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RESEARCH ARTICLE

THE BIO EVOLUTIONARY CHRONOLOGY OF APPEARANCE OF SUBSTRATE - SUBSTANCE MATERIAL BASIS DATED 06 OCTOBER ACCORDING TO A BRIEF EVOLUTIONARY TIME TABLE OWING TO HORIZANTAL GENE TRANSFER LEADING TO FURTHER CREATION OF SCIENTIFIC GROUND OF NCM MEDICINE AND INTEGRATION OF TRADITIONAL AND MODERN MEDICINES

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ABSTRACT

Horizantal gene transfer during which genes are inserted into a genome by viruses, plasmids, and other foreign agents at example of archaea and bacteria cells had been served a more important role in the formation of substrate - substance basis, leading to origin of species during bioevolutionary time, also leading to further creation of NCM medicine and integration of Traditional and Modern medicines, which lasted from October 06 was day (one day is equal to 42 million years) - 3,6 bya years ago until December 31-1:00 a.m (40 mya) first monkeys, 9:00 p.m (5-6 mya) first hominins, 10:30 p.m (2,5 mya) - first stone tools, 11:22 p.m (0,5 mya) -first use of fire, 11:59 p.m (30 000 ya) - Cave paintings, 11:59:35 p.m (12 000 ya) -farming, 11:59:55 p.m (2 000 ya) - common era begins, 11:59:59 p.m (500 ya) -Renaissance. The recent literature date, relating to that archaea and bacteria are the deepest branches of the tree of life, the two groups are similar in morphology and share some fundamental biochemistry, including the genetic code have been confirmed that the day of formation of substrate - substance basis leading to further creation of NCM medicine and integration of Traditional and Modern medicines is October 06 (3,6 bya years ago when life established, first fossils - accorting to a brief evolutionary time table, because in the interval of this day, which lasted 42 million years, had been created the basic elements of membrane - redoxy potentials three state line systems as one is unseparable part of the full 9 stepped cycle of proton, electron conductance inside human body, leading to formation of RNA, DNA, ribosome, genetic code. What about general features of bioevolutional events happened in the October 06, 3,6 bya years ago was the early forms of life establishment in the form of Archea owing to natural geochemically sustained proton gradients of LUCA had been existed in the geochemical origin - hydrothermal vent of this time, giving the fundaments of following appearance of Bacteria, facilitating ecological spread and divergence by Horizantal gene transfer during which genes are inserted into a genome by viruses, plasmids, and other foreign agents at example of archaea and bacteria. The formation of substrate - substance basis during bioevolutionary time, leading to further creation of NCM medicine and integration of Traditional and Modern medicines within October 06 - 3,6 bya years ago had been conducted owing to transformation- the genetic alteration of a cell resulting from the introduction, uptake and expression of foreign genetic material (DNA or RNA. By us have been established that the day of formation of substrate- substance basis leading to further creation of NCM medicine after 3,59 bya years of these historical events and integration of Traditional and Modern medicines is October 06 (3,6 bya, life established, first fossils)- because in the interval of this day, which lasted 42 million years, had been created the basic elements of membrane - redoxy potentials three state line systems as one is unseparable part of the full 9 stepped cycle of proton, electron conductance inside human body, leading to formation of RNA, DNA, ribosome, genetic code. The membrane - redoxy potentials three state line systems formed during October 06 was day (one day is equal to 42 million years) - 3,6 bya years agoas one is unseparable part of the full 9 stepped cycle of proton, electron conductance inside human body, leading to formation of RNA, DNA, ribosome, genetic code had been coded 3000 years ago had been coded by abstract triple code as Khii, Shar, Badgan (K.S.B) in Traditional medicine, when intellectual capacity of humans was developed in high level to find the triple code as (K.S.B).

