RESEARCH ARTICLE

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Whole Exome Sequencing Revealed Rare Variants in *BRCA2, RAD51D, FANGC, CYP24A1* Genes in Breast/Ovarian Cancer Patients from a Small Buryat Ethnic Group

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Abstract

Objective: Breast cancer is a public health problem with increasing incidence, prevalence, and mortality worldwide. Germline variants in the DNA repair genes *BRCA1/2* are involved in the pathogenesis of hereditary breast/ovarian cancer. However, for many ethnic groups that are isolated geographically worldwide, founder variants of breast cancer still have not been found. In this study, we provide whole exome sequencing data performed in a group of breast/ovarian cancer patients who belong to the Buryats. **Methods:** Our study included 56 Buryat patients with histologically confirmed primary breast/ovarian cancer who completed an anonymous questionnaire about basic information and nationality. Genomic DNA was isolated from peripheral blood leukocytes. Libraries were prepared using a BGI Optimal DNA Library Prep kit (MGI, China). An Agilent SureSelect Human All Exon V6 kit (Agilent, USA) was used for hybridization. High-throughput sequencing was performed on a DNA nanoball sequencing platform DNBSeq-G400 (MGI, China). **Result:** In the overall group of patients with signs of hereditary breast/ovarian cancer, likely pathogenic/pathogenic variants were detected in 16% (9/56). We have discovered likely pathogenic/pathogenic variants that can either directly (*BRCA2*, *RAD51D, FANCG*) or indirectly (*POLR2C, FOXL2, GDF9, CYP21A4*) initiate breast/ovarian cancer. For the first time, three rare germinal variants in the *BRCA2* gene were detected in a small Buryat ethnic group. Further studies are required to confirm their role in the pathogenesis of breast /ovarian cancer in this ethnic group. We found that the *RAD51D* gene variant c.757C>T is recurrent and was observed in 4% of Buryat patients with breast/ovarian cancer. **Conclusion:** For the first time, rare germinal variants in the *BRCA2*, *RAD51D*, *FANGC, CYP24A1* genes were detected in a small Buryat ethnic group. Our data are consistent with existing data showing that variants in the *RAD51D* gene may be involved in the pathogenesis of breast/ovarian cancer. We also showed that the Mongolic-speaking Buryat populations exhibited strong genetic resemblance to those of Chinese.

Keywords: Germline variants- breast cancer- ethnic groups- Buryat- non-Caucasian

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Introduction

Breast cancer is a public health problem with increasing incidence, prevalence and mortality worldwide [1]. Germline variants in the DNA repair genes *BRCA1/2* are involved in the pathogenesis of breast/ovarian cancer. The presence of these variants may lead to the manifestation of the hereditary breast/ovarian cancer syndrome at a young age. The *BRCA1/2* founder effect or the accumulation of certain variants in these genes has been described for some populations. These populations are known as genetic isolates due to their cultural or geographic isolation over many generations, either by preference for conservation culture and/or religion, or by geographical or societal restrictions [2]. The detection of *BRCA1/2* founder variants allows for more efficient and cost-effective genetic testing and cancer prevention strategies in populations where these variants are prevalent. By focusing on a smaller set of variants, testing becomes more rapid and affordable. This allows for early detection and preventive measures for high-risk individuals, potentially preventing the development of breast and ovarian cancers.

However, for many ethnic groups isolated

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geographically worldwide, founder variants of breast cancer still have not been found. It is possible that in these groups the breast cancer development will be caused by variants in genes other than *BRCA1/2*. Whole genome or whole exome sequencing methods are needed to expand the gene spectrum and study both coding and non-coding gene sequences in these ethnic groups. In this regard, the Buryats, as a small indigenous ethnic group of Siberia, represent an ideal population for current testing.

The Buryat people are descendants of Mongol populations that settled in the meadow-steppe region around Lake Baikal at the boundary of the northern forest. The Buryat language belongs to the Mongolic language family. At the last census, the Buryat population numbered over 400,000 individuals [3]. In our previous work, we have demonstrated that the Buryat and other native Siberian groups are genetic isolates due to their cultural and geographic isolation over many generations [4]. Since 2014, we have focused on the search for *BRCA1/2* founder variants in the Buryat ethnic group. We are currently continuing studies to identify variants involved in breast/ovarian cancer in non-Caucasian patients belonging to the indigenous Buryat people, a poorly studied ethnic group in Siberia. In this study, we provide whole exome sequencing data performed in a group of breast/ovarian cancer patients who belong to the Buryats.

