cell viability, which prevented the formation of ice crystals that injured cell walls [9]. Apparently, slow freezing, suitable for esophageal and colon cancer, was not applicable to the stomach tumor tissue. We will take it into account in the further development of cryopreservation protocols.

Conclusions. Protocols 2 and 3 with slow freezing of samples should be used for cryopreservation of human esophageal and colon cancer xenografts. Gastric cancer samples require other cryopreservation methods due to the low efficiency of the existing ones.

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N.V. Zaitseva, O.A. Kazakova, A.A. Mazunina, V.B. Alekseev, O.V. Dolgikh

GENETIC AND IMMUNOLOGICAL MARKERS OF THE FORMATION OF METABOLIC SYNDROME IN SCHOOL CHILDREN (ON THE EXAMPLE OF THE PERM REGION)

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ZAITSEVA Nina Vladimirovna – Academician of the Russian Academy of Sciences, MD, Professor, scientific director of FBSI Federal Scientific Center for Medical and Preventive Health Risk Management Technologies, e-mail: znv@fcrisk.ru; ORCID: 0000-0003-2356-1145; **KAZAKOVA Olga Alekseevna** – junior researcher at the laboratory of Immunogenetics of FBSI Federal Scientific Center for Medical and Preventive Health Risk Management Technologies; e-mail: chakina2011@yandex.ru; ORCID: 0000-0002-0114-3930; **MAZUNINA Alena Aleksandrovna** – junior researcher at the laboratory of Immunogenetics of FBSI Federal Scientific Center for Medical and Preventive Health Risk Management Technologies; e-mail: alena-osa@bk.ru; tel. +7(342) 236-39-30. ORCID: 0000-0002-3579-4125; **ALEKSEEV Vadim Borisovich** – MD, Director of Federal Scientific Center for Medical and Preventive Health Risk Management Technologies; e-mail: root@fcrisk.ru; tel. +7(342)236-39-30. ORCID: 0000-0001-5850-7232; **DOLGIKH Oleg Vladimirovich** – MD, Head of the Department of Immunobiological Diagnostics of FBSI Federal Scientific Center for Medical and Preventive Health Risk Management Technologies; e-mail: oleg@fcrisk.ru; tel. +7(342)236-39-30. ORCID:0000-0003-4860-3145

The problem of the formation of metabolic syndrome in children is becoming more and more urgent every year, which is associated with excess nutrition, physical inactivity, increased psycho-emotional stress, therefore, timely identification of immune and genetic markers of predisposition to the development of this pathology will allow identifying possible health risks at an early stage and preventing their implementation in adulthood. **The aim of the study:** To evaluate the indicators of immune status and genetic polymorphism of candidate genes as markers of the development of metabolic syndrome in school children (on the example of a secondary school in Perm). **Materials and methods.** The study involved 214 school-age children. Three groups were formed, ranked according to the body mass index criterion: observation group1 with metabolic syndrome (BMI SDS >2.0), observation group2 with excess body weight (BMI SDS >1.0 <2), comparison group – absence of excess body weight (BMI SDS <1.0). The evaluation of immune (IL 1B, IL 4, CD19+), neuroregulatory (leptin), metabolic (glucose, HDL, triglycerides), genetic (ADRB rs1042413, PPARA rs4253778) indicators was carried out. **Results and discussion.** It was found that the group of children with metabolic syndrome and excess body weight in relation to the comparison group was characterized by an increase in CD19+ expression by 1.3 times, a decrease in the content of anti-inflammatory cytokine IL4 by 1.5 times, overexpression of pro-inflammatory cytokines (IL1b by 1.9 times), leptin by 2.0 times, an imbalance of lipid-carbohydrate metabolism (reduction of HDL by 7%, against the background of an increase in triglyceride levels by 17% and glucose levels by 8%), significant changes in the frequencies of genotypes associated with metabolic syndrome (increased frequency by 2.7 times of the typical AA genotype of the ADRB2 gene rs1042713, OR=3.79 CI:1.25-11.47; p<0.05, as well as by 4.6 times of the variant CC genotype of the PPARA gene rs4253778 OR=5.00; CI:0.97-25.89; p<0.05). **Conclusion.** Candidate immunological (CD19+, IL 1b, IL4) and genetic (ADRB2 rs1042713, PPARA rs4253778) markers are recommended to be used as indicators for identifying early signs of metabolic syndrome in school-age children living in the Perm region.

