

# **Chapter 1**

An Actinide Dependent Shadow Biosphere of  
Archaea and Viroids and Its Messenger Digoxin  
- Role in Schizophrenia, Autism and  
Seizure Disorder

## Introduction

Global warming induces a genomic change in humans. Global warming induces endosymbiotic archaeal and RNA viroidal growth. The porphyrins form a template for the formation of RNA viroids, DNA viroids, prions, isoprenoids and polysaccharides. They can symbiose together to form primitive archaea. The archaea can further induce HIF alpha, aldose reductase and fructolysis resulting in further porphyrinogenesis and archaeal self-replication. The primitive archaeal DNA is integrated along with RNA viroids which are converted to their corresponding DNA by the action of redox stress induced HERV reverse transcriptase into the human genome by the redox stress induced HERV integrase. The archaeal DNA sequences that are integrated into the human genome forms endogenous archaeal human genomic sequences akin to HERV sequences and can function as jumping genes regulating genomic DNA flexibility. The integrated endogenous genomic archaeal sequences can get expressed in the presence of redox stress forming endosymbiotic archaeal particles which can function as a new organelle called the archaeons. The archaeon can express the fructolytic pathway constituting an organelle called the fructosome, cholesterol catabolic pathway and digoxin synthetic forming an organelle called the steroidelle, the shikimic acid pathway forming an organelle called the neurotransminoid, antioxidant vitamin E and vitamin C synthetic organelle called the vitaminocyte as well as the glycosaminoglycan synthetic organelle called glycosaminoglycoid. The archaeon secreting RNA viroids is called the viroidelle.

The endosymbiotic actinidic archaea forms the basis of life and can be considered as the third element in the cell. It regulates the cell, the neuro-immune-endocrine system and the conscious / unconscious brain. The endosymbiotic actinidic archaea can be called as the elixir of life. A definite

population of endosymbiotic actinidic archaea is required for the existence and survival of life. A higher density of endosymbiotic actinidic archaeal population can lead to human disease. Thus actinidic archaea are important for survival of human life and can be considered as crucial to it. Symbiosis by actinidic archaea is the basis of evolution of humans and primates. The increase in endosymbiotic archaeal growth can lead to the induction of homo neanderthalis. This endosymbiotic archaea induced neanderthalisation of the species leads to human disease like metabolic syndrome X, neurodegenerations, schizophrenia and autism, autoimmune disease and cancer. The reduction in endosymbiotic archaeal growth by a high fibre, high medium chain triglyceride and legume protein ketogenic diet, antibiotics from higher plants like *Curcuma longa*, *Embllica officianalis*, *Allium sativum*, *Withania somnifera*, *Moringa pterygosperma* and *Zingiber officianalis* and transplantation of colonic microflora from normal homo sapien population can lead to deneanderthalisation of species and treatment of the above mentioned diseased states. The colonic microflora of neanderthalised diseased states like metabolic syndrome X, neurodegenerations, schizophrenia and autism, autoimmune disease and cancer when transferred to the normal homo sapien species leads to generation and induction of homo neanderthalis. Thus primate and human evolution is symbiotic event which can be induced the modulating symbiotic archaeal growth. Human populations can be divided into matrilineal Neanderthal population in South Indian Dravidians, Celts, Basques, Jews and Berbers and the Cro-Magnon population seen in Africa and Europe. The symbiotic archaeal colonization decides which species - Neanderthal or Cro-Magnon to which the society belongs to. It is tempting to postulate symbiotic microflora and archaea determining the family behavior and traits as well as societal and caste behavior and traits. The cell has been postulated by Margulis to be a symbiotic association of bacteria and viruses. Similarly, the

family, the caste, the community, nationalities and the species itself is determined by archaeal and other bacterial symbiosis.

Symbiosis by microorganisms especially archaea drives the evolution of the species. In such a case symbiosis can be induced by transfer of microflora symbionts and evolution induced. Endosymbiosis by archaea as well as archaeal symbionts in the gut can modulate the genotype, the phenotype, the social class and the racial group of the individual. The symbiotic archaea can have horizontal and vertical transmission. Endosymbiotic archaeal growth leads to neanderthalisation of the species. The neanderthalised species is matrilineal society and includes the Dravidians, the Celts, the Basques and the Berbers. The inhibition of the endosymbiotic archaeal growth leads to evolution of the homo sapiens. This includes the Africans, Aryan invaders of North India and the Aryan derived European population. Symbiosis mediated evolution depends on the gut flora and the diet. This has been demonstrated in the *drosophila pseudoobscura*. The *drosophila* mates only with other individuals eating the same diet. When the *drosophila* gut microflora is altered by feeding antibiotics they mate with other individuals eating different diets. The diet consumed by the *drosophila* regulates its gut microflora and mating habits. The combination of the human genome and the symbiotic microbial genome is called the hologenome. The hologenome especially its symbiotic microbial component drives human evolution as well as animal evolution. The evolutionary distance between species of wasp depends on the gut microflora. The human gut microflora regulates the endocrine, genetic and neuronal systems. Humans and primate evolution depends on endosymbiotic archaea and gut microflora. The endosymbiotic archaeal growth determines the racial differences between the matrilineal Harappan / Dravidian societies and the patriarchal Aryan society. The matrilineal Harappan / Dravidian society was neanderthalic and had

increased endosymbiotic archaeal growth. Endosymbiotic archaeal growth and neanderthalisation can lead to autoimmune disease, metabolic syndrome X, neurodegeneration, cancer, autism and schizophrenia. The Neanderthal gut flora and endosymbiotic archaea was determined by the non vegetarian ketogenic high fat high protein diet consumed by them in the Eurasian steppes. The homo sapiens including the classical Aryan tribes and African ate a high fibre diet and had lower archaeal growth both endosymbiotic and gut. The dietary fibre intake determines the microbial diversity of the gut. The high fibre intake is associated with increased generation of short chain fatty acids - butyric acid by the gut flora. Butyrate is a HDAC inhibitor and leads to increased generation and incorporation of endogenous retroviral sequences. The high dietary fibre intake related increased HERV sequences leads to increased synaptic connectivity and a dominant frontal cortex as seen in homo sapien species. The neanderthalic species consume a ketogenic non vegetarian high fat high protein low fibre diet. This leads to decreased generation of endogenous HERV sequences and reduced genomic flexibility in neanderthalic species. This produces smaller cerebral cortex and a dominant cerebellar cortex in the neanderthalic brain. The homo neanderthalic species by the low dietary fibre intake starve their microbial self. This leads to increased endosymbiotic and gut archaeal growth. The mucous membrane lining the gut becomes thinned out as the gut bacteria eats up the mucous lining of the gut. This results in leakage of endotoxin and archaea from the gut to the blood breaching the barrier and produces a chronic immunostimulatory inflammatory state which forms the basis of autoimmune disease, metabolic syndrome, neurodegeneration, oncogenic and psychiatric disorders. The Neanderthal species eat a low fibre diet and have a deficiency of microbiota accessed carbohydrate generating short chain fatty acid. There is a deficiency of butyrate generated in the gut from the dietary fibre which can produce suppression of the chronic inflammatory process. The Neanderthals