Materials and Methods

Our study included 56 Buryat patients with histologically confirmed primary breast/ovarian cancer (3 patients with ovarian cancer) who completed an anonymous questionnaire about basic information and nationality. Thirty nine percent of patients were diagnosed with cancer prior to age 50. Two percent of patients (1/56) were diagnosed with metachronous breast cancer. Thirty nine percent of patients (22/56) had sings of hereditary cancer. Seven percent of patients (4/56) were young and had a history of hereditary cancer (Table 1). The clinical information was based on the medical documentation. All patients signed informed consent to participate in this study.

Genomic DNA isolated from peripheral blood leukocytes by standard procedures. Libraries were prepared using a BGI Optimal DNA Library Prep kit (MGI, China). An Agilent SureSelect Human All Exon V6 kit (Agilent, USA) was used for hybridization. High-throughput sequencing was performed on a DNA nanoball sequencing platform DNBSeq-G400 (MGI, China) (depth of coverage is 103.9x, Q30 reflects a base call accuracy of 95%). Exome sequencing data were processed using the DRAGEN Bio-IT platform v.3.9.5 (Illumina, USA) and aligned to the hg38 reference human genome. The quality of sequencing data was controlled using the MultiQC v.1.11 software. Annotation of the variants was done using the OpenCRAVAT software [5]. All found variants passed the filtering ($p < 0.005$). Variants are classified as pathogenic, likely pathogenic, uncertain significance, likely benign, and benign according to the 2015 guidelines of American College of Medical Genetics and Genomics and the Association for Molecular Pathology – ACMG/AMP [6]. Likely pathogenic/Pathogenic variants were confirmed by Sanger sequencing (Figure 1 a-g).

This study reflects high quality variants. High-quality variants were defined as (1) FILTER = PASS, (2) QUAL > 100, (3) Depth coverage ≥ 26X, and (4) Variant fraction ≥ 38%. Variants that did not fulfil these requirements were considered low-quality variants and not reported.

Results

In the overall group of patients with signs of hereditary breast/ovarian cancer, Likely pathogenic/Pathogenic variants were detected in 16% (9/56). Table 2 presents whole exome sequencing data in a group of Buryat women with breast/ovarian cancer.

According to bioinformatics analysis, we have found different classes of germinal variants from benign to pathogenic. Benign variants were discarded. We do not present conflicting, unknown variants due to the fact that their analysis is quite complex, the analysis of these variants is labor-intensive and will be continued. In this short report, we present only variants that are likely pathogenic or pathogenic in accordance to ACMG/AMP or ClinGen VCEP (Table 3).

We have discovered Likely pathogenic/pathogenic variants that can either directly (*BRCA2*, *RAD51D*, *FANCG*) or indirectly (*POLR2C, FOXL2, GDF9, CYP24A1*) initiate breast/ovarian cancer. For the first time, rare pathogenic variants, mainly in the *BRCA2* gene, not common among Slavs, were detected in three Buryat patients with breast/ovarian cancer. A pathogenic variant in the *BRCA2* gene c.9052A>G was found in a 43-year-old

Table 1. Clinical and Anamnestic Characteristics of Patients

Characteristics of patients	% (n)
Diagnosis	
Breast cancer	5(53/56)
Ovarian cancer	95(3/56)
Age	
≤ 50	61(34/56)
≥ 50	39(22/56)
Family history	
Yes	39(22/56)
No	38(21/56)
Unknown	23(13/56)
Tumor side	
Left	28(15/56)
Right	46(26/56)
Unknown	26(15/56)
Stage	
1	21(11/56)
2	23(13/56)
3	16(9/56)
4	14(8/56)
Unknown	26(15/56)

