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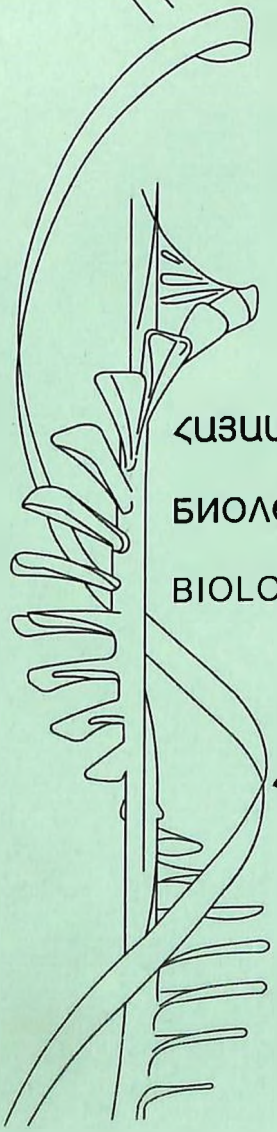
НАЦИОНАЛЬНАЯ АКАДЕМИЯ НАУК РЕСПУБЛИКИ АРМЕНИЯ
NATIONAL ACADEMY OF SCIENCES OF THE REPUBLIC OF ARMENIA



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БИОЛОГИЧЕСКИЙ ЖУРНАЛ АРМЕНИИ

BIOLOGICAL JOURNAL OF ARMENIA

Հատոր LXXII, ՀԱՎԵԼՎԱԾ, 2020

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ՀՀ ԳԱԱ «Գիտություն» հրատարակչություն

Լույս է տեսնում 1948 թվականից, հոդվածները հրատարակվում են հայերեն, ռուսերեն կամ անգլերեն լեզուներով
Выходит с 1948 года, статьи публикуются на армянском, русском или английском языках
Journal is published since 1948, the articles are published in Armenian, Russian or English

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Հայաստանի Կենսաբանական Հանդես, 2020

ՀԱՅԱՍՏԱՆԻ ԿԵՆՍԱԲԱՆԱԿԱՆ ՀԱՆԴԵՍ
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IN MEMORIAM

ARMEN A. GALOYAN
1929–2012

Armen A. Galoyan, President of the Armenian Association of Biochemists (AAB), Academician of National Academy of Sciences of RA, member of the Medical Academy of RA, Editor-in-Chief of the journal "Neurochemistry" (issue of Russian Acad. Sci. and Armenian Nat. Acad. Sci.) died on 4th October 2012. He was Head of a joint Laboratory on Neurohormones Biochemistry (Institute of Biochemistry of NAS RA and A. Bach Institute of Biochemistry of RAS), and Scientific Councillor to the Institute of Biochemistry of NAS RA and Chairman of the Institute Scientific Council.

Acad. A. Galoyan was born in 1929 in v. Small Parni (currently v. Anushavan of the Shirak region of RA) and graduated from the Yerevan Medical Institute in 1953. He received his Candidate degree in biological sciences from the Koltsov Institute of Developmental Biology, USSR Academy of Sciences, Moscow in 1956, under the supervision of academician Ch.S.Koshtoiants. He received Doctoral degree in biological sciences in 1964 and became Professor of biochemistry in 1966. In 1971 A. Galoyan became Corresponding member of NAS RA (Chemistry of

Physiologically Active Compounds) and in 1986 Academician of NAS RA (biochemistry). He started to work in the H. Buniatian Institute of Biochemistry of NAS RA from 1958 and served as Director of the Institute of Biochemistry during 1981-2006. Acad. A. Galoyan was a member of many international communities and received numerous honorary awards. The detailed scientific pathway of Acad. A. Galoyan is presented below.

During the past 20 years Acad. A. Galoyan was among the leading investigators in Neuroendocrine Immunology, signalling molecules of the immune system of the brain. He initiated these studies in Armenian and Russian research institutions, simultaneously leading the Departments of Neurohormone Biochemistry at the H.Buniatian Institute of Biochemistry NAS RA in Yerevan and the A.N. Bach Institute of Biochemistry RAS in Moscow. Several overseas laboratories have also participated in these studies via international collaborative grant programs. For the years of meticulous investigations Acad. A. Galoyan and co-workers have succeeded in discovering and chemically identifying a number of hypothalamic neuroactive peptides, the synthetic analogues of which are now available. The immunomodulatory and neuroprotective effects of these compounds were demonstrated, and the findings were published in peer-reviewed journals and book chapters (for reviews see Galoyan A.A. 2004 Brain Neurosecretory Cytokines: Immune Response and Neuronal Survival. Kluwer Academic / Plenum Publishers, New York, p. 188; Lajtha A., Galoyan A., Besedovsky H., 2008 Handbook of Neurochemistry and Molecular Neurobiology: Neuroimmunology, 3rd Edition. Springer, New York). He was author/co-author of 500 full papers, 247 abstracts and 20 patents.

Acad. A. Galoyan was a President of the Armenian Association of Biochemists from 1981 until his death. The Armenian biochemical

community is deeply grieved by the loss of Acad. A. Galoyan and will always remember him as a distinguished and very active scientist.

"...Most scientists are experts only in very narrow areas; able to approach only very specific aspects of a problem, but complex problems need approach from more than a narrow side. Galoyan combining medicine, chemistry, endocrinology, and immunology in his approaches is a rare individual, one of only very few these days who can be creative and innovative in a complex field. The accomplishments in his studies are more than impressive, they represents a major breakthrough. We salute an important leading member of the neuroscience community. Dr. Galoyan's findings have great potential for developing new therapeutic clinical procedures, not only in neurological but also in cardiological and endocrine pathological changes.... According to Galoyan a new area of neuroendocrine cardiology is established. His works shows a potential action neuropeptides formed in the brain on the rest of the organism. It is admirable how Galoyan could accomplish so much under circumstances that were not necessarily favorable and thus required a great deal of creativity, imagination and talent."

Professor A. Lajtha and Professor A. Galoyan

Professor Abel Lajtha,
Director of Center for Neurochemistry (NY)
Editor-in-chief of "Neurochemical Research"
Preface on Special Issue in Honor of Professor Armen Galoyan
Neurochem Res. (2010), 35:835-836.

It was first in a sad personal note by his daughter Karina then in a release from his scientific secretary at the H. Buniatian Institute of Biochemistry in Yerevan, Arme-nia that I, and we, learned with great sorrows of the passing of our dear friend and distinguished colleague Armen Galoyan.

I knew the name Armen Galoyan since the early 1960s when, first with such a proposal in the literature, he was writing about cardiotropic activities of extracts of the hypothalamus (1962–1964) at a time when we were actively involved in the isolation and characterization of hypothalamic peptides controlling pituitary functions. I met him for the first time in 1972 in Yerevan on the occasion of the International Symposium on Neurochemistry organized by him and in which he showed their early results on cardioactive extracts of hypothalamic origin. We had just isolated and established the molecular structure (1969) of the hypothalamic thyrotropin releasing factor (TRF) and I remember discussing extensively with him the methodol-ogy and equipment he and his group would need to proceed and similarly characterize their cardiotropic peptides. On my invitation he came to my newly established laboratory at the Salk Institute in 1973.

