phic loci, while in stable COPD association was shown only with the rs536715 locus. Our data indicated that *SIRT3* (rs3782116) gene locus is the specific marker of frequent exacerbations COPD phenotype.

The associations of *SIRT3* gene loci with age-associated diseases in which oxidative stress and cellular senescence play a key role were extensively investigated [11].

The *SIRT6* (rs107251) is associated with the development of both COPD phenotypes. *SIRT6* exhibits ADP-ribosyltransferase and histone deacetylase activity, and plays role in DNA repair [9]. In the study [3], a decrease of *SIRT6* levels was shown in respiratory epithelial cells of COPD patients due to cigarette smoke exposure. An association of *SIRT6* gene loci with cardiovascular diseases has been shown; cardiovascular diseases are often a comorbid pathology in COPD and have similar pathogenetic mechanisms associated with oxidative stress and cellular senescence [1].

**Conclusion.** As a result of the study, we have identified significant associations with the development of various COPD phenotypes with polymorphic variants of the *SIRT1* (rs3818292), *SIRT3* (rs536715) and *SIRT6* (rs107251) genes. A specific marker for COPD phenotype with frequent exacerbations is the *SIRT3* (rs3782116) gene locus. The data obtained confirm the hypothesis of a significant role of NAD-dependent protein deacetylases from the sirtuin family and the mechanisms of cellular senescence in the hereditary predisposition to COPD development.

## Reference


1. Song X., Wang H., Wang C., Ji G., Jiang P., Liang D., Wang X. Association of Sirtuin Gene Polymorphisms with Susceptibility to Coronary Artery Disease in a North Chinese Population. Biomed. Res. Int. 2022; 2022: 4294008. doi: 10.1155/2022/4294008.
2. Korytina G.F., Akhmadishina L.Z., Aznabaeva Y.G., Kochetova O.V., Zagidullin N.S., Kzhyshkowska J.G., Zagidullin S.Z., Viktorova T.V. Associations of the NRF2/KEAP1 pathway and antioxidant defense gene polymorphisms with chronic obstructive pulmonary disease. Gene. 2019; 692: 102-112. doi: 10.1016/j.gene.2018.12.061.
3. Takasaka N., Araya J., Hara H., Ito S., Kobayashi K., Kurita Y., Wakui H., Yoshii Y., Yumino Y., Fujii S., Minagawa S., Tsurushige C., Kojima J., Numata T., Shimizu K., Kawaishi M., Kaneko Y., Kamiya N., Hirano J., Odaka M., Morikawa T., Nishimura S.L., Nakayama K., Kuwano K. Autophagy induction by SIRT6 through attenuation of insulin-like growth factor signaling is involved in the regulation of human bronchial epithelial cell senescence. J. Immunol. 2014; 192(3): 958-968. doi: 10.4049/jimmunol.1302341.
4. Barnes P.J., Baker J., Donnelly L.E. Cellular Senescence as a Mechanism and Target in Chronic Lung Diseases. Am. J. Respir. Crit. Care Med. 2019; 200(5): 556-564. doi: 10.1164/rccm.201810-1975TR.
5. Finkel T., Deng C.X., Mostoslavsky R. Recent progress in the biology and physiology of sirtuins. Nature. 2009;460(7255): 587-591.doi: 10.1038/nature08197.
6. Ragland M.F., Benway C.J., Lutz S.M., Bowler R.P., Hecker J., Hokanson J.E., Crapo J.D., Castaldi P.J., DeMeo D.L., Hersh C.P., Hobbs B.D., Lange C., Beaty T.H., Cho M.H., Silverman E.K. Genetic Advances in Chronic Obstructive Pulmonary Disease. Insights from COPDGene. *Am J. Respir. Crit. Care. Med*. 2019;200(6): 677-690. doi: 10.1164/rccm.201808-1455SO.
7. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: 2023 report [Internet]. Available from https://goldcopd.org/2023-gold-report-2/
8. Kirkham P.A., Barnes P.J. Oxidative stress in COPD. Chest. 2013; 144(1): 266-273. doi: 10.1378/chest.12-2664.
9. Kugel S., Mostoslavsky R. Chromatin and beyond: the multitasking roles for SIRT6. Trends Biochem. Sci. 2014; 39(2): 72-81. doi:10.1016/j.tibs.2013.12.002.
10. Zhang J.R., Li C.Y., Zhang J., Lv X.J. Roles of sirtuin family members in chronic obstructive pulmonary disease. Respir. Res. 2022; 23(1): 66. doi: 10.1186/s12931-022-01986-y.
11. Sun W., Liu C., Chen Q., Liu N., Yan Y., Liu B. SIRT3: A New Regulator of Cardiovascular Diseases. Oxid. Med. Cell Longev. 2018; 2018: 7293861. doi: 10.1155/2018/7293861.
12. Rajendrasozhan S., Yang S.R., Kinnula V.L., Rahman I. SIRT1, an antiinflammatory and antiaging protein, is decreased in lungs of patients with chronic obstructive pulmonary disease. Am. J. Respir. Crit. Care Med. 2008; 177(8): 861-870. doi: 10.1164/rccm.200708-1269OC.
13. Dikalova A.E., Itani H.A., Nazarewicz R.R., McMaster W.G., Flynn C.R., Uzhachenko R., Fessel J.P., Gamboa J.L., Harrison D.G., Dikalov S.I. Sirt3 Impairment and SOD2 Hyperacetylation in Vascular Oxidative Stress and Hypertension. Circ. Res. 2017; 121(5): 564-574. doi: 10.1161/CIRCRESAHA.117.310933.
14. Cao L., Liu C., Wang F., Wang H. SIRT1 negatively regulates amyloid-beta-induced inflammation via the NF-κB pathway. Braz. J. Med. Biol. Res. 2013; 46(8): 659-669. doi: 10.1590/1414-431X20132903.
15. Wu Q.J., Zhang T.N., Chen H.H., Yu X.F., Lv J.L., Liu Y.Y., Liu Y.S., Zheng G., Zhao J.Q., Wei Y.F., Guo J.Y., Liu F.H., Chang Q., Zhang Y.X., Liu C.G., Zhao Y.H.. The sirtuin family in health and disease. Signal Transduct. Target Ther. 2022; 7(1): 402. doi: 10.1038/s41392-022-01257-8.


