

**BIOGRAPHICAL SKETCH**

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NAME: **Kuppusamy, Periannan**

eRA COMMONS USER NAME (credential, e.g., agency login): kuppusamy01

POSITION TITLE: Professor of Radiology, Medicine, Engineering, and Chemistry

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Madras, Chennai, India	BSc	1975	Chemistry, Math, Physics
University of Madras, Chennai, India	MSc	1977	Chemistry
Indian Institute of Technology, Chennai, India	PhD	1985	Advanced EPR Spectroscopy/Applications
National Inst. of Health, NIA, Baltimore, MD	Fogarty Research Fellow	1987	Mol. Cellular Biochemistry
John Hopkins University, Baltimore, MD	Cardiovascular Research Fellow	1990	Cardiovascular Disease

**A. Personal Statement**

I am an internationally recognized scholar and accomplished scientist in the unique and state-of-the-art discipline of electron paramagnetic resonance (EPR) spectroscopy and imaging. I have over 35 years of continuous interest and experience in the use of EPR technology for biomedical applications.

My overall expertise includes detection and imaging of oxygen and oxygen-free radicals<sup>1-4</sup>; myocardial ischemia-reperfusion injury; stem-cell therapy for cardiac repair; ROS pathophysiology and vascular remodeling in heart failure; tumor physiology, oxygenation, and drug resistance; small-molecule therapeutics for heart and cancer; noninvasive measurement of tissue oxygenation; molecular probes for free radical biology and medicine; EPR spectroscopy, imaging software, and instrumentation.

I have been a prolific contributing author on over 400 peer-reviewed scientific publications, reviews, and book chapters. As of 10/15/2021, I have 26,272 [citations](#) of my research publications including 7,527 in the last 5 years. The *h-index* of my publications is 78, while my *i10* index is 315.

As a recognition for my outstanding contributions to the biomedical EPR field, I was awarded the Silver Medal for Biology and Medicine by the International EPR Society in 2006. I was also awarded the honorary title of "Doctor Honoris Causa" by the University of Pécs, in Pécs, Hungary in 2008 in recognition of research in cardiovascular field. I was the recipient of the 2014 Piette Award by the EPR Society and "Distinguished Alumni Award" from Indian Institute of Technology (IIT), Chennai in 2015.

Innovation in research is critically important for the continued success of any researcher. I have consistently demonstrated innovation in my research and have received continuous funding with multiple awards from numerous sources, including the National Institutes of Health (NIH) and the American Heart Association. My research has transformed into several patents and licensing.

I have active collaborations with experts in chemistry, engineering, and biomedical fields to develop novel sensors, methods, and instrumentation that use EPR spectroscopy to measure and image free radicals and oxygen. My laboratory has developed highly sensitive microcrystalline oxygen-sensing paramagnetic probes for biological oximetry. The patented technology is capable of noninvasive and repeated determination of oxygen concentration (pO<sub>2</sub>) from single cells to the whole body in animals and humans. Development of a clinical version of this technology (instrumentation) is in progress.

I am the inventor of a novel class of oxygen sensors, called OxyChip, for direct and repeated measurements of oxygen concentration (pO<sub>2</sub>) from topical (skin) to deep tissues. The OxyChip is currently in Phase I clinical trial, supported by a P01 award from the National Cancer Institute.

My current research interests include oxygen biology and oximetry. My lab is working on the effect and mechanisms of supplemental oxygenation for mitigation of hypoxia-mediated tumor aggression/metastasis and inhibition of growth. We are working with several tumor models including ovarian, breast, pancreas, and colon cancer, and have demonstrated the beneficial effect of supplemental oxygen as an adjuvant therapy.

**My role in the project:** I will oversee the sensor development, characterization, functional evaluation in animal models, and biocompatibility studies including testing using ISO/ASTM guidelines. I will work closely with the Co-Investigators and directly supervise all other investigators in the project.

1. Zweier JL, Kuppusamy P. (1988) Electron paramagnetic resonance measurements of free radicals in the intact beating heart: A technique for detection and characterization of free radicals in whole biological tissues. *Proceedings of the National Academy of Sciences USA* 85, 5703-5707
2. Kuppusamy P, Chzhan M, Vij K, Shteynbuk M, Lefer DJ, Gianella E, Zweier JL (1994) Three-dimensional spectral-spatial EPR imaging of free radicals in the heart: A technique for imaging tissue metabolism and oxygenation. *Proceedings of the National Academy of Sciences USA* 91, 3388-3392
3. Zweier JL, Wang P, Samouilov A, Kuppusamy P (1995) Enzyme-independent formation of nitric oxide in biological tissues. *Nature Medicine* 1, 804-809
4. Ahmad R, Kuppusamy P (2010) Theory, instrumentation, and applications of electron paramagnetic resonance oximetry. *Chemical Reviews* 110, 3212-3236