In the following years the contributions of his laboratory became milestones in totally new concepts and with dem-onstration at the molecular level of cardioactive peptides of both hypothalamic (1978) and atrial (1979) origins, new cytokines from hypothalamus as unique regulators of immune competent cells in bone marrow. The primary structures of these brain immunomodulators were fully established (2001) with proline-rich polypeptides (PRPs) as major constituents. Galoyan introduced the terms of neu-roendocrine immune system and neuroendocrine immu-nology. Then he and his group demonstrated and reported extensively on antibacterial,

immunotropic, neuroprotec-tive and even antitumor properties of these PRPs and their analogues for the treatment of infectious, immune, neuro-degenerative and cardiovascular diseases (2001–2009).

Armen Galoyan and co-workers published over 700 papers in world-widely known journals. The novel scien-tific results reported and discussed at numerous interna-tional symposia are summarized in three fundamental monographs under his name and in the Handbook of Neurochemistry and Molecular Neurobiology, 3rd ed., v. Neuroimmunology (2008). His latest book Brain Immune System Signal Molecules in Protection from Aerobic and Anaerobic Infections (Springer) was published last month...

Besides being a member of the Armenian academy of Sciences and director of the joint laboratory on Neuro-hormone Biochemistry with the Bach Institute of Bio-chemistry of the Armenian republic, Armen Galoyan was a fully accredited member of numerous scientific institutions throughout the world.

In closing, let me say that I also happen to know that the name of Armen Galoyan was suggested to the nominating committee of the Nobel Prize for Physiology or Medicine on at least two occasions in the last few years.His contribution will survive him and expand in the years to come.

Nobel laureate R. Guillemin and professor A. Galoyan

Roger Guillemin, MD, PhD
Distinguished Professor, The Salk Institute, La Jolla California
Nobel Prize for Physiology or Medicine 1977

The journal (Neurochemical Research), and publisher Springer, would like to express its sadness in the passing of a dear friend and long-time editor Professor Armen Galo-yan. He was recently honored on the occasion of his 80th birthday—Neurochemical Research 35(6), 2010. In the words of Abel Lajtha, "It is admirable how Galoyan could accomplish so much under circumstances that were not necessarily favorable and thus required a great deal of creativity, imagination, and talent." The neuroscience community loses a leading member.

Arne Schousboe, Editor-in-Chief
Henry Sershen, Managing Editor
Abel Lajtha, former Editor-in-Chief

A. Schousboe and A. Galoyan

INTERNATIONAL ONLINE CONFERENCE DEDICATED TO THE 90TH ANNIVERSARY OF ACADEMICIAN ARMEN GALOYAN "NEUROBIOLOGY IN THE 21ST CENTURY" ARMENIA, YEREVAN, 2020

CONFERENCE PROGRAM

16.12.2020 Day I

18:00 - Opening Ceremony

18:30 – Karina Galoian (USA)
Cancer Stem Cells (CSC) as a Therapeutic Target in 3D Tumor Models of Human Chondrosarcoma: An Encouraging Future for Proline Rich Polypeptide-1 (PRP-1)

18:55 – Questions

19:10 – Silva Abrahamyan (RA)
Morpho-functional study of the effect of hypothalamic proline-rich polypeptide-1 and elucidation of the underlying mechanisms of its action in rats with different neurodegenerative models, as well as in mice with Ehrlich ascites carcinoma model.

19:35 - Questions

19: 45 – Naira Sahakyan (RA)

Essential oils of basil cultivars affect the activity of antioxidant enzymes in neuronal microglial cells

20:10 - Questions

20:20 – Arshak Aleksanyan (USA)
Epigenetic Cell Reprogramming Approach for Neural Cell Generation

20:50 - Questions

17.12.2020 Day 2

18:00 – Narine Khachatryan (RA)
Quantitative changes of neuroactive amino acids in the brain and pancreas of rats in the conditions of the experimental diabetes mellitus

18:25 - Questions

18:35 – Ruzan Petrosyan (RA)
Immunogenetics and Anthropology as an help for patients with Ethnic Diseases

19:00 - Questions

19:10- Kristine Danielyan (RA)
New ways of experimental stroke treatment

19:35 – Questions

19:45 – Anush Ghambaryan (RF, Fr)
Neurocomputational model of value-based decisio-making in uncertain and changing environment

19:55 - Poster presentation and discussion

20:20 - The Closing Ceremony

APPLICATION OF THE BIODEGRADABLE POLYMER LAYERS CARRYING THE CHEMOTHERAPEUTIC AGENTS APPLICABLE FOR THE TREATMENT OF GLIOBLASTOMA

Alaverdyan M.A.[1], Danielyan K.E.[1]*, Chailyan S.G.[1], Harutyunyan L.R.[2]

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Targeted delivery of the medicines is the most modern direction in pharmacology, because of the elimination of the negative side effects of the applicable medicines. Polyethylene glycol (PEG) is biodegradable compounds, which is approved for the utilization in the clinical settings. In our work we have used the PEG as well as the polyvinyl butyral as well as polyvinyl acetate, polyvinyl alcohol for the local treatment of the glioblastoma. One of the thin layers of the polymers were synthetized by simultaneous mixing with the methotrexate. The thin adsorbing layers were consisted from the 2 parts: the layer adhering on the brain matter and the layer carrying the chemotherapeutic medicine.

The polymerization was initiated with the following reagents: ethyl alcohol (96%), water, dodecyl phthalate (95%, ACROS ORGANIC, USA). The homogeneity of the layers was checked with the light microscope. Before the preliminary utility the polymer layers they were checked in vivo to clarify the intensity of the adhesion. The layers were sterilized by the evaporated gases of peroxide, as well as gentamicin, glutaraldehyde, formaldehyde, iodine alcohol solutions.

The best brain tissue adhering agent was the polyvinyl acetate, which was carrying the methotrexate. The polyvinyl alcohol was protecting the entire layers composition from the organic fluids and preserving the medicine from the fast degradation.

We were able to synthetize the polymers, which were carrying 1 mg of the methotrexate on the unit of the layer's surface. The final version of the layers was sterilized with the gases of the peroxide (10 %) and gentamycin.

Key words: glioblastoma, polyethylene glycol, methotrexate. polyvinyl acetate, polyvinyl alcohol.

EPIGENETIC CELL REPROGRAMMING APPROACH FOR NEURAL CELL GENERATION

Alexanian A.R.

