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NANOTECHNOLOGICAL APPROACH IN BIOLOGICAL
INFORMATION TRANSFER CORRECTION

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MEDICINAL EVOLUTION

During the history of humanity, people have tried to solve the mystery of diseases, or, what are scientifically known as malfunctions of biological information transfer. Although not fully understanding the depth of the problems, from Biblical times up to the middle of the 19th century people have tried to cure diseases empirically, based on remedies extracted from botanicals that exist in nature. Today, we can conclude that this was an attempt to stimulate self-healing processes that naturally exists in the body.

On the other hand, the 20th century pharmaceutical industry has been successful in creating a big variety of powerful drugs. Their efforts were aimed at the development of a 'singular active ingredients' with specific curative effects. Usually, those singular active ingredients are acting on one (1) specific pathway of biological information transfer. Typically, to have an effect, these singular pharmaceutical agents should be administered in high dosages, often causing side effects.

Even though modern pharmaceutical industries gave us a huge leap forward, we are on a considerable distance away from the normalization of internal informational links. In other words, modern treatment is not aimed to increase self-healing processes, nor the stability of the functional activity in living organisms.

The Status Quo in the functional activity of living organisms is only possible with the stability of their internal informational links (biological information transfer). The transfer of biological information in living organisms has a complex multi-step character and includes vertical and horizontal links with multitude feedback at various stages (see below).

The restoration of the malfunctioning biological information transfer is only possible by manipulating with the minute amount of bioactive substances, naturally existing in the living organisms. This became possible only after development of Nanotechnology of Bioactive Complexes Modeling (Nano-ComplexesTM), which has had the ability to manipulate not only with nano (10^{-9}), but also with pico (10^{-12}) quantities of bioactive substances. That bioactive Nano-ComplexesTM has the ability to stimulate physiological mechanisms of the organism by restoring the genetically determined chain of cellular signaling.

FUNDAMENTAL SCIENTIFIC RESEARCH

Our fundamental scientific research was focused on inter- and intracellular signaling of hormones and biologically active substances in area of post-aggressive reactions of the organism. Major interest was focused on the study of pathogenesis of stress conditions and tanatogenesis after severe trauma and shock conditions.

The problem of shock is huge, and probably, one of the most represented in medical literature. During such trauma and shock conditions, the body mobilizes all its defense systems, helping naturally to resist death. To discover the interaction of these defense systems, we had to develop new methods of research and analysis - thousands of inter-related parameters were measured simultaneously (circulatory, cellular signaling, hormonal, and other regulatory subsystems) and the beauty of the human 'design' became evident. It required the development of completely new methodology of study, development of a new not-existed test system. The entire system of biological information communication and intricate biochemical pathways become understandable and tangible. These were the first steps of bio-nanotechnology.

Even though the original goal was to create new drug for treatment of shock, after 15 years of experiments it was evident that it is impossible to create any new substance/drug, which can be helpful to significantly reduce the lethality after severe trauma and shock conditions. With this data, it became obvious that no new molecules needed to be developed, and that everything what our bodies required has already been created and placed within and our cells knew best how to fix themselves. Only when "communication breakdown" occurred, the damage started becoming permanent and deterioration setting in. Modeling and mapping of those naturally existing biological information systems was the next logical step.

WHAT'S OUR GOAL? To activate self-healing processes that naturally exists in the living organism simultaneously with specific curative effects by normalizing internal biological information transfer.

