ყაზახეთის რესპუბლიკაში B ჰეპატიტის საწინააღმდეგო ვაქცინაციის შეტანამ პროფილაქტიკური აცრების კალენდარში განსაზღვრა ავადობის მნიშვნელოვანი შემცირება 18 წლამდე ასაკის მოსახლეობაში. 5-წლიანი პერიოდის კვლევის შედეგებმა ცხადყო, რომ ქრონიკული ვირუსული B ჰეპატიტით ავადობას აქვს შემცირების ტენდენცია. ქრონიკული B ჰეპატიტით დაავადების რაოდენობა 2012 წელს იყო 35,4 შემთხვევა 100 000 მოსახლეზე, ხოლო 2016 წელს ეს მაჩვენებელი შემცირდა 5,8-ით (16,4%) და შეადგინა 29,6 შემთხვევა 100 000 მოსახლეზე.

განხილულ პერიოდში ქრონიკული B ჰეპატიტის შემთხვევების ყველაზე მნიშვნელოვანი შემცირება აღინიშნა 2015 წელს (27,9 შემთხვევა 100 000 მოსახლეზე); შემდეგ, 2016 წელს ავადობამ უმნიშვნელოდ იმატა – 1,7-ით (6%) 100 000 მოსახლეზე. 2012-2016 წწ. აღინიშნა დელტა ჰეპატიტით ავადობის შემთხვევების ზრდა 50%-ით 18 წელზე მეტი ასაკის პირებში, რამაც შეადგინა 0,57 შემთხვევა 100 000 მოსახლეზე. ბოლო ეპიდემიოლოგიური კვლევების მონაცემების მიხედვით, C ჰეპატიტის ინფექციის გავრცელება (ანტი-HCV-ს აღმოჩენის საფუძველზე) ვარირებს რეგიონებს შორის, თუმცა, მთლიანობაში ქვეყანაში გავრცელებამ შეადგინა 483 000 (3,1%) პაციენტი.

ავტორების მიერ მოცემულია C ჰეპატიტის პროგნოზირებადი ელიმინაციის პარადიგმა. დღევანდელ დღეს აქტუალურია ღვიძლის სტეატოზის შესწავლა მეტაბოლური დარღვევების ზრდის გლობალურ ზრდასთან დაკავშირებით ყაზახეთში.

EPIGENETIC MODIFICATION UNDER THE INFLUENCE OF PEPTIDE BIOREGULATORS ON “AGED” HETEROCHROMATIN

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Following the completion of the Human Genome Project, the strategic direction of modern genetics moved toward functional genomics. This field is concerned with the functions of mapped genes, determining the functions of DNA located in non-coding areas, and developing new technologies for the comparative analysis of gene expression. Non-coding DNA, often comprising repetitive sequences of nucleotides, is localized in heterochromatin. There are various types of heterochromatin, including structural and facultative heterochromatin, nucleolar organizer region (NORs) heterochromatin, and telomeric heterochromatin. However, the functions of heterochromatin remain largely unclear.

Facultative heterochromatin - heterochromatinization chromatin (condensed euchromatin or heterochromatin regions, which mainly consist of “closed” - transcribable genes) occur in aging [4,5] and are generally hypoacetlated and methylated indicating of an epigenetic change [1,11,14]. Hypermethylation causes heterochromatinization and thus results in gene silencing [12]. The fact that such histone modifications are reversible – offers potential usage in therapy [15].

In the present investigation are considered eligible the modification of heterochromatin (total heterochromatin, constitutive – pericentromeric and telomeric heterochromatin, nucleolus organizer regions (NORs) heterochromatin and facultative heterochromatin) under the influence of peptide bioregulators (tetrapeptides: Ala-Glu-Asp-Gly -Epitalon; Lys-Glu-Asp-Ala – Livagen; Ala-Glu-Asp-Pro - Cortagen and dipeptide Lys-Glu - Vilon) in lymphocyte cultures of healthy individuals, aged 20-88 years.

