NIH Biographical Sketch Common Form

Name: Natarajan, Sathish Kumar

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0001-7491-8592

Position Title: Associate Professor

Organization and Location:University of Nebraska-Lincoln / Nutrition & Health Sciences, Lincoln, Nebraska, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
University of Nebraska Medical Center, Omaha, Nebraska, United States	Postdoctoral Fellow	08/2012	06/2014	Cholangiocyte Lipoapoptosis in Fatty Liver Disease
University of Nebraska-Lincoln, Lincoln, Nebraska, United States	Postdoctoral Fellow	11/2008	06/2012	Supplementation of Proline prevents Apoptosis
Tamilnadu Dr. MGR Medical University, Chennai, Tamilnadu, India	Doctor of Philosophy (PHD)	06/2001	10/2008	Biomedical Sciences
University of Madras, Chennai, Tamilnadu, India	Master of Science (MS)	06/1999	05/2001	Biochemistry
University of Madras, Chennai, Tamilnadu, India	Bachelor of Science (BS)	05/1996	05/1999	Biochemistry

Appointments and Positions

2024 - present Associate Professor, University of Nebraska-Lincoln / Nutrition & Health Sciences, Lincoln, Nebraska, United States

2016 - 2024 Assistant Professor, University of Nebraska-Lincoln/ Nutrition & Health Sciences, Lincoln, Nebraska, United States

2014 - 2015 Lecturer, University of Nebraska Medical Center/ Biochemistry and Molecular Biology, Omaha, Nebraska, United States

2012 - 2014 Postdoctoral Research Associate, University of Nebraska Medical Center / Biochemistry and Molecular Biology, Lincoln, Nebraska, United States

Products

Products Closely Related to the Proposed Project

1. Sahoo PK, Ravi A, Liu B, Yu J, Natarajan SK. Palmitoleate protects against lipopolysaccharide-induced inflammation and inflammasome activity. J Lipid Res. 2024 Nov;65(11):100672. PubMed Central PMCID: PMC11585775.
2. Natarajan SK, Ingham SA, Mohr AM, Wehrkamp CJ, Ray A, Roy S, Cazanave SC, Phillippi MA, Mott JL. Saturated free fatty acids induce cholangiocyte lipoapoptosis. Hepatology. 2014 Dec;60(6):1942-56. PubMed Central PMCID: PMC4553418.
3. Natarajan SK, Bruett T, Muthuraj PG, Sahoo PK, Power J, Mott JL, Hanson C, Anderson-Berry A. Saturated free fatty acids induce placental trophoblast lipoapoptosis. PLoS One. 2021;16(4):e0249907. PubMed Central PMCID: PMC8062006.
4. Natarajan SK, Stringham BA, Mohr AM, Wehrkamp CJ, Lu S, Phillippi MA, Harrison-Findik D, Mott JL. FoxO3 increases miR-34a to cause palmitate-induced cholangiocyte lipoapoptosis. J Lipid Res. 2017 May;58(5):866-875. PubMed Central PMCID: PMC5408604.
5. Sahoo PK, Krishnamoorthy C, Wood JR, Hanson C, Anderson-Berry A, Mott JL, Natarajan SK. Palmitate induces integrated stress response and lipoapoptosis in trophoblasts. Cell Death Dis. 2024 Jan 11;15(1):31. PubMed Central PMCID: PMC10784287.

Other Significant Products Highlighting Contributions to Science

1. Thompson M, Ulu A, Yuil-Valdes AG, Mukherjee M, Thoene M, Van Ormer M, Slotkowski R, Lyden E, Anderson Berry A,

Hanson CK, Nordgren TM, Natarajan SK. Omega-6 and Omega-3 Fatty Acid-Derived Oxylipins from the Lipoxygenase Pathway in Maternal and Umbilical Cord Plasma at Delivery and Their Relationship with Infant Growth. Int J Mol Sci. 2022 Jan 9;23(2) PubMed Central PMCID: PMC8775763.

