BIOGRAPHICAL SKETCH

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NAME: Nagajyothi, Jyothi Falguni

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

POSITION TITLE: Director/Member of Hackensack University Medical Center, New Jersey
Member/Professor at Center for Discovery and Innovation, Hackensack Meridian Health

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
Bangalore University, India	B.S	04/1986	Chemistry, Biology
Bangalore University, India	M.S	04/1988	Biochemistry
University of Mysore, India	PhD	06/2001	Biochemistry
Albert Einstein College of Medicine, NY	Postdoctoral	12/2007	Pathology, Biochemistry

A. Personal Statement

I am a Director/Professor at the Center for Discovery and Innovation, Hackensack University Medical Center, NJ, USA. Over the last 15 years, my research has focused primarily on the role of lipid metabolism and adipose tissue pathophysiology in acute and chronic infectious diseases. Thus, my area of expertise encompasses the immuno-metabolic effects of lipid metabolism and adipose tissue on infectious disease progression and outcome, and vice versa. In particular, I have demonstrated that deregulated lipid metabolism results in the pathogenesis of Chagas cardiomyopathy (CCM) and pulmonary TB infection. CCM is a major cause of mortality and morbidity in Chagas disease-endemic regions of Latin America. It also is imposing an increasing public health burden in the US due to immigration from endemic areas. Chagas disease is caused by the parasite *Trypanosoma cruzi*. The pathogenesis of CCM traditionally has been studied as an inflammatory disease. My research team was the first to demonstrate that adipose tissue physiology and immuno-metabolic functions influence cardiac immune balance and CCM pathogenesis. I have received NIH funding to investigate the role of host lipid metabolism in Chagas disease. Currently, I am the PI on RO1 grants aimed at elucidating the connection between adipose tissue physiology and cardiac pathology. During the last five years, my research focus has expanded to dissecting the crosstalk between adipose tissue physiology and tuberculosis (TB). Similar to *T. cruzi*, both the virulent and attenuated strains of *Mycobacterium tuberculosis* (Mtb) invade and persist in adipose tissue (PMID: 29109018). Our recent publications indicate a strong association between adipose tissue pathophysiology and TB activation (PMID: 30992360). My laboratory demonstrated that an acute loss of fat cells increases the pathogenesis of pulmonary TB (PMID: 30992360). This research program is critically important because obesity, insulin resistance, and diabetes are becoming more prevalent in endemic areas of tropical diseases and have a strong potential to influence the course of infectious diseases. I was recently awarded an RO1 grant to investigate the role of adipose tissue and adipomes in the pathogenesis of pulmonary tuberculosis. My expertise in: (i) adipocyte physiology and pathology relevant to infectious diseases, (ii) illustrating the link between infectious diseases and metabolic syndromes like insulin resistance and Type 2 diabetes, (iii) characterizing the intercellular cross-talks between adipocyte signaling and other cell types including immune cells, (iv) developing diet and drug-induced metabolic syndrome models, (v) immuno-metabolic studies, and (v) analyzing and quantitating adipomics and lipidomics all make me perfectly positioned to successfully carry

out the studies related to adipose pathophysiology and host immuno-metabolism in the context of infectious and non-infectious diseases.

Publications relevant to the on-going research studies:

1. Ayyappan JP, Lizardo K, Wang S, Yurkow E, Nagajyothi J* (2020) Inhibition of SREBP Improves Cardiac Lipidopathy, Endoplasmic Reticulum Stress and Modulates Chronic Chagas Cardiomyopathy. Journal of American Heart Association (https://www.ahajournals.org/doi/pdf/10.1161/JAHA.119.014255).
2. Ayyappan JP, Usha G, Lizardo K, Vinnard C, Subbian S, Perlin D and Nagajyothi JF* (2019) Adipose tissue regulates pulmonary pathology during TB infection. 10 (2) e02771-18; DOI: 10.1128/mBio.02771-18. PubMed PMID: 30992360
3. Ayyappan JP, Lizardo K, Wang S, Yurkow E, **Nagajyothi J** (2019) Inhibition of ER Stress by 2-Aminopurine Treatment Modulates Cardiomyopathy in a Murine Chronic Chagas Disease Model. PubMed PMID: 30879276.
4. Nagajyothi F, Desruisseaux MS, Machado FS, Upadhya R, Zhao D, Weiss LM, Scherer PE, Tanowitz HB (2012) Response of adipose tissue to early infection with Trypanosoma cruzi (Brazil Strain). J Infect Dis. doi: 10.1093/infdis/jir840 PMID: 22293433.