I.E. Nikolaeva, A.S. Golderova, V.G. Ivanova, M.P. Kirillina., T.I. Nikolaeva

# MATURATION OF MONOCYTES INTO DENDRITIC CELLS BY MORPHOLOGICAL SIGNS IN BREAST CANCER

DOI 10.25789/YMJ.2023.83.04

УДК 57.085.23; 616-006.66

Medical Institute, M.K. Ammosov North-Eastern Federal University: **NIKOLAEVA Irina Eduardovna** – research associate, medbiotech@s-vfu.ru; **GOLDEROVA Aitalina Semyonovna** – MD, research associate, Professor; **IVANOVA Violetta Grigoryevna** – 6th year student; **NIKOLAEVA Tatiana Ivanovna** – PhD, Associate Professor, chief physician of the Yakut Republican oncological dispensary; **KIRILLINA Maria Petrovna** – PhD in Biology, research scientist, head of the lab. Yakut Science Centre of Complex Medical Problems; e-mail: kirillinamp@mail.ru , 89142779959.

Taking into account the complex maturation process of dendritic cells under culturing conditions, as well as the available data of morphological characteristics at various pathological conditions, we find it interesting to assess the features of cell morphology in oncological patients. The purpose of this study was to assess the morphological characteristics of the processes of maturation of dendritic cells in breast cancer. In cancer patients, the potential for cellular viability and maturation compared to healthy individuals is reduced in the early days of cultivation, probably due to the cytotoxicity of chemotherapy and radiation therapy at the time of the study. Cell analysis in the last days of cultivation indicates that the processes of activation of monocyte maturation in dendritic cells in in vitro were significantly higher in oncobols than in healthy individuals.