2. Muthuraj PG, Pattnaik A, Sahoo PK, Islam MT, Pattnaik AK, Byrareddy SN, Hanson C, Anderson Berry A, Kachman SD, Natarajan SK. Palmitoleate Protects against Zika Virus-Induced Placental Trophoblast Apoptosis. Biomedicines. 2021 Jun 4;9(6) PubMed Central PMCID: PMC8226770.
3. Muthuraj P. Fetal Programming in Maternal Obesity. Diabesity. 2020; 6(3):36-39. Available from: DOI:10.15562/diabesity.2020.71
4. Ulu A, Sahoo PK, Yuil-Valdes AG, Mukherjee M, Van Ormer M, Muthuraj PG, Thompson M, Anderson Berry A, Hanson CK, Natarajan SK, Nordgren TM. Omega-3 Fatty Acid-Derived Resolvin D2 Regulates Human Placental Vascular Smooth Muscle and Extravillous Trophoblast Activities. Int J Mol Sci. 2019 Sep 7;20(18) PubMed Central PMCID: PMC6770915.
5. Hahka T, Sekar D, Sahoo PK, Ravi A, Freel C, Krishnamoorthy C, Ramamurthy S, Rapoza R, Drakowski R, Akbar A, VanOrmer M, Thoene M, Hanson CK, Nordgren T, Natarajan SK, Anderson Berry A. RvD2 mitigates TNFα-Induced mitochondrial reactive oxygen species through NRF2 signaling in placental trophoblasts. Front Physiol. 2025;16:1547940. PubMed Central PMCID: PMC12000658.

Certification:

I certify that the information provided is current, accurate, and complete. This includes but is not limited to information related to domestic and foreign appointments and positions.

I also certify that, at the time of submission, I am not a party to a malign foreign talent recruitment program.

Misrepresentations and/or omissions may be subject to prosecution and liability pursuant to, but not limited to, 18 U.S.C. §§ 287, 1001, 1031 and 31 U.S.C. §§ 3729-3733 and 3802.

Certified by Natarajan, Sathish Kumar in SciENcv on 2026-02-10 18:51:51

NIH BIOGRAPHICAL SKETCH SUPPLEMENT

Name: Natarajan, Sathish Kumar

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0001-7491-8592

Position Title: Associate Professor

Organization and Location: University of Nebraska-Lincoln / Nutrition & Health Sciences, Lincoln, Nebraska, United States

Personal Statement

I am a tenured Associate Professor in the Department of Nutrition & Health Sciences, University of Nebraska-Lincoln and my research focus is to develop novel therapeutic nutrient approaches against maternal obesity-induced placenta and fetal organ damage during pregnancy thereby preventing offspring from developing metabolic disease later in their life. As a Principal Investigator of this application, I will provide overall direction for the project that aims to a) Determine the mechanism of palmitoleate protection against lipotoxicity in the placenta and fetal liver during maternal obesity (MO); b) Elucidate the protective role of palmitoleate against MO-induced ER Stress in the placenta and fetal tissues; and c)Ascertain the protective role of palmitoleate against inflammation in the placenta, fetal brain and fetal brain in MO using in vitro, ex vivo and in vivo experimental approaches. I have broad background and expertise in studying the mechanism of cell injury in human placental damage during acute fatty liver of pregnancy, placental infection, protective nutrient signaling and apoptotic signaling pathways, mitochondrial function, and mitochondrial fatty acid oxidation disorders, which positions me well to lead this project. I had demonstrated placental damage and mitochondrial dysfunction during acute fatty liver of pregnancy and currently studying the protective role of omega-7 and omega-3 fatty acid against cell death signaling pathway, I have also established the pro-apoptotic role of FoxO3 and microRNA-34a in cholangiocyte lipoapoptosis in metabolic dysfunction-associated steatotic liver disease (MASLD) and have identified that palmitoleate protects against palmitate-induced cholangiocyte lipoapoptosis and trophoblast lipoapoptosis. Further, I have also established the protective role of palmitoleate against lipopolysaccharide-induced inflammation and NLRP3 inflammasome activity in placental trophoblasts, human monocyte-derived macrophages and mouse bone marrow-derived macrophages. I have ongoing projects to study the beneficial role of dietary macadamia nuts against maternal obesity-induced complications from USDA-NIFA-AFRI standard grant (2023-67017-40223) and Hatch multistate enhanced program grant from University of Nebraska to study the beneficial role of dietary palmitoleate against maternal obesity related complications. I have served as an ad hoc grant reviewer for the NICHD, special emphasis panel in NIEHS, early career reviewer to NIDDK, Graduate Fellowship Panel reviewer to NSF and DoD I have 66 peer-reviewed publications including pre-print, editorial comment and a book chapter. These articles have been placed in journals like Hepatology, Cell Death & Disease, Cell Death & Discovery, Journal of Lipid Research, International Journal of Molecular Sciences, and Journal of Virology. I have been cited in 2,817 documents including editorial comments (Source: Scopus.com, ID#9035955300; h-index:24). In summary, I have necessary expertise, leadership to mentor graduate students and postdoctoral fellows and successfully complete the proposed goals of this project.