B. Positions and Honors

Positions and Employment

1988-1990	Lecturer, Vijaya First Grade College, Bangalore University, India
1990-1991	Senior Research Assistant, Central Silk Research & Training Institute, India
1991-2001	Scientist, Central Food Technological & Research Institute, India
2001-2007	Research Associate, Department of Pathology, Albert Einstein College of Medicine, NY
2007-2009	Associate, Department of Pathology, Albert Einstein College of Medicine, NY
2009-2012	Instructor, Department of Pathology, Albert Einstein College of Medicine, NY
2012-2015	Assistant Professor, Department of Pathology, Albert Einstein College of Medicine, NY
2015- 2018	Assistant Professor of Microbiology, Biochemistry, Molecular Genetics, Rutgers, NJ
2017- 2020	Director, Center for Infectious Diseases Metabolomics, PHRI Rutgers, NJ
2018- 2020	Associate Professor of Microbiology, Biochemistry, Molecular Genetics, Rutgers, NJ
Aug 2015 -	Adjunct Assistant Professor, Department of Pathology, Albert Einstein College of Medicine
June 2020-	Adjunct Member, Public Health Research Institute, Rutgers, NJ
June 2020-	Adjunct Associate Professor, Microbiology, Biochemistry, Molecular Genetics, Rutgers, NJ
June 2020-	Director/ Member Scientist, Hackensack University Medical Center, Hackensack, NJ
June 2020-	Director/Member, Center for Discovery and Innovation, Nutley, NJ
June 2020-	Professor, Dept. of Medical Sciences, Hackensack Meridian Health School of Medicine at Seton Hall (forthcoming), Nutley, NJ

Honors

1998-2000	Deutscher Akademisher Austauschdienst (DAAD) fellowship awarded by the Government of Germany (PhD program at the University of Hannover, Germany).
2012-2014	NIH/NHLBI R21HL112099 (PI)
2015-2020	NIH/NHLBI R01 HL122866 (PI)
2016-2018	NIH/NIAID R21 AI124000 (Co-Investigator)
2018-2020	NIH/NIAID R21 AI134656 (Co-investigator)

C. Contributions to Science

Link between adipocyte physiology and acute and chronic infectious diseases: I have shown that adipose tissue acts as a reservoir for pathogens like *T. cruzi* (parasite) and *M. tuberculosis* (bacterium) in both animals and humans during Chagas disease and in animal models of TB, respectively. These pathogens target adipose tissue, invading adipocytes and using their fat stores for replication and as an energy source during acute infection. Indeed, my laboratory has used several different mouse models to demonstrate that

adipocytes play a major role in determining parasitemia, cardiac parasite load, and cardiac pathology during acute *T. cruzi* infection. Also, we showed a significant association between adipocyte physiology and lung pathology during Mtb infection.

a. Combs TP, **Nagajyothi**, Mukherjee S, de Almeida CJ, Jelicks LA, et al. The adipocyte as an important target cell for Trypanosoma cruzi infection. J Biol Chem. 2005 Jun 24;280(25):24085-94. PubMed PMID: 15843370
b. **Nagajyothi F**, Zhao D, Machado FS, Weiss LM, Schwartz GJ, et al. Crucial role of the central leptin receptor in murine Trypanosoma cruzi (Brazil strain) infection. J Infect Dis. 2010 Oct 1;202(7):1104-13. PubMed PMID: 20726767; PubMed Central PMCID: PMC2932826.
c. **Nagajyothi F**, Desruisseaux MS, Thiruvur N, Weiss LM, Braunstein VL, et al. Trypanosoma cruzi infection of cultured adipocytes results in an inflammatory phenotype. Obesity (Silver Spring). 2008 Sep;16(9):1992-7. PubMed PMID: 19186325; PubMed Central PMCID: PMC2771879.
d. Wen JJ, **Nagajyothi F**, Machado FS, Weiss LM, Scherer PE, Tanowitz HB, Garg NJ (2014) Markers of oxidative stress in adipose tissue during Trypanosoma cruzi infection. Parasitol Res. 2014 Jun 20. PubMed PMID: 24948102, PubMed Central PMCID: PMC4374356

Role of host lipids in the pathogenesis of Chagasic cardiomyopathy: Chagas disease is caused by the parasite *T. cruzi*. Even after 100 years since its discovery, the mechanisms involved in the parasite invasion and the pathogenesis of Chagas disease are not completely understood. My laboratory demonstrated that *T. cruzi* has high affinity for host lipoproteins and utilizes the LDL receptor for invasion. These discoveries were a major turning point in understanding the pathogenesis of Chagas disease. We showed that the parasites bound to LDL bring in cholesterol into the cell during invasion, elevating intracellular cholesterol and causing cardiac lipidopathy. We also demonstrated increased cholesterol accumulation in heart sections of cardiomyopathic Chagas patients, which is a novel mechanism for the pathogenesis of Chagas disease.

