BIOGRAPHICAL SKETCH

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NAME: Arthur, Subha

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

POSITION TITLE: Associate Professor

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
Women's Christian College University of Madras, Chennai, India	BSc	03/1995	Botany, Zoology & Chemistry
University of Madras, Chennai, India	MSc	04/1997	Molecular Biology
Dr. ALM Institute of Basic Medical Sciences University of Madras, Chennai, India	PhD	02/2004	Molecular Biology-Microbiology
Section of Digestive diseases, Dept. of Medicine, WVU, Morgantown, WV 26505.	Post doctorate Research	12/2009	Gastrointestinal physiology

A. Personal Statement

My primary research focus for more than a decade has been in the area of intestinal ion and nutrient transport processes, with emphasis on their regulation in pathophysiological states such as inflammatory bowel disease and obesity. First as a post-doctoral researcher and now as a junior faculty member, I have focused my research toward understanding the mechanisms of regulation of intestinal nutrient and ion transporters, which resulted in 17 publications between 2014 and 2019. I have directed undergraduate, graduate students and medical students on their research projects and have experience coordinating a group of researchers to complete a research project. As one of the junior investigators of the Marshall University's COBRE ACCORD grant (P20GM121299-01A1), I was trained to work as an independent researcher on all aspects of research to achieve academic excellence, which I believe has enhanced my effectiveness and responsibilities to act as a principal investigator.

B. Positions and Honors

Positions and Employment

2004-05 Lecturer, Dept. of Biotechnology, SIST, Chennai, India.

2005-09 Postdoctoral researcher, Section of Digestive diseases, Dept. of Medicine, WVU.

2010-13 Research Associate, Section of Digestive diseases, Dept. of Medicine, WVU.

2013- 20 Assistant Professor, Department of Clinical and Translational Sciences,
Marshall University School of Medicine, Huntington WV.

2020- Associate Professor, Department of Clinical and Translational Sciences,
Marshall University School of Medicine, Huntington WV.

Other Experiences and Professional Memberships

2005-10 Trainee member, American Gastroenterological Association.

2010- Member, American Gastroenterological Association

Honors

1995 Alma Stockey Convocation Prize, Women's Christian College, Chennai, India.

1995 Dr. Anna Zachariah Prize, Women's Christian College, Chennai, India.

1995 P.X.Rengasami and Sinnadurai Memorial Prize, Women's Christian College, Chennai, India.

1998 Junior Research Fellow, Rameshwardas Birla Smarak Kosh, Mumbai, India.

2001 Senior Research Fellow, Lady Tata Memorial Trust, Mumbai. India.

2017 Faculty Award presented by Marshall BMS graduate students.

C. Contribution to Science

1 My research focus over the last few years has been to understand the role of intestinal bile acid transporter ASBT in obesity-associated dyslipidemia, which is central to most of the complications of obesity. Bile acids that facilitate lipid absorption in the intestine are known to be increased in obesity leading to the disruption of bile acid and lipid homeostasis. However, it was unknown how ASBT, the sole intestinal mediator of bile acid absorption, is regulated in obesity. With this relevance, my coauthors and I have demonstrated for the first time that in obesity, the dyslipidemia that leads to many of the complications of the condition, may be partly due to deregulation of intestinal bile acid absorption. We have shown in two in vivo models of obesity, namely Zucker rat model of monogenic obesity and TALLYHO mouse model of polygenic obesity, and as well as in human obesity that ASBT expression was significantly increased in the distal ileum. Moreover, we also demonstrated in Zucker rats and in an in vitro model of rat intestinal epithelial cells that the increased ASBT expression is likely due to the transcriptional regulation by the nuclear receptor Farnesoid X receptor. These results of the study further indicated that in obesity, the increase in FXR stimulates not only the assimilation of bile acids by increasing ASBT, but also the subsequent intracellular handling and export of bile acids by augmenting the appropriate bile-acid-handling proteins such as IBABP and OSTα. Given the importance of bile acids in dyslipidemia associated with obesity, the knowledge gained from this study has laid a strong foundation to better understand the regulation of intestinal bile acid absorption in obesity, which may lead to new and more efficacious treatment options for obesity.

Sundaram S, Palaniappan B, Nepal N, Chaffins S, Sundaram U, **Arthur S**. Mechanism of Dyslipidemia in Obesity-Unique Regulation of Ileal Villus Cell Brush Border Membrane Sodium-Bile Acid Cotransport. Cells. 2019;8(10). Epub 2019/10/19. doi: 10.3390/cells8101197. PubMed PMID: 31623375; PMCID: PMC6830326.

