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Research on the evolution and development of autonervous system

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Abstract—The development of the basic construction of vertebrates, the metameric system, the sympathetic nervous system, the lymphatic vessel system, the capillary system and the bone marrow hemopoietic system have been investigated from the viewpoint of the gravity-evolutionary theory. The definitive structures and organs of the vertebrates are the bone and respiratory apparatus of the gut. All animal cells have a cellular respiratory system composed of mitochondria. The hemopoietic system in bone marrow, blood cells, and the cardiovascular system are the structures of the organ system between the outer (gut) respiration of gills and lungs and inner (cellular) respiration of mitochondria. The author has successfully developed hybrid artificial bone marrow by applying biomechanical stimuli to sintered apatite; this took on the characteristics of bone marrow hemopoiesis peculiar to higher vertebrates after migrating onto land. The author has also developed a hybrid-type artificial dental root that took on the characteristics of the gompholic tooth peculiar to mammals. By this approach, the author has suggested that evolution occurs according to the mechanical functions of the animal in response to gravitational energy. Establishment of the basic construction of mammals was verified by means of experimental evolutionary studies that showed the Heterodontus (dog shark) had developed into an archetype mammal directly during terrestrialization. These evolutionary phenomena can be seen as a revolutionary transformation of morphology due to biomechanical responses to environmental changes of energy triggering gene expression of cells. Through the establishment of the mammalian system, the tissue immune system is disclosed and a new concept for immune diseases is developed. Diseases of the immune system seem to be related to disorders of the cellular respiration of mitochondria caused by intracellular infections of non-pathogenic micro-organisms in the gut system.

Keywords: Morphology; gravity; evolution; metameric system; biomechanics; immune diseases; vertebrates; phylogenesis-ontogenesis; archetype; immune system.

INTRODUCTION

The development of the basic construction of vertebrates, this is, the metameric system as well as the sympathetic nervous system, the lymphatic system, the

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capillary system, and the bone marrow hemopoietic system are investigated from the viewpoint of gravitational influence on evolution, that is, the so-called gravity evolutionary theory, which the author proposed and verified using ceramic artificial bone marrow chambers (Nishihara, 1987, 1999).

The definition of a vertebrate is a chordate having a bony backbone, with differing degrees of ossification. The structures and organs defined as being characteristic of vertebrates are the spine, and the gut respiratory system (the gill and lung system). The definitive structures and organs are the bone and respiratory apparatus of the gut (Torry, 1987). Moreover, all organisms have the cellular respiration system of mitochondria. What is the structure of the organ system between the outer (gut) respiration of gills and lungs and inner (cellular) respiration of mitochondria? It is the hemopoietic system in bone marrow, blood cells, and the cardiovascular system. Therefore, if the definitive substance of bones is synthesized, then, using them, the riddles of the evolution of the vertebrates can be solved by developing artificial bone marrow chambers inducing the hemopoietic system (Nishihara, 1987, 1999).

The author has successfully developed hybrid artificial bone marrow by applying biomechanical stimuli to sintered apatite (Nishihara *et al.*, 1992, 1994). This took on the characteristics of bone marrow hemopoiesis peculiar to higher vertebrates after migrating to land.

The author has also developed a hybrid-type artificial dental root that took on the characteristics of the gompholic tooth peculiar to mammals (Nishihara, 1993, 2003a). In this way, the author has clarified that evolution occurs according to the mechanical functions of the animal in response to gravitational forces. In order to elucidate the law of evolution, the author has developed trilateral research that integrates morphology, including embryology and phylogeny, the functional study of molecular biology, and molecular genetics concerning remodeling with biomechanics (Nishihara, 1998). The author has also devised an experimental evolutionary study method that applies trilateral research to work of every phylogenetic stage representing phylogeny (Nishihara *et al.*, 1996). From these studies the author has tried to reinterpret Wolff's Law (1870), Lamarck's Use and Disuse Theory (1809) and Haeckel's Biogenetic Law (Alberch, 1994) with the current level of science using biomechanics and molecular biology. The author used artificial bone marrow organs made of synthetic apatite and Ti-electrodes as well as using an artificial dental root inducing the cementum (fibrous bone) and hemopoietic nest by biomechanics. The author, moreover, verified Lamarck's Use and Disuse Theory. Following that, the author carried out research on the basic construction of vertebrates from the viewpoint of the Gravity Influencing Evolutionary Theory (Gravity Evolutionary Theory, Nishihara, 2003).

