Annals of Case Reports & Reviews

Research Article

Valeryevna KK. 2026(5): 1000465
doi: 10.39127/2574-5747/acrr: e465

Features of Knee Osteoarthritis in Patients with Single Nucleotide Polymorphisms of the GDF-5, TGFA, And TGFB1 Genes

Korochina Kristina Valeryevna*

Candidate of Medical Sciences (PhD), Associate Professor of the Department of Internal Medicine, Orenburg State Medical University, Russia, Orenburg,

***Corresponding author:** Korochina Kristina Valeryevna, E-mail: kris_kor@inbox.ru

Citation: Valeryevna KK (2026) Features of Knee Osteoarthritis in Patients with Single Nucleotide Polymorphisms of the GDF-5, TGFA, And TGFB1 Genes. Annal Cas Rep Rev: ACRR-465.

Received Date: 21 June, 2026; **Accepted Date:** 26 June, 2026; **Published Date:** 30 June, 2026

Abstract

Osteoarthritis (OA) is a polygenic disease, and data on the influence of single nucleotide polymorphisms (SNPs) on knee joint involvement are contradictory.

***Objective:** to investigate the effect of SNP Rs143384 of the Growth and differentiation factor 5 (GDF-5) gene, Rs3771501 of the Transforming growth factor-alpha (TGFA) gene, and Rs75621460 of the Transforming growth factor-beta (TGFB1) gene on the clinical features of advanced knee OA.*

***Materials and Methods:** The study included 80 patients with knee OA grades 3–4, with no history of trauma or concomitant knee joint pathology of another etiology. All patients underwent a general clinical examination, completed clinical-functional scales (Visual Analogue Scale [VAS], Knee Injury and Osteoarthritis Outcome Score [KOOS], Western Ontario and McMaster University Osteoarthritis Index [WOMAC]), and molecular genetic testing for SNP using real-time polymerase chain reaction, followed by statistical analysis of the data.*

***Results:** In the analysis of the Rs143384 polymorphism of the GDF-5 gene, patients with the homozygous A/A genotype had the highest mean age and more pronounced clinical signs according to the KOOS scale; patients carrying the A allele (G/A, A/A) were characterized by a shorter clinical duration of knee OA and a higher body mass index. When assessing the Rs3771501 of the TGFA gene, the G/G genotype group had a higher proportion of men and showed the highest pain scores on VAS, WOMAC, and KOOS; in patients with the G allele in both homozygous and heterozygous states, the clinical duration of knee OA was significantly shorter. Regarding the Rs75621460 of the TGFB1 gene, the absence of the A/A genotype and a low frequency of the G/A genotype were noted; therefore, no significant features were found.*

***Conclusions:** The A allele of the GDF-5 gene and the G allele of the TGFA gene are associated with a more rapid progression of knee OA. The A allele of the GDF-5 gene is linked to a higher body mass index and more severe clinical manifestations. The G allele of the TGFA gene is associated with male sex and more pronounced knee pain.*

***Keywords:** osteoarthritis, knee joint, SNP, polymorphism, mutation, Rs143384, Rs3771501, Rs75621460.*

Background

Osteoarthritis (OA) is the most common musculoskeletal disorder, with a predicted increase in incidence and marked clinical and pathogenetic variability. The most relevant form of this disease is primary OA, which is determined by an "endogenous" factor—genetic predisposition—that shapes its phenotypic features and serves as a background for the layering of "exogenous" influences.

OA is a polygenic disease resulting from the inheritance of multiple risk alleles [1]. The most important genes are those involved in musculoskeletal development, particularly GDF-5 (Growth and differentiation factor-5). It encodes a protein that is a member of the superfamily of signaling molecules and is involved in chondrogenesis, the formation of synovial joints, maintenance of ligament and tendon structure, as well as the maintenance of cartilage homeostasis in adults [2].

