BIOGRAPHICAL SKETCH

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NAME: **Shilpa Iyer**

eRA COMMONS USER NAME (credential, e.g., agency login): **SI3SNIH**

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)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Ferguson College, Pune, India	BS	1990-1993	Zoology
University of Pune, Pune, India	MS	1993-1995	Genetics
The University of Georgia, Athens, GA	PhD	2002-2006	Molecular Genetics
University of Virginia, Charlottesville, VA	Postdoctoral Fellow	2006-2010	Mitochondrial Genetics

A. Personal Statement

I am broadly interested in understanding the molecular mechanisms of and developing therapies for mitochondrial diseases, aging and cancer. My graduate training focused on understanding the genetic requirements for protecting the ends of telomeres, which provided clues to molecular mechanisms of telomere length regulation in rare human cancers. My post-doctoral training focused on clinical translational development of mitochondrial gene therapy for Parkinson's disease. As a research scientist, I was able to leverage my graduate and post-doctoral training to further my research goals by developing customized cellular models for mitochondrial disease. In my current position as an assistant professor, my lab is working on understanding the relationships between mutant mitochondrial DNA, bioenergetics, mitochondrial dynamics, oxidative stress and tissue-specific cell responses. We are also interested in developing novel drug discovery platforms for improving bioenergetics in cellular models for mitochondrial disorders. Over the years, I have demonstrated a successful record of accomplishment of publications, fellowships and federal funding from Arkansas Bioscience Institute, National Institutes of Health and Department of Defense.

Recent publications relevant to this project:

a. Meshrkey F, Cabrera Ayuso A, Rao RR, **Iyer S**. Quantitative analysis of mitochondrial morphologies in human induced pluripotent stem cells for Leigh syndrome. Stem Cell Res. 2021 Oct 12;57:102572
b. Bakare AB, Meshrkey F, Lowe B, Molder C, Rao RR, Zhan J, **Iyer S**. MitoCellPhe reveals mitochondrial morphologies in single fibroblasts and clustered stem cells. Am J Physiol Cell Physiol. 2021 Oct 1;321(4):C735-C748.
c. Bakare AB, Rao RR, **Iyer S**. Cell-Permeable Succinate Increases Mitochondrial Membrane Potential and Glycolysis in Leigh Syndrome Patient Fibroblasts. Cells. 2021 Aug 31;10(9)
d. Bakare AB, Dean J, Chen Q, Thorat V, Huang Y, LaFramboise T, Lesnefsky EJ, **Iyer S**. Evaluating the Bioenergetics Health Index Ratio in Leigh Syndrome Fibroblasts to Understand Disease Severity. Int J Mol Sci. 2021 Sep 26;22(19).
e. Bakare AB, Daniel J, Stabach J, Rojas A, Bell A, Henry B, **Iyer S**. Quantifying Mitochondrial Dynamics in Patient Fibroblasts with Multiple Developmental Defects and Mitochondrial Disorders. Int J Mol Sci. 2021 Jun 10;22(12).

Current and recent funded projects in my lab include:

DoD PR151666
Iyer (PI);
10/2016- 03/2023
Patient-Specific Human Induced Pluripotent Stem Cells for Mitochondrial Diseases

DoD PR192433
Balachandran (PI) Iyer Role:co-PI
09/2020- 08/2023
Heart-on Chip for Drug Efficacy Testing for Mitochondrial Diseases

NIH 1P20GM139768-01
Iyer (PI)
04/2021-02/2023
Bioenergetics Core- Arkansas Integrative Metabolism Research Center

NIH 1R21HD094394-01A1
Iyer (MPI).
01/2019- 12/2022
Development of quantitative biomarkers for mitochondrial disorders

NIH 1R15NS080157-01A1
Iyer (PI)
04/2013 – 08/2018
mtDNA heteroplasmy during development and differentiation: An in-vitro approach.

