SUDHEESH A P

Postdoctoral Associate
Ke Lab of Quantitative RNA Biology
The Jackson Laboratory,
Bar Harbour, Maine, USA 04609

PERSONAL PROFILE

A professional self motivated researcher with years of experience and expertise in RNA biology

ACHIEVEMENTS

Young inspiring scientist , 2019
Young Scientist Research award, 2018
Meritorious student award, 2017
KSCSTE Award, 2012

CONTACT DETAILS

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ACADEMIC HISTORY

Ph.D. in Biotechnology, Rajiv Gandhi Centre for Biotechnology (Manipal Academy of Higher Education), Kerala, India (2019)

Master of Science in Biotechnology, Mahatma Gandhi University, Kerala, India (2012)

Diploma in Medical Biotechnology, Bharathiar University, Tamil Nadu, India (2010)

Bachelor of Science in Biotechnology, Bharathiar University, Tamil Nadu, India (2010)

RESEARCH EXPERIENCE

Postdoctoral Associate, The Jackson Laboratory, 2020
Laboratory Supervisor : Shengdong Ke, Ph.D.
Research Area : Mechanism of m6A modification and its role in cancer progression

Senior Research Fellow, RGCB, Trivandrum, 2014-2019
Supervisor : Rakesh Laishram, Ph.D.
Thesis title : Mechanism and Regulation of Star-PAP mediated 3'-end Processing and Alternative Polyadenylation

Junior Research Fellow, RGCB, Trivandrum, 2012-2014
Research Guide: Dr. E Sreekumar, Ph.D.
Project title: Characterization of Neurovirulence of Chikungunya virus (CHIKV) in Animal and Cell based Models.

Master of Science Thesis, Mar Athanasius College, 2012.

Research Guide: Anu Yamuna Joseph, Ph.D.

Project title: A LAMP Based Molecular Diagnostic Method for the detection of *Leptospira*.

PUBLICATIONS

Sudheesh AP, Mohan, N., Francis, N, Rakesh S Laishram and Anderson, R., 2019. Star-PAP controlled Alternative Polyadenylation coupled poly(A) tail length regulates expression in Hypertrophic heart. *Nucleic acids research*. gkz875

Sudheesh, A.P. and Rakesh S Laishram., 2018. Nuclear phosphatidylinositol- phosphate type I kinase α-coupled Star-PAP polyadenylation regulates cell invasion. *Molecular and cellular biology*, 38(5), pp.e00457-17.

Mohan, N*., **Sudheesh A.P***., Francis, N., Anderson, R. and Rakesh S Laishram., 2015. Phosphorylation regulates the Star-PAP-PIPKIα interaction and directs specificity toward mRNA targets. *Nucleic acids research*, 43(14), pp.7005-7020. (*Equal first authorship).

Kandala, D., Mohan, N., Vivekananda, A., **Sudheesh, A.P**., Reshmi, G., and Rakesh S. Laishram. 2016. CstF and 3'-UTR *cis*-element determine Star-PAP specificity for target mRNA selection by excluding PAPα. *Nucleic Acid Res.* 44 (2): 811-823.

AWARDS & ACHIEVEMENTS

- Young Inspiring Scientist, 3rd Annual Conference of Bermuda Principles, 2019
- Young Scientist Research Award-Biology, Dr. KV Rao Scientific Society, India, 2018
- Meritorious Student Award, Rajiv Gandhi Centre for Biotechnology, Trivandrum, 2017
- Best Poster Award, 9th RNA Group Meet, Banaras Hindu University, India, 2017
- ASBMB International Travel Award, ASBMB Annual Meeting, Chicago, USA, 2017
- Best Poster Award, 85th Society of Biological Chemists (India) meeting, Central Food Technological Research Institute, India, 2016
- KSCSTE Award, Government of Kerala, Kerala, India for Master's dissertation, 2012

FELLOWSHIPS

- Senior Research Fellowship, Department of Biotechnology, Government of India, 2016
- National Eligibility Test, Union Grants Commission, Government of India, 2015
- Junior Research Fellowship, Department of Biotechnology, Government of India, 2014
- Junior Research Fellowship, Kerala State Council for Science Technology and Environment, India, 2013
- INSPIRE Fellowship, Department of Science & Technology, Government of India, 2013