Cell Reprogramming & Therapeutics LLC, Milwaukee, WI

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Advances in cell reprogramming technologies to generate patient-specific cells of a desired type will revolutionize the field of regenerative medicine. Over the last decade, several cell reprogramming methods such as nuclear transfer, cell fusion and transfection or transduction with pluripotent factors have been developed. However, the majority of these technologies require the exposure of cell nuclei to large reprogramming molecules via transfection, transduction, cell fusion, or nuclear transfer. These methods raise several technical, safety, and ethical issues. Chemical genetics is an alternative approach to cell reprogramming that uses small, cell membrane penetrable substances to regulate multiple cellular processes, including cell plasticity. Recently, using a chemical genetics approach (a combination of small molecule modulators of epigenetic target enzymes and neural inducing factors) we have been able to turn human mesenchymal stem cells (hMSCs) directly into neuronal progenitors that have the potential to generate different neuronal subtypes, such as dopaminergic, cholinergic, and GABAergic cells when further grown in appropriate neuronal differentiation media. The therapeutic effects of these cells on several neurological disorders have been demonstrated.

CANCER STEM CELLS AS A THERAPEUTIC TARGET IN 3D TUMOR MODELS OF HUMAN CHONDROSARCOMA: AN ENCOURAGING FUTURE FOR PROLINE RICH POLYPEPTIDE-1

Caroline J. Granger[1], Alexandra Moran[2], Aaron K. Hoyt[1], Sheila Conway[2] and Karina Galoian[2]

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Chondrosarcomas are malignant bone neoplasms relatively insensitive to chemotherapy and radiation, a property attributed by the self-renewing and stroma-perpetuating cancer stem cells (CSC). In the absence of effective adjuvant therapies, surgical resection remains the standard of care and investigations into novel targets are critical to the development of effective systemic therapies. Proline rich polypeptide (PRP-1), a 15-amino acid mammalian target of rapamycin complex-1 (mTORC1) inhibitor, has previously demonstrated cytostatic properties and antineoplastic regulation of the Wnt pathway in JJ012 human chondrosarcoma cells. This study utilizes spheroids, a dependable in vitro model of 3D solid tumors, to determine PRP-1's ability to eliminate properties of anchorage independent growth and metastatic potential. A better understanding of the mechanism by which this occurs in the CSC population of human chondrosarcoma could identify novel targets for future therapeutics.

Cultured JJ012 cells, a subset treated with PRP-1, underwent ALDEFLUOR® assay with N,N-diethylaminobenzaldehyde (DEAB) as negative control, to measure aldehyde dehydrogenase (ALDH) activity (a recognized marker of CSC's) and sorted into bulk JJ012, $ALDH^{high}$ and PRP-1 treated $ALDH^{low}$ via flow cytometry. All PRP-1 treatments were administered in a dose response manner. All cell fractions underwent clonogenic colony formation comparing PRP-1 treated colonies vs control. Cell cycle and apoptosis analysis using propidium iodide was completed using spheroids grown and treated with PRP-1 and analyzed via flow cytometry. Additionally, PRP-1 treated and control spheroids were grown for assessment of early apoptosis and cell death using a modified annexin V/Pi apoptosis assay followed by flow cytometry.

Clonogenic dose-response assay demonstrated a dose of 5 μg/mL PRP-1 to be most effective in eliminating colonies formed by JJ012 bulk

(92%, $p < 0.0002$) and $ALDH^{high}$ CSC population (80.5%, $p < 0.0005$). $ALDH^{low}$ non-CSC population was affected to a lesser extent at all doses (maximum reduction 53.5%, $p < 0.0013$). Qualitative analysis of spheroid growth displayed unequivocal reduction with increasing dosage of PRP-1 (Figure 1). Cell cycle analysis of spheroids displayed a 6% increase in apoptosis after treatment with PRP-1 and most notably a shift in cycling to G1/S phase arrest. Annexin V analysis displayed an overall decrease in spheroid viability by 59.2% with 7.6% cells shifting from viable cells into early apoptosis and 51.6% shifting from viable to dead by another mechanism after treatment with PRP-1.

The results display the effectiveness of PRP-1 in eliminating anchorage independent colony formation and thus malignant potential of chondrosarcoma CSCs. Spheroid formation, a reliable 3D tumor model and hallmark of metastatic potential conferred by CSCs, was markedly reduced by PRP-1. Additional reduction occurred in the non-CSC bulk tumor population, indicating a concomitant decline in tumor stromal cells following exposure to PRP-1. Spheroid cell cycle analysis demonstrates PRP-1's cytostatic function in CSCs by G1/S phase arrest, and insinuates death induction properties in CSCs by increased apoptosis. Annexin V analysis further displays these properties, accomplished both by late apoptosis and cell death by another mechanism. These findings ratify that PRP-1 effectively reduces CSC viability in a reliable spheroid chondrosarcoma tumor model. Further studies are necessitated in chondrosarcoma animal models to improve our understanding of the effects of PRP-1 on both neoplastic and non-neoplastic tissue.

GENERAL PROTEASE INHIBITORS STABILIZE ALBUMIN MICROPARTICLE AS THE POTENTIAL CARRIERS OF PROMEDICINES

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Albumin is supporting the osmotic pressure in blood. This plasma protein is able to carry medicines such as warfarin, ibuprofen, chlorpromazine, and naproxen, copper, zinc, and calcium ions. Binding of the compounds to albumin, changes their targeting effects as well as the circulation time. Consequently, albumin might serve as an affective carrier for the prolongation of the medicines' circulation time.

In our current work we prepared the albumin based biological microcarriers as it was presented in our previous publication (Aganyants H, Danielyan K; International Nano Letters, 2016), which were placed to the trypsinolysis, mimicking the blood protease-rich environment. Also, the protein based microcarriers structure was containing the general inhibitors of the proteases.

The polymerization of the albumin was performed with two aldehydes: formaldehyde as well as the glutaraldehyde. The best aldehyde, initiating the effective polymerization was chosen. In 72 hours it was measured the lysis by the spectrophotometric methods (Cary 60, Agilent, USA). Also, by the contrast phase microscope there were taken the pictures, which were analyzed for the particle count. The statistical analyses were performed by ONE-WAY-ANOVA as well as t-student test.

Inhibitors in the structure of the nanoparticles might prevent lysis process. The particles are more stable in ethanol vs water environment. Development of the albumin nanoparticles with the prolonged time of circulation is proposed.

Key words: Albumin microparticles, inhibitors, proteases, lyses

NEUROCOMPUTATIONAL MODEL OF VALUE-BASED DECISIO-MAKING IN UNCERTAIN AND CHANGING ENVIRONMENT

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A fundamental assumption in classical economics is that reward probabilities and reward magnitudes (computational components) are integrated in optimal way, multiplicatively for deriving option values and making choices. To explain repeatedly reported systematic violation of optimal decision-making, behavioral economists have proposed prospect theory. According to that, humans do optimal integration of computational components as described in expected utility theory, but make computations based on distorted representation of reward probabilities and values (subjective valuation). Although this approach can explain human choices, it cannot dissociate sub-optimality (of computational strategy) from distortion of computational components, hence, may conclude models that fit human behavior, but are not indicative of underlying computational mechanisms. This, first, undermines the core aim of behavioral economics, that is, to understand human behavior per se, second, abridges the potential of model-based study of neural mechanisms in the brain. A recent study hypothesized an alternative additive strategy of option value derivation (model MIX) and contrasted this sub-optimal strategy with both optimal multiplicative strategy (model OPT) and subjective valuation (model DIST). Two follow-up studies manipulated reward parity via low (basic level of rewards) and high (five times larger rewards) conditions in each of gain vs loss reward representation conditions. The reward parity manipulation aimed as testing diminishing sensitivity, and gain-vs-loss manipulation aimed at checking

loss aversion tendency (both are behavioral tendencies observed in behavioral economics studies).