**Keywords:** cultivation, monocytes, dendritic cells, morphology, breast cancer.

**Introduction.** Anticancer vaccines are designed to induce an immune response against tumor antigens. Despite decades of research and development, only a few anti-cancer vaccines have been approved for human use. The success of

these anti-cancer vaccines depends on several factors, including the type of antigens used, the microenvironment of the tumor, the immune landscape of the tumor and various vaccine formulations [5]. Dendritic cells (DCs) are the main antigens that process and represent antigens through the molecules of the main histosis complex MHC I and II to innate and adaptive immune systems [11, 8, 4, 6].

DCs can be grown (differentiated) in large quantities under special laboratory conditions and have become widely studied on experimental models. DCs are rare among peripheral blood leukocytes (less than 1%) and typically exhibit complex phenotypic and functional heterogeneity of the population. Several subtypes of DC with unique and specific functions, morphology and localization: 1) Langerhans cells are described; 2) Myeloid dendritic cells; 3) Dendritic cells derived from monocytes; 4) Lymphoid dendritic cells; 5) Plasmocyte dendritic cells.

Immature DCs have a rounded and smooth surface, while mature DCs have a rough surface with multiple pseudotypes. In the immature state of DC, lower levels of bone-inducing molecules such as CD80, CD86, CD83, and MHC II are expressed and secrete lower levels of immunostimulating cytokines such as IL-12, IL-10, and TNF. In contrast, mature DCs express high levels of bone-inducing molecules and immunostimulating cytokines, indicating that DCs are in phenotypically and functionally mature state [3]. Immature DCs with low levels of activation and high phagocytic ability absorb antigens and mature, acquiring a more active phenotype. After maturation, DCs form dendrites and rapidly migrate to lymph nodes to enhance immune response [7].

An important difference between the properties of newborn babies and adult DCs is the more pronounced suppression of mitogenic activity in cultures with a competitive influence of conventional and modulated DCs [2]. Under the influence of Kureha polysaccharide, immature dendritic cells develop into mature dendritic cells with reduced antigen capture, but also high expression of key surface molecules of MHC-II class, CD40, CD80, CD86 and CD83, as well as larger IL-12p70 and TNF-α [9].

Immature dendritic cells were observed to have large rounded cells, almost without processes. Towards maturation, cells acquire dendritic process elongated forms. These changes occur before and after activation on dendritic cells of patients and on dendritic cells of conditionally healthy persons. The study results are based on the fact that the maturation capacity of dendritic cells in osteomyelitis disease is not impaired. The ability of dendritic cells isolated from peripheral blood monocytes, patients with chronic osteomyelitis caused by Staphylococcus aureus to maturation under the influence of in vitro activators is not impaired [1].

In the study [10] a comparison was made of maturation of DCs from monocytes of patients with cirrhosis of liver and healthy persons. Higher DC output from monocytes was found in patients with cirrhosis of the liver. However, with phenotyping of CD14+ cells, there was no significant difference between cirrhosis of the liver and healthy donors in terms of DC output from CD14+ precursors. The study concluded that when using adequate conditions for DC maturation and T-cell DC absorption from cirrhosis patients, they retain the same ability to activate, mature and present the antigen as healthy donors.

