

group and the group of patients with lung cancer. The most statistically significant differences in the frequencies of alleles and genotypes were observed by the polymorphic variant 857G> A. In patients compared with healthy ones, there is a decrease in the incidence of mutant NAT2 * 857G allele - 64.2% and 78.3%, respectively, $\chi^2 = 42.52$; $p < 0.05$; OR = 2.02; 95% CI = 1.10 - 3.78 and an increase in the frequency of wild NAT2 * 857A allele - 35.8%, 21.7%, respectively $\chi^2 = 42.52$; $p < 0.05$; OR = 6.47; 95% CI = 3.52 - 11.98. In the group of patients, the frequency of the NAT2 * 857A allele (35.8%, $\chi^2 = 42.52$, $p < 0.05$, OR = 6.47, 95% CI = 3.52-11.98), and the heterozygous genotype NAT2 * 857G/A (71.6%, $\chi^2 = 13.43$, $p = 0.0002$, OR = 0.23, 95% CI = 0.10-0.53), but the frequency of homozygous genotype decreased NAT2 * 857G/G (28.4%, $\chi^2 = 10.95$, $p = 0.0009$, OR = 3.79, 95% CI = 1.66-8.78) compared with the control - 21.7%, 36.6% and 60.1% respectively. In the analysis of associations of polymorphic variants 481C> T, 590G> A and 857G> A of the NAT2 gene with the development of lung cancer in Yakutia, allelic variants and genotypes of the NAT2 gene were established, contributing to the development of lung cancer in individuals of Yakut ethnicity. The markers of increased risk of developing lung cancer in the Yakuts are the NAT2 * 857A allele and the NAT2 * 857G/A genotype; the NAT2 * 857G allele, the NAT2 * 857G/G genotype are low-risk markers.

Prospects for further research. The associations of polymorphic variants 481C> T, 590G> A and 857G> A of NAT2 gene with development of lung cancer in Yakutia have been studied for the first time. Genetic markers of increased and decreased risk of lung cancer in the Yakuts have been identified. It has been revealed that the markers of increased risk of developing lung cancer for the Yakuts are the NAT2 * 857A allele and the NAT2 * 857G/A genotype, the NAT2 * 857G allele, the NAT2 * 857G/G genotype are markers of reduced risk. The mutations associated with lung cancer will help to form risk groups for the prevention of cancer for people working with genotoxic factors and smokers.