For the original study 25 subjects with no general medical, neurological, psychiatric or addictive history were recruited. For the first and second follow-up studies 31 and 30 subjects were recruited, respectively. The experimental task of the study was one-armed bandit task. For estimating model-free parameters all models were fitted to experimental data separately for each participant by maximizing the model log-likelihood (LLH). To maximize LLH, slice sampling procedure with uniform priors was used. Then, gradient ascent starting from the best sample was used to get optimized estimates of parameters maximizing LLH. Each participant of the original study was tested in three fMRI sessions. Statistical parametric maps of local brain activations were computed in every subject using the standard general linear model.

The original study confirmed both behavioral and neural superiority of model MIX (additive strategy) over model OPT and model DIST according to Bayesian Information Criterion. Moreover, the study found model MIX is the general model of decision-making while model OPT is only a special case.of model MIX in uncertain and changing environment. The follow-up studies confirmed the main conclusion of the original study. Besides, follow-up studies did not find evidence against the normalization step of MIX model algorithm (no diminishing sensitivity); and did not find evidence supporting differential behavior in gain and loss domains (no loss aversion).

The study revealed that humans employ a sub-optimal valuation and choice algorithm in uncertain and changing environments, and found no evidence of behavioral tendencies such as diminishing sensitivity and asymmetrical risk-taking in gain and loss domains.This results contribute to the view that decision-making in environments with incomplete information may give rise to computational strategies that are not necessarily optimal in terms of normative frameworks but might ensure both behavioral flexibility and effective learning.

THE ROLE OF NOS AND ANTIOXIDANT ACTIVITY IN SOME DERIVATIVES OF L-ARGININE

Ghazaryan. S.H. [1], Alchudzhyan N. Kh.[2], Movsisyan N.H.[2], Barkhudaryants I.M.[1], Hovakimyan S.S. [1], Paghutyan N.H. [1]

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The discovery of NO as a universal regulatory molecule possessing the properties of a biological messenger was a consequence of the development of a number of scientific areas, including immunology, physiology and pharmacology of the cardiovascular system, toxicology, neurobiology, etc.

The regulatory effect of NO in all systems is ensured by its generation from L-arginine, catalyzed by constitutive isoforms of NO synthesis (NOS) - endotenal and neuronal NOS.

Along with regulatory functions, NO also detects cytotactic / cytostatic activity, acting as one of the main effectors of the cellular immunity system. This NO activity is ensured by the functioning of the inducible form of NOS, the synthesis of which in immunocompetent cells is initiated by cytokines, endoxins and other biologically active agents.

The above serves as the basis for the planning of new derivatives of L-arginine both in the form of lithium salts due to the carboxyl group of the amino acid and in the form of new N-substituted derivatives of the same amino acid.

So, NOS activity was judged by the number of nitrite / nitrate anions (in μg / ml blood) formed during 24 hours of incubation, which were determined by the diazotization reaction, spectrophotometrically at a wavelength of 546 nm.

To determine the effect of lithium salts of tret-butyloxycarbonyl-L-arginine, N^{ω}-tosyl-N^{α}-benzyloxycarbonyl – L-arginine, N^{α}, N^{ω}, N^{ω}-tricarbobenzoxy - L-arginine and tret-butyloxycarbonyl-L-arginine during the peroxidation process (POL), we determined the level of lipid peroxides in the non-enzymatic (ascorbate-dependent) system of peroxidation according to the yield of the final product - malonic dialdehyde (MDA). The

data obtained indicate the feasibility of finding new, more effective substances in a number of derivatives of the amino acid L-arginine.

Key words: NOS, NO-syntaza, L-arginine, derivatives of the amino acid, malonic dialdehyde, MDA

THE ROLE OF MICROELEMENTS CONTAINING AMINO ACIDS IN THE DEVELOPMENT OF THE BODY

Ghazaryan S.H., Barkhudaryants I.M., Alaverdyan Zh.R., Hovakimyan S.S., Paghutyan N.H.
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In the case of the formation of a pathogenic excess of microelements (ME) in the environment, it is necessary to carry out comprehensive measures to adjust their quantity in environmental objects aimed at regulating the intake of ME into the body. It should be noted that the same trace elements in a different dosage and possible forms are necessary for the normal functioning of human and animal organisms.

Such chemical elements include: iron, copper, cobalt, zinc, molybdenum, manganese, strontium, boron, selenium, fluorine, iodine, which are used in medicine.

At present, the number of such biogenic chemical elements is growing, as the physiological role outside the new and new chemical elements, and their.

Studies are included in research plans - lithium, cadmium, cesium, barium, titanium, vanadium, chromium, antimony, arsenic, mercury, bismuth, and discoveries in the field of biogeochemistry and biology are possible.

Experimenters and clinicians describe the very important effects of these cations with amino acids in one molecule.

Based on the studies, it can be concluded that Li +, Zn (II), Ag (I) containing derivatives of amino acids and peptides have a wide spectrum of pharmacological action, that is, they have antioxidant, fibrolitic, antimutagenic, radioprotective, antidepressant, psychotropic activities.

Key words: microelements, Lithium, Li, Silver, Ag, Zink, Zn, antioxidant, radioprotective

ANTI-CONVULSION AND PSYCHOTROPIC ACTIVITY OF N- AND C-SUBSTITUTED DERIVATIVES OF NEUROAMINO ACIDS

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The great interest of pharmacologists and clinicians is attracted to the various properties of certain derivatives of neuroamino acids. One of the groups of biologically active substances is neuroactive amino acids, for which the mediating role and functions of modulators of various processes in the body are proved. GABA-based drugs have long been used as neurotropic, with anticonvulsant, psychotropic, nootropic, neuroprotective properties.

Recently, during therapy with antiepileptic drugs, mainly of the second generation, there has been a tendency to optimize treatment aimed at the use of anticonvulsants with advanced combined properties. So, epileptic mood disorders, twilight dizziness, epileptic psychoses, epileptic personality changes, disorders of the emotional sphere are known. A new direction in treatment allows such drugs to be used in various related fields of neurology and psychiatry, when it becomes necessary to alleviate emotional stress, cause relaxation and sedation.

