ISSN 2518-1629 (Online),
ISSN 2224-5308 (Print)

ҚАЗАҚСТАН РЕСПУБЛИКАСЫ
ҰЛТТЫҚ ҒЫЛЫМ АКАДЕМИЯСЫНЫҢ
Өсімдіктердің биологиясы және биотехнологиясы институтының

Х А Б А Р Л А Р Ы

ИЗВЕСТИЯ

НАЦИОНАЛЬНОЙ АКАДЕМИИ НАУК
РЕСПУБЛИКИ КАЗАХСТАН
Института биологии и биотехнологии растений

N E W S

OF THE NATIONAL ACADEMY OF SCIENCES
OF THE REPUBLIC OF KAZAKHSTAN
of the Institute of Plant Biology and Biotechnology

БИОЛОГИЯ ЖӘНЕ МЕДИЦИНА СЕРИЯСЫ

♦

СЕРИЯ БИОЛОГИЧЕСКАЯ И МЕДИЦИНСКАЯ

♦

SERIES OF BIOLOGICAL AND MEDICAL

4 (328)

ШІЛДЕ – ТАМЫЗ 2018 ж.
ИЮЛЬ – АВГУСТ 2018 г.
JULY – AUGUST 2018

1963 ЖЫЛДЫҢ ҚАҢТАР АЙЫНАН ШЫҒА БАСТАҒАН
ИЗДАЕТСЯ С ЯНВАРЯ 1963 ГОДА
PUBLISHED SINCE JANUARY 1963

ЖЫЛЫНА 6 РЕТ ШЫҒАДЫ
ВЫХОДИТ 6 РАЗ В ГОД
PUBLISHED 6 TIMES A YEAR

АЛМАТЫ, ҚР ҰҒА
АЛМАТЫ, НАН РК
ALMATY, NAS RK

«ҚР ҰҒА Хабарлары. Биология және медициналық сериясы».
ISSN 2518-1629 (Online),
ISSN 2224-5308 (Print)
Меншіктенуші: «Қазақстан Республикасының Ұлттық ғылым академиясы» РҚБ (Алматы қ.)
Қазақстан республикасының Мәдениет пен ақпарат министрлігінің Ақпарат және мұрағат комитетінде 01.06.2006 ж. берілген **№5546-Ж** мерзімдік басылым тіркеуіне қойылу туралы куәлік

Мерзімділігі: жылына 6 рет.
Тиражы: 300 дана.

Редакцияның мекенжайы: 050010, Алматы қ., Шевченко көш., 28, 219 бөл., 220, тел.: 272-13-19, 272-13-18,
www:nauka-nanrk.kz / biological-medical.kz

Типографияның мекенжайы: «Аруна» ЖК, Алматы қ., Муратбаева көш., 75.

«Известия НАН РК. Серия биологическая и медицинская».
ISSN 2518-1629 (Online),
ISSN 2224-5308 (Print)
Собственник: РОО «Национальная академия наук Республики Казахстан» (г. Алматы)
Свидетельство о постановке на учет периодического печатного издания в Комитете информации и архивов Министерства культуры и информации Республики Казахстан **№5546-Ж**, выданное 01.06.2006 г.

Периодичность: 6 раз в год
Тираж: 300 экземпляров

Адрес редакции: 050010, г. Алматы, ул. Шевченко, 28, ком. 219, 220, тел. 272-13-19, 272-13-18,
www:nauka-nanrk.kz / biological-medical.kz

Адрес типографии: ИП «Аруна», г. Алматы, ул. Муратбаева, 75

News of the National Academy of Sciences of the Republic of Kazakhstan. Series of biology and medicine.
ISSN 2518-1629 (Online),
ISSN 2224-5308 (Print)
Owner: RPA "National Academy of Sciences of the Republic of Kazakhstan" (Almaty)
The certificate of registration of a periodic printed publication in the Committee of information and archives of the Ministry of culture and information of the Republic of Kazakhstan N 5546-Ж, issued 01.06.2006

Periodicity: 6 times a year
Circulation: 300 copies

Editorial address: 28, Shevchenko str., of. 219, 220, Almaty, 050010, tel. 272-13-19, 272-13-18,
http://nauka-nanrk.kz / biological-medical.kz

Address of printing house: ST "Aruna", 75, Muratbayev str, Almaty

N E W S
OF THE NATIONAL ACADEMY OF SCIENCES OF THE REPUBLIC OF KAZAKHSTAN
SERIES OF BIOLOGICAL AND MEDICAL
ISSN 2224-5308
Volume 4, Number 328 (2018), 63 – 68