Establishment of the basic construction of archetypical vertebrates during the primitive evolution of vertebrates is thought to occur by means of gene duplication of the hemichordate ascidia. Prior to that, during the dawn of vertebral evolution the hemichordate ascidia, which integrated the respiration, nutrition, and excretion systems into only one tube of the gut, evolved from Bryozoa, which have a pterobranchial skin respiration system. Conventionally, primordial revolution of the establishment of the metameric system from monometameric ascidia had been completely unrecognized; also, development of the sympathetic nervous system had been only slightly investigated.

From the evolution of the vertebrate, mammals are conventionally thought to have evolved after three kinds of vertebrate revolutions. The first is the nativity of the Acantoidii; the second, terrestrialization; and the third, the birth of mammals. However, the author could find only two stages. These were verified by means of experimental evolutionary studies that showed the Heterodontus (dog shark) had developed into an archetype mammal directly during terrestrialization. These evolutionary phenomena can be seen as a revolutionary transformation of morphology due to biomechanical responses to environmental changes. Through these transitions, various kinds of concerns develop between morphology and the function of organs in the human body from the standpoint of basic construction of the vertebrates. Through this new theory of evolution, the immune system was studied and a new concept for immune disease was developed. Immune system diseases are a disorder of cellular respiration of mitochondria caused by intracellular infections of non-pathogenic micro-organisms in the gut system.

DEVELOPMENT OF BASIC CONSTRUCTION OF VERTEBRATES

Living organisms, including multi-cellular creatures and higher animals, have enormously diversified shapes. Are there any basic designs for the bodies of higher organisms? What is the initiating factor in evolution? The questions that occurred first in the sciences of life were those related to morphology and function. In modern science, the first person who noticed the presence of archetypes as the basis for higher organisms, including animals and plants, was the poet Goethe, who established the new scientific area of 'Morphologie'. He defined Morphologie as a science whose ultimate objective is to clarify the mechanisms of morphological transformation. He also studied vertebrate archetypes up to human beings. Goethe stated that even the body of a human being 'has reached today's shape through transformations every moment after the creation of life, starting from the prototype in the Archeozoic age'. Goethe's lifelong theme was the importance of 'the principles of modification of shapes', which was later called phylogeny by Haeckel.

In those days, Lamarck and Cuvier in France greatly contributed, as did Goethe, to the establishment of a new scientific field, which is called 'life sciences' today. Lamarck made 'Biologie' independent from natural history (Lamarck and Treviranus, 1802) through studies of invertebrates and proposed the evolutionary concept that the archetypes of living beings are changed by external as well as internal biomechanical factors according to the Use and Disuse Theory (Lamarck, 1809). This was a more definite scientific realization of Goethe's Morphologie of the modification of archetypes under biomechanical influences. On the other hand, Cuvier established the basics of comparative vertebrate anatomy at the age of 27, and proposed the principle of the dependence and correlation of organs (1795). However, under the patronage of Napoleon, he advocated the theory of the unchangeability of life and made efforts to abolish Lamarck's concept of evolution.

The essence of the Use and Disuse theory is biomechanics and the substance of biomechanics is dependent upon the earth's gravity (Nishihara, 2003a).

While various living beings exist on the earth, there are comparatively few basic macromolecular substances that are common to all living beings, namely, nucleic acids constituting genes and amino acids constituting proteins. There are various substances for skeletal systems related to morphology and, since the substances are not the same, the basic morphology and the modifications appropriate to each kind seem to be different.

The skeletal systems of organisms on earth can be divided approximately into five kinds: (1) the cellulose system for plants, (2) silicate system for diatoms, (3) calcium carbonate system for shellfish and coral, (4) chitin system for insects, prawns and spiders, and (5) the collagen apatite phosphate system for vertebrates. To those listed above only the last two skeletal systems have effective response mechanisms to biomechanical stimulation. Because of this, invertebrates with only chitin and vertebrates display a morphology associated with functions.