References

1. Clinical pharmacogenetics. / Sychev D.A. [et al.] edited by V.G. Kukis, N.P. Bochkova. – M.: Geotar-Media, 2007. – P.248.
2. Ravegnini G, Sammarini G, Hrelia P, Angelini S. Key Genetic and Epigenetic Mechanisms in Chemical Carcinogenesis. *Toxicol Sci.* 2015 Nov;148(1):2-13. doi:10.1093/toxsci/kfv165.
3. Antonova O, Toncheva D, Grigorov E. Bladder cancer risk from the perspective of genetic polymorphisms in the carcinogen metabolizing enzymes. *J BUON.* 2015 Nov-Dec;20(6):1397-406.
4. Wang S, Hao J, Wang H, Fang Y, Tan L. Efficacy and safety of immune checkpoint inhibitors in non-small cell lung cancer. *Oncoimmunology.* 2018 Apr 24;7(8):e1457600. doi: 10.1080/2162402X.2018.1457600.
5. Kim AS, Ko HJ, Kwon JH, Lee JM. Exposure to Secondhand Smoke and Risk of Cancer in Never Smokers: A Meta-Analysis of Epidemiologic Studies. *Int J Environ Res Public Health.* 2018 Sep 11;15(9). pii: E1981. doi: 10.3390/ijerph15091981.
6. Eckhardt M, Zhang W, Gross AM, Von Dollen J, Johnson JR, Franks-Skiba KE, Swaney DL, Johnson TL, Jang GM, Shah PS, Brand TM, Archambault J, Kreisberg JF, Grandis JR, Ideker T, Krogan NJ. Multiple Routes to Oncogenesis are Promoted by the Human Papillomavirus-Host Protein Network. *Cancer Discov.* 2018 Sep 12. pii: CD-17-1018. doi: 10.1158/2159-8290.CD-17-1018.
7. Ju J, Chen A, Deng Y, Liu M, Wang Y, Wang Y, Nie M, Wang C, Ding H, Yao B, Gui T, Li X, Xu Z, Ma C, Song Y, Kvensakul M, Zen K, Zhang CY, Luo C, Fang M, Huang DCS, Allis CD, Tan R, Zeng CK, Wei J, Zhao Q. NatD promotes lung cancer progression by preventing histone H4 serine phosphorylation to activate Slug expression. *Nat Commun.* 2017 Oct 13;8(1):928. doi:10.1038/s41467-017-00988-5.
8. Fayez D, Saliminejad K, Irani S, Kamali K, Memariani T, Khorram Khorshid HR. Arylamine N-acetyltransferase 2 Polymorphisms and the Risk of Endometriosis. *Avicenna J Med Biotechnol.* 2018 Jul-Sep;10(3):163-167.
9. Wang Y, Wang Z, Xu J, Li J, Li S, Zhang M, Yang D. Systematic identification of non-coding pharmacogenomic landscape in cancer. *Nat Commun.* 2018 Aug 9;9(1):3192. doi: 10.1038/s41467-018-05495-9.
10. Hwang IW, Kim K, Kwon BN, Kim HJ, Han SH, Lee NR, Choi EJ, Cho HI, Jin HJ. Association of glutathione S-transferase M1 and T1 null/present polymorphism with physical performance in the Korean population. *Genes Genomics.* 2018 Sep 10. doi: 10.1007/s13258-018-0737-6.

Key words: lung cancer, polymorphic variant, N-acetyltransferase-2 (NAT2).

Accepted for printing on 20 Aug 2018

DOI: 10.29256/v.02.02.2018.escbm71

PROGNOSTIC ROLE OF IL-4, IL-2 AND TLR-2 FOR PREDICTING OF COURSE OF FOOD ALLERGY IN CHILDREN

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Food allergy (FA) is considered as one of the main health problems of early childhood and is considered as the first step of "atopy march". It was proved, that important role in further development of allergic diseases has IL-4. Promising positive results of target therapy of atopic dermatitis with anti-IL-4 antibodies underline importance of this signaling protein. The aim of the study was to evaluate possible prognostic role of IL-4 for predicting of the long-term effects of the correction of barrier dysfunction in children with food allergy in comparison with IL-2 and TLR-2.

Materials and methods. 88 patients with skin symptoms of food allergy aged from 1 month to 18 years were included into the study. Treatment of all patients lasted 10 days and included elimination of the causative product, skin emollient and *Bacillus clausii*. Blood samples were collected after fasting in cooling vacutaner and after that

it was immediately centrifugated (4°C for 3.000 × 30 min). For levels of IL-2, IL-4 detection ELISA method was used (Human IL-2 Platinum ELISA and Human IL-4 Platinum ELISA, produced by Affymetrix eBioscience, Austria). TLR-2 in serum was detected by ELISA Kit for TLR-2 (Cloud-Clone Corp). Course of the disease was assessed during 1-year follow-up period of the course of treatment. Frequency and duration of each exacerbation was assessed in points: 0 – without change, 1 – little improvement, 2 – much improvement, 3 – remission/full control.

Results. Statistical analysis of the obtained results showed that levels of IL-4 were significantly important only for the frequency of the exacerbations ($U = 28,0; p = 0,01$). Duration of the exacerbation did not differ in children with different levels of IL-4. IL-2 and TLR-2 expression had no association with long-term effects in children who received treatment aimed on the barrier dysfunction correction ($p > 0,05$).

Key words: food allergy, IL-4, epidermal barrier, treatment, emollient.