B. Positions and Honors

Positions and Employment

2002 – 2006	Graduate Research Assistant, University of Georgia, Athens
2006 – 2010	Postdoctoral Scholar, University of Virginia, Charlottesville, VA
2010 – 2016	Research Assistant Professor, Virginia Commonwealth University, Richmond, VA
2016 – Present	Assistant Professor, Biological Sciences, University of Arkansas, Fayetteville, AR

Other Experience and Professional Memberships

2009 – Present	United Mitochondrial Disease Foundation
2009 – Present	Bioblast International Scientific Committee
2016 – Present	American Society for Biochemistry and Molecular Biology
2012 – Present	European Cooperation in Science and Technology for Mapping Mitochondrial Fitness
2012	Instructor, High resolution respirometry international workshop, Oroboros, Innsbruck, Austria
2016	Judge, 20th Annual ASBMB (American Society for Biochemistry and Molecular Biology), Undergraduate Poster Competition, San Diego
2016 – Present	Working Group 1& 4- European Cooperation in Science and Technology for Mapping Mitochondrial Fitness, as part of the MITOEAGLE (Mitochondrial Evolution, Age, Gender, Lifestyle, Environment) network, Austria
2017	Planning Committee, Mitochondrial Medicine Southeast Regional Symposium
2019	Proposal Reviewer, City University of New York, Office of Award Pre-Proposal Support Program.
2019	Proposal Reviewer, Department of Defense CDMRP
2020	Proposal Reviewer, National Institute of Health

Honors and Awards

1994	Summer Research Fellowship: Department of Biotechnology India (National)
1995 – 1996	Rajiv Gandhi Fellowship: For innovative research and science; Jawaharlal Nehru Center for Advanced Scientific Research, Indian Institute of Sciences, Bangalore, India
2002	American Association for Cancer Research (AACR-AFLAC) Scholar-in Training Award
2004	American Federation for Aging Research Scholarship (Glenn/AFAR): Research in the Biology of Aging
2005	Training Scholarship: NIH funded HEST (Human Embryonic Stem Cell Toolbox) Workshop

2005 – 2006	NIH Genetics (merit) Training Grant Fellowship: Dept of Genetics, UGA
2007	Parkinson's Disease Foundation, Postdoctoral Research Fellowship
2007	American Parkinson Disease Association, Postdoctoral Research Fellowship
2008	United Mitochondrial Disease Foundation: Burroughs Wellcome Travel award
2009	Femtech Fellowship: O2k-Course on High-Resolution Respirometry, Austria
2012	United Mitochondrial Disease Foundation: Burroughs Wellcome Travel Scholarship
2020	Connor Faculty Fellow, J. William Fulbright College of Arts and Sciences

C. Contribution to Science

1. Mitochondrial Regulation in Stem Cell Self-renewal and Differentiation.

In recent projects funded by DoD and an NIH-AREA grant, my lab has focused on generating customized induced pluripotent stem cell models for understanding pathophysiology and developing therapies for mitochondrial disorders. Other projects include understanding the role of cell cycle regulators in stem cell differentiation, and the role of mitochondria in maintaining self-renewal in neural progenitors.

a. Grace HE, Galdun III P, Lesnefsky EJ, West FD, **Iyer S.** mRNA reprogramming of T8993G Leigh's syndrome fibroblast cells to create induced pluripotent stem cell models for mitochondrial disorders. Stem Cells and Development. 28(13):846-859. 2019. PMID: 31017045
b. Alsayegh, K.A., Sheridan, S., **Iyer, S**., and Rao, R.R. Knockdown of CDK2AP1 in Human Embryonic Stem Cells reduces the threshold for differentiation. PLoS One 13(5): e0196817. 2018. PMID: 29734353.
c. Rao, R.R. and **S. Iyer**. Stem cells, neural progenitors, and engineered stem cells. Methods in Molecular Biology- Neuronal Cell Death. 1254:255-67**.** 2015**.** PMID: 25431071.
d. **Iyer, S**., Xiao, E., Alsayegh, K., Eroshenko, N., Riggs, M.J., Bennett, J.P. Jr., and Rao, R.R: Mitochondrial gene replacement in human pluripotent stem cell-derived neural progenitors. Gene Therapy. May;19(5):469-75. 2012. PMID: 21918550

2. Mitochondrial Gene Therapy for Neurodegenerative and Mitochondrial Disorders.

My training in genetics led me to explore mitochondrial gene therapy as an approach to treat neurodegenerative and mitochondrial disorders. My research has shown that triggering biogenesis is an important step to improving problems related to energy failure in metabolic diseases. My research led to the development of a gene therapy technology for introducing healthy mitochondrial DNA into diseased cells for restoring genomic integrity and mitochondrial function. This work has been well received by the scientific community and has been awarded postdoctoral fellowships as well as travel awards to numerous scientific meetings.

