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# Disclosure of Mechanisms of the Mammalian Life System and Selye's Stress Theory

Katsunari NISHIHARA

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# Disclosure of Mechanisms of the Mammalian Life System and Selye's Stress Theory

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Katsunari NISHIHARA

NISHIHARA Institute, HARA Bldg. 3F, 6-2-5 Roppongi, Minato-ku, Tokyo, Japan

**Key words:** stress; energy metabolism; life system

## 1. Selye's Stress Theory and Energy

Selye's theory, proposed in 1936, stated that mammalian creatures have reactions to the secretion of not only adrenalin from the suprarenal glands medulla, but also adrenocortico hormone from the hypophysis–suprarenal glands hormonal system, to prevent any disorder of the organism under adverse stimuli, physical, mental or emotional, internal or external, such as bacterial infection, fatigue, starvation, cold, blows, noise, chemical and pharmacological absorption, impressions, and restlessness which tends to disturb homeostasis. If these compensating reactions are inadequate or inappropriate, they may lead to maladies. Selye called these adverse stimuli "stressors", and proposed the concept of Selye's syndrome, namely the general adaptation syndrome. He stated that the general adaptation syndrome is the sum of all non-specific, systemic reactions of the body which occur after long, continued exposure to stress. The alarm reaction is sum of all non-specific systemic phenomena elicited by sudden exposure to stimuli to which the organism is quantitatively or qualitatively not adapted. Selye discovered that humans fall ill not only by bacterial infection or inappropriate nutrition, fatigue or starvation, but also by energy, such as cold or noise. In this paper the author intends to disclose

*Address for correspondence: Katsunari Nishihara, DMsc. DMD., NISHIHARA Institute, HARA Bldg. 3F, 6-2-5 Roppongi, Minato-ku, Tokyo, JAPAN

the real meaning of Selye's stress theory. Disclosing the true mechanism of the hypophysis-suprarenal glands hormonal system is to realize the mechanism of the life system of mammalian multicellular organisms. To know the real mechanism of Selye's stress theory we have to realize what life is.

Life has not yet been scientifically defined even in the 21st century. The author defines life as follows: life is a hydrocolloid matter of organic substances with various kinds of minerals encapsulated by phospholipid membranes in which a part or the whole structure remodels itself by means of energy metabolism. Consequently, this organic system can overcome aging by remodeling, namely the renewal of tissues or cells. Therefore, remodeling concomitant with energy metabolism is essential for life. However, in conventional life science, energy metabolism is completely overlooked. In multicellular animals, tremendously different cells are differentiated into organs and tissue. However, almost all cells except matured erythrocytes in mammals have organelle for energy metabolism, namely mitochondria.

## 2. Mitochondria and Energy Metabolism

The most remarkable and differently shaped organelle in various cells are mitochondria, which generate a high-energy bonding substance, ATP, to metabolize and control all kinds of life activities. After the initial stage of fertilization, cell division starts and cells proliferate and change to develop various shaped cells in various organs with the same nucleic code and with the same mitochondrial DNA. All specialized cells in specialized organs have characteristic specialized functions. These functions are supported directly by their mitochondrial facilities. Not only the function of the cells, but morphological structural components are also supported by mitochondrial activities. Therefore, the cell membrane is also controlled by the mitochondrial function. Membranes of tissue or organ cells, except blood cells, have a strict contact inhibition phenomenon. This is also regulated by mitochondria. The leukocyte membrane has a species-specific antigen of MHC (major histocompatibility antigen complex, namely HLC), which is also controlled by their mitochondrial function.

To observe the issue of evolution from protozoa to multicellular animals, not only the cell membrane, namely cells and cell co-relations, but also the differentiation of endo-, exo-, and meso-dermal cells as well as neural and muscular cells, digestive gut cells, and cardio-lympho vessels are all completely supported by mitochondrial function. We have no relic animal or fossil exhibiting how phylogenetic-stage archetype multicellular animals evolved from protozoa. However, in the vertebrates, we have the archetype shark, i.e., chondrichthyes, which after landing became amphibians, reptiles

and mammalian-type reptiles. Therefore, we can consider how landed sharks (terrestrialized chondrichthyes) changed their basic construction of the archetype vertebrates to mammalian-type animals. Living phenomena are systems struggling for self-continuation by utilizing energy from the incorporation and decomposition of environmental factors, so that life can be said to essentially depend on the environment. Therefore, by extension, all vital reactions can be considered biomechanical responses to environmental factors.