Material and methods. We used molecular-cytogenetic methods. We studied chromosomes in 40 lymphocyte cultures obtained from 20 healthy individuals of 75-88 years and 10 cultures from young 10 individuals - 20 to 40 years. In lymphocyte cultures were studied: total heterochromatin (differential scanning calorimeter); constitutive heterochromatin (activity of ribosomal genes of acrocentric chromosome – NORs, pericentromeric C-heterochromatin (C-band) and telomeric heterochromatin) and facultative heterochromatin (sister chromatid exscanges – (SCE) with 5-bromdeoxyuridin (BrdU) [8].

Description of the preparations

Epithalon (Ala-Glu-Asp-Gly) reinforces the organism’s resistance to stresses, regulating neuro-endocrine system and prolongs the average life expectancy;

Livagen (Lys-Glu-Asp-Ala) increases the average level of protein synthesis in aging, renovates liver proteins and induces the activation of protein synthesis in hepatocytes;

Cortagen (Ala-Glu-Asp-Pro) in humans demonstrated a pronounced therapeutic effect on the structural and functional recovery of the damaged peripheral nerve tissue;

Vilon (Lys-Glu) stimulates lowering for the risk of premature aging, has an antitumor activity and stimulates functioning of the immune system and reparative processes, strengthens the resistance of organisms to stress activities, favors prolongation of the average life span [3].

The bioregulators kindly was provided by professor Vladimir Khavinson (Institute Bioregulation and Gerontology, St. Petersburg, Russia).

Results and discussion. *Differential Scanning calorimeter*

The heat absorption curves corresponding to denaturation processes in intact lymphocytes and in lymphocyte cultures treated by peptides (Ala-Glu-Asp-Gly; Lys-Glu-Asp-Ala, Ala-Glu-Asp-Pro, and Lys-Glu) indicate that the treatment of cells with peptides induced heat redistribution and should be attributed to the local decondensation (deheterochromatinization) of loops of up to the 30 nm fibers and partial decondensation of

transcribed chromatin transformation of 10 nm filaments into 5 nm filaments in old individuals (75-88 years) in comparison with young - 20-40 years individuals. Thus, we can conclude that the peptide bioregulators (Ala-Glu-Asp-Gly; Ala-Glu-Asp-Pro, Lys-Glu-Asp-Ala and Lys-Glu) unfolds the highest levels of chromatin organization, that induces deheterochronatinization of total (structural and facultative) chromatin in intact cells of old individuals (Table).

Variability of facultative heterochromatin based on the SCE test. The results of studies on the induction of SCEs by peptide bioregulators (tetrapeptides: Ala-Glu-Asp-Gly, Lys-Glu-Asp-Ala, Ala-Glu-Asp-Pro and dipeptide Lys-Glu) in lymphocyte cultures of aged individuals are shown in Table. The analysis showed that Epitalon induced a significant increase in SCE counts in A, C, D and G group chromosomes. Epitalon-treated cells from old individuals corresponding to an average of 8.4±0.5 SCE/per cell (for intact cultures of the same individuals, this value was 5.9±0.2 SCE/cell); Livagen (Lys-Glu-Asp-Ala) induced a significant increase in SCE counts in A, B, C, D, E and G group chromosomes with statistic relevance (an average of 9.2±0.4 SCE/cell); Cortagen (Ala-Glu-Asp-Pro) significantly increased SCE counts in A, C and D group chromosomes (an average of 10.1±0.3 SCE/cell) in comparison with intact cells and the bioregulator Vilon (Lys-Glu) significantly increased SCE counts in A, C, D, E and G group chromosomes (an average of 9.9±0.6 SCE/per cell).