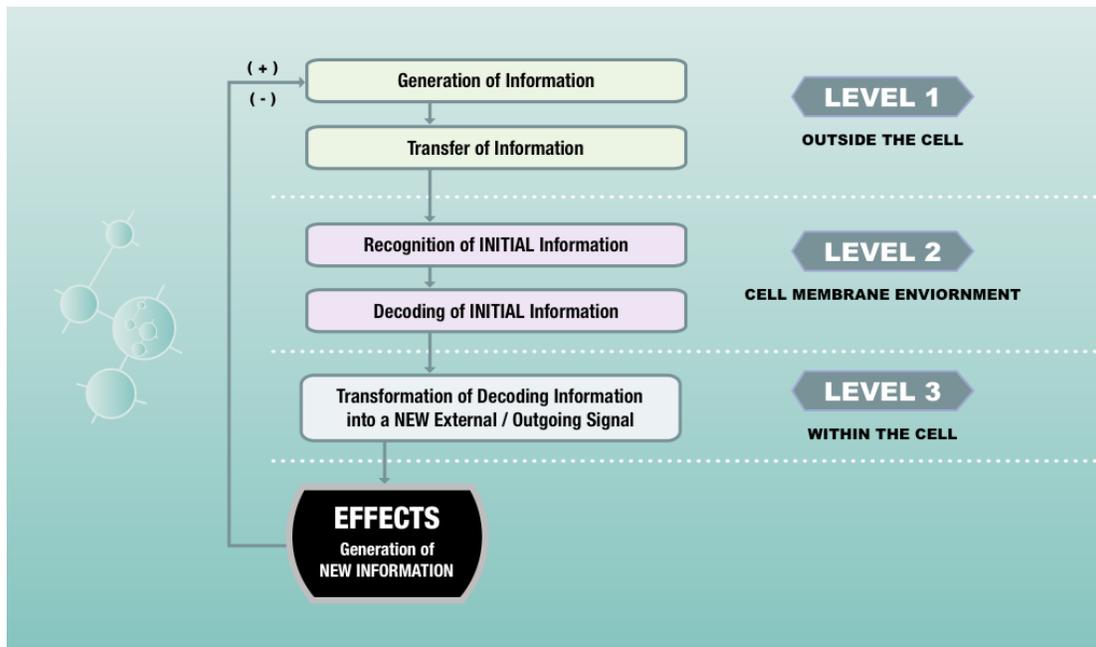
HOW? With a certain extend we can state that Normalization of Biological Information Transfer equal to Activation of Self-Healing Processes.

For better understanding of technological platform oriented toward development of new products for Activation of Self-Healing Processes it is necessary to describe the new scientific concept, which is behind this development.

THE CONCEPT OF BIOLOGICAL INFORMATION TRANSFER IN LIVING ORGANISMS

Stability in the functional activity of living organisms and its adaptation to newly developing situations is only possible with the permanent communication of internal biological informational systems, i.e., only with the informational stability of a living organism. The transfer of biological information and realization of its effects in living organisms has a complex multi-step character and includes vertical and horizontal links with a multitude of feedbacks at various stages.

Chart 1: BIOLOGICAL INFORMATION TRANSFER IN LIVING ORGANISM



Structurally, this complex multi-step biological information transfer can be subdivided into three basic levels (see chart 1):

- Generation and Transfer of Information
- Recognition and Decoding of Initial Information
- Intracellular Transformation of Decoded Information into a New External/Outgoing Signal.

Level 1: The generation of initial information takes place within specialized organs synthesizing and secreting specific biologically active substances. The information being generated represents only the First Degree Messengers. In other words, they are only the carriers of the initial information, which is necessary to modulate on final stages of entire information chain. To this group belongs majority of biologically active substances, hormones, etc. substances that have specific receptors on/in cells of the target organs.

Very often the place of synthesis and secretion of the First Degree Messengers is at a considerable distance from the place of final realization (cells and target organs). The most frequent (although not the only) way of transporting these substances to the cells and targeting organs via the blood circulatory system.

Another type of First Degree Messengers is the typical pharmaceutical agent. Due to its stereochemical structure these agents can affect various specific cell receptors.

Level 2: Second level of biological information transfer is characterized by Recognition and Decoding of initial information. This important element of information transfer involves the Recognition of the First Degree Messengers and is carried out by strictly specific cell receptors. These receptors are typically located either on the surface of cell membrane (membrane receptors), or within the cells (cytosol and/or nuclear receptors). After the initial information carried out by the First Degree Messenger is recognized by cellular receptors, it is decoded and then processed for further information transfer.