## 3. Two Major Life Systems

To realize the life system of multicellular vertebrates two major life systems are compared.

*1) Prokaryote and eukaryote.*

There are two major life systems at the cellular level, namely prokaryote and eukaryote. The former are bacteria with a haploid DNA helix and the latter are protozoa, yeast, mold and multicellular organisms, namely the so-called animals. In the cells of the latter there is a diploid DNA helix having various kinds of organelle, i.e., mitochondria, Golgi apparatus and an endoplasmic reticulum.

*2) Protozoa, namely monocellular creatures and multicellular animals*

There are two major animals on earth, namely monocellular animals of protozoa and multicellular animals. In the latter, the most progressively evolved are the vertebrates. The basic construction of protozoa and a cell of a multicellular animal are quite similar. However, all the apparatus essentially required for protozoa are organelle in cells and those of the multicellular animal are organs constructed with numerous cells. Development of the more highly evolved animals of the vertebrates in the cosmos required essential and necessary conditions: sound substances with mass, especially water, oxygen, and other elements, and nutrition under sunlight energy as well as moderate gravity energy.

*3) Plants and the vertebrates*

The origin of the Vertebrates is Ascidia, which is also the origin of higher plants. Ascidia have gills and muscle as well as roots made of cellulose. Special ascidia, losing gut respiration and digestion, had to respirate with skin epithelial and subcutaneous cells and to absorb nutrition directly by means of roots, thus becoming plants. Plant leaf cells have mitochondria and chloroplasts. The differences at the cellular level between plants and animals are only

chloroplasts and cellulose cell walls; other nuclei, organelle and cytoplasm are the same.

The characteristic difference between plants and animals is movement. The animals, namely the vertebrates, are the vehicle of the gut respiratory and digestive system. The locomotive system is essentially skeletal muscles, which develop concomitant with the neural brain system. In creatures without muscles, no neural-cerebral system develops.

## 4. Basic Construction of the Vertebrates

The origin of the vertebrates is a gastulura-type coelenterate, which is constructed with endo- and exoderm with mesenchymal gel. Epithelio-muscle cells are derived from both endo- and exodermal cells. The gastulura-type gut epithel absorbs oxygen and nutrition, digests, and disintegrates, generating energy. With this energy the animal proliferates their cells and move toward nutrition; following that, with surplus nutrition, the animal commences self reproduction. Mammalia, especially Eutheria, always respirate, digest and circulate blood and lymphofluid by means of the vascular system and heart pump and respiration apparatus. Organisms require energy for remodeling. In addition, animals require enormous amounts of energy for muscle movement through activity. Almost all energy metabolism in animals is supported by mitochondria. Plants don't move by themselves, except as pollen, or at the cellular level. Therefore, they have no neural system or muscle. Mitochondria in plant cells only support metabolism, catabolism, and remodeling. Some protozoa have various kinds of organelle including photo- as well as chemosensors. Naturally, they have absorbing, digesting, assimilating, dissimilating, remodeling, reproducing, and excretory systems. All of the structure at the cellular level is regulated by not only genome cords of the nucleus, but also in cooperation with the nucleic acid of mitochondria. For the development of multicellular vertebrates, moderate gravity energy, just like 1G of the earth, is inevitable. Under sunlight and gravity energy, animals live and move toward the head, this gives rise to the basic construction of the animal body, upper and lower, cranial and caudal polarization by light energy, and the law of inertia, i.e., gravity action.

This involved the development of bone marrow hemopoiesis with matured non-nuclear erythrocyte, the parasympathetic nervous system, the capillary system, the lymphatic system, and the immune system.

