BIOGRAPHICAL SKETCH

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NAME: Kanwaljeet S. Anand, MBBS, D.Phil.

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

POSITION TITLE: Professor of Pediatrics, Anesthesiology, Perioperative & Pain Medicine

EDUCATION/TRAINING:

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date	FIELD OF STUDY
M.G.M. Medical College, University of Indore, India	MBBS	10/1981	Medicine
Jesus College, University of Oxford, Oxford, U.K.	D.Phil.	07/1986	Clinical Research

A. Personal Statement

My overall aim is to probe the social ecology of early childhood using hair cortisol concentrations (HCC) and hair oxytocin concentrations (HOC) as summative measures of stressful vs. supportive experiences in their environment. In subsequent projects, these measures will be used to investigate the long-term physical health and mental health outcomes following childhood trauma and critical illness. First, we will establish the normative ranges for hair cortisol and hair oxytocin in healthy preschool children and identify the demographic and psychosocial factors that explain the variability in these biomarkers. Second, we will quantify protein biomarkers in hair, including inflammatory cytokines and other mechanistic proteins that reflect illness vs. wellness in early childhood. Third, we will measure these neurohormones and candidate cytokines in specific patient populations to reveal specific molecules and expression profiles with diagnostic value, or those that change with specific therapies. My research training occurred as a Rhodes Scholar at University of Oxford studying stress responses to surgery, and continued in a postdoctoral fellowship at Harvard Medical School, where I proposed the first scientific rationale for pain-related stress in newborns. Over 30 years, my research has contributed extensive knowledge about early development of pain/stress, established novel approaches for analgesia/anesthesia, investigated the long-term effects of pain/stress, and the mechanisms underlying opioid tolerance and anesthetic neurotoxicity in the immature brain. I have designed multiple randomized clinical trials and other clinical cohort studies, including the International NEOPAIN trial funded by NICHD, the NeoOpioid Consortium funded by the European Commission, and studies funded via collaborative research networks launched by NIMH, NINDS, and NICHD. With my clinical training and decades of experience in pediatric critical care, extensive research experience, track record of previous NIH and other competitive funding, and history of successful collaborations, I feel that I am qualified to serve as Principal Investigator for the proposed project. Publications relevant to the proposed research project include:

1. Slominski R, Rovnaghi CR, **Anand KJS**. Methodological considerations for hair cortisol measurements in children. ***Therapeutic Drug Monitoring*** 2015; 37(6): 812-820. PMID: 25811341. PMCID: PMC4581896.
2. Palmer FB, **Anand KJS**, Graff JC, Murphy LE, Qu Y, Völgyi E, Rovnaghi CR, Moore A, Tran QT, Tylavsky FA. Early adversity, socioemotional development, and stress in urban one-year-old children. ***Journal of Pediatrics***, 2013; 163(6): 1733-1739. PMID: 24070827.
3. Slopen N, Roberts A, LeWinn KZ, Bush NR, Rovnaghi CR, Tylavsky F, **Anand KJS**. Maternal experiences of trauma and hair cortisol in early childhood in a prospective cohort. ***Psychoneuroendocrinology***, 2018; 98:168-176. PMID: 30170311
4. **Anand KJS**, Rigdon R, Rovnaghi CR, Qin F, Tembulkar S, Bush N, LeWinn K, Tylavsky FA, Davis R, Barr DA, Gotlib IH. Measuring socioeconomic adversity in early life. ***Acta Paediatrica*** 2018 (in press).

B1. Positions held

1993-1997 Assistant Professor of Pediatrics, Anesthesiology, Psychiatry, Emory University, Atlanta, GA.
1997-2000 Associate Professor, Pediatrics, Anesthesiology & Anatomy, University of Arkansas, Little Rock.
2000-2009 Professor of Pediatrics, Anesthesiology, Pharmacology & Neurobiology, Morris & Hettie Oakley Chair of Critical Care Medicine, University of Arkansas for Medical Sciences, Little Rock, AR.
2009-2015 Professor of Pediatrics, Anesthesiology, Anatomy & Neurobiology, St. Jude Chair of Critical Care Medicine, University of Tennessee Health Science Center, Memphis, TN.
2015-present Professor of Pediatrics, Anesthesiology, Perioperative & Pain Medicine, Stanford University School of Medicine, Palo Alto, CA.