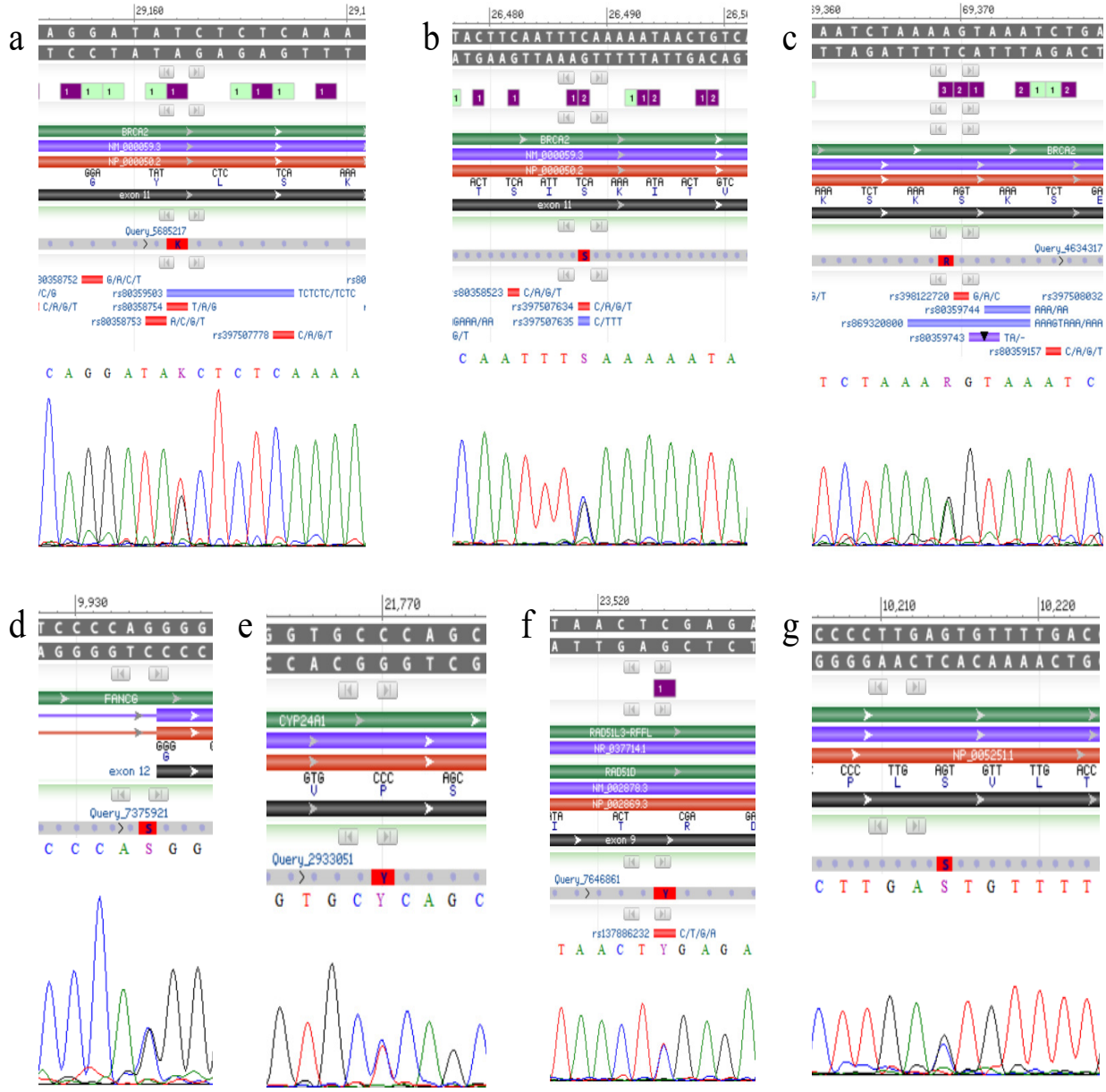

Figure 1. a-g. Detection of the genes variants by Sanger sequencing. a - is the positive sample, the canonical forward sequence of the *BRCA2* gene (c.5286T>G); b - is the positive sample, the canonical forward sequence of the *BRCA2* gene (c.2612C>G); c - is the positive sample, the canonical forward sequence of the *BRCA2* gene (c.9052A>G); d - is the positive sample, the canonical forward sequence of the *FANCG* gene (c.1481-1G>C); e - is the positive sample, the canonical forward sequence of the *CYP24A1* gene (c.1508C>T); f- is the positive sample, the canonical forward sequence of the *RAD51D* gene (c.757C>T); g - is the positive sample, the canonical forward sequence of the *GDF9* gene (c.1283G>C).

patient diagnosed with breast cancer. A pathogenic variant of the *BRCA2* gene c.5286T>G was found in a 70-year-old patient with ovarian cancer. A pathogenic variant of the *BRCA2* gene c.2612C>G was found in a 68-year-old patient diagnosed with ovarian cancer.

A pathogenic variant in the *RAD51D* gene c.757C>T was observed in two unrelated individuals. One of these individuals, a 61-year-old patient with ovarian cancer had a family history of breast cancer in first-degree relatives (mother). Another, a 47-year-old patient was diagnosed with breast cancer. Also, a 43-yers old breast cancer patient was found to have likely pathogenic splice site variant in *FANCG* c.1481-1G>C gene associated with Fanconi anemia.