A Genome-wide association study (GWAS) using a database of 441,757 individuals from the UK Biobank identified ten important loci, with Rs143384 being the most significant polymorphism [3]. The study by Meng W. et al. (2019) [4] identified two loci that reached genome-wide significance, among which this polymorphism was also present. At the same time, the study by Pedrinha I.S. et al. (2024) [5] showed no statistically significant differences in the frequency of this single-nucleotide polymorphism (SNP) between OA patients and a control group in a Brazilian population.

In searching for the "effector" or "risk" allele of this gene, some contradictions have been found. Most studies indicate that for this mutation, the risk allele is the A allele (e.g., Tachmazidou I. et al., 2019 [6]). A meta-analysis of GWAS data by C.G. Boer et al. (2021) [7] on mixed European and Asian samples (nine populations were studied) also established an association between the A allele of Rs143384 in the *GDF-5* gene and the

development of knee OA. In the study by Yan S. et al. (2021) [8], carriers of the A allele had an approximately 1.35-fold increased risk of OA compared to carriers of the G allele.

At the same time, several studies have not found statistically significant patterns; for example, in the study by Shin M.H. et al. (2012) on 2,462 individuals over 50 years of age in a Korean population, no significant differences in genotype frequencies of this gene between patients and healthy controls were observed [9]. The associations of the polymorphism with affected joints are also unclear: in the study of Tachmazidou I. et al. (2019) [6], the Rs143384 polymorphism of the *GDF-5* gene is associated with an increased risk of OA at any joints, while other studies associate it with knee Oa (e.g., Yiwen T. et al., 2024 [3]; Boer C.G. et al., 2021 [7]). Some studies have revealed associations of this polymorphism with female sex (Yiwen T. et al., 2024 [3]). A recent experimental study demonstrated that the SNP polymorphism of this gene does not by itself change GDF-5 expression but may exert a modulating effect through local epistatic interactions [10].

The genes with a predominant influence on proliferative processes in joints belong to the TGF (Transforming growth factor) family. Rs3771501 of the TGF-α gene is one of the most extensively studied polymorphisms. However, data on which allele of this gene constitutes the "risk" allele remain inconclusive in the literature. GWAS have identified associations of the A allele with OA in European populations (Tachmazidou I. et al., 2019 [6]) and in mixed samples of Europeans, Asians, and Americans of European descent (C.G. Boer et al., 2021 [7]). On the other hand, a study by E. Zengini et al. (2018) [11] in a European population established an association of the G allele with OA. A comprehensive review postulates that Rs3771501 of the TGF-α gene has been replicated at genome-wide significance and is associated with OA in males regardless of the localization [12].

Another SNP polymorphism belonging to the TGF gene family, namely Rs75621460 of the TGFB1 gene, is also of considerable importance for OA development. The study by Rice S.J. et al. (2020) [13] demonstrated its association with chondrocyte hypertrophy, which is a key feature of structural tissue remodelling in joints affected by this disease. At the same time, the study by Limer K.L. et al. (2009) [14] on a sample of over 3,000 individuals did not confirm statistically significant differences between the experimental and control groups.

Unfortunately, most studies have been conducted by foreign authors, and the Russian population has remained largely unexplored in this regard, which determined the relevance of the present work.

Objective: to investigate the effect of the most significant SNP polymorphisms (in terms of OA development) on the clinical features of advanced knee OA.

Materials and Methods

The study included 80 patients with knee OA grades 3-4 who were admitted to the traumatology and orthopedics department of the V.I. Voinov Orenburg Regional Clinical Hospital for total knee arthroplasty.

Inclusion criteria:

- knee joint pain and other clinical signs typical of OA;
- diagnosis of knee OA according to the Altman R.D. criteria (1991) [15];
- radiographic grade 3–4 according to Kellgren–Lawrence (1957) [16];
- patient's informed consent to participate in the study.

Exclusion criteria:

- concomitant knee joint pathology of non-rheumatological origin;
- acute and chronic viral infectious diseases;
- long-term prior use of disease-modifying drugs (SYSADOA) or glucocorticoids;
- conditions that prevented adequate patient participation (e.g., encephalopathy, psychiatric disorders).

The general clinical examination included collection of complaints and medical history, rheumatological physical examination, and assessment of body mass index (BMI).