In the second revolution of vertebrates, i.e., terrestrialization in the Devonian period, two dramatic changes occurred in the change from water to air as the habitat with a concomitant change in gravitational force (from 1/6G, due to buoyancy, to 1G), as well as in the change from branchial to

pulmonary respiration. The terrestrialization of Heterodontus (dog shark) led to dramatic changes in the following 12 major areas: 1) cardiovascular system, 2) capillaries, 3) lympho system, 4) autonomic nervous system, 5) homothermal system, 6) skeletal system, 7) bone marrow hemopoietic system, 8) tissue immune system, 9) external respiratory system, 10) pyramidal tract system, 11) erythrocyte development, and 12) placoid mineral loss (fur). These changes in evolution occur as metaplasia, which means the change of cell type with the same genetic code by means of gene expression, is triggered by physicochemical stimuli, including energy (Nishihara, 2003). Metamorphosis is disclosed to be a phenomenon of metaplasia. In pathological terminology, this means a change of cells from one type into another with the same genetic code by biomechanical stimuli, i.e., via physicochemical changes, including energy.

## 5. Evolutionary Changes in the Second Revolution of the Vertebrates and Role of Mitochondria in Muscle Cells

In the second revolution of the vertebrates, the author hypothesizes that the increased gravitational action of the earth after landing affects the blood pressure of chondrichthyes through their intensive movement to escape suffocation by moving toward water (Nishihara, 2003). With elevated blood pressure, streaming potential increases (Petrov *et al*, 1989) and the increased currents trigger the gene expression of chondrocytes to develop strong somatomuscle of the animal conjugated with the pyramidal tract of the cerebral motor nervous system, as blood and lympho vessels, osseous tissue, together with bone marrow hemopoiesis as well as erythrocyte enucleation, the cardiovascular system, lympho-vessel formation, the sympathetic nervous system along with the capillary system, and major histocompatibility antigens (MHC) in conjugation with the homothermal system. All these systems are induced by mitochondrial cytokines developed by elevated energy metabolism of muscles in chondrichthyes during landing. The author verified these by means of experimental evolutionary research methods.

In the second revolution, mitochondria in somato-muscles required oxygen. This assures that mitochondria in muscle cells as well as in cells of all kinds of organs and viscera synthesize some kind of trilateral cytokine of nerve, blood vessel, and muscle-growth factors to develop the pyramidal tract neuron system with respective muscles with the capillaries and the blood and lymphovessal system. Consequently, somato muscles controlled by pyramidal tract neurons are conjugated with capillaries and the sympathetic nervous system developed into brain, visceral organs, and the auto-nervous system. Before the stage of mammalian-type reptiles there were no nutritional

capillaries even in the heart or brain. The heart was derived from branchial hematopoietic nests. Therefore, the heart itself generates hematopoietic cells in archetype vertebrates. The number of mitochondria in protozoa or yeast are only 2-3 or 6-8, and in mammalian cells they are 800~3000. From this fact, we can know how high-level energy metabolism developed in mammals. All vascular systems have smooth muscle cells in their walls. At this stage, the sympathetic nervous system developed from the ganglion of the parasympathetic nervous system. During the development of the sympathetic nervous system, neurons in the cerebral cortex proliferate in mammalian type reptiles and control somato motor muscles by means of the pyramidal tract. At this stage, the bone marrow hemopoietic system, together with the functioning of MHC, as well as the homothermal system were established. The function of MHC is for remodeling and cell-metabolism as well as antibody formation of immunoglobulin, as leukocytes depend completely upon cellular respiration and energy metabolism of mitochondria in white blood corpuscles. As mentioned above, the mammalian sympathetic nervous system developed along with capillaries derived from the ganglion of parasympathetic nerves. Therefore, it has no control over the central nervous system of the brain and spine. As a result, through capillaries and sympathetic nerves, the body surface of skin is connected to viscera as well as to the brain, spine, bone marrow, and joints. Thus, the archetype shark evolved into mammalian-type reptiles by means of mitochondria through cytokines excreting into tissue fluid, which induced capillaries in conjugation with vessel muscles and neural fibers of autonomous nerves. From this hypothesis the author considers that at the initial evolution of the multi-cellular organism coelenterate, namely, archetype Hydrozoa, developed from a concentrated multi-protozoa organism, namely, a multicellular organism. Constructions of a monocellular structure, protozoa, are controlled by DNA as well as mitochondrial DNA. In multi-cellular organisms all constructions and development and differentiation as well as functions of cells among multiple cells are controlled by mitochondria in each cell and mitochondria can function by means of hormones in the blood stream. Therefore, in these organisms, some kind of receptor or acceptor as well as controller to secrete hormone to control mitochondria in whole cells systemically in the visceral brain system, i.e., the limbic system in archetype animals, which incorporate not only energy but also nutrition, toxins, and bacteria and viruses just as somato-sensors control muscle movement through the neuron and neural system. This is considered from disclosure of the controlling mechanism of the basic construction of mammalia by means of mitochondrial functions.