a. **Nagajyothi F**, Weiss LM, Silver DL, Desruisseaux MS, Scherer PE, Herz J, Tanowitz HB. (2011) *Trypanosoma cruzi* Utilizes the Host Low Density Lipoprotein Receptor in Invasion. PLoS Negl Trop Dis 5(2): e953. Pubmed PMID: 21408103.
b. Johndrow C, Nelson R, Tanowitz H, Weiss LM, **Nagajyothi F** (2014) *Trypanosoma cruzi* infection results in an increase in intracellular cholesterol. Microbes Infect. 16(4):337-44. Pubmed PMID: 24486184.
c. **Nagajyothi F**, Machado FS, Burleigh BA, Jelicks LA, Scherer PE, Mukherjee S, Lisanti MP, Weiss LM, Garg NJ, Tanowitz HB. Mechanisms of Trypanosoma cruzi Persistence in Chagas Disease. Cell Microbiol. 2012 Feb 6. doi: 10.1111/j.1462-5822.2012.01764. Pubmed PMID: 22309180.
d. **Nagajyothi F**, Zhao D, Weiss LM, Tanowitz HB. (2012). Curcumin treatment provides protection against Trypanosoma cruzi infection. Parasitol Res. Pubmed PMID: 22215192, PubMed Central PMCID: PMC3556637

Role of diet and metabolic drugs in acute and chronic infectious diseases: We have provided abundant evidence that whole body lipid homeostasis is altered during acute *T. cruzi* infection. Consistent with these observations, my laboratory also demonstrated that diet and metabolic drugs play important roles in the pathogenesis of Chagas disease both during acute and chronic stages. For instance, a high-fat diet modulated cardiac pathology and increased infected mouse survival in the murine acute Chagas model compared with mice fed on a carbohydrate-rich diet. However, during chronic stages of infection, a high-fat diet aggravated cardiac pathology and dysfunction. We also demonstrated a link between diet, adipogenesis, lipolysis and hepatomegaly during acute and chronic *T. cruzi* infection using murine models. These studies are particularly important as the epidemics of diabetes and obesity are emerging in the endemic regions of Chagas disease, where they have significant potential to alter the pathogenesis of Chagas disease.

a. **Nagajyothi F**, Weiss LM, Zhao D, Koba W, Jelicks LA, et al. High fat diet modulates Trypanosoma cruzi infection associated myocarditis. PLoS Negl Trop Dis. 2014 Oct;8(10):e3118. PubMed PMID: 25275627; PubMed Central PMCID: PMC4183439.

b. Brima W, Eden DJ, Mehdi SF, Bravo M, Wiese MM, Stein J, Almonte V, Zhao D, Kurland I, Pessin JE, Zima T, Tanowitz HB, Weiss LM, Roth J, **Nagajyothi** (2015) The brighter (and evolutionarily older) face of the metabolic syndrome: evidence from Trypanosoma cruzi infection in CD-1 mice. Diabetes Metab Res Rev. PMID: 25613819, PubMed Central PMCID: PMC4427523.
c. Lizardo, K., Almonte, V., Law, C., Aiyyappan, J.P., Cui, M.H. and **Nagajyothi, J.F**. (2017) Diet regulates liver autophagy differentially in murine acute Trypanosoma cruzi infection. Parasitology research, 116(2), pp.711-723. PMID: 27987056, PubMed Central PMCID: PMC5283091
d. Lizardo K, Ayyappan JP, Cui MH, Balasubramanya R, Jelicks LA, Nagajyothi JF (2018) High fat diet aggravates cardiomyopathy in murine chronic Chagas disease. Microbes Infect. PubMed PMID: PMID: 30071300

Complete List of Published Work in My Bibliography: (Jyothi F Nagajyothi and Fnu Nagajyothi)

http://www.ncbi.nlm.nih.gov/sites/myncbi/collections/bibliography/43934482/sort=date&direction=ascending

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

Ongoing Research Support

01/10/2020 – 12/31/2024
RO1 AI150765-01 NIH/NIAID
Jyothi Nagajyothi (PI)
Immunometabolic regulations of pulmonary TB pathogenesis by adipose tissue
The overarching goal of this proposal is to: (i) Examine the importance of fat loss as a risk factor for TB disease progression and severity; and (ii), dissect the role of adipocyte-derived factors in regulating immuno-metabolic mechanisms underlying pulmonary pathogenesis.

Completed Research Support

2015/04/01-2020/03/31
1R01HL122866, NIH/NHLBI
Jyothi Nagajyothi (PI)
Pathogenic contribution of lipid homeostasis to chagasic Cardiomyopathy
This grant examines the role of adipose tissue in the pathogenesis of Chagas disease cardiomyopathy.

05/15/2018-04/30/2020
R21 AI134656 NIH
Role: Co-Investigator (5% effort)
Regulation of *T. brucei* infection by RNA binding proteins
Our goal is to uncover the mechanism by which trypanosomes accomplish this regulatory feat. By determining the biological differences between the African trypanosomes and their mammalian hosts, we will identify new biochemical approaches and drug targets to replace the inadequate therapies currently in place.

2012/07/15-2015/07/14
1R21 1HL112099-01A, NIH/NHILB
Jyothi Nagajyothi (PI)
Role of lipoproteins in Chagas Disease

Overlap: None