Biophysical Reviews (2023) 15:1425–1861
https://doi.org/10.1007/s12551-023-01150-w

ABSTRACT

The 7th Congress of Biophysicists of Russia - conference proceedings

Abstracts

Published online: 11 October 2023

of affected tissues, was significantly higher in HTLP (already after 4 hours - 46%) than Glyciram (25% after 6 hours).
Given the previously obtained data on immunomodulatory activity [3] and interferon-inducing activity, it can be concluded that HTLP has anti-inflammatory activity mediated through the activation of cytokine cascades of immunocompetent cells. Anti-inflammatory activity and lack of side effects make HTLP an important subject for further study.
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S9.713. The blockade of electrostatic interactions between virus and cell the novel way for protection against highly contagious SARS-CoV-2 and influenza strains

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Insertion of four positively charged amino acids into the spike protein molecule cause the significant increase of SARS-CoV-2 contagiousness. Fusion of coronavirus and target cell can be induced by the Coulumb force based on viral's own electric charge. Insertion of three new positively charged amino acids (arginine, histidine, lysine) dramatically increases positive electric charge of Omikron strain spike protein (five times higher than other SARS-Cov-2 strains).Electrostatic interactions between the positively charged virus spike protein and negatively charged target cell receptors induce virus-cell fusion and replication in the the target cells due to attractions of opposite electric charges. The Spike protein of highly contagious variant Kraken of Omicron strain (infects more than 20 persons) contains a great number of positively charged amino acids. The similar positive charge of SARS-Cov-2 and antiviral antibodies can dramatically reduce their electrostatic interactions and induce coronavirus immune escape. Highly contagious nature of Omikron strain can be based on the electrostatic interactions between the positively charged spike protein amino acids and negatively charged cell target receptors. The positively charged amino acids(arginine, lysine) were discovered in haemagglutinin molecule of highly contagious H1N1 virus strain. The protective compositions based on positively charged molecules were developed to fight against highly infective virus strains of SARS-Cov-2 and influenza H1N1. The positively charged protective electrostatic barrier can block electrostatic interactions between positively charged virus sites and negatively charged target cell receptors. Cationic liposomes with positively charged amino acids (arginine and its metabolite NO), low-grade oxidized microelements, electron acceptors (xanthohumol, thymoquinone, oxidized glutathione and sodium thiosulfate) can solve the problem. The protective composition against highly contagious SARS-Cov-2 strains has been developed. It includes positively charged molecules: arginine-based cationic lecithine liposomes, electron acceptors: xanthohumol(from hop extract), sodium thiosulfate. Myrrh essential oil, extract of Nigella sativa, medium-chain triglycerides were included to improve the target effect of the composition. Composition against H1N1 flu virus includes positively charged molecules:spermidin, cationic steroid squalamine and arginine based lecithin liposomes. Myrrh essential oil, hop and ginseng oil extracts, carrageenan, succinate and medium chain triglycerides were included into composition to improve its protective effect. Antiviral effects were studied in Vero and MDCK cell culture infected with coronavirus and H1N1 virus, dynamics of PCR-test and clinical manifestations of the disease were studied in patients infected with SARS-Cov-2 and H1N1 flu virus. Intranasal electrostatic barrier induced by drug composition inhibited virus entry and replication in target cells, blocked viral proteases, coronavirus and H1N1 haemagglutinin receptors, activated protective interferon synthesis, T-cell immune response, and decreased the level of proinflammatory cytokines. Coronavirus content was decreased in cell cultural environment by more than 1000 times 2 days after incubation with the protective drug composition. Antiviral spray inhibited SARS-Cov-2 replication by 92-94% two days after starting treatment and caused the completed virus dissapperanse for 3-5 day treatment (based on PCR-test).Increased loss of disease symptoms was stated based on the signs of rhinitis, pharyngitis and laryngotracheitis. Clinical signs of recovery were observed on 3-6 after starting treatment in 85% cases of the main group and in 13% of the control group. Comparable results were obtained using the composition to protect against highly contagious H1N1 influenza virus

