ORIGINAL ARTICLES

УДК 616.233-002.2-02:575.174.015.3
https://doi.org/10.20538/1682-0363-2023-3-36-42

Association of *MnSOD* and *GPX1* gene polymorphisms with a risk of chronic dust-induced bronchitis

Zhukova A.G.[1, 2], Kazitskaya A.S.[1, 2], Yadykina T.K.[1], Gulyaeva O.N.[1]

[1] *Research Institute for Complex Problems of Hygiene and Occupational Diseases*
23, Kutuzova Str., Novokuznetsk, 654041, Russian Federation

[2] *Kuzbass Humanitarian Pedagogical Institute, Kemerovo State University*
23, Tsiolkovskogo Str., Novokuznetsk, 654041, Russian Federation

ABSTRACT

Aim. To assess the association of the *MnSOD* (rs4880) and *GPX1* (rs1050450) gene polymorphisms with a risk of developing chronic dust-induced bronchitis in workers of the coal mining industry.

Materials and methods. The study included 182 coal miners with prolonged exposure to high concentrations of coal dust, including 116 people with a previously established diagnosis of chronic dust-induced bronchitis (CDB) and 66 people without pathology of the bronchopulmonary system, working under the same sanitary and hygienic conditions. Polymorphisms of the *MnSOD* (rs4880) and *GPX1* (rs1050450) genes were studied using polymerase chain reaction.

Results. For the first time, we established a statistically significant association between the polymorphisms of the *MnSOD* (rs4880) and *GPX1* genes (rs1050450) and CDB. Thus, the chance of detecting the homozygous A/A (Val/Val) *MnSOD* genotype in miners with CDB was 2 times higher than in the comparison group (χ^2 – 5.42; p = 0.02; odds ratio (OR) 2.21; 95% confidence interval (CI) 1.13–4.33), while the chance of detecting the homozygous G/G (Pro/Pro) *GPX1* genotype in miners with CDB was almost 6 times higher than in the comparison group (χ2 – 21.47; p = 0.001; OR 5.89; 95% CI 2.65–13.08). It was found that the combination of AA/GG genotypes of the *MnSOD/GPX*1 genes was significantly associated with a 1.5-fold risk of developing CDB (χ^2 – 11.49; p < 0.001; relative risk (RR) 1.59; 95% CI 1.36–1.84), while the chance of detecting this combination of genotypes in miners with bronchopulmonary pathology was 15 times higher than in the comparison group (OR 15.09; 95% CI 1.99–114.64).

Conclusion. Carriage of homozygous genotypes A/A at the rs4880 *MnSOD* locus and G/G at the rs1050450 *GPX1* locus was shown to be a marker of genetic predisposition to the development of CDB. The combination of homozygous genotypes of the studied AA/GG *MnSOD/GPX1* genes indicated a 1.5-fold risk of developing CDB. Carrying one of the three combinations of the *MnSOD* and *GPX1* genotypes (GG/AA, AA/AA, and AG/AA) indicated resistance to the development of CDB.

Keywords: gene polymorphism, *MnSOD, GPX1*, coal and rock dust, chronic dust-induced bronchitis

Conflict of interest. The authors declare the absence of obvious or potential conflict of interest related to the publication of this article.

Source of financing. This work was carried out according to the state assignment within the budgetary topic of the Research Institute for Complex Problems of Hygiene and Occupational Diseases No. AAAA-A19-119013190126-6.

Conformity with the principles of ethics. All patients signed an informed consent to participate in the study. The study was approved by the Biomedical Ethics Committee at the Research Institute for Complex Problems of Hygiene and Occupational Diseases (Protocol No. 3, § 1 of 04.28.2022).

For citation: Zhukova A.G., Kazitskaya A.S., Yadykina T.K., Gulyaeva O.N. Association of *MnSOD* and *GPX1* gene polymorphisms with a risk of chronic dust-induced bronchitis. *Bulletin of Siberian Medicine.* 2023;22(3):36–42. https://doi.org/10.20538/1682-0363-2023-3-36-42.

