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**

The focus of my research group is to understand the interplay between lipid metabolism, adipose tissue function, and the pathogenesis of diseases such as Chagas cardiomyopathy (CCM), tuberculosis (TB), COVID-19, and breast cancer. My lab has been at the forefront of studying how pathogens like *Trypanosoma cruzi, Mycobacterium tuberculosis,* and *SARS-CoV-2* invade adipocytes, leading to metabolic dysfunction that promotes cardiac and/or lung pathology in CCM, TB, and COVID-19. We pioneered the discovery of adipocyte-derived extracellular vesicles, known as adipomes, which have been shown to regulate immune responses and metabolic pathways in both infectious and non-infectious diseases. Our research has expanded to explore how adipose tissue dysfunction—driven by obesity, insulin resistance, and metabolic syndrome—worsens the severity of TB, CCM, and cancer, with a specific focus on how adipomes from pathological adipocytes may influence tumorigenesis and metastasis in breast cancer. Additionally, we are investigating the sex-specific roles of adipomes in modulating immune cell responses and their impact on disease outcomes. In summary, my lab specializes in studying the immuno-metabolic effects of adipocyte signaling and lipid metabolism in disease progression, as well as developing models to understand how systemic conditions like obesity and diabetes influence both infectious and non-infectious diseases.

Ongoing and recently completed projects that I would like to highlight include:

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

Completed Research Support

01/04/2015-03/31/2020

1R01HL122866, NIH/NHLBI
Jyothi Nagajyothi (PI)
Pathogenic contribution of lipid homeostasis to chagasic Cardiomyopathy

05/15/2018-04/30/2020
R21 AI134656 NIH
Jyothi Nagajyothi (Co-Investigator)
Regulation of T. brucei infection by RNA binding proteins

Citations:

1. Thangavel H, Dhanyalayam D, Kim M, Lizardo K, Sidrat T, Lopez JG, Wang X, Bansal S, **Nagajyothi JF**. Adipocyte-released adipomes in Chagas cardiomyopathy: Impact on cardiac metabolic and immune regulation. iScience. 2024 Apr 5;27(5):109672. doi: 10.1016/j.isci.2024.109672. PMID: 38660407; PMCID: PMC11039351.
2. Thangavel H, Lizardo K, Dhanyalayam D, De Assis S, **Nagajyothi JF**. Diets Differently Regulate Tumorigenesis in Young E0771 Syngeneic Breast Cancer Mouse Model. J Clin Med. 2023 Jan 4;12(2):413. doi: 10.3390/jcm12020413. PMID: 36675341; PMCID: PMC9862441.
3. Oswal N, Lizardo K, Dhanyalayam D, Ayyappan JP, Thangavel H, Heysell SK, Nagajyothi JF. Host Metabolic Changes during Mycobacterium Tuberculosis Infection Cause Insulin Resistance in Adult Mice. J Clin Med. 2022 Mar 16;11(6):1646. doi: 10.3390/jcm11061646. PMID: 35329973; PMCID: PMC8948975
4. Alkabab YMA, Biswas S, Ahmed S, Paul K, Nagajyothi J, Banu S, Heysell S. Differentiating transient from persistent diabetic range hyperglycemia in a cohort of people completing tuberculosis treatment in Dhaka, Bangladesh. PLoS One. 2021 Nov 23;16(11):e0260389. doi: 10.1371/journal.pone.0260389. PMID: 34813631; PMCID: PMC8610235.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

June 2020-	Professor, Dept. of Microbiology and Immunology, Georgetown University, Washington, DC
June 2020-	Director/Member, Center for Discovery and Innovation, Nutley, NJ
June 2020-	Director/ Member Scientist, Hackensack University Medical Center, Hackensack, NJ
June 2020-2022	Adjunct Member, Public Health Research Institute, Rutgers, NJ
June 2020-2022	Adjunct Associate Professor, Microbiology, Biochemistry, Molecular Genetics, Rutgers, NJ
Aug 2015 -	Adjunct Assistant Professor, Department of Pathology, Albert Einstein College of Medicine
2018- 2020	Associate Professor of Microbiology, Biochemistry, Molecular Genetics, Rutgers, NJ
2017- 2020	Director, Center for Infectious Diseases Metabolomics, PHRI Rutgers, NJ
2015- 2018	Assistant Professor of Microbiology, Biochemistry, Molecular Genetics, Rutgers, NJ
2012-2015	Assistant Professor, Department of Pathology, Albert Einstein College of Medicine, NY
2009-2012	Instructor, Department of Pathology, Albert Einstein College of Medicine, NY
2007-2009	Associate, Department of Pathology, Albert Einstein College of Medicine, NY
2001-2007	Research Associate, Department of Pathology, Albert Einstein College of Medicine, NY
1991-2001	Scientist, Central Food Technological & Research Institute, India
1990-1991	Senior Research Assistant, Central Silk Research & Training Institute, India
1988-1990	Lecturer, Vijaya First Grade College, Bangalore University, India

Honors

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

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 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 J**F (2018) High fat diet aggravates cardiomyopathy in murine chronic Chagas disease. Microbes Infect. PubMed PMID: PMID: 30071300

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

Complete List of Published Work in My Bibliography: (Jyothi F Nagajyothi and Fnu Nagajyothi)
https://www.ncbi.nlm.nih.gov/sites/myncbi/jyothi.nagajyothi.1/bibliography/public/