## 6. Basic Construction of the Mammalia and Function of Mitochondria in Cells

All life phenomena, including morphology, and function, remodeling, and the genito-urinary system of protozoa, completely depend upon the energy metabolism of their mitochondria and the genome function of their nucleus. Adult Eutheria, multicellular mammalia, have circa $60\times10^{12}$ cells, and many kinds of organs and structures. As they have complicated correlated functions, they can move as if constructed from one cell just like protozoa. The fertilized oosperm cell divides into multiple cells, develop into complicated gastulura, branchilura, neurura, and embryos. In the 21st century, no scientist has considered in medicine or the life sciences how human ontogeny, i.e., development, takes place and how the multicellular human body is constructed from a newborn baby with $3\times10^{12}$ cells to an adult with $6\times10^{13}$ cells with close correlation, systemically, and a cooperating system among tissue cells and organs, which are constructed from enormous numbers of cells. We have to recognize initially that the multicellular human body acts as a whole, systemically, as if it was a single-cellular organism of protozoa. Second, prokaryote bacteria cannot form a multicellular organism, but only eukaryote can develop into a multicellular creature. Mitochondria are thought to be aerobic bacteria parasiting into eukaryote cells $1.8\times10^{9}$ years ago.

Let us consider evolution from protozoa to a multi-cellular organism. What is the most different structural part of cells between protozoa and the latter? The most remarkable different parts are the innumerable organelle mitochondria and the structure of the cell membrane. The structure of the cell membrane is also controlled by both nuclear and mitochondrial genes. In the human body, there are various cells in several different evolutionary stages. Leukocytes correspond to the stage of protozoa. Therefore, they can penetrate through small pit holes of blood or lympho-vessels with amoeboid movement. They can invade even cerebral liquor and a fetus through placenta. Now, consider the differences of the membrane of leukocytes and other organ cells. Leukocytes have MHC (major histocompatibility antigen, namely HLA) in its membrane. All cells in the human body, except matured erythrocytes, have genes of MHC. However, genes of MHC in cells, except leukocytes, are dormant.

Mitochondria are living organisms in living cells and control all $6\times10^{13}$ cells as a whole, in adult mammals systemically, and correlates all cells as one creature as a united system. Comparing the human body to a nation, various organs are states or prefectures, cities or towns, or large communities. Each cell, having eight hundred to three thousand mitochondria, are like a union of a community, factory, or large, well-run department store. Then what are the

enumerous mitochondria? Mitochondria are just like citizens in a nation-state. Only citizens can support the nation. Likewise, only vivid mitochondria can sustain the human body. Without mitochondrial functions, humans could never maintain their health. Complexion, color, looks and expression of the face, vigor and vitality, fatigue, tiredness, and exhaustion, all of these body states indicate mitochondrial conditions.

We can know the deterioration of their mitochondria, if some important organs loose their function, e.g., a heart attack is a dysfunction of mitochondria in cardiac muscles, dementia is a dysfunction of mitochondria in neurons in the cortex of the cerebrum, and nephritis is bacterial infection resulting dysfunction of mitochondria in glomerulus and mesangium. These dysfunctions of mitochondria occur as a result of improper energy metabolism, chronic fatigue, and intracellular infection of enterobacteria or viruses.

Various kinds of environmental energies, e.g., heat and cold, light and sound, atmospheric pressure, gravity and moisture, including the bio-energy of emotion, religion, spirit, fear and death of intimate life, and thought and ideology, influence directly all mitochondria in $6\times10^{13}$ cells. As well, energy metabolism of animals, namely movement and behavior, and emotion, are supported and influenced reciprocally by mitochondria. By these energies, mitochondria in all body cells become lively or exhausted. Not only energy but also toxic substances, intracellular parasitic microbes, and nutrition influence mitochondria.