have got the fermentation by-product deficiency syndrome. The induction of neanderthalic species depends on the low fibre intake induced high archaeal density endosymbiotic and the gut microflora. The homo sapiens species consume a high fibre diet generating large amounts of short chain fatty acid butyrate which inhibits endosymbiotic and gut archaeal growth. The microbial self of the homo sapien species is more diverse than that of the neanderthalic species and the archaeal population density is less. This results in a protection against chronic inflammation and the induction of diseases like autoimmune disease, metabolic syndrome, neurodegeneration, oncogenic and psychiatric disorders. The homo sapien species have a higher intake of dietary fibre contributing to around 40 g/day and a diverse microbial gut flora with less of archaeal population density. The butyrate generated from dietary fibre produces an immunosuppressive state. Thus the symbiotic microflora with less of archaeal density induces a homo sapien species. This can be demonstrated by experimental induction of evolution. A high fibre high MCT diet as well as antibiotics derived from higher plants and fecal microbiota transfer from sapien species can inhibit the Neanderthal metabolonomics and phenotype and induce the evolution of homo sapiens. A low fibre high fat high protein diet as well as fecal microbiota transfer from the Neanderthal species can produce Neanderthal metabolonomics and phenotype inducing the evolution of homo neanderthalis. Transfer of colonic microflora predominantly archaea and modulation of endosymbiotic archaea by a paleo diet and antibiotics from higher plants can lead to interconversion of human species between homo neanderthalis and homo sapiens. The hologenome especially the microbial flora endosymbiotic/gut drives human and animal evolution and can be experimentally induced. Symbiotic microflora drives evolution. Every animal, every human species, different communities, different races and different caste have their signature endosymbiotic and gut microflora which can be transmitted

vertically and horizontally. Thus symbiosis drives human and animal evolution. The colonic and endosymbiotic archaea and other microbes like clostridial clusters determine the species, race, caste, community and personal identity of the individual. The identity of the individual - personal, community, caste, race, nationality and species is determined by the colonic and endosymbiotic archaeal and clostridial clusters. Predominant archaeal symbiosis produces homo neanderthalis and less prominent archaeal symbiosis and dominant clostridial clusters in the gut produces the homo sapien species. Each individual, race, nationality, caste, creed and community have the endosymbiotic and colonic microbiota signature. This colonic and endosymbiotic microbiota signature is transferable by the change of endosymbiotic and colonic microbiota from one group to another. Thus the evolution and identity based on individuality, race, nationality, caste and creed can be induced.

This can be interpreted on the basis of Villarreal hypothesis of group identity and cooperativity of RNA collectives. Archaeal symbiosis in the gut and in the tissue spaces determines speciation of human beings as homo sapiens and homo neanderthalis. The endosymbiotic archaea can secrete RNA viroids and viruses and there is a viroid-archaeal host relationship between the two. A dynamic state of virus lysis and persistence can occur in archaea suggesting that viral addiction can occur in archaea. The RNA viroids in the archaea coordinate their behavior by information exchange, modulation and innovation generating new sequence based content. This occurs due to a phenomenon of symbiosis in contrast to the concept of survival of the fittest. The generation of new RNA viroidal sequences is a result of practical competence of living agents to generate new sequences by symbiosis and sharing. This represents highly productive RNA viroidal quasi-species consortia for the evolution, conservation and plasticity of genomic environments. The behavioural motives of the RNA

are single stem loop structures. They have self folding and group building capabilities depending upon functional needs. The evolution process depends upon what Villareal calls RNA stem loop consortia. The whole entity can function only if participatory groups of RNA viroids can get their function coordinated. There is competent denovo generation of new sequences by cooperative action and not by competition. These RNA viroidal group consortia can contribute to the host identity, group identity and group immunity. The term used for this is RNA viroidal sociological behavior. The RNA viroids can build groups that invade the archaea and compete as a group for limited resources such host genomes. A key behavioural motif is able to integrate a persistent life style into the archaeal colony with the addiction module forming competing viroidal groups that are counter balancing each other together with the archaeal/host immune system. This leads to creation of an identity for the archaeal colony and the homo neanderthalis host. Viroids can kill their host and also colonize their host without disease and protect the host from similar viruses and viroids. Together with lysis and protection we see a viroid colonized host that is both symbiotic and innovative acquiring new competent codes. Thus the viroid-host relationship is a pervasive, ancient force in the origin and evolution of life. Cumulative evolution at the level of RNA viroids is like a ratchet effect used for transmission of cultural memes. This learning accumulates so that every new generation must not repeat all innovative thoughts and techniques. Quasi-species of RNA viroids are cooperative and exclusive of other quasi-species. They have group recognition differentiating self-groups and non-self-groups allowing for quasi-species to promote the emergence of group identity. With group identity via counter related addiction modules two opposing components must be present and work coherently and define the group as a whole. Biological identity is constituted by dynamic interaction of cooperative groups. Virus addiction module is an essential strategy for existence

of life in the virosphere. Viruses are transmissible and can persist in specific host population leading to a form of group immunity / identity since identical but uncolonized host population remains susceptible to a killing action of lytic viruses. In this way we see that viruses are necessary providing opposing functions for addiction (persistence/protection and lytic/killing). Viroids can function as consortia, an essential interacting group and provide a mechanism from which consortial function could emerge in the origin of protobiotic life. Genetic parasites can act as a group (qs-c). But for this group to be coherent they must attain group identity and this is typically via an addiction strategy. Antiviral and proviral system in the archaea will themselves emerge in the host from virus derived information. The archaeal viruses themselves provide the critical function required for antiviral defence. The opposing functions are the basis of addiction modules. Thus the emergence of group identity becomes an essential and early event in the emergence of life. This is coherent to the basically group behavior of RNA viroids in archaea. This group selection and group identity are needed to create information coherence and network formation and to establish a system of communication - code competent interactions. This identity serves as information also for the ones that do not share this identity. This is the beginning of self/non-self differentiating capability. In this way viroids promote the emergence of group identity in archaeal colonies and host humans. The archaeal colony identity depends upon the colonizing set of RNA viroids producing a coherent network that is inclusive opposing functions and favours the persistence of parasite derived new information. On the basis of population-based functions of RNA DNA can be considered as a habitat for consortia RNA. Thus RNA viroids of the archaea are involved in complex multicellular identity. This is called as the Gangen hypothesis by Villarreal. The Gangen describes the emergence of commonly shared code use, group membership and collective living function of RNA

