Journal of Carcinogenesis
Covering Genesis to Therapeutics

Journal of Carcinogenesis, ISSN: 1477-3163
2025; Vol 24: Issue 3s, https://carcinogenesis.com/

TP53 Arg72Pro Gene Polymorphism and Risk of Breast Cancer among Kabardino-Balkarian population

Bittueva Madina M.*, Bogotova Zalina I., Paritov Anzor U., Khandohov Tahir Kh., Akhmetova Farida M., Nastaeva Saida R.

Federal State Budgetary Educational Institution of Higher Education

«Kabardino-Balkarian State University named after H.M. Berbekov»

E-mail*: madbi@mail.ru

ABSTRACT

Tumor suppressor gene (TP53 or P53) is considered as the most frequently mutated gene in almost all forms of human cancer. In addition to mutations that inactivate p53 functions, numerous single nucleotide polymorphisms (SNPs) have been identified in the p53 gene that also affect the molecular function of the p53 protein. The most frequently studied SNPs in the p53 pathway were identified in codon 72 (rs1042522). This variant leads to an arginine-to-proline amino acid substitution, altering the apoptotic function of p53. We investigated the occurrence of the Arg72Pro polymorphism (rs1042522) of the p53 gene in breast cancer patients in Kabardino-Balkaria (Russia).

Keywords: *Breast Cancer, P53 Gene, Arg72pro Polymorphism, Kabardino-Balkarian Population*

How to Cite: Bittueva Madina M., Bogotova Zalina I., Paritov Anzor U., Khandohov Tahir Kh., Akhmetova Farida M., Nastaeva Saida R., (2025) TP53 Arg72Pro Gene Polymorphism and Risk of Breast Cancer among Kabardino-Balkarian population, *Journal of Carcinogenesis*, *Vol.24, No.3s,* 294-296.

1. INTRODUCTION

During the course of evolution, multicellular organisms have developed the ability to eliminate defective and malfunctioning cells from their tissues. Almost all mammalian tissue cells contain the p53 protein, which serves as a local representative of the organism's interests. Upon receiving a signal about a metabolic disorder or genetic damage inside the cell, the p53 protein can stop the cell from progressing through the growth and division cycle and initiate repair processes. If the metabolic disorder or genomic damage is too severe, after the signal from the p53 protein, apoptosis mechanisms are activated. The consequence of this is rapid cell death. Elimination of defective cells is necessary, since otherwise there is a threat to the health and viability of the organism. The constant presence of a latent but intact apoptotic mechanism represents a constant threat to the nascent cancer cell. This explains the need for the normal functioning of p53 gene [1].

Numerous studies have confirmed that the wild-type allele of p53 functions to suppress cell proliferation, and as a result, the p53 gene was eventually classified as a tumor suppressor gene. By 1987, it became apparent that point mutations in p53 alleles were common in the genomes of a wide variety of human tumor cells [2]. Data accumulated from various studies have shown that the p53 gene is mutated in 30–50% of common human malignancies. Indeed, of all the genes studied to date in the genomes of human cancer cells, p53 is the gene found to be most frequently mutated, present in a mutant form in the genomes of nearly one-third of all human tumors [3].

In addition to mutations that inactivate p53 function, many single nucleotide polymorphisms (SNPs) have been identified in the p53 gene that also affect the molecular function of the p53 protein as a guardian of the genome [4,5]. As is known, genetic polymorphisms can lead to a deficiency in protein function and stability. The p53 mutation database of the International Agency for Research on Cancer (IARC) contains 29 common polymorphisms in the non-coding region of p53. Among these SNPs of the p53 gene, one known SNP that occurs in codon 72, the Arg72Pro polymorphism (rs1042522), is the most common. The p53 codon Arg72Pro is a C/G variation of the p53 gene on human chromosome 17p13 [6].

The incidence of malignant neoplasms in the world is steadily increasing, and according to statistics, approximately 46 thousand women are diagnosed with breast cancer each year. In Kabardino-Balkaria, breast cancer ranks first in the incidence of malignant neoplasms [7].

The aim of our research was to study the frequency of the single nucleotide polymorphism Arg72Pro (rs1042522) of the p53 gene in patients with breast cancer in Kabardino-Balkaria.

2. MATERIAL AND METHODS

For a comparative analysis of the frequency of occurrence of the single nucleotide polymorphism Arg72Pro (rs1042522) in patients with breast cancer in Kabardino-Balkaria, a collection of DNA samples of peripheral blood lymphocytes was used. The study included DNA samples of 128 patients with breast cancer (the diagnosis was verified morphologically) and 117 healthy volunteers women forming a control group. The analysis of the status of amplification products was carried out by the allele-specific PCR (AS-PCR) method and the electrophoretic detection method.

DNA was isolated from whole blood using the QIAamp DNA Blood Mini Kit (Qiagen, Germany). The polymerase chain reaction (PCR) was performed using the allele-specific (AS) polymerase reaction kit from Litekh Research and Production Company. PCR fragments were separated in 2% agarose gel.

The structure of the forward and reverse primers was as follows: (p53R72P-F) 5'-GTCCTCTGACTGCTCTTTTCACCCATCTAC-3' and, respectively, (p53R72P-R) 5'-GGGATACGGCCAGGCATTGAAGTCTC-3'.