Decoding of the incoming signal is possible due to conformational changes of the receptor structure and the activation of cell membrane and/or intracellular decoding systems. Both decoding factors are strictly specific and are activated only after the complex of First Degree Messenger + Cellular Receptors has been formed.

Realization of the processes taking place on Level 2 to a great extent depends on the functional activity of transmembrane and intracellular conjunction agents, such as specialized bioactive lipids, structural proteins, and bioactive carbohydrates, as well as on other cell membrane structural components.

Level 3: Initial biological information decoded on a second level should be transformed into an intracellular signaling level, thus materialized into a Generation of New Biological Information.

Transformation happening on a third level is unique in its character and structure. First two levels of biological information transfer have nature of a molecular signaling transmission; while on a third level its transfers into a cellular biochemical reaction. The transformation of molecular signaling into a biochemical reaction materializes in the synthesis of new information substances.

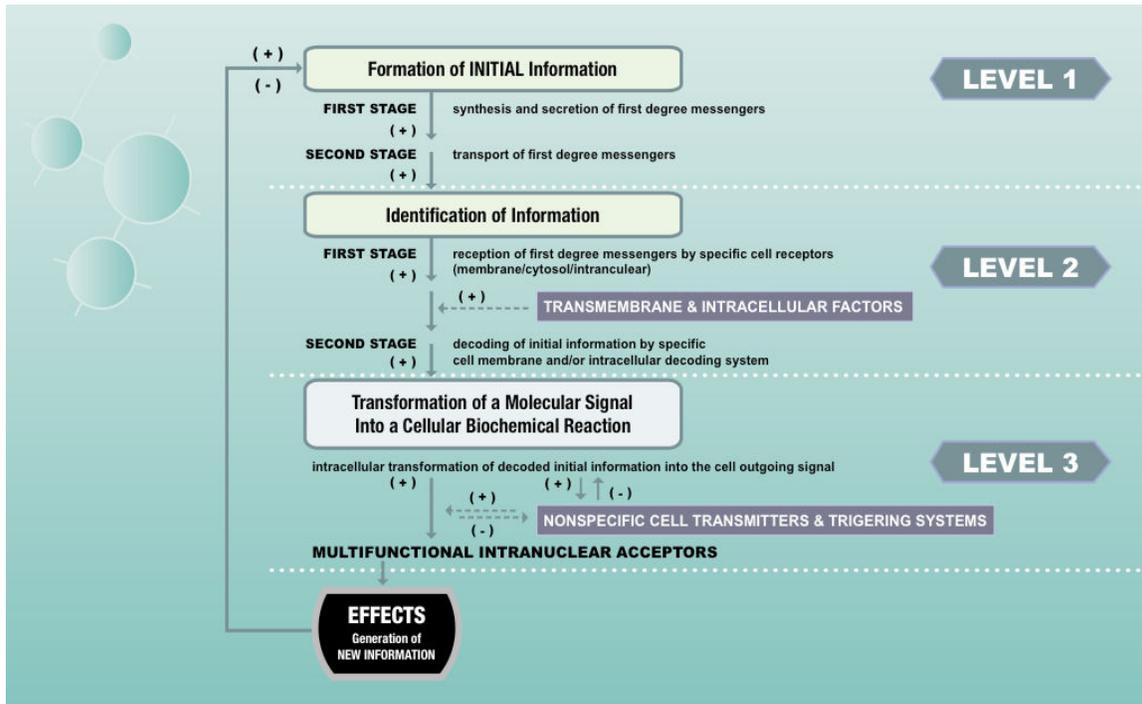
It is important to point out that the third level of information transfer has more integrated nature than the transfer of information on the previous two levels. More precisely, for each First Degree Messenger exists specific cellular receptor, but there is no a specific intracellular pathway. Otherwise if on first two levels of biological information transfer exist a specific substance and a specific decoding system, on a third level there are only few specific pathways of molecular signaling transformation into a cellular biochemical response (for example by means of cyclic nucleotides, inositol triphosphate-diacylglycerol line, Ca⁺⁺ - calmodulin pathway, specific intracellular cascade system, etc.).