In this regard, we synthesized and studied the neurotropic properties of the new 15 N- and C-substituted derivatives of GABA (N-p-alkoxybenzoyl GABA) and their lithium and zinc salts. The correct combination of the obtained amino acid derivatives with lithium and zinc cations is also attractive in the sense that these cations are used for the treatment and prevention of manic-depressive psychosis and various affective conditions.

We investigated the anticonvulsant properties of the compounds according to the tests: corazole, nicotine, thiosemicarbazide convulsions,

maximal electroshock, arecoline tremor, etc. As a result of the studies, active compounds for antagonism with corazole were identified, some of which (the most active) were studied on the psychotropic effect on the models : "Open field", "elevated cross-shaped labyrinth", "forced swimming", "rotating rod". 50% effective doses of the compounds, therapeutic and / or protective indices were calculated.

Among the studied amino acids, the most active compounds identified were N-p-propoxybenzoyl, N-p-isopropoxybenzoyl, N-p-butoxybenzoyl and N-p-isobutoxybenzoyl radicals. Derivatives are most active in the test of corazole seizures Zn in comparison with GABA bases and lithium salts, but they are much more toxic than them. GABA base muscle relaxation and their lithium salts are caused in doses much higher than the effective doses, and zinc derivatives - in doses very close to therapeutic ones.

Key words: γ-aminobutyric acid, neuroamino acids, GABA, Zink, Lithium derivatives, anticonvulsant

PROTECTIVE EFFECTS OF GALARMINE AND VENOM OF NAJA OXIANA ON SUBSTANTIA NIGRA OF RATS IN A MODEL OF PARKINSON'S DISEASE.

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Parkinson's disease is the most common movement disorder in a wide range of neurodegenerative diseases, primarily resulting from the death of the dopaminergic neurons of the substantia nigra and associated with the gradual degradation of the individual. Therapy aimed at slowing down the death of dopaminergic neurons can be effective. A comparative study of the morphofunctional state of the cellular structures of rats substantia nigra neurons of the Parkinson's disease rotenone model and also on this model with treatment by venom of the Central Asian cobra *Naja naja oxiana* (NOX) and with the introduction of galarmine has been carried out.

Analysis of the results of the study shows that with the introduction of galarmine and small doses of venom, an increase in phosphatase activity is observed, the normal morphological picture is preserved, positive changes in the structural properties of the substantia nigra neurons are compared with the Parkinson's disease model, and galarmin is more effective. The data obtained suggest that galarmine and small doses of NOX venom act as a neuroprotective agents.

Key words: *Parkinson's disease, substantia nigra, galarmine, NOX venom, neuroptotection.*

ALCOHOL, DIABETES MELLITUS AND ITS IMPROVEMENT

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Diabetes mellitus (DM) is one of the diseases of the century and it has not been fully studied yet. Over 400 million people on our planet suffer from diabetes and most of them consume alcoholic beverages. The research aimed to create a model of 1-st form diabetes by alloxan in laboratory white rats, study the behavior of sick rats under the influence of ethanol and try to improve the state of diabetes caused by alloxan by giving the animals an amino acid mixture.

The experiments were carried out in two series. 32 healthy male white rats were divided into 4 groups. All animals except the control group, were intraperitoneally (i/p) injected with alloxan at a dose of 150 mg/kg body wt. In 3 days after the injection (confirming stable DM image) the blood glucose level increased 5-fold compared with the control group. The following symptoms have been observed in animals with DM: increased use of water by animals (more than 120 ml), excessive urination, abrupt weight loss, hair loss, depression. Animals in one group were i/p injected with 25% ethyl alcohol at a dose of 2.5 g/kg and with an amino acid mixture (100 mg/kg GABA, 50 mg/kg glutamine, 100 mg/kg β-alanine) in another group.

On the 4th day of alloxan administration, the ethanol decreased the glucose content by 24.2%, and the amino acid mixture by 32.4% and on the 5th day 26.3% and 33%, respectively, i.e.the use of these two substances has a positive effect on the amount of glucose in the blood.

The behavior of all animals was recorded using "Open field" test. Animal behavior has dramatically changed under the influence of alloxan: motor, orientation-research activity and emotion decreased,depression occurs. The action of alloxan was so strong, that the single injection of ethanol or amino acids mixture did not make visible changes, which would probably be with prolonged use of these substances.

All values are presented as mean ± standard error (MEAN ± SEM). Data were statistically analyzed by Sigma Stat test. A statistically significant comparison test was performed with ONE WAY ANOVA. The reliability of the mean differences between the control and experimental groups was observed at $p < 0.05$.

Results of this study show that the single administration of ethanol and the amino acid mixture have hypoglycemic action in Alloxan induced diabetic model, which is mediated via increased peripheral utilization of glucose, but do not act on the animals behavior.

INVESTIGATION OF THE EFFECT OF GALARMIN ON THE PERIPHERAL BLOOD COMPOSITION OF MICE WITH THE INFECTION OF METHICILLIN-RESISTANT STRAIN OF *STAPHYLOCOCCUS AUREUS* (MRSA)

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Staphylococcus aureus (*S. aureus*) and particular its methicillin-resistant strains (MRSA) are emerging one of the major health threats in many countries worldwide and are responsible for the majority of severe cases of intra- and community-acquired staphylococcal infections.

Discovered by A.A. Galoyan proline-rich polypeptides (PRPs) isolated from the neurosecretory nuclei of the bovine hypothalamus and neurohypophysis (*N. paraventricularis and N. supraopticus*) represent a new family of hypothalamic neuropeptides. It has been shown that PRP-1 or Galarmin possesses cytokine activities and exhibits a wide range of biological functions, including immunomodulating, antioxidant, antitumor, neuroprotective and antibacterial properties.

The influence of Galarmin on hemotological and serological parameters of peripheral blood of infected mice was studied. Under the influence of the Galarmin, a redistribution of blood cells, a change in the absolute number of leukocytes and platelets, as well as a dose-related increase in the percentage of lymphocytes was observed. The summaryzed data show the complex and non-specific effect of Galarmin on the immunological parameters of the blood of infected animals.

CHANGES IN FIBRIN-STABILIZING FACTOR ACTIVITY UNDER THE ACTION OF HYPOTHALAMIC PROLINE- RICH PEPTIDES

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Proline rich peptides (PRP) have been found in various animal species from invertebrates to mammals. The presence of a large number of proline amino acid residues in the structure of PRP gives them the opportunity to easily interact with various protein molecules, including those involved in key biochemical reaction cascades. Peptides of this family are characterized by low toxicity to mammalian cells. Such a peptide is the neuromodulator PRP-1, which belongs to the family of hypothalamic neuropeptides. PRP-1 consists of 15 amino acid residues, has cytokine properties with a wide spectrum of biological activity, including immunomodulating, antioxidant, antitumor, neuroprotective and antibacterial properties, it also regulates humoral and cellular immunity. The next proline-rich peptide of the hypothalamus GX-NH_2 studied by us, is an analog of galarmine (PRP-1), consisting of 10 amino acid residues, where the last proline is amidated. The

peptide is characterized by well-defined antineurodegenerative and antibacterial properties, is a stable compound, its proteolytic breakdown in the blood proceeds rather slowly.