CONFERENCES ATTENDED

- 10th RNA Group Meeting, Rajiv Gandhi Centre for Biotechnology, Trivandrum, 2019 (*Organize*)
- 3rd Annual Conference Bermuda Principles- Bermuda, 2019 (*Talk*)
- 9th RNA Group Meeting, Banaras Hindu University, India, 2017 (*Poster*)
- Experimental Biology'17- Annual Meeting of the American Society for Biochemistry and Molecular Biology, Chicago, USA, 2017 (*Poster*)
- 85th meeting of the Society of Biological Chemists (India), Central Food Technological Research Institute, Mysuru, India, 2016 (*Poster*)
- 33rd Annual convention of Indian Association for Cancer Research, Rajiv Gandhi Centre for Biotechnology, India, 2014

TECHNICAL EXPERTISE

- **Molecular Biology and Biochemistry:** Isolation of plasmid and genomic DNA, RNA isolation, Site directed mutagenesis, Molecular cloning, shRNA and CRSIPR cloning, Radioactive DNA/RNA labeling, *In vitro* Transcription, PCR, Quantitative Real time (qRT) PCR, and 3'-RACE, Electrophoresis (Agarose, Formaldehyde, Native and Denaturing SDS/Urea PAGE), Protein expression and purification, Chromatography based protein purification (affinity and size exclusion), Western blotting, protein interactions- Immunoprecipitation, (IP/Co-IP), GST-Pull down, RNA-Protein interaction -RNA Immunoprecipitation (RIP), RNA EMSA, UV/chemical-cross linking, In vitro assays (Polyadenylation and cleavage assays), Polysome profiling, Cellular sucrose fractionation, CRISPRa/i genomics and UV/Visible Spectroscopy.

- **Cell Biology:** Mammalian cell culture, Transfections, siRNA and stable knockdowns, Immunofluorescence and Bright Field Microscopy, Stable cell generation, Aseptic techniques, Reporter Assays, Invasion assays, Plaque assays, Viral culture and cultivation.
- **Microbiology:** Bacterial Culture, Transformation, Biochemical characterization and Culturing and identification of microbes
- **Animal experience:** SCID Models, BALB/c Mouse (Tumor and Viral studies)
- **Computer/Software Skills:** Microsoft office, Adobe Photoshop, BioEdit, ImageJ, Clone Manager, SnapGene, SerialCloner, Gene Ontology and functional analysis tools.

MEMBERSHIPS

- American society of Biochemistry and molecular biology
- The RNA Society

MENTORSHIP / MANAGEMENT

- Mentored undergraduate/master students for the partial fulfillment of their thesis dissertation, involved experimental designing, training of basic molecular and biochemical techniques, evaluation for the completion of thesis.
- Laboratory maintenance, annual and regular purchase of consumables and non-consumables.

LANGUAGE SKILLS

English (IELTS Qualified)
Malayalam
Tamil
Hindi

HOBBIES

Swimming & Cycling
Travelling
Cooking
Voluntary teaching and Social service

RESEARCH EXPERIENCE

Mechanism of m^{6}A mRNA modification and its role in cancer cell progression

Eukaryotic mRNA undergoes various processing steps before it matures for translation, which includes capping, splicing and polyadenylation. However, recent research has highlighted that similar to DNA, mRNA also undergoes nucleotide modifications that could have profound role in determining its fate. The most prevalent internal mRNA modification is m^{6}A (N^6-methyladenosine), a reversible chemical modification that a methyl group is added to adenosine nucleotide at the N^6 position. Interestingly, studies revealed that ~40% of the eukaryotic transcriptome contain multiple m6As' per transcript. Even though they were found to be involved in mRNA stability, translation and localization, the underlying molecular mechanism is largely unknown. Reflecting the diverse molecular functions of m^{6}A, many studies have shown that the enzymes/associated protein factors- writers, readers and erasers, are critically involved in human diseases including cancer.

Thus the mechanism study of m^{6}A mRNA modification holds the great potential for novel therapeutic breakthrough. Under this context, my work is focused on the mechanism study of m^{6}A mRNA modification and its dysregulation in cancer progression.