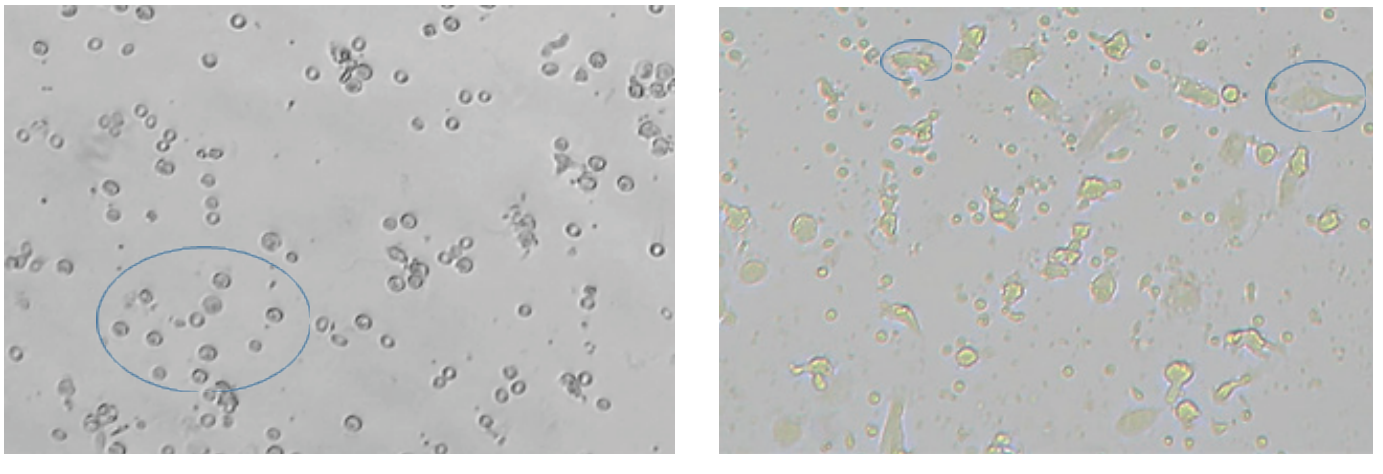
Dendritic cell maturation is a complex heterogeneous process that can give different distinctive functional properties. In studies by Chinese scientists [12] tested the influence of surractin on the maturation of dendritic cells. The results showed that mature DCs form longer processes than immature DCs. Surfactin can induce morphological, phenotypic, and functional maturation of dendritic cells and in this process NF-κB has been involved in signaling.

Thus, given the complex process of maturation of dendritic cells under cultivation, as well as the available data of morphological characteristics at various pathological conditions, it seems interesting to us to assess the features of cell morphology in oncological patients.

The purpose of this study was to assess the morphological characteristics of the processes of maturation of dendritic cells in breast cancer.

**Material and methods of research.** The research was carried out on the basis of the laboratory of medical biotechnologies of the Medical institute NEFU. Venous blood of 19 patients with a verified diagnosis of breast cancer with informed voluntary consent was given to SBU RS(Y) «Yakut Republican Oncological Dispensary». Dendritic cells were isolated from adult venous blood monocytes. The control group consisted of 4 practically healthy volunteers without inflammatory, autoimmune and oncological diseases.

All studies were carried out in sterile conditions and laminar box. Venous blood is taken sterily into vacueters containing EDTA (Lab-Vac), the volume of venous blood was about 18 ml (2 vials of 9 ml) and diluted with an equal volume of the nutrient medium RPMI-1640 («Biolot», Russia). Mononucleic cells were isolated by the standard method, by



Drawing. Images of cells under an inverted microscope (lens 40): 2 day of cultivation (left) prevails round cells, 7 day (right) - elongated cells (examples of cells are highlighted by an oval)

**The ratio of the number of counted cells in the dynamics, $\left(\begin{smallmatrix} Me \\ Q1;Q3 \end{smallmatrix}\right)$**

| Cultivation days | Cages | Control group (16 fields of vision) | Cancer group (76 fields of vision) | p… |
|---|---|---|---|---|
| 2-й | «Round»/ Immature | 113.00 (74.75; 138.00) | 89.00 (42.00; 126.00) | 0.184 |
| | «Elongated»/ Ripening | 27.00 (18.25; 46.75) | 18.00 (13.00; 27.00) | 0.024 |
| 7-й | «Round»/ Immature | 69.00 (47.50; 87.5) | 12.00 (6.00; 25.75) | 0.000 |
| | «Elongated»/ Ripening | 27.50 (22.25; 35.00) | 18.00 (9.75; 25.00) | 0.001 |

centrifugation in the gradient density Ficoll (LLC «PanEco») 1500 rev/min for 40 min. and centrifuged twice at 1000 rev/min by 10 min. For the adhesion of monocytes to the bottom of the cultural vials of 75 cm2preliminary incubated at 1.5 h at 5% CO2 at 37oC. The non-attached cells (lymphocytes) were washed with incomplete RPMI medium (OOO «BioloT», Russia). 10 ml of RPMI (OOO «BioLOT», Russia) with 20% of FBS500SA (LLC «Diaem») was added to the attached monocytes as well as growth factors and differentiation factors - GM-CSF (40 microns) and IL-4 (40 microns), which were applied to 1-5 days.