In studying the effects of PRP-1 and GX-NH_2 on the hemostatic system, it is shown that, depending on the dose, they significantly accelerate blood coagulation, increase the amount of fibrinogen, reduce prothrombin time and plasma tolerance to heparin, and act differently on fibrinolytic activity. The data suggest that PRP-1 suppresses the fibrinolytic activity of the blood plasma, and depending on the dose prolongs the time of fibrinolysis by 20-65%, in contrast, GX-NH_2 accelerates blood thrombolytic activity by 23-45%. Based on the foregoing, PRP-1 and GX-NH_2 was studied to evaluate their effect on the activity of the last enzyme of the blood coagulation cascade - fibrinstabilizing factor XIII (FXIII).

In the final phase of the coagulation cascade with the help of thrombin and Ca^{+2}, FXIII turns into an active transglutaminase (FIIIa), which is necessary for maintaining hemostasis, since the active enzyme stabilizes fibrin by crosslinking its α - and γ - chains, strengthens the fibrin clot with covalent bonds, protecting it from rapid removal by the fibrinolytic system. Congenital deficiency of FXIII is accompanied by severe hemorrhagic syndrome, causing life - threatening bleeding diathesis, the clinical consequences of which are well studied.

The lack of activity of factor XIII disrupts the formation of physiological fibrin, which can lead to bleeding. A decrease in factor activity can be observed in liver diseases (hepatitis, cerrosis, cancer with liver metastases), systemic lesions of the hematopoietic apparatus, under the influence of indirect anticoagulants, with congenital anomalies and etc., and may also be a consequence of the appearance in the blood of an enzyme inhibitor. The activity of FXIII increases in patients with thromboembolic complications, atherosclerosis, postoperative interventions, with the growth of tumors and metastases, in women in labor.

Test compounds were used in several doses. Depending on the dose, they mainly suppress the activity of factor XIII, but at a low dose (1 μg / 100 g) PRP-1 increases the enzyme activity by 16% and, at 2.5 μg / 100 g, on the contrary, significantly suppresses it (58%). GX-NH_2 acts on factor

XIII only at a dose of 1 μg/100 g, inhibiting its activity by 26%. With an increase in the dose of both peptides to 5 μg / 100 g, the activity of factor XIII does not change (table 1.).

Table 1. Dose-dependent change in the activity of FXIII under action of hypothalamic proline rich peptides PRP-1 and GX-NH_2

Dose	1 μg /100g	2.5 μg /100g	5 μg /100g
Title the drug	FXIII activity (%)		
PRP-1	+16	-58	–
GX-NH_2	-26	–	–

Significant differences between control and experience ($p \leq 0,05$)

All diseases caused by high or low activity of factor XIII in the blood are found by laboratory study of its activity. Given the influence of the hypothalamic proline rich peptides tested by us on factor XIII activity, we suggest that among the measures already taken, we can offer their application as regulators of enzyme activity.

THE CAVES OF THE ARMENIAN HIGHLANDS AS WITNESSES MILLIONS OF YEARS OF LIFE IN ARMENIA AND ARTSAKH

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This article is devoted to the description of the cave complexes in the territory of Armenia (including Gegarkunik region) and Artsakh, both old and the new oness. A comparative analysis of the literature data on the haplotyping of the Azokh paleontrope and the inhabitants of modern

Armenia also had been carried out. An identical haplotype R1b of an ancient man who had lived in the Azokh cave and modern Armenians which are the residents of Syunik and Zangezur, and lake Sevan area (Gegarkunik region) had been found. The presence of caves on the territory of Armenia and Artsakh with found human remains and the identity of the haplotypes of ancient and modern humans in the territory habitation of the Armenian population proves the anciety of human life in this territory and considers the Armenian Highlands and Artsakh as the cradle of the formation of the Armenian ethnos and Armenian civilization. Haplotype R1b indicates that Armenians man kind belongs to the Caucasoid type. Identical are alsothe immunological data having recieved during the study of certain diseases (Familial Mediterranean Fever) in the Armenians of Armenia and Artsakh

Key words: Azokh paleontrope, Armenia, Artsakh, Haplotype R1b, Caves, Mediterranean fever, T-lymphocytes

NEUROIMMUNOLOGICAL AND BIOCHEMICAL CRITERIA FOR DIFFERENTIATION, DIAGNOSIS OF THE DISEASE AND PREDICTING THE DEVELOPMENT OF RENAL COMPLICATIONS IN FAMILIAL MEDITERRANEAN FEVER (FMF) IN ARMENIANS OF THE REPUBLIC OF ARMENIA AND ARTSAKH

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Molecular-genetic (MEFV mutation determination), neuroimmunological (T- cell E-rosette formation test (E-RFT) with incubation with selective adrenomimetic agent salbutamol and without it had been created in immunological laboratory of the Republica Children's Hospital immunological laboratory RA), biocemistry investigations (determination of the blood ß-lipoproteins) had been done in Armenians with MEFV from Republic of Armenia and the Republic of Artsach. The results obtained had shown, that these tests can be used as a differential and diagnostic criteria for FMF and as a

criteria for the effectivity of colchicintherapy, as well as predictive criteria for the development of amyloidosis and immunosupression.

ESSENTIAL OILS OF BASIL CULTIVARS AFFECT THE ACTIVITY OF ANTIOXIDANT ENZYMES IN NEURONAL MICROGLIAL CELLS

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Plants of the Ocimum genus (Lamiaceae family) are rich in essential oils (EO) and used for various purposes including the treatment and prevention of various diseases. The qualitative and quantitative composition of essential oils of Ocimum species, cultivated in high altitude Armenian landscape was quite different and the main components of *O. basilicum* var. *purpureum*; *O. basilicum* var. *thyrsiflora* and *O.* x *citriodorum* oils belong to the class of oxygenated monoterpenes. Investigated EOs possess remarkable antioxidant activity. They inhibit the tyrosinase activity, the enzyme responsible not only for the melanin production, but also for various aging-related metabolic processes. Investigated EOs had no any significant effect on catalase at the protein levels, but alters its activity in neuroglial BV-2 different cell lines. Treatment of the neuroglial cell lines with the sub-cytotoxic concentrations of three mentioned EOs influence also the activity of acetyl-CoA oxidase type 1.

The microglial cells play a pivotal role as the neuroprotective agents against neuroinflammation. Different data included in the present article are

stating that plant origin substances can play a role of regulators of enzymatic antioxidant capacity of cells. EOs extracted from the Ocimum different cultivars are able to trigger the activity of acetyl-CoA oxidase type 1 (or palmytoil-CoA oxidase type 1), which can serve as a basis of regulation of redox deviation in WT cells. So, it can be suggested them to be applied for the prevention of some processes, which can influence on the aging, as the process of ageing is commonly associated with mitochondrial dysfunction, oxidative stress caused by the increased level of free radical production, dysfunction of the microglia, high blood pressure and so on.