viroids. Communication is a code depended interaction and transmission of infectious code defines the origin of the virosphere. This issue refers to the idea of collective of RNA viroids with inherent toxic and antitoxic features should be able to transmit or communicate these agents and their features to a nearby competing population. It strongly favours the survival of RNA viroidal population with compatible addiction modules that will inhibit agent toxicity and allow persistence of new agents. This is thus the survival of the persistently colonized set which is an inherently symbiotic and consortial process. It also promotes increasing complexity and identity/immunity of the host collective via a new agent colonization, and stable addition. Thus the transmission of RNA agents attains both communication and recognition of group membership. In this way the emergence of the virosphere must had been an early event in the origin of life and group identity. Viruses and viroids are genetic parasites and the most abundant living entities on earth. The virosphere is a network of infectious genetic agents. Evolution, conservation and plasticity of genetic identities are the result of cooperative consortia of RNA viroids that are competent to communicate. Thus the archaeal viroidal consortia can symbiotically share and communicate producing new sequences and give an identity to the archaeal colony. The low fibre diet and extreme temperatures of the Eurasian steppes leads to archaeal multiplication and induction of the homo neanderthalis species. The archaeal colony's characteristics are determined by the cooperative consortia of RNA viroids in the archaea and the archaeal colony identity determines the homo neanderthalis identity. Thus the archaeal colonies with their quasi-species consortia of RNA viroids determine the homo neanderthalis identity. The new sequence generation by the RNA viroidal consortia's symbiotic sharing character contributes to the diversity in the behavior and creativity of the homo neanderthalis population. The archaeal RNA viruses and viroids and the archaeal colonies themselves protect the homo

neanderthalis population from retroviral infections. Thus the homo neanderthalis population is retroviral resistant and the quasi-species consortia of archaea and archaeal viroids gives them a group identity as retroviral resistant. Thus the quasi-species consortia of archaea and RNA viroids give homo neanderthalis colonies their identity and idea of self. The homo neanderthalis is resistant to retroviral infection like the Australian aboriginals and the endogenous retroviral sequences in the Neanderthal genome are limited. This leads to lack of plasticity and dynamicity of the human genome and the cerebral cortex is ill-developed with a dominant impulsive cerebellar cortex in the homo neanderthalis population. This produces the impulsive creative surrealistic spiritual neanderthalic brain. As the extreme of temperature goes off and the ice age ends the archaeal population density also comes down. This also can result from the consumption of a high fibre diet in the African continent. The high fibre diet digested by clostridial clusters in the colon promotes butyrate synthesis and butyrate will induce HDAC inhibition and expression of retroviral sequences in the primate genome. This leads to increase in endogenous retroviral sequences in the human genome, increasing genomic dynamicity and the evolution of complicated cerebral cortex dominant brain with its complex synaptic connectivity in the homo sapiens. This leads onto a logical, commonsensical, pragmatic and practical homo sapiens brain. The homo sapiens due to lack of archaea and the RNA viroids are susceptible retroviral infection. Thus the archaeal colonies and RNA viroidal quasi-species consortia determine the evolution of the human species and the brain networks. Thus extremes of temperature, fibre intake, archaeal colony density, RNA viroidal quasi-species, group identity and retroviral resistance decides on the evolution of homo sapiens and homo neanderthalis as well as the brain networks. The present extremes of temperature and low fibre intake in civilized society can lead to increase in archaeal population densities and quasi-species RNA viroidal

networks generating a new homo neanderthalis in a new neanderthalic anthropocene age as opposed to the present homo sapien anthropocene age. The archaeal population densities and quasi-species RNA viroidal networks determine homo sapien / homo neanderthalis species, racial, caste, community, national, sexual, metabolic, phenotypic, neuronal, psychiatric, psychological, immune, genotypic and individual identity. The archaea secretes the trephone digoxin which can edit the RNA viroids and generate new sequences. Archaeal dipolar magnetite and porphyrins in the setting of digoxin induced membrane sodium potassium ATPas inhibition can produce a pumped phonon system mediated quantal perceptive state and quantal communication in the RNA viroidal symbiotic system generating new sequences by steroidal digoxin enzymatic editing action. This gives rise to archaeal RNA viroidal quasi-species symbiotic diversity and identity to species, race, caste, sex, culture, individual and national identity.

The human brain can be considered as a modified archaeon colony network. The archaeon are eternal and can last for billions of years. The human brain is basically an information storage system. The archaeon has got dipolar magnetite and porphyrins and can function as quantal computer. The archaeal colony with its dipolar magnetite and porphyrin in the setting of archaeal digoxin induced membrane sodium potassium ATPase inhibition can function as a pumped phonon system mediating quantal perception. The archaeon in the brain is capable of information storage at a point in time and space. The experiences and information stored in the archaeon is immortal and eternal. The archaeon can have a wave particle existence and can exist in multiple quantal possible states and can inhabit multiple quantal multiverses. The interaction between information stored in quantal computers in multiple different archaeon systems all over the universe by the quantal interactions

results in eternal existence of information in quantal multiverses. The information in the quantal multiverses can have a particulate existence creating a newer mode by quantal interactions between information stored at multiple points of time. This creates the particulate mythic world of human existence. These are what are called as Samsaras. The mind is uploaded into information in the neuronal archaeal colony network and its quantal computers. The information stored in the archaeal colony network mediated quantal state is eternal and can be considered as a digital version of the brain, a mind downloading technique or whole brain emulation. The archaeal colony network stores the human experiences in an eternal manner and can contribute to biological reincarnation.