Coelenterates and Pterobranchia, having no skeleton, are able to change their morphology relatively freely in conformity with their functions. Invertebrates that developed a chitin-based skeleton evolved into organisms such as crabs and insects with social organizations, but because of their external skeleton, their remodeling system of ecdysis was limited, and therefore they failed to achieve larger sizes.

The collagen apatite-based internal skeleton of vertebrates was able to change its shape by remodeling in response to external as well as internal forces during movement under the earth's gravity. Also, they were able to grow to huge sizes and to adapt and propagate, forming considerably diversified species.

Therefore, it can be said that the bone structure is the defining characteristic of the vertebrates. For this reason, the mechanisms of bone evolution in vertebrates can be clarified by investigating bone characteristics. Bone is a connective tissue calcified by hydroxyapatite, so that collagen seems to be as important a substance as apatite for characterizing the vertebrates. The archetype of the bone structure is derived from a carapace called aspidin, which is a composite of dentine and bone forming the armor of the Pisces in the Archeozoic era. Calcium which existed in high concentrations in the Archeozoic sea was absorbed in the gut from sea water and metabolized by mitochondria in muscle and secreted from aspidin on the skin surface. The aspidin may also have had a storage function for phosphates, which were in short supply in the sea.

The starting point of the evolution of the vertebrates is the incorporation of respiratory apparatus into the gill cleft from the cutaneous respiration system of Pterobranchia, and the acquisition of an apatite bone structure. Therefore, the archetype of our mammalian human ancestors can be seen in the dog shark

(*Heterodontus japonicus*) of which constructive parts around the mouth coincide with those of the human embryo.

Since animals cannot synthesize energy sources independently from their immediate environment, the fundamental characteristic of animals is related to movement in search of food.

In morphological evolution, empirical laws exist which state that the form changes according to the method of using the body, i.e. repeated action, just as in the Use and Disuse theory. That is to say, the characteristics of constant behavior determine form and structure. Repetitive behavior can be seen as a function in many cases, and, therefore, form changes in accordance with function. Because of this, the evolution of form occurs depending on changes in the environment. Environmental change promotes change in biomechanics in a broad sense, i.e. physico-chemical stimuli including energy.

ESTABLISHMENT OF THE BASIC CONSTRUCTION OF ARCHETYPE VERTEBRATES IN EVOLUTION

The primordial revolution

In this stage, metameric organisms developed through a process of genome duplication from the ascidian (urochordate monosomite organisms). Relics of this primordial revolutionary stage are the Amphioxus and Cyclostomata. After metameric organisms (vertebrates with a homeobox), metamorphic changes occurred as the result of biochemical stimuli with no alteration to the basic structure of the homeobox genome.

The primordial vertebrate, i.e. hemichordate ascidian organism with a monosomite form, began with the acquisition of a gut for an absorbing and excreting system, that is, respiration, nutrition, hemopoiesis, generation, and urination. Ascidian has a dorsal chord, but it is a monosomite organism, while the vertebrates are multisomite organisms. Development from monosomite animals to multisomite vertebrates is thought to have occurred by geneduplication, a concept proposed by S. Ohno.

Through several cycles of gene-duplication of ascidian genomes, a cyclosalpa-type organism, which is a continuous ascidian-like chain with serial single gut of archetype independent vertebrae, evolved. This organism moved in sea water. The first front ascidia formed the head and face. Water and food were taken by the mouth while each branchial aperture opened during water aspiration to provide oxygen, which was absorbed through the gills. When the openings closed, digestion of food began in the gut. After that, food debris was discharged from the anus. Following the development of the anus, the gut of all somites in the tail part of cyclosalpa disappear completely. In this way, the tail, i.e. the serial somites without the gut developed. From this primordial vertebral evolution, archetype vertebrates like Amphioxus and Cyclostomata developed. This mechanism of development depends upon the Use and Disuse theory based on biomechanical energy. Maintenance of this system required a hard-tissue notochord, namely, the series of somites that became the vertebrae.

The first revolution

The Silurian period saw the appearance of spiny sharks (Acanthodii), with jaws, calcified teeth and a carapace of hydroxyapatite acquired through forward movement. Descendants of these are to be found today as cartilaginous fishes (Chondrichtyes), i.e. sharks and rays.