This data indicates that each of the studied peptide bioregulators has a selective effect on definite chromosomes. Higher level of SCEs (deheterochromatinization) were registered in telomeric heterochromatin and dicreased (heterochromatinization) in the medial regions of chromosome arms; The SCE processes do not occur or are less in heterochromatin or heterochromatinized chromosome regions. Therefore, the increased frequency of SCEs under the influence of bioregulators demonstrates the decondensation (deheterochromatinization) of the condensed during the aging chromosome regions, followed by the release of the repressed genes located there [10,13].

Transcriptional activity of ribosomal genes.

The associative activity of the strands of acrocentric chromosomes positively correlates with the intensity of Ag-staining that depends on the activity of the ribosomal genes located in NORs. The absence of silver staining (caused by condensation of the stalks) also testifies to the inactivation of ribosomal genes.

The data obtained from the analysis of Ag-positive NORs in cultured lymphocytes, intact and treated with bioregulators, obtained in the case of old donors, are shown in the Table. It was shown that peptide bioregulators (Ala-Glu-Asp-Gly, Lys-Glu-Asp-Ala, Ala-Glu-Asp-Pro, and Lys-Glu) strongly increased the amount of Ag-positive NORs in all acrocentric chromosomes involved or not involved in associations, in comparison with intact cells ($p<0.001$). In particular, the number of Ag-positive NORs of acrocentric chromosomes involved in association corresponded to 2.32±0.12 for Epitalon; to 2.49±0.14 for Livagen; to 2.20±0.11 for Cortagen and 2.39±0.11 for Vilon; for per bioregulator - treated cells, this data is significantly higher than the corresponding index for intact culture cells (Table). Our results are in accordance with the previous data [8]. In particular, hormones, various growth factors and chemicals induced chromosome decondensation (in old age as well) resulting in increased transcriptional activity of nucleolar organizer regions [7,8]. An increase in the amount and size of Ag-positive NORs, and an increase in the number of acrocentric chromosomes involved in associations in the cultures obtained from old individuals and treated with peptide bioregulators, indicated deheterochromatinization of satellite stalks, when compared with control values. This can lead to the intensification of protein synthesis because of the activation of ribosomal genes in aged individuals [2,6].

Heteromorphism of structural pericentromeric C-heterochromatin. The data on heteromorphism of structural pericentromeric heterochromatin (C-segments) in intact lymphpcytes and in lymphpcytes treated by peptide bioregulators (Ala-Glu-Asp-Gly; Lys-Glu-Asp-Ala, Ala-Glu-Asp-Pro, and Lys-Glu) of old individuals for chromosomes 1, 9 and 16 are presented in the Table.

The data reflecting variability of large (d and e) and small (a and b) C-segment variant frequencies in separate chromosomes appeared to be equal in the case of the tested bioregulators. It should be noted that in the cells, treated with Cortagen (Ala-Glu-Asp-Pro) and Vilon (Lys-Glu), the distribution of C-segment variants for chromosomes 1, 9 and 16 remained stable and did not differ in old people ($p>0.05$).

Table. Influence of peptide bioregulators (Epitalon, Livagen, Cortagen and Vilon) on reactivation of chromatin from old individuals

Experimental conditions	Association of acrocentric chromosomes per cell	Facultative heterochromatin (SCE per cell)	Total heterochromatin	Structural heterochromatin(C- bends) Chromosomes		
				1	9	16
Control (20-40yr.)	1.33±0.06	7.7±0.4	Stable condition	Stable condition	Stable condition	Stable condition
Control (75-88yr.)	1.17±0.05	5.9±0.2	Heterochromatinized	Heterochromatinized	Stable condition	Stable condition
Epitalon	2.32±0.12	8.4±0.5	Deheterochromatinized	Deheterochromatinized	Deheterochromatinized	Stable condition
Livagen	2.49±0.14	9.2±0.4	Deheterochromatinized	Deheterochromatinized	Deheterochromatinized	Stable condition
Cortagen	2.20±0.11	10.1±0.3	Deheterochromatinized	Heterochromatinized	Stable condition	Stable condition
Vilon	2.39±0.11	9.9±0.6	Deheterochromatinized	Heterochromatinized	Stable condition	Stable condition

