BIOGRAPHICAL SKETCH

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NAME: Arthur, Subha

eRA COMMONS USERNAME (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 DateMM/YYYY | FIELD OF STUDY |
| --- | --- | --- | --- |
| Women’s Christian College, Chennai, India | BSc | 03/1995 | Botany, Zoology, Chemistry |
| University of Madras, Chennai, India | MSc | 04/1997 | Molecular Biology |
| University of Madras, Chennai, India | PhD | 02/2004 | Microbiology |
| West Virginia University, Morgantown | Post-doctoral | 12/2009 | Gastroenterology |

1. Personal Statement

My research interests broadly focus on understanding intestinal ion and nutrient transport processes, with emphasis on their regulation in pathophysiological states such as inflammatory bowel disease and obesity. My current work aims to decipher the functional and molecular mechanisms underlying increased intestinal bile acid absorption in obesity, with the ultimate goal of identifying potential therapeutic targets to alleviate obesity and its associated dyslipidemia which are the primary drivers of several chronic metabolic disorders such as cardiovascular disease and diabetes, the major contributors of premature mortality in this country. Using two etiologically distinct rat models of obesity—genetic and diet-induced—my lab has demonstrated that intestinal bile acid absorption, mediated by the apical sodium-dependent bile acid co-transporter (ASBT) in villus cells, is significantly elevated in obesity. Notably, high-fat diet exposure upregulated ASBT expression prior to the onset and progression of dyslipidemia, suggesting that increased intestinal bile acid absorption via ASBT may be the initiating event in obesity-related lipid abnormalities. Further investigations revealed that ASBT is upregulated not only at the cellular level, but also along the crypt-villus and caudal-oral axes of the small intestine. This multilayered upregulation of ASBT in obesity likely amplifies net bile acid absorption and contributes to enhanced fat absorption, implicating dysregulated ASBT as a central player in the pathogenesis of obesity. Ongoing research is focused on elucidating the intracellular mechanisms that regulate ASBT in proximal and distal small intestine to identify a novel, intestine-specific target to reverse ASBT-mediated bile acid hyperabsorption, thereby mitigating obesity-associated dyslipidemia and other metabolic disorders.

Sundaram S, Jagadeesan A, Paulraj RS, Sundaram U, **Arthur S**. Novel Expression of Apical Bile Acid Transport (ASBT) More Proximally Than Distal Ileum Contributing to Enhanced Intestinal Bile Acid Absorption in Obesity. Int J Mol Sci. 2024 Oct 25;25(21):11452. doi: 10.3390/ijms252111452. PMID: 39519005; PMCID: PMC11547122.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific appointment

2020-Present Associate Professor, Department of Clinical and Translational Sciences,

 Marshall University, Huntington WV.

2013-2020 Assistant Professor, Department of Clinical and Translational Sciences,

 Marshall University, Huntington WV.

2010-2013 Research Associate**,** Section of Digestive diseases, Dept. of Medicine, WVU**.**

2010- Present Member, American Gastroenterological Association

2010-2013 Research Associate**,** Section of Digestive diseases, Dept. of Medicine, WVU**.**

2005-2009 Postdoctoral researcher, Section of Digestive diseases, Dept. of Medicine, WVU**.**

2005-2010 Trainee member, American Gastroenterological Association.

2004-2005 Lecturer, Dept. of Biotechnology, SIST, Chennai, India.

Honors

2017 The 2017 Faculty Award by Marshall BMS graduate students.

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

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

1995 Alma Stockey Convocation Prize, Women’s Christian College (WCC), Chennai, India.

1995 Dr. Anna Zachariah Prize, WCC, Chennai, India.

1. P.X.Rengasami and Sinnadurai Memorial Prize, WCC, Chennai, India.

C. Contributions to Science

1. 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 bile acid absorptive mechanism, is regulated in obesity. My coauthors and I demonstrated for the first time that dyslipidemia that is central to most of the disorders of obesity occurs primarily due to increased intestinal bile acid absorption. Moreover, we also demonstrated in Zucker rat model of obesity and in an in vitro model of rat intestinal epithelial cells that the increased ASBT expression in obesity is due to the transcriptional upregulation by the nuclear receptor Farnesoid X receptor. Further, FXR stimulates not only the absorption of bile acids by increasing ASBT, but also the subsequent intracellular handling and export of bile acids by upregulating the expression of bile-acid-handling proteins IBABP and OST resulting in increased bile acid levels entering portal vein and systemic circulation. In a recent study we also demonstrated that ASBT-mediated bile acid absorption and FXR expression are also significantly increased along the proximal length of the small intestine in obesity. This is a very significant observation since ASBT was known hitherto to be expressed only in the distal ileum of the small intestine. This was further substantiated by significant reduction in bile acid levels in obese Zucker rats both in the distal ileum as well as in the cecum, indicating that bile acids are absorbed actively throughout the small intestine, resulting in reduced levels entering the distal intestine and cecum and increased levels entering systemic circulation. Given the importance of bile acids in dyslipidemia associated with obesity, the knowledge gained from these studies have 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, Jagadeesan A, Paulraj RS, Sundaram U, **Arthur S**. Novel Expression of Apical Bile Acid Transport (ASBT) More Proximally Than Distal Ileum Contributing to Enhanced Intestinal Bile Acid Absorption in Obesity. Int J Mol Sci. 2024 Oct 25;25(21):11452. doi: 10.3390/ijms252111452. PMID: 39519005; PMCID: PMC11547122.

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.

1. 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:HCO3 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.

**Arthur S**, Palaniappan B, 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.

1. 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 the malabsorption of glutamine. This finding is extremely significant as glutamine is the essential building block of proteins and malabsorption of this nutrient results in progression of the 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. These series of publications 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.

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.

**Arthur S**, Sundaram U. Inducible nitric oxide regulates intestinal glutamine assimilation during chronic intestinal inflammation. Nitric Oxide. 2015 Jan 30; 44:98-104 (PMID: 25524833).

1. Malnutrition is the least understood complication of chronic alcoholism. Therefore, to better understand alcohol dependent malnutrition, we investigated how moderate alcohol consumption may affect the intestinal absorption of essential dietary nutrients. We demonstrated that the absorption of essential dietary nutrients such as glucose and amino acid glutamine mediated by Na-dependent co-transports SGLT1 and B0AT1 respectively were indeed downregulated in the small intestine establishing the role of intestinal nutrient transporters in malnutrition associated with alcohol consumption. The results of the studies describe possible mechanisms for the onset of malnutrition commonly seen in chronic alcoholics and thus has potential implications for the treatment of moderate ethanol-dependent malnutrition.

Molly Butts, Raja Singh Paulraj, Jennifer Haynes, **Subha Arthur**, Soudamani Singh and Uma Sundaram. Moderate Alcohol Consumption Inhibits Sodium-Dependent Glutamine Co-Transport in Rat Intestinal Epithelial Cells in Vitro and Ex Vivo. Nutrients 2019, 11(10), 2516; [PMID:31635319](https://doi.org/10.3390/nu11102516.%20PMID%3A31635319).

Butts M, Singh S, Haynes J, **Arthur S**, Sundaram U. Moderate Alcohol Consumption Uniquely Regulates Sodium-Dependent Glucose Co-Transport in Rat Intestinal Epithelial Cells In Vitro and In Vivo. The Journal of nutrition. 2020;150(4):747-55. Epub 2019/11/27. doi: 10.1093/jn/nxz277. PubMed PMID: 31769840; PMCID: PMC7138678.

**Complete list of Published Work in MyBibliography:**

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