Clinical-and-functional assessment was performed using the Visual Analogue Scale (VAS), the Knee Injury and Osteoarthritis Outcome Score (KOOS), and the Western Ontario and McMaster University Osteoarthritis Index (WOMAC).

Molecular genetic testing of patient material (buccal swab samples obtained using a swab system) was carried out in all participants to detect SNPs: Rs143384 of the GDF-5 gene, Rs3771501 of the TGFA gene, and Rs75621460 of the TGFB1 gene, using real-time PCR (CFX 96 Thermal Cycler).

Statistical analysis was performed using Statistica 10.0 software. Quantitative data were presented as medians with interquartile ranges (Me [Q lower; Q upper]). The frequency of categorical variables (e.g., OA grades) was expressed as percentages. Differences between study groups were assessed using the Mann–Whitney U-test. For comparisons of qualitative variables and their frequencies between groups, Pearson's chi-squared test was applied. The significance level was set at $p < 0.05$.

Results and Discussion

The study included 13 (16%) men and 67 (84%) women. The median age of patients was 66 [58; 73] years. The distribution of gene polymorphisms in this sample is presented in Table 1. As can be seen from the table, for the GDF-5 and TGFA genes, the frequency of minor alleles was quite high, whereas for TGFB1, the vast majority of patients had the G/G genotype, and the A/A variant was not detected at all.

Table 1: *Distribution of alleles of the GDF-5 (Rs143384), TGFA (Rs3771501), and TGFB1 (Rs75621460) genes among patients with gonarthrosis.*

Rs 143384 GDF-5	
G/G	24 (30,0%)
G/A	41 (51,3%)
A/A	15 (18,7%)
Rs 3771501 TGFA	
A/A	16 (20,0%)
A/G	38 (47,5%)
G/G	26 (32,5%)
Rs75621460 TGFB1	
G/G	75 (93,8%)
G/A	5 (6,2%)
A/A	0 (0%)

Next, the clinical features of knee OA were examined depending on the presence of a particular allele for each of the studied genes. When assessing Rs143384 (Table 2), the group of patients with the homozygous A/A genotype was found to have the highest mean age, while the clinical duration of knee OA in patients with the A allele in both homozygous and heterozygous states was approximately 5 years shorter than in those with the G/G variant. No gender-specific distribution of this SNP polymorphism was observed; however, it was noted that patients carrying the A allele (G/A, A/A) had a higher BMI. Evaluation of clinical-functional scales (VAS and WOMAC) revealed no statistically significant differences between the study groups; for the KOOS scale, a trend toward lower scores (i.e., more pronounced clinical features) was observed in the subscales "Symptoms," "Activities of Daily Living," and "Sport " in the group of patients with the A/A genotype.

Table 2: *Clinical features of knee OA in patients with the Rs143384 SNP polymorphism of the GDF-5 gene.*

Genotype / Parameter	G/G	G/A	A/A	Statistical significance, p-value
Age, years	67,5 [63,0; 70,5]	65 [57,0; 68,0]	72 [63,0; 76,0]	0,036
Sex, n (%)	М – 3 (12,5%) Ж – 21 (87,5%)	М – 9 (22%) Ж – 32 (78%)	М – 2 (13,3%) Ж – 13 (86,7%)	0,560
Duration of OA, years	15 [10; 20]	9,5 [5; 15]	10 [7,5; 22,5]	0,101
Knee OA grade	3 – 17 (70,8%) 4 – 7 (29,2%)	3 – 32 (78%) 4 – 9 (22%)	3 – 9 (60%) 4 – 6 (40%)	0,398
BMI, kg/m²	30,2 [27,3; 33,8]	33,3 [31,1; 36,1]	34,5 [32,8; 36,1]	0,158
Clinical-and-functional scales				
VAS, mm	7,5 [5,0; 8,5]	6,0 [5,0; 8,0]	6,5 [5,0; 8,0]	0,977
WOMAC, pain, points	33,5 [24,5; 43,5]	34,0 [27,0; 38,0]	35,0 [30,0; 41,0]	0,800
WOMAC, stiffness, points	15,0 [9,0; 17,0]	14,0 [12,0; 17,0]	14,5 [13,0; 16,0]	0,926
WOMAC, function, points	103,0 [78,0; 136,0]	109,0 [85,0; 144,0]	116,0 [92,0; 132,0]	0,875
WOMAC, total, points	148,0 [116,0; 196,0]	157,0 [130,0; 183,0]	159,0 [143,0; 182,0]	0,902
KOOS, pain,%	44,4 [36,1;50,0]	38,9 [33,3; 47,2]	41,6 [33,3; 44,4]	0,333
KOOS, symptoms, %	42,8 [32,1; 46,4]	39,2 [28,6; 50,0]	32,1 [28,6; 42,8]	0,115
KOOS, activities of daily living, %	45,6 [39,7; 48,5]	42,6 [32,3; 50,0]	39,0 [32,3; 47,1]	0,197
KOOS, sport, %	25,0 [10,0; 45,0]	25,0 [10,0; 35,0]	10,0 [0,0; 25,0]	0,125
KOOS, quality of life, %	18,8 [12,5; 25,0]	23,8 [12,5; 25,0]	21,9 [12,5; 25,0]	0,823