Chromosome 1 and 9 appeared to be deheterochromatinized (the decrease of large bands in size) in Epitalon and Livagen- treated cells. The rate of heteromorphism for appointed chromosomes was significant ($p<0.001$). A difference from the control indices was not noticed for chromosome 16. It should be noted that in the cells, treated with Cortagen (Ala-Glu-Asp-Pro) and Vilon (Lys-Glu) (Table), large and small C-segment variants in chromosomes were registered with approximately the same <frequency in intact cells, and differences between the indices compared were not significant (Table). The results indicated that each peptide bioregulator selectively deheterochromatinizes 1, 9 and 16 chromosome C-segment variants.

Conclusion. Epigenetic process – heterochromatinization progress with aging and can deactivate many previously functioning active genes. It blocks certain stages of normal metabolic processes in the cell, which inhibits many specific enzymes and leads to aging pathologies. The action of genetic systems reveals general rules in the behavior of such systems, such as the connection between the structural and functional interrelationships between the "directing" and "directed" structures. In this respect, it should be noted that heterochromatinised regions in chromosomes can reversed by many physical and chemical agents, hormones and peptide bioregulators [5,7,9]. Peptide bioregulators (tetrapeptides: Ala-Glu-Asp-Gly; Lys-Glu-Asp-Ala, Ala-Glu-Asp-Pro, and dipeptide Lys-Glu) generally affects the remodeling of facultative heterochromatin (deheterochromatinization). Peptide bioregulators induce: 1. Unrolling -deheterochromatinization of total heterochromatin, constitutive (pericentromeric, telomeric, and nucleolar organizer regions (NOR)) and facultative heterochromatin; 2. Higher level of SCEs (deheterochromatinization) were registered in telomeric heterochromatin and decreased (heterochromatinization) in the medial regions of chromosome arms; 3. Each peptide bioregulator selectively deheterochromatinizes a specific region of chromosomes releasing inactive (once active) genes, which, apparently, can contributes to the targeted treatment of aging diseases.

The proposed genetic mechanism responsible for constitutive and facultative heterochromatin remodeling (deheterochromatinization) of old age may lead for the prolongation of the life span and to the development strategy of therapeutic treat of the aging pathologies.

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SUMMARY

EPIGENETIC MODIFICATION UNDER THE INFLUENCE OF PEPTIDE BIOREGULATORS ON "AGED" HETEROCHROMATIN

[1,2]Lezhava T., [1,2]Jokhadze T., [2,3]Monaselidze J., [1,2]Buadze T., [1,2]Gaiozishvili M., [1,2]Sigua T.

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Following the completion of the Human Genome Project, the strategic direction of modern genetics has moved toward functional genomics, to explore the functions of non-coding regions of DNA. These non-coding regions are localized in heterochromatin. The functions of heterochromatin largely remain unclear. Facultative heterochromatin occurs in aging.

The effect of synthetic peptide bioregulators (tetrapeptides: Ala-Glu-Asp-Gly; Lys-Glu-Asp-Ala; Ala-Glu-Asp-Pro and dipeptide - Lys-Glu) on total heterochromatin, constitutive (structural) and facultative heterochromatin in cultured lymphocytes of individuals aged 75-88 and 20 - 40 years have been studied.

We used a molecular-cytogenetic methods: differential scanning calorimetry; activity of ribosomal genes of acrocentric chromosome satellite stalks – NORs; C-heterochromatin; sister chromatid exchanges (SCE).

The results showed that peptide bioregulators: 1. induce unrolling - deheterochromatinization of total heterochromatin, constitutive (pericentromeric, telomeric, and nucleolar organizer

regions (NOR)) and facultative heterochromatin; 2. induce higher level of SCEs (deheterochromatinization), were registered in telomeric heterochromatin and decreased (heterochromatinization) SCEs level in the medial regions of chromosome arms; 3. each peptide bioregulator selectively deheterochromatinizes a specific region of chromosomes releasing inactive (once active) genes, which, apparently, can contribute to the targeted treatment of aging diseases.

