Stanford

Shwetha Shivaprasad

Postdoctoral Research Fellow, Microbiology and Immunology

NIH Biosketch available Online Curriculum Vitae available Online

Bio

BIO

I am Shwetha Shivaprasad, a postdoctoral researcher in the laboratory of Dr.Peter Sarnow, Department of Microbiology and Immunology, Stanford University.

Originally I hail from a small town in Southern India, Hassan which is in the state of Karnataka. It is a place well known for its delightful coffee and skillful stonework architecture. I completed my schooling in Hassan and moved to Manipal University in Karnataka for my Bachelors in Biotechnology. The degree included a six month project in immunology that I carried out in the Biochemistry department of the Indian Institute of Science (IISc). IISc is ranked first among all the research institutes in India. After my Bachelors, I pursued a Masters degree in M.S.University of Baroda in the state of Gujarat, where I was awarded the gold medal for obtaining the highest GPA. I also secured an All India Rank of 3 and a five year scholarship for PhD studies awarded by the Government of India.

I was a PhD candidate in the Department of Microbiology and Cell Biology at the Indian Institute of Science. My research in the field of virology under the guidance of Dr. Saumitra Das revealed novel regulators of viral replication and pathogenesis and I published my findings in several peer reviewed journals. At Stanford, I continue to work on virus-host interactions with specific emphasis on the dengue virus.

HONORS AND AWARDS

- School of Medicine Dean's Postdoctoral Fellowship, Stanford University (07/2017- 06/2018)
- Kishore Vaigyanik Protsahan Yojna scholarship for research in the Basic Sciences, Department of Science and Technology, Government of India (2005-2010)
- Gold medal for highest GPA, Maharaja Sayajirao University of Baroda, India (2010)
- Graduate student research fellowship, Council of Scientific and Industrial research, Government of India (2010-2015)
- Best poster award in the 4th Molecular Virology Meet, Rajiv Gandhi Centre for Biotechnology, India (04/2015)

PROFESSIONAL EDUCATION

- Doctor of Philosophy, Indian Institute of Science (2016)
- Master of Science, Maharaja Sayajirao University Baroda (2010)
- Bachelor of Science, Manipal University (2008)

STANFORD ADVISORS

- Peter Sarnow, Postdoctoral Faculty Sponsor
- Peter Sarnow, Postdoctoral Research Mentor

LINKS

- My Bibliography: https://www.ncbi.nlm.nih.gov/sites/myncbi/1B9hnmlDq7p54/bibliography/51911050/public/?sort=date&direction=ascending

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

The Flaviviridae family of viruses are arthropod-borne human pathogens predominant in tropical regions of the world. Their ability to thrive in both vertebrate and invertebrate hosts make them ideal candidates to study cross species barriers to viral propagation and species specific adaptations in the viral genome. Some of the best examples of structural and functional adaptations of the virus to different hosts can be seen with the Dengue virus.

Dengue is a mosquito borne flavivirus that affects upto 340 million people in a year. The dengue positive strand RNA genome is highly structured with several long range RNA-RNA interactions. These structures act as riboswitches to regulate the viral life cycle. For example, the 5' and 3' ends of the viral genome have complementary regions that allow the RNA to alternate between linear and circular conformations, thereby regulating the translation replication switch. There are many examples of such cis acting elements dispersed throughout the 11kb Dengue genome that regulate viral infection. These RNA structures are also involved in interactions with host RNA and protein molecules in a structure and/or sequence dependent manner. Through such interactions, dengue virus is able to subvert the biochemical machineries of both mammalian and mosquito cells and establish successful infection in two different host organisms. Since the physiological and biochemical processes in humans and arthropods are fundamentally different, the virus faces different selective pressures in the two hosts. As the virus replicates, it generates a genetically diverse population from which different variants are selected for in a host specific manner. The dengue 3'UTR contains a regulatory RNA sequence which evolves differently in mosquitoes and mammalian cells. During transmission from humans to mosquitoes, large deletions and mutations accumulate in the 3'UTR which affect the immunomodulatory ability of the virus. They promote survival in mosquito cells but are rapidly cleared in mammalian cells because they generate a higher immune response. In my project, I plan to study the structural and mechanistic determinants of dengue virus adaptation to human and mosquito hosts.

Goals of my study:

1. Global mapping of RNA structures and interactions in Dengue infected mammalian and mosquito cells using in vivo crosslinking (PARIS).

Base pairing between different regions of the dengue RNA (structures) and between dengue RNA and host RNA molecules (interactions) are known to modulate the viral life cycle and viral pathogenesis. Dengue RNA adopts alternative RNA structures that bring distant regulatory motifs of the genome together to facilitate viral translation and replication. At the same time, interactions between the dengue RNA and specific host RNA molecules such as microRNAs adds additional levels of regulation to the viral life cycle. Our goal is to generate a global map of RNA duplexes that are formed in virus infected cells, which could potentially uncover many new structures and interactions that are of consequence to viral propagation.

2. Identification of host proteins interacting with mammalian and mosquito adapted variants of Dengue using the RAPID assay.

Host switching generates different clonal variants of dengue in mammalian cells and mosquito cells. Most of the variants contain mutations in the stem loop 2 of the 3'UTR. These mutations alter the pattern of subgenomic viral RNA fragments (sfRNAs) that are generated in the mosquito and mammalian cells leading to differential triggering of the immune response in the two hosts. In our experiments, we aim to identify host proteins that interact differentially with the mammalian and mosquito adapted variants of dengue genomic RNA, with specific emphasis on the 3' untranslated region. The findings from our study will help us understand the mechanistic determinants of viral fitness in different hosts.

Publications

PUBLICATIONS

- **Reversible HuR-microRNA binding controls extracellular export of miR-122 and augments stress response** *EMBO REPORTS*

Mukherjee, K., Ghoshal, B., Ghosh, S., Chakrabarty, Y., Shwetha, S., Das, S., Bhattacharyya, S. N.
2016; 17 (8): 1184-1203

- **HuR Displaces Polypyrimidine Tract Binding Protein To Facilitate La Binding to the 3 ' Untranslated Region and Enhances Hepatitis C Virus Replication** *JOURNAL OF VIROLOGY*
  Shwetha, S., Kumar, A., Mullick, R., Vasudevan, D., Mukherjee, N., Das, S.
  2015; 89 (22): 11356-11371

- **The beta hairpin structure within ribosomal protein S5 mediates interplay between domains II and IV and regulates HCV IRES function** *NUCLEIC ACIDS RESEARCH*
  Bhat, P., Shwetha, S., Sharma, D. K., Joseph, A. P., Srinivasan, N., Das, S.
  2015; 43 (5): 2888-2901

- **Serum proteomics of hepatitis C virus infection reveals retinol-binding protein 4 as a novel regulator** *JOURNAL OF GENERAL VIROLOGY*
  Gouthamchandra, K., Kumar, A., Shwetha, S., Mukherjee, A., Chandra, M., Ravishankar, B., Khaja, M. N., Sadhukhan, P. C., Das, S.
  2014; 95: 1654-1667

- **Circulating miRNA profile in HCV infected serum: novel insight into pathogenesis** *SCIENTIFIC REPORTS*
  Shwetha, S., Gouthamchandra, K., Chandra, M., Ravishankar, B., Khaja, M. N., Das, S.
  2013; 3