UDC 617.7-007.681-056.7

Zh. B. Tileules, O. H. Hamdieva, S. B. Zajpanova, G. A. Kojshekenova, B. O. Bekmanov

«Institute of General Genetics and Cytology» CS MES RK, Almaty, Kazakhstan.
E-mail: janerke.tleules@mail.ru azadahamdieva@gmail.com saule1kz@mail.ru
ms.gulshat7@mail.ru bobekman@rambler.ru

ANALYSIS OF *MYOCILIN (MYOC)* AND *NEUROTROPHIN 4 (NTF4)* GENES IN PATIENTS WITH GLAUCOMA IN KAZAKHSTAN

Abstract. Primary Open-Angle Glaucoma being the most common type of glaucoma has a great socio-medical significance and it is a major focus for scientific researching in ophthalmology. In 21-50% of cases the disease is the result of genetic causes and for descendants of people with glaucoma, the risk of this pathology is 10 times higher. Mutations causing Primary Open-Angle Glaucoma have been identified in *MYOC/TIGR* gene, which encodes a 57kDa protein known as myocilin and in the gene *NTF4* that codes a dimeric peptide (28kD). In this study we investigated the frequency of mutations in *MYOC/TIGR* and *NTF4* genes in Kazakhstan population. The study was conducted involving 85 patients diagnosed with primary glaucoma and 100 individuals as a control group. The results of our research show that T353I, D208E in *MYOC/TIGR* gene and R206W polymorphisms in *NTF4* gene among Kazakhstan population has no influence on the POAG progression while R76K SNP in *MYOC/TIGR* gene can be as a genetic factor which affects the development of POAG type of glaucoma.

Keywords: POAG, polymorphism, *MYOC/TIGR*, *NTF4*.

Introduction. Glaucoma is a neurodegenerative disease which is characterized by progressive damage to ganglion cells, optic nerve fibers, and visual field defects. It is one of the main reasons of irreversible blindness in the world. Primary Open-Angle Glaucoma (POAG) is a basic form of primary glaucoma. Glaucoma is a treatable disease if it is detected early, however, many patients get being diagnosed only after the loss of visual field, since glaucoma is typically asymptomatic at the early stages [1].

An estimated 66.5 million people were identified as having open-angle and angle-closure glaucoma by 2010 and it tends to reach 79.6 million by 2020. Binocular blindness in 2010 was observed in 8.4 million patients with glaucoma, and by 2020 it is going to rise to 11.2 million [2]. According to J. Goldberg's estimates, the number of glaucoma patients will reach 120 million by 2030 [3]. Since 2011, 24 750 patients with glaucoma have been registered in Kazakhstan [4].

Primary open-angle glaucoma (POAG) is described distinctly as a multifactorial optic neuropathy that is progressive, and irreversible, with a characteristic acquired loss of optic nerve fibers. POAG is a chronic disease. It may be hereditary. Genetic predisposition is a distinctive feature of primary glaucoma and confirmed in 50% of cases. Currently, there are 4 causative genes and 70 candidate genes associated with the development of POAG [5]. The well-recognized genes associated with POAG include *myocilin* (*MYOC/TIGR*) [6, 7], *optineurin* (*OPTN*) [8] and *neurotrophin-4* (*NTF4*) [9]. In the past 2 years, large scale genetic studies that have examined the blood samples of thousands of glaucoma patients have been instrumental in the discovery of more common genetic risk factors for POAG. For glaucoma, these genetic factors include changes in the DNA sequences or actual loss of DNA, and several different genes have been implicated [10]. How these genes cause or influence the likelihood of developing POAG is of major interest. The definition of a mutation in these genes is important for the diagnosis of glaucoma and genetic counseling of patients.

MYOC/TIGR gene located in chromosome 1q24.3 and expressed in many ocular tissues, including the trabecular meshwork. Therefore, the alternative name for this gene is *TIGR* (*gene trabecular mesh-*

work-induded glucocorticoid response protein). The gene has 3 exons of size 604, 126, and 782 bp. *MYOC* is expressed as a 2.3 kb transcript and the translated product is predicted to contain 504 amino acids (58 kDa) [11]. Myocilin mutations, in general, are more strongly associated with POAG and JOAG than other forms of glaucoma [12, 13].

The next gene is neurotrophin (*NTF4*). Cytogenetic Location: 19q13.33, which is the long (q) arm of chromosome 19 at position 13.33. *NTF4* is translated as pre-pro-neurotrophin. The gene is organized in 2 exons and encodes a polypeptide of 210 amino acids. Neurotrophin protein is dimeric polypeptide with a molecular weight of 28 kDa and they are important regulators of neural survival, development, function, and plasticity. *NTF4* gene is expressed in most parts of the brain and in other tissues [14].