B2. Selected Honors:

1994 Inaugural **"Young Investigator Award" for Pediatric Pain**, International Association for Study of Pain
2000 **"Jeffrey Lawson Award"** for Advocacy in Children's Pain Relief from the American Pain Society
2003 Chair, Neonatal Pain Task Force, FDA/NICHD Newborn Drug Development Initiative
2005 Editorial Board, ***Pain***, official journal of the International Association for the Study of Pain.
2006 Member, ALSDAC Advisory Committee of the Food & Drug Administration, U.S. Public Health Service
2007 Chair, International Research Committee, Society for Critical Care Medicine.
2007 **"Mentor of the Year" Award**, Department of Pediatrics, University of Arkansas for Medical Sciences
2007 Member of the American Board of Pediatrics, Sub-Board of Critical Care Medicine (2007-13).
2008 **"Salute to Greatness" Individual Award**, Dr. Martin Luther King, Jr. Commission, State of Arkansas
2008 Invited Speaker at the House of Commons, British Parliament, January 28th, 2008.
2008 Consultant for the National Academy of Sciences, Institute of Laboratory Animal Research
2009 **"Nils Rosén von Rosenstein Medal"**, Swedish Academy of Medicine & Swedish Pediatric Association
2011 **Mentor Award**, School of Graduate Studies, University of Arkansas for Medical Sciences, Little Rock.
2011 Invited Scientific Expert, ALSDAC Committee, Center for Drug Evaluation and Research, FDA.
2011 Council Member, Special Interest Group for Pediatric Pain, International Association for Study of Pain
2013 Keynote Address, ***9th Annual "In Praise of Medicine"*** Erasmus University Medical Center, Rotterdam.
2015 Keynote Speaker, **Journées Nationales de Néonatologie,** The Pasteur Institute, Paris, France.
2015 International Fellow, **Leading Causes of Life Initiative**, Wake Forest University, Winston-Salem, NC.
2015 Executive Committee, Pediatric Pain Research Network, Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, & Networks (ACTTION)
2016 Member, NICHD Special Emphasis Panel/Scientific Review Group 2016/01 ZHD1 DSR-K (90)
2016 Member, Center for Scientific Review 2016/10 ZRG1 PSE-D (90), Neurological, Aging & Musculoskeletal Epidemiology (NAME) Study Section
2017 Member, Center for Scientific Review, 2018/01 SBIB-H82, Clinical Fetal & Pediatric Applications
2017 Member, Consensus Task Force, Ethical Guidelines for Pediatric Pain Research, The MayDay Fund
2018 Chair, Center for Scientific Review, 2018/02 SBIB-H82, Clinical Fetal & Pediatric Applications
2018 Honorary Doctorate, Faculty of Medicine and Health, University of Örebro, Örebro, Sweden

C. Contributions to Science

1) Current controversy exists regarding normative references ranges for cortisol in children. We developed a novel assay measuring hair cortisol concentrations (HCC) in children and proposed that diurnal variations, or changes related to age, or sex, or puberty do not affect HCC values, therefore, measuring hair cortisol may represent an alternative approach to defining the normative cortisol values for children. We examined the relationship of maternal variables to hair cortisol levels and the social-emotional development of 1 year-olds, suggesting that hair cortisol mediates the effects of early adversity on social-emotional development. We recently found that maternal exposures to prenatal traumatic life events were associated with increased hair cortisol levels in preschool children. We identified a clinical profile of nervous system dysregulation in children and found it was associated with multiple adverse childhood experiences (ACEs), mediated possibly via neuroendocrine, neuroimmune and neurenteric pathways (including HPA axis dysregulation).
   a) Slominski R, Rovnaghi CR, **Anand KJS**. Methodological considerations for hair cortisol measurements in children. ***Therapeutic Drug Monitoring*** 2015; 37(6): 812-820. doi: 10.1097/FTD.00000000000209. PMID: 25811341. PMCID: PMC4581896.
   b) Slopen N, Roberts A, LeWinn KZ, Bush NR, Rovnaghi CR, Tylavsky F, **Anand KJS**. Maternal experiences of trauma and hair cortisol in early childhood in a prospective cohort. ***Psychoneuroendocrinology***, 2018; 98:168-176. PMID: 30170311