## **B. Positions, Scientific Appointments, and Honors**

### **Positions & Employment**

2013-present Professor, Department of Radiology, Geisel School of Medicine, Dartmouth College, NH  
2013-present Professor, Department of Medicine, Geisel School of Medicine, Dartmouth College, NH  
2020-present Professor (Adjunct), Department of Chemistry, Dartmouth College, Hanover, NH  
2019-present Professor (Adjunct), Thayer School of Engineering, Dartmouth College, Hanover, NH  
2008-2013 Associate Director (Research), Division of Cardiovascular Medicine, OSU  
2005-2013 Professor, Department of Internal Medicine, Ohio State University, Columbus, OH  
2005-2013 Professor (Adjunct), Department of Biomedical Engineering, OSU, Columbus, OH  
2005-2011 Director, Small Animal Imaging Shared Resource, Ohio State University  
2005-2010 Associate Director, Dorothy M. Davis Heart and Lung Research Institute, OSU  
2002-2005 Associate Professor, Department of Internal Medicine, Ohio State University, Columbus, OH  
2002-2013 Director, Center for Biomedical EPR Imaging, Ohio State University, Columbus, OH  
2001-2002 Associate Professor, Department of Medicine, Johns Hopkins University, Baltimore, MD  
1992-2001 Assistant Professor, Department of Medicine, Johns Hopkins University, Baltimore, MD  
1990-1992 Instructor, Department of Medicine, Johns Hopkins University, Baltimore, MD  
1990-2002 Associate Director, EPR Center, Johns Hopkins University, Baltimore, MD

### **Other Experience & Honors**

2015 Distinguished Alumni Award, Indian Institute of Technology (IIT), Chennai  
2011 Lumley Interdisciplinary Research Award by College of Engineering, Ohio State University  
2008 Honorary Doctorate ("*Doctor Honoris Causa*") awarded by the University of Pecs, Pecs, Hungary for Medical Sciences  
2006 Silver Medal in Biology/Medicine award by International EPR Society in recognition of development of EPR imaging and *in vivo* EPR for biological applications  
2006 Research Investigator Award by American Tamil Medical Association (ATMA) for outstanding achievements in biomedical research  
2006 Distinguished Mentor Award by Davis Heart and Lung Research Institute for recognition of outstanding mentoring and teaching activities in the institute  
2005-2013 William D. and Jacquelyn L. Wells Chair in Imaging Research  
1996-2001 Established Investigator Award, American Heart Association (National Center)

## **Editorships, Review & Professional Memberships**

2013-present Editorial Board, J Radiology and Radiation Therapy  
2012-present Editorial Board, Clinical Biochemistry  
2003-present Editorial Board, Antioxidants and Redox Signaling  
2010-present Editorial Board, ROS  
2012-present Editorial Board, Clinical Biochemistry  
2004 & 2007 Guest Editorship, Antioxidants and Redox Signaling  
2008 Guest Editorship, Israel Journal of Chemistry  
2012 Guest Editorship, Cell Biochemistry and Biophysics (2012)  
1998-present Grant Review Peer-review committee member of several NIH, NCI, NIBIB, NIEHS Study Sections and reviewer of several international proposals.

Memberships: Past & Current: American Association for the Advancement of Science; American Cancer Society; American Chemical Society; American Heart Association; American Physiological Society; American Society for Pharmacology and Experimental Therapeutics; Biophysical Society; International EPR Society; Society for Free Radical Biology and Medicine; International Society for Heart Research; International Society for Magnetic Resonance in Medicine.

## **C. Contributions to Science**

**1. EPR Spectroscopy and Imaging:** I am a pioneer in the development and application of low-frequency (1.2 GHz) EPR spectroscopy for biological systems including small animals (mice), organs, and tissues. I have also developed instrumentation (hardware), software, and procedures for imaging of free radicals and oxygen in biological systems. Some of the outstanding contributions of my imaging research include *in vivo* imaging of heterogeneity and oxygenation in murine tumors, whole-body imaging of nitric oxide generation in mice, and noninvasive imaging of tumor redox status. The original developments led to the adaptation of the EPR imaging technology by several laboratories around the world. In recognition of my seminal contribution to *in vivo* EPR and EPR imaging for biological applications, I was awarded a Silver Medal in Biology/Medicine in 2006 by the International EPR Society.

