

## Bio-data

A. Name of the Candidate: Jomon Joseph

B. Broad Subject Area: Life Sciences

C. Specialization: Molecular Cell Biology

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E. Educational Qualification:

Sl.No.	Degree	University	Year	Subjects	Percentage
1.	B.Sc (Agri)	University of Agricultural Sciences, Bangalore	1990	Agricultural Sciences	3.48 / 4.00 (CGPA)*
2.	M.Sc (Agri)	University of Agricultural Sciences, Bangalore	1993	Crop Physiology	3.86 / 4.00 (CGPA)*
3.	Ph.D.	Indian Institute of Science, Bangalore	2000	Biochemistry	-
4.	Post Doc	National Institutes of Health, Bethesda, USA	2005	Molecular Cell Biology	-

\* Cumulative Grade Point Average

F. Details of professional training and research experience, specifying period.

### SCIENTIST (2005-present)

#### National Centre for Cell Science, Pune – 7

My lab has been broadly interested in studying specific endoplasmic reticulum (ER) domains enriched in a subset of nucleoporins called 'Annulate Lamellae (AL)'. The cellular functions of this unexplored organelle are currently unclear, which is the major focus of my lab. Our work showed that Nup358, a nucleoporin present in the AL, plays a novel role in the microRNA (miRNA) pathway by coupling the miRNA-induced silencing complex with the target mRNA (Sahoo et al., 2017). Further studies from my lab also showed AL to be present at the ER-mitochondrial contact sites (ERMCS) and support a role of Nup358 in a few functions associated with the ERMCS such as calcium homeostasis, autophagy, and mTOR signaling (Kalarikkal et al., 2021) (Kalarikkal et al., 2024). Another major contribution from my lab is the finding that Nup358 is involved in the regulation of cell polarity during directed migration and neuronal differentiation (Murawala et al., 2009). Moreover, Nup358 was identified as a SUMO E3 ligase for the polarity kinase aPKC and thereby modulating the polarized epithelial structures called 'microridges' in zebrafish (Yadav

et al., 2017; Magre et al., 2019). Nup358 was also shown to localize to the cytoplasmic replication factories produced by the vaccinia virus and to be involved in viral infection (Khuperkar et al., 2017). My recent finding suggests that Nup358-mediated DDX19 SUMOylation modulates mRNA export (Banerjee et al., 2022). Recently, we also found that Nup358, annulate lamellae (AL)-resident nucleoporin, regulates ERMCSs via inhibition of mTORC2/Akt and activation of GSK3 $\beta$  (Kalarikkal et al., 2024). Our findings are expected to help identify the underlying reasons and intervention strategies for acute necrotizing encephalopathy (ANE), a neurological disorder linked with causal mutations in Nup358 and neurodegenerative diseases.

In brief, my lab is addressing a fundamental question in biology; the functions of an underexplored cell organelle, annulate lamellae (AL). I am one of the very few scientists across the globe working on the biology of AL, pioneering the field. Our study elegantly showed that AL, and particularly the AL-component Nup358, is involved in regulating miRNA-mediated suppression of mRNA translation, viral infection, ER-mitochondria contact site dynamics, growth factor signaling and autophagy. As mutations in Nup358 cause viral infection-induced 'acute necrotizing encephalopathy (ANE)' and nucleoporin functions are compromised in many neurodegenerative diseases, seminal contributions from my lab may have far-reaching implications in fundamental and disease biology.

## **POST DOCTORAL RESEARCH (2000-2005)**

**Laboratory of Gene Regulation & Development, NICHD / NIH, Bethesda, USA**

Advisor: **Dr. Mary Dasso**

The role of Ras-like nuclear (Ran) protein and Small Ubiquitin-like Modifier (SUMO) in regulating mitotic events was investigated during the post doctoral period. In addition to the well-characterized function in nuclear transport, Ran is implicated in regulating mitotic spindle assembly, nuclear assembly, and mitotic progression. Our work showed that the nucleoporin Nup358 (also called RanBP2) in complex with the Ran GTPase activating protein (RanGAP1) is localized to kinetochores in a microtubule-dependent manner during mitosis. Furthermore, we showed that Nup358-RanGAP1 complex plays a critical role in mediating proper kinetochore-microtubule interactions. This unexpected role for Nup358 at the kinetochore has opened new avenues for further research into the non-traditional roles of nucleoporins. The research work involved cell biology techniques (immunofluorescence, confocal microscopy, live cell imaging, microinjection of proteins into cells), RNA interference (design of small interfering RNAs, transfection and knocking-down expression specific proteins in mammalian cells) and biochemical studies (HPLC, immunoprecipitation, immunoblotting) using mammalian cell cultures and *Xenopus* egg extracts.

## **DOCTORAL RESEARCH (1993-2000)**

**Biochemistry Department, Indian Institute of Science, Bangalore, India**

Advisor: **Dr. H.S. Savithri**

During the doctoral work, I characterized a plant virus with respect to its genome organization and regulation of polyprotein processing. Results from the work concluded that Pepper Vein Banding Virus (PVBV), a major virus infecting chili pepper, is a distinct member of the Potyvirus group of plant viruses. Further, bacterial

expression of the coat protein showed that it could self-assemble into distinct virus-like particles (VLPs) in bacteria. The work also showed for the first time that the VLPs formed from a potyviral coat protein could encapsidate its own messenger RNA. Further, I identified critical residues required for catalysis and substrate binding of a potyviral protease (NIa protease) using site-directed mutagenesis. In addition, I helped characterizing two more plant viruses, a flexuous filamentous virus causing mosaic disease of sugarcane (*Saccharum officinarum* L.) and a tobacco mosaic virus strain isolated from tomato. The work involved propagation and isolation of plant viruses, RNA isolation, cDNA synthesis, cloning, DNA sequencing, nucleotide and amino acid sequence analysis, expression and purification of recombinant viral proteins, and site-directed mutagenesis.

## **M. Sc. RESEARCH (1990-1993)**

**Crop Physiology Department, Univ. Agricultural Sciences, Bangalore, India**

Advisor: **Dr. M. Udayakumar**

A group of plant proteins called Absciscic Acid (ABA) responsive proteins (ARPs) that are induced during salt stress in finger millet were characterized. I also developed specific polyclonal antibodies against partially purified ARPs. Using immunological methods, these proteins were shown to be potential biological markers for screening for plant genotypes with higher salt tolerance. Work involved induction of ARPs by saline stress in finger millet seedlings, purification of heat-resistant basic proteins, immunization and development of polyclonal antibodies in rabbits, Western blot and ELISA.

## **G. Details of employment.**

Scientist 'G' at the National Centre for Cell Science (NCCS) – 2022 - onwards  
Scientist 'F' at the National Centre for Cell Science (NCCS) – 2016 - 2021.  
Scientist 'E' at the National Centre for Cell Science (NCCS) – 2010 to 2016.  
Scientist 'D' at the National Centre for Cell Science (NCCS) – 2005 to 2010.

## **H. Professional recognition, awards