In addition, we found likely pathogenic variants previously described as genes involved in primary ovarian insufficiency [7]. Among them, likely pathogenic variants of *POLR2C* c.77C>G, *FOXL2* c.1045C>G, *GDF9* c.1283G>C were detected in young Buryat breast cancer patients. Likely pathogenic variant of *FOXL2* c.1045C>G was found in a 43-year-old female patient diagnosed with breast cancer and bearing pathogenic non-coding splice site c.1481-1G>C in *FANCG* gene.

Likely pathogenic variant of *GDF9* c.1283G>C was found in two Buryat breast cancer patients (41- and 68-year-old). Likely pathogenic variant of *POLR2C* c.77C>G gene was detected in two Buryat breast cancer patients (40- and 65-year-old).

Table 2. Likely Pathogenic/Pathogenic Variants in Buryat Patients with Breast/Ovarian Cancer According to the whole Exome Sequencing Data Analysis

Gene, ID SNP	HGVS	MAF (GnomAD_genomes, Global)	Patient age, diagnosis
BRCA2 gene rs80358754	NM_000059.4: c.5286T>G p.Tyr1762Ter	G=0.000007	70-year-old, ovarian cancer
BRCA2 gene rs397507634	NM_000059.4: c.2612C>G p.Ser871Ter	A=0.000007	68-year-old, ovarian cancer
BRCA2 gene rs431825373	NM_000059.4: c.9052A>G p.Ser3018Gly	MAF None	43-year-old, breast cancer
FANCG gene rs2131053141	NM_004629.2: c.1481-1G>C	MAF None	43-year-old, breast cancer
CYP24A1 gene rs766440228	NM_000782.5: c.1508C>T p.Pro503Leu	A=0.0000486	47-year-old, breast cancer
RAD51D rs137886232	NM_002878.4: c.757C>T p.Arg253Ter	T=0.00003(ALFA, Global)	47-year-old, breast cancer, 61-year-old, ovarian cancer (mother BC)
POLR2C gene rs770336099	NM_032940.3: c.77C>G p.Thr26Ser	G=0.00002	43-year-old, breast cancer, 65-year-old breast cancer
FOXL2 gene rs201840174	NM_023067.4: c.1045C>G p.Arg349Gly	C=0.0002	43-year-old, breast cancer patient with FANCG gene variant
GDF9 gene rs118080183	NM_005260.7: c.1283G>C p.Ser428Thr	G=0.0001	41-year-old, breast cancer, 68-year-old breast cancer

Interestingly, a likely pathogenic variant of xenobiotic metabolism genes was also discovered. A 47-year-old breast cancer patient was found to have a likely pathogenic variants c.1508C>T in the *CYP24A1* gene.

Discussion

Buryats are the largest ethnic group, including Mongolian, Chinese, and Siberian Buryats, with a population of around 545,000 to 690,000 people [8]. In the Russian Federation, this ethnic group numbers

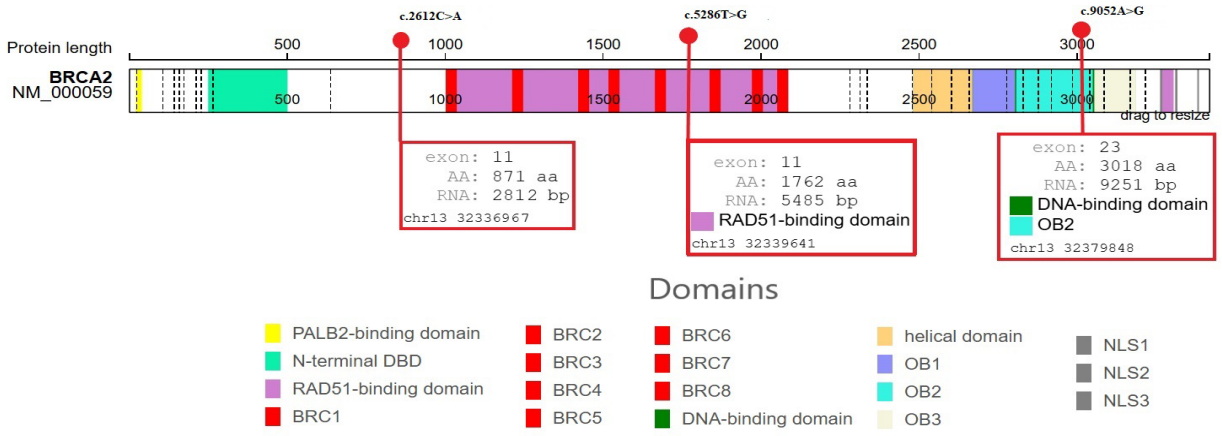

Figure 2. Functionally Significant Domains of the *BRCA2* Gene (*RAD51*-Binding and DNA-Binding Domains). The location of *BRCA2* gene variants (c.5286T>G, c.2612C>G, c.9052A) is shown in red.