The proposed genetic mechanism responsible for the remodeling of constitutive and facultative heterochromatin emphasizes the importance of external and internal factors in the development of diseases and may lead to the development of a strategy for the therapeutic treatment of senile pathology.

Keywords: association, acrocentric chromosomes, bioregulators, heterochromatin, NOR, SCE.

РЕЗЮМЕ

ЭПИГЕНЕТИЧЕСКАЯ МОДИФИКАЦИЯ ГЕТЕРОХРОМАТИНА ПРИ СТАРЕНИИ ПОД ДЕЙСТВИЕМ ПЕПТИДНЫХ БИОРЕГУЛЯТОРОВ

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После завершения проекта «Геном человека» стратегическое направление современной генетики переместилось в сторону функциональной геномики. Эта область связана с изучением функций картированных генов, определением функций ДНК, расположенных в некодирующих областях. Некодирующая ДНК, часто содержащая повторяющиеся последовательности нуклеотидов, локализована в гетерохроматине. Функции гетерохроматина в значительной степени остаются неясными.

Изучено влияние синтетических пептидных биорегуляторов (тетрапептиды: Ala-Glu-Asp-Gly; Lys-Glu-Asp-Ala; Ala-Glu-Asp-Pro и дипептид Lys-Glu) на общий гетерохроматин, конститутивный (структурный) и факультативный гетерохроматин в культивируемых лимфоцитах лиц в возрасте 75-88 и 20-40 лет.

Использованы молекулярно-цитогенетические методы - дифференциальная сканирующая калориметрия; методика выявления и учета: активности рибосомных генов спутничных нитей акроцентрических хроматид - ЯОР; С-гетерохроматина; сестринских хроматидных обменов (СХО).

Результаты показали, что при старении пептидные биорегуляторы: 1) вызывают раскручивание - дегетерохроматинизацию общего гетерохроматина, конститутивного (прицентромерного, теломерного и ядрышкообразующих областей - ЯОР) и факультативного гетерохроматина; 2) индуцируют повышение уровня СХО, регистрируемых в теломерном гетерохроматине (дегетерохроматинизация) и снижают уровень СХО в медиальных областях хромосомных плеч (гетерохроматинизация); 3) каждый пептидный биорегулятор селективно дегетерохроматинизирует определенный специфический участок хромосом, высвобождая неактивные (когда-то активные) гены, что, по-видимому, может способствовать целенаправленному лечению болезней старения.

Предлагаемый генетический механизм, ответственный за ремоделирование конститутивного и факультативного гетерохроматина, подчеркивает значимость внешних и внутренних факторов в развитии заболеваний и может привести к разработке стратегии терапевтического лечения старческой патологии.

რეზიუმე

„დაბერებული“ ჰეტეროქრომატინის ეპიგენეტიკური მოდიფიკაცია პეპტიდური ბიორეგულატორების ზეგავლენით

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[1]ივ. ჯავახიშვილის სახ. თბილისის სახელმწიფო უნივერსიტეტი, გენეტიკის კათედრა; [2]ივ. ჯავახიშვილის სახ. თბილისის სახელმწიფო უნივერსიტეტი გენეტიკის ინსტიტუტი; [3]ე.ანდრონიკაშვილის სახ. ფიზიკის ინსტიტუტი, ფიზიკის ლაბორატორია, თბილისი, საქართველო

„ადამიანის გენომის“ პროექტის დასრულების შემდეგ თანამედროვე გენეტიკის სტრატეგიულმა მიმართულებამ ფუნქციური გენომიკისაკენ გადაინაცვლა, რაც დნმ-ის არამაკოდირებელი უბნების ფუნქციების კვლევასაც გულისხმობს. ეს არამაკოდირებელი უბნები ჰეტეროქრომატინშია ლოკალიზებული. ჰეტეროქრომატინის ფუნქციები მნიშვნელოვანწილად გაურკვეველი რჩება.