✉ *Zhukova Anna G.,* nyura_g@mail.ru

Ассоциация полиморфизмов генов *MnSOD* и *GPX1* с риском развития хронического пылевого бронхита

Жукова А.Г.[1, 2], Казицкая А.С.[1, 2], Ядыкина Т.К.[1], Гуляева О.Н.[1]

[1] *Научно-исследовательский институт комплексных проблем гигиены и профессиональных заболеваний (НИИ КПГПЗ)*
Россия, 654041, г. Новокузнецк, ул. Кутузова, 23

[2] *Кузбасский гуманитарно-педагогический институт (КГПИ), Кемеровский государственный университет (КемГУ)*
Россия, 654041, г. Новокузнецк, ул. Циолковского, 23

РЕЗЮМЕ

Цель. Оценить связь полиморфных локусов генов *MnSOD* (rs4880) и *GPX1* (rs1050450) с риском развития хронического пылевого бронхита у работников основных профессий угледобывающей отрасли.

Материалы и методы. В исследование включены 182 работника угольных шахт с длительным воздействием высоких концентраций угольно-породной пыли, среди которых 116 человек с ранее установленным диагнозом «хронический пылевой бронхит» (ХПБ), 66 – лица без патологии бронхолегочной системы, работающие в тех же санитарно-гигиенических условиях. Полиморфизмы генов *MnSOD* (rs4880) и *GPX1* (rs1050450) изучали с помощью полимеразной цепной реакции.

Результаты. Впервые для полиморфизмов генов ферментов антиоксидантной защиты – *MnSOD* (rs4880) и *GPX1* (rs1050450) установлена статистически значимая ассоциация с ХПБ. Так, шанс обнаружить гомозиготный генотип A/A (Val/Val) *MnSOD* у шахтеров с ХПБ в 2 раза выше, чем в группе сравнения (χ^2 – 5,42; p = 0,02; отношение шансов (ОШ) 2,21; 95%-й доверительный интервал (95%-й ДИ) 1,13–4,33), тогда как шанс обнаружить гомозиготный генотип G/G (Pro/Pro) *GPX1* у шахтеров с ХПБ почти в 6 раз выше, чем в группе сравнения (χ^2 – 21,47; p = 0,001; ОШ 5,89; 95%-й ДИ 2,65–13,08). Выявлено, что сочетание генотипов AA/GG генов *MnSOD*/*GPX1* статистически значимо связано с полуторакратным риском развития ХПБ (χ^2 – 11,49; p < 0,001; относительный риск 1,59; 95%-й ДИ 1,36–1,84), тогда как шанс обнаружить это сочетание генотипов у шахтеров с патологией бронхолегочной системы в 15 раз выше, чем в группе сравнения (ОШ 15,09; 95%-й ДИ 1,99–114,64).

Заключение. Показано, что маркером генетической предрасположенности к развитию ХПБ является носительство гомозиготных генотипов A/A в локусе rs4880 *MnSOD* и G/G в локусе rs1050450 *GPX1*. Сочетание гомозиготных генотипов изученных генов AA/GG *MnSOD/GPX1* свидетельствует о полуторакратном риске развития ХПБ. Носительство одного из трех сочетаний генотипов генов *MnSOD* и *GPX1*: GG/AA, AA/AA и AG/AA свидетельствует о резистентности к формированию ХПБ.

Ключевые слова: полиморфизм генов, *MnSOD, GPX1*, угольно-породная пыль, хронический пылевой бронхит

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Работа выполнена по государственному заданию в рамках бюджетной темы Научно-исследовательского института комплексных проблем гигиены и профессиональных заболеваний (№ АААА-А19-119013190126-6).

Соответствие правилам этики. Все пациенты подписали информированное согласие на участие в исследовании. Исследование одобрено комитетом по биомедицинской этике НИИ КПГПЗ (протокол № 3, §1 от 28.04.2022).

Для цитирования: Жукова А.Г., Казицкая А.С., Ядыкина Т.К., Гуляева О.Н. Ассоциация полиморфизмов генов *MnSOD* и *GPX1* с риском развития хронического пылевого бронхита. *Бюллетень сибирской медицины.* 2023;22(3):36–42. https://doi.org/10.20538/1682-0363-2023-3-36-42.