Mutations in the *MYOC/TIGR* and *NTF4* genes result in damage to actin fibers in the trabecular meshwork [15] and a decrease in neurotrophin signal [16]. Mutations in these genes are responsible for the development of glaucoma from 2% to 20%.

The main goal of this study is to investigate the polymorphism of *MYOC/TIGR* (rs772312298, rs2234926, D208E) and *NTF4* (rs121918427) genes in patients with glaucoma in population of Kazakhstan.

Materials and methods. The study was conducted involving 85 patients diagnosed with primary glaucoma. These materials were collected in the Kazakh Research Institute of Eye Diseases and in the Medical Centre Hospital of President's Affairs Administration of the Republic of Kazakhstan. As a control group, people were selected who did not suffer from this disease and they were chosen depending on the age, gender and ethnic composition of patients with glaucoma. Genomic DNA was extracted from 200 µl of whole blood using a kit (*ThermoFisher Scientific,* USA). The concentration of the DNA molecule was determined using a DNA fluorometer (*BioPhotometer plus*, *Eppendorf*, Germany), and the quality was determined by agarose gel electrophoresis.

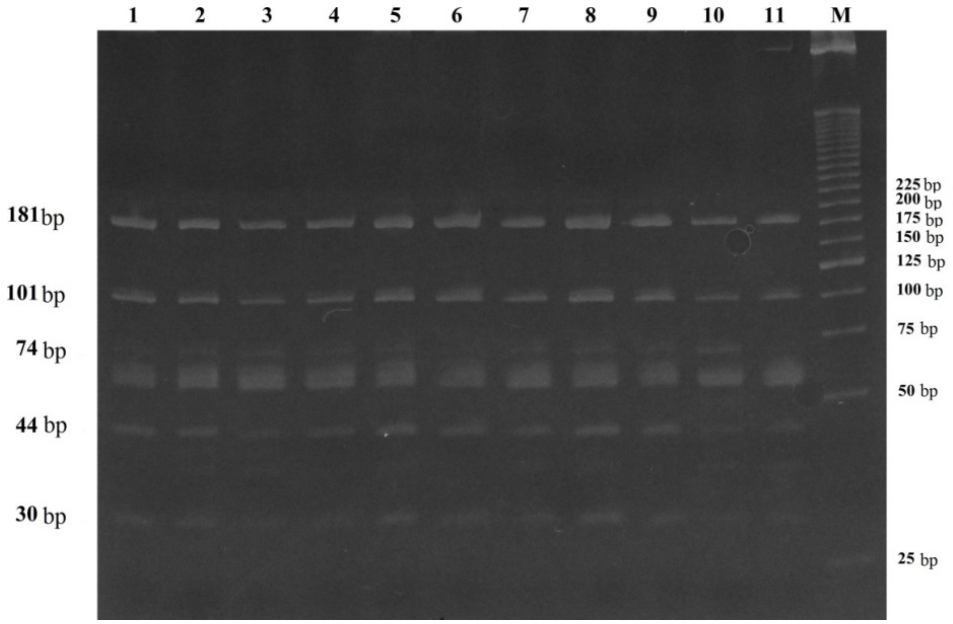
Genotyping of polymorphisms was carried out by polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP). The volume of the reaction mixture for PCR is 20 µl: 50-100 ng of genomic DNA, 5 pmol of primer and Master Mix (*ThermoFisher Scientific,* USA). For the PCR thermal cycle, a touchdown annealing temperature of 62°C minus 0.2°C per cycle for 35 cycles was used in a thermal cycler (*Mastercylcer nexus, Eppendorf,* Germany). Patients with POAG and members of the control group were also screened by restriction analysis. Restriction enzymes were mixed with each sample and incubated with their corresponding buffers overnight at 37°C (*ThermoFisher Scientific,* USA). Primer pairs and restriction enzymes are listed in table 1. DNA fragments were detected by electrophoresis on 2% agarose or 12% polyacrylamide gels.