2. Diabetes and hypertension are the major metabolic disorders associated with obesity. The contribution of gut as an effector of diet associated obesity and the consequent metabolic disorders, primarily diabetes and obesity, is not fully understood. My co-authors and I have demonstrated recently, not only in two in vivo models of obesity but also in obese human intestine, that the

sodium dependent absorption of glucose, mediated by SGLT1, is significantly increased in the obese intestine. Moreover, this stimulation was coupled to increased absorption of chloride through $Cl:HCO_3$ exchangers DRA and PAT1. However, the Na:H exchanger, which is traditionally known to be coupled to SGLT1, was not affected. These alterations in the sodium and glucose absorptive processes will lead to an increase in glucose and NaCl absorption, which provides the pathophysiologic basis for the deregulation of glucose and NaCl homeostasis of diabetes and hypertension, respectively, in obesity. These data provided new knowledge to develop more efficacious treatment targets to combat obesity-associated diabetes and hypertension.

Palaniappan B, **Arthur S**, Sundaram VL, Butts M, Sundaram S, Mani K, Singh S, Nepal N, Sundaram U. Inhibition of intestinal villus cell Na/K-ATPase mediates altered glucose and NaCl absorption in obesity-associated diabetes and hypertension. FASEB journal: official publication of the Federation of American Societies for Experimental Biology. 2019; 33(8):9323-33. Epub 2019/05/21. doi: 10.1096/fj.201802673R. PubMed PMID: 31107610; PMCID: PMC6662973.

3. I have documented through a series of publications, both as the primary investigator and as a co-investigator, that intestinal Na-glutamine co-transporters B0AT1 and SN2 are altered during chronic intestinal inflammation resulting in glutamine malabsorption. This finding is extremely significant as glutamine is the essential building block of proteins and malabsorption of this nutrient results in progression of inflammatory bowel disease. I have further shown with my co-investigators that these alterations are due to the direct effect of immune inflammatory mediators on Na-glutamine co-transporters in the enterocytes and could be efficiently reversed to normal, not only with a broad spectrum immune modulator such as a glucocorticoid but also with specific inhibitors of inflammatory mediators/pathways. The publications listed below, established that malabsorption of glutamine is an actively regulated process by the intestinal cells and is completely revocable. This information is extremely vital as it lays the stage to formulate efficacious treatment modalities for this chronic condition that is without a medical cure and commonly requires a lifetime of care.

Arthur S, Manoharan P, Sundaram S, Rahman MM, Palaniappan B, Sundaram U. Unique Regulation of Enterocyte Brush Border Membrane Na-Glutamine and Na-Alanine Co-Transport by Peroxynitrite during Chronic Intestinal Inflammation. International journal of molecular sciences. 2019;20(6). Epub 2019/03/29. doi: 10.3390/ijms20061504. PubMed PMID: 30917504; PMCID: PMC6470611.

Arthur S, Singh S, Sundaram U. Cyclooxygenase pathway mediates the inhibition of Na-glutamine co-transporter B0AT1 in rabbit villus cells during chronic intestinal inflammation. PloS one. 2018;13(9):e0203552. Epub 2018/09/08. doi: 10.1371/journal.pone.0203552. PubMed PMID: 30192835; PMCID: PMC6128596.

Singh S, **Arthur S**, Sundaram U. Unique regulation of Na-glutamine cotransporter SN2/SNAT5 in rabbit intestinal crypt cells during chronic enteritis. Journal of cellular and molecular medicine. 2018;22(3):1443-51. Epub 2017/12/23. doi: 10.1111/jcmm.13257. PubMed PMID: 29271063; PMCID: PMC5824387.

Complete list of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/myncbi/1DwhNN2y2tO5Y/bibliography/public/

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

Ongoing Research Support:

1P20GM121299-01A1 Center of Biomedical Research Excellence (COBRE)
Appalachian Center for Cellular transport in Obesity Related Disorders (ACCORD)
Sundaram (PI) Feb. 2018- Feb.2021
Title: Regulation of intestinal bile acid absorption in obesity
Role: Junior Investigator (PI of project 1 - 50% effort)
Note: Current submitted RO1 will replace above support in the COBRE grant

Veteran Affairs Merit grant: I01BX003443-01A2
Sundaram (PI) July 2017- June 2021
Title: Regulation of intestinal NaCl absorption
Role: Co-investigator (25% effort)

Completed Research Support

Appalachian Centre for Clinical and Translational Sciences 02/2015-01/2016
Title: Regulation of sodium dependent bile acid absorption in obesity.
Role: PI

NIH P20GM103434-15 Next Generation Sequencing pilot grant 08/2015-07/2016
Title: Molecular mechanism of ASBT regulation by high fat diet.
Role: PI