INTRODUCTION

Chronic dust-induced bronchitis (CDB) in miners is a special form of bronchial inflammation in response to exposure to high concentrations of coal dust with the development of diffuse atrophic and sclerotic changes, accompanied by impaired bronchial motility and respiratory failure [1, 2]. The key mechanism of the pathological response to long-term coal dust exposure is excessive activation of free radical processes (FRP) and changes in the activity of antioxidant defense enzymes [3–5].

Manganese superoxide dismutase (MnSOD) and glutathione peroxidase (GPx) are the key antioxidant enzymes which provide the first line of defense against oxidative stress [6–9]. Experiments on long-term exposure to coal dust showed changes in the expression of antioxidant defense components in different organs in rat models, including MnSOD, catalase, and GPx [10].

There are practically no studies that describe genetic variations in antioxidant defense in individuals with long-term exposure to coal dust at work. Among the antioxidant enzymes in CDB, the polymorphism of the glutathione-S-transferase (GSTT) gene family is the most studied one. The glutathione S-transferase gene family provides resistance of cells and tissues to toxic substances and products of lipid peroxidation. It has been shown that carriers of the *GSTT1*+ genotype which is responsible for normal production of the enzyme are most susceptible to the development of CDB, and carriers of the *GSTT1* null-genotype are resistant to CDB development [11, 12].

The aim of the study was to assess the association of the *MnSOD* (rs4880) and *GPX1* (rs1050450) gene polymorphisms with a risk of developing CDB in workers of the coal mining industry.

MATERIALS AND METHODS

Individuals employed in the main mining occupations in south Kuzbass mines (an underground tunneller, a stope miner, a mining machine operator) aged 39–58 years were examined in the clinic of the Research Institute for Complex Problems of Hygiene and Occupational Diseases. A total of 182 coal miners with long-term exposure to high concentrations of coal dust (exceeding the maximum permissible concentration by up to 35 times), including 116 miners previously diagnosed with chronic dust-induced bronchitis (CDB), were examined. Occupational bronchopulmonary pathology was diagnosed after the examination at the clinic of the Research Institute for Complex Hygiene Problems and Occupational Diseases by the medical expert board using federal guidelines.

The comparison group (66 workers) that underwent a preventive medical examination consisted of individuals without bronchopulmonary pathology, working under the same sanitary and hygienic conditions. The examined groups of miners are comparable in age and work experience, the difference between the groups is statistically insignificant ($p > 0.05$). The average work experience of miners with CDB was 24.39 ± 0.5 years, in the comparison group – 23.1 ± 1.2 years. The average age of miners with CDB was 48 ± 0.6 years, in the comparison group – 46 ± 0.7 years.

The following inclusion criteria were used in the study: Russian ethnicity; male gender; employment in the main occupations in the coal mines of south Kuzbass; at least 10 years of working underground; signed voluntary informed consent to participate in the study; clinically confirmed diagnosis of CDB for individuals included in the experimental group. The exclusion criteria were as follows: belonging to indigenous or settler descendant ethnic groups; mental disorders; malignant neoplasms and autoimmune diseases; refusal to sign an informed consent to participate in the study. For the comparison group, an additional exclusion criterion was any bronchopulmonary pathology, including both occupational and general somatic pathology.

For genetic studies, venous blood was taken on an empty stomach in vacutainers with K_3EDTA as an anticoagulant. Extraction of genomic DNA from blood cells was performed by phenol – chloroform extraction followed by ethanol precipitation [13]. Polymorphic variants of the genes were analyzed by real-time polymerase chain reaction using competitive TaqMan probes complementary to the polymorphic DNA sequence on DTprime-4 (DNA-Technology LLC, Moscow, Russian Federation). Test systems for molecular genetic analysis were developed by the Institute of Chemical Biology and Fundamental Medicine of the Siberian Branch of the Russian Academy of Sciences and synthesized by SibDNK LLC (Novosibirsk, Russian Federation). *MnSOD* (rs4880) and *GPX1* (rs1050450) gene polymorphisms were studied.