შესწავლილია სინთეზური პეპტიდური ბიორეგულატორების (ტეტრაპეპტიდების Ala-Glu-Asp-Gly; Lys-Glu-Asp-Ala; Ala-Glu-Asp-Pro და დიპეპტიდის Lys-Glu) გავლენა ზოგად ჰეტეროქრომატინზე, კონსტიტუციურ (სტრუქტურულ) და ფაკულტატურ ჰეტეროქრომატინზე 75-88 და 20-40 წლის ინდივიდთა კულტივირებულ ლიმფოციტებში.

გამოყენებულია მოლეკულურ-ციტოგენეტიკური მეთოდები - დიფერენციული მასკანირებელი კალორიმეტრია; აკროცენტრულ ქრომოსომათა აქტიური რიბოსომული გენების სიხშირის დადგენა; C -ჰეტეროქრომატინის; შვილეულ ქრომატიდთა გაცვლების (შქგ) აღრიცხვის მეთოდები.

შედეგებმა აჩვენა,რომ დაბერებისას პეპტიდური ბიორეგულატორები: 1. იწვევენ ზოგადი ჰეტეროქრომატინის,კონსტიტუციური (პერიცენტრომერული,ტელომერული და ბირთვაკწარმომქმნელი რაიონების - ბწრ) და ფაკულტატური ჰეტეროქრომატინის გაშლას - დეჰეტეროქრომატინიზაციას; 2. ინდუცირებენ ქრომოსომათა ტელომერულ ჰეტეროქრომატინში რეგისტრირებული შქგ-ს დონის მატებას (დეჰეტეროქრომატინიზაცია) და აქვეითებენ შქგ-ს დონეს ქრომოსომული მხრების მედიალურ უბნებში (ჰეტეროქრომატინიზაცია); 3. თითოეული პეპტიდური ბიორეგულატორი სელექციურად ახდენს რა ქრომოსომის სპეციფიკური უბნის დეჰეტოქრომატინიზაციას და ათავისუფლებს არააქტიურ (ოდესღაც აქტიურად მოფუნქციე) გენებს,რამაც, როგორც ჩანს, შეიძლება ხელი შეუწყოს სიბერის ავადმყოფობათა მიზანმიმართულ მკურნალობას.

წარმოდგენილი გენეტიკური მექანიზმი, რომელიც პასუხისმგებელია კონსტიტუციური და ფაკულტატური ჰეტეროქრომატინის რემოდელირებაზე, ხაზს უსვამს დაავადებათა განვითარებაში გარეგანი და შინაგანი ფაქტორების მნიშვნელობას, და შეიძლება საფუძვლად დაედოს სიბერის პათოლოგიათა თერაპიული მკურნალობის სტრატეგიის შემუშავებას.

EPINEURIAL SUTURES, POLYETHYLENE GLYCOL HYDROGEL AND FIBRIN GLUE IN THE SCIATIC NERVE REPAIR IN RATS: FUNCTIONAL AND MORPHOLOGICAL ASSESSMENTS IN EXPERIMENT

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Mechanical damage to the peripheral nerve is a fairly common type of injury, which is characterized by a complex of long-term neurological disorders [2,4,10,11,19,28,33,38,41] and require significant financial costs [2,4,10,17,23,25,33,37,44]. Regeneration of the damaged nerve is a staged process and depends on a number of factors: the level and extent of damage, time from damage and microsurgical restoration, the method of microsurgery, revascularization [9]. The search for new and effective microsurgical techniques in the restoration of peripheral nerves is not complete.

