

THE ROLE OF ADAPTIVE VARIANTS OF THE EDAR GENE IN THE DEVELOPMENT OF BREAST CANCER.

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TIKHONOV D.G.

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Annotation. There are suggestions in the literature about the involvement of the 370A EDAR allele in the development of breast cancer. Unfortunately, the question of what the frequency of the allele is among patients with breast cancer has not been clarified, and studies, even using the case-control method, have not been conducted to clarify the role of this mutation in its development. It is unclear what role the 370A mutation of the EDAR gene plays in the low incidence of breast cancer in Yakut women.

Keywords: gene, EDAR, mutation 370A, breast cancer, Yakuts

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Introduction. It is considered that mutation 370A of the ectodysplasin A receptor EDAR gene (nucleotide mutation designated 1540C, rs3827760) occurred as a result of adaptive selection among the East Asian population. The authors calculated that this allele appeared about 30,000 years ago in Central China [1]. Another group of researchers believes that adaptive selection of this mutation occurred 20,000 years ago in Beringia [2].

The 370A allele causes multiple phenotypic expressions (pleiotropic effect) in humans and mice, including thick and straight hair, mammary duct branching, the frequency of eccrine glands, and shovel-like incisors [1, 3-5]. The degree of spade-like teeth depends on the heterozygosity or homozygosity of the allele. In this connection,

the spade-shaped feature of teeth can become a marker for the presence of the 370A EDAR allele. It should be noted that in humans, the expression of the phenotype on the degree of branching of the milk ducts has not been clarified. Thus, Latin Americans carrying this allele had low mammary gland density according to the results of mammography, although this cannot directly indicate the degree of branching of the mammary gland ducts [6]. It was found that among Hispanic women, the frequency of the 370A allele of the EDAR gene was higher than among white Spanish-speaking women, but on the other hand, the age-standardized breast cancer rate was lower [6]. However, it should be noted that, until now, the frequency of this allele among breast cancer patients has not been

determined. This mutation may be linked to protection against breast cancer. In this report, we attempt to analyze the results of studies of the 370A allele, its frequency in global populations, phenotypic manifestations, and possible role in the development of breast cancer.

The 370A EDAR mutation is believed to be associated with metabolic syndrome and a predisposition to diabetes (carriers have a high body mass index, higher levels of triglycerides, very low-density lipoproteins, glycated hemoglobin, pre-diabetes, and diabetes status) [6], which confirms the idea that genes inherited from previous generations are probably "inadequately or imperfectly adapted to modern environmental conditions" [7], as a result of which they can cause a high incidence of

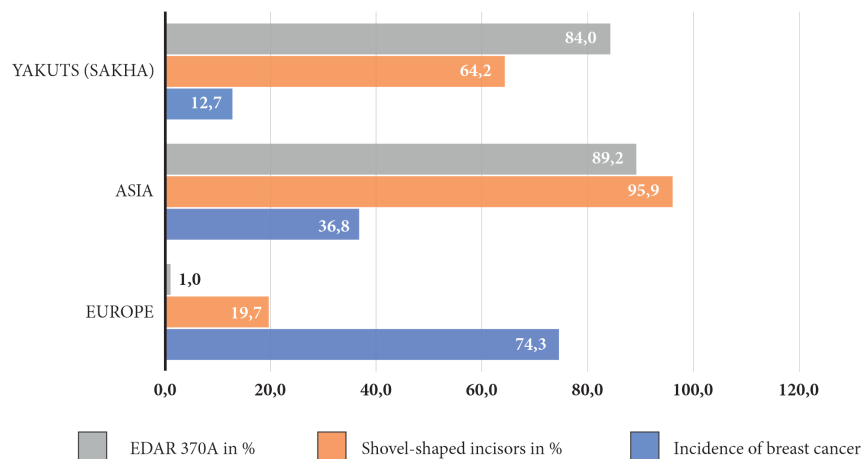


Figure 1. Incidence of breast cancer per 100,000 population, incidence of scapular incisors, and EDAR 370A among the Sakha (Yakuts), Asia, and Europe

osteoarthritis, type 2 diabetes, and other diseases of civilization.

Coletta D. K. et al. suggested that the EDAR 370A variant may be associated with differences in the manifestation of breast cancer in Latinos [6]. Among the central Yakuts, the shovel-like shape of incisors is observed in 64.2% of individuals [8], and the frequency of the 370A allele of the EDAR gene in the ALFRED database is 0.84 [9]. At the same time, their age-standardized incidence of breast cancer (world standard) is one of the lowest in the world and ranges from 6.8 to 18.3 in different years,

with an average of 12.7 per 100,000 people [10]. The frequency of the allele according to the 1000 Genome Project in Europe is 0.24, in East Asia it is 0.87, according to dbSNP, in Europe it is 0.01, in Africa it is 0.01, in Asia it is 0.89, in East Asia it is 0.92, in American Indians it is 0.19, and in South Asia it is 0.1 [11], and the incidence of breast cancer is high in Europe and low in Asia (see Figure 1).

Thus, the literature suggests that the 370A EDAR allele is involved in the development of breast cancer. But, unfortunately, until now, the question of what the frequency

of the allele among breast cancer patients is has not been clarified; not even a case-control study has been conducted to define the role of this mutation in its development. What role the 370A EDAR gene mutation plays in the low incidence of breast cancer in Yakut women is also unknown.

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About authors

TIKHONOV Dmitry Gavrilievich, MD, Professor, Senior Research Officer of the Scientific research Center of the medical Institute of the North-Eastern Federal University, 677008, Yakutsk, St. Petrovsky. 5, Russia, <https://orcid.org/0000-0003-3385-9471>, e-mail: Tikhonov.dmitri@yandex.ru.