The roots of Western civilisational disease can be related to the starvation of the colonic microflora. The colonic microflora depends upon complex carbohydrates derived from dietary fibre. The processed food of high protein, fat and sugars is digested and absorbed in the stomach and small intestine. A very little of it reaches the colon and widespread use of antibiotics in medicine has produced mass extinction of the colonic microflora. The colonic microflora is extremely diverse and the diversity is lost. There are 100 trillion bacteria in the colon belonging to 1200 species. They regulate the immune system by inducing the T-regulatory cells. A high fibre diet contributes to colonic microbiota diversity. Interaction with farm animals like cows and dogs also contributes to the colonic microflora diversity. The typical Western diet of high fat, high protein and sugars decreases the colonic microbiota diversity and increase colonic/endosymbiotic archaea producing methanogenesis. The colonic archaea feed upon the mucous lining of the colon and produces leakage of archaea into the blood and tissue system producing endosymbiotic archaea. This results in a chronic inflammatory state. The high fibre diet of Africans, South

Americans and Indians produces increased colonic microbiota diversity and increase in clostridial clusters generating SCFA in the gut. High fibre diet is protective against metabolic syndrome and diabetes mellitus. Metabolic syndrome is related to degeneration, cancer, neuropsychiatric illness and autoimmune disease. A high fibre diet of upto 40 g/day can be called as a gut diet. The colonic microflora especially the clostridial cluster digests the fibre generating short chain fatty acids which regulates immunity and metabolism. High fibre diet increases the colonic mucus secretion and the thickness of the mucus lining. A high fibre diet produces increase in clostridial clusters and mucous secretion. This produces a strong gut blood barrier and prevents metabolic endotoxemia which produces a chronic inflammatory response. High dietary fibre intake and the diversity of the colonic microflora with prominent SCFA producing clostridial clusters are interrelated. The clostridial clusters metabolise the complex carbohydrate in dietary fibre to short chain fatty acids butyrate, propionate and acetate. They increase the T-regulatory function. A high fibre diet increases the bacteroides and reduces the firmecutes of the colonic microflora. A high fibre diet is associated with a low body-mass index. A low fibre diet produces increase in colonic archaeal growth as well as endosymbiotic tissue and blood archaea. This produces more of methanogenesis rather than short chain fatty acid synthesis contributing to immune activation. A low fibre diet is associated a high body-mass index and chronic systemic inflammation. Germ-free mice show cardiac, pulmonary and liver atrophy. Gut microflora is required for the generation of organ systems. The gut microflora is also required for generation of T-regulatory cells. High fibre intake produces more colonic microbiota diversity and increase in clostridial clusters and fermentation by products like butyrate which suppresses inflammation and increases T-regulatory cells. A low fibre diet produces increase in archaeal growth, methanogenesis, destruction of the mucus lining and leakage of the

colonic archaea producing endosymbiotic tissue and blood archaea. This produces an immune hyperreactivity contributing to the modern plagues of civilization - metabolic syndrome, schizophrenia, autism, cancer, autoimmunity and degenerations. The gut microbiota drives human evolution. The humans don't host the gut microbiota but the gut microbiota host us. The human system forms an elaborate culture laboratory for the propagation and survival of the microbiota. The human system is induced by the microbiota for their survival and growth. The human system exists for the microbiota and not the other way round. The same mechanism holds good in plant systems. Plant started the colonized earth as they started symbiosing with bacteria in the roots systems which can derive nutrients from the soil. Human beings form a mobile culture laboratory for the more effective propagation and survival of the microbiota. The microbiota induces the formation of specialized immune cells called innate lymphoid cells. The innate lymphoid cells will direct the lymphocytes not to attack the beneficial bacteria. Thus the endosymbiotic archaea and the gut archaea induce human, primate and animal evolution to generate structures for them to survive and propagate. The source of endosymbiotic archaea, the third element of life is the colonic archaea that leaks into the tissue spaces and blood systems due to breach in the gut blood barrier. The increase in colonic archaea is due to the starvation of the gut microbiota consequent to a low fibre diet. This results in increase in colonic archaeal growth and destruction of clostridial clusters and bacteroides. The increase colonic archaeal growth in the presence of gut starvation due to low fibre diet eats up the mucus lining and produces breakages in the gut blood barrier. The colonic archaea enters the blood stream and produces endosymbiosis generating endosymbiotic archaea and various new organelle - fructosoids, steroidelle, vitaminocyte, viroidelle, neurotransminoid, porphyrinoids and glycosaminoglycoids.

The increase in endogenous EDLF, a potent inhibitor of membrane  $\text{Na}^+\text{-K}^+$  ATPase, can decrease this enzyme activity. The results showed increased endogenous EDLF synthesis as evidenced by increased HMG CoA reductase activity, which functions as the rate limiting step of the isoprenoid pathway. Studies in our laboratory have demonstrated that EDLF is synthesized by the isoprenoid pathway. The endosymbiotic archaeal sequences in the human genome get expressed by redox stress and osmotic stress of global warming. This results in induction of HIF alpha which will upregulate fructolysis and glycolysis. In the setting of redox stress all glucose gets converted to fructose by the induction of enzymes aldose reductase and sorbitol dehydrogenase. Aldose reductase converts glucose to sorbitol and sorbitol dehydrogenase converts sorbitol to fructose. Since fructose is preferentially phosphorylated by ketohexokinases the cell is depleted of ATP and glucose phosphorylation comes to a halt. Fructose becomes the dominant sugar that is metabolized by fructolysis in expressed archaeal particles in the cell functioning as organelle called fructosoids. The fructose is phosphorylated to fructose 1-phosphate which is acted upon by aldolase B which converts it into glyceraldehyde 3-phosphate and dihydroxy acetone phosphate. Glyceraldehyde 3-phosphate is converted to D 1,3-biphosphoglycerate which is then converted to 3-phosphoglycerate. The 3-phosphoglycerate is converted to 2-phosphoglycerate. 2-phosphoglycerate is converted to phosphoenol pyruvate by the enzyme enolase. Phosphoenol pyruvate is converted to pyruvate by the enzyme pyruvic kinase. The archaeaon induces HIF alpha which upregulates fructolysis and glycolysis but inhibits pyruvate dehydrogenase. The forward metabolism of pyruvate is stopped. The dephosphorylation of phosphoenol pyruvate is inhibited in the setting of pyruvic kinase inhibition. Phosphoenol pyruvate enters the shikimic acid pathway where it is converted to chorismate. The shikimic acid is synthesized by a pathway starting from glyceraldehyde

