

BIOGRAPHICAL SKETCH

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NAME: Raman, Lakshmi

eRA COMMONS USER NAME (credential, e.g., agency login): Irama1

POSITION TITLE: Associate Professor of Pediatrics

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
Chennai Medical College, Chennai, India	MBBS	1989	Medicine
Royal College of Physicians, London, UK	DCH	1993	Pediatrics
Royal College of Physicians, London, UK	MRCP	1994	Pediatrics
SUNY Downstate Medical Center, Brooklyn, NY	Resident	1997-2001	Pediatrics
University of Minnesota, Minnesota, MN	Fellow	2001-2004	Pediatric Critical Care

A. Personal Statement

As the Medical Director of the Extracorporeal Membrane Oxygenation (ECMO) program I have primarily focused by efforts on education and research apart from overseeing the clinical care of these patients. In education we do training for incoming fellows and specialists who assist in caring for the ECMO pump on a yearly basis and I oversee the curriculum. I also direct a 3-day National ECMO course once a year which has been endorsed by the Extra Corporeal Life Support Organization (ELSO) and serve as the first course to be endorsed by ELSO.

My research focus has been to evaluate the neurological injury in patients who are on Extracorporeal life support, otherwise commonly referred to as Extracorporeal Membrane Oxygenation (ECMO). My collaboration to study this started with Dr. Busch even prior to his arrival at University of Texas Southwestern Medical Center In the past few years, we have evaluated the cerebral blood flow changes using multi-channel near infrared spectroscopy and trans-cranial Doppler in non-cardiac patients undergoing ECMO therapy in collaboration with Dr. Tian at the University of Texas at Arlington. The proposed study funded in part by the American Heart Association has been evaluating disturbances in cerebral autoregulation. I have also been collaborating with Dr. Ann Stowe who was previously in the neurorepair lab to study neuroinflammation and autoreactivity to CNS specific antigens and this work was recently published in critical care medicine. With my role as the Medical Director of the ECMO program at Children's Medical Center of Dallas I am interested in finding ways to predict neurological events on ECMO.

With my leadership and focus on ECMO, I have recently published my work that I have done both locally and nationally with ELSO community. I continue to present my work at National and International meetings. My preclinical work also included the role for CNS autoreactivity in long-term deficits in a mouse model of perinatal hypoxia, which is a press release article in the *Journal of Leukocyte Biology*. I also serve as a reviewer for Neuroscience Letters, Journal of Pediatric Surgical Research, ASAIO and serve on the review committee for fellow clinical grants and abstracts with Pediatric Academic Society. I also serve on the editorial board for ASAIO. I have been appointed to the steering committee at ELSO to chair the protocols, guidelines and grant committee. I also serve on the National committee for education and scientific review with ELSO data registry.

1. Tian F, Morriss MC, Chalak L, Venkataraman R, Ahn C, Liu H, Raman L, 2017. Impairment of cerebral autoregulation in pediatric extracorporeal membrane oxygenation associated with neuroimaging abnormalities. (*Neurophotonics*: 2017 Oct; 4 (4): 041410). PMID: 28840161

2. Fenghua Tian, Christopher Jenks, Donald Potter, Raman L Regional cerebral abnormalities using frequency-domain near-infrared spectroscopy during Pediatric extracorporeal membrane oxygenation (*ASAIO: Dec 2016*): PMID: 27922887
3. Sterling B. Ortega, Xiangmei Kong, Ramgopal Venkataraman, Allen M Savendra, Steven G Kernie, Ann M Stowe and Raman L: Perinatal chronic hypoxia induces cortical inflammation, hypomyelination, and peripheral myelin-specific T cell autoreactivity *Journal of Leucocyte Biology*, 2016 January). PMID: 26038434
4. Sterling B. Ortega, PhD., Poornima Pandiyan, MD, Jana Windsor, MSc, Vanessa O. Torres, BS., Uma M. Selvaraj, MTech, Amy Lee, MD, Michael Morriss, MD, Fenghua Tian, PhD., Lakshmi Raman, MD, Ann M. Stowe, PhD: A Pilot Study Identifying Brain-Targeting Adaptive Immunity in Pediatric Extracorporeal Membrane Oxygenation Patients With Acquired Brain Injury, *CCM Journal* March 2019, Volume 47, Number 3