Keywords: metabolic syndrome, body mass index, PPARG gene, ADRB2 gene, cytokines, CD, schoolchildren.

Introduction. The peculiarities of the development of the child's body, as well as bad habits, sedentary lifestyle, excess nutrition, genetic predisposition, increased emotional stress lead to the formation of metabolic syndrome in children become risk factors for the development of cardiovascular diseases in adulthood. If earlier the diagnosis of metabolic syndrome was applicable only to the adult

population, today the manifestations of this syndrome are noted in children and adolescents with greater frequency [1].

Metabolic syndrome combines a complex of symptoms including metabolic, hormonal and psychosomatic disorders. For children, the exogenous contributing factors to the development of this syndrome are inactivity, excessive food intake and stress, and the markers accompanying this change are carbohydrate and lipid imbalance, hormonal and immune disorders [2,3].

Russian statistics show that the percentage of children with obesity and malnutrition is growing, and overweight is observed in every fifth child of school age [4].

Physical inactivity of modern children in combination with improper diet and increased psycho-emotional stress during the educational process has a negative impact on the health of children, which is expressed in increased fatigue, irritability, eating disorders, decreased immunity and quality of life of children in general [5].

Excess and unbalanced nutrition contributes to the development of immune disorders. The state of metabolism and the immune system directly depend on the gut microbiome, where an excess of some substances affects the deficiency of others, which disrupts the extraction of energy from consumed foods, contributing additional calories, as well as fueling lipogenesis and gluconeogenesis [6].

The central system regulating the feeling of satiety is the dopaminergic system, where dopamine and leptin act as key neuropeptides in the regulation of metabolism. An increase in leptin in the blood leads to a feeling of satiety and, accordingly, a decrease in the intake of additional energy from food, correlates with the amount of fat mass in the human body, having a long-term effect on brain mechanisms. Thus, with prolonged accumulation of triglycerides, the release of leptin into the blood by adipocytes increases. Pro-inflammatory cytokines and elevated glucose levels also contribute to the release of leptin, while leptin potentiates the pyrogenic effect of IL1. It is known that leptin has a direct relationship with the level of dopamine involved in the regulation of metabolism. Chachhiani I. and co-authors suggest that elevated concentrations of leptin in the first stages of inflammation can stimulate cortisol synthesis, thereby inhibiting the effects of the hypothalamic-pituitary-adrenal axis [7-9].

Genetic predisposition makes a decisive contribution to the development of metabolic syndrome. Thus, the PPARA gene is expressed in tissues with a high level of mitochondrial oxidation (liver, heart, vascular walls), is activated by fatty acids, participates in lipid oxidation and lipoprotein metabolism, thereby counteracting the formation of metabolic syndrome and aging. The PPARG receptor has anti-inflammatory and antiproliferative effects. The expression product of the ADRB2 gene is a lipolytic receptor in fat cells, and is associated with lipid mobilization. The Arg16Gly and Gln27Glu polymorphisms of the ADRB2 gene are associated with the development of metabolic syndrome and pathology of the cardiovascular system in adults [10,11].

The determination of markers associated with the development of metabolic syndrome in children is associated with certain difficulties associated with the peculiarities of the development of the child's body, puberty, mental disorders, and also associated with gender. For example, girls are more susceptible to the development of metabolic syndrome during puberty, which is due to hormonal transformations. The lipid profile may also depend on age, while there is no clearly defined range of insulin norms for children of different ages, especially during puberty.