3-phosphate. Glyceraldehyde 3-phosphate combines with the pentose phosphate pathway metabolite sedoheptulose 7-phosphate which is converted to erythrose 4-phosphate. The pentose phosphate pathway is upregulated in the presence of the suppression of glycolytic pathway. Erythrose 4-phosphate combines with phosphoenol pyruvate to generate shikimic acid. Shikimic acid combines with another molecule of phosphoenol pyruvate to generate chorismate. The chorismate is converted to prephenic acid and then to parahydroxy phenyl pyruvic acid. Parahydroxy phenyl pyruvic acid is converted to tyrosine and tryptophan as well as neuroactive alkaloids. The shikimic acid pathway is structured in expressed archaeon organelle called the neurotransminoid. The fructolytic intermediates glyceraldehydes 3-phosphate and pyruvate are the starting points of the DXP pathway of cholesterol synthesis. Glyceraldehyde 3-phosphate combines with pyruvate to form 1-deoxy D-xylulose phosphate (DOXP) which is then converted to 2-C methyl erythritol phosphate. 2-C methyl erythritol phosphate can be synthesized from erythrose 4-phosphate a metabolite of the shikimic acid pathway. DXP combines with MEP to form isopentenyl pyrophosphate which is converted to cholesterol. Cholesterol is catabolized by archaeal cholesterol oxidases to generate digoxin. The digoxin sugars digitoxose and rhamnose are synthesized by the upregulated pentose phosphate pathway. Glycolytic suppression leads to upregulation of the pentose phosphate pathway. The expressed archaeon organelle concerned with cholesterol catabolism and digoxin synthesis is called the steroidelle. The suppression of glycolysis and stimulation of fructolysis results in upregulation of the hexosamine pathway. Fructose is converted to fructose 6-phosphate by ketohexokinases. The fructose 6-phosphate is converted to glucosamine 6-phosphate by the action of glutamine fructose 6-phosphate amidotransferase (GFAT). Glucosamine 6-phosphate is converted to UDP N-acetyl glucosamine which is then converted to N-acetyl glucosamine and various amino sugars.

UDP glucose is converted to UDP D-glucuronic acid. UDP D-glucuronic acid is converted to glucuronic acid. This forms the uronic acid synthetic pathway. Uronic acids and hexosamines form repeating units of glycosaminoglycans. In the setting of glycolytic suppression and fructolytic metabolism fructolysis leads to increase synthesis of hexosamines and GAG synthesis. The GAG synthesizing archaeaon particles are called the glycosaminoglycoids. The expressed archaeaon particles are capable of synthesizing antioxidant vitamin C and E. The UDP D-glucose is converted to UDP D-glucuronic acid. UDP D-glucuronic acid is converted to D-glucuronic acid. D-glucuronic acid is converted to L-gulonate by enzyme aldoketoreductases. L-gulonate is converted to L-gulonolactone by lactonase. L-gulonolactone is converted to ascorbic acid by the action of archaeal L-gulo oxidase. The vitamin E is synthesized from shikimate which is converted to tyrosine and then to parahydroxy phenyl pyruvic acid. Parahydroxy phenyl pyruvic acid is converted to homogentisate. Homogentisate is converted to 2-methyl 6-phytyl benzoquinone which is converted to alpha tocopherol. 2-methyl 6-phytyl benzoquinone is converted to 2,3-methyl 6-phytyl benzoquinone and gamma tocopherol. Vitamin E can also be synthesized by the DXP pathway. Glyceraldehyde 3-phosphate and pyruvate combined to form 1-deoxy D-xylulose 5-phosphate which is converted to 3-isopentenyl pyrophosphate. 3-isopentenyl pyrophosphate and dimethyl allyl pyrophosphate combined to form 2-methyl 6-phytyl benzoquinone which is converted to tocopherols. The ubiquinone another important membrane antioxidant and part of the mitochondrial electron transport chain is synthesized by the shikimic acid pathway and DXP pathway. The isoprenoid moiety of ubiquinone is contributed from the DXP pathway and the rest of it by tyrosine catabolism. The tyrosine is generated by the shikimic acid pathway. The archaeaon particles concerned with the synthesis of vitamin C, vitamin E and ubiquinone which are all antioxidants are called the vitaminocyte.

The human brain synthesizes an endogenous membrane sodium-potassium ATPase inhibitor digoxin which plays a role in neuro-immuno-endocrine integration and pathogenesis of several neuropsychiatric diseases. Endomyocardial fibrosis (EMF) along with the root wilt disease of coconut is endemic to Kerala with its radioactive actinide beach sands. Actinides like cerium producing intracellular magnesium deficiency due to cerium-magnesium exchange sites in the cell membrane have been implicated in the etiology of EMF.<sup>1</sup> Endogenous digoxin, a steroidal glycoside has also been related to the etiology of EMF due to the intracellular magnesium deficiency it produces.<sup>2</sup> Organisms like phytoplasmas and viroids have also been demonstrated to play a role in the etiology of these diseases.<sup>3, 4</sup> Endogenous digoxin has also been related to the pathogenesis of schizophrenia, autism and primary seizure disorder.<sup>2</sup> The possibility of endogenous digoxin synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered.<sup>5-7</sup> Davies has put forward the concept of a shadow biosphere of organisms with alternate biochemistry present in earth itself.<sup>8</sup> An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states is described.<sup>6</sup>

## Methods

Informed consent of the subjects and the approval of the Ethics committee of the Institute were obtained for the study. The following groups were included in the study: - schizophrenia, autism and primary seizure disorder/primary generalized epilepsy. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline,

(II) same as I+cholesterol substrate, (III) same as II+cerium 0.1 mg/ml, (IV) same as II+ciprofloxacin and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond.<sup>9</sup> Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 °C for 1 hour. The following estimations were carried out: - Cytochrome F420, free RNA, free DNA, muramic acid, polycyclic aromatic hydrocarbon, hydrogen peroxide, dopamine, pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA reductase, digoxin and bile acids.<sup>10-13</sup> Cytochrome F420 was estimated fluorimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). Polycyclic aromatic hydrocarbon was estimated by measuring hydrogen peroxide liberated by using glucose reagent. The statistical analysis was done by ANOVA.