c) Elbers J, Rovnaghi CR, Golianu B, **Anand KJS**. Clinical profile associated with Adverse Childhood Experiences: The advent of nervous system dysregulation. ***Children*** 2017; 4 (11). pii: E98. doi: 10.3390/children4110098. PMID: 29140276 PMCID: PMC5704132.
d) Rovnaghi CR, **Anand KJS**. Pathways to nervous system dysregulation. ***Internal Medicine Review*** 2018; (in press).

2) In the 1980's, surgical operations were being performed in infants and young children with minimal or no anesthesia. We investigated the hormonal-metabolic stress responses of infants undergoing surgery and proposed the mechanisms by which early adverse experiences can lead to the long-term changes in brain development and behavior.
   a) **Anand KJS**, Causon RC, Christofides ND, Brown MJ, Bloom SR, Aynsley-Green A. Can the human neonate mount an endocrine and metabolic response to surgery? ***Journal of Pediatric Surgery*** 20:41-48, 1985. PMID: 3973812.
   b) **Anand KJS**, Scalzo FM. Can adverse neonatal experiences alter brain development and subsequent behavior? ***Biology of the Neonate***; 77(2): 69-82, 2000. PMID: 10657682.
   c) **Anand KJS**. Pain, plasticity, and premature birth: a prescription for permanent suffering? ***Nature Medicine***, 6(9): 971-973, 2000. PMID: 10973310.
   d) Bhutta AT, Cleves MA, Casey PH, Cradock MM, **Anand KJS**. Cognitive and behavioral outcomes of school-aged children who were born preterm: A meta-analysis. ***JAMA*** 288(6): 728-737, 2002. PMID: 12169077

3) We designed, executed and reported the first randomized, placebo-controlled clinical trials to show that adequate anesthesia can reduce the hormonal-metabolic stress responses of newborns and thereby decreasing their morbidity and mortality following surgery in the neonatal period.
   a) **Anand KJS**, Sippell WG, Aynsley-Green A. Randomized trial of fentanyl anesthesia in preterm neonates undergoing surgery: Effects on the stress response. ***Lancet*** i (8527):243-248, 1987. PMID: 2879174.
   b) **Anand KJS**, Sippell WG, Schofield N McC, Aynsley-Green A. Does halothane anaesthesia decrease the metabolic and endocrine stress responses of newborn infants undergoing operation? ***British Medical Journal*** 296: 668-672, 1988. PMID: 3128362.
   c) **Anand KJS**, Hickey PR. Halothane-morphine compared with high-dose sufentanil for anesthesia and postoperative analgesia in neonatal cardiac surgery. ***New England Journal of Medicine*** 326:1-9, 1992. PMID: 1530752.

4) Results from the randomized clinical trials listed above led to the first scientific rationale for development of the pain system in early life. This presented a framework for pain assessment in neonates, which allowed us to launch some of the pivotal multicenter randomized clinical trials of neonatal analgesia / anesthesia.
   a) **Anand KJS**, Hickey PR. Pain and its effects in the human neonate and fetus. ***New England Journal of Medicine*** 317: 1321-1329, 1987. PMID: 3317037.
   b) **Anand KJS**, Hall RW, Desai NS, et al. Effects of pre-emptive morphine analgesia in ventilated preterm neonates: Primary outcomes from the NEOPAIN trial. ***Lancet,*** 2004, 363: 1673-1682. PMID: 15158628.
   c) **Anand KJS**, Eriksson M, Boyle EM, et al. Assessment of continuous pain in newborns admitted to NICUs in 18 European countries. ***Acta Paediatrica*** 2017, 106(8): 1248-1259. PMID: 28257153.
   d) **Anand KJS**. Defining Pain in Newborns: Need for a new taxonomy? ***Acta Paediatrica*** 2017; 106(9): 1438-1444. DOI: 10.1111/apa.13936, PMID: 28556311.