Archetype Cyclostomata continued to move forward speedily. Energy metabolism of the muscles increased and excreted large amounts of minerals from the muscles, which functioned via electron transmission in mitochondria through increased cellular respiration as a result of muscle movement. Consequently, placioids made of cartilage evolved into bone with an enamel substance and Acantoidii developed. This is the first revolution in vertebral evolution.

Use of bone made of collagen apatite compounds for hard tissue made adaptation and propagation possible for the vertebrates. The fact that the hydroxyapatite is based on calcium which is indispensable for life, and phosphate which is indispensable for cytological respiration, as well as energy and nucleic acid metabolism are considered to have far-reaching significance.

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, all vital reactions can be considered biomechanical responses to environmental factors.

BASIC CONSTRUCTION OF MAMMALS

This involved development of bone marrow hemopoiesis, the parasympathetic nervous system, capillary system, 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 a 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 (Nishihara, 2003c). In addition, the cartilaginous endoskeleton ossified. Salamanders and lungfish are relics of this evolutionary stage.

During terrestrialization, drastic changes of biomechanic stimuli in a broad sense, occurred. These include energy without mass, e.g. force of gravity, as well as substance with mass, e.g. oxygen. They are known as the following five physicochemical stimuli: (1) Gravity of 1/6G in water (buoyancy) to 1G on land or 6 times stronger energy; (2) 0.7% oxygen content in sea water to 21% in air, or 30 times greater; (3) Water as a life-medium containing minerals becomes 1/800 lighter as air without minerals; (4) Complete 'wetness' in water to complete 'dryness' in air; and (5) Highly viscous water versus extremely low viscosity of air.

As the result of gravitational action, the dog shark could adapt by increasing blood pressure as it struggled to try to escape suffocation by returning to water. Consequently, endoskeleton cartilage developed into osseous tissue with bone marrow hemopoiesis. Thirty times increased oxygen content caused the sixth gill epithelial membranes to develop air sacks of the lungs during respiration in the struggle to escape suffocation. Dryness as well as the lack of minerals in the air influenced the placoids (dermal teeth) to develop fur, which are in fact placoids made of collagen without minerals. The high viscosity of water brought about the streamlined shapes of organisms in water. The extremely low viscosity of air brought about common shapes without streamlining after terrestrialization. This is epitomized by the changes in morphology and functions in the organs of archetype vertebrates after land migration, as seen by respiratory gills, the dermal region, and inner skeletons. 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.

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, 2003c). With elevated blood pressure, streaming potential increases (Petrov *et al.*, 1989) and the increased currents trigger the gene expression of chondrocytes to develop osseous tissue, together with bone marrow hemopoiesis as well as erythrocyte-enucleation, the cardiovascular system, lymphatic-vessel formation, the pyramidal tract of the cerebral motor nervous system, the sympathetic nervous system along with the capillary system and major histocompatibility antigens (MHC) in conjugation with the homothermal system. The author verified these processes by means of experimental evolutionary research methods (Nishihara, 2000).

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 cytokine nerve growth factor to generate capillaries and the lymphovessal system. Consequently, capillaries and the sympathetic nervous system proliferate and develop into brain, visceral organs, as well as somato-muscles. Before the stage of archetype animals there were no nutritional capillaries even in the heart and brain. The heart was derived from branchial hematopoietic nests. Therefore, the heart itself generates hemato cells.

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.

But we may ask, what is the nervous system? This question is most important to solve the riddle of the brain. The nervous system was differentiated together with muscle cells. However, conventional research overlooks this. As a result, research has not been able to solve the brain system riddle. The cerebrum of archetype animals is composed of a visceral brain, which controls somato-muscles by means of the extra-pyramidal tract as well as visceral muscles.

The parasympathetic nervous system is extremely old. Even the initial developmental stage of vertebrates, such as the monosomite ascidian, had this. The parasympathetic nervous system developed together with the gut system. Therefore, the parasympathetic nervous system belongs to the visceral smooth muscle group. These systems function by cholinergic stimuli. Therefore, the preganglion nervous system of sympathetic nerves is not correct as it actually belongs to the parasympathetic nervous system because of cholinergic fibers. What then were the major factors in the development of capillaries and sympathetic nerves? The former developed from the extensive increase of movement requiring oxygen and the latter from thermal changes in the air in the environment. Thus, the surface skin of the somatic motor system has a connection with somato organs, e.g. brain, and visceral organs, such as the heart and the intestines, via the autonomic nervous system.

