



Chapter

4

**Archaeon Synthesis of Pah From
Cholesterol Regulates Cell Function**

Introduction

Endomyocardial fibrosis (EMF) along with the root wilt disease of coconut is 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 Polycyclic aromatic hydrocarbons have been related to the pathogenesis of schizophrenia, malignancy, metabolic syndrome x, autoimmune disease and neuronal degeneration.⁴ The possibility of polycyclic aromatic hydrocarbon 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 in the above mentioned disease states is described.^{7, 9} Polycyclic aromatic hydrocarbon synthesized by endosymbiotic archaea can contribute to global warming. Global warming has been related to the changing patterns of disease and infections.

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 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+ciprofloxacin 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 Cholesterol substrate was prepared as described by Richmond.¹⁰ Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 °C for 1 hour. The following estimations were carried out: - Cytochrome F420 and polycyclic aromatic hydrocarbon.¹¹⁻¹³ 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. 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 rutil increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutil 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 PAH.*

| Group | CYT F420% (Increase with Rutile) | | CYT F420% (Decrease with Doxy+Cipro) | | PAH % change (Increase with Rutile) | | PAH % change (Decrease with Doxy+Cipro) | |
|---------|--|------|--|------|---|------|---|------|
| | Mean | ±SD | Mean | ±SD | Mean | ±SD | Mean | ±SD |
| Normal | 4.48 | 0.15 | 18.24 | 0.66 | 4.45 | 0.14 | 18.25 | 0.72 |
| Schizo | 23.24 | 2.01 | 58.72 | 7.08 | 23.01 | 1.69 | 59.49 | 4.30 |
| Seizure | 23.46 | 1.87 | 59.27 | 8.86 | 22.67 | 2.29 | 57.69 | 5.29 |
| AD | 23.12 | 2.00 | 56.90 | 6.94 | 23.26 | 1.53 | 60.91 | 7.59 |
| MS | 22.12 | 1.81 | 61.33 | 9.82 | 22.83 | 1.78 | 59.84 | 7.62 |
| NHL | 22.79 | 2.13 | 55.90 | 7.29 | 22.84 | 1.42 | 66.07 | 3.78 |
| DM | 22.59 | 1.86 | 57.05 | 8.45 | 23.40 | 1.55 | 65.77 | 5.27 |
| AIDS | 22.29 | 1.66 | 59.02 | 7.50 | 23.23 | 1.97 | 65.89 | 5.05 |
| CJD | 22.06 | 1.61 | 57.81 | 6.04 | 23.46 | 1.91 | 61.56 | 4.61 |
| Autism | 21.68 | 1.90 | 57.93 | 9.64 | 22.61 | 1.42 | 64.48 | 6.90 |
| EMF | 22.70 | 1.87 | 60.46 | 8.06 | 23.73 | 1.38 | 65.20 | 6.20 |
| F value | 306.749 | | 130.054 | | 391.318 | | 257.996 | |
| 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 There was also an increase in polycyclic aromatic hydrocarbon synthesis in the system. The PAH synthesis was inhibited by antibiotics and stimulated by addition of cerium. The archaeal endosymbiont can aromatize cholesterol to generate PAH.¹⁶ The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms.¹⁷

Archaeal PAH can intercalate with DNA and RNA modulating their function. PAH intercalation of DNA can produce HERV expression. PAH can induce photon mediated redox stress. The PAH induced redox stress can produce histone deacetylase inhibition resulting in endogenous retroviral (HERV) reverse transcriptase and integrase expression. This can integrate the HERV RNA complementary DNA into the noncoding region of eukaryotic non coding DNA using HERV integrase as has been described for borna and ebola viruses.¹⁹ The noncoding DNA is lengthened by integrating HERV RNA 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.²⁰ The integrated viroids and archaea can undergo vertical transmission and can exist as genomic parasites.¹⁸⁻²⁰ This increases the length and alters the grammar of the noncoding region producing memes or memory of acquired characters as well as eukaryotic speciation and individuality.²¹ The HERV RNA complementary DNA can function as jumping genes producing a dynamic genome important in storage of synaptic information, HLA gene expression and developmental gene expression. The HERV RNA can regulate mRNA function by RNA interference.¹⁸ The phenomena of RNA interference can modulate T cell and B cell function, insulin signalling lipid metabolism, cell growth and differentiation, apoptosis, neuronal transmission and euchromatin/heterochromatin expression. The PAH can also intercalate with RNA modulating its function. The expression of HERV RNA covered with a phospholipid membrane can contribute to the pathogenesis of acquired immunodeficiency syndrome. Archaeal PAH can regulate genomic function. The archaeal PAH intercalating with DNA can induce DNA mutations and oncogene activation contributing to cellular dedifferentiation and proliferation. Archaeal PAH can induce malignant transformation.²²

The archaeal PAH can regulate the nervous system including the NMDA/GABA thalamo-cortico-thalamic pathway mediating conscious perception.^{4, 23} NMDA/GABA receptors can be modulated by PAH increasing NMDA activity and inducing GAD.⁴ 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 state²³ inducing quantal perception with nanoarchaeal sensed gravity producing the orchestrated reduction of the quantal possibilities to the macroscopic world.^{4, 23} Archaeal PAH can bind membranes, proteins and DNA generating exciplexes and biophoton emission. Biophotons generate a quantal state mediating quantal perception. The archaeal PAH induced NMDA excitotoxicity can contribute to the pathogenesis of schizophrenia and autism. Archaeal PAH induced NMDA excitotoxicity can also contribute to cell death and neuronal degeneration.²⁴ Archaeal PAH induced redox stress can also contribute to neuronal degeneration.

Archaeal PAH can induce AHR dependent regulatory T cells (Tregs). The activation of the AHR-Treg pathway suppresses autoimmune disease. PAH by producing redox stress can also generate immune activation. Thus archaeal PAH has a biphasic role in immunoregulation.^{25, 26} Archaeal PAH can generate insulin resistance and contribute to metabolic syndrome x. Archaeal PAH by photo-oxidation generates redox stress contributing to insulin resistance. Small particulate matter or nanoparticles in the blood generated by PAH can produce vasospasm and cardiovascular/ cerebrovascular disease.^{27, 28}

The PAH synthesized by endosymbiotic archaea can contribute to global warming. This may be the main contributory factor for global warming. Archaeal PAH can induce HERV expression and its integration back into the genomic DNA enlarging the noncoding region of the genome. The increase in the length of noncoding region and the differences in it contribute to eukaryotic and primate evolution. It is the increase in noncoding region length that led to

the evolution of primates and humans. Pollution and global warming mediated by archaeal PAH is a method of eukaryotic evolution. Global warming increases the carbon dioxide in the atmosphere and contributes to more archaeal growth. The increase in archaeal growth leads to increased synthesis of PAH and increased global warming. Global warming contributes to evolutionary innovation.

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