## Results

The parameters checked as indicated above were: - cytochrome F420, free RNA, free DNA, muramic acid, polycyclic aromatic hydrocarbon, hydrogen peroxide, serotonin, pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA reductase, digoxin and bile acids. Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of cerium increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of cerium increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables 1-7 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

**Table 1.** *Effect of cerium and antibiotics on muramic acid and dopamine.*

Group	DOPAMINE % (Increase with Cerium)		DOPAMINE % (Decrease with Doxy)		Muramic acid % change (Increase with Cerium)		Muramic acid % change (Decrease with Doxy+Cipro)	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
Normal	4.41	0.15	18.63	0.12	4.34	0.15	18.24	0.37
Schizo	21.88	1.19	66.28	3.60	23.02	1.65	67.61	2.77
Seizure	22.29	1.33	65.38	3.62	22.13	2.14	66.26	3.93
Autism	22.76	2.20	67.63	3.52	22.79	2.20	64.26	6.02
F value	403.394		680.284		348.867		364.999	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

**Table 2.** *Effect of cerium and antibiotics on free DNA and RNA.*

Group	DNA % change (Increase with Cerium)		DNA % change (Decrease with Doxy)		RNA % change (Increase with Cerium)		RNA % change (Decrease with Doxy)	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
Normal	4.37	0.15	18.39	0.38	4.37	0.13	18.38	0.48
Schizo	23.28	1.70	61.41	3.36	23.59	1.83	65.69	3.94
Seizure	23.40	1.51	63.68	4.66	23.08	1.87	65.09	3.48
Autism	22.12	2.44	63.69	5.14	23.33	1.35	66.83	3.27
F value	337.577		356.621		427.828		654.453	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

**Table 3.** *Effect of cerium and antibiotics on HMG CoA reductase and PAH.*

Group	HMG CoA R % change (Increase with Cerium)		HMG CoA R % change (Decrease with Doxy)		PAH % change (Increase with Cerium)		PAH % change (Decrease with Doxy)	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
Normal	4.30	0.20	18.35	0.35	4.45	0.14	18.25	0.72
Schizo	22.91	1.92	61.63	6.79	23.01	1.69	59.49	4.30
Seizure	23.09	1.69	61.62	8.69	22.67	2.29	57.69	5.29
Autism	22.72	1.89	64.51	5.73	22.61	1.42	64.48	6.90
F value	319.332		199.553		391.318		257.996	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

**Table 4.** Effect of cerium and antibiotics on digoxin and bile acids.

Group	Digoxin (ng/ml) (Increase with Cerium)		Digoxin (ng/ml) (Decrease with Doxy+Cipro)		Bile acids % change (Increase with Cerium)		Bile acids % change (Decrease with Doxy)	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
Normal	0.11	0.00	0.054	0.003	4.29	0.18	18.15	0.58
Schizo	0.55	0.06	0.219	0.043	23.20	1.87	57.04	4.27
Seizure	0.51	0.05	0.199	0.027	22.61	2.22	66.62	4.99
Autism	0.53	0.08	0.205	0.041	22.21	2.04	63.84	6.16
F value	135.116		71.706		290.441		203.651	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

**Table 5.** Effect of cerium and antibiotics on pyruvate and hexokinase.

Group	Pyruvate % change (Increase with Cerium)		Pyruvate % change (Decrease with Doxy)		Hexokinase % change (Increase with Cerium)		Hexokinase % change (Decrease with Doxy)	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
Normal	4.34	0.21	18.43	0.82	4.21	0.16	18.56	0.76
Schizo	20.99	1.46	61.23	9.73	23.01	2.61	65.87	5.27
Seizure	20.94	1.54	62.76	8.52	23.33	1.79	62.50	5.56
Autism	21.91	1.71	58.45	6.66	22.88	1.87	65.45	5.08
F value	321.255		115.242		292.065		317.966	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

**Table 6.** Effect of cerium and antibiotics on hydrogen peroxide and delta amino levulinic acid.

Group	H <sub>2</sub> O <sub>2</sub> % (Increase with Cerium)		H <sub>2</sub> O <sub>2</sub> % (Decrease with Doxy)		ALA % (Increase with Cerium)		ALA % (Decrease with Doxy)	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
Normal	4.43	0.19	18.13	0.63	4.40	0.10	18.48	0.39
Schizo	22.50	1.66	60.21	7.42	22.52	1.90	66.39	4.20
Seizure	23.81	1.19	61.08	7.38	22.83	1.90	67.23	3.45
Autism	23.52	1.49	63.24	7.36	23.20	1.57	66.65	4.26
F value	380.721		171.228		372.716		556.411	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

**Table 7.** Effect of cerium and antibiotics on ATP synthase and cytochrome F420.

Group	ATP synthase % (Increase with Cerium)		ATP synthase % (Decrease with Doxy)		CYT F420 % (Increase with Cerium)		CYT F420 % (Decrease with Doxy)	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
Normal	4.40	0.11	18.78	0.11	4.48	0.15	18.24	0.66
Schizo	23.67	1.42	67.39	3.13	23.24	2.01	58.72	7.08
Seizure	23.09	1.90	66.15	4.09	23.46	1.87	59.27	8.86
Autism	22.60	1.64	66.86	4.21	21.68	1.90	57.93	9.64
F value	449.503		673.081		306.749		130.054	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

**Table 8**

	Serum fructose		Serum fructokinase		Aldolase B		Total GAG	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
Normal	2.50	0.195	8.50	0.405	3.50	1.304	3.50	0.707
Schizo	31.14	4.446	22.19	2.634	11.63	3.081	21.50	1.714
Autism	28.66	5.089	24.09	2.146	12.30	1.621	22.60	3.054
Bipolar	29.88	5.150	22.29	1.641	10.87	1.895	23.47	2.878
F value	17.373		13.973		13.903		21.081	
p value	< 0.01		< 0.01		< 0.01		< 0.01	

**Table 9**

	Total TG		Serum ATP levels		Uric acid		Anti-aldolase	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
Normal	124.00	3.688	2.50	0.405	5.70	0.369	7.50	1.704
Schizo	244.00	31.383	0.72	0.102	8.65	0.701	1.35	0.319
Autism	284.30	19.743	0.87	0.072	8.14	0.538	1.35	0.218
Bipolar	289.89	23.406	0.74	0.115	9.59	0.783	1.80	0.402
F value	16.378		59.169		14.166		55.173	
p value	< 0.01		< 0.01		< 0.01		< 0.01	

**Table 10**

	Anti-enolase		Anti-pyruvatekinase		Anti-GAPDH	
	Mean	±SD	Mean	±SD	Mean	±SD
Normal	1.50	0.358	50.40	5.960	5.20	0.363
Schizo	0.40	0.142	22.02	11.954	1.31	0.235
Autism	0.20	0.060	19.27	2.201	1.20	0.205
Bipolar	0.39	0.124	18.93	6.447	1.78	0.355
F value	14.091		21.073		58.769	
p value	< 0.01		< 0.01		< 0.01	