Photographs were taken of field of view with native (unpainted) cells in the cultivated vials under the inverted microscope (JSC «LOMO», Russia) with an increase of x10 and x40 on the 2nd and 7th days of cultivation. Clear images with uniform cell distribution throughout the microscope's field of vision were selected for counting. The initial concentration of cells in the examined slurry on the day of planting in vials was within 1-1.5 million cells per ml. A total of 16 fields of vision of healthy persons and 76 areas of vision of oncobols were selected for analysis. The differentiation of the analyzed cells has been made according to morphological form into two types: 1 - «round cells», i.e. rounded cell shape without cell processes (immature) and 2 - «elongated cells», i.e. cells with elongated shapes and cells with processes (ripening).

Statistical analysis was carried out using IBM SPSS Statistics 19.0. The Kolmogorov-Smirnov test was used to determine whether the data corresponded to normal distribution law. The equality of the sample averages was tested using the Student parametric t-criterion (in the case of a normal distribution) and the Mann-Whitney non-parametric U-criterion for independent samples (in the case of deviation from the normal distribution). The criterion χ2was used to assess whether or not the two categorical variables were connected. The data are presented in the table as Me (median), Q1 and Q3 (quartiles 25 and 75%). The results were considered statistically significant at the achieved level of significance p <0.05. The study was conducted in full compliance with the ethical recommendations of the Helsinki Declaration of the World Medical Association and the Basics of the Russian Federation Law on Health Protection of Citizens (1993).

**Results and discussion.** A comparative analysis of the data showed that the number of round cells on the second day of cultivation did not reveal statistically significant differences, although the median of round cells in the control group was 1.31 times higher than that of oncobols (tables). However, we found a significant difference in the number of elongated cells on the second day of cultivation, so in the group of oncobols their number was significantly lower (p=0.024) than in the control group. The percentage of elongated cells in the healthy group was 19.28%, and in the cancer group it was 16.82%. On the second day of cultivation, the morphological characteristic of cells according to the degree of change in the form of monocytes into an elongated group in oncobols tends to decrease (χ2 = 51.56; p=0.056) compared to control group. Thus, in the early days of cultivation, the maturation process is somewhat delayed in cancer patients.

Analysis of the obtained cell count data for the seventh day of cultivation indicates that the total number of cells in oncobols decreased from 2 days of cultivation by 3.56 times, when as in the control group - 1.45 times. This significant percentage of loss, i.e. the low viability of oncobols cells to culturing conditions, may be due to the cytotoxic effect of chemotherapy and radiation therapy received at the time of the patient's study with breast cancer.

Comparative analysis of the data on the 7th day of cultivation showed that the number of round and elongated cells was statistically significantly lower in oncobols (p=0,000 and p=0,001, respectively). Nevertheless, it should be noted that the percentage of elongated cells in oncobols was 45.85%, which is 1.56 times higher than in the control group (29.32%), with the ratio of round and elongated cells having statistically significant difference (χ2 = 82.14; p=0.010) and the share of elongated cells is significantly higher in oncobles. Thus, in the last days of cultivation, despite the significantly low content of cells, the processes of activating the maturation of monocytes into dendritic cells under in vitro conditions were higher in oncobles than in healthy individuals.

**Conclusion.** Thus, the morphological analysis we have obtained indicates that the degree of maturation of dendritic cells from peripheral blood monocytes under culturing conditions has a significant difference between breast cancer patients and healthy individuals. In cancer patients, the potential for cellular viability and maturation compared to healthy individuals is reduced in the early days of cultivation, probably due to the cytotoxicity of chemotherapy and radiation therapy at the time of the study. Cell analysis in the last days of cultivation indicates that the processes of activation of monocyte maturation in dendritic cells in in vitro were significantly higher in oncobols than in healthy individuals. The data we have obtained require further in-depth study in order to find ways to improve the effectiveness of the use of autologous dendritic cell oncoduction in breast cancer patients.