- a) **Kuppusamy P**, Chzhan M, Wang P, Zweier JL (1996) Three-dimensional gated EPR imaging of the beating heart: Time-resolved measurements of free radical distribution during the cardiac contractile cycle. Magnetic Resonance in Medicine 35, 323-328
- b) **Kuppusamy P**, Afeworki M, Shankar RA, Deborah C, Krishna MC, Hahn SM, Mitchell JB, Zweier JL (1998) *In vivo* electron paramagnetic resonance imaging of tumor heterogeneity and oxygenation in a murine tumor model. Cancer Research 58, 1562-1568
- c) **Kuppusamy P**, Shankar RA, Roubaud VM, Zweier JL (2001) Whole body detection and imaging of nitric oxide generation in mice following cardiopulmonary arrest: Detection of intrinsic nitrosoheme complexes. Magnetic Resonance in Medicine 45, 700-707
- d) **Kuppusamy P**, Li H, Ilangovan G, Cardounel AJ, Zweier JL, Yamada K, Krishna MC, Mitchell JB (2002) Noninvasive imaging of tumor redox status and its modification by tissue glutathione levels. Cancer Research 62, 307-312

**2. Probes and Methods for *in vivo* EPR Oximetry:** I pioneered the development of innovative oxygen-sensing probes, called LiNc-BuO, OxyChip, SPOTChip, and MicroChip for accurate, reliable and repeated measurement of oxygen concentration in tissues using EPR technology. The probes are made of paramagnetic oxygen-sensing crystals of LiNc-BuO embedded in polydimethylsiloxane (PDMS) polymer. When implanted into tissue, the probes allow subsequent measurements to be made noninvasively and repeatedly over long periods, of several months or more, in animal models and human subjects. I have established the use of this probe for noninvasive monitoring of oxygen concentration in a variety of applications including myocardial ischemia/reperfusion injury, cellular cardiomyoplasty (cell therapy), cancer therapy, and wound healing. The FDA has issued an investigational device exemption (IDE) status for OxyChip. A Phase 1 (safety & efficacy) clinical trial of OxyChip in cancer patients is in progress, supported by a P01 grant from NCI.

- a) Pandian RP, Dolgos M, Marginean C, Woodward PM, Hammel PC, Manoharan PT, **Kuppusamy P** (2009) Molecular packing and magnetic properties of lithium naphthalocyanine crystals: hollow channels enabling permeability and paramagnetic sensitivity to molecular oxygen. Journal of Materials Chemistry 19(24): 4138-4147

- b) Hou H, Khan N, Gohain S, Kuppusamy ML, **Kuppusamy P** (2018). Pre-clinical evaluation of OxyChip for long-term EPR oximetry. Biomedical Microdevices 20(2):29.
- c) Kmiec MM, Tse D, Mast JM, Ahmad R, **Kuppusamy P** (2019). Implantable microchip containing oxygen-sensing paramagnetic crystals for long-term, repeated, and multisite in vivo oximetry. Biomedical Microdevices 21(3):71 (2019)
- d) **Kuppusamy P**, Kmiec, MM, Tse D, Mast JM, Ahmad, R. Estimation of pO<sub>2</sub> histogram from a composite EPR Spectrum of multiple random implants. Biomedical Microdevices, 22(1):3 (2019).

**3. Oxygen in Cardiovascular Disease and Treatment:** I have studied the molecular mechanisms and the role of oxygen in cardiovascular diseases including the treatment of myocardial injury (MI) and stem-cell therapy. Specifically, my research focused on understanding the oxygen-sensing mechanism and signal transduction at the molecular level that led to transcriptional and post-translational regulation of p53, PTEN, and PI3K in MI, coronary and pulmonary vascular remodeling, and RV failure. I have shown a definitive role for oxygen in the regulation of cardiomyocyte apoptosis/survival (via p53/NOS3), vascular-cell proliferation and migration (via ROS/PTEN), and tumor growth (via HIF-1/p53). All these studies have important implications in the understanding and treatment of cardiovascular diseases.

- a) Khan M, Meduru S, Mohan IK, Kuppusamy ML, Wisel S, Kulkarni A, Rivera BK, Hamlin RL, **Kuppusamy P** (2009) Hyperbaric oxygenation enhances transplanted cell graft and functional recovery in the infarct heart. Journal of Molecular Cellular Cardiology 47(2): 275-287
- b) Khan M, Meduru S, Gogna R, Madan E, Citro L, Kuppusamy ML, Sayyid M, Mostafa M, Hamlin RL, **Kuppusamy P** (2012) Oxygen cycling in conjunction with stem cell transplantation induces NOS3 expression leading to attenuation of fibrosis and improved cardiac function. Cardiovascular Research 93(1) 89-99
- c) Gogna R, Esha M, Khan M, Pati U, **Kuppusamy P** (2013) p53's choice of myocardial death or survival: Oxygen protects infarct myocardium by recruiting p53 on NOS3 promoter through regulation of p53-Lys118 acetylation. EMBO Molecular Medicine 5: 1662-1683
- d) Prabhat AM, Kuppusamy ML, Naidu SK, Meduru S, Reddy PT, Dominic A, Khan M, Rivera BK, **Kuppusamy P** (2018). Supplemental oxygen protects heart against acute myocardial infarction. Frontiers in Cardiovascular Medicine 5:114. *PMCID: PMC6120988*