## Discussion

### Archaeal Cholesterol Catabolism in Relation to Psychiatric Disease

The archaeon steroidelle DXP pathway and the upregulated pentose phosphate pathway contribute to digoxin synthesis. There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source.<sup>14, 15</sup> The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by cerium induced increase in enzyme activities.<sup>16</sup> There was also an increase in archaeal HMG CoA reductase activity indicating increased cholesterol synthesis by the archaeal mevalonate pathway. The archaeal beta hydroxyl steroid dehydrogenase activity indicating digoxin synthesis and archaeal cholesterol hydroxylase activity indicating bile acid synthesis were increased.<sup>7</sup> The archaeal cholesterol oxidase activity was increased resulting in generation of pyruvate and hydrogen peroxide.<sup>15</sup> The pyruvate gets converted to glutamate and ammonia by the GABA shunt pathway. The archaeal aromatization of cholesterol generating PAH, serotonin and dopamine was also detected.<sup>17</sup> The archaeal glycolytic hexokinase activity and archaeal extracellular ATP synthase

activity were increased. The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms.<sup>18</sup>

## **Archaeal-Viroidal Human Genomic Sequences and Psychiatric Disease**

There was an increase in free RNA indicating self replicating RNA viroids and free DNA indicating generation of viroid complementary DNA strands by archaeal reverse transcriptase activity. The actinides modulate RNA folding and catalyse its ribozymal action. Digoxin can cut and paste the viroidal strands by modulating RNA splicing generating RNA viroidal diversity. The viroids are evolutionarily escaped archaeal group I introns which have retrotransposition and self splicing qualities.<sup>19</sup> Archaeal pyruvate can produce histone deacetylase inhibition resulting in endogenous retroviral (HERV) reverse transcriptase and integrase expression. This can integrate the RNA viroidal complementary DNA into the noncoding region of eukaryotic noncoding DNA using HERV integrase as has been described for borna and ebola viruses.<sup>20</sup> The noncoding DNA is lengthened by integrating RNA viroidal complementary DNA with the integration going on as a continuing event. The archaea genome can also get integrated into human genome using integrase as has been described for trypanosomes.<sup>21</sup> The integrated viroids and archaea can undergo vertical transmission and can exist as genomic parasites.<sup>20, 21</sup> This increases the length and alters the grammar of the noncoding region producing memes or memory of acquired characters.<sup>22</sup> The viroidal complementary DNA can function as jumping genes producing a dynamic genome important in storage of synaptic information, HLA gene expression and neurodevelopmental gene expression. The alteration in DNA sequences produced by viroidal complementary DNA jumping genes can lead onto schizophrenia and primary seizure disorder. The RNA viroids can regulate mRNA function by RNA interference.<sup>19</sup> The

phenomena of RNA interference can modulate T-cell and B-cell function, neuronal transmission and euchromatin / heterochromatin expression. The RNA viroid induced mRNA interference can modulate dopaminergic, glutamatergic and serotonergic synaptic transmission contributing to the pathogenesis of schizophrenia and primary seizure disorder.

The presence of muramic acid, HMG CoA reductase and cholesterol oxidase activity inhibited by antibiotics indicates the presence of bacteria with mevalonate pathway. The bacterial with mevalonate pathway include streptococcus, staphylococcus, actinomycetes, listeria, coxiella and borrelia.<sup>23</sup> The bacteria and archaea with mevalonate pathway and cholesterol catabolism had a evolutionarily advantage and constitutes the isoprenoidal clade organism with the archaea evolving into mevalonate pathway gram positive and gram negative organism through horizontal gene transfer of viroidal and virus genes.<sup>24</sup> The isoprenoidal clade prokaryotes develop into other groups of prokaryotes via viroidal / virus as well as eukaryotic horizontal gene transfer producing bacterial speciation.<sup>25</sup> The RNA viroids and its complementary DNA developed into cholesterol enveloped RNA and DNA viruses like herpes, retrovirus, influenza virus, borna virus, cytomegalo virus and ebstein barr virus by recombining with eukaryotic and human genes resulting in viral speciation. Bacterial and viral species are ill defined and fuzzy with all of them forming one common genetic pool with frequent horizontal gene transfer and recombination. Thus the multi and unicellular eukaryote with its genes serves the purpose of prokaryotic and viral speciation. The multicellular eukaryote developed so that their endosymbiotic archaeal colonies could survive and forage better. The multicellular eukaryotes are like bacterial biofilms. The archaea and bacteria with a mevalonate pathway uses the extracellular RNA viroids and DNA viroids for quorum sensing and in the generation of symbiotic

biofilm like structures which develop into multicellular eukaryotes.<sup>26, 27</sup> The endosymbiotic archaea and bacteria with mevalonate pathway still uses the RNA viroids and DNA viroids for the regulation of multicellular eukaryote. Pollution is induced by the primitive nanoarchaea and mevalonate pathway bacteria synthesized PAH and methane leading on to redox stress. Redox stress leads to sodium potassium ATPase inhibition, inward movement of plasma membrane cholesterol, defective SREBP sensing, increased cholesterol synthesis and nanoarchaeal / mevalonate pathway bacterial growth.<sup>28</sup> Redox stress leads on to viroidal and archaeal multiplication. Redox stress can also lead to HERV reverse transcriptase and integrase expression. The noncoding DNA is formed of integrating RNA viroidal complementary DNA and archaea with the integration going on as a continuing event. The archaeal pox like dsDNA virus forms evolutionarily the nucleus. The integrated viroidal, archaeal and mevalonate pathway bacterial sequences can undergo vertical transmission and can exist as genomic parasites. The genomic integrated archaea, mevalonate pathway bacteria and viroids form a genomic reserve of bacteria and viruses which can recombine with human and eukaryotic genes producing bacterial and viral speciation. Bacteria and viruses have been related to the pathogenesis of schizophrenia and primary seizure disorder. Borrelia, toxoplasma, chlamydia, mycoplasma, retroviruses, herpes virus, influenza virus and borna virus contribute to the neuropathogenesis of schizophrenia.<sup>29-31</sup> Herpes virus is implicated in the pathogenesis of primary seizure disorder. The change in the length and grammar of the noncoding region produces eukaryotic speciation and individuality.<sup>32</sup> Changes in the length of noncoding region can lead onto disorders of consciousness like schizophrenia and autism.<sup>33</sup> The human endogenous retroviruses and change in the length and grammar of the noncoding region has been described in schizophrenia. The integration of nanoarchaea, mevalonate pathway prokaryotes and viroids in to the eukaryotic

and human genome produces a chimera which can multiply producing biofilm like multicellular structures having a mixed archaeal, viroidal, prokaryotic and eukaryotic characters which is a regression from the multicellular eukaryotic tissue. This results in a new neuronal, metabolic, immune and tissue phenotype leading to human diseases like schizophrenia and primary seizure disorder. The microchimeras formed can lead to polyploidy. Neuronal polyploidy and microchimeras have been described in schizophrenia.