## 7. Animal Movement, Morphology and the Correlation between Gravity

Locomotive movement is the most characteristic property of animals compared to plants, both of which are originally derived from Ascidia. Animal movement under gravity requires enormous energy for muscle contraction. Energy substances are synthesized in mitochondria as ATP (adenosine-triphosphate). The development of muscle inevitably induced the nervous system concomitant with the cardiovascular system and the cardiovascular system inevitably derived the gut respiration and digestive absorptive system. Also the muscle-neural system derived concomitant with the sensor system against external circumstances. These sensors are constructed along with the epithel mesenchyme corresponding function. All of these derivations are supported by energy substances and are generated by mitochondria.

Common sensors are for muscle movement. The representative sensors are the cerebrum, the neural system, the eye, the ear, the nose, haptics in cutaneous tissue, and the tooth. The muscle-neural system requires sensors for space and time and movement energy. For the cardiovascular system, sensors for

 

gravity and pressure are necessary. Animals are a vehicle of the visceral gut system moving toward food and reproduction. In the animal body there are various sensors for movement against environmental energy: sensors of the eye to light, the ear to sound, the cuniculi and sense of balance to gravity, the sense of touch to pressure, the tooth to mastication, namely, collision of food and pressure, and the spindle in muscle to movement.

Let us go back to the question of the influence of gravity. It has to be remarked that all organisms are constructed with water-soluble colloids of organic substances, even skeletal osseous tissue. Looking attentively, gravitational force acts in an important way on the shape of substances in a liquid state. This is more pronounced with water soluble, high molecular colloids, like those that compose living body tissues. Mammals have three kinds of sensors against gravity and dynamic energy: 1) the cuniculi of the inner ear functions as a gyro-compass in the neural cranium due to gravity, 2) the teeth for mastication, create a functionary collision of substance with mass, and 3) muscle spindles in muscles function in muscle contraction. There are also famous physiological studies of skeletal deformities by Julius Wolff (1836–1902), known as Wolff's Law on the functional adaptation of bone morphology. However, this law is restricted to very narrow conditions and over-use of the constant bias function results in discrepancies of shape and function. The gravity action effect upon the mediums of blood and lymphofluids, and the biomechanical force on the human body, are converted into hydrodynamics concomitant with movement. Hydrodynamics induce streaming potential and, by this, bone morphogenetic proteins (BMP) are induced through the gene expression of mesenchymal cells in connective tissue, which then differentiate into osteoclasts, osteoblasts and myoblasts, conjugated with hemopoietic cells. As a result of these mechanisms, bone remodeling takes place and deformities occur as a result of unilateral, improper gravitational action.

Jean-Baptiste Lamarck (1784–1829) proposed in 1809 the Use and Disuse theory for animal evolution. Wolff's Law is a part of Lamarck's theory, instructed only by skeletal morphology within one generation. Lamarck's theory has important limiting conditions of use, namely not to go beyond normal growth and healthful conditions. What does it mean when mammals use organs beyond normal growth and healthful conditions? Theoretically, mammals then fall ill. Mammalian babies can never eat anything during the suckling period. If they do, immune diseases such as dermatitis and epilepsy take place. As noted earlier, adult humans have several human-characteristic behaviors and structural defects compared to standard Eutheria (Mammalia). As a result of these behaviors and defects, humans can easily fall ill by means of improper energy accepted and intracellular infection by non-pathogenic enterobacteria.

## 8. The Overall System to Control Mitochondria in Whole Cells Directly in Mammalia

There should be special acceptors as well as controllers in multicellular organisms, especially mammals, which control energy metabolism over all cells in the body. The special supervising acceptor for systemic energy metabolism in whole cells in mammals are the suprarenal glands, which are also supervised by the hypophysis by means of hormones. The suprarenal glands secrete adrenalin and mineral- and glyco-corticosteroid hormones, both of which control mitochondrial energy metabolism in whole cells. These controls of mitochondrial metabolism in whole cells are the most important system in mammals. The accepting apparatus for these hypophysis-suprarenal glands systems are the epithelial body, the thymus, Waldyer's lympho-adenoid rings, and gut-associated lymphoid tissue (GALT). This system was disclosed as Selye's stress theory. However Selye did not know that hypophysis and suprarenal glands were acceptors and controllers of various stimuli, which influence the animal body. The hypophysis secretes an adrenocorticotropic hormone as a controller of the total stimuli impacting the living energy system of the animal.