## Reference

1. Rubtsova J.P., Aleynik D.J., Zhivtsov O.P., [et al.] Sozrevanie in vitro dendritnyh kletok zdorovyh lic i pacientov s hronicheskim osteomielitom, vyzvannym Staphylococcus aureus [Maturation in vitro dendritic cells of healthy individuals and patients with chronic osteomyelitis caused by Staphylococcus aureus]. Infekciya i immunitet [Infection and immunity. 2019; 9 (1): 87-94 (In Russ.).] doi: 10.15789/2220-7619-2019-1-87-94

2. Tsaturov M.E., Talaev V.Y., Matveichev A.V. [et al.] Tolerogennye dendritnye kletki sozrevanie i funkcii v eksperimentah in vitro [Tolerant dendritic cells maturation and functions in in vitro experiments]. Medicinskij al'manah [Medical almanac. 2010; 2: 263-266.

3. Banchereau, J., Briere F., Caux C., Davoust J., Lebecque S., Liu Y.J., Pulendran B., Palucka K. Immunobiology of dendritic cells. Annu. Rev. Immunol. 2000; 18: 767–811.

4. Dudek A.M., Martin S., Garg A.D., Agostinis P. Immature, Semi-Mature, and Fully Mature Dendritic Cells: Toward a DC-Cancer Cells Interface That Augments Anticancer Immunity. Frontiers in immunology. 2013; 4: 438.

5. Grimmett E., Al-Share B., Basem Alkassab M [et al.] // Cancer vaccines: past, present and future; a review article. Discover Oncology. 2022. Volume 13. Article number: 31

https://doi.org/10.1007/s12672-022-00491-4
6. Liu K, Nussenzweig MC. Origin and development of dendritic cells. Immunol Rev. 2010 Mar;234(1):45-54. doi: 10.1111/j.0105-2896.2009.00879.x. PMID: 20193011.
7. Kim M.K, Kim J. Properties of immature and mature dendritic cells: phenotype, morphology, phagocytosis, and migration. RSC Adv. 2019 Apr 10;9(20):11230-11238. doi: 10.1039/c9ra00818g. PMID: 35520256; PMCID: PMC9063012.
8. Steinman RM. The dendritic cell system and its role in immunogenicity. Annu Rev Immunol. 1991;9:271-96. doi: 10.1146/annurev.iy.09.040191.001415. PMID: 1910679.
9. Tan Y., Meng Y., Wang Z., Shan F., Wang Q., Zhang N. Maturation of morphology, phenotype and functions of murine bone marrow-derived dendritic cells (DCs) induced by polysaccharide Kureha (PSK). Hum Vaccin Immunother. 2012 Dec 1; 8(12): 1808–1816
10. Tanoue S, Chang LY, Li Y, Kaplan DE. Monocyte-derived dendritic cells from cirrhotic patients retain similar capacity for maturation/activation and antigen presentation as those from healthy subjects. Cell Immunol. 2015 May;295(1):36-45. doi: 10.1016/j.cellimm.2015.02.008. Epub 2015 Feb 25. PMID: 25734547; PMCID: PMC4405471
11. Wculek S.K, Cueto F.J, Mujal A.M, Melero I, Krummel M.F, Sancho D. Dendritic cells in cancer immunology and immunotherapy. Nat Rev Immunol. 2020;20(1):7–24
12. Xu W, Liu H, Wang X, Yang Q. Surfactin Induces Maturation of Dendritic Cells in vitro. Biosci Rep. 2016 Oct 6;36(5):e00387. doi: 10.1042/BSR20160204. PMID: 27534429; PMCID: PMC5052710.

S.A. Fedorova, S.A. Popova, M.I. Mordosova, M.I. Starostina

DOI 10.25789/YMJ.2023.83.05

УДК 613.31:616-018

# GENERATION LENGTH IN THE YAKUT POPULATION IN 18th-19th CENTURIES

The intergenerational time interval in the Sakha people (Yakuts) was determined by an analysis of genealogical data of 712 families from Namsky, Verkhnekolymsky, Srednekolymsky, Nizhnekolymsky and Elgetsky districts recorded in the 18th – 19th centuries. The male generation interval in the Yakuts averaged 35.7 years, the female generation interval was 30.5 years, which is much higher than the mean general intervals used earlier in population-genetic studies for calculating the time of genetic divergence by the Y chromosome (31-32 years) and mtDNA (25-28 years).