Mechanism and Regulation of Star-PAP mediated 3'-end Processing and Alternative Polyadenylation

In this study, we investigate Star-PAP mediated APA, mechanism of target UTR selection, signals that regulate its target mRNA selection, and cellular implications. We demonstrated recognition sequence elements around the polyadenylation signal at the 3'-UTR drives the Star- PAP specificity. Moreover, both Star-PAP and PAPα compete with each other for cleavage factors but with a preference for Star-PAP. We show that changing these regulatory sequences in the UTR could change the regulatory PAP. We demonstrated that this mechanism of Star- PAP poly(A) site selection is involved in the regulation of APA where Star-PAP generates the longest but translationally predominant transcript in contrast to the earlier view of shorter UTR associated with higher protein levels. Using NQO1, we show that the Star-PAP regulated distal- most site has a longer poly(A) tail and thus not the miRNA binding determine

the translatability of NQO1 APA isoforms. We observed that the Star-PAP and PIPKIα regulated common mRNA targets are involved in cellular processes in cancer such as proliferation, invasion and metastasis. The Star-PAP-PIPKIα interaction is required for the regulation of 3′-end processing of mRNAs encoding anti-invasive or metastatic factors. Further, the Star-PAP expression exhibited a negative co-relation with cellular invasiveness in breast cancer cells in a cellular Star-PAP level-dependent manner. Moreover, we show that the serine 6 (S6) phosphorylation at the ZF region on Star-PAP controls the specificity of Star-PAP poly(A) site selection. This phosphorylation site is involved in Star-PAP recognition of target UTR/poly(A) site and PIPKIα interaction. The work thus opens up newer avenues in addressing the problem of cancer therapy.

Characterization of Neurovirulence of *Chikungunya* Virus (CHIKV) in Animal and Cell based Models

Neurovirulence is one of the recent complications identified during infections by the re-emerging strains of CHIKV. Since isolating a clinical strain from the human brain was technically challenging, we had to develop the neuroadaptive and neurovirulent virus. I was associated with the phenotype and infectivity characterization using several biochemical and cell biological assays like plaque assay, plaque purification and cytopathic effect determination and Immunofluorescence. Further, the genotypic characterization of the neurovirulent and neuroinvasive strains of CHIKV was done by whole genome sequencing, which also could shed light on the evolutionary significance of mutations in the viral genome. We identified critical mutations responsible for increased virulence and host adaptability in CHIKV.

Loop-mediated isothermal amplification (LAMP) based rapid and sensitive method for diagnosis of Leptospirosis

Leptospirosis is one among the emerging disease which, if left untreated, can cause many complications like Hepatic failures, Meningitis and even death. We have developed a loop-mediated isothermal amplification (LAMP) assay for the rapid and sensitive detection of Leptospirosis. In the present study, a LAMP test assay was designed using LAMP for the detection of *Leptospira* species. This study validates LAMP as an alternative molecular diagnostic tool and confirms the utility for the rapid and effective detection of Leptospira infections.

RESEARCH INTEREST

- **Fields of Interest:** RNA biology, Cell and Molecular Biology, Biochemistry, Disease Biology- Neurological disorders and Cancer, Virology
- **Areas of Interest:** mRNA modifications-m6A, mRNA processing- Polyadenylation, RNA editing, mRNA stability, RNA binding proteins, Regulatory RNAs (lncRNAs and miRNAs)

REFERENCE

- **Shengdong Ke, Ph.D.**
  Assistant Professor
  The Jackson Laboratory
  Bar Harbor, Maine-04609, US
  Email ID: Shengdong.ke@jax.org
  Mobile #: 207-288-6539

- **Rakesh S Laishram, Ph.D.**
  Scientist E-II and Swarnajayanti Fellow
  Rajiv Gandhi Centre for Biotechnology (RGCB) Trivandrum – 695 014, India
  E-mail ID: laishram@rgcb.res.in
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- **Arumugam Rajavelu, Ph.D.**
  Faculty Scientist
  Rajiv Gandhi Centre for Biotechnology (RGCB) Trivandrum – 695 014, India
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- **Dr. E Sreekumar, Ph.D.**
  Scientist E-II
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