What are these total stimuli to the animal? They are substance without mass, i.e., energy and substance with mass, including oxygen, nutrition, parasitic microbes, and toxins.

Energy stimuli are heat and cold thermodynamics and atmospheric pressure, light-electromagnetic waves, sound, moisture, and biological energy.

Besides these acceptors and the common energy sensors mentioned above, mammals also have receptors and incorporate organs of the branchial respiratory and digestive gut system against toxins, parasitic microbes, namely viruses, mycoplasma, bacteria, parasites, toxic proteins, and amines. They are tonsilla or lympho adenoid tissue and thymus, Peyer patch, epithelial body, cervical sinus, hypophysis, and suprarenal glands, which are almost all derived from branchial organs, and the gut visceral system. The above-mentioned concept of acceptors and controllers have been overlooked by conventional research. The hypophysis and suprarenal glands are acceptors not only for pressure, thermal stimuli, light and sound, but also various kinds of substance with mass, e.g., parasitic viruses and bacteria as well as toxins. The Peyer patch is the acceptor for proteins, amines, toxins, viruses and bacteria.

For the gut-visceral system, not only sensors for energy, namely the eye, ear, and skin, but also the sensors on acceptors for substance with mass, namely the tongue, taste buds, hypophysis, thymus, GALT, and suprarenal glands, which are also the incorporation system of viruses, bacteria, toxins and energy, and all sensors, submit to the gut-visceral system.

The hypophysis and suprarenal glands, as well as cervical sinus are also receptors of energy. Conventionally, sensors are limited to energy. However, all substances with or without mass, which enter the body from outside, are absorbed and acknowledged by the body and transmitted through the blood stream over whole body cells. Animals use enormous energy during peristaltic movement of the gut visceral muscles as well as locomotive movement of somatomuscles. Plants do not have locomotive movement, therefore plants use energy substance generated by mitochondria only for cellular respiration, namely metabolism, remodeling and reproduction. We have to remember the energy conservation theory, which states stating that in the ultimate condition substance with mass is equivalent to energy without mass. Life of higher animals like vertebrates is the circulating system of energy metabolism under sunlight energy as well as earth and moon gravity energy streams, which circulate in the animal body by the energy of metabolized nutrition absorbed from digested food.

## 9. Electromagnetic Energy and Force

The embryogenic tooth germ and eye germ are histologically precisely the same. The eye is a sensor for electromagnetic waves (energy) and the tooth is a sensor for hydrodynamic waves (energy) of the masticating apparatus to crush food, namely the collision of substance with mass, i.e., dynamic force action under gravity energy.

Here, we have to consider energy, the correlation between force and substance with mass. The cosmos quintessentially comprises (1) space (and pressure), (2) time and (3) light (electromagnetic waves), which have a close relativity correlation, (4) substance with mass, and (5) thermodynamic energy, which rules over the other four. The author has disclosed what gravitational energy is as follows: gravitational force exclusively belongs to and acts on substances with mass and does not act in the ambit pertaining to electromagnetic energy. In the ultimate condition, a substance with mass is in equilibrium with energy; for example, ultra-high temperature plasma, in which mass is converted into tremendous energy. However, at that instant, energy loses its attractive force, i.e., gravitation. These forces belong exclusively to substances with mass. Therefore, if they lose mass, they simultaneously lose their gravitational force.

Substances with mass have three states: solid, liquid and gaseous. Substances characterized by mass undergo (physical and/or chemical) modifications at a certain rate when they gain or lose thermal energy. Solid and liquid substances collide with each other. By these explosive collisions, substances with mass change into space, light and thermodynamic energy. In the case of a release of

energy, the lowest asymptotic limit exists for thermodynamic equilibrium at –273.13 °C (absolute zero).

Mammals utilize, for the life system, energy without mass as well as substances with mass equivalently under the energy conservation theory. The origin of the life system started initially from absorbing nutrition, oxygen and minerals, namely substance with mass, concomitant with absorbing energy. Therefore, the higher Mammalia have the absorbing system of energy and food, namely substance with mass. We call the former "sensor" or "receptor" and the latter "the gut absorbing system." The gut absorbing system is a receptor (absorber) for substance with mass from a standpoint of the energy conservation theory.