Table 3. Variants Interpretation in According to ACMG/AMP or ClinGen VCEP

Gene, ID SNP	HGVS	VAF,%	ACMG/AMP evidence criteria	ClinGen VCEP/ evidence criteria	Variant interpretation
BRCA2 gene rs80358754	NM_000059.4 c.5286T>G p.Tyr1762Ter	53		PVS1, PM3_Support, PM5_Strong, PP1_Strong, PP3_Support, PP4_Strong	Pathogenic
BRCA2 gene rs397507634	NM_000059.4 c.2612C>G p.Ser871Ter	50		PVS1, PM3_Support, PM5_Strong, PP1_Strong, PP3_Support, PP4_Strong	Pathogenic
BRCA2 gene rs431825373	NM_000059.4 c.9052A>G p.Ser3018Gly	45		PVS1_Strong, PS3, PM2_Support, PM3_Support, PP1_Very_Strong, BP4_Support	Pathogenic (Likely pathogenic ClinVar)
FANCG gene rs2131053141	NM_004629.2 c.1481-1G>C	45	PVS1_Strong, PM2, PP3, PP4		Likely pathogenic
CYP24A1 gene rs766440228	NM_000782.5 c.1508C>T p.Pro503Leu	53	PM1, PM3, PP3, PP4		Likely pathogenic
RAD51D rs137886232	NM_002878.4 c.757C>T p.Arg253Ter	38	PVS1, PS4, PM4, PP1, PP3, PP4		Pathogenic
POLR2C gene rs770336099	NM_032940.3 c.77C>G p.Thr26Ser	50	PM1, PP3_Moderate, PP4, PP5		Likely pathogenic
FOXL2 gene rs201840174	NM_023067.4 c.1045C>G p.Arg349Gly	42	PS3_Support, PS4_Support, PM3, PP1, PP3, PP5		Likely pathogenic
GDF9 gene rs118080183	NM_005260.7 c.1283G>C p.Ser428Thr	56	PS3, PP3, PP4, PP5		Likely pathogenic

over 400,000 individuals. Nowadays, the study of ethnic-specific genetic variants associated with breast/ovarian cancer in the Buryat population is ongoing, and the precise mechanisms underlying hereditary breast and ovarian cancer in this group remain unknown.

We have previously detected two pathogenic variants in non-*BRCA* genes in 38 Buryat breast cancer patients using targeted sequencing (data not shown) [4]. Among them is a pathogenic variant in the *RAD51D* gene c.757C>T that observed in two unrelated individuals aged under 40. One of these patients had a family history of late-onset stomach cancer in second-degree relatives. The second pathogenic variant was found in the *PTEN* gene c.406T>C in a 38-year-old breast cancer patient with no family history. In addition, no pathogenic variants of the *BRCA1/2* genes or founder variants were detected in young Buryat women using targeted sequencing.

For a long time, young Buryats diagnosed with breast cancer were tested for the presence of 8 *BRCA 1/2* variants (common among Slavs) using the real-time PCR. In case of a negative test result, Buryat breast/ovarian cancer patients with signs of hereditary cancer were not observed for early cancer prevention. This situation was observed until the including high-throughput sequencing in health insurance. Currently, it is well established that the Slavic founder variants of *BRCA1/2* are absent in the Buryat ethnic group [9]. On the other hand, in the oncology practice, variants in non-*BRCA* genes (*CHECK2, PALB2, MUTYH, PTEN*, etc.) is not a potential targets for drug therapy. Current recommendations for patients bearing variants in the *CHECK2, PALB2, MUTYH, PTEN* genes and their healthy relatives usually include disease surveillance and control. However, since 2024, a new drug, TRUQAP (capivasertib) AstraZeneca, has become available in many countries around the world for patients with very rare variants in the *PTEN* gene [10]. The emergence of new drugs or expanded recommendations for the use of existing ones may be of great importance for ethnic groups in which variants in genes other than *BRCA* are prevalent.