It is relevant today to identify immunological and genetic markers of the formation of metabolic syndrome in children under conditions of increased psycho-emotional stress associated with the educational process.

The aim of the study: To evaluate the indicators of immune status and genetic polymorphism of candidate genes as markers of the development of metabolic syndrome in school children (on the example of a secondary school in Perm).

Materials and methods. The study involved 214 children (7-17 years old) attending secondary general educational institutions in Perm. The observation and comparison groups were formed based on the assessment of body mass index and divided into groups of children according to the WHO classification: observation group1 – children with metabolic syndrome (BMI SDS >2.0) (12.3±0.7 years), observation group2 - overweight children (BMI SDS >1.0 <2) (11.3±0.5 years), the comparison group – children with no excess body weight (BMI SDS <1.0) (11.6 ± 0.3 years).

The lipid, carbohydrate, and immune profiles were evaluated for the examined children, as well as the polymorphism of candidate genes in the development of metabolic disorders.

The level of triglycerides and HDL was assessed by photometric method, the level of glucose in serum and plasma was determined by glucose oxidase method on the Keylab BPC+Biosed device.

The level of absolute and relative expression of CD19+ B-lymphocytes was assessed by the method of membrane immunofluorescence using FACSCalibur (Becton Dickinson) device.

The level of proinflammatory cytokines TNF and IL4, as well as the level of leptin, were evaluated by the method of enzyme-linked immune blood analysis on the BioTEC Elx808 device.

The polymorphism of candidate genes was evaluated by real-time polymerase chain reaction on a Bio RAD CFX96 device with an assessment of allelic discrimination. The features of polymorphism of candidate genes are investigated: *ADRB2* Arg16Gly rs1042713, *PPARA* G2528C rs4253778.

Statistical analysis was carried out using parametric and nonparametric research models in the Statistica 10.0 program, with an assessment of X-mean, SD-deviation, SE-error, W-normality of distribution, Student's t-test, Mann-Whitney U-test, p- significance level. Statistical analysis of candidate genes was evaluated using multiplicative, general, dominant and recessive inheritance models, with the evaluation of indicators x2- chi-square criterion, OR- odds score, CI – confidence interval, p – significance level. The results were considered significant at $p<0.05$.

Results and discussion. The immune profile of the children of observation group 1 relative to the comparison group was characterized by a significant change in cellular regulation indicators: an increase in the absolute and relative expression levels of CD19+ B-lymphocytes by 1.3 and 1.2 times, respectively.

The lipid profile of the children of the observation group1 relative to the comparison group was characterized by a significantly increased triglyceride level by 1.5 times (1.15±0.20 mmol/dm3 versus 0.78±0.04 mmol/dm3) and a reduced HDL level by 1.2 times, carbohydrate metabolism was characterized by a significant increase in blood glucose by 8% ($p<0.05$) (Tab.1).

The assessment of the immune profile showed that the children of observation group 2, relative to the comparison group, are characterized by an increase in the expression of cytokine IL1b by 1.9 times and a decrease in IL4 by 1.5 times.

In the children of the observation group2, relative to the comparison group, HDL levels were significantly lowered by 8% and triglyceride levels were increased by 18% and leptin by 2.1 times ($p<0.05$).

Thus, it was found that excess body weight in school-age children is accompanied by hormonal dysregulation in the form of hyperproduction of the peptide hormone leptin, which promotes proliferation and activation of monocytes and macrophages, accompanied by increased production of proinflammatory cytokines [12]; features of immune regulation (overexpression of CD19+ B-lymphocytes, IL1beta proinflammatory cytokines, insufficient expression of anti-inflammatory cytokine IL4), however, in the studies of N.Y. Grishkevich and co-authors, analysis of lymphocyte subpopulations in the blood of obese children showed a decrease in absolute and relative expression of B-lymphocytes [13]; an imbalance of markers of carbohydrate and lipid metabolism (high expression of glucose and triglycerides in the blood, a decrease in HDL levels), where the main change in the lipid composition of the blood in metabolic syndrome is precisely an increase in triglycerides and a decrease in HDL [14].