## 10. The Cell Respiration System, the Immune System, and the Stimuli Acceptor System

The system directly influencing mitochondria is the hypophysis of the suprarenal glands system, which supervise energy metabolism of mitochondria in whole cells of animals. What are the substances influencing energy metabolism of mitochondria in whole cells? These are 1) energy, heat and cold, pressure, moisture, light, sound, and electricity; 2) nutrition, minerals, vitamins, water, oxygen, namely substance with mass; 3) toxic substances and parasitic microbiles; bacteria, mycoplasma, and viruses. Initially, Selye's stressor included microbial infection. However, in recent therapeutics for intractable immune diseases, bacterial infections are completely overlooked. For actual animal life, stressors include not only energy as well as nutrition but also toxins, bacteria and viruses, namely substance with mass. Even for energy, the conventional Selye's Stress theory overlooked dynamic force, gravity energy, muscle movement, and these receptors.

Therefore, the hypophysis-suprarenal glands system have to include the all-integrated absorbing and acceptor system of not only energy but also nutrition as well as viruses and bacteria.

The gut system is the absorbing acceptor system of both energy and substance with mass. There are three parts, 1) the branchial respiratory gut, 2) digestive tract of the gut absorbing system, and 3) excretory tract, namely the genito-urinary system.

All nutrition, minerals, vitamins, oxygen, as well as viruses and bacteria are recepted and absorbed into blood or leukocytes and delivered to almost all cells throughout the blood stream and lympho stream. At this time, microbes absorbed in leukocytes from the M cell of Peyer's patch are disseminated into cells by contaminated leukocytes. This gives rise to intra-cellular infection

of organ cells or tissues cells by non-pathogenic entero-virus or bacteria, and mycoplasma.

If intracellular infection occurs in some organ, the function of the cells of that organ deteriorate because of the dysfunction of mitochondria caused by contaminated bacteria or viruses. This is an immune disease.

The conventional interpretation of Selye's stress theory has been just half the story because of overlooking intracellular infection of the cells in the organism. Consequently, bacterial or viral contamination in all cells in whole body occurs. The initial stage of intractable immune diseases starts from intracellular contamination of hypophysis-suprarenal glands through Waldeyer lympho adenoid tissue or gut associated lymphoid tissue absorbing into leukocytes entero bacteria or viruses by cooling the gut. After that, dysfunction in secreting the adrenocrticotropic hormone takes place, and intracellular infection over all cells in whole body occurs. This is the cause of intractable immune diseases. Thus, Selye's stress theory is now completely disclosed under the energy conservation theory.

In conclusion, multicellular animals live under sunlight and gravity energy of the earth and moon, and incorporate substances with mass from the gut. Using both energy and substance with mass, creatures remodel themselves in conjugation with energy metabolism by means of mitochondria. The vertebrates have not only sensors to recognize different energies including, sound, touch, cold, hot, pressure, and moisture, but also acceptors to process oxygen, minerals, nutrition, toxins, and microbes, such as viruses and bacteria. Thus, creatures live by accepting both energy and substance with mass. Acceptors of energy are sensors of the eyes, ears, static organs and muscle spindles as well as all somato and visceral organs, and acceptors of substance with mass, including microbes, are the gut system incorporating into blood or lymphofluid various kind of substances. These substances, including nutrition, toxins, oxygen as well as microbes, are distributed into cells of the whole body. Therefore, the control center of the substance-distributing system in blood and lymphofuluid to cells in the whole body is the direct regulation system of mitochondria. This control center is the hypophysis-suprarenal gland system. Dysfunction of this hypophysis-suprarenal gland system by intracellular infection or by malnutrition, e.g., a complete lack of vitamins B or C, induce systemic dysfunction of mitochondria in whole body cells.

The author discloses the mechanism of the hypophysis-suprarenal gland system as the direct control system of cellular energy metabolism of mitochondria in whole cells in the animal body and this is the immune system. The immune facility is the remodeling capacity conjugated with energy metabolism. Therefore, the hypophysis-suprarenal gland system, i.e., the direct

control system of mitochondrial metabolism in whole cells is the controlling system of energy metabolism as well as the acceptor of the stimuli of energy and substances with mass including bacteria.

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**Errors and Corrections table**

P174

Section 4, line 2 gel→cells

P 178

Section 7, line 8 sensor→sensory