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INTRODUCTION

Examples of Common Descent have been appeared in the case of Human Chromosome 2. Compelling evidence of the shared common ancestry of humans with the great apes is the fusion event which occurred when two chromosomes common in apes fused to form chromosome 2 in humans. Endogenous retroviruses are residual DNA sequences found in the genomes of virtually all living organisms as a result of ancient viral infections. Since the retroviral sequences are incorporated into the DNA of the host organism, such sequences are inherited in the offspring. Such analyses of endogenous retroviruses often reveal speciation events and how closely related two species may be, as observed in the shared endogenous retroviruses between humans and other primate species. A some study found the genomes of 40 animals (including 10 primates, four Caenorhabditis worms, and 12 Drosophila insects) contained genes which the researchers concluded had been transferred from bacteria and fungi by horizontal gene transfer. For example, the most common gene to be used for constructing phylogenetic relationships in prokaryotes is the 16S ribosomal RNA gene since its sequences tend to be conserved among members with close phylogenetic distances, but variable enough that differences can be measured. However, in recent years it has also been argued that 16s rRNA genes can also be horizontally transferred. Horizontal gene transfer poses a possible challenge to the concept of the last universal common ancestor (LUCA) at the root of the tree of life first formulated by Carl Woese, which led him to propose the Archaea as a third domain of life. Common descent describes how, in evolutionary biology, a group of organisms share a most recent common ancestor. There is "massive" evidence of common descent of all life on Earth from the last universal common ancestor (LUCA). It have been reported identifying a set of 355 genes from the LUCA, by comparing the genomes of the three domains of life, archaea, bacteria, and eukaryotes.

Common ancestry between organisms of different species arises during speciation, in which new species are established from a single ancestral population. Organisms which share a more-recent common ancestor are more closely related. The most recent common ancestor of all currently living organisms is the last universal ancestor, which lived about 3.9 billion years ago. The two earliest evidences for life on Earth are graphite found to be biogenic in 3.7 billion - year - old metasedimentary rocks discovered in western Greenlanda and microbial matfossils found in 3.48 billion - year - old sandstone discovered in Western Australia. All currently living organisms on Earth share a common genetic heritage, though the suggestion of substantial horizontal gene transfer during early evolution has led to questions about the monophyly (single ancestry) of life. 6,331 groups of genes common to all living animals have been identified; these may have arisen from a single common ancestor that lived 650 million years ago in the Precambrian. The recent literature date, relating to that archaea and bacteria are the deepest branches of the tree of life, the two groups are similar in morphology and share some fundamental biochemistry, including the genetic code have been confirmed that the day of formation of substrate - substance basis leading to further creation of scientific ground of NCM medicine and integration of Traditional and Modern medicines is October 06 (3,6 bya years ago when life established, first fossils - according to a brief evolutionary time table, because in the interval of this day, which lasted 42 million years, had been created the basic elements of membrane -redoxy potentials three state line systems as one is unseparable part of the full 9 stepped cycle of proton, electron conductance inside human body, leading to formation of RNA, DNA, ribosome, genetic code (Ambaga, 2016). All cells power ATP synthesis through chemiosmotic coupling, in which the ATP synthase (ATPase) is powered by electrochemical differences in H^+ or Na^+ concentration across membranes. The ATPase is universally conserved and shares the same deep phylogenetic split as the ribosome, implying that both were present in LUCA. The deepest branches in the tree of life are entirely populated by autotrophs, which also depend on chemiosmotic coupling to drive carbon metabolism via proteins such as the energy-converting hydrogenase (Ech) and ferredoxin. But there are serious objections to the idea that LUCA was chemiosmotic. Pumping protons across membranes requires sophisticated proteins, which are only useful in membranes impermeable to protons. Unlike the ATPase, no ion pumps are universally conserved. The pathways for heme and quinone synthesis (the major cofactors of respiratory proteins) also differ in archaea and bacteria, although their distribution is complicated by lateral gene transfer, as is reconstruction of the phylogenetic origins of respiratory ion pumps. But it seems likely that both lipid membranes and active pumping are evolutionarily distinct in archaea and bacteria. It is hard to reconcile these fundamental differences with the universality of the ATPase. On the face of it, LUCA was chemiosmotic, yet did not have a modern phospholipid membrane or active ion pumps.

