Chapter 4

Global Warming Induced Endosymbiotic Actinidic Archaeal Synthesis of Bile Acids from Cholesterol Regulates Cellular Function

Introduction

Climate change and related stress leads to increased porphyrin synthesis leading onto porphyrinuria and porphyria. The stimulus for porphyrin synthesis comes from heme deficiency. Heme suppresses ALA synthase. Stress induces heme oxygenase which converts heme to carbon monoxide and bilirubin. Thus heme is depleted from the system. Heme oxygenase is induced by environmental stress. Climatic changes of global warming and ice age can induce heme oxygenase. Heme oxygenase is also induced by EMF pollution of the environment. Thus there is increased porphyrin synthesis from succinyl CoA and glycine. The porphyrins can self organize to form macromolecular structures which can self replicate to form a porphyrin organism.[1] The photon induced transfer of electrons along the macromolecule can lead to light induced ATP synthesis. The porphyrins can form a template on which RNA and DNA can form generating viroids. The porphyrins can also form a template on which prions can form. They all can join together - RNA viroids, DNA viroids, prions - to form primitive archaea. Thus the archaea are capable of self replication on porphyrin templates. The self replicating archaea can sense gravity which gives rise to consciousness. They can also sense the anti-gravity fields which gives rise to the unconscious brain. Thus there can be both self replicating archaea and anti-archaea regulating the conscious and unconscious brain. Thus the climate change stress mediated increased porphyrin synthesis leads to prefrontal cortex atrophy, cerebellar dominance, cerebellar cognitive affective disorder, quantal perception and neanderthalisation of the population. The porphyrions are self replicating supramolecular organisms which forms the precursor template on which the viroids, prions and nanoarchaea originate. Stress induced template directed abiogenesis of porphyrions, prions, viroids and archaea is a

continuous process and can contribute to changes in brain structure and behavior as well as disease process.

Endomyocardial fibrosis along with the root wilt disease of coconut is also endemic to Kerala with its radioactive actinide beach sands. Actinides like rutile as well as organisms like phytoplasmas and viroids have been implicated in the etiology of these diseases.[1-4] Bile acids are considered as steroidal hormones with endocrine, metabolic and neuroregulatory functions. Bile acids has been related to the pathogenesis of schizophrenia, malignancy, metabolic syndrome x, autoimmune disease and neuronal degeneration.[4] The possibility of endogenous bile acid synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered.[5-8] An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states is described.[7, 9]

The induction of the Warburg phenotype results in inhibition of pyruvate dehydrogenase and defective generation of acetyl CoA. Acetyl CoA is the substrate for cholesterol synthesis by the isoprenoid pathway. This results in defective cholesterol synthesis and cholesterol deficient state. Defective cholesterol synthesis and catabolism can lead to cholesterol depletion and low cholesterol levels. Low cholesterol level can result in bile acid deficiency and systemic disease.

Materials and Methods

The following groups were included in the study: - endomyocardial fibrosis, Alzheimer's disease, multiple sclerosis, non-Hodgkin's lymphoma, metabolic syndrome x with cerebrovascular thrombosis and coronary artery disease, schizophrenia, autism, seizure disorder, Creutzfeldt Jakob's disease and

acquired immunodeficiency syndrome. 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+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond.[10] Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37℃ for 1 hour. The following estimations were carried out: - Cytochrome F420 and bile acids.[11-13] Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). Informed consent of the subjects and the approval of the ethics committee were obtained for the study. The statistical analysis was done by ANOVA.

Results

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 rutile increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in table 1 as

percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

Table 1. *Effect of rutile and antibiotics on cytochrome F420 and archaeal bile acids.*

Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)		Bile acids % change (Increase with Rutile)		Bile acids % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.48	0.15	18.24	0.66	4.29	0.18	18.15	0.58
Schizo	23.24	2.01	58.72	7.08	23.20	1.87	57.04	4.27
Seizure	23.46	1.87	59.27	8.86	22.61	2.22	66.62	4.99
AD	23.12	2.00	56.90	6.94	22.12	2.19	62.86	6.28
MS	22.12	1.81	61.33	9.82	21.95	2.11	65.46	5.79
NHL	22.79	2.13	55.90	7.29	22.98	2.19	64.96	5.64
DM	22.59	1.86	57.05	8.45	22.87	2.58	64.51	5.93
AIDS	22.29	1.66	59.02	7.50	22.29	1.47	64.35	5.58
CJD	22.06	1.61	57.81	6.04	23.30	1.88	62.49	7.26
Autism	21.68	1.90	57.93	9.64	22.21	2.04	63.84	6.16
EMF	22.70	1.87	60.46	8.06	23.41	1.41	58.70	7.34
F value	306.749		130.054		290.441		203.651	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Discussion

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source.[6, 14] 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 rutile induced increase in enzyme activities.[15] The archaeal cholesterol hydroxylase activity indicating bile acid synthesis were increased.[8]

The archaeal bile acids are steroidal hormones which can bind GPCR and modulate D2 regulating the conversion of T4 to T3 which activates uncoupling proteins reducing redox stress. Bile acids can activate the transcription factor NRF ½ inducing NQO1, GST, HOI reducing redox stress. Bile acids are neuroprotective and help to prevent neurodegenerative process. Bile acids can bind FXR regulating insulin receptor sensitivity. Bile acid deficiency leads to insulin resistance and metabolic syndrome x. Bile acids can bind PXR inducing the bile acid shunt pathway of cholesterol detoxification.[25] Bile acid deficiency leads to cholesterol toxicity. Bile acid binding to FXR receptor inhibits tissue fibrosis and connective tissue deposition. Bile acid deficiency may play a role in MPS and collagen deposition in EMF, CCP, MNG and mucoid angiopathy. Bile acids can bind macrophage GPCR and VDR producing immunosuppression and inhibiting NFKB. This helps to modulate the archaea and viroid induced chronic immune activation. Bile acid deficiency can contribute to autoimmune disease. 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 and schizophrenia / autism. Bile acids tend to have an inhibitory effect on cell proliferation and prevent malignant transformation.[16]

Archaeal bile acids binding to VDR has an inhibitory effect on cell proliferation. Bile acids thus can modulate cell death and cell proliferation. It can regulate metabolism via modulating mitochondrial uncoupling proteins and via FXR insulin receptor sensitivity. Bile acids can modulate limbic lobe and

brain functions via GPCR receptor and olfactory pathways. Bile acids can regulate immune function via macrophage GPCR and VDR. Archaeal bile acids can produce neuro-immuno-endocrine integration. Archaeal bile acids deficiency can contribute to the pathogenesis of endomyocardial fibrosis, Alzheimer's disease, multiple sclerosis, non-Hodgkin's lymphoma, metabolic syndrome x with cerebrovascular thrombosis and coronary artery disease, schizophrenia, autism, seizure disorder, Creutzfeldt Jakob disease and acquired immunodeficiency syndrome.

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