In present study, we performed whole exome sequencing to continue searching for recurrent or founder variants in the Buryat ethnic group patients with breast/ovarian cancer. We did not restrict an age of the patients, since it is well known that more than 60% of women who inherit a harmful change in *BRCA1* or *BRCA2* will develop breast cancer during their lifetime [11]. It is important to note that three pathogenic variants of the *BRCA2* gene (c.5286T>G, c.2612C>G, c.9052A) we identified for the first time. A pathogenic variant in the *BRCA2* gene

c.9052A>G was identified in a 43-year-old young patient diagnosed with breast cancer. This missense variant has been described in the PubMed ClinVar database; overall population frequency has not been studied, and it was classified from uncertain significance to probably pathogenic in 2024. The c.9052A>G variant, also known as p.S3018G, located in coding exon 22 of the *BRCA2* gene, results from an A to G substitution at nucleotide position 9052. The serine at codon 3018 is replaced by glycine, an amino acid with similar properties. This alteration was identified once in an individual diagnosed with breast cancer living in Italy [12].

The variant in the *BRCA2* gene c.5286T>G (population frequency 0.0000) was detected in a 70-year-old patient with ovarian cancer. Previously, the *BRCA2* c.5286 T>G has been identified in 17 ovarian cancer patients from various regions of the Russian Federation, including Moscow, Novosibirsk, Irkutsk, Kirov, Chelyabinsk regions, Yakutia, and Primorsky Krai. This variant is also mentioned as a new founder variant in Russia, but without specifying the ethnic group [13]. According to Grigory A. Janus, 2023, the frequency of *BRCA2* c.5286 T>G was 3.4% (20/589) in the regions of the Russian Federation [14]. The authors summarize that this gene variant is common among the "northern Russians", who are a population that is genetically closer to the Finno-Ugrians than to the Slavs. It should be noted that in this study we first identified the c.5286T>G variant in a patient with ovarian cancer belonging to the Buryat ethnic group.

A pathogenic variant c.2612C>G in the *BRCA2* gene was found in a 68-year-old female patient diagnosed with ovarian cancer. This variant results in a stop codon that is described in ClinVar with a general population frequency of 0.00000 according to the PubMed SNP database. This variant was previously described in a one Chinese (c.2612C>G) and a one Vietnamese (c.2612C>G) breast cancer patients [15, 16]. Thus, all three variants of the *BRCA2* gene that we identified are rare germline variants, not typical for Slavs, and further studies are required to confirm their role in the breast/ovarian cancer pathogenesis in the Buryat ethnic group.

We also studied the location of these variants into the functionally significant domains of the *BRCA2* gene, which can be an indicator predicting the effectiveness of PARP inhibitors [17]. The *BRCA2* gene variant c.5286T>G is located in the important RAD51-binding domain, the variant c.9052A>G in the DNA-binding domain, in contrast to the variant c.2612C>G. Thus, the presence of *BRCA2* gene variants c.5286T>G and c.9052A>G may be associated with a long-term response to PARP inhibitor therapy (Figure 2).

Regarding non-BRCA genes, a pathogenic variant in the *RAD51D* gene c.757C>T, was rediscovered in two unrelated individuals in our study. This suggests that the variant *RAD51D* c.757C>T is recurrent and is observed in 4% (4/94) of breast/ovarian cancer Buryat patients. Yao H., 2022 found that *RAD51D* germline variants are more frequent in ovarian cancer Chinese patients with family history of cancer. In addition, the authors showed that patients with *RAD51D* germline variants might benefit from PARPis treatment [18].

High-performance whole exome sequencing method allowed to detect a likely pathogenic non-coding splice site c.1481-1G>C germline variant in *FANCG* gene in a 43-year-old female patient diagnosed with breast cancer. This variant is involved in Fanconi anemia, a rare, autosomal recessive genetic disease characterized by aplastic anemia, congenital defects, endocrinological abnormalities, and an increased cancer incidence, including breast cancer [19, 20].

A likely pathogenic variant in the *CYP24A1* gene/oncogene c.1508C>T not directly associated with an increase risk of breast cancer was found in a 47-year-old female breast cancer patient. *CYP24A1* is an enzyme expressed in the mitochondrion that catalyzes hydroxylation reactions which lead to the degradation of 1,25-dihydroxyvitamin D3, the physiologically active form of vitamin D. Is known that *CYP24A1* gene-induced vitamin D insufficiency promotes breast cancer growth [21].Vitamin D deficiency has been found to be associated with a variety of cancers, including prostate, multiple myeloma, colorectal and breast cancer [22].

Rare likely pathogenic gene variants associated with primary ovarian failure *POLR2C* c.77C>G, *FOXL2* c.1045C>G, *GDF9* c.1283G>C were also found in Buryat breast cancer patients. Primary ovarian failure is a heterogeneous disease and its molecular etiology is unclear. Moreover, 50–90% of cases is idiopathic and likely involves a substantial genetic contribution. Approximately 50% of the deleterious gene variants causing premature ovarian failure were found in genes involved in meiosis, DNA damage repair and transcription, and translation fidelity. Variants in these genes could predispose to cancer risk in women with premature ovarian failure [23]. Further studies are required to confirm the role of these germinal variants in ethnic breast cancer patients belonging to the Buryat ethnic group.