Statistical analysis of the results obtained was carried out using the IBM SPSS Statistics 22 software (license agreement No. 20/604/3–1 of 22.04.2016). The normality of the distribution of quantitative variables (age and work experience of patients) was

checked using kurtosis and asymmetry parameters. Quantitative variables were presented as the mean (*M*) and the standard error of the mean (*m*). Under normal distribution, Student's parametric *t*-test was used to compare two independent samples. The critical significance level (*p*) at which the null hypothesis would be rejected was 0.05.

The correspondence of the actual distribution of polymorphic variants of the *MnSOD* and *GPX1* genes to the theoretically expected one was determined according to the Hardy – Weinberg equilibrium. Pearson's χ^2 value was calculated to assess differences in the distribution of genotypes in patients with CDB and healthy individuals. The critical value of the significance level of differences was $p = 0.05$. The significance of differences in parameters was assessed by calculating the odds ratio (OR) and relative risk (RR) with the determination of the limits of the 95% confidence interval (CI). If the OR is more than 1, it means that the chances of finding a risk factor are higher in the group with an outcome (disease). If 95% CI does not include 1, that is, both limits are > 1 or < 1, a conclusion is made about the statistical significance of the identified association between the factor and the outcome at $p < 0.05$.

RESULTS AND DISCUSSION

The correspondence of the actual distribution of *MnSOD (*rs4880) and *GPX1 (*rs1050450) gene polymorphisms to the theoretically expected one was determined according to the Hardy – Weinberg equilibrium (Table 1). In the comparison group, the frequency of the A allele of the *GPX1* gene was two times higher than the frequency indicated in the dbSNP database of the NCBI open access information resource for the general population (0.6924 compared to 0.3219). However, no deviation of the obtained data from the expected frequencies was observed, the significance level was above 0.05 both for each genotype (χ^2 – 0.26–1.17–1.32; $p > 0.05$) and the total (χ^2 – 2.75; $p > 0.005$). For the *MnSOD* gene, no deviations from the frequency indicated in the dbSNP database were observed in both study groups.

The results obtained indicated that the Hardy – Weinberg equilibrium conditions were met (Table 1) with $p > 0.05$ for all studied genotypes, which made it possible to interpret the data obtained and conduct further analysis using the Pearson's χ^2 test to assess the distribution of genotypes between miners with CDB and individuals in the comparison group.

Table 1

Distribution of alleles and genotypes of the *MnSOD (*rs4880) and *GPX1 (*rs1050450) genes in the study groups

Group	Gene	Genotype	Absolute numbers	Genotype frequency, %	Allele frequency, %	Theoretically expected genotype frequency, %	Theoretically expected number of individuals with a given genotype	Heterozygosity	χ^2 Hardy–Weinberg
CDB	*MnSOD*	*A/A*	48	41.4	61.6	38.0	44	47.3	0.35
		A/G	47	40.5	–	47.3	55		1.13
		G/G	21	18.1	38.4	14.7	17		0.9
		Total	116	1	1	1	116		2.38
Comparison group		*A/A*	16	24.25	50.0	25.0	16.5	50.0	0.02
		A/G	34	51.5	–	50.0	33		0.03
		G/G	16	24.25	50.0	25.0	16.5		0.02
		Total	66	1	1	1	66		0.06
CDB	*GPX1*	*A/A*	14	12.9	32.1	10.3	11	43.6	0.67
		A/G	42	38.5	–	43.6	48		0.64
		G/G	53	48.6	67.9	46.1	50		0.15
		Total	109	1	1	1	109		1.46
Comparison group		*A/A*	34	52.3	69.2	47.9	31	42.6	0.26
		A/G	22	33.9	–	42.6	28		1.17
		G/G	9	13.8	30.8	9.5	6		1.32
		Total	65	1	1	1	65		2.75

*$p > 0.05$.

In the course of our study, the *MnSOD (*rs4880) and *GPX1 (*rs1050450) gene polymorphisms were considered separately. A molecular genetic study of *MnSOD* and *GPX1* gene polymorphisms revealed statistically significant differences between patients with CDB and the comparison group (Table 2). The chance of detecting the homozygous A/A genotype in *MnSOD (*rs4880) in miners with CDB was two

times higher than in the comparison group (χ^2 – 5.42; $p < 0.02$; OR – 2.21; 95% CI 1.13–4.33).