Honors

2023	Dinsdale Family Faculty Award, Institute of Agriculture and Natural Resources, UNL
2022	Annual Research Symposium Alumni Presentation, Biochemistry and Molecular Biology, University of Nebraska Medical Center
2019	Honorable Mention: Best Undergraduate Mentor Award, Academic Affairs, University of Nebraska-Lincoln
2016	Thematic Best Poster Award, American Society for Biochemistry and Molecular Biology
2015	Travel Award to attend Industry Colloquium, Novel Targets and Therapies in Liver Disease, American Association for the Study of Liver Disease (AASLD)
2006	Young Scientist Travel Award, 20th IUBMB Conference, Kyoto, Japan
2004	Shakuntala Amir Chand Prize, Indian Council of Med Research (ICMR). Ministry of Education, Government of India

Contributions to Science

1. Free Fatty Acid-induced Trophoblast and Cholangiocyte Lipoapoptosis: Maternal obesity and Metabolic syndrome-Associated Steatotic Liver Disease (MASLD) patients have elevated levels of circulating saturated free fatty acids (FFAs). We have demonstrated that lipotoxic saturated FFAs induce caspase-dependent trophoblast lipoapoptosis. Lipoapoptosis is defined as

programmed cell death induced by high levels of fatty acid exposure. I have also established the pro-apoptotic role of forkhead family of transcription factor class O (FoxO) 3 and microRNA-34a in cholangiocyte lipoapoptosis in MASLD (Formerly referred as non-alcoholic fatty liver disease, NAFLD). I have recently demonstrated that palmitate induces integrated stress response in trophoblast lipoapoptosis which involve activation of cJun N-terminal kinase and FoxO3-dependent p53 upregulated modulator of apoptosis (PUMA). We have also shown the role of CHOP activation in palmitate-induced trophoblast lipoapoptosis. Further, palmitate was also shown to activate extracelluar signal-regulated kinase and stress granules as a cell survival response. Palmitoleate, an omega-7 monounsaturated fatty acid (present in high levels in macadamia nuts & oil), has been shown to be protective against hepatocyte lipoapoptosis, cholangiocyte- and trophoblast lipoapoptosis, respectively. I have also demonstrated that palmitoelate prevents lipopolysaccharide induced inflammation and NLRP3 inflammasome activity in trophoblasts, human monocyte-derived macrophages and mouse bone marrow-derived macrophages. These data suggest that palmitoleate treatment can also be a nutritional therapy for the prevention of obesity-induced complications.

