

Endosymbiotic Actinidic Archaeal Synthesis of Neurotransmitters by Cholesterol Catabolism Regulates Brain Function

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Abstract

Aims and Objectives: 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 EMF. Bacterial synthesis of neurotransmitters plays a role in quorum sensing and motility. The possibility of endogenous neurotransmitter synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered in EMF and systemic diseases like neuronal degeneration, psychiatric disease, metabolic syndrome x, autoimmune disease and malignancy.

Methodology: 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. The following estimations were carried out:- Cytochrome F420, dopamine, serotonin, noradrenaline, acetyl choline and glutamate.

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 and rutile to the patient's plasma produced the same changes but the extent

of change was more in patient's sera as compared to controls.

Conclusion: Actinidic archaea can synthesize neurotransmitters via cholesterol catabolism. The archaeal neurotransmitters can regulate the brain and autonomic nervous system contributing to neuronal degeneration, psychiatric disease, metabolic syndrome x, autoimmune disease and malignancy.

Key words: Archaea; Actinide; Cholesterol; Neurotransmitters; Disease

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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 EMF^[1,2,3,4]. Bacterial synthesis of neurotransmitters plays a role in quorum sensing and motility. The possibility of endogenous neurotransmitter synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered in EMF and systemic diseases like neuronal degeneration, psychiatric disease, metabolic syndrome x, autoimmune disease and malignancy^[5-8]. An actinide dependent shadow biosphere of archaea in the above mentioned disease states is described^[7,9].

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, dopamine, serotonin, noradrenaline, acetyl choline and glutamate^{[11]-}

^{13]}. Cytochrome F420 was estimated fluorimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). 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 tables 1-3 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 Glutamate

Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)		Glutamate% change (Increase with Rutile)		Glutamate% change (Decrease with Doxy+Cipro)		
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	
Normal	4.48	0.15	18.24	0.66	4.34	0.21	18.43	0.82	
Schizo	23.24	2.01	58.72	7.08	20.99	1.46	61.23	9.73	
Seizure	23.46	1.87	59.27	8.86	20.94	1.54	62.76	8.52	
AD	23.12	2.00	56.90	6.94	22.63	0.88	56.40	8.59	
MS	22.12	1.81	61.33	9.82	21.59	1.23	60.28	9.22	
NHL	22.79	2.13	55.90	7.29	21.19	1.61	58.57	7.47	
DM	22.59	1.86	57.05	8.45	20.67	1.38	58.75	8.12	
AIDS	22.29	1.66	59.02	7.50	21.21	2.36	58.73	8.10	
CJD	22.06	1.61	57.81	6.04	21.07	1.79	63.90	7.13	
Autism	21.68	1.90	57.93	9.64	21.91	1.71	58.45	6.66	
EMF	22.70	1.87	60.46	8.06	22.29	2.05	62.37	5.05	
		F value 306.749 P value < 0.001		F value 130.054 P value < 0.001		F value 321.255 P value < 0.001		F value 115.242 P value < 0.001	

Table 2
Effect of Rutile and Antibiotics on Noradrenaline and Acetyl Choline

Group	Noradrenaline % (Increase with Rutile)		Noradrenaline % (Decrease with Doxy+Cipro)		Acetyl choline % (Increase with Rutile)		Acetyl choline % (Decrease with Doxy+Cipro)	
	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
AD	22.65	2.48	60.19	6.98	23.67	1.68	66.50	3.58
MS	21.14	1.20	60.53	4.70	22.38	1.79	67.10	3.82
NHL	23.35	1.76	59.17	3.33	23.34	1.75	66.80	3.43
DM	23.27	1.53	58.91	6.09	22.87	1.84	66.31	3.68
AIDS	23.32	1.71	63.15	7.62	23.45	1.79	66.32	3.63
CJD	22.86	1.91	63.66	6.88	23.17	1.88	68.53	2.65
Autism	23.52	1.49	63.24	7.36	23.20	1.57	66.65	4.26
EMF	23.29	1.67	60.52	5.38	22.29	2.05	61.91	7.56
F value 380.721		F value 171.228		F value 372.716		F value 556.411		
P value < 0.001		P value < 0.001		P value < 0.001		P value < 0.001		

Table 3
Effect of Rutile and Antibiotics on Dopamine and Serotonin

Group	DOPAMINE % (Increase with Rutile)		DOPAMINE % (Decrease with Doxy+Cipro)		5 HT % change (Increase with Rutile)		5 HT % 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
AD	23.66	1.67	65.97	3.36	23.09	1.81	65.86	4.27
MS	22.92	2.14	67.54	3.65	21.93	2.29	63.70	5.63
NHL	23.81	1.90	66.95	3.67	23.12	1.71	65.12	5.58
DM	24.10	1.61	65.78	4.43	22.73	2.46	65.87	4.35
AIDS	23.43	1.57	66.30	3.57	22.98	1.50	65.13	4.87
CJD	23.70	1.75	68.06	3.52	23.81	1.49	64.89	6.01
Autism	22.76	2.20	67.63	3.52	22.79	2.20	64.26	6.02
EMF	22.28	1.52	64.05	2.79	22.82	1.56	64.61	4.95
F value 403.394		F value 680.284		F value 348.867		F value 364.999		
P value < 0.001		P value < 0.001		P value < 0.001		P value < 0.001		

DISCUSSION

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesise and use cholesterol as a carbon and energy source^[6,14]. The archeal 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 oxidase activity results in generation of pyruvate^[14]. The pyruvate gets converted to glutamate

and GABA by the GABA shunt pathway. The pyruvate generated by cholesterol oxidase activity can also get converted to acetyl CoA and acetyl choline. The archaeal aromatization of cholesterol generating norepinephrine, serotonin and dopamine was also detected^[16]. The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms^[17].

The archaea and viroids can regulate the nervous system including the NMDA/GABA thalamocorticothalamic pathway mediating conscious perception^[4,18]. NMDA/GABA receptors can be modulated by cholesterol catabolism generated glutamate and GABA. The archaea can regulate limbic lobe transmission with archaeal cholesterol aromatase/ring oxidase generated norepinephrine, dopamine, serotonin and acetyl choline^[16]. The increased integration of archaea into the neuronal genome can produce increased cholesterol oxidase and aromatase mediated monoamine and NMDA transmission producing schizophrenia and autism. The archaeal cholesterol catabolism generated glutamate can produce NMDA excitotoxicity producing neuronal degeneration. The archaeal glutamate and GABA synthesis can play a role in neurodegeneration, autism and schizophrenia.

Archaeal cholesterol catabolism generated glutamate and serotonin can produce immune activation and acetyl choline can produce immunosuppression. The balance between the two sets of immunostimulatory and immunosuppressive neurotransmitters can contribute to autoimmune disease. Parasympathetic neuropathy and vagal blockade can lead to autoimmune disease. Immunity is regulated by the vagal reflex. Archaeal cholesterol catabolism generated glutamate and GABA can regulate insulin secretion from the pancreatic beta cells contributing to metabolic syndrome x. Metabolic syndrome x has been attributed to alteration in the sympathetic/parasympathetic balance. There is vagal suppression and sympathetic overactivity. This produces hyperinsulinism, immune activation and metabolic syndrome x. Sympathetic overactivity and vagal blockade can lead to vasospasm, microangiopathy and vascular disease. Sympathetic overactivity and parasympathetic blockade can produce malignant cell proliferation. The Warburg phenotype can be induced by vagal blockade induced immune activation^[19]. Thus the archaeal synthesis of acetyl choline and catecholamines can regulate the sympathetic and parasympathetic nervous system contributing to metabolic syndrome x, autoimmune disease and malignancy.

The archaeal neurotransmitters may control the human nervous system regulating visceral functions and consciousness.

REFERENCES

[1] Hanold, D. & Randies, J. W. (1991). Coconut Cadang-

- Cadang Disease and Its Viroid Agent. *Plant Disease*, 75, 330-335.
- [2] Valiathan, M. S., Somers, K., Kartha, C. C. (1993). *Endomyocardial Fibrosis*. Delhi: Oxford University Press.
- [3] Edwin, B. T. & Mohankumaran, C. (2007). Kerala Wilt Disease Phytoplasma: Phylogenetic Analysis and Identification of a Vector. *Proutista Moesta, Physiological and Molecular Plant Pathology*, 71(1-3), 41-47.
- [4] Kurup, R. & Kurup, P. A. (2009). *Hypothalamic Digoxin, Cerebral Dominance and Brain Function in Health and Diseases*. New York: Nova Science Publishers.
- [5] Eckburg, P. B., Lepp, P. W. & Relman, D. A. (2003). Archaea and Their Potential Role in Human Disease. *Infect Immun*, 71, 591-596.
- [6] Smit A. & Mushegian, A. (2000). Biosynthesis of Isoprenoids via Mevalonate in Archaea: The Lost Pathway. *Genome Res*, 10(10), 1468-84.
- [7] Adam, Z. (2007). Actinides and Life's Origins. *Astrobiology*, 7, 6-10.
- [8] Schoner, W. (2002). Endogenous Cardiac Glycosides, a New Class of Steroid Hormones. *Eur J Biochem*, 269, 2440-2448.
- [9] Davies, P. C. W., Benner, S. A., Cleland, C. E., Lineweaver, C.H., McKay, C.P., Wolfe-Simon, F. (2009). Signatures of a Shadow Biosphere. *Astrobiology*, 10, 241-249.
- [10] Richmond, W. (1973). Preparation and Properties of a Cholesterol Oxidase from Nocardia Species and its Application to the Enzymatic Assay of Total Cholesterol in Serum. *Clin Chem*, 19, 1350-1356.
- [11] Snell, E. D. & Snell, C. T. (1961). *Colorimetric Methods of Analysis* (Vol. 3A). New York: Van Nostrand.
- [12] Glick, D. (1971). *Methods of Biochemical Analysis* (Vol. 5). New York: Interscience Publishers.
- [13] Colowick, Kaplan, N.O. (1955). *Methods in Enzymology* (Vol. 2). New York: Academic Press.
- [14] Van der Geize R., Yam, K., Heuser, T., Wilbrink, M. H., Hara, H., Anderton, M. C.. (2007). A Gene Cluster Encoding Cholesterol Catabolism in a Soil Actinomycete Provides Insight into Mycobacterium Tuberculosis Survival in Macrophages. *Proc Natl Acad Sci USA*, 104(6), 1947-52.
- [15] Francis, A. J. (1998). Biotransformation of Uranium and Other Actinides in Radioactive Wastes. *Journal of Alloys and Compounds*, 271(273), 78-84.
- [16] Probian C., Wülfing, A., Harder, J. (2003). Anaerobic Mineralization of Quaternary Carbon Atoms: Isolation of Denitrifying Bacteria on Pivalic Acid (2,2-Dimethylpropionic acid). *Applied and Environmental Microbiology*, 69(3), 1866-1870.
- [17] Vainshtein M., Suzina, N., Kudryashova, E., Ariskina, E. (2002). New Magnet-Sensitive Structures in Bacterial and Archaeal Cells. *Biol Cell*, 94(1), 29-35.
- [18] Lockwood, M. (1989). *Mind, Brain and the Quantum*. Oxford: B. Blackwell.
- [19] Wallace, D. C. (2005). Mitochondria and Cancer: Warburg Addressed. *Cold Spring Harbor Symposia on Quantitative Biology*, 70, 363-374.