**4. Hypoxia in Cancer Progression and Therapy:** The oxygen level in solid malignancies is a critical parameter affecting clinical outcomes, particularly for radiation therapy. The dependence of radiation therapy's efficacy on oxygen levels in tumors appears to be more significant than stage, tumor morphology, or tumor size. The oxygen level is also an important factor in tumor response to surgical and chemotherapeutic approaches. I have studied hypoxia and its role in the progression and treatment of solid tumors. I have also showed how mitigation of tumor hypoxia, for example by administration of enriched oxygen, can inhibit tumor growth and/or enhance certain chemotherapy/radiation treatment outcomes.

- a) Selvendiran K, Bratasz A, Kuppusamy ML, Tazi MF, Rivera BK, **Kuppusamy P** (2009) Hypoxia induces chemoresistance in ovarian cancer cells by activation of signal transducer and activator of transcription 3 (STAT3). International Journal of Cancer 125(9): 2198-2204
- b) Selvendiran K, Kuppusamy ML, Ahmed S, Bratasz A, Meenakshisundaram G, Rivera BK, Khan M, **Kuppusamy P** (2010) Oxygenation inhibits ovarian tumor growth by downregulating STAT3 and cyclin-D1 expressions. Cancer Biology & Therapy 10(4): 386-390
- c) Gogna R, Madan E, **Kuppusamy P**, Pati U (2012) Re-oxygenation causes hypoxic tumor regression through restoration of p53 wild-type conformation and post-translational modifications. Cell Death & Disease 3: e286
- d) Mast JM, **Kuppusamy P** (2018). Hyperoxygenation as a Therapeutic Supplement for Treatment of Triple Negative Breast Cancer. Frontiers in Oncology 8:527. *PMCID: PMC6256245*

**5. Clinical Oximetry:** My most recent contribution to science is the successful adaptation of the *in vivo* EPR oximetry—methods and probes—for safe, noninvasive, and repeated measurement of tissue pO<sub>2</sub> in human subjects. Measurement of oxygen concentration in the tumor of cancer patients using OxyChip is currently under phase I (safety and feasibility) clinical trial at Dartmouth-Hitchcock Medical Center.

- a) Kmiec MM, Hou H, Kuppusamy ML, Drews TM, Prabhat AM, Petryakov SV, Demidenko E, Schaner PE, Buckey JC, Blank A, **Kuppusamy P**. Transcutaneous oxygen measurement in humans using a paramagnetic skin adhesive film. Magnetic Resonance in Medicine 81:781-794 (2019)
- b) Schaner PE, Tran LB, Zaki BI, Swartz HM, Demidenko E, Williams BB, Siegel A, **Kuppusamy P**, Flood AB, Gallez, B. The impact of particulate electron paramagnetic resonance oxygen sensors on fluorodeoxyglucose imaging characteristics detected via positron emission tomography. Science Reports 11(1): 4422 (2021).
- c) Schaner P E, Pettus JR, Flood AB, Williams BB, Jarvis LA, Chen EY, Pastel DA, Zuurbier RA, diFlorio-Alexander RM, Swartz HM and **Kuppusamy P**. OxyChip Implantation and Subsequent Electron Paramagnetic Resonance Oximetry in Human Tumors Is Safe and Feasible: First Experience in 24 Patients. Frontiers in Oncology, 10: 572060 (2020).
- d) Schaner PE, Williams BB, Chen EY, Pettus JR, Schreiber WA, Kmiec MM, Jarvis LA, Pastel DA, Zuurbier RA, DiFlorio-Alexander RM, Paydarfar JA, Gosselin BJ, Barth RJ, Rosenkranz KM, Petryakov SV, Hou H, Tse D, Pletnev A, Flood AB, Wood VA, Hebert KA, Mosher RE, Demidenko E, Swartz HM, and **Kuppusamy P**. First-In-Human Study in Cancer Patients Establishing the Feasibility of Oxygen Measurements in Tumors Using Electron Paramagnetic Resonance with the OxyChip. Frontiers in Oncology. 11:743256 (2021).

### **Complete List of Published Work in My Bibliography**

<http://www.ncbi.nlm.nih.gov/sites/myncbi/periannan.kuppusamy.1/bibliography/40848246/public/?sort=date&direction=ascending>