One can readily observe reduced diversity (but not intensity) of biological information transfer on the third level, which ensures the universal stability of the biological signal transfer. All of this is expressed in the closed-system character of the intracellular information volume throughout the Second Degree Messengers and their analogs.

Effective transformation of the decoded signal into an intracellular biological response to a great extent depends on the functional activity of non-specific cellular transmitters and triggering systems. Transmission of the intracellular information leads to the activation of specific chromatin acceptor locations, which initiates multiple specific effects with transcription processes being initially modulated. The final effect of this complex chain of information transfer is stimulation/suppression of DNA synthesis, which expresses in the synthesis (generation) of new information substances.

If structurally the transfer of biological information in living organisms is expressed in terms of three levels, it physically materializes in the form of informational blocks shown on Chart 2. It is important to point out that the transfer of biological information by blocks actually corresponds to the levels of information transfer.

Chart 2: STRUCTURE OF BIOLOGICAL INFORMATION TRANSFER



First Informational Block: The first informational block involves the formation of initial information and includes two stages: (a) Synthesis and Secretion of First Degree Messengers, or introduction of non-naturally occurring substances, like pharmaceutical drugs; (b) transporting of First Degree Messengers to the targeted organs and its cells.

Second Informational Block: The second informational block involves identification of information and comprises of two stages: (a) reception of First Degree Messengers by specific cellular receptors; (B) decoding of initial information by specific cell membrane and/or intracellular decoding system.

Third Informational Block: The third informational block involves the transformation of a molecular signal into a cellular biochemical reaction. This transformation includes a set of intracellular transformers and decoders of initial information and their transmitters, thus resulting into the cellular final outgoing signal - synthesis of new information substances.

When any of the steps of biological information transmission is troubled it results on pathology. Various pathologies have their basic dysfunction in biological information transfer.

Present methods of correction/treatment of the different pathologies basically are aimed towards attempting to reconstruct the transfer of biological information by means of interacting directly with the First Degree Messengers and/or indirectly through the change in its activity/amount. Some pharmaceutical agents are capable to affect on a cellular level. Otherwise, modern pharmaceutical treatment is capable to influence the First Level of Information Transfer and sometime to touch first stages of a Second Level.

By referring to Charts 1 and 2 it can be seen to what degree present therapeutic methods of treatment are inadequate and inefficient to ensure the informational stability of the organism.

Another problem with such approach is the dosage of therapeutic agents. To achieve biological information transmission, the usage amount of pharmaceutical substances very often exceeds physiological dosage by thousands of times, thus creating new non-physiological pathways. In addition, the physiological and biochemical responses from 'therapeutic' and 'physiological' dosages of bioactive substances are very different. Frequently, unusual and non-physiological effects are observed when the same bioactive substance is used in amounts exceeding the physiological level.

Current therapeutic practices are not without side effects. This results in a failure to restore the disrupted metabolism (disrupted transfer of biological information). The new non-physiological regulation quickly gets out of order, thereby creating more and more disruptions in the normal biological information transfer and making the organism's informational transfer unstable and vulnerable to its adaptation to new extreme conditions.

WHERE IS THE SOLUTION?

The principals of the discovered scientific concept and its practical implementation are based on fundamental ruling that the restoration of the information stability in the living organism is possible only by:

- Reconstructing biological information transfer by restoring the genetically determined chain of information transfer.
- Restoring the genetically determined chain of information transfer by acting simultaneously on all the levels of the information transfer mechanism.
- Ensuring the stability of information flow of the organism by supporting all the basic elements responsible for biological information transfer.

Restoration of body's natural biological information transfer, i.e. reconstruction of the genetically determined chain of biological information transfer is only possible by means of creating natural biologically active complexes containing all informational systems necessary for normal biological information transfer.