According to some authors “Phylogenetic relationship” refers to the relative times in the past that species shared common ancestors. 16s rRNA gene, a highly conserved component, is the most widely used gene marker for genus and species identification and taxonomic significance in bacteria and archaea. Also, 18S rRNA is commonly used in fungi for phylogenetics since it has more hypervariable domains than 16S. Common descent describes how, in evolutionary biology, a group of organisms share a most recent common ancestor. There is "massive evidence of common descent of all life on Earth from the last universal common ancestor (LUCA). It has been reported identifying a set of 355 genes from the LUCA, by comparing the genomes of the three domains of life, archaea, bacteria, and eukaryotes. The shikimate pathway (shikimic acid pathway) is a seven step metabolic route used by bacteria, archaea, fungi, algae, some protozoan, and plants for the biosynthesis of folates and aromatic amino acids (phenylalanine, tyrosine, and tryptophan). One of example of common biochemistry are these that all known forms of life are based on the same fundamental biochemical organization: genetic information encoded in DNA, transcribed into RNA, through the effect of protein- and RNA-enzymes, then translated into proteins by (highly similar) ribosomes, with ATP, NADPH and others as energy sources. Analysis of small sequence differences in widely shared substances such as cytochrome c further supports universal common descent. Some 23 proteins are found in all organisms, serving as enzymes carrying out core functions like DNA replication. The fact that only one such set of enzymes exists is convincing evidence of a single ancestry. 6,331 genes common to all living animals have been identified; these may have arisen from a single common ancestor that lived 650 million years ago in the Precambrian. The genetic code (the "translation table" according to which DNA information is translated into amino acids, and hence proteins) is nearly identical for all known lifeforms, from bacteria and archaea to animals and

plants. The universality of this code is generally regarded by biologists as definitive evidence in favor of universal common descent. Fungi and bacteria could have contributed to the phenylpropanoid pathway in ancestral land plants for the synthesis of flavonoids and lignin through horizontal gene transfer. Analysis of DNA sequences suggests that horizontal gene transfer has occurred within eukaryotes from the chloroplast and mitochondrial genomes to the nuclear genome.

RESULT AND CONCLUSION

Horizantal gene transfer during which genes are inserted into a genome by viruses, plasmids, and other foreign agents at example of archaea and bacteria cells had been served a more important role in the formation of substrate - substance basis, leading to origin of species during bioevolutionary time, also leading to further creation of NCM medicine and integration of Traditional and Modern medicines, which lasted from October 06 was day (one day is equal to 42 million years) - 3,6 bya years ago until December 31-1:00 a.m(40 mya) first monkeys, 9:00 p.m (5-6 mya) first hominins, 10:30 p.m (2,5 mya) - first stone tools, 11:22 p.m (0,5 mya) - first use of fire, 11:59 p.m (30 000 ya) - Cave paintings, 11:59:35 p.m (12 000 ya)-farming,11:59:55 p.m (2 000 ya)-common era begins, 11:59:59 p.m (500 ya)-Renaissance. What about general features of bioevolutional events happened in the October 06, 3,6 bya years ago was the early forms of life establishment in the form of Archea owing to natural geochemically sustained proton gradients of LUCA existed in the geochemical origin - hydrothermal vent of this time, giving the fundaments of following appearance of Bacteria, facilitating ecological spread and divergence by Horizantal gene transfer during which genes are inserted into a genome by viruses, plasmids, and other foreign agents at example of archaea and bacteria. The formation of substrate - substance basis during bioevolutionary time, leading to further creation of scientific ground of NCM medicine and integration of Traditional and Modern medicines within October 06 - 3,6 bya years ago had been conducted owing to transformation - the genetic alteration of a cell resulting from the introduction, uptake and expression of foreign genetic material (DNA or RNA), and transduction - the process in which bacterial DNA is moved from one bacterium to another by a virus (a bacteriophage, or phage) and bacterial conjugation - a process that involves the transfer of DNA via a plasmid from a donor cell to a recombinant recipient cell during cell - to - cell contact, also through virus - like elements encoded by the host that are found in some species. It should be emphasize that in case of ancient cells - as Archaea, the creation of proton gradient as first forms of the basic elements of membrane - redoxy potentials three state line systems - one is unseparable part of the full 9 stepped cycle of proton, electron conductance inside human body, leading to formation of RNA, DNA, ribosome, genetic code by using a sodium - proton antiporter (SPAP) formed by inorganic barrier of geochemical origin - hydrothermal vent. Common general characteristics of last universal common ancestor (LUCA) including three domains of life as the archaea, bacteria, and eukaryotes had proton gradient formation from various sources of donators with corresponding acceptors of electrons because of permanent proton and electron flows. The composition of cell membranes and mechanism of DNA replication have some differences in the the archaea, bacteria, serving the big role in divergency, conditioning the furture formation ofvarious forms of life as Nomember 04 was day 2,4 bya years ago, free oxygen, Nomember 14 was day 2,0 bya years ago, complex single cells, Nomember 21 was day 1,7 bya years ago, evidence of multicellular organisms, December 08 - sexual reproduction (1 bya), December 15 – land fungi and plants (700 mya), December 17 – First soft bodied animals (590 mya), December 19 – First vertebrates - Cambrian explosion (530 mya), December 20 – first land plants (470 mya), December 21 – Fish, complex land plants and land animals (425 mya), December 22 – Insects (400 mya), December 23 – Winged Insects, reptiles (350 mya), December 25 – Mammal-like reptiles (256 mya), December 26 – Dinosaurs (235 mya), True animals (220 mya), December 28 – Birds (150 mya), December 29 – Flowering plants (100 mya), December 30 – First definite primates (55 mya), December 31-1:00 a.m (40 mya) first monkeys, 9:00 p.m(5-6 mya) first hominins.

