not known to us, either sick or surrounding, because they have long since left the patient and can not be eliminated, the patient himself has to be treated, his composition, his organs, his strength. Here is the secret of my treatment, which I bring to you as a gift "(14). A holistic approach underlies traditional Chinese medicine. A Chinese doctor thinks how to restore the health of a person as a whole, and not just how to cure the disease or diseased organs (15).

The second concept, which appeared in Europe in the 19th century and dominates in Western medicine today, rightly paying attention to the idealism of the first, requires finding a material substratum of the disease and ironic over the medicine of the countries of the East. A vivid representative of this concept, Rudolf Virchow, is the founder of cellular (cellular) pathology, in which painful processes are reduced to changes in the vital activity of the smallest parts of the animal organism-cells (16). Virkhov considered an anachronism to raise the question of the general disease of the whole organism and refused the principle of treating the patient, and not the disease, saying "to consider the disease as the suffering of the whole organism and to call for the treatment of healthy organs and systems - absurd!". Traditional eastern medicine today in the West is considered pseudoscience. The development of natural science led in the 19th and 20th centuries to rapid progress in the field of biology, based on the achievements of natural fundamental sciences, and unrecognizably changed medicine. The cause of the disease today is seen not even cell damage, but in molecular defects that arise as a result of the violation of the genetic apparatus of the cell, and the task of medicine is seen in the selection of such drugs that will eliminate the existing molecular defect. In fact, it is proposed to treat not even a disease, but defects of molecules (3,4). At first glance, Western methodology completely dominates in modern medicine and the holistic view of the nature of man and disease is forever forgotten. However, paradoxically this sounds, it is the latest achievements in molecular biology, the decoding of the human genome and the ability to quickly peruse individual genomes can unite two seemingly irreconcilable philosophical concepts of medicine. Yes, the disease has a material substrate. At the heart of the origin of diseases are very specific changes in cells and macromolecules, but it is the unique characteristics of each person that predetermine the possibility of the occurrence of a disease, the effectiveness of a medicine.

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THE PROTEINS OF NERVOUS TISSUE INVOLVED IN NEURODEGENERATIVE DISORDERS. BIOINFORMATIC STUDY

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Neurodegenerative diseases are associated with the changing of properties of the nervous tissue proteins, leading to aggregation and precipitation [1]. One of the most important proteins of the nervous tissue is huntingtin (Htt) [2]. A unique feature of this protein is the recurring sequence of glutamine residues near the N-terminus of the polypeptide chain. The number of glutamine repeats in Htt of healthy people varies, but does not exceed 35. The development of Huntington's chorea is a consequence of a mutation in the first exon (EX1) by the type of short tandem-CAG repeats, resulting in an increase in the number of recurring glutamine residues, the number of which can reach 250 or more. The time of onset of the disease and its severity directly depend on the number of repetitions [1,3]. It is assumed that in the mutant protein mHtt the polyglutamine region acquires a toxic conformation in the form of the ß-structure, as a result of which the protein aggregates and precipitates as amyloid fibrils [4]. At least ten neurodegenerative diseases are caused by polyglutamine expansion in the nervous tissue proteins, including Huntington's chorea, spinal and bulbar muscular atrophy, and polyglutamine spinocerebellar ataxia [5]. So, Htt is a target in the development of new effective medicines created with the help of computer design. The 3D structure of Htt has not been clarified yet. In particular, only the structure of the initial N-terminal fragment of 430 amino acids (AA), including a repetition of 17 glutamine residues, was established [6]. To solve this problem, computer simulation methods are found [7,8]. In the case of Htt, the main difficulty is the uniquely long length of its polypeptide chain, comprising 3142 AA. For such a long chain, it is impossible to find pattern proteins. Therefore, we proposed an approach consisting in modeling 3D structures of individual sections of the Htt polypeptide chain, combining the latter into a whole molecule eventually.

The key proteins of the neural tissue also include the channels of the transient potential (TRP channels) that regulate the flow of cations into the cell and are activated by such pathogens as temperature, mechanical action, chemoattractants etc. In mammalian organisms, there are 28 TRP channels, divided into 6 subfamilies: TRPC 1-7, TRPV 1-6, TRPM 1-8, TRPA 1, TRPP 1-3 and TRPML 1-3. All subfamilies of TRP channels are widely represented in the central nervous system, especially in the hippocampus, cerebellum and amygdala. In the peripheral nervous system, TRPs are localized in the ganglia of the posterior roots, where they are directly involved in the temperature and pain sensitivity [9]. In experimental models of neurodegenerative diseases, it has been established that TRP channels belonging to different subfamilies play a different role in the development of these diseases [10-12]. Thus, in the experimental model of Parkinson's disease, the expression of TRPM2, TRPM7 induces oxidative stress reactions and the appearance of a hypoxic state, which leads to the death of neurons; while inhibition of expression slows the process of cell death [10]. Expression of TRPV1, TRPV4 is associated with the of ischemic conditions and causes depolarization of the hippocampal neurons, intracellular accumulation of Ca2 + ions followed by apoptosis of cells [11]. On the other hand, in the same model, the induced overexpression of TRPC1 inhibits the development of apoptosis and promotes the survival of neurons of the black substance, preventing the reduction of the mitochondrial membrane potential [12]. In this study, attempts have been made to establish features of similarity and differences in AA sequences and 3D structures of TRP proteins using bioinformatics methods. The fulfillment of certain specific functions by proteins depends on the spatial configuration of their molecules, which in turn is due to the AA sequence. In the foreign literature, the role of TRP-receptors in neurology is described mainly for: TRPV1, TRPV4, TRPC1, TRPM2, TRPM7. These proteins were selected for comparative bioinformatic analysis.