a. **Iyer, S**. Novel therapeutic approaches for Leber's hereditary optic neuropathy. Discovery Medicine. 15(82):141-9. 2013. PMID: 23545042.
b. **Iyer, S**., Bergquist, K.E., Young, K., Gnaiger, E., Rao, R.R., and Bennett, Jr., J.P. Mitochondrial gene therapy improves respiration, biogenesis and transcription in G11778A Leber's hereditary optic neuropathy and T8993G Leigh's syndrome cells. Human Gene Therapy. 23(6):647-57. 2012**.** PMID: 22390282.
c. **Iyer, S**., Thomas, R. R; Portell, F. R; Dunham, LD; Quigley C. K; Bennett, Jr.,J.P Jr.: Recombinant Mitochondrial Transcription Factor A with N-terminal Mitochondrial Transduction Domain Increases Respiration and Mitochondrial Gene Expression. Mitochondrion. 9(3): 196-203, 2009. PMID: 19460293.
d. Keeney, P.M., Quigley, C.K., Dunham, L.D., Papageorge, C.M., **Iyer, S.**, Thomas, R.R., Schwarz, K.M., Trimmer, P.A., Khan, S.M., Portell, F.R., Bergquist, K.E., and Bennett, Jr., J.P. Mitochondrial Gene Therapy Augments Mitochondrial Physiology in a Parkinson's Disease Cell Model. Human Gene Therapy. 20(8):897-907. 2009. PMID: 19374590

3. Telomere End Protection and Genome Stability.

My graduate training in yeast genetics led to understanding the genetic requirements for protecting the ends of the chromosomes for maintaining genomic integrity. This work led to identifying a novel gene mutation which triggered an atypical recombination repair pathway observed in a subset of cancer cells, accompanied

by numerous publications, awards and fellowships from the American Association for Cancer Research and American Foundation for Aging Research.

a. McEachern, M.J., **Iyer, S**., Fulton, T.B., and Blackburn, E.H. Telomere fusions caused by mutating the terminal region of telomeric DNA. Proceedings of the National Academy of Sciences, USA. 97(21): 11409-11414. 2000. PMID: 11016977.
b. McEachern, M.J., and **S. Iyer**. Short telomeres in yeast are highly recombinogenic. Molecular Cell. 7: 695-704. 2001. PMID: 11336694
c. **Iyer, S**., Chadha, A.D., and McEachern, M.J. A mutation in the STN1 gene triggers an ALT-like Recombinational Telomere Elongation and Rapid Deletion in Yeast. Molecular and Cellular Biology. 18: 8064-73. 2005. PMID: 16135798.
d. **Iyer, S**., Carter, SD., McEachern M.J., and Astrom, S.U. Role of nonhomologous end-joining components in telomere metabolism in K. lactis. Genetics,175 (3):1035-45. 2007. PMID: 17237517.

4. Science Education and Public Awareness.

I also have made significant contributions to outreach and science education. I directed a transdisciplinary Bioenergetics program involving 16 students from 8 disciplines in the Arts and STEM, who researched and created novel educational modules on bioenergetics and energy deficiency disorders. Project outcomes were exhibited at the Science Museum of Virginia (3 months; 120,000 visitors) in Spring 2015. Subsequently, my team has developed a novel science-based strategy board game explaining inter-organelle communication as it pertains to the mitochondria.

a. **Iyer**, **Shilpa,** Rao, Raj, Joyce, Myles, Richards, Austin, Gordon, Khandi, Wyatt, Chase. "The Great Cellular Reef"-. TXu 2-155-133/ 2019-09-03. Registered Copyright 2019.
b. Tompkins E, Faris S, Hughes L, Maurakis E, Lesnefsky EJ, Rao, RR, and **Iyer. S.** Arts, Science, Engineering and Medicine Collaborate to Educate Public on Bioenergetics. Research Reports. 1(1):e1-e9. 2017. PMID: 29756092
c. **Shilpa Iyer**, Matthew Woolman, Raj Rao, Andrew Ilnicki, Jeffrey Foster, Benjamin Leach, Douglas Fuchs, David Saul, Beza Telke, Khanh Tran. "Might!TM A Bioenergetics Game"- VAu001297334 / 2016-07-05. Registered Copyright 2016.

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