When analyzing the Rs3771501 polymorphism of the TGFA gene (Table 3), the following patterns were observed. Although the number of women significantly exceeded the number of men in the overall patient sample, the G/G genotype group had a slightly higher proportion of men compared to the other groups. No age-related distribution features were identified, nor were there any associations with BMI. However, the mean clinical duration of knee OA in patients with the G allele in both homozygous and heterozygous states was significantly shorter than in those with the A/A variant of this gene. Regarding clinical-and-functional scales, patients with the G/G genotype had higher pain scores on VAS and the WOMAC "Pain" subscale. When evaluating the KOOS questionnaire, the lowest scores in the "Pain" subscale were found in patients with the A/G and G/G genotypes, which also corresponds to the most pronounced pain levels in these subgroups.

Table 3: *Clinical features of gonarthrosis in patients with the Rs3771501 SNP polymorphism of the TGFA gene.*

Genotype / Parameter	A/A	A/G	G/G	Statistical significance, p-value
Age, years	68,5 [62,5; 74,0]	65 [59,0; 70,0]	67,0 [60,0; 72,0]	0,591
Sex, n (%)	М – 1 (6,3%) Ж – 15 (93,7%)	М – 4 (10,5%) Ж – 34 (89,5%)	М – 7 (26,9%) Ж – 19 (73,1%)	0,191
Duration of OA, years	18,5 [10,0; 22,5]	10,0 [7,5; 18,5]	10,0 [5,0; 15,0]	0,174
Knee OA grade	3 – 8 (50%) 4 – 8 (50%)	3 – 30 (78,9%) 4 – 8 (21,1%)	3 – 18 69,2%) 4 – 8 (30,8%)	0,138
BMI, kg/m²	32,4 [28,4; 36,8]	33,6 [30,8; 35,4]	32,5 [28,9; 36,1]	0,936
Clinical-and-functional scales				
VAS, mm	6,0 [5,0; 8,0]	5,0, [4,5; 8,0]	8,0 [6,0; 9,0]	0,015
WOMAC, pain, points	29,0 [19,0; 38,0]	31,0 [24,0; 38,0]	35,0 [33,0; 43,0]	0,111
WOMAC, stiffness, points	13,0 [7,0; 16,0]	14,0 [11,0; 17,0]	15,0 [12,0; 18,0]	0,355
WOMAC, function, points	106,0 [62,0; 134,0]	105,0 [85,0; 136,0]	111,5 [83,0; 147,0]	0,581
WOMAC, total, points	149,0 [97,0; 182,0]	146,0 [123,0; 188,0]	165,0 [130,0; 212,0]	0,485
KOOS, pain,%	45,8 [41,7; 50,0]	38,9 [33,3; 47,2]	41,7 [33,3; 50,0]	0,285
KOOS, symptoms, %	35,7 [32,1; 45,4]	35,7 [28,6; 50,0]	32,1 [28,6; 42,8]	0,846
KOOS, activities of daily living, %	44,1 [38,2; 50,0]	44,1 [33,1; 49,3]	42,6 [32,3; 48,5]	0,787
KOOS, sport, %	25,0 [10,0; 40,0]	22,5 [10,0; 52,5]	25,0 [5,0; 30,0]	0,969
KOOS, quality of life, %	25,0 [12,5; 31,3]	18,8 [12,5; 25,0]	18,8 [12,5; 25,0]	0,348