Accepted for printing on 28 Aug 2018

DOI: 10.29256/v.02.02.2018.escbm72

STUDY OF THE ACTION OF CHROMIUM-CONTAINING BIOPREPARATIONS FROM SPIRULINA ON INSULIN ACTIVITY IN RATS

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Trivalent chromium is essential to normal carbohydrate, lipid and protein metabolism. Chromium is biologically active as part of an oligopeptide– chromodulin – potentiating the effect of insulin by facilitating insulin binding to receptors at the cell surface [1]. In recent decades, the Cr (III) picolinate (CrPic) is used as a nutritional supplement with an effective ability to alleviate the symptoms of type 2 diabetes. On the other hand, CrPic has some disadvantages. In acidic media, when pH is reduced, the complex hydrolyses to release picolinic acid - a determinant factor in the low rate of gastrointestinal absorption of chromium. The results of the research on the toxic effects of CrPic have been reviewed in some publications, while the statements described still bear contradictory characters [2, 3]. In order to exclude the adverse effects of Cr (III) compounds on the human body, the use of chromium-containing natural supplements such as chromium enriched yeasts [4] or high chromium-containing spirulina and other bioactive substances is very important [5, 6, 7]. The goal of present research was study of the effect of new chromium containing preparations from spirulina on insulin activity in rats in experimental alloxanic type II diabetes.

Materials and Methods. The spirulina food additive – „SpiruCr1” was obtained with the method previously developed in Scientific Research Laboratory “Phycobiotechnology” [8]. Cyanobacterium *Spirulina platensis* was grown in presence of chromium glycinate [Cr(Gly)3]Cl (5-30 mg/l) and in both lighting regimes: continuous illumination and with photoperiod 14/10 hours, spirulina productivity and chromium accumulation in biomass were studied. The maximum stimulatory effect of chromium glycinate on productivity of spirulina, as well as chromium accumulation in biomass were established. Chromium glycinate was supplemented portioned in concentrations of 40 mg / l on the first and the 3rd day of cultivation. Cultivation of spirulina was carried out for 10 days with photoperiod regime: night / day (10/14 hours). Biomass was separated from the culture liquid by filtration, washed with distilled water and supposed to lyophilization for obtaining of spirulina food additive. „SpiruCr1”. Injectable preparation „BioRCr1” was obtained from chromium enriched spirulina biomass by extraction and purification [6]. These preparations were tested as remedies for increasing of the insulin activity in rats in experimentally induced type II of diabetes. The research was carried out in RS Laboratory “Human and Animal Ecophysiology”, Insitute of Research and Innovation, Moldova State University. The experiments were performed on four groups of rats with average weight 250-300g. 1 – Control group (healthy rats), the second, third and fourth groups included the rats with experimental induced type II diabetes by administering of alloxan, a chemical substance that causes the destruction of beta- cells of the pancreas - responsible for insulin synthesis. The rats of the third group were fed on a food supplement «SpiruCr1» for 10 days and subsequently their insulin activity has been determined. The fourth group of rats was treated intraperitoneally with the injectable preparation «BioRCr1» for 10 days with testing of insulin activity. Insulin activity was determined by immuno-fermentative method (biochemical analyzer STAT-FAX 4500).

Results. The chromium containing products - the food additive «SpiruCr1» and the biopreparation «BioRCr1» are natural, including high content of chromium (up to 10mg/g and 1.2mg/g of Cr, respectively), amino acids, and oligopeptide and other bioactive substances. The effects of chromium containing preparations obtained from chromium enriched spirulina biomass on insulin activity in rats were established. The obtained results are presented in Table 1.

Table 1

Change in insulin activity in rats following administration of the chromium containing preparations

Experimental groups	Insulin activity, mIU/ml
1. Healthy rats (control)	5,00
2. Rats with alloxanic diabetes	0,27
3. Rats with alloxanic diabetes treated with „SpiruCr1”	7,80
4. Rats with alloxanic diabetes treated with „BioRCr1”	7,20