Key words: *Ocimum*; essential oil; **Oxygenated monoterpenes**; microglia; palmytoil-CoA oxidase

РОЛЬ ПЛАЗМИД КИШЕЧНОЙ ПАЛОЧКИ ПРИ КАНЦЕРОГЕНЕЗЕ

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Получвнные нами данные, относительно транслокации *E. coli* у больных с канцерогенезом, а также электронно- микроскопические исследования выявили, что если кишечник, где просходят изменения с микробом, иногда необратимые (образование бесструктурных протопластов) является наименее, благоприятной средой для *E. coli* то кровь и тем более опухольнаиболее блогоприятные условия для её существования.

Плазмида это репликон, которая кодирует не основные для жизнедеятельности бактериальной клетки функции, но даёт бактерии преимущвства при попадании в неблагоприятные условия.

Выделяемые нами плазмиды из *E. coli* здоровых и больных онкологией людейдаютнам возможность продвинуться вперёд в

области онкологии, поскольку плазмиды являются удобной моделью для эксперимвнтов по искусственной реконструкции генетического материяла.

КОЛИЧЕСТВЕННЫЕ ИЗМЕНЕНИЯ НЕЙРОАКТИВНЫХ АМИНОКИСЛОТ В МОЗГУ И ПОДЖЕЛУДОЧНОЙ ЖЕЛЕЗЕ КРЫС В НОРМЕ И ПРИ ЭКСПЕРИМЕНТАЛЬНОМ САХАРНОМ ДИАБЕТЕ

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Было проведено сравнительное изучение содержания и обмена нейроактивных аминокислот в мозге и поджелудочной железе. В частности изучена утилизация их амидов как возможных источников ГАМК, играющей важную роль не только в деятельности мозга, но и в эндокринной и экзокринной функциях панкреаса. Подтверждено сходство в количественном распределении и метаболизме нейроактивных аминокислот в обоих органах,наличие высокоактивной фосфатакивируемой глутаминазы в митохондриальной фракции поджелудочной железы, показан аналогичный характер генерации ГАМК из глутамина при подавлении ГАМК-трансаминазы (ГАМК-Т) ее специфическим ингибитором этаноламин-О-сульфатом (ЭОС). Показано, что аспарагин как в мозге, так и в поджелудочной железе может быть возможным источником глутамина, а следовательно ГАМК. α-кетоглутарат в гомогенатах мозга усиливает выход глутамина и аспартата при инкубации с аспарагином. Добавление в инкубационную среду глутамата снимает подобный эффект α-кетоглутарата при одновременном усилении выхода аммиака. В гомогенатах поджелудочной железы α-кетоглутарат также вызывает повышение выхода глутамина и глутамата, но без влияния на уровень аспартата. Подтверждено ГАМК генерирующее действие как отдельного введения ЭОС и глутамина,так и в особенности их совместного внутрибрюшинного введения.

Исходя из данных о стимулирующем действии ГАМК на пролиферацию β-клеток, синтез и высвобождение инсулина, а также противовоспалительных, трофических и иммуномодуляторных свойств этой аминокислоты нами было исследовано влияние предварительного введения ГАМК-генерирующих соединений, глутамина и ЭОС на содержание и метаболизм нейроактивных аминокислот в мозге и поджелудочной железе и уровень глюкозы в крови интактных и подвергнутых воздействию диабетогенов (стрептозотоцин и аллоксан) крыс. Показано более эффективное ГАМК-генерирующее действие предварительного совместного введения глутамина и ЭОС, вызывающего заметное подавление гипергликемического эффекта стрептозотоцина. Преимущество использования глутамина и ЭОС вместо ГАМК заключается в преодолении ими гемато-энцефалического барьера и активации ГАМК ергических систем мозга, участвующих в регуляции содержания глюкозы в крови. Выявлены существенные различия в эффектах стрептозотоцина и аллоксана на содержание нейроактивных аминокислот в мозге и панкреасе крыс. Так стрептозотоцин вызывает статистически значимое снижение концентрации нейроактивных аминокислот как в мозге, так и в поджелудочной железе, тогда как аллоксан, не влияя на их уровень в мозге, приводит к повышению концентрации глутамата и глутамина без существенного изменения уровня ГАМК в поджелудочной железе. Отсутствие эффекта алоксана на содержание нейроактивных аминокислот мозга, по-видимому,связано с непреодолимостью гемато-энцефалического барьера для этого диабетогена. Предварительное внутрибрюшинное трехдневное введение ЭОС и глутамина снимает эффекты стрептозотоцина и аллоксана на уровень нейроактивных аминокислот в органах крыс. Показана большая эффективность ЭОС в предупреждении гипергликемии, вызываемой аллоксаном, чем стрептозотоцином, что по-видимому связано с различиями в механизмах цитотоксического действия диабетогенов.

На культуре островковых β-клеток поджелудочной железы в опытах in vitro показано усиление флюоресценции инсулина при добавлении ЭОС, ГАМК или глутамина, особенно выраженное в случае первого. Добавление стрептозотоцина к культуре островковых β-клеток поджелудочной железы вызывает резкое тушение флюоресценции инсулина, которое подавляется как ЭОС, так и ГАМК и глутамином. Полученные данные свидетельствуют о перспективности применения ГАМК-генерирующих агентов (глутамин, агонисты ГАМК, ингибиторы ГАМК-трансаминазы) в профилактике и лечении сахарного диабета.

К.С. - нейроактивные аминокислоты, этаноламин-О-сульфат, глутамин, мозг, панкреас, диабет

ԳԱԼԱՐՄԻՆԻ և ՆՐԱ ԱԾԱՆՑՅԱԼՆԵՐԻ ԱԶԴԵՑՈՒԹՅՈՒՆԸ ՈՐՈՇ ՖՈՍՖԱՏԱԶՆԵՐԻ ԱԿՏԻՎՈՒԹՅԱՆ ՎՐԱ ՍՊԻՏԱԿ ԱՌՆԵՏՆԵՐԻ ՏԱՐԲԵՐ ՕՐԳԱՆՆԵՐՈՒՄ

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[2] ՀՀ ԳԱԱ Կենսաքիմիայի ինստիտուտ

Ածխաջրաֆոսֆատային փոխանակության ֆերմենտների ակտիվության կարգավորման ուսումնասիրությունը օրգանիզմի տարբեր ֆիզիոլոգիական և ախտաբանական պայմաններում առանձնակի հետաքրքրություն է ներկայացնում սպիտակուցների, ճարպերի և ածխաջրերի փոխանակության ընդացքում նրանց ունեցած կարևոր ֆիզիոլոգիական նշանակության, և կլինիկայում որպես տարբեր հիվանդությունների (քաղցկեղ, լյարդի և ոսկրային հիվանդություններ, նյարդային համակարգի խանգարումներ և