Next, the features of knee OA were studied from the perspective of the Rs75621460 polymorphism of the TGFB1 gene (Table 4). Due to the small number of patients in the G/A subgroup, no significant trends were identified regarding the effect of either allele of the gene on the clinical characteristics of knee OA, with the exception of the disease stage (grade 4 was more frequently observed in the G/A group).

Table 4: *Clinical features of gonarthrosis in patients with the Rs75621460 SNP polymorphism of the TGFB1 gene.*

Genotype / Parameter	G/G	G/A	Statistical significance, p-value
Age, years	65,0 [59,0; 72,0]	66,0 [57,0; 66,0]	0,654
Sex, n (%)	М – 13 (17,3%) Ж – 62 (82,7%)	М – 1 (20%) Ж – 4 (80%)	0,879
Duration of OA, years	10,0 [6,0; 20,0]	10,0 [9,0; 15,0]	0,870
Knee OA grade	3 – 56 (74,7%) 4 – 19 (25,3%)	3 – 2 (40%) 4 – 3 (60%)	0,093
BMI, kg/m²	32,8 [29,8; 35,7]	33,7 [32,9; 36,3]	0,564
Clinical-and-functional scales			
VAS, mm	6,0 [5,0; 8,0]	8,0 [6,0; 9,0]	0,206
WOMAC, pain, points	34,0 [27,0; 40,0]	36,0 [34,0; 38,0]	0,496
WOMAC, stiffness, points	14,0 [12,0; 17,0]	14,0 [14,0; 16,0]	0,905
WOMAC, function, points	110,0 [85,0; 136,0]	120,0 [96,0; 127,0]	0,933
WOMAC, total, points	155,0 [125,0; 191,0]	170,0 [146,0; 182,0]	0,839
KOOS, pain,%	41,6 [33,3; 47,2]	38,9 [36,1; 47,2]	0,792
KOOS, symptoms, %	39,3 [28,6; 46,4]	35,7 [21,4; 50,0]	0,711
KOOS, activities of daily living, %	44,1 [35,3; 48,5]	42,6 [38,2; 44,1]	0,587
KOOS, sport, %	25,0 [10,0; 50,0]	50,0 [40,0; 90,0]	0,227
KOOS, quality of life, %	18,8 [12,5; 25,0]	18,8 [12,5; 25,0]	0,730

The conducted study allows for a preliminary assessment of the clinical features of gonarthrosis with regard to the SNP polymorphisms Rs143384 of the GDF-5 gene, Rs3771501 of the TGFA gene, and Rs75621460 of the TGFB1 gene. For a number of parameters, the statistical significance level of $p < 0.05$ was not reached, likely due to the relatively small sample size; thus, at $p = 0.1–0.2$, only trends toward certain disease characteristics can be suggested. The study anticipates an

expansion of the patient sample in the future. Nevertheless, the data obtained already allow us to suggest that the A allele of the GDF-5 gene is a pathological variant, which is consistent with the majority of literature sources [3, 6, 8]. It is associated with a more rapid development of OA as well as with a higher BMI in patients, which was also noted in the study [17]. In contrast to [3], the authors did not find any association of this SNP polymorphism with female sex. In the presence of the homozygous A/A genotype, a trend toward more pronounced clinical manifestations of knee OA was observed according to the KOOS scale.

For the TGFA gene, the G allele is likely the risk allele, since its presence was associated with a shorter clinical duration of knee OA (i.e., faster progression to late stages). For the homozygous G/G genotype, a trend toward more pronounced pain was revealed, as detected by three scales (VAS, WOMAC, and KOOS). Furthermore, this variant was more common in males.