S9.714. The contribution of NOS to the increase in NO production in the heart during motor activity limitation

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The significant role of nitric oxide (NO) in many processes, including heart activity, as well as insufficiency of information about the functions of NO during changes in motor activity predetermine the importance of studies in this direction. During the course of life, the level of motor activity often changes downward under the influence of some environmental requirements. If a person changes his lifestyle so that his motor activity becomes low by necessity, his organism must adapt to the new condition. In these cases, a specific adaptation develops, which boils down to structural and metabolic dysfunctions of many organs and body systems. Movement deficit is accompanied by the development in the body of phenomena unfavorable for health (detrained cardiovascular system, atrophy of skeletal musculature and atherosclerosis, and osteopenia, etc.).
One of the most effective and direct methods of detecting and quantifying NO in biological samples is the method of spin trap EPR spectroscopy. The spin trap method is based on the reaction of the NO radical with the spin trap. A complex of Fe2+ with diethyldithiocarbamate (DETC) was used to capture NO and form the stable ternary complex (DETC)2–Fe2+–NO. This complex is paramagnetic (SFe = 1/2 and IN = 3/2) and can be detected by the EPR method. The complexes are characterized by an easily recognizable EPR spectrum with a g-factor of g = 2.035 and a triplet hyperfine structure. The amount of NO was estimated from the intensity of the characteristic EPR signal belonging to the (DETC)2–Fe2+–NO complex. The signals were compared for the integral intensity values, since the integral intensity of the EPR signal is directly proportional to the concentration of paramagnetic complexes. Thirty minutes after drug administration, the rat anesthetized with urethane was fixed on the operating table and cut, and the removed organs were quickly dried and frozen in liquid nitrogen in capillaries for measurements. The EPR spectra of the prepared samples were recorded on an ER-200E-SRC Bruker EMX/plus X-band EPR spectrometer with an ER 4112HV temperature attachment at 77 K. The following parameters were kept constant in all experiments: microwave power of 30 mW, modulation of 5 G, amplification of 4 ×

104 , time constant of 100 ms, spectrum recording time of 50 s, and number of accumulations of 8. The computer of an Aspect 3000 spectrometer from Bruker was used to accumulate and record the spectra. Immediately before the measurement, the finished sample truncated according to the shape of the measurement cuvette is weighed. The weight of the samples needed to be about 100 mg. The amplitude of the EPR spectra was always normalized to the weight of the sample and to the amplitude of the EPR signal of the reference sample. Application of L-NAME after 1 month spent under conditions of movement deficit led to a decrease in NO levels to the values registered in the control group (natural motor activity). Consequently, the increase in the amount of NO in the heart of rats under motion deficit may be due to the contribution of NOS.

S9.715. The dynamics of bursting activity determines the efficiency of intermodular connections in modular networks in vitro