B. Positions and Honors

Positions and

Employment

1997-2000	Resident, Department of Pediatrics, SUNY-Down State Medical Center, Brooklyn, NY
2000-2001	Chief Resident, Department of Pediatrics, SUNY Down State Medical Center, Brooklyn, NY
2001-2004	Fellow, Pediatric Critical Care Medicine, Department of Pediatrics, University of Minnesota, Minneapolis, MN
2004-2008	Assistant Professor, Department of Pediatrics, Hennepin County Medical Center, Minnesota, MN
2008-2017	Assistant Professor, Department of Pediatrics, UT Southwestern Medical Center, Dallas, TX
2017-	Associate Professor, Department of Pediatrics, UT Southwestern Medical Center, Dallas, TX

Other Experience and Professional Memberships

2000-	American Academy of Pediatrics
2004-	Society of Critical Care
2008-	Society for Pediatric Research

Honors

1984	Distinction in Anatomy & Biochemistry, University of Madras, India
1988	Distinction in Surgery, University of Madras, India
2001	Jay H. Fisher Memorial Award for Excellence in teaching, SUNY, NY
2001	Sixth Annual Residents' Night Award, Academy of Medicine of Richmond, NY

C. Contribution to Science

1. **Chronic hypoxia and the developing brain:** During my early training in Critical Care fellowship, I focused on understanding the effects of chronic hypoxia on the developing brain in particular the developing hippocampus. We investigated this on a rat model of chronic hypoxia as the hippocampal development in the rat is very similar to the developing human brain where the hippocampal development occurs postnatally. We studied the neurometabolic profile of the hippocampus in these rats using a 9.4 tesla magnet and for the first time demonstrated that chronic hypoxia causes decreased brain energy consumption with suppressed excitatory neurotransmission and reduced neuronal integrity. Following this we evaluated the dendritic arborization of the hippocampus which suggested a persistence of the immature pattern associated with delayed trace and delay fear conditioning in these rats.
 - a. Raman L, Tkac I, Ennis K, Gruetter R, Georgieff M.K., Rao R. In vivo effect of chronic hypoxia on the neurochemical profile of the developing rat hippocampus. *Brain Res. Dev Brain Res* 156:202-209, 2005. PMID: 16099307
 - b. Raman L, Hamilton KIL, Gewirtz JC, Rao R. Effects of chronic hypoxia in developing rats on dendritic morphology of the CA1 subarea of the hippocampus and on fear-potentiated startle. *Brain Res* 1190: 167-174, 2008. PMID: 18083146
 - c. Raman L, Georgieff M.K., Rao R. The role of chronic hypoxia in the development of neurocognitive abnormalities in preterm infants with bronchopulmonary dysplasia. *Dev Sci* 9(4): 359-367, 2006. PMID: 16764609