With regard to Rs75621460 of the TGFB1 gene, further research is needed, as the current results, given the low frequency of the polymorphic G/A variant, do not allow any clear trends to be established.

Conclusion

The prevalence and impact of polymorphisms of the GDF-5 (Rs143384), TGFA (Rs3771501),
and TGFB1 (Rs75621460) genes on the features of advanced knee OA have been studied. It has been shown that the A allele of the GDF-5 gene is associated with a more rapid development of OA, a higher BMI in patients, and more pronounced clinical manifestations according to the KOOS scale. The G allele of the TGFA gene is also associated with the shortest clinical duration of knee OA, male sex (in the homozygous state), and more pronounced joint pain, as verified by multiple scales.

References

1. Aubourg G., Rice S.J., Bruce-Wootton P., Loughlin J. Genetics of osteoarthritis // Osteoarthritis Cartilage. 2022. Vol. 30, Iss. 5. P. 636–649. DOI: 10.1016/j.joca.2021.03.002.
2. Sun K., Guo J., Yao X., Guo Z., Guo F. Growth differentiation factor 5 in cartilage and osteoarthritis: a possible therapeutic candidate // Cell Prolif. 2021. Vol. 54. No. 3. Art. e12998. DOI: 10.1111/cpr.12998.
3. Yiwen T., Qi P.,Tengda C., Luning Y.,Mainul H., Tania D., Weihua M. A Genome-wide Association Study Identifies Novel Genetic Variants Associated with Knee Pain in the UK Biobank (N = 441,757) // medRxiv 2024.09.16.24313726; doi: 10.1101/2024.09.16.24313726.
4. Meng W., Adams M.J., Palmer C.N.A.; Shi J., Auton A., Ryan K.A., Jordan J.M., Mitchell B.D., Jackson R.D., Yau M.S., McIntosh A.M., Smith B.H. Genome-wide association study of knee pain identifies associations with GDF5 and COL27A1 in UK Biobank // Communications biology. 2019. Vol. 2 321. DOI: 10.1038/s42003-019-0568-2.
5. Pedrinha I. S., Cardoso J. V., Faria J. L. R., Mozella A., Abbud L. F., de Campos G. J., Machado J.A., de Sousa E. B. Analysis of polymorphism in the gene that codes the differential growth factor 5-GDF5 in patients with knee osteoarthritis // Osteoarthritis and Cartilage. 2024. Vol. 32, P. 488-489. DOI: 10.1016/j.joca.2024.02.725.
6. Tachmazidou I., Hatzikotoulas K., Southam L., Esparza-Gordillo J., Haberland V., Zheng J., Johnson T., Koprulu M., Zengini E., Steinberg J., Wilkinson J.M., Bhatnagar S., Hoffman J.D., Buchan N., Süveges D.; arcOGEN Consortium; Yerges-Armstrong L., Smith G.D., Gaunt T.R., Scott R.A., McCarthy L.C., Zeggini E. Identification of new therapeutic targets for osteoarthritis through genome-wide analyses of UK Biobank data // Nature genetics. 2019. Vol. 51,2. P. 230-236 DOI: 10.1038/s41588-018-0327-1.
7. Boer C.G., Hatzikotoulas K., Southam L., Stefánsdóttir L., Zhang Y., Coutinho de Almeida R., Wu T.T., Zheng J., Hartley A., Teder-Laving M., Skogholt A.H., Terao C., Zengini E., Alexiadis G., Barysenka A., Bjornsdottir G., Gabrielsen M.E., Gilly A., Ingvarsson T., Johnsen M.B., Jonsson H., Kloppenburg M., Luetge A., Lund S.H., Mägi R., Mangino M., Nelissen R.R.G.H.H., Shivakumar M., Steinberg J., Takuwa H., Thomas L.F., Tuerlings M.; arcOGEN Consortium; HUNT All-In Pain; ARGO Consortium; Regeneron Genetics Center; Babis G.C., Cheung J.P.Y., Kang J.H., Kraft P., Lietman S.A., Samartzis D., Slagboom P.E., Stefansson K., Thorsteinsdottir U., Tobias J.H., Uitterlinden A.G., Winsvold .B, Zwart J.A., Smith G.D., Sham P.C., Thorleifsson G., Gaunt T.R., Morris A.P., Valdes A.M., Tsezou A., Cheah K.S.E., Ikegawa S., Hveem K., Esko T., Wilkinson J.M., Meulenbelt I., Michael Lee M.T., van Meurs J.B.J., Styrkársdóttir U., Zeggini E. Deciphering osteoarthritis genetics across 826,690 individuals from 9 populations // Cell. 2021. Vol. 184(24). P. 6003-6005. DOI: 10.1016/j.cell.2021.11.003. Erratum for: Cell. 2021 Sep 2;184(18):4784-4818.e17. DOI: 10.1016/j.cell.2021.07.038.
8. Yan S., Nie H., Bu G., Yuan W., Wang S. The effect of common variants in GDF5 gene on the susceptibility to chronic postsurgical pain // Journal of orthopaedic surgery and research. 2021. Vol. 16(1). P. 420. DOI: 10.1186/s13018-021-02549-5.
9. Shin M. H., Lee S. J., Kee S. J., Song S. K., Kweon S. S., Park D. J. et al. Genetic association analysis of GDF5 and ADAM12 for knee osteoarthritis // Joint Bone Spine. 2012. Vol. 79. No. 5. P. 488–491. DOI: 10.1016/j.jbspin.2011.10.016.
10. Coveney C. R., Maridas D., Chen H., Muthuirulan P., Liu Z., Jagoda E. et al. Complex regulatory interactions at GDF5 shape joint morphology and osteoarthritis disease risk // Arthritis Rheumatol. 2025. Vol. 77. No. 11. P. 1488–1502. DOI: 10.1002/art.43231.
11. Zengini E., Hatzikotoulas K., Tachmazidou I., Steinberg J., Hartwig F.P., Southam L., Hackinger S., Boer C.G., Styrkarsdottir U., Gilly A., Suveges D., Killian B., Ingvarsson T., Jonsson H., Babis G.C., McCaskie A., Uitterlinden A.G., van Meurs J.B.J., Thorsteinsdottir U., Stefansson K., Davey Smith G., Wilkinson J.M., Zeggini E. Genome-wide analyses using UK Biobank data provide insights into the genetic architecture of osteoarthritis // Nature genetics. 2018. Vol. 50(4). P. 549-558. DOI: 10.1038/s41588-018-0079-y.
12. Novakov V.B., Novakova O.N., Churnosov M.I. [Genome-wide studies of knee osteoarthritis: review]. Travmatologiya i ortopediya Rossii [Traumatology and Orthopedics of Russia]. (In Russian). DOI: 10.21823/2311-2905-2021-27-1580.