Table 1 – Primer pairs and restriction enzymes for PCR-RFLP analysis

Polymorphism	Primer pair (5′→ 3′)	Codon changes	Nucleotide changes	Restriction enzyme
T353IR: T353IF:	GCTACCCTTCTAAGGTTCACATAC ATTGGCGACTGACTGCTTAC	$Thr^{353}Ile$	1058 (C→T)	*Hpy*CH4III
R76KR: R76KF:	CTTCTGTGCACGTTGCTGCA CTGGTCCAAGGTCAATTGGT	$Arg^{76}Lys$	227 (G→A)	*Bsm*AI
D208ER: D208EF:	CATAGTCAATCCTTGGGC CTGCAGACCTGCTCTGACAA	$Asp^{208}Glu$	624 (C→G)	*Bsm*AI
R206WR: R206WF:	CCGGAGTCTGCATTTCTTAGT GAAGGAGGCTGGAAGAGATTAC	$Arg^{206}Trp$	616 (C→T)	*Apa*I

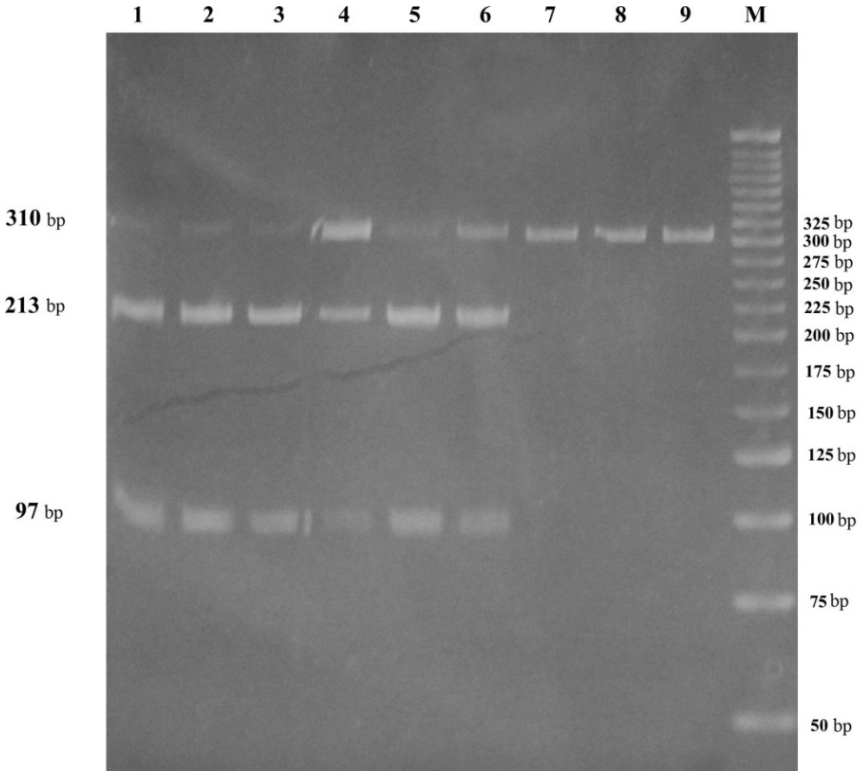
When processing the PCR products with restriction enzymes, the following DNA fragments were obtained: Thr/Thr-181, 101, 44, 30 bp.; Arg/Arg – 310 bp., Arg/Lys -310, 213, 97 bp, Lys/Lys - 213, 97 bp; Asp/Asp - 207,126 bp; Arg/Arg-501,86,71 bp.

Results and discussion. In order to observe *MYOC* and *NTF4* polymorphism by PCR-RFLP methods 85 patients suffering from glaucoma and 100 glaucoma-free individuals as a control group were included in genetic case-control studies. The genotype distribution based on SNPs are shown in figures 1 and 2.



M – DNA Ladder 25 bp (*ThermoFisher Scientific*, USA), 1-11 – CC genotype.

Figure 1 – R76K SNP genotyping results by PCR-RFLP method



M – DNA Ladder 25 bp (*ThermoFisher Scientific*, USA),
1, 2, 3, 5 – GG genotype, 4, 6 – GA genotype, 7, 8, 9 – AA genotype.

Figure 2 – Results of R76K SNP polymorphism by PCR-RFLP method

The frequencies of R76K polymorphisms in glaucoma patients and healthy control group are tabulated in table 2.

Table 2 – Genotype frequencies of the studied R76K G>A polymorphism in population

SNP	Genotypes	Patients group n=85	Patients group n=100	x^2	OR	CL 95%	P
R76K G>A	GG	0.682	0.970	26.59	0.07	0.02 – 0.23	3.0E-7
	GA	0.259	0.030		11.29	3.24 –39.30	
	AA	0.059	0.000		13.73	0.75 -252.07	

It this study R76K SNP has been detected in 27 glaucoma patients (22-Arg/Lys, 5-Lys/Lys) and in 3 individuals (3-Arg/Lys) from the control group.

R76K polymorphism is nucleotide change resulted in *G* being replaced by *A* (c.227G>A) in exon1 of *MYOC/TIGR* gene predicting amino acid change (substitution of Arg by Lys). The research carried out in Germany shows that R76K SNP was detected in 40 out of 112 glaucoma patients and in 3 patients there was identified Lys76Lys mutation at a polymorphic level [17].