The basic technical method of restoring the spatial integrity of the injured nerve is neuroraphy [14,16,31] – suturing the ends of the nerve "end-to-end" through epi- or perineurium with a biocompatible monofilament. The disadvantages of the method are time and financial cost, high manual qualification requirements for the surgeon, as well as the persistence of xenogenic suture material and incomplete spatial isolation of the injured area – additional triggers of local inflammatory reactions [3,13,29], which generally limit and slow down the regenerative growth of nerve fibers. All this motivates the development of sutureless sealed coaptation – adhesive, laser, photochemical [3,7,13-15,22,29,40,43,45,47], nanocomposite [18] or electrowelded [34].

The listed types of direct connection of nerve stumps, first of all, epineural suture (ES), are used in cases of easy, tension-free coaptation of nerve ends; otherwise recovery requires a graft [26]. The efficiency of regeneration and functional recovery is determined by the level of regeneration of nerve fibers through the sutured area, and if there are several such areas, as in the case of a graft, the number of regenerating nerve fibers in the distal nerve decreases. Grinsell D. and Keating C.P. note that at the level of one suture zone loses about 50% of nerve fibers, and after two suture areas - 75% [20].

The efficiency of functional recovery of the limb is influenced by both the level of nerve regeneration and the state of denervated muscles during reinnervation, such as malnutrition, fibrotic changes. The question arises of improving nerve regeneration by neuroraphy with innovative biodegradable polymers that would ensure the adhesion of the nerve ends and sufficient strength of this connection. The synthetic and biodegradable substances currently used in such way have partially realized this potential. Prospective data are available on the use of adhesives based on polyethylene glycol hydrogel (PEG) and fibrin glue (FG) [39]. The advantages of adhesives are ease of use, safety, less trauma to the nerve endings compared to ES, lower connective tissue density at the level of coaptation. However, there are concerns about the strength of connection of the nerve ends, so several ESs are still used to avoid "failure" of the suture [24]. Also, PEG and FG should not interfere with the regeneration of nerve fibers in the distal end of the nerve. Thus, FG is considered as an alternative to the microenvironment in conduits [12,32,35]. There is evidence for longer biodegradation of PEG in the damaged nerve and its better adhesion and strength compared to FG [30,42]. That is why a comparative analysis of the effectiveness of damaged nerve regeneration after different methods of neuroraphy is useful for neurosurgical practice.

The aim of the study was to evaluate the effectiveness of sciatic nerve regeneration after neuroraphy by ES, PEG and FG.

Material and methods. *The animal model.* The study was carried out with 30 white not purebred male rats (250±25 g, 5-6 months of age). Rats were randomly selected into the experimental groups:

Group № 1. Control – intact rats;

Group № 2. Shame-operated – a linear skin incision on the lateral surface of the femur was performed, the left sciatic nerve was isolated and mobilized. This was followed by layer-by-layer restoration of soft tissue integrity without nerve manipulation;

Group № 3. The complete transection (CT) of the sciatic nerve – the actions, as in the group № 2 with the additional complete transection of the sciatic nerve, the endings of the nerve were not connected, but remained freely in the wound. This was followed by layer-by-layer restoration of soft tissue integrity without nerve manipulation;

Group № 4. Epineural sutures (ES) – the actions, as in group № 2 with an additional complete transection of the sciatic nerve and its subsequent fixation end-to-end by epineurial neuroraphy with the atraumatic needle (4-6 epineurial sutures with a polyamide thread № 10/0);

Group № 5. Polyethylene glycol (PEG) – DuraSeal hydrogel – the actions as in group № 2 with an additional complete cross-section of the sciatic nerve and its subsequent fixation with use of hydrogel DuraSeal®, (Covidien LLC, USA) and 2 "fixating sutures".

Group № 6. Fibrin glue (FG) – Tisseel glue – the actions, as in group № 2 with an additional complete transection of the sciatic nerve and its subsequent fixation with Tisseel® fibrin glue and 2 "fixating sutures";

The surgery was performed under general anesthesia (xylazine 15 mg/kg and ketamine 70 mg/kg, intraperitoneally), according to the rules of asepsis and antiseptics. An access to the sciatic nerve in group 3 was performed as follows: an animal