Otherwise, the restoration of self-healing processes is only possible by imitation of naturally existing biological information transfer.

NANOTECHNOLOGICAL PLATFORM (Informational Nanocomplexes)

Practical implementation of the discovered scientific concept and restoration of genetically determine chain of information transfer had required the development of new, non-existed technologies, which would allow manipulating in nano & pico-amount of active substances.

Based on the fundamental research, BIONOVA developed several proprietary nanotechnologies, which could be used as a technological platform for creation of multiple products oriented toward enhancement of self-healing processes, with specific

curative effects. This technological platform is based on development of nanotechnology of bioactive complex modeling (Nano-Complexes™), which has the ability to manipulate not only with nano (10^{-9}), but also with pico (10^{-12}) quantities of active substances. Developed universal technological platform enables to create physiological approach for treatment of multiple human dysfunctions and diseases.

Developed technological platform has the ability to imitate naturally existing in the human body bioactive complexes. That bioactive Nano-Complexes™ stimulates the physiological mechanisms of the organism by restoring the genetically determined chain of cellular signaling.

Today, BIONOVA's technological platform is based on cutting edge technology inventions, which can be grouped into two categories:

Opti-Path™

Nanotechnology of Biologically Active Complexes Modeling (Nano-Modules™)

- Nano-Modules™ are formulated to contain all the necessary active substances to restore normal function of a specific metabolic pathway. The type, concentration and quantity of the substances in the complex depend on the pathway being corrected.
- Nano-Modules™ are an imitation of biological information transfer systems existing in a human organism.
- The efficiency and safety of Nano-Modules™ is insured by concentration of the active agents that are completely governed by the living organism's buffering principle.

NuCell-Direct™

Nanotechnology of Delivery System

- The composition and structure of NuCell-Direct™ Delivery System approximates the structure of a human cell membrane.
- NuCell-Direct™ provides entrapped active ingredients with the extraordinary stability to the extreme physical and chemical conditions.
- Promotes direct delivery of the actives to the target tissue
- NuCell-Direct™ provides with time-release effects of the incorporated active ingredients.

For detail description each of the above technologies, see in the following additions of this magazine.

TECHNOLOGICAL APPLICATION

Today, BIONOVA already developed group of proprietary nanotechnologies, collectively known as NANO-TECH-CARE™:

- NANO-SKIN-TECH™ – new generation of skin care products
- NANO-NUTRI™ – new generation of nutritional products
- NANO-CEUTICAL™ – new generation of pharmaceutical products
- NANO-DEFENSE™ – new generation of bio-warfare products

SUMMARY

The presenting scientific concept has been based on multiple years of fundamental scientific research of inter- and intracellular signaling of hormones and biologically active substances in area of post-aggressive reactions of the organism, such as study of pathogenesis of stress conditions and thanato-genesis (mechanisms of death) after severe trauma and shock conditions.

RESEARCH DATA: After 15 years of experiments it became understandable that it is impossible to create any new substance/drug, which can be helpful to significantly reduce the lethality after severe shock. The enormous amount of data obtained in this research led to the understanding of biological information transfer within cells and the effect when those information transfers failed. It has been discovered that it was impossible to create a new substance that would help the body to recover from severe trauma and shock conditions. Instead of creating and administering new molecules that were foreign to the body, the best approach to future medicine would be starting using substances that already naturally existed within the body.

SCIENTIFIC CONCEPT DEVELOPMENT: This was a first step in modeling and mapping of naturally existed biological information system. “The Concept of Biological Information Transfer in Living Organisms” was born. The basic idea of this concept is that restoration of the malfunctioning biological information transfer is only possible by creating biologically active nanocomplexes containing all the necessary information (substances) ensuring normal biological information transfer.