According to the data, the variation T353I c.1058C>T in exon3 of *MYOC* gene can be one of the main reasons for developing POAG with increased intraocular pressure [15]. The reported findings on glaucoma genetics in Chinese Han population add to a growing body of evidence supporting that hypothesis. However, the genomic analyses of populations in Caucasus and Africa revealed that there is no genetic association of mutation T353I with glaucoma. Thus, genetic variations of *MYOC* gene can be varied among different ethnicity [16]. D208E mutations of *MYOC/TIGR* gene are causes of amino acid changes (Asp to Glu) due to the 624-cytosine nucleotide in exon2 of this gene is substituted by guanine. F. Mabuchi et al. reports that Asp208Glu mutations have been found in 4 hypertensive glaucoma patients and 3 POAG patients, at the same time it was revealed in 1 individual from the control group in Japan [18]. In addition, Japanese researchers investigated the distribution of Asp208Glu polymorphism among 99 glaucoma patients and their families also, in which Asp208Glu SNP has been indicated in one of the patients' mother and the researchers considered Asp208Glu polymorphism as an occasional neutral change with no effect on the gene's output [26]. Consequently, genetic variations of *MYOC* gene can be varied among different ethnicity.

The studies were carried out in China showed that R206W polymorphism in *NTF4* gene is a rare example of mutation. This SNP was indicated only in one of the 174 patients [27]. The research held by Pasutto found that named SNP was indicated in 4 glaucoma patients out of 399 from the experimental group and in none of the controls [28]. Abundant studies lead us to conclude that R206W polymorphism is a very rare SNP. Indeed, as a result of our study R206W polymorphism has been detected in neither case belong to the test group nor the control group.

By the frequency of T353I, D208E and R206W polymorphisms in *MYOC* gene and in *NTF4* respectively, there is no statistically significant difference between patients with POAG and individuals from control group. The available data point to the low frequency of above-mentioned polymorphisms. Our study has revealed that R76K is the most frequent polymorphism in Kazakhstan population. According to literary sources, the frequency of R76K SNP in Asia's population is higher than in Europe. The results of our research suggest that T353I, D208E and R206W polymorphisms in Kazakhstan population are the matter of neutral SNPs and could not be determined as a genetic reason of POAG progression, whereas R76K SNP has a strong association with POAG form of glaucoma.

REFERENCES

[1] Alekseev V.N., Aljab'eva Zh.Ju., Amirov A.N. (2014) Glaukoma. Nacional'noe rukovodstvo, Russia. ISBN 978-5-9704-2035-5 (in Russian)

[2] Quigley H.A., Broman A.T. (2006) The number of people with glaucoma worldwide in 2010 and 2020 // Br J Ophthalmol; 90: 262–7. DOI: 10.1136/bjo.2005.081224 (in Eng.)

[3] Goldberg I. Glaucoma in the 21st Century, Hartcourt. Health Communication. London: Mosby Int., 2000. P. 4-8 (in Eng.)

[4] http://www.inform.kz/ru/glaukoma-yavlyaetsya-glavnoy-problemoy-oftal-mologii-minzdrav-rk_a 3009168

[5] Kiseleva O.A., Zhuravleva A.N., Halilov Sh.A. Nasledstvennost' – faktor riska ili odno iz zven'ev v patogeneze pervichnoj glaukomy? // Oftal'mologija. 2011. N 4. P. 4-7 (in Russian)

[6] Wiggs J.L., Pasquale L.R. Genetics of glaucoma // Hum Mol Genet. 2017. Aug 1; 26(R1): R21-R27. doi: 10.1093/hmg/ddx184. (in Eng.)

[7] Stone E.M., Fingert J.H., Alward W.L., et al. Identification of a gene that causes primary open angle glaucoma // Science. 1997; 275: 668–70. DOI: 10.1126/science.275.5300.668 (in Eng.)

[8] Rezaie T., Child A., Hitchings R., et al. Adult-onset primary open-angle glaucoma caused by mutations in optineurin // Science. 2002; 295: 1077–9. DOI: 10.1126/science.1066901 (in Eng.)

[9] Alward W.L., Kwon Y.H., Khanna C.L., et al. Variations in the myocilin gene in patients with open-angle glaucoma // Arch Ophthalmol. 2002; 120: 1189–1197. doi:10.1001/archopht.120.9.1189 (in Eng.)

[10] Pasutto F., Matsumoto T., Mardin C.Y., Sticht H., Brandstätter J.H., Michels-Rautenstrauss K., et al. Heterozygous NTF4 mutations impairing neurotrophin-4 signaling in patients with primary open-angle glaucoma // Am J Hum Genet. 2009; 85: 447–56. DOI: 10.1016/j.ajhg.2009.08.016 (in Eng.)