2. **Neurogenesis and inflammation in chronic hypoxia:** After satisfying my visa requirement for 4 years post training, I moved to the current position at UTSW. Initially, I was in a developmental biology lab where I studied the effect of chronic hypoxia on hippocampal neurogenesis in a transgenic mouse model that expresses green fluorescent protein in the progenitor cell population. We found that chronic hypoxia significantly impaired hippocampal neurogenesis and this was mediated through the mTOR pathway. We further found that erythropoietin was able to rescue some of the depletion seen in hippocampal neurogenesis. With change of mentorship, I collaborated with Dr. Stowe in the neurorepair lab and studied the effects of perinatal hypoxia on myelination and CNS inflammation. We found that the inflammation leads to long-term depletion of myelin with concurrent motor deficits. The result was recently published in *Journal of leukocyte biology* and was chosen as a highlighted article with a dedicated editorial and most accessed article in the 6 months since the publication.
- Raman L, Kong X., Gilley J., Kernie S.G. Chronic hypoxia impairs murine hippocampal development and depletes the postnatal progenitor pool by attenuating mTOR signaling. (*Pediatr Res* 70: 159-165, 2011). PMID: 21532529
 - Raman L, Kong X, Kernie S.G. Pharmacological inhibition of the mTOR pathway impairs hippocampal development in mice (*Neuroscience letters*-2013; April 29; 541:9-14). PMID: 23395832
 - Eugene Chung, Xiangmei Kong, Mark P Goldberg, Ann M Stowe, Raman L. Erythropoietin Mediated Neuroprotection in a pediatric mouse model of chronic hypoxia (*Neuroscience Letters*-2015; April 29; 541:9-14). PMID: 2589777
 - Sterling B. Ortega, Xiangmei Kong, Ramgopal Venkataraman, Allen M Savendra, Steven G Kernie, Ann M Stowe and Raman L: Perinatal chronic hypoxia induces cortical inflammation, hypomyelination, and peripheral myelin-specific T cell autoreactivity (*Journal of Leucocyte Biology*, 2016 January). PMID: 26038434
3. **Extracorporeal membrane oxygenation (ECMO) therapy and its implications:** Since I assumed leadership in the clinical arena as the Medical Director of the ECMO program for Children's Medical Center, Dallas, TX. I redirected my research interest to ECMO therapy with particular emphasis on neurological monitoring and injury on ECMO. We have done some preliminary data acquisition initially using multi-channel near infrared spectroscopy to correlate with neurological injury which has been published in *ASAIO journal* as a case series. I was successful in obtaining an American Heart Grant to study cerebral autoregulation. We now have about 30 neonatal and pediatric patients supported on ECMO, where we show that significant disturbances in cerebral autoregulation resulting in phase coherence abnormalities that correlate with abnormal neuroimaging and was published in *Neurophotonics*. Furthermore, with the robust data base we have compiled at our ECMO Center of Excellence, we have complete and on-going retrospective studies.
- Raman L, Heidi Dalton: Year in Review: Extracorporeal Membrane Oxygenation (*Respiratory Care*: July 2016: Vol: 61(7)): PMID: 27381702
 - Pilar Anton-Martin, Raman L, Jefferson Tweed, Nikhil Thatte, Vinai Modem, Janna Journeycake: Pre ECMO coagulopathy does not increase the occurrence of hemorrhage during extracorporeal support: (*The International Journal of Artificial Organ*: 2017; 40 (5): 250-255): PMID: 28430304
 - Christopher Jenks, Jefferson Tweed, Kristin Gigli, Ramgopal Venkataraman Raman L: An International Survey on Ventilator, Tracheostomy and Extubation Practices Among Extracorporeal Membrane Oxygenation Centers: (*ASAIO J*: 2017, May 18): PMID: 28525418
 - Christopher Jenks, Ayesha Zia, Ramgopal Venkataraman and Raman L: High Hemoglobin Is an Independent Risk Factor for the Development of Hemolysis During Pediatric Extracorporeal Life Support: (*Journal of Intensive Care Medicine* 2017 Jan): PMID: 28486865
 - Pilar Anton-Martin, Janna Journeycake, Vinai Modem, Sailaja Golla, Raman L, Jefferson Tweed, Cindy Darnell-Bowens: Coagulation profile is not a predictor of acute cerebrovascular events in pediatric ECMO patients (*ASAIO J* 2017 July 3): PMID: 28678046
 - Ryan P Barbaro, Matthew L Paden, Yigit S Guner, Raman L, Lindsay M Ryerson, Peta Alexander, Viviane Nasir, Melania M. Bembea, Peter T Rycus, Ravi R Thiagarajan: Pediatric Extracorporeal Life Support Organization Registry International Report 2016: (*ASAIO J*, 2017 July/Aug; 63 (4): 456-463): PMID: 28557863
 - Nasr VG, Raman L, Barbaro RP, Guner Y, Tonna J, Ramanathan K, Federico P, Thiagarajan RR, Alexander PMA: Highlights from the Extracorporeal Life Support Organization Registry: 2006-2017: *ASAIO J* 2018, Jul 25