5) Changes in clinical practice led to indiscriminate opioid use with an increasing incidence of opioid tolerance and withdrawal. We examined the mechanisms underlying opioid tolerance and their impact on early brain development; documented the prevalence of opioid tolerance and withdrawal in critically ill children in a multicenter study and its relationships to the variability of clinical practices for opioid analgesia.
   a) Liu JG, Rovnaghi CR, Garg S, **Anand KJS**. Opioid receptor desensitization contributes to thermal hyperalgesia in infant rats. ***European Journal of Pharmacology***, 491 (2-3): 127-136, 2004. PMID: 15140629
   b) **Anand KJS**, Willson DF, Berger J, Harrison R, Meert KL, Zimmerman J, Carcillo J, Newth CJL, Prodhan P, Dean JM, Nicholson CE. Tolerance and withdrawal from prolonged opioid use in critically ill children. ***Pediatrics*** 125(5): e1208-1225, 2010. PMID: 20403936
   c) **Anand KJS**, Clark AE, Willson DF, Berger J, Meert KL, Zimmerman JJ, Harrison R, Carcillo JA, Newth CJL, Bisping S, Holubkov R, Dean JM, Nicholson CE. Opioid Analgesia in Mechanically Ventilated

Children: Results from the multicenter MOTIF study. ***Pediatric Critical Care Medicine***, 14(1): 28-36, 2013. PMID: 23132396

d) **Anand KJS**. Revisiting a dilemma: repetitive pain vs. opioid exposures? ***Acta Paediatrica*** 105(7): 736-7, 2016. doi: 10.1111/apa.13442. PMID: 27272629

D. Additional Information: Research Support and/or Scholastic Performance

My scholarly contributions include more than 300 papers, chapters and books, with an H-index of >60.
Many of my publications are listed in Scopus: http://www.scopus.com/authid/detail.url?authorId=7101749758

Ongoing Research Support:

1 K08 HL118118 (Schwingshackl) 02/01/2014 – 05/31/2019
National Heart, Lung & Blood Institute (NIH/NHLBI)
The role of 2-pore domain potassium channels in Acute Lung Injury
Major goals of this project are to develop novel therapeutic targets including stretch-activated ion channels for treating ARDS in children and adults.
Role: Co-Mentor

5 K23 HD082782 (Chidambaran) 09/01/2014 – 06/30/2019
Eunice Kennedy Shriver National Institute for Child Health & Human Development (NIH/NICHD)
Morphine Pharmacogenomics to Predict Risk of Respiratory Depression in Children
Major goals of this project are to identify specific genetic biomarkers that can increase the risks of opioid side effects including respiratory depression after postoperative analgesia.
Role: Co-Mentor

Stanford University School of Medicine (Anand) 10/01/2015 – 09/30/2020
Child Health Research Institute
Identifying potential biomarkers for measuring pain and stress in critically ill children
Major goals of this grant are to set up the Pain/Stress Neurobiology Laboratory focused on investigating the mechanims, measurements, and outcomes of pain/stress in infants and children.

Child Health Research Institute (Anand) 01/01/2018 – 06/30/2019
Biomarkers of Risk and Resilience in Preschool Children
Major goals of this project are to develop and validate a novel ELISA-based assay for measuring hair oxytocin concentrations (HOC) and to collect pilot data from preschool children and their parents currently living in Santa Clara County.

1 R41 DA046983 (Gholami, Anand) 09/01/2018 – 08/30/2019
National Institute for Drug Abuse (NIH/NIDA)
Measuring Infant Pain Objectively using Sensor Fusion & Machine Learning Algorithms
Major goals of this project are to differentiate acute pain from baseline or non-painful events in hospitalized infants and newborns and to develop sensor fusion frameworks for integrating the physiological data from multiple clinical and non-clinical sensors.

1 S10 OD026962-01 (Chien) 02/01/2019 – 01/31/2020
NIH Office of the Director (Priority Score=10 from ***ZRG1 BCMB-T(30)***, awaiting notice of grant award)
Xevo TQ-XS Triple Quadrupole Mass Spectrometer System
Major goals of this project are to fund a Triple Quadrupole Mass Spectrometer for supporting a range of funded projects involving targeted peptide and small molecule quantitation, including the hair cortisol and hair oxytocin proposed for this project.
Role: Co-Investigator.