[11] Astahov Ju.S., Rahmanov V.V. Nasledstvennost' i glaukoma // Oftal'mologicheskie vedomosti. 2012; 4 (4): 51-7 (in Russian)

[12] Resch Z.T., Fautsch M.P. Glaucoma-associated myocilin: a better understandingbut much more to learn. Exp Eye Res 2009; 88: 704-712. DOI: 10.1016/j.exer.2008.08.011 (in Eng.)

[13] Chi P.P., Yuk F.L., Baojian F., Larry B., Win Ch.T., Wing Sh.L., Dorothy S.P. TIGR/MYOC Gene Sequence Alterations in Individuals with and without Primary Open-Angle Glaucoma // Invest Ophthalmol Vis Sci. 2002 Oct; 43(10):3231-5 (in Eng.)

[14] Ibanez C.F. Neurotrophin-4: the odd one out in the neurotrophin family. Neurochem. Res. 21: 787-793, 1996. (in Eng.)

[15] Kelly W., Ryo K., Xiang Sh., Beatrice Y.J.T. Yue. Extracellular myocilin affects activity of human trabecular meshwork cells. Journal of Cellular Physiology, 17 February 2004. doi: 10.1002/jcp.10478 (in Eng.)

[16] Kollu N.R., Srujana N., Subhabrata Ch. Complex genetic mechanisms in glaucoma: An overview // Indian J Ophthalmol. 2011 Jan; 59(Suppl1): S31-S42. doi: 10.4103/0301-4738.73685 (in Eng.)

[17] Lam D.S., Leung Y.F., Chua J.K., Baum L., Fan D.S., Choy K.W., Pang C.P. Truncations in the TIGR gene in individuals with and without primary open-angle glaucoma // Invest Ophthalmol Vis Sci 2000; 41:1386-91 (in Eng.)

[18] Mabuchi F., Yamagata Z., Kashiwagi K., Tang S., Iijima H., Tsukahara S. Analysis of myocilin gene mutations in Japanese patients with normal tension glaucoma and primary open-angle glaucoma // Clin Genet 2001; 59:263-8. doi: 10.1016/j.ophtha.2012.02.044. (in Eng.)

[19] Ray K., Mukhopadhyay A., Acharya M. Recent advances in molecular genetics of glaucoma. Mol Cell Biochem 2003; 253: 223-31. DOI: https://doi.org/10.1023/A:1026059800470 (in Eng.)

[20] Weisschuh N., Neumann D., Wolf C., Wissinger B., Gramer E. 'Prevalence of myocilin and optineurin sequence variants in German normal tension glaucoma patients' // Mol Vis. 2005; 11: 284-287. http://www.molvis.org/molvis/v11/a33/ (in Eng.)

[21] Fingert J.H., Heon E., Liebmann J.M., Yamamoto T., Craig J.E., Rait J., Kawase K, Hoh S.T., Buys Y.M., Dickinson J., Hockey R.R., Williams-Lyn D., Trope G., Kitazawa Y., Ritch R., Mackey D.A., Alward W.L., Sheffield V.C., Stone E.M. Analysis of myocilin mutations in 1703 glaucoma patients from five different populations // Hum Mol Genet 1999; 8: 899-905. https://doi.org/10.1093/hmg/8.5.899 (in Eng.)

[22] Alward W.L., Fingert J.H., Coote M.A., Johnson A.T., Lerner S.F., Junqua D., Durcan F.J., McCartney P.J., Mackey D.A., Sheffield V.C., Stone E.M. Clinical features associated with mutations in the chromosome 1 open-angle glaucoma gene (GLC1A) // N Engl J Med 1998; 338: 1022-7. DOI: 10.1056/NEJM199804093381503 (in Eng.)

[23] Xiao-Min Zh., Yan Y., Ning F., Hong-Bo Ch., Xiao-Hong L., Yun W., Wen-Han Y., Su-Ping C., Xu-Yang L. Single nucleotide polymorphism of MYOC affected the severity of primary open angle glaucoma // Int J Ophthalmol. 2013; 6(3): 264–268. doi: 10.3980/j.issn.2222-3959.2013.03.02 (in Eng.)

[24] Huang X., Li M., Guo X., Li S., Xiao X., Jia X., Liu X., Zhang Q. 'Mutation analysis of seven known glaucoma-associated genes in Chinese patients with glaucoma' // Invest Ophthalmol Vis Sci. 2014; 55: 3594-3602. doi: 10.1167/iovs.14-13927 (in Eng.)