- h. Dalton HJ, Lequier L, Raman L: RBC Exposure in Pediatric Extracorporeal Membrane Oxygenation: confusion without consensus: Pediatric Critical Care Medicine: 2018 Aug: 19(8): 787-788
- i. Viviane G. Nasr, Lakshmi Raman, Ryan P. Barbaro, Yigit Guner, Joseph Tonna, Kollengode Ramanathan, Pappalardo Federico, Ravi R. Thagarajan, and Peta M. A. Alexander: Highlight from the Extracorporeal Life Support Organization Registry: 2006-2017, ASAIO Journal 2018.
- j. Amy E. Lee, Poornima Pandiyan, Ming-Mei Liu, Monica A. Williams, Allen D. Everett, Gregory P. Mueller, Michael Craig Morris, Lakshmi Raman, Deborah Carlson, and Joshua W. Gatson: Tau Is Elevated in Pediatric Patients on Extracorporeal Membrane Oxygenation: ASAIO Journal 2018 Pediatric Circulatory Support
- k. Jamie Weller, Lakshmi Raman, Ali McMichael: Anticoagulation and monitoring in pediatric extracorporeal membrane oxygenation: The Egyptian Journal of Critical Care Medicine 6 (2018) 69-71
- l. The use of Extracorporeal Membrane Oxygenation in life-threatening foreign body aspiration: case series, review of ELSO registry data and systematic literature review” – Accept for publication in The Journal of Emergency Medicine

D. Research Support

Completed Research Support

15BGIA25860045 Raman (Co-PI) 07/1/15-6/30/17
 Evaluation of Neurological risks with cerebral autoregulation impairments in Neonatal Extracorporeal support
 The goal of this study is to evaluate potential impairments in cerebral autoregulation in neonatal ECMO and correlate these severities with MRI in post ECMO survivors.
 Role: Collaborator

Institutional Grant, UT Southwestern Medical Center, Dallas, TX Raman (PI) 08/01/2015-07/2015
 Maintenance of cerebral perfusion pressure in moderate to severe traumatic brain injury attenuates CNS inflammation of TBI
 The goal of this study is to evaluate potential autoregulation impairments in pediatric traumatic brain injury patients with moderate to severe brain injury and determine the range of CPP that minimizes leukocyte egress into the brain.
 Role: Principal Investigator

Junior Investigator CCRAC Award, UT Southwestern Medical Center, Dallas, TX 08/01/08-07/31/2011
 Perot Brain and Nerve Injury Center, Dallas, TX
 Children's Medical Center Dallas, Dallas, TX
 Role of chronic hypoxia on progenitor stem cell pool in the hippocampus
 The goal of this study was to show the effect of chronic hypoxia on the progenitor stem cell pool using immunohistochemistry and investigating the underlying mechanism
 Role: Principal Investigator

Minneapolis Medical Research Foundation 07/01/2005-06/30/2008
 Brain Energy Metabolism in Chronic Hypoxia
 The goal of this study was to demonstrate the long term effects of Chronic Hypoxia on creating kinase and MAP-2 expression and the chronic hypoxia predisposes of secondary injury.
 Role: Principal Investigator

Viking Children's Fund Grant, Minnesota Vikings Foundation, Minnesota, MN 09/01/2004 - 08/31/2005
 Effect of Chronic Hypoxia on the Developing Rat Hippocampus
 The goal of this study was to show the effect of chronic hypoxia on the dendritic arborization both during hypoxia and long term and the role of chronic hypoxia on hippocampal behavior of fear potentiated startle.
 Role: Principal Investigator