### **Archaeal Digoxin and Disorders of Consciousness**

The archaea and viroids can regulate the nervous system including the NMDA / GABA thalamo-cortico-thalamic pathway mediating conscious perception.<sup>2, 34</sup> NMDA / GABA receptors can be modulated by digoxin induced calcium oscillations resulting in NMDA / glutamic acid decarboxylase (GAD) activity induction, PAH increasing NMDA activity and inducing GAD as well as viroid induced RNA interference modulating NMDA / GABA receptors.<sup>2</sup> The cholesterol ring oxidase generated pyruvate can be converted by the GABA shunt pathway to glutamate and GABA. Increased NMDA transmission has been described in schizophrenia and primary seizure disorder. The dipolar PAH and archaeal magnetite in the setting of digoxin induced sodium potassium ATPase inhibition can produce a pumped phonon system mediated Frohlich model superconducting state inducing quantal perception with nanoarchaeal sensed gravity producing the orchestrated reduction of the quantal possibilities to the macroscopic world.<sup>2, 34</sup> Schizophrenia and autism are described as disorders of consciousness and increased integration of archaea and viroids into the genome can contribute to its neuropathogenesis.

## **Archaeal and Viroidal Sequences in Human Genome, Hemispheric Dominance and Consciousness**

The archaea can regulate limbic lobe transmission with archaeal cholesterol aromatase / ring oxidase generated norepinephrine, dopamine, serotonin and acetyl choline.<sup>17</sup> Increased dopaminergic and serotonergic transmission is important in the pathogenesis of schizophrenia and autism. The higher degree of integration of the archaea into the genome produces increased digoxin synthesis producing right hemispheric dominance and lesser degree producing left hemispheric dominance.<sup>2</sup> Right hemispheric dominance has been described in schizophrenia, autism and primary seizure disorder. The increased integration of archaea into the neuronal genome can produce increased cholesterol oxidase and aromatase mediated monoamine and NMDA transmission producing schizophrenia, autism and primary seizure disorder. The archaeal bile acids are chemically diverse and structurally different from human bile acids. The archaeal bile acids can bind olfactory GPCR receptors and stimulate the limbic lobe producing a sense of social identity. The dominance of archaeal bile acids over human bile acids in stimulating the olfactory GPCR - limbic lobe pathway leads to loss of social identity resulting in autism and schizophrenia.<sup>35</sup> Archaea and RNA viroid can bind the TLR receptor induce NF $\kappa$ B producing immune activation and cytokine TNF alpha secretion. The archaeal DXP and mevalonate pathway metabolites can bind  $\gamma\delta$  TCR and digoxin induced calcium signaling can activate NF $\kappa$ B producing chronic immune activation.<sup>2, 36</sup> The archaea and viroid induced chronic immune activation and generation of superantigens can lead on to autoimmune disease. Immune activation and autoimmunity is important in the pathogenesis of schizophrenia, autism and primary seizure disorder. Autoantibodies have been described in schizophrenia, autism and primary seizure disorder. Archaea, viroids and digoxin can induce the host AKT PI3K, AMPK, HIF alpha and NF $\kappa$ B producing the Warburg metabolic

phenotype.<sup>37</sup> The increased glycolytic hexokinase activity, decrease in blood ATP, leakage of cytochrome C, increase in serum pyruvate and decrease in acetyl CoA indicates the generation of the Warburg phenotype. There is induction of glycolysis, inhibition of PDH activity and mitochondrial dysfunction resulting in inefficient energetics. Mitochondrial dysfunction can lead onto NMDA excitotoxicity and cell death important in schizophrenia, autism and primary seizure disorder. Cholesterol oxidase activity, increased glycolysis related NADPH oxidase activity and mitochondrial dysfunction generates free radicals important in the pathogenesis of schizophrenia, autism and primary seizure disorder. The accumulated pyruvate enters the GABA shunt pathway and is converted to citrate which is acted upon by citrate lyase and converted to acetyl CoA, used for cholesterol synthesis.<sup>37</sup> The pyruvate can be converted to glutamate and ammonia which is oxidised by archaea for energy needs. The increased cholesterol substrate leads to increased archaeal growth and digoxin synthesis leading to metabolic channeling to the mevalonate pathway. Hyperdigoxinemia is important in the pathogenesis of schizophrenia, autism and primary seizure disorder.<sup>2</sup> The Warburg phenotype can contribute to the pathogenesis of schizophrenia and autism by augmenting the bacterial shikimic acid pathway. The upregulated glycolysis consequent to the Warburg phenotype produces phosphoenol pyruvate, a basic substrate for the bacterial shikimic acid pathway which can synthesize monoamines and neuroactive alkaloids. The shikimic acid pathway can generate dopamine and serotonin producing the increased monoaminergic transmission in schizophrenia and autism. The shikimic acid pathway can also synthesize the neuroactive alkaloids strychnine, nicotine, morphine, mescaline and LSD important in the pathogenesis of schizophrenia and autism. Endogenous neuroactive alkaloids have been described in schizophrenia, autism and primary seizure disorder by several workers.<sup>2</sup> The upregulated glycolysis can also contribute to increased

NMDA and GABA transmission in the thalamo-cortico-thalamic pathway. The glycolytic pathway produces phosphoglycerate which is converted to phosphoserine and then serine which activates the NMDA receptor. The glycolytic enzyme glyceraldehyde 3-phosphate dehydrogenase is a GABA receptor kinase and activates GABA transmission. Thus the archaea and viroid induced Warburg phenotype can contribute to the pathogenesis of schizophrenia, autism and primary seizure disorder. The archaeal cholesterol catabolism can deplete the cell membranes of cholesterol resulting in alteration in lipid microdomains and their related neurotransmitter receptor contributing to the altered NMDA, serotonergic and dopaminergic transmission in schizophrenia, autism and primary seizure disorder.

### **Archaeal and Viroidal Sequences in Human Genome - A New Neuronal Phenotype**

In schizophrenia, autism and primary seizure disorder the paper presents data on: (1) Detection of a shadow biosphere of archaea, viroid and mevalonate pathway bacteria, (2) Bacterial cholesterol synthesis and catabolism are important in pathogenesis, and (3) The integration of viroid and archaea into the neuronal genome creates a new phenotype.

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