[25] Kim H.J., Suh W., Park S.C., Kim C.Y., Park K.H., Kook M.S., Kim Y.Y., Kim C.S., Park C.K., Ki C.S., Kee C. 'Mutation spectrum of CYP1B1 and MYOC genes in Korean patients with primary congenital glaucoma' // Mol Vis. 2011; 17: 2093-2101. <http://www.molvis.org/molvis/v17/a228> (in Eng.)

[26] Ishikawa K., Funayama T., Ohtake Y., Tanino T., Kurosaka D., Suzuki K., Ideta H., Fujimaki T., Tanihara H., Asaoka R., Naoi N., Yasuda N., Iwata T., Mashima Y. 'Novel MYOC gene mutation, Phe369Leu, in Japanese patients with primary open-angle glaucoma detected by denaturing high-performance liquid chromatography' // J Glaucoma. 2004; 13: 466-471. DOI: 10.1097/0.ijg.0000138204.6d (in Eng.)

[27] Eranga N. Vithana, Monisha E. Nongpiur, Divya Venkataraman, Stephanie H. Chan, Jagadeesh Mavinahalli and Tin Aung Identification of a novel mutation in the NTF4 gene that causes primary open-angle glaucoma in a Chinese population // Mol Vis. 2010; 16: 1640–1645. Published online 2010 Aug 15 (in Eng.)

[28] Pasutto F., Matsumoto T., Mardin C.Y., Sticht H., Brandstatter J.H., Michels-Rautenstrauss K., Weisschuh N., Gramer E., Ramdas W.D., van Koolwijk L.M., Klaver C.C., Vingerling J.R., Weber B.H., Kruse F.E., Rautenstrauss B., Barde Y.A., Reis A. Heterozygous NTF4 mutations impairing neurotrophin-4 signaling in patients with primary open-angle glaucoma // Am J Hum Genet. 2009; 85: 447-56. doi: 10.1016/j.ajhg.2009.08.016 (in Eng.)

Ж. Б. Тілеулес, О. Х. Хамдиева, С. Б. Зайпанова, Г. А. Қойшекенова, Б. О. Бекманов

ҚР БҒМ ҒК «Жалпы генетика және цитология институты» РМК, Алматы, Қазақстан

ҚАЗАҚСТАНДА ГЛАУКОМАМЕН АУЫРАТЫН НАУҚАСТАРДА МИОЦИЛИН (*MYOC)* ЖӘНЕ НЕЙРОТРОФИН 4 (*NTF4)* ГЕНДЕРІН ТАЛДАУ

Аннотация. Қазіргі таңда біріншілік ашық бұрышты глаукома офтальмология саласындағы медициналық-әлеуметтік мәнге ие басым бағыттардың бірі болып саналады. Глаукома 21-50% жағдайда генетикалық негізделген, глаукомамен ауыратын науқастардың ұрпақтарында осы аурудың даму қаупі 10 есеге жоғары болатындығы анықталған. Біріншілік ашық бұрышты глаукома ауруын тудыратын мутациялар 57кДа миоцилин белогын кодтайтын *MYOC/TIGR* және 28 кДа димерлі полипептидті кодтайтын *NTF4* гендерінде анықталған. Бұл жұмыста Қазақстан популяциясында *MYOC/TIGR* және *NTF4* гендеріндегі мутациялардың кездесу жиілігі анықтау қарастырылған. Зерттеуге біріншілік ашық бұрышты глаукомамен ауыратын 85 науқас және бақылау ретінде 100 сау адамдардан жиналған қан үлгілері қолданылды. Зерттеу нәтижесінде *MYOC/TIGR* геніндегі T353I, D208E және *NTF4* геніндегі R206W мутациялары мен глаукома ауруының дамуы арасында байланыстың болмайтындығы, ал *MYOC/TIGR* геніндегі R76K SNP мутациясының аталған аурудың дамуына әсер ететіндігі анықталды.

Түйін сөздер: БАБГ, полиморфизм, *MYOC/TIGR*, *NTF4*.