2. Placenta and Liver Lipotoxicity in Acute Fatty Liver of Pregnancy: I started my research career by developing an animal model for fatty acid oxidation disorder-induced hepatic microvesicular steatosis using valproic acid and showed that the co-administration of the peroxisome proliferator, clofibrate, results in protection against the oxidative damage seen in subcellular organelles and decreases hepatic microvesicular steatosis. Later, my work revealed a novel mechanism of placental damage in acute fatty liver of pregnancy (AFLP), a rare autosomal recessive disease that occurs during the third trimester of pregnancy. AFLP is a catastrophic illness resulting in progressive maternal liver dysfunction and secondary systemic compromise that poses a significant challenge to the fetus and mother. We had shown that defect due to genetic mutation in fatty acid oxidizing enzymes results in placental mitochondrial damage/dysfunction and oxidative stress in the placenta and systemic oxidative stress, which acts as a source of maternal liver damage in AFLP patients. Further, we had demonstrated that arachidonic acid from the placenta of AFLP patient's damages hepatocyte mitochondria by enhancing the levels of mitochondrial-derived free radicals, in an in vitro culture system. More importantly, the arachidonic acid also resulted in lipoapoptosis of cultured hepatocytes as evidenced by an increase in the caspase 3 activity. My work clearly showed that lipoapoptosis occurs even at low concentrations of toxic arachidonic acids reflective of pathology observed in AFLP patients.
3. Omega-3 fatty acid metabolism in the placenta. Our work demonstrated that omega-3 fatty acid-derived lipid mediators regulate placental trophoblast function. We have also demonstrated the expression of Resolvin D2 (RvD2) receptor, GPR18 expression in placental trophoblasts and have observed an increase in membrane localization of GPR18 with RvD2 supplementation in trophoblasts. I have shown that RvD1 and RvD2 derived from docosahexaenoic acid (DHA) were increased in maternal circulation in settings of adverse health or inflammation. Further, we observed the role of RvD2 in the inflammation resolution in trophoblasts. Supplementation of RvD2 prevents against tumor necrosis factor alpha exposure related mitochondrial reactive oxygen species by way of activating NRF2 transcription factor. We have also recently demonstrated that both omega-3 and omega-6 derived oxylipins influence fetal birth length and weight percentiles. We have also shown that placental inflammation in hypertensive disorders of pregnancy compared to normotensive placentae. These accomplishments show case my lab expertise in studying placental lipid metabolism.
4. Zika Virus induces endoplasmic reticulum (ER) stress and apoptosis in placental trophoblasts and Neuronal cells: Zika virus infection in pregnant women is highly associated with Congenital Zika Syndrome and the development of microcephaly, intra uterine growth retardation and ocular damage in the fetus. Recent advances in Zika virus infection suggest that the virus is transmitted to the fetal organs including brain via infecting the placenta. Infection of the placenta during the first and second trimester plays a crucial role in Zika virus transmission from maternal circulation to the fetus resulting in Congenital Zika Syndrome. We had recently demonstrated that Zika virus induces the activation of ER stress and mitogen activated protein kinase's (MAPK). Activation of cJun N-terminal kinase (JNK) plays a critical role in Zika virus-induced placental trophoblast apoptosis. We also have preliminary data to show that Zika virus induces apoptosis in neuroblastoma cell and retinal pigmental epithelial cells. Further, we had demonstrated that supplementation of palmitoleate dramatically protects ZIKV-induced placental trophoblast and neuronal apoptosis. The identification of palmitoleate protection against Zika virus-induced apoptosis will result in potential nutrient therapy against placental damage and fetal brain caused due to Zika virus infection. These accomplishments show case my lab expertise in studying placental viral infection and protective role for palmitoleate against Zika virus infection.
5. Established that proline and pipecolate metabolism promote cell survival. Proline catabolism can lead to the formation of superoxide and induces apoptosis while biosynthesis or accumulation of proline appears to be protective against oxidative stress. These opposing properties suggest proline has a pivotal role in mediating redox homeostasis under different conditions. We have provided evidence that proline supplementation protects mammalian cells via Akt-FoxO3 signaling pathways for cell survival during stress. Similar to proline, pipecolate also protects mammalian cells against oxidative stress-induced cell death. My work demonstrated a novel findings and established that pipecolate oxidase is present in the mitochondria besides to its home, peroxisomes. Identifying nutrients and small molecules that are cytoprotective related to current proposal.

Certification:

I certify that the information provided is current, accurate, and complete. This includes but is not limited to information related to domestic and foreign appointments and positions.

I also certify that, at the time of submission, I am not a party to a malign foreign talent recruitment program.

Misrepresentations and/or omissions may be subject to prosecution and liability pursuant to, but not limited to, 18 U.S.C. §§ 287, 1001, 1031 and 31 U.S.C. §§ 3729-3733 and 3802.

Certified by Natarajan, Sathish Kumar in SciENcv on 2026-02-1018:51:51