The sympathetic nervous system functions only by adrenalin. During the development of the sympathetic nervous system, neurons in the cerebral cortex proliferated 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 are established.

The function of MHC is for remodeling and cell-metabolism as well as antibody formation of immunoglobulin A, as leukocytes depend completely upon cellular respiration and energy metabolism of mitochondria in white blood corpuscles. The body temperature of the homothermal system is generated by means of oxidative phosphorylation in mitochondria. This is the reason why the mammalian immune system of leukocytes, i.e. antibody formation as well as bacterial phagocytes and digestion strictly depend upon a body temperature of 37°C. If body temperature lowers by one degree, leukocytes lose their immune functions. The terrestrialization of Heterodontus (dog shark) led to dramatic changes in the following 12 major areas: (1) cardiovascular system, (2) capillaries, (3) lymphatic 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.

As mentioned above, the mammalian sympathetic nervous system developed along with capillaries derived from the ganglion of parasympathetic nerves. Therefore, it had 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.

DISCLOSURE OF THE MECHANISMS OF EVOLUTION OF THE IMMUNE SYSTEM AND THE ONSET OF HUMAN IMMUNE DISEASES

What happened to the immune system during terrestrialization? The immune system is composed of various kinds of hemocytes. During the development of bone marrow hemopoiesis, erythrocytes lose their nuclei and leukocytes differentiate with functioning HLA in their surface membrane. Erythrocytes without nuclei cannot maintain amoeboid movement, therefore, they remain in the blood vessels. Leukocytes continue to have amoeboid movement, so they can move into lymphoid vessels as well as intracellular space. Lymphoid vessels act as the major immune system of white blood corpuscles, into which the autonomous nervous system has its networks. The function of white blood corpuscles, i.e. the cytotogical digestive system, depends upon little higher temperatures than the homothermal system of each respective animal. Cytological digestion of leukocytes is carried out by the energy generated by their mitochondria.

These drastic changes in evolution occurred according to Lamarck's Use and Disuse theory, and all phenomena are based on the metaplasia of cells. Also, all drastic phenomena in evolution are sustained by the energy metabolism of mitochondria in all cells in an organism. From the standpoint of evolution, as well as from the basic construction of the vertebrates, the author questions why intractable immune diseases which comprise almost all human maladies, have risen recently in all the advanced countries.

Thinking about the establishment of the eukaryotes, in which parasitic aerobic bacteria had infected intracellularly as mitochondria, it can be easily understood that in higher animal cells, various microbes, e.g. virus, mycoplasma, bacteria, and some kinds of Protozoa can cause parasitic infections. If these microbes have pathogenicity, maladies occur in animals. Today, if we have no effective antibiotics against pathogenic bacteria, we could never overcome either epidemic or pathogenic contagious diseases. The immune system as a defence mechanism is very weak and there is almost no protective system against parasitic infections.

Self and non-self immunology is now in vogue around the world. However, this immunology is effective only for tissue immunity in organ transplants, but almost useless against infectious diseases.

Archetype vertebrate chondrichthyes (and sharks) are known to have the MHC gene. However, they have no tissue immune system; and, as their leukocytes do not phagocyte, bacteria and microbes can coexist in shark blood. They have no lymph system as their erythrocytes have a nucleus like leukocytes. Therefore, their leukocytes do not have their own vascular system of lymphoid vessels. The author successfully verified the immuno-tolerance of chondrichthyes by means of transplantation of various shark organs into mammals (Nishihara, 2004).

From this research, the author has determined that the renewal metabolism of cells in the immune system of mammals is a remodeling system by means of MHC or HLA in the cell membrane. In the human body, one trillion out of 60 trillion cells are remodeled per day during sleep. This is the function of the tissue immune system of leukocytes. The loss of this function in mammals is known as immunotolerance. This tissue immunity has developed into the most sophisticated system in mammals during evolution. The development has been in parallel with evolution of bone marrow hemopoiesis, the lung respiration system, the sympathetic nervous system, the cerebral motor of the pyamidal tract system, the cardiovascular capillary system, the completion of erythrocyte differentiation, and the homothermal system.