Ж. Б. Тілеулес, О. Х. Хамдиева, С. Б. Зайпанова, Г. А. Қойшекенова, Б. О. Бекманов

РГП «Институт общей генетики и цитологии» КН МОН РК, Алматы, Казахстан

АНАЛИЗ ГЕНОВ МИОЦИЛИНА (*MYOC*) И НЕЙРОТРОФИН 4 (*NTF4*) У БОЛЬНЫХ ГЛАУКОМОЙ В КАЗАХСТАНСКОЙ ПОПУЛЯЦИИ

Аннотация. Первичная открытая глаукома, являющаяся наиболее распространенной формой глаукомы, имеет большое социально-медицинское значение и является основным направлением научных исследований в области офтальмологии. В 21-50% случаев заболевание обуславливается генетически, а у потомков людей, болевших глаукомой, риск этой патологии в 10 раз выше. Мутации, вызывающие первичную открытую глаукому, были идентифицированы в гене *MYOC/TIGR*, который кодирует белок, известный как миоцилин (57 кДа), и в гене NTF4, который кодирует димерный пептид (28kD). В данном исследовании мы изучали частоту мутаций в генах *MYOC/TIGR* и NTF4 среди населения Казахстана. Исследование проводилось с участием 85 пациентов с первичной глаукомой и 100 человек в качестве контрольной группы. Результаты наших исследований показывают, что полиморфизмы T353I, D208E в гене *MYOC/TIGR* и R206W в гене *NTF4* среди населения Казахстана не влияют на прогрессию ПОУГ, тогда как R76K SNP в генах *MYOC/TIGR* может быть генетическим фактором, который влияет на развитие глаукомы типа ПОУГ.

Ключевые слова: ПОУГ, полиморфизм, *MYOC/TIGR*, *NTF4*.

Author's information:

Tileules Zhanerke – Master student, Institute of General Genetics and Cytology of the Ministry of Education and Science of the Republic of Kazakhstan; Almaty, janerke.tleules@mail.ru

Hamdieva Ozada – Scientific Researcher, Institute of General Genetics and Cytology of the Ministry of Education and Science of the Republic of Kazakhstan; Almaty, azadahamdieva@gmail.com

Zajpanova Saule – Scientific Researcher, Institute of General Genetics and Cytology of the Ministry of Education and Science of the Republic of Kazakhstan; Almaty, saule1kz@mail.ru

Kojshekenova Gulshat – Scientific Researcher, Institute of General Genetics and Cytology of the Ministry of Education and Science of the Republic of Kazakhstan; Almaty, ms.gulshat7@mail.ru

Bekmanov Bakhytzhan – PhD, Institute of General Genetics and Cytology of the Ministry of Education and Science of the Republic of Kazakhstan; Almaty, bobekman@rambler.ru

Publication Ethics and Publication Malpractice in the journals of the National Academy of Sciences of the Republic of Kazakhstan

For information on Ethics in publishing and Ethical guidelines for journal publication see http://www.elsevier.com/publishingethics and http://www.elsevier.com/journal-authors/ethics.

Submission of an article to the National Academy of Sciences of the Republic of Kazakhstan implies that the described work has not been published previously (except in the form of an abstract or as part of a published lecture or academic thesis or as an electronic preprint, see http://www.elsevier.com/postingpolicy), that it is not under consideration for publication elsewhere, that its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright-holder. In particular, translations into English of papers already published in another language are not accepted.

No other forms of scientific misconduct are allowed, such as plagiarism, falsification, fraudulent data, incorrect interpretation of other works, incorrect citations, etc. The National Academy of Sciences of the Republic of Kazakhstan follows the Code of Conduct of the Committee on Publication Ethics (COPE), and follows the COPE Flowcharts for Resolving Cases of Suspected Misconduct (http://publicationethics.org/files/u2/New_Code.pdf). To verify originality, your article may be checked by the Cross Check originality detection service http://www.elsevier.com/editors/plagdetect.

The authors are obliged to participate in peer review process and be ready to provide corrections, clarifications, retractions and apologies when needed. All authors of a paper should have significantly contributed to the research.

The reviewers should provide objective judgments and should point out relevant published works which are not yet cited. Reviewed articles should be treated confidentially. The reviewers will be chosen in such a way that there is no conflict of interests with respect to the research, the authors and/or the research funders.

The editors have complete responsibility and authority to reject or accept a paper, and they will only accept a paper when reasonably certain. They will preserve anonymity of reviewers and promote publication of corrections, clarifications, retractions and apologies when needed. The acceptance of a paper automatically implies the copyright transfer to the National Academy of Sciences of the Republic of Kazakhstan.

The Editorial Board of the National Academy of Sciences of the Republic of Kazakhstan will monitor and safeguard publishing ethics.

Правила оформления статьи для публикации в журнале смотреть на сайте:

www:nauka-nanrk.kz

ISSN 2518-1629 (Online), ISSN 2224-5308 (Print)

http://www.biological-medical.kz/index.php/ru/

Редактор *М. С. Ахметова, Т. М. Апендиев, Д. С. Аленов*
Верстка на компьютере *Д. Н. Калкабековой*

Подписано в печать 11.07.2018.
Формат 60x881/8. Бумага офсетная. Печать – ризограф.
9,2 п.л. Тираж 300. Заказ 4.