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Numerous studies have investigated the complex organization of the brain's structural and functional networks, but the relationship between topology and information processing is still not well understood. In recent years, it has been shown that brain neural networks have a modular organization that promotes efficient integration and separation of information, resistance to damage, and rapid adaptation. Modular systems combine the properties of functional differentiation and integration. The segregation of neuronal cultures into related areas (modules) makes it possible to obtain the dynamics of spontaneous activity corresponding to the modular systems' properties. Each module has its own spontaneous burst dynamics, and some bursts propagate from one module to another, initiating a response burst in the Target module. Microfluidic techniques enable the formation of neural networks with a controlled number of modules and intermodule connections. Combination with microelectrode arrays these methods provide high spatial and temporal resolution for investigating functional interaction Our work aimed to investigate the relationship between the intramodular activity of neuronal cultures in vitro and the effectiveness of intermodular interaction.
Research methods. The study was performed on an experimental model of primary cell cultures of the hippocampus of C57BL/6 mouse embryos. A microfluidic chip was developed using soft lithography from polydimethylsiloxane (PDMS). Cell cultivation was performed in two chambers connected by asymmetric microchannels creating a directional connection between the Source and the Target networks. The chip was combined with a microelectrode array with 60 electrodes (Multichannel systems, Germany). Bioelectrical activity was registered using the MEA2100-2x60-System-E device (Multichannel systems, Germany) with a sampling frequency of 20 kHz. Spike and burst detection was performed using previously developed software and the MatLab software package [1]. Data are presented as median and percentile.
Results. Our study showed that the spontaneous activity observed in the modules can be classified into two types based on the distribution of burst's characteristics as the Spike rates in a burst and the Duration of a burst. The neural networks with a cluster of "large" bursts exhibited higher levels of intramodular activity, including longer bursts and a greater number of spikes per burst.
At the same time, such dynamics corresponded to increased levels of inter-module activity, which consisted of bursts propagating from the Source to the Target module. The percentage of bursts propagating was 23% (+16.75 -4; n = 11) in neural networks with a cluster of "large" bursts. In neural networks with activity without "large" bursts, the percentage of propagated bursts was less than 4% (+2 -12.25; n = 9; $p<0.05$; Mann-Whitney test).
Conclusions. The efficiency of module interaction, expressed as the percentage of Source module bursts that initiate a burst in the Target module, depends not only on the formed connection, but also on the intramodular activity.
This work was supported by the Russian Science Foundation (21-75-10154), https://rscf.ru/project/21-75-10154/.
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S9.716. The effect of Uridine on physiological activity in blood lymphocytes in the Rotenone model of Parkinson's disease in rats

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Parkinson's disease (PD) is a chronic neurodegenerative disease associated with the death of dopaminergic substantia nigra neurons. It is known that one of the causes of PD is mitochondrial dysfunction associated with a decrease in their energy efficiency and the development of oxidative stress. In our work, the effect of uridine on the activity of the key mitochondrial enzyme succinate dehydrogenase (SDH) and cytosolic -lactate dehydrogenase (LDH) in blood lymphocytes on smears and on serum malondialdehyde (MDA) levels in rotenone-induced parkinsonian model was investigated. Previous works by our group has shown that uridine leads to an increase in the formation of uridine diphosphate in the cell, an activator of mitochondrial ATP-dependent potassium channel (mitoKATP-channel). Activation of mitoKATP-channel leads to a decrease in oxidative stress [1, 2], which is why we used uridine in the PD model to treat mitochondrial dysfunction in rats.
Materials and Methods: The study was performed on male Wistar rats (n=25) weighing 280-320 g, kept at the ITEB RAS in compliance with the rules of the European Convention for the Treatment of Laboratory Animals. To simulate PD in rats, a rotenone solution (SIGMA) was used at a dose of 1.7 mg/kg animal weight, administered by subcutaneous chronic injection for 28 days, according to the scheme of 2 days of dosing, 2 days of rest. Rotenone is a cellular respiration inhibitor; it blocks electron transfer from glandular clusters of complex I to ubiquinone. Uridine was administered intraperitoneally at a concentration of 30 mg/kg animal weight with a frequency of 2 days of dosing and 2 days of rest.
The activities of SDH (a biomarker of aerobic mitochondrial respiration) and LDH (a biomarker of anaerobic respiration - glycolysis) were measured by the CBC method in immobilized blood lymphocytes on smears [3]. The CBC method is based on the reduction reaction of nitroblue tetrazolium chloride to dark blue diformazan (DF) at the second site of the mitochondrial respiratory chain. Thin blood smears were fixed for 30 sec with 60 % acetone and 10 mM HEPES, pH 5.2 - 5.4, then stained in incubation medium containing: 125 mM KCl, 10 mM HEPES, 1.22 mM NST for 1 hour at 37°C, pH 7.2 ±0.05 and additives; 5mM succinic acid was the main assay to characterize LDH activity and 5mM lactic acid, 5mM malonic acid and 0.5mM NAD - LDH activity. Smears were studied under 1000X magnification using a Leica DM-2000 microscope. Cytomorphological and quantitative analysis of color micrographs of lymphocytes was performed using