It has been shown that the A/A (Val/Val) genotype of the *MnSOD* gene causes a change in the secondary structure of the *MnSOD* signal sequence (from α-helix to β-sheet structure), resulting in a decrease in the transport of the antioxidant enzyme into mitochondria [14]. In addition, a change in the secondary structure reduces the activity of *MnSOD* by 30–40% and the efficiency of detoxification of superoxide anion radicals [6, 8, 15], which is one of the factors of excessive FRP activation. Thus, earlier rat model experiments focusing on long-term exposure to coal dust showed a decrease in SOD activity by 1.9 times and an increase in the sensitivity of lung tissue to FRP induction *in vitro* [10].

The study of the *GPX1 (*rs1050450) gene polymorphism showed that the chance of detecting the homozygous genotype G/G (Pro/Pro) in miners with CDB was almost 6 times higher than in the comparison group (χ^2 – 21.47; $p = 0.001$; OR – 5.89; 95% CI 2.65–13.08). Previously, carriers of the G/G (Pro/Pro) genotype had high activity of glutathione peroxidase (GPx1) and a high level of free radical oxidation products in blood plasma. In addition, the G/G (Pro/Pro) *GPX1* genotype provides a more intense antioxidant response to damaging effects compared to the G/A (Pro/Leu) and A/A (Leu/Leu) genotypes [9]. In turn, the homozygous genotype A/A is the genotype of resistance to the development of CDB, the frequency of which in the comparison group was 4 times higher than in miners – 52.31% and 12.85%, respectively.

Table 2

Distribution of *MnSOD* and *GPX1* genotypes in the comparison group and in patients with chronic dust-induced bronchitis

Gene	Genotype	Comparison group, abs. (%)	CDB, abs. (%)	χ^2; p	OR, 95% CI
MnSOD (rs4880)	*A/A* (Val/Val)	16 (24.24)	48 (41.38*)	5.42; 0.02	2.21; 1.13; 4.33
	A/G (Ala/Val)	34 (51.52)	47 (40.52)		0.64; 0.35; 1.18
	G/G (Ala/Ala)	16 (24.24)	21 (18.10)		0.69; 0.33; 1.44
GPX1 (rs1050450)	*G/G* (Pro/Pro)	9 (13.84)	53 (48.62*)	21.47; 0.001	5.89; 2.65; 13.08
	A/G (Pro/Leu)	22 (33.85)	42 (38.53)		0.82; 0.43; 1.55
	A/A (Leu/Leu)	34 (52.31)	14 (12.85*)		0.13; 0.06; 0.28

* – significance of differences compared to the comparison group.

Table 3

Combinations of *MnSOD (*rs4880) and *GPX1* (rs1050450) gene polymorphisms in coal industry employees

Group	Combination of genotypes			
	AA/GG	*GG/AA*	*AA/AA*	*AG/AA*
CDB patients	23	1	5	9
Comparison group	1	8	11	17
χ^2; p	11.49; $p < 0.001$	12.20; $p < 0.001$	8.91; $p = 0.003$	12.52; $p < 0.001$
OR 95% CI	15.09 1.99–114.64	0.06 0.01–0.48	0.21 [0.07–0.63	0.22 0.09–0.54
RR, 95% CI	1.59 1.36–1.85	0.16 0.03–1.04	0.46 0.22–0.95	0.49 0.29–0.84

Note: the table presents the combinations of genotypes that have a statistically significant association with the development of chronic dust-induced bronchitis and resistance to its development.

Next, we determined whether there were significant differences in combinations of genotypes of the *MnSOD*/*GPX1* antioxidant enzyme genes between coal miners with CDB and healthy individuals (Table 3). The analysis showed that the combination of AA/GG genotypes of the *MnSOD*/*GPX1* genes had a statistically significant association with a 1.5-fold risk of developing CDB (χ^2 – 11.49; $p < 0.001$; RR – 1.59; 95% CI 1.36–1.84), while the odds of detecting this combination of genotypes in miners with bronchopulmonary pathology were 15 times higher than in the comparison group (OR – 15.09; 95% CI 1.99–114.64). This may be due to a significant decrease in MnSOD activity and excessive activation of GPx1 and FRP in organs, in particular in the lungs [16]. Carriers of the combination of AA/GG

genotypes who have a high genetic risk of developing CDB should be advised to change their job, have a regular health checkup, and participate in preventive measures if they were previously exposed to coal dust.