այլն) ինֆորմացիոն մարկերներ կիրառման առումով: Ածխաջրաֆոսֆորային փոխանակության նոր կարգավորիչների որոնումը հանդիսանում է ժամանակակից կենսաբժշկության խնդիրներից մեկը: Հիպոթալամուսի պրոլինով հարուստ պեպտիդ-1-ը ցուցաբերում է կենսաբանական ակտիվության լայն սպեկտր՝ իմունամոդուլյատոր, հակաուռուցքային, նեյրոպաշտպանիչ, հակաօքսիդանտային և արյունաստեղծ: Ելնելով վերոհիշյալից պեպտիդը առանձնակի հետաքրքրություն է ներկայացնում ածխաջրաֆոսֆորական փոխանակության կարգավորման գործում ինչպես առողջ, այնպես էլ ախտահարված օրգանիզմում: Ուսումնասիրվել է այդ պեպտիդի ազդեցությունը ֆոսֆո-մոնոէսթերազների (հիմնային և թթու ֆոսֆատազներ) ակտի-վության կարգավորման գործում:

Հետիշեմիկ փոփոխություններից կարևորագույններից են համարվում հիշողության և ուսուցման գործընթացի խանգարումները, որոնք կաթվածից հետո զարգացող կլինիկայում ամենահաճախ հանդիպող շեղումներից են: Այսպես, վիճակագրական տվյալները վկայում են, որ սուր իշեմիկ խանգարումներից հետո կախված տարբեր գործոններից, 20-80% հիվանդների մոտ արձանագրվում է հիշողության և կոգնիտիվ խանգարումները:

Այսպիսով, գալարմինը օրգանիզմի մի շարք ախտածին վիճակներում հանդիսանում է ածխաջրաֆոսֆորային փոխանակության կարգավորիչ: Այս տվյալները ճանապարհ են հարթում բժշկության մեջ նրա գործնական կիրառման համար ածխաջրաֆոսֆորային փոխանակության ֆերմենտների ակտիվության կարգավորման գործում նոր դեղանյութերի մշակման ուղղությամբ:

Հետազոտությունների արդյունքները ցույց են տվել, որ գալարմինի ազդեցության ներքո (in vitro) սպիտակ առնետների օրգաններում հիմնային և թթվային ֆոսֆատազների ակտիվությունը ենթարկվում է նշանակալից փոփոխության: Երիկամներում, լյարդում և սրտամկանում նկատվում է նշված

ֆերմենտների ակտիվության բարձրացում 20-50%: Երիկամների ՀՖ-ի ակտիվությունը հասնում է 90%, մինչդեռ ուղեղի նույն ֆերմենտի ակտիվությունը ընկճվում է 30%: Ստացված տվյալները վկայում են, որ ուղեղի պրոլինով հարուստ պոլիպեպտիդը մասնակցում է տարբեր օրգանների փոխանակության պրոցեսներում:

ՆԱԴՐԻ ՊԱՐՈՒՆԱԿՈՂ ԼԻՊՈՊՐՈՏԵԻՆԻ (ՆԼՊ) և ՆԱԴՐԻ ՕՔՍԻԴԱԶԻ (NOX) ՄԻՋև ԿԱԶՄՎԱԾ ՍՈՒՊԵՐՕՔՍԻԴ-ԳԵՆԵՐԱՑՆՈՂ ԱՍՈՑԻԱՏԻ ՍՏԱՑՈՒՄ և ՆԼՊ-ՈՎ ԱՌՆԵՏԻ ՈՍԿՐԱԾՈՒԾԻ ԲՋԻՋՆԵՐԻ, ԿՈՐԻԶՆԵՐԻ ՈՒ ՄԻՏՈՔՈՆԴՐԻՈՒՄՆԵՐԻ ԹԱՂԱՆԹՆԵՐԻ և ԻՄՈՒՆԱՅԻՆ ԲԶԱԹԱՂԱՆԹՆԵՐԻ NOX-ԵՐԻ ԱԿՏԻՎԱՑՈՒՄ

Սիմոնյան Ռ.Մ.[1], Բաբայան Մ.Ա.[1], Սիմոնյան Գ.Մ.[1], Ֆեսչյան Ս.Մ.[2], Սիմոնյան Մ.Ա.[1]

[1]ՀՀ ԳԱԱ Հ.Բունիաթյանի անվան Կենսաքիմիայի ինստիտուտ
[2] Երևանի Մ.Հերացու անվան Պետական բժշկական համալսարան
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Առաջին անգամ սպիտակ առնետների ուկրածուծի բջիջների, կորիզների ու միտոքոնդրիումների թաղանթներից անջատվել ու մաքրվել են սուպերօքսիդ (O_2^-)-գեներացնող ասոցիատի իզոձևեր, կազմված ՆԱԴՐԻ պարունակող լիպոպրոտեինից (ՆԼՊ) ու ՆԱԴՐԻ օքսիդազի թերմինալ իզոձևերի գումարային ֆրակցիայից (Nox1+Nox2) [ՆԼՊ-Nox]: Վակուում լիոֆիլացումից հետո ՆԼՊ-Nox-ի ասոցիատի իզոձևերի տեսակարար քանակները, ստացված 1գ ոսկրածուծի բջիջների, կորիզների ու միտոքոնդրիումների թաղանթներից համապա-

տասխանաբար կազմում են 21,3±2,1մգ, 25,2±3,0մգ, 32,0±3,4մգ ($p<0,05$, $n=6$): Ստացված ՆԼՊ-Nox-ի ասոցիատի իզոձևերի մաքսիմալ օպտիկական կլանումները տեսանելի մարզում 412 նմ–ում են (թույլ կլանում) և 280 նմ-ում :

Անջատված ՆԼՊ-ի իզոձևերը ցուցաբերում են վերականգնիչ (հակաօքսիդանտային) ակտիվություն, խթանելով էրիթրոցիտների ու լեյկոցիտների O_2^--գեներացնելու ակտիվությունը: Նշված ասոցիատները O_2^--եր գեներացնում են անմիջական և ոչ թե «համակցման» մեխանիզմով, տեղափոխելով ՆԼՊ-ի ՆԱԴՐՀ–ի էլեկտրոնը ասոցացված Nox–ի հեմային խմբի Fe(III)-ով (որպես էլեկտրոնի տեղափոխման կամրջակ) դեպի O_2 վերականգնելով այն մինչև O_2^-: Ոսկրածուծի ասոցիատներով O_2^--երի գեներացման տեսակարար ակտիվությունը էրիթրոցիտների թաղանթներից անջատված ասոցիատների համեմատ ավելի է 1,5-1,7 անգամ: Որպես O_2^--երի գոյացման բնական, եռանդուն և անընդհատ գործող նոր համակարգեր, առաջարկվում է դրանք օգտագործել որպես հակամանրէային ու հակավիրուսային ագենտներ, իսկ ՆԼՊ-ն որպես իմունադեֆիցիտի նվազեցման միջոց՝ էքսպերիմենտում:

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