The software used for bioinformatics research is available for free. To work with Chimera 1.11.2 software the limited access was previously obtained. The search for primary protein structures in the FASTA format was carried out using the UniProt databases http://www.uniprot.org/ and NCBI Protein http://www.ncbi.nlm.nih.gov/protein. To create a library of proteins homologous to the protein of interest, multiple alignment was performed in UniProt using the BLAST algorithm, based on local alignment of the regions of the protein being studied with the proteins included in the database. For the alignment, the default parameters were used: Target database - UniProtKB, E-Threshold - 10, Matrix - Auto, Filtering - none, Gapped - yes, Hits - 250. Information on tertiary protein structures was taken in RCSB PDB http://www.rcsb .org/pdb/home/home.do. For proteins whose tertiary structure is not determined by X-ray diffraction analysis, 3D modeling of the template proteins in SWISS-MODEL was simulated https://swissmodel.expasy.org/. Alignment of tertiary protein structures was performed in RCSB PDB via the online software Sequence and Structure Alignment, using jCE (java Combination Extension) algorithm [13] with default parameters http://www.rcsb.org/pdb/workbench/workbench.doaction=menu. Structural similarity of the compared proteins was judged by such indicators as Score, Z-score and RMSD [14]. To merge the 3D structures of 11 Htt fragments into a single 3D model, we used Chimera 1.11.2 https://www.cgl.ucsf.edu/chimera/

Taken from the UniProt database http://www.uniprot.org/ the primary structure of Htt in the FASTA format, including 3142 AA, was conditionally divided into 11 sites of ~ 300 AA (142 AA in 11 sites) in each. For each site, we searched for a template protein with a known tertiary structure using the BLAST algorithm and based on the 3D model template on the SWISS-MODEL server https://swissmodel.expasy.org/.

The resulting 11 models were loaded into Chimera 1.11.2, where they were linked together by peptide bonds to form the 3D model of Htt. The results are presented in the .pdb file format, available for further use in any software for bioinformatic work with proteins.

Our approach explicates on the functional role of Htt, which has not yet been clarified [1, 2]. Based on the alignment results of AA sequences, the identified template proteins for each site belonged to different groups in their functional role, which suggests the polyfunctionality of Htt. It is interesting to note that very similar results regarding the possible physiological role of individual segments of the Htt polypeptide chain were obtained on the basis of structural alignment [8]. In particular, the protein-template for the 1-300 AA segment, based on our alignment of the AA sequences

and the structural alignment carried out by the authors, identified the signal proteins PDB ID 5HIU and PDB ID 3IOR respectively, for the segment 301-600 AA structural protein (PDB ID 2OF3) and the contractile protein (2ENY (A), for the 601-900 segment of the AA hydrolase PDB ID 2IAE and PDB ID 2IBI (A) .The structural analogs for the chain 901-1800 chain of AA were not identified in this work. [8]. Among the possible functional activities of Htt the serine/threonine protein phosphatase 2A (PP2A) is an extremely important phosphatase involved in various aspects of cell function [15].

The expression of the subfamily TRPVs and TRPMs correlates with the induction of apoptosis of the cell, while TRPC promotes the survival of neurons in ischemic injury conditions. The results of the alignment of AA sequences and 3D structures of TRP proteins are related to ischemic injury of the nervous tissue indicate that the identity and similarity of the TRPV1 and TRPM7 sequences was 10% and 24%, respectively, with respect to 3% and 14% in the case of TRPC1 and TRPV1. A similar regularity is established in comparing the 3D structures of these proteins. Pairwise alignment of 3D structures of proteins was used and the values, whose value increases with the increase in the structural similarity of the compared proteins (Score and Z-score), in the first case, were 769.14 and 5.46, and in the second 343.29 and 4.07, respectively. To characterize the average distance between atoms of superimposed 3D structures of proteins, the root-mean-square deviation (RMSD) is used. The more similar the structures, the denser they overlap, than smaller the value of the indicator. With pairwise alignment of the TRPV1 and TRPM7 structures, the RMSD was 3.04, while in aligning of TRPC1 and TRPV1, 3.42. Thus, the results of alignment of 3D structures of selected representatives of TRP proteins indicate that the different functional role of TRP proteins can be due to differences in their primary and tertiary structures.

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OXIDATIVE STRESS AND BRONCHIAL HYPERSENSITIVITY TO LOW TEMPERATURE AND OSMOTIC FACTORS

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To study the role of oxidative stress (OS) in the formation of bronchial hypersensitivity to the action of low temperatures and osmotic factors, we proposed a method for the determination of oxidatively modified lipids in an exhaled air condensate [1]. The method consists in recording the UV absorption spectra of lipid extracts from exhaled breath condensate