Three combinations of polymorphic genotypes of the *MnSOD*/*GPX1* genes: GG/AA (χ^2 – 12.20; $p < 0.001$; OR – 0.06; 95% CI 0.01–0.48; RR – 0.16; 95% CI 0.03–1.04), AA/AA (χ^2 – 8.91; $p = 0.003$; OR – 0.21; 95% CI 0.07–0.63; RR – 0.46; 95% CI 0.22–0.95), and AG/AA (χ^2 – 12.52; $p < 0.001$; OR – 0.22; 95% CI 0.09–0.54; RR – 0.49; 95% CI 0.29–0.84) are associated with resistance to the development of CDB (Table 3). This may be due to preserved normal activity of the antioxidant defense enzymes MnSOD and GPx1 and maintenance of a normal redox balance.

CONCLUSION

Based on the obtained results, we can conclude that the carriage of homozygous genotypes A/A at the rs4880 *MnSOD* locus and G/G at the rs1050450 *GPX1* locus is a marker of genetic predisposition to the development of CDB, and their combination AA/GG in the *MnSOD/GPX1* genes indicates a 1.5-fold risk of developing CDB. The rs1050450 *GPX1* polymorphism homozygous for the A allele forms resistance to CDB development. Carrying one of the three combinations of genotypes in the *MnSOD* and *GPX1* genes (GG/AA, AA/AA and AG/AA) also indicates resistance to CDB.

REFERENCES

1. Perret J.L., Plush B., Lachapelle P., Hinks T.S., Walter C., Clarke P. et al. Coal mine dust lung disease in the modern era. *Respirology*. 2017;22(4):662–670. DOI: 10.1111/resp.13034.
2. Mu M., Li B., Zou Y., Wang W., Cao H., Zhang Y. et al. Coal dust exposure triggers heterogeneity of transcriptional profiles in mouse pneumoconiosis and vitamin D remedies. *Part Fibre Toxicol*. 2022;19(1):7. DOI: 10.1186/s12989-022-00449-y.
3. Kaur S., Gill M.S., Gupta K., Manchanda K. Effect of occupation on lipid peroxidation and antioxidant status in coal-fired thermal plant workers. *Int. J. Appl. Basic Med. Res*. 2013;3(2):93–97. DOI: 10.4103/2229-516X.117065.
4. Ulker Oc., Yucesoy B., Demir O., Tekin Io., Karakaya A. Serum and BAL cytokine and antioxidant enzyme levels at different stages of pneumoconiosis in coal workers. *Hum. Exp. Toxicol*. 2008;27(12):871–877. DOI: 10.1177/0960327108098332.
5. Pavlovskaya N.A., Rushkevich O.P. Biologic markers for early diagnosis of effects caused by exposure to coal dust in miners. *Russian Journal of Occupational Health and Industrial Ecology.* 2012;(9):36–42 (in Russ).
6. Alhobeira H.A., Mandal R.K., Khan S., Dar S.A., Mahto H., Saeed M. et al. Link between MnSOD Ala16Val (rs4880) polymorphism and asthma risk is insignificant from sequential meta-analysis. *Bioinformation*. 2020;16(11):789–800. DOI: 10.6026/97320630016789.
7. Ekoue D.N., He C., Diamond A.M., Bonini M.G. Manganese superoxide dismutase and glutathione peroxidase-1 contribute to the rise and fall of mitochondrial reactive oxygen species which drive oncogenesis. *Biochim. Biophys. Acta Bioenerg*. 2017;1858(8):628–632. DOI: 10.1016/j.bbabio.2017.01.006.
8. Hernando B., Gil-Barrachina M., Tomás-Bort E., Martinez-Navarro I., Collado-Boira E., Hernando C. The effect of long-term ultra-endurance exercise and SOD2 genotype on telomere shortening with age. *J. Appl. Physiol*. 2020;129(4):873–879. DOI: 10.1152/japplphysiol.00570.2020.
9. Jablonska E., Gromadzinska J., Peplonska B., Fendler W., Reszka E., Krol M.B. et al. Lipid peroxidation and glutathione peroxidase activity relationship in breast cancer depends on functional polymorphism of GPX1. *BMC Cancer.* 2015;15:657. DOI: 10.1186/s12885-015-1680-4.
10. Zhukova A.G., Mikhailova N.N., Sazontova T.G., Zhdanova N.N., Kazitskaya A.S., Bugaeva M.S. et al. Participation of free-radical processes in structural and metabolic disturbances in the lung tissues caused by exposure to coal-rock dust and their adaptogenic correction. *Bull. Exp. Biol. Med.* 2020;168(4):439–443. DOI: 10.1007/s10517-020-04727-7.
11. Gafarov N.I., Zakharenkov V.V., Panev N.I., Burdein A.V., Puzyrev V.P., Rudko A.A. Chronic occupational bronchitis in workers of coal mining enterprises in Kouzbass: role of endogenous factors. *Russian Journal of Occupational Health and Industrial Ecology.* 2010;(3):37–40 (in Russ.).
12. Gafarov N.I., Zakharenkov V.V., Panev N.I., Kucher A.N., Freydin M.B., Rudko A.A. The role of genetic factors in the development of chronic dust bronchitis in workers of coal mining enterprises in Kuzbass. *Hygiene and Sanitation.* 2013;92(4):44–47 (in Russ.).
13. Sambrook J., Russell D.W. Purification of nucleic acids by extraction with phenol: chloroform. *Cold Spring Harb. Protoc.* 2006;1:pdb.prot4455. DOI: 10.1101/pdb.prot4455.
14. Xitong Y., Sulian Y., Hongyang X., Dan L., Yuanyuan Z., Guangming W. Superoxide dismutase gene polymorphism is associated with ischemic stroke risk in the china Dali region han population. *Neurologist.* 2021;26(2):27–31. DOI: 10.1097/NRL.0000000000000301.
15. Flekac M., Skrha J., Hilgertova J., Lacinova Z., Jarolimkova M. Gene polymorphisms of superoxide dismutases and catalase in diabetes mellitus. *BMC Med. Genet*. 2008;9:30. DOI: 10.1186/1471-2350-9-30.
16. Bastaki M., Huen K., Manzanillo P., Chande N., Chen C., Balmes J.R. et al. Genotype-activity relationship for Mn-superoxide dismutase, glutathione peroxidase 1 and catalase in humans. *Pharmacogenet. Genomics*. 2006;16(4):279–286. DOI: 10.1097/01.fpc.0000199498.08725.9c.