NANO-TECH-CARE™: The next step was a development of several technologies, based on bioengineering of biologically active nanocomplexes. This development based on BIONOVA’s proprietary nanotechnological approach, which is used as a technological platform for creation of multiple products oriented toward enhancement of self-healing processes. This technological platform is based on development of Nanotechnology of Bioactive Complex Modeling, which has the ability to manipulate not only with nano (10^{-9}), but also with pico (10^{-12}) quantities of active substances. Developed universal technological platform enables to cure multiple human dysfunctions and diseases.

CONCLUSION: Regardless of the nature of the disease/condition, we are dealing with complex dysfunction in a biological information transfer. It is impossible to restore such complex dysfunction by intervening with high dosage of the singular active substances. It requires completely different and complex approach, not to devastate already unstable system of biological information transfer. The only way to restore biological information transfer would be through physiological restoration of self-healing processes.

რეზიუმე

ბიბლიური წლებიდან მოყოლებული მე-19 საუკუნის მეორენახევრამდე ადამიანები ცდილობდნენ ემკურნალათ დაავადებებისთვის ემპირიული წესით. მე-20 საუკუნის ფარმაცევტულმა მრეწველობამ თუმცა შეძლო ძლიერ მოქმედი მრავალი სამკურნალწამლო საშუალებების შექმნა, მაგრამ მათი ძალისხმევა მიმართული იყო იმგვარი საშუალებების შესაქმნელად, რომლებსაც შეეძლოთ ორგანიზმში დიდი მოცულობის ინფორმაციის შეტანა. ეს მიდგომა კი შორს დგას იმ რეალობისაგან რომელსაც ორგანიზმში აქვს ადგილი.

ამ თვალსაზრისით საგულისხმოა ის ფაქტი, რომ ბიოლოგიური ინფორმაციის გადატანა მოიცავს სამ ეტაპს, რომლებშიც შესაძლოა გამოყოფილი იყოს ქვე ეტაპებიც.

პირველი ეს არის პირველადი ინფორმაციის რეალიზაციის ეტაპი და ის მოიცავს ორ ქვე ეტაპს: ბიოლოგიურად აქტიური ნივთიერებების ორგანიზმში დაგროვებას (მათი სინთეზი ორგანიზმის სხვადასხვა უჯრედების მიერ, ორგანიზმში მედიკამენტების შეყვანა და სხვა) და მათ სამიზნე უჯრედებამდე ტრანსპორტს. მეორე, ეს არის მეორადი ინფორმაციის რეალიზაციის ეტაპი და ის მოიცავს ასევე ორ ქვეეტაპს: პირველადი "მესენჯერის" უჯრედის ციტოპლაზმის მემბრანაზე მიმაგრებას და მათ მიერ მოტანილი ინფორმაციის უჯრედის ციტოპლაზმასა და ბირთვში შეტანას. მესამე ეს არის ბიოლოგიური ინფორმაციის ბიოქიმიური რეაქციის სახით რეალიზაცია. თუ კი ბიოლოგიური ინფორმაციის გადაცემის პირველი - ორი ეტაპი მკვეთრად სპეციფიურია და აქედან გამომდინარე სხვადასხვა სახითაა წარმოდგენილი, მესამე ეტაპი – ნაკლებად სპეციფიკური და შედარებით ერთფეროვანია.

პრობლემის გადაჭრა ალბათ ბიოლოგიური ინფორმაციის გადაცემის სამივე ეტაპზე ერთდროული ზემოქმედებაა. ამგვარი ზემოქმედება კი შესაძლებელია მოხერხდეს ნანოტექნოლოგიური მიდგომების გამოყენებით, როცა აქტიური ნივთიერება აღებულია ნანო (10^{-9} გრ) ან პიკო (10^{-12} გრ) ზომებში. ამ თვალსაზრისით "ბიონოვას" ტექნოლოგიური პლათფორმა ეფუძნება Opti-PathTM და NuCell-DreetTM სისტემების შექმნასა და გამოყენებას, რაც გარკვეული ოპტიმიზმის საფუძველს ქმნის.