A significant limitation of our study is the analysis of only likely pathogenic/pathogenic variants in the Buryat ethnic group. However, in Buryat patients with breast/ovarian cancer, rare germline likely pathogenic/pathogenic variants in *RAD51D*, *BRCA2*, *FANGC* genes were found. Further studies are required to evaluate the impact of variants in the *CYP24A1* gene and genes associated with primary ovarian failure in breast cancer. There is a recurrent pathogenic variant of the *RAD51D* gene in breast/ovarian cancer Buryat patients. Moreover, our data are consistent with data showing that variants in the *RAD51D* gene may be involved in the pathogenesis of ovarian cancer, for example, in the Chinese population.

In conclusions, for the first time, rare germinal variants in the *BRCA2* gene, which are not typical for Slavs, were detected in a small Buryat ethnic group. Further studies are required to confirm their role in the pathogenesis of breast /ovarian cancer in this ethnic group. We found that the *RAD51D* gene c.757C>T is recurrent and is observed in 4% (4/94) of patients with breast/ovarian cancer. Our data are consistent with data showing that variants in the *RAD51D* gene may be involved in the pathogenesis of ovarian cancer, for example, in the Chinese population. We also showed that Mongolic-speaking Buryat populations exhibited strong genetic resemblance to Chinese.

Author Contribution Statement

All authors contributed equally to the concept, literature search, writing manuscript, critical revision, and finalizing the manuscript.

Acknowledgements

General

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Institutional review board statement

This study and the protocols used was approved by the Institutional Review Board (IRB) of Cancer Research Institute, Tomsk National Research Medical Center, Russian Academy of Science, Tomsk, Russia1 (ЭЗ № 07-2025/4, 29/09/2025)

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Data Availability

Data available on reasonable request

Ethical Declaration

The study was approved by the Ethics Committee of the Cancer Research Institute of Tomsk National Research Medical Center (Protocol No. 10 of September 24, 2022).

Conflict of Interest

The authors declare no potential conflict of interest.

