	2	0.46	0.040404%	0.000398%	0.000881%	gnomAD	European (non-Finnish)
172	*BRCA2*	c.8020_8021dupAA p.I2675fs*2	Frameshift	LP	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
173	*BRCA2*	c.8021A>G p.K2674R	Missense	LP	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
174	*BRCA2*	c.8092G>A p.A2698T	Missense	VUS	2	0.46	0.040404%	0.003537%	0.024030%	gnomAD	African/ African-American
175	*BRCA2*	c.8117A>G p.N2706S	Missense	VUS	1	0.23	0.020202%	0.006719%	0.052260%	gnomAD	South Asian
176	*BRCA2*	c.8155A>G p.I2719V	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
177	*BRCA2*	c.8322-47G>T	Intronic	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
178	*BRCA2*	c.8324T>G p.M2775R	Missense	VUS	1	0.23	0.020202%	0.003184%	0.006481%	gnomAD	European (non-Finnish)
179	*BRCA2*	c.8359C>T p.R2787C	Missense	VUS	1	0.23	0.020202%	0.000398%	0.002891%	gnomAD	Latino/ Admixed American
180	*BRCA2*	c.8395delA p.R2799Dfs*22	Frameshift	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
181	*BRCA2*	c.8452G>A p.V2818I	Missense	VUS	2	0.46	0.040404%	0.000398%	0.000880%	gnomAD	European (non-Finnish)
182	*BRCA2*	c.8478C>A p.Y2826*	Nonsense	P	4	0.92	0.080808%	0.000398%	0.003267%	gnomAD	South Asian
183	*BRCA2*	c.8487+39T>C	Intronic	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
184	*BRCA2*	c.8649A>G p.P2883P	Synonymous	VUS	2	0.46	0.040404%	0.000000%	0.000000%	gnomAD	
185	*BRCA2*	c.8878C>T p.Q2960*	Nonsense	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
186	*BRCA2*	c.67+1G>A	Intronic	P	6	1.38	0.121212%	0.000000%	0.000000%	gnomAD	
187	*BRCA2*	c.8930delA p.Y2977Ffs*11	Frameshift	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
188	*BRCA2*	c.8940delA p.E2981Kfs*7	Frameshift	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
189	*BRCA2*	c.8953+80G>A	Intronic	VUS	1	0.23	0.020202%	0.012700%	0.025900%	gnomAD	European (non-Finnish)
190	*BRCA2*	c.9038C>T p.T3013I	Missense	VUS	1	0.23	0.020202%	0.024480%	0.047480%	gnomAD	European (non-Finnish)
191	*BRCA2*	c.9052_9057delAGTAAA p.K3019_3020del	Inframe del	LP	3	0.69	0.060606%	0.003548%	0.032120%	gnomAD	African/ African-American
192	*BRCA2*	c.8881G>A p.G2961S	Missense	VUS	6	1.38	0.121212%	0.000000%	0.000000%	gnomAD	
193	*BRCA2*	c.9253del p.T3085Qfs*19	Frameshift	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
194	*BRCA2*	c.9317G>A p.W3106*	Nonsense	P	5	1.15	0.101010%	0.000000%	0.000000%	gnomAD	
195	*BRCA2*	c.9370_9381delAACCTCCA GTGG p.N3124_W3127del	Inframe del	LP	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
196	*BRCA2*	c.9370_9383delAAC CTCCAGTGGCGinsCT p.R3128delinsL	Missense	LP	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
197	*BRCA2*	c.9382C>T p.R3128*	Nonsense	P	1	0.23	0.020202%	0.002122%	0.020030%	gnomAD	African/ African-American
198	*BRCA2*	c.9397_9398delTC p.S3133fs*16	Frameshift	LP	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
199	*BRCA2*	c.9501+4A>G	Intronic	VUS	2	0.46	0.040404%	0.001195%	0.016360%	gnomAD	Other
200	*BRCA2*	c.9502-12T>G	Intronic	VUS	1	0.23	0.020202%	0.010620%	0.027750%	gnomAD	Other
201	*BRCA2*	c.9556G>C p.A3186P	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
202	*BRCA2*	c.9586A>G p.K3196E	Missense	P	1	0.23	0.020202%	0.009546%	0.028220%	gnomAD	Latino/ Admixed American

203	*BRCA2*	c.9613_9614delGCinsCT p.A3205L	Missense	LP	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
204	*BRCA2*	c.9682delA p.S3228Vfs*21	Frameshift	P	1	0.23	0.020202%	0.000400%	0.000883%	gnomAD	European (non-Finnish)
205	*BRCA2*	c.9717G>A p.W3106*	Nonsense	P	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
206	*BRCA2*	c.9730G>T p.V3244F	Missense	VUS	1	0.23	0.020202%	0.001194%	0.010880%	gnomAD	East Asian
207	*BRCA2*	c.9772G>A p.E3258K	Missense	VUS	1	0.23	0.020202%	0.000000%	0.000000%	gnomAD	
208	*BRCA2*	c.9839C>A p.P3280H	Missense	P	2	0.46	0.040404%	0.001592%	0.016310%	gnomAD	Other
209	*BRCA2*	c.9934A>G p.I3312V	Missense	VUS	3	0.69	0.060606%	0.001592%	0.016300%	gnomAD	Other
210	*BRCA2*	c.9976A>T p.K3326*	Nonsense	LP	2	0.46	0.040404%	0.646800%	1.091000%	gnomAD	European (Finnish)

ACMG Class.: ACMG (American College of Medical Genetics and Genomics) Classification; Freq.: frequency, gnomAD: The Genome Aggregation Database; P: pathogenic; LP: likely pathogenic; VUS: variant of uncertain significance