The results of the genetic analysis showed significant changes in the frequencies of alleles and genotypes of candidate genes between the study groups that differ according to the SDS BMI criterion: the PPARA G2528C rs4253778 peroxisome activator gene and the ADRB2 Arg16Gly rs1042713 adrenoreceptor gene (Table 2).

The frequency of homozygous wild genotype AA of the adrenergic receptor gene ADRB2 Arg16Gly rs1042713 was significantly increased in children of the observation group1 relative to the comparison group by 2.7 times, inherited by the dominant type, with allele A (OR=2.31; CI:1.11-4.82; p<0.05) and genotype AA (OR=3.79 CI:1.25-11.47; p<0.05) significantly increase the likelihood of developing metabolic syndrome.

For children of the observation group2, relative to the comparison group, an increase in the frequency of the variant homozygous CC genotype of the PPARA G2528C rs4253778 gene by 4.6 times, inherited by recessive type, was found, and the odds assessment indicates the likely participation of this genotype in metabolic disorders and the formation of excess body weight (OR=5.00; CI:0.97-25.89; p<0.05).

Thus, it was found that the variant allele of the PPARA gene is associated only with excess body weight, when the modified oxidation-peroxidation program can be adjusted by diet, which is sufficient to stop the increase in clinical manifestations of obesity. The transcription factor PPARA regulates the expression of several dozen genes involved in the regulation of cellular differentiation, inflammatory response, glucose and lipid metabolism [15]; whereas the polymorphism of the ADRB2 catecholamine regulation gene under the conditions of the intensity of the educational process triggers a hormonal mechanism associated with leptin overexpression, which leads to more pronounced changes in BMI towards its increase with the development of metabolic syndrome and the need for its drug correction. According to Mitra S. research and the co-authors showed an association of polymorphism of the ADRB2 gene with changes in HDL levels, and the AA genotype of the gene was associated with higher blood glucose levels in children [16].

Conclusion. The present study of the immunological and genetic profile of school-age children (7-17 years old), living in the Perm region, exposed to psycho-emotional stress of the academic load has substantiated the indicator indicators of early diagnosis of the formation of metabolic syndrome and overweight, characterizing violations of immune and metabolomic regulation, including markers of cellular regulation B-lymphocytes

Table 1

The results of a comparative analysis of the immune and metabolomic profile of the studied groups of children according to the SDS BMI criterion.

Indicator	Standard	Observation group1	Observation group2	Comparison group	p1	p2
CD19+ abs	0.09-0.66 (*10^9/л)	0.38±0.04	0.30±0.02	0.29±0.01	0.0320	0.5370
CD19+ rel	6-25 (%)	14.43±0.84	12.97±0.56	11.91±0.27	0.0060	0.1040
ИIL1b	0-6 (пг/мл)	2.97±0.65	4.81±0.97	2.54±0.21	0.5460	0.0320
IL4	0-4 (пг/мл)	1.77±0.36	1.50±0.15	2.28±0.23	0.2560	0.0080
Glucose	3.33-5.55 (ммоль/дм3)	5.018±0.09	4.72±0.08	4.64±0.04	0.0010	0.4180
Triglycerides	0.3-1.7 (ммоль/дм3)	1.15±0.09	0.91±0.07	0.77±0.02	0.0000	0.0590
HDL	0.8-2.2 (ммоль/дм3)	1.46±0.08	1.59±0.04	1.72±0.03	0.0040	0.0290
Leptin	1.1-27.6 (нг/мл)	33.31±9.78*	15.75±1.15	7.49±0.78	0.1320	0.0000

Note: *- significant difference with the norm, abs- absolute, rel- relative, p1- significant differences between groups of observation1/comparison; p2-significant differences between groups of observation2/comparison.