**Keywords:** generation length, Yakuts, population.

**Introduction.** Generation interval (sometimes referred to as the generation length) is the most important parameter for calculating the mutation rate at microsatellite repeats in the Y chromosome and autosomal loci, in mitochondrial DNA, as well as for calculating the time of genetic divergence. In early genetic studies, the mean generation interval of 25 and 30 years was used for the paternally inherited Y chromosome; 20 years – for the maternally inherited mtDNA; and 20 and 25 years – for autosomes [15]. In particular, in the Zhivotovsky's fundamental work on assessing the mutations rate at the Y chromosome STR loci in populations with short-term documented histories – in Polynesians of New Zealand and Gypsies of Bulgaria, the male generation interval was estimated as ~25 years [19]. This value has been used by many authors to calculate the time of the most recent common ancestor in the reconstruction of the genetic history of various ethnic groups [1,10-12,14]. Later, an estimate of about ~30 years was considered more reasonable for male generation interval, and ~25–28 years – for female generation interval [1,15]. Only in one study of the genetic history of the Iberian population by the Y-chromosome, the male generation length was assumed to be 35 years [16].

However, one should take into account differences in marriage traditions and demographic characteristics in various populations (age of first marriage, adult mortality rate), which can greatly affect the intergenerational time interval. In order to clarify this indicator for the Yakut population, we determined the male and female generation intervals according to the genealogical data of the Yakuts of the $18^{th}$ – $19^{th}$ centuries.

**Materials and Methods.** The generation intervals were calculated by a direct count in deep-rooted pedigrees of Central and Northern Yakuts, restored according to the census records of 1768, 1795, 1816, and 1858; church registers for the period from 1768 to 1918; and the materials of the 1917 census [6-9]. The sample included genealogical data of 120 families of the Modut *nasleg* (community) [8, Tables 1-14] and 64 families of the Khatyryk nasleg [9, Tables 1-2] of Namsky district; 58 families of the I Baidun nasleg [6, Tables 88-93] and 96 families IV Myatyuzhsky nasleg [6, Tables 94-101] of Verkhnekolymsky district; 187 families of the II Baidunsky nasleg [6, Tables 1-12] and 90 families of the I Kangalassky nasleg [6, Tables 14-22] of Srednekolymsky district; 55 families of the I Myatyuzhsky nasleg of Nizhnekolymsky district [6, Tables 102-104); and 42 families of the Indigirka Yakuts of Elgetsky* disctrict [7, tables 2, 4]. **Note*. Elgetsky district was founded after 1770; it occupied a vast territory in the basin of the upper, middle and lower reaches of the Indigirka River. Since the 1930s, most of the territory of Elgetsky district has been part of modern Abysky and Momsky districts, and the smaller part belongs to Allaikhovsky district. The name of Elgetsky district is almost forgotten today.

The male generation interval $I_m$ (father-child), which is of interest for the study of the Y-chromosome, is calculated as the mean age of the father at birth of all his children. The female generation interval $I_f$ (mother-child), which is used in the study of mtDNA, is defined as the mean age of the mother at birth of all her children. For the population as a whole, the generation interval in a given time period is equal to the weighted average of the total generation intervals for the families included in it. The overall human generation interval required for studies using autosomal loci is calculated by the formula $I_o = (I_f + I_m)/2$ [15]. These generation intervals, $I_m$, $I_f$, and $I_o$, depend only on the reproductive adults; people who do not have children cannot influence these indicators. Thus, childhood mortality and infertility do not affect the values of the generation interval of a population.

In addition to the intergenerational

M.K. Ammosov North-Eastern Federal University, Institute of Natural Sciences, Yakutsk, Russia: **FEDOROVA Sardana A.** – PhD, Senior Researcher, sardaanafedorova@mail.ru; **POPOVA Saryalla A.** – student, popovasaryalla@icloud.com; **MORDOSOVA Maria L.** – student, mariamordosova053@gmail.com; **STAROSTINA Maria I.** – Ph.D., Researcher, Institute of Psychology, maria_star2001@mail.ru