The association between the Arg72Pro polymorphism of *p53* gene and breast cancer risk was determined as an odds ratio (OR) within a 95% confidence interval (CI) based on multivariate logistic regression analyses where the **p** value less than 0.05 will be defined as statistically significant.

Ethical approval. This study was performed in line with the principles of the Declaration of Helsinki. Informed voluntary consent was obtained from each of the participants included in the study.

3. RESULTS

The frequencies of single nucleotide polymorphism of the p53 Arg72Pro gene in breast cancer patients and controls are presented in Table 1.

Table 1.: Frequency of Arg72Pro polymorphism of the p53 gene

Genotype	***Patients (n=128)*** ***Cases No (%)***	***Control (n=117)*** ***Cases No (%)***	*OR*	*95 % CI:*	***p***
Pro/Arg	**42 (32.8%)**	**47 (40.2%)**	0.727	0.4315 to 1.2262	**0.232**
Pro/Pro	**31 (24.2%)**	**18 (15.4%)**	1.758	0.9224 to 3.3495	**0.086**
Arg/Arg	**55 (42.9%)**	**52 (44.4%)**	0.942	0.5681 to 1.5612	**0.816**

Among women (n=128) with breast cancer, a high frequency of carriage of the Arg/Arg polymorphism was revealed - 42.9%, heterozygous carriers of the polymorphism accounted for 32.8% and carriage of the Pro/Pro polymorphism was detected in 24.2% of cases. Among healthy women, the frequency of carriage of the Arg/Arg polymorphism was 44.4%, heterozygous carriers of the polymorphism accounted for 40.2% and carriage of the Pro/Pro polymorphism was detected in 15.4% of cases.

We have found that carriage of the Pro/Pro as polymorphic marker Arg72Pro of the TP53 gene may be associated with the risk of developing breast cancer in women of Kabardino-Balkaria (p=0.086). However, it still did not cross the threshold of a statistically significant marker.

Various studies have attempted to find an association between p53 variants in their ability to bind components of the transcriptional apparatus, activate transcription, induce apoptosis, and suppress transformation of primary cells [6]. These findings could be partially explained by the fact that p53 protein encoded by the Arg allele is more efficient for inducing apoptosis. Nevertheless, the p53 protein encoded by Pro allele has been mostly efficiently related to DNA repair.

According to a meta-analysis conducted on 17 studies, including 12,226 cases and 10,782 controls, the associations of TP53 codon 72 polymorphisms with breast cancer were analyzed [8]. Overall, no associations of TP53 codon 72 polymorphisms with breast carcinoma were observed (for Arg/Arg vs Pro/Pro: OR = 1.20; 95%CI = 0.96-1.50; for dominant model: OR = 1.12; 95%CI = 0.96-1.32; for recessive model: OR = 1.13; 95%CI = 0.98-1.31). In the subgroup analysis by ethnicity, statistically similar results were obtained when the data were stratified as Asians, Caucasians and

Africans.

In the future, along with polymorphisms, it is proposed to study the carriage of mutations in the p53 gene in this sample, as well as their relationship with the nature and course of the disease. Integration of genetic profiling into personalized medicine approaches is necessary to improve the primary diagnosis and treatment of breast cancer.

REFERENCES

[1] R. A. Weinberg. The biology of cancer. Garland Science. 331-390 (2014).

[2] D.I. Linzer and A.J. Levine. Cell. 17, 43-52 (1979). https://pubmed.ncbi.nlm.nih.gov/222475/

[3] International Agency for Research on Cancer, TP53 genetic variations in human cancer, IARC release. https://www.iarc.who.int/news-events/new-release-of-the-iarc-tp53-database/

[4] M .Tada, K Furuuchi, M Kaneda, J Matsumoto, M Takahashi, A Hirai, Y Mitsumoto, R D Iggo, T Moriuchi Inactivate the remaining p53 allele or the alternate p73? Preferential selection of the Arg72 polymorphism in cancers with recessive p53 mutants but not transdominant mutants/ Carcinogenesis. 2001 Mar;22(3):515-7. doi: 10.1093/carcin/22.3.515. / https://pubmed.ncbi.nlm.nih.gov/11238194/

[5] Marin MC, Jost CA, Brooks LA, Irwin MS, O'Nions J, Tidy JA, et al. A common polymorphism acts as an intragenic modifier of mutant p53 behaviour. Nat Genet. 2000;25:47–54 /https://pubmed.ncbi.nlm.nih.gov/10802655/

[6] Thomas M, Kalita A, Labrecque S, et al. Two Polymorphic Variants of Wild-Type p53 Differ Biochemically and Biologically. Mol Cell Biol. 1999;19:1092–100. doi: 10.1128/mcb.19.2.1092. https://pubmed.ncbi.nlm.nih.gov/9891044/

[7] https://protiv-raka.ru/analytics/epidemiologiya-rmzh-v-interaktivnyh-diagrammah (2025).

[8] Wenlei Zhuo, Yunsong Zhang, Zhaolan Xiang, Lei Cai, Zhengtang Chen. Polymorphisms of TP53 codon 72 with breast carcinoma risk: evidence from 12226 cases and 10782 controls /https://pmc.ncbi.nlm.nih.gov/articles/PMC3225858/