Table 2

The results of a comparative analysis of the frequencies of alleles and genotypes of candidate genes in the studied groups of children differing by the SDS BMI criterion

Groups	Gen	Genotype	X^2(p)	OR(CI)	allele	X^2(p)	OR(CI)
Observation1/ Comparisons	*ADRB2* Arg16Gly rs1042713	AA	6.44 (0.0112)	3.79* (1.25-11.47)	A	5.23 (0.0222)	2.31* (1.11-4.82)
		AG		0.76 (0.26-2.19)			
		GG		0.46 (0.14-1.47)	G		0.43 (0.21-0.90)
Observation2/ Comparisons	*PPARA* G2528C rs4253778	GG	4.73 (0.0296)	1.00 (0.46-2.16)	G	0.42 (0.5164)	0.81 (0.43-1.53)
		GC		0.72 (0.31-1.64)			
		CC		5.00 (0.97-25.89)	C		1.23 (0.65-2.33)

Note: X2 is chi-squared, p - significance level, OR – odds ratio, CI - confidence interval, * -reliability of the results.

CD19+, pro- and anti-inflammatory cytokines IL1b, IL4, an indicator of neuropeptide regulation (leptin) associated with polymorphism of alleles and genotypes of candidate genes of the adrenoreceptor gene ADRB2 rs1042713 (A allele and AA genotype) and the PPARA peroxisome receptor gene rs4253778 (CC genotype).

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S.I. Sofronova, A.N. Romanova, V.M. Nikolaev, M.P. Kirillina

THE FREQUENCY OF METABOLIC SYNDROME AND ITS COMPONENTS IN THE NON-INDIGENOUS POPULATION OF SOUTH YAKUTIA

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A one-stage study of the working non-indigenous population of South Yakutia was conducted. A high incidence of abdominal obesity, lipid-metabolic disorders has been shown. Dyslipidemia, arterial hypertension and metabolic syndrome, mainly represented by a three-component, were most often registered in men compared to women. The relationship of blood pressure with triglyceride and glucose levels was obtained.

Keywords: metabolic syndrome, dyslipidemia, arterial hypertension, non-indigenous population, South Yakutia.

Metabolic syndrome (MS) remains a global epidemic in the XI century, increasing its growth rates, causing terrible complications such as type 2 diabetes, stroke, myocardial infarction, etc. Often, the presence of MS exacerbates the course of cardiovascular pathology, increasing the risk factors for its development. Its prevalence in the world ranges from 10 to 30% according to foreign and domestic authors, depending on various criteria for its diagnosis [4;9;10]. According to some estimates, it reaches up to 1/3 of the world's population [7]. The total cost of treatment and economic losses associated with this syndrome are estimated in trillions. The study of MS in the working non-indigenous population of the North is relevant, research in this field is extremely scarce. The spread of MS and its patients becoming younger is the main reason for the relevance of the study. It is also due to the high risk of developing cardiovascular diseases and their mortality in the industrial cities of the Far North.

The aim of the study was to assess the frequency of occurrence of metabolic syndrome and its components in non-indigenous residents of South Yakutia.

Materials and methods of research. A one-time population study of the working population of non-indigenous nationality in the Aldan district of the Republic of Sakha (Yakutia) was conducted. According to the list of employees of industrial and social spheres, every 3rd employee was invited for examination. The response rate was 75%. 174 residents of the Aldan district of working age were analyzed, 66 of them were men, whose

Yakut Science Centre of Complex Medical Problems: **SOFRONOVA Sargylana Ivanovna** – PhD, Researcher of YSC CMP, ORCID: 0000-0003-0010-9850, sara2208@mail.ru,; **ROMANOVA Anna Nikolaevna** – MD, director of YSC CMP, ORCID: 0000-0002-4817-5315; **NIKOLAEV Vyacheslav Mikhailovich** – PhD, researcher, nikolaev1126@mail.ru; **KIRILLINA Maria Petrovna** – PhD, researcher of YSC CMP, kirillinamp@mail.ru