13. Rice S.J., Tselepi M., Roberts J., Loughlin J. Molecular genetic and epigenetic analysis of the osteoarthritis risk
14. Limer K.L., Tosh K., Bujac S.R., McConnell R., Doherty S., Nyberg F., Zhang W., Doherty M., Muir K.R., Maciewicz R.A. Attempt to replicate published genetic associations in a large, well-defined osteoarthritis case-control population (the GOAL study) // Osteoarthritis and Cartilage. 2009. Vol. 17(6). C. 782-789. DOI: 10.1016/j.joca.2008.09.019.
15. Altman R.D. Criteria for classification of clinical osteoarthritis // The Journal of rheumatology. Supplement. 1991. Vol. 27. P. 10-12.

residing downstream of the gene TGFB1 // Osteoarthritis and Cartilage. 2020. Vol. 28, P. 339.
16. Kellgren J.H., Lawrence J.S. Radiological assessment of osteoarthrosis // Annals of the rheumatic diseases. 1957. Vol. 16,4. P. 494-502. doi: 10.1136/ard.16.4.494.
17. Novakov V.B., Novakova O.N., Churnosov M.I. Analysis of associations of candidate gene polymorphism with the development of knee osteoarthritis in obese patients. Yakut Medical Journal. 2023;(3):68-71.