Authors' information

Zhukova Anna G. – Dr. Sci. (Biology), Associate Professor, Head of the Laboratory for Molecular Genetic and Experimental Research, Research Institute for Complex Hygiene Problems and Occupational Diseases; Head of the Department of Natural Sciences, Kuzbass Humanitarian Pedagogical Institute, Kemerovo State University, Novokuznetsk, nyura_g@mail.ru, https://orcid.org/0000-0002-4797-7842

Kazitskaya Anastasia S. – Cand. Sci. (Biology), Senior Researcher, Laboratory for Molecular Genetic and Experimental Research, Research Institute for Complex Hygiene Problems and Occupational Diseases; Associate Professor of the Department of Natural Sciences, Kuzbass Humanitarian Pedagogical Institute, Kemerovo State University, Novokuznetsk, anastasiya_kazitskaya@mail.ru, https://orcid.org/0000-0001-8292-4810

Yadykina Tatiana K. – Cand. Sci. (Biology), Leading Researcher, Laboratory for Molecular Genetic and Experimental Research, Research Institute for Complex Hygiene Problems and Occupational Diseases, Novokuznetsk, yadykina.tanya@yandex.ru, https://orcid.org/0000-0001-7008-1035

Gulyaeva Olga N. – Senior Researcher, Laboratory for Molecular Genetic and Experimental Research, Research Institute for Complex Hygiene Problems and Occupational Diseases, Novokuznetsk, Gulyaich1973@mail.ru, https://orcid.org/0000-0003-2225-6923

(✉) **Zhukova Anna G.,** nyura_g@mail.ru

Received 21.06.2022;
approved after peer review 23.11.2022;
accepted 16.02.2022