We must then ask what are the intractable immune diseases that are now appearing in in advanced countries, especially Japan, France and the USA? Intractable immune diseases, including self-immune maladies, develop by the intracellular contamination of parasitic non-pathogenic enteromicrobes, which are incorporated into leukocytes from lympho-adenoid follicles, i.e. GALT (gut associated lymphoid tissues). The more famous ones are Waldeyer's adeno lymphoid ring and the Peyer patch. From this, the non-pathogenic indigenous parasitic microbiota are incorporated into the follicles where microbes are digested and immunoglobulin A is generated. However, by breathing though the mouth, or by cooling the gut with cold liquids or ice cream, bacteria or viruses are incorporated into leukocytes and leukocytes disseminate these parasitic bacteria in circulating blood. This gives rise to unrecognized intracellular infections of various kinds of cells in major organs. Common pathogenic bacteria bring about diseases by contamination of the medium, i.e. blood or lymphatic fluid, or on the surface of the gut, e.g. the lungs and intestines. However, intracellular infections by non-pathogenic parasitic enterobacteria bring about no infectious diseases or toxicoses, but allergic diseases and immune system diseases instead.

These allergic diseases, e.g. atopic dermatitis as well as collagen diseases, myositis, ulcerative colitis, asthma, and mycoplasma pneumonia, are intracellular infections of non-pathogenic or only weakly pathogenic microbes.

Conventionally, intracellular infections have been known as viral infections or protozoa malaria. What happens during intracellular contamination by non-pathogenic bacteria? In intracellular infections by aerobic or anaerobic bacteria, the energy metabolism of mitochondria of the infected cells is disturbed. Aerobic bacteria consume intracellular oxygen and anaerobic bacteria consume nutrition glycolysis which allows pyruvic acid to be metabolized for the oxidative phosphorylation in mitochondria. Therefore, despite aerobic or anaerobic bacteria, facultative aerobiosis or obligate anaerobes without pathogenicity, all cells infected are caused by the disturbed cellular respiration of mitochondria. By breathing though the mouth, lower body temperature, cooling of the gut by cold drinks or ice cream, overtension of the sympathetic nerves, shortage of sheep (i.e. relief from gravity), and an overtired state, all allow parasitic non-pathogenic enterobacteria to be incorporated into leukocytes through lympho-adenoid follicles in the gut (Nishihara, 2000). These over-reactions of energy induce the intracellular infection of leukocytes, which are brought about by the mistaken use of the human body. Through the lymphatic vessels, these contaminated leukocytes are incorporated into venous vessels and the leukocytes disseminate bacteria into various cells in different organs via the bloodstream. Each specialized organ has highly differentiated cells with specialized functions. All cell functions are regulated by the energy metabolism of mitochondria. Therefore, if cells of some specialized organs, e.g. brain, kidney, spleen or pancreas, or some structure, e.g. joint, subcutaneous tissue, or bone marrow, are contaminated by parasitic enterobacteria disseminated by infected leukocytes, these organs cannot continue to function normally. And, in some cases, these contaminated structures allow the granulation of tissue to develop. These are joint rheumatitis, matrix pneumonia, histocytosis, sarcoidosis, and atopic dermatitis.

The major causal factor of evolution is energy. The modality of evolution is in accordance with Lamarck's Use and Disuse theory. The major cause of intractable immune diseases is also energy. These diseases are now occurring according to the Use and Disuse theory by the mistaken usage of the mouth for breathing, shortage of natural sleep, shortage of sunlight absorption, cooling the gut and an over-tired condition, which result in the deterioration of mitochondria in all cells of the body, as well as intracellular infections by parasitic bacteria.

SUMMARY

The basic construction of the vertebrates has been investigated from the viewpoint of gravity as a causal factor in evolutionary theory. The initial stage of the revolution of vertebral evolution, i.e. the primordial revolution in which the monosomite ascidian developed into polymetameric organisms, is thought to occur as a result of geneduplication. Lamarck's Use and Disuse theory corresponding to gravity as well as the development of the sympathetic nervous system are studied together with bone marrow hemopoiesis, the tissue immune system, capillaries and lymphovessel development, and the homothermal system. From this research, the author has determined that the causes of human-specific intractable immune diseases are intracellular contamination by parasitic nonpathogenic enteromicrobes, which are disseminated by leukocytes.

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