References

1. Sanvisens A, Vidal-Vila A, Puigdemont M, Viñas G, Roqué-Lloveras A, Del Barco S, et al. Population-based analysis of breast cancer incidence and mortality: Overall and age-specific temporal trends over 40-year period in girona, spain. Breast Cancer Res Treat. 2025;212(1):97-105. https://doi.org/10.1007/s10549-025-07704-8.
2. Marafi D. Founder mutations and rare disease in the arab world. Dis Model Mech. 2024;17(6). https://doi.org/10.1242/dmm.050715.
3. Leonard WR, Sorensen MV, Mosher MJ, Spitsyn V, Comuzzie AG. Reduced fat oxidation and obesity risks among the buryat of southern siberia. Am J Hum Biol. 2009;21(5):664-70. https://doi.org/10.1002/ajhb.20903
4. Gervas P, Molokov A, Schegoleva A, Kiselev A, Babyshkina N, Pisareva L, et al. New germline mutations in non-brca genes among breast cancer women of mongoloid origin. Mol Biol Rep. 2020;47(7):5315-21. https://doi.org/10.1007/s11033-020-05612-2.
5. Pagel KA, Kim R, Moad K, Busby B, Zheng L, Tokheim C, et al. Integrated informatics analysis of cancer-related variants. JCO Clin Cancer Inform. 2020;4:310-7. https://doi.org/10.1200/cci.19.00132.
6. Richards S, Aziz N, Bale S, Bick D, Das S, Gastier-Foster J, et al. Standards and guidelines for the interpretation of sequence variants: A joint consensus recommendation of the american college of medical genetics and genomics and the association for molecular pathology. Genet Med. 2015;17(5):405-24. https://doi.org/10.1038/gim.2015.30.
7. Chapman C, Cree L, Shelling AN. The genetics of premature ovarian failure: Current perspectives. Int J Womens Health. 2015;7:799-810. https://doi.org/10.2147/ijwh.S64024.
8. Zelenskaya EM, Lifshits GI, Nikolaev KY, Donirova OS, Altayev VD, Apartsin KA, et al. The frequency of the minor polymorphisms in the cyp2c19, vegfr-2 genes, and clinical outcomes in russian and buryat patients with acute coronary syndrome. Genet Test Mol Biomarkers. 2020;24(6):338-42. https://doi.org/10.1089/gtmb.2019.0216.
9. Gervas P, Aleksey MY, Nataliya BN, Kollantay O, Evgeny CL, Cherdyntseva NV. A systematic review of the prevalence of germline brca mutations in north asia breast cancer patients. Asian Pac J Cancer Prev. 2024;25(6):1891-902. https://doi.org/10.31557/apjcp.2024.25.6.1891.
10. Turner NC, Oliveira M, Howell SJ, Dalenc F, Cortes J, Gomez Moreno HL, et al. Capivasertib in hormone receptor-positive advanced breast cancer. N Engl J Med. 2023;388(22):2058-70. https://doi.org/10.1056/NEJMoa2214131.
11. Godet I, Gilkes DM. Brca1 and *BRCA2* mutations and treatment strategies for breast cancer. Integr Cancer Sci Ther. 2017;4(1). https://doi.org/10.15761/icst.1000228.
12. Stella S, Vitale SR, Massimino M, Martorana F, Tornabene I, Tomarchio C, et al. In silico prediction of brca1 and *BRCA2* variants with conflicting clinical interpretation in a cohort of breast cancer patients. Genes (Basel). 2024;15(7):943. https://doi.org/10.3390/genes15070943.
13. Kechin A, Boyarskikh U, Barinov A, Tanas A, Kazakova S, Zhevlova A, et al. A spectrum of brca1 and *BRCA2* germline deleterious variants in ovarian cancer in russia. Breast Cancer Res Treat. 2023;197(2):387-95. https://doi.org/10.1007/s10549-022-06782-2.
14. Yanus GA, Sokolenko AP, Imyanitov EN. Northern origin of the *BRCA2* c.5286 t > g founder allele. Breast Cancer Res Treat. 2024;204(1):191. https://doi.org/10.1007/s10549-023-07202-9.
15. Kwong A, Shin VY, Ho JC, Kang E, Nakamura S, Teo SH, et al. Comprehensive spectrum of brca1 and *BRCA2* deleterious mutations in breast cancer in asian countries. J Med Genet. 2016;53(1):15-23. https://doi.org/10.1136/jmedgenet-2015-103132.
16. Wen WX, Allen J, Lai KN, Mariapun S, Hasan SN, Ng PS, et al. Inherited mutations in brca1 and *BRCA2* in an unselected multiethnic cohort of asian patients with breast cancer and healthy controls from malaysia. J Med Genet. 2018;55(2):97-103. https://doi.org/10.1136/jmedgenet-2017-104947.
17. Labidi-Galy SI, Rodrigues M, Sandoval JL, Kurtz JE, Heitz F, Mosconi AM, et al. Association of location of brca1 and *BRCA2* mutations with benefit from olaparib and bevacizumab maintenance in high-grade ovarian cancer: Phase iii paola-1/engot-ov25 trial subgroup exploratory analysis. Ann Oncol. 2023;34(2):152-62. https://doi.org/10.1016/j.annonc.2022.11.003.
18. Yao H, Li N, Yuan H. Clinical characteristics and survival analysis of chinese ovarian cancer patients with *RAD51D* germline mutations. BMC Cancer. 2022;22(1):1337. https://doi.org/10.1186/s12885-022-10456-z.
19. Fang CB, Wu HT, Zhang ML, Liu J, Zhang GJ. Fanconi anemia pathway: Mechanisms of breast cancer predisposition development and potential therapeutic targets. Front Cell Dev Biol. 2020;8:160. https://doi.org/10.3389/fcell.2020.00160.
20. D'Andrea AD. Susceptibility pathways in fanconi's anemia

and breast cancer. N Engl J Med. 2010;362(20):1909-19. https://doi.org/10.1056/NEJMra0809889.
21. Osanai M, Lee GH. Cyp24a1-induced vitamin d insufficiency promotes breast cancer growth. Oncol Rep. 2016;36(5):2755-62. https://doi.org/10.3892/or.2016.5072.
22. Gupta D, Vashi PG, Trukova K, Lis CG, Lammersfeld CA. Prevalence of serum vitamin d deficiency and insufficiency in cancer: Review of the epidemiological literature. Exp Ther Med. 2011;2(2):181-93. https://doi.org/10.3892/etm.2011.205.
23. Federici S, Rossetti R, Moleri S, Munari EV, Frixou M, Bonomi M, et al. Primary ovarian insufficiency: Update on clinical and genetic findings. Front Endocrinol (Lausanne). 2024;15:1464803. https://doi.org/10.3389/fendo.2024.1464803.