Accordind to the more appropriate model (Sojo *et al.,* 2014), a early cell as Archea of this early evolutionary time with a semi-permeable membrane sits at the interface between an alkaline and an acidic fluid. The fluids are continuously replenished and otherwise separated by an inorganic barrier. Hydroxide ions (OH^-) can flow into the cell from the alkaline side by simple diffusion across the membrane, with protons (H^+) entering in a similar manner from the acidic side. Other ions (Na^+, K^+, Cl^-, not shown) diffuse similarly, as a function of their permeability, charge, and respective internal and external concentrations on each side. Inside the protocell, H^+ and OH^- can neutralize into water, or leave towards either side. Internal pH thus depends on the water equilibrium and relative influxes of each ion. A protein capable of exploiting the natural proton gradient sits on the acidic side, allowing energy assimilation via ATP production, or carbon assimilation via CO_2 fixation. The authors hypothesize that a sodium-proton antiporter (SPAP) provided the first step towards modern membranes. SPAP increases the free energy available from natural proton gradients by ~60%, enabling survival in 50-fold lower gradients, thereby facilitating ecological spread and divergence. In sight of hypothesis that natural proton gradients could drive carbon and energy metabolism in LUCA, in the absence of active ion pumps, faces a serious drawback. Because fluids are electrically balanced, the transfer of H^+ ions down a concentration gradient, from an acid solution into a cell, transfers positive charge into the cell, generating a membrane potential that opposes further influx. The system swiftly reaches equilibrium, in which electrical charges and concentration differences are offset (Sojo V, Pomiankowski A, Lane N, 2014) Equilibrium is death: natural proton gradients could only drive carbon and energy metabolism in LUCA. Sojo *et al.* 2014 assume that the external pH does not change on either side of the cell, as external fluids are replenished by continuous flow from large reservoirs as hydrothermal fluids or the ocean, this belong to October 06 was day (one day is equal to 42 million years) - 3,6 bya years, when life established, first fossils. According to Sojo *et al.* (2014) membrane bioenergetics are universal, yet the phospholipid membranes of archaea and bacteria the deepest branches in the tree of life are fundamentally different. This deep divergence in membrane chemistry is reflected in other stark differences between the two domains, including ion pumping and DNA replication. The analysis shows that such gradients can power carbon and energy metabolism, but only in leaky cells with a proton permeability equivalent to fatty acid vesicles. Sojo *et al.* (2014) had been demonstrated that reconstructing the traits of the last universal common ancestor (LUCA) requires constraining the relationships between the three domains of life, the archaea, bacteria, and eukaryotes. Archaea and

bacteria share core biochemistry, including the genetic code, transcription machinery, and ribosomal translation, but differ for unknown reasons in fundamental traits including cell membrane and cell wall, glycolysis, ion pumping, and even DNA replication. The differences in membrane lipids may be the key to this major unsolved problem in biology. Phospholipid side chains are typically isoprenoids in archaea and fatty acids in bacteria [15]. While this could reflect adaptive evolution, archaea and bacteria also differ in the stereochemistry of the glycerol-phosphate headgroup Archaeal lipids have an **sn**-glycerol-1-phosphate (G1P) headgroup, while bacteria use the mirror structure **sn**-glycerol-3-phosphate (G3P). There is no persuasive selective explanation for these opposite stereochemistries. The enzymes involved, glycerol-1-phosphate-dehydrogenase (G1PDH) in archaea and glycerol-3-phosphate-dehydrogenase (G3PDH) in bacteria. Protons enter the cell through membrane proteins, and directly through the lipid phase of the membrane (Sojo V, Pomiankowski A, Lane N, 2014) and the overall rate of proton influx depends on the difference in proton concentration and electrical charge between the outside and inside of the cell membranesit is existed more close relationship between the proton permeability and the lipid phase of the membrane, and the rate of loss of protons from inside, also it is existed mutual dependence between the steady-state proton concentration inside the cell relative to the outside, giving the free energy ($-\Delta G$) available to drive carbon and energy metabolism including the bioenergetic route map leading from a leaky LUCA dependent on natural proton gradients, to the first archaea and bacteria with highly distinct ion-tight phospholipid membranes.

According to A brief evolutionary time table - (one day is equal to 42 million years) September 02 -formation of solar system, September 14-4,5 bya yeaers ago-eartth formed, October 06 was day (one day is equal to 42 million years) -3,6 bya years ago, life established, first fossils), October 27 was day -2,7 bya years ago, photosynthesis, Nomember 04 was day 2,4 bya years ago, free oxygen, Nomember 14 was day 2,0 bya years ago, complex single cells, Nomember 21 was day 1,7 bya years ago, evidence of multicellular organisms, December 08 - sexual reproduction (1 bya), December 15 – land fungi and plants (700 mya), December 17 – First soft bodied animals (590 mya), December 19 – First vertebrates - Cambrian explosion (530 mya), December 20 – first land plants (470 mya), December 21 – Fish,complex land plants and land animals (425 mya), December 22 – Insects (400 mya), December 23 – Winged Insects, reptiles (350 mya), December 25 – Mammal- like reptiles (256 mya), December 26 – Dinosaurs (235 mya), True animals (220 mya), December 28 – Birds (150 mya), December 29 – Flowering plants (100 mya), December 30 – First definite primates (55 mya), December 31-1:00 a.m(40 mya) first monkeys, 9:00 p.m(5-6 mya) first hominins, 10:30 p.m(2,5 mya)-first stone tools, 11:22 p.m (0,5 mya)-first use of fire, 11:59 p.m (30 000 ya) - Cave paintings, 11:59:35 p.m (12 000 ya)-farming, 11:59:55 p.m (2 000 ya)-common era begins, 11:59:59 p.m (500 ya)-Renaissance. Such bioevolutionary based chronology have been confirmed that in n the time interval as 11:59:55 p.m (2 000 ya) - common era begins, 11:59:59 p.m (500 ya) -Renaissance according to A brief evolutionary time table - (one day is equal : 00 a.m(40 mya) first monkeys, 9:00 p.m (5-6 mya) first hominins, 10:30 p.m (2,5 mya) -first stone tools, 11:22 p.m (0,5 mya) - first use of fire, 11:59 p.m (30 000 ya)-Cave paintings, 11:59:35 p.m (12 000 ya) - farming had appeared the abstract triple theory of rLung, Mkhris, Badgan 3000 years ago in Tibetian medicine, when cognitive function of humans was able to code these by abstract three notions, which had been reflected the membrane - redoxy potentials three state line systems as one is unseparable part of the full 9 stepped cycle of proton, electron conductance inside human body, leading to formation of RNA, DNA, ribosome, genetic code.

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In research attempts to find the bioevolutionary time of formation of substrate - substance basis leading to further creation of NCM medicine and integration of Traditional and Modern medicines we have been usedthe comparative - differentative approach as “substance - external patterns - abstraction”, which allowed to us distinguish that, from all theories of Traditional and Modern medicines, what is substance, what are external patterns, what is abstraction. By us have been established that the day of formation of substrate - substance basis leading to further creation of NCM medicine after 3,59 bya years of these historical events and integration of Traditional and Modern medicines is October 06 (3,6 bya, life established, first fossils) - because in the interval of this day, which lasted 42 million years, had been created the basic elements of membrane - redoxy potentials three state line systems as one is unseparable part of the full 9 stepped cycle of

Figure 1. The full 9 stepped cycle of proton, electron conductance

proton, electron conductance inside human body, leading to formation of RNA, DNA, ribosome, genetic code. The scientific evidence of forming of substrate - substance basis leading to further creation of NCM medicine and integration of Traditional and Modern medicines is October 06 (3,6 bya, life established, first fossils) are follows as the biochemical capacity to use water as the source for electrons in photosynthesis evolved once, in a common ancestor of extant cyanobacteria. The geological record indicates that this transforming event took place early in our planet's history, at least 2450-2320 million years ago (Ma), and possibly much earlier. Light is captured by antenna complexes and transferred to two large bio-solar systems, photosystem I and II, which catalyze the transmembrane charge separation. This drives the photosynthetic process and provides the energy for production of the high - energy substrate ATP and reduced hydrogen in the form of NADPH. The photosystems are functionally coupled by the cytochrome b6f complex, the membrane intrinsic plastoquinone pool and lumenal electron carriers. The reactions of the electron transport chain lead to an electrochemical proton gradient, which drives synthesis of ATP by the molecular motor, the ATP synthase. Thylakoid membranes are the site of the light - reactions of photosynthesis, and they are crucial to the photosynthetic lifestyle of cyanobacteria. Genome sequencing has provided a large amount of information on the genetic basis of nitrogen metabolism and its control in different cyanobacteria. 2-oxoglutarate has turned out to be the central signalling molecule reflecting the carbon/nitrogen balance of cyanobacteria. In such way by us established that the first day of creation of integration of Traditional and Modern Medicine and foundation of NCM medicine was 06 October - 3,6 bya-life formed, first fossils according (Biological anthropology, p.120) to a Brief Evolutionary timetable (one day is equal to 40 million years), because when formed the RNA able to replicate itself act as a code for the synthesis of proteins and appeared the three states of membrane structures with electron, proton transport systems related to membrane structures, three state of redoxy potential line system - the biochemical capacity to use water as the source for electrons in photosynthesis evolved once, in a common ancestor of extant cyanobacteria. The geological record indicates that this transforming event took place early in our planet's history, at least 2450 - 2320 million years ago (Ma), and possibly much earlier. Light is captured by antenna complexes and transferred to two large bio-solar systems, photosystem I and II, which catalyze the transmembrane charge separation. This drives the photosynthetic process and provides the energy for production of the high-energy substrate ATP and reduced hydrogen in the form of NADPH. The photosystems are functionally coupled by the cytochrome b_6f complex, the membrane intrinsic plastoquinone pool and lumenal electron carriers.

The membrane - redoxy potentials three state line systems formed during October 06 was day (one day is equal to 42 million years) - 3,6 bya years agoas one is unseparable part of the full 9 stepped cycle of proton, electron conductance inside human body, leading to formation of RNA, DNA, ribosome, genetic code had been coded 3000 years ago had been coded by abstract triple code as Khii, Shar, Badgan (K.S.B) in Traditional medicine, when intellectual capacity of humans was developed in high level to find the triple code as (K.S.B).

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