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Bio-Science Research Centre
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Goals: (1) To develop new drugs for the metabolic syndrome based on the concept that it is a disorder of the brain that has its origins in the perinatal period due to sub-optimal metabolism of polyunsaturated fatty acids.

(2) To develop gamma-linolenic acid as a drug for the treatment of human glioma.

(3) To study the interactions between genes and environment in these clinical conditions by using microarrays and SiRNA techniques.

Research Experience: Have been in research for more than 30 years (since 1976). I am well versed with most modern biological research techniques, and also have extensive supervisory experience both at undergraduate and graduate level.

Clinical Experience: I was formerly Professor of Internal Medicine in India for more than 10 years, teaching graduates and specialist candidates in Internal Medicine, Endocrinology, Rheumatology and Diabetology. I have extensive experience in patient care, management of diverse type of clinical conditions and clinical research and trials.

Areas of specialization and interest:

Research: Essential fatty acids, eicosanoids, cytokines, free radicals, nitric oxide, melatonin and their role in various clinical conditions with special interest in angiogenesis and its role in cancer. Liposomal, nano and SiRNA delivery of drugs for cancer and metabolic syndrome.

Clinical: More than 30 years of clinical experience in the areas of Internal Medicine, Endocrinology, Diabetology and Rheumatology, and oncology.

Publications: More than 370 research papers in various journals.

Patents: 5 awarded:

1. Methods for selectively occluding blood supplies to neoplasias US 6,426,367 B1 awarded on July 30, 2002).

2. Method of stabilizing and potentiating the action of anti-angiogenic substances (US 6,380,253 B1 awarded on April 30, 2002).
3. Method of stabilizing and potentiating the action of anti-angiogenic substances (US 6,617,354 awarded on September 9, 2003).
4. Method of stabilizing and potentiating the action of anti-angiogenic substances (US 7,666,910 awarded on February 23, 2010)
5. Method(s) of preventing, arresting, reversing and treatment of atherosclerosis, letter of allowance received.

Another 10 are pending.

Present Position/Title: Professor of Biomedical Engineering and Director
Bio-Science research Centre
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Education: Date of Birth: 28th June 1950

Institution and Location	Degree	Year Rec'd	Field	
Andhra Medical College,	M.B;B.S.	1973	Medicine Surgery, Obstet & Gynec	Visakhapatnam, India
Osmania Medical College,	M.D. (Internal Medicine)	1981	General	Hyderabad, India.
National Academy of Medical Sciences, New Delhi, India.	FAMS	1992	Medicine	

Research and Professional Experience:

1. Senior Research Fellow of ICMR (Indian Council of Medical Research) and CSIR (Council of Scientific and Industrial Research, India) from 1976 to 1981- 6 years.
2. Research Associate of ICMR from 1981-1983 - 3 years - Both positions at Department of Genetics, Osmania University, Hyderabad, India)
3. Scientist, Efamol Research Institute, Kentville, NS, Canada from 1984 to 1986- 2 years.
4. Associate Professor of Clinical Pharmacology and Medical Research and Medicine, Nizam's Institute of Medical Sciences, Hyderabad, India from 1986 to 1989 - 3 years.
5. Professor of Medicine, Nizam's Institute of Medical Sciences, Hyderabad, India from 1990 to August 1996.
6. Professor and Chief, Division of Internal Medicine, Clinical Immunology and Biochemistry, L.V. Prasad Eye Institute, Hyderabad-500034, India from August 1996 to July 1999.

7. EFA Sciences, LLC, Norwood, MA, USA as Chairman & Research Director-August 1999-June2004 (5 years)
8. Research Professor of Surgery, Nutrition, and Physiology SUNY Upstate Medical University Syracuse, NY, USA-2003-2004 (1 and ½ years)
9. Research Director, IKP Centre for Technologies in Public Health (ICTPH), Chennai, India from 1st October 2007 to May 2009 (2 ½ years)

Other academic affiliations:

1. Visiting faculty to the Faculty of Medicine, National University of Singapore since 1991.
2. Visiting Scientist to Flinders University Medical School in 1982.
3. Visiting Faculty to Long Island Jewish Medical Centre, NY, USA in 1992.
4. Visiting Faculty to Oklahoma State University in 1994 for 3 months to work on Monoclonal antibody technology with Prof. John L Sherwood of Department of Plant Pathology.
5. Honorary Professor of Endocrinology and Metabolism, Sri Venkateswara Institute of Medical Sciences (SVIMS), Tirupati, India – 1992-1996.
6. Visiting Professor of Research to SUNY Upstate Medical University, Syracuse, NY from April 2002 to March 2004.
7. Chief Scientific Officer and Adviser to Userspace Corporation, Seattle, WA, USA from 2006-2007 (one year).
8. Visiting Professor to Athens University, Greece-since 2004-current.
9. Honorary Vice-Dean and Research Professor, Caribbean Medical University, Curacao, The Netherlands-from 2007-2008 (6 months).
10. Chairman of Scientific Advisory Committee, Functional Foods Centre, Richardson, TX, USA-from 2006-current.
11. Visiting Faculty to Department of Engineering and Bioinformatics, Andhra University, Visakhapatnam since 2006-2008 (2 years).

Clinical Interests:

Broad Specialty : Internal Medicine

Sub-specialties : Endocrinology and Diabetology, Clinical Immunology including Rheumatology and oncology

Total experience more than 26 years since 1981.

Total Research Experience:

30 years in research since 1976.

Research Interests:

Essential fatty acids, eicosanoids, cytokines, free radicals and melatonin in various disease processes including mutagenesis, carcinogenesis, cancer, diabetes mellitus, essential hypertension, coronary heart disease, peptic ulcer disease and osteoporosis.

Honors and Awards:

1. **Awarded Ramalingaswami Fellowship by Department of Biotechnology of India for research in India from 2008-2013.**
2. **Shakuntala Amirchand** prize of ICMR in Experimental Medicine-1988.
3. Dr. Coelho Memorial Prize of Association Physicians of India in Experimental Medicine-1992.
4. Regional Research Award of Japanese Society of Clinical chemists-1992.
5. Elected as Fellow of the National Academy of Medical Sciences-1992.
6. **Shanti Swaroop Bhatnagar prize in Medical Sciences-1992.**
7. **Elected as** Fellow of the Indian College of Physicians (FICP) in 1993.
8. Bobba Dharma Rao Prize in Medicine, Karnataka Association of Physicians of India, Bangalore-1994.
9. Distinguished Citizen award by Pramukh Swamy Maharaj of Aksharadham, Ahmedabad-1992.
10. Yagnavalki Sangham award-1992.

Membership in Societies

Life Member of:

1. Association of Physicians of India.
2. Indian Association for Cancer Research.
3. Indian Society of Oncology.
4. Indian Rheumatism Association.
5. National Council on Hypertension.
6. International College of Nutrition.
7. Diabetic Association of India.
8. The Indian Society of Human Genetics.

9. Indian Society of Critical Care Medicine.
10. Association for the promotion of DNA fingerprinting and other DNA technologies.
11. Indian Society of Parenteral and Enteral Nutrition.
12. Society of Biological Chemists (India).
13. South Asian Society on Atherosclerosis and Thrombosis.

Member of:

1. New York Academy of Sciences, USA.
2. American Association for the Advancement of Science.

Member of the Editorial Board of the journals:

1. Medical Science Monitor: published from Poland.
2. **Editor-in-Chief, Lipids in Health and Disease-published by BioMed Central, U.K.**
3. The European Journal of General Medicine
4. Current Nutrition and Food Science, USA
5. Journal of the Association of Physicians of India
6. Current Pharmaceutical Biotechnology, USA
7. Open Nutrition Journal, Open Nutrition Reviews, Open Nutrition Letters published by Bentham Science Publishers, USA
8. Journal of Applied Research in Clinical and Experimental Therapeutics, USA
9. Frontiers in Biosciences, NY, USA
10. Diabetes Review Letters
11. The Open Colorectal Cancer Journal
12. Gene Therapy and Molecular Biology

Significant contributions and projects undertaken:

1. Developing essential fatty acids and their metabolites as potential anti-cancer drugs.
2. Investigating the possible use of gamma-linolenic acid and eicosapentaenoic acid as anti-peptic ulcer agents.

3. Clinical trials under progress as to the possible use of essential fatty acids and their metabolites in the treatment of systemic lupus erythematosus and rheumatoid arthritis.
4. Investigating the possibility that an altered EFA metabolism could be responsible for insulin resistance and hyperinsulinemia and obesity.
5. Potential use of LCPUFAs and L-arginine-nitric oxide system in preserving the integrity of beta cells of the pancreas.
6. To investigate the role of perinatal supplementation of long-chain polyunsaturated fatty acids as a strategy to prevent adult diseases.

Number of Ph.D.'s guided: So far 12.

12 students obtained Ph.D. in biochemistry under my guidance in India. The details are as follows:

<u>Name of the student</u>	<u>Title of the thesis</u>
1. Revati Koratkar 1992	A study of the anti-mutagenic actions of prostacyclin and its mechanisms
2. K. Vijay Kumar 1993	Biochemical studies in essential hypertension with particular reference to free radicals, essential fatty acids and prostaglandins
3. P. Sangeetha Sagar 1993	Effect of gamma-linolenic acid on tumor cells in vitro
4. G. Ramesh 1994	Effect of cis-unsaturated fatty acids on tumor cells in vitro and in vivo
5. G. Sravan Kumar 1994	Influence of alpha-linolenic and eicosapentaenoic acids on the growth of mouse myeloma cells in vitro.
6. M. Padma 1994	A study of the modulation of signal transduction by cis-unsaturated fatty acids
7. N. Madhavi 1994	A study of the effect(s) of cis-unsaturated fatty acids on drug-sensitive and resistant tumor cells in vitro.
8. V. Manjari 1998	Investigation into the effect of cis-unsaturated fatty acids on peptic ulcer disease
9. I.K. Mohan 1998	Investigation into the role of L-arginine, nitric oxide and polyunsaturated fatty acids in diabetes mellitus.
10. C. Arun Kumar 1999	Investigation into the anticancer activities of melatonin in vivo
11. M. M. Sailaja Devi 2000	Investigation into the role of prostaglandins in chemical induced diabetes mellitus.
12. Y. Suresh 2000	Investigation into the role of polyunsaturated fatty acids in chemical induced diabetes mellitus.

Research Projects (in India) completed:

1. Investigation into the effect of cis-unsaturated fatty acids on tumor cells in vitro; from 1987-1991 (4 years) Funded by Department of Science and Technology, India.
2. Investigation into the role of free radicals in human essential hypertension; from 1988 to 1991 (3 years) Funded by Indian Council of Medical Research
3. Investigation into the mechanism(s) of tumoricidal actions of essential fatty acids and their metabolites from 1989 to 1992 funded by Indian Council of Medical Research
4. Investigation into the mechanism(s) of genoprotective action of prostacyclin from 1992 to 1996, funded by Indian Council of Medical Research.
5. Investigation into the mechanism(s) of tumoricidal action of essential fatty acids from 1998 to 1999 (1 year) funded by Indian Council of Medical Research

Invited guest speaker/speaker at the following International Conferences:

1. International Congress on Prostaglandins, the IV International Washington Spring Symposium-1984.
2. The Second International Congress on Essential Fatty Acids, Prostaglandins and Leukotrienes - 1985.
3. International Congress on Radiation induced injury, Inflammation, and eicosanoids - Washington, 1986.
4. International Conference on Interferon and other cytokines, Heidelberg, Germany - 1987.
5. International Congress on Tumor Necrosis Factor and other cytokines, Kyoto, Japan - 1988.
6. UNESCO/COSTAM workshop on Lipid soluble antioxidants in Biochemistry of Nutrition and Environmental Health, Penang, Malaysia - 1991.
7. International Congress on Clinical Biochemistry, Kyoto, Japan, 1991.
8. International Symposium on Polyunsaturated Fatty Acids, Tokyo, Japan - 1992.
9. 6th International Conference on Superoxide and Superoxide dismutase, Kyoto, Japan - 1993.
10. American Oil Chemists' Society meeting, San Diego, Texas, USA-1995.
11. IV World congress of International Society for Adaptive Medicine: A satellite symposium on Myocardial preservation and Cellular adaptation, held at Madras, India December 14-16, 1995.
12. 8th APLAR Congress of Rheumatology, Melbourne, Australia, 21-26 April 1996.

13. AOCS Conference on PUFAs in Infant Nutrition: Consensus and Controversies, Barcelona, Spain: November 7 to 9, 1996.
14. 4th International Congress on Essential Fatty Acids and Eicosanoids, Edinburgh, U.K.: July 20-25, 1997.
15. ISSFAL congress at Lyon, France from June 1st to 5th 1998.
16. American Diabetes Association annual conference at Chicago, USA from July 13th to 15th 1998.
17. The SmithKline Beechem Research Symposium on The Insulin Resistance Syndrome: Molecular mechanisms linking Obesity, insulin resistance and cardiovascular disease, 14-16 April 1999, Robinson College, Cambridge, UK.
18. Annual meeting of the American Oil Chemists' Society, San Diego, April 2000.
19. Annual meeting of the association of Physicians of India, January 2001 and January 2002; title of the invited lectures: "Recent Advances in Metabolic Syndrome" and "Hyperlipidemias".
20. Gordon Research Conference on "Inflammation in dental Diseases" in Feb 2003; the title of the invited lecture: "Metabolic Syndrome X is an inflammatory condition" at Ventura, CA, USA.
21. APICE Congress at Naples, Italy in November 2003; the title of the invited talk: "Insulin in the critically ill".
22. 7th International Symposium on Atherosclerosis and cardiovascular diseases at Athens, Greece in December 2003; title of the invited talk: "Metabolic Syndrome X-some new concepts and suggestions".
23. Conference on Nutraceuticals in Cardiovascular Diseases, Texas, USA, June 2004; title of the invited talk: Nutritional factors in the prevention and treatment of cardiovascular diseases.
24. Annual meeting of the American Oil Chemists' Society, May 2005, Salt Lake City, USA and the title of the invited talk: Anti-cancer actions of gamma-linolenic acid and its derivatives.
25. Invited speaker at 2nd International Symposium on Functional Foods, Dallas, Texas; November 15-16, 2005. Title of the talk: A perinatal strategy to prevent adult disease.
26. Invited speaker at APICON-2006-Annual Conference of the Association of Physicians of India, Patna, Bihar, Jan 2006. Title of the talk: Gamma-linolenic acid therapy of human gliomas.
27. Visiting Professor to the University of Athens, Greece from December 18-22, 2005 to give lectures on Methodological issues in Metabolic Syndrome X.
28. Invited speaker at 3rd International conference on "Functional Foods and phytotherapy for the prevention and treatment of chronic disease" held at Richardson, TX, USA from October 14-15, 2006 and gave two lectures: (i) Prevention and treatment of cardiovascular diseases by nutritional factors, and (ii) Nutrigenomics.

29. Invited speaker at 10th International symposium on atherosclerosis and related risk factors at Athens, Greece from 29th November to 2nd December 2006. Title of the talk is: “Low grade systemic inflammation in metabolic syndrome with its origins in the perinatal period”.
30. Invited speaker at 2nd Panhellenic congress on atherosclerosis from 8th December to 11th December 2006. Title of the talk is: “Beneficial actions of polyunsaturated fatty acids in cardiovascular diseases: But, how and why?”
31. Invited to conduct a one-day pre-conference workshop entitled: “Understanding the potential of lipid based formulations” on 11th December 2006 during the conference on “Strategies to enhance Solubility and Drug absorption” organized by Informa Life Sciences at Amsterdam, The Netherlands.
32. Invited speaker at 4th International Conference on “Functional Foods” at Richardson, TX, USA in October 2007.
33. Invited speaker at International conference on Atherosclerosis, Athens, Greece, in December 2007.
34. Invited expert member on “Perinatal Nutrition of Infants” sponsored by Child Health Foundation, 2008.
35. Invited speaker at 5th International conference on Functional Foods at Baton Rouge, TX from 15-18th October 2008 and delivered a talk entitled: Obesity: Genes, brain, gut, and environment.
36. Invited speaker at 6th International conference on Functional Foods at Texas Women’s University, Denton, TX, USA from December 4-5, 2009. Title of the talk: Mechanisms involved in the pathogenesis of diabetes mellitus.
37. Invited speaker at 7th International conference on Functional Foods at Texas Women’s University, Denton, TX, USA in December, 2010. Title of the talk: Is type 2 diabetes mellitus a disorder of the brain?

Current Research Interests:

My current research interests are focused on three areas:

1. **To develop γ -linolenic acid (GLA) as a therapeutic tool for the treatment of glioma:** My previous studies revealed that GLA selectively kills tumor cells but not normal cells in vitro. The mechanism of this tumoricidal action of GLA is attributed to its ability to enhance free radical generation and enhanced formation of lipid peroxides only in tumor cells. GLA induced apoptosis of tumor cells. In addition, GLA decreased the anti-oxidant content of tumor cells, enhanced the expression of p53, and suppressed the activity of oncogenes. In an extension of these studies, it was noted that GLA is able to prevent BP and other chemical-induced genetic damage and abrogate induction of tumors in animal models. Based on these in vitro and in vivo studies, preliminary human studies were performed which showed that intra-tumoral injection of GLA can also regress human glioma without any significant side effects. It is my desire to perform more pre-clinical toxicology studies and ultimately develop GLA as an anti-glioma drug. I also plan to develop analogues of GLA as possible anti-cancer molecules for other cancers.
2. **Polyunsaturated fatty acids as modulators of hypothalamic function and its involvement in the development of the metabolic syndrome:** Brain is rich in polyunsaturated fatty acids arachidonic acid (AA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). There is reasonable

evidence to suggest that perinatal and early childhood supplementation of these PUFAs could influence the development of metabolic syndrome X in adult life. The mechanism of this action of PUFAs could be due to their ability to influence the hypothalamic appetite/satiety set point during the perinatal period. This is supported by the observation that breast fed children are less prone to develop metabolic syndrome. It will be my goal to investigate how perinatal feeding of PUFAs influences the production of various neurotransmitters (serotonin, dopamine, NPY, leptin, etc.) in various parts of hypothalamus, insulin receptors in the brain and their function; rennin-angiotensin system in the brain, and pancreatic beta cell function.

- 3. To study the role of PUFAs in neuronal function:** PUFAs form an important constituent of all cell membranes including neurons. But, very little is known how these PUFAs influence neuronal function. I wish to study using in vitro and in vivo methods the role of PUFAs in neuronal function. Particularly, I wish to study the ability of various PUFAs to alter neuronal cell membrane fluidity, secretion of serotonin, dopamine, and acetylcholine by neurons in vitro; the expression of receptors for these neurotransmitters on the cell membrane; the affinity of neurotransmitters to their respective receptors; and finally how this knowledge can be translated to an in vivo situation and for improvement of cognitive function.

Current international collaborations:

1. ATTICA Study with Dr. Demosthenes Panagiotakos of Athens, Greece. This study is looking at the influence of diet and life style factors in the incidence and progression of type 2 diabetes mellitus, and coronary heart disease.
2. **Indo-Argentine project in collaboration with Dr. Aldo R Eynard. In this study we are studying the mechanism of protection of beta cells of pancreas by polyunsaturated fatty acids. This is being funded by DST.**
3. GLA in glioma. In this study we are studying the pre-clinical and phase 1 study of GLA (Gamma-linolenic acid) in the treatment of glioma. This is being done in collaboration with Dr. Laszlo Puskas of Szeged, Hungary and is being funded by Hungarian Academy of Sciences.
4. Study of insulin as a cardioprotective agent in collaboration with Prof. Gao of China. In this study we are evaluating the mechanism of protection of cardiac tissue from ischemia-reperfusion injury by insulin. This is being funded by Chinese government funds.
5. Exercise and its mechanisms of protection against obesity and type 2 diabetes mellitus. This is being done in collaboration with Dr. Edith of Portugal. We are looking at pro- and anti-inflammatory cytokines, beta cells mass, intracellular IL-6 and TNF content in beta cells before and after exercise.

Names and addresses of potential referees:

1. Dr Aldo R Eynard, MD PhD
Histologia y Embriologia Instituto de Biologia Celular
Professor Catedra de Biologia Celular
Casilla de Correos
220 5000 Cordoba
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2. Benny K H Tan, MD PhD
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3. Dr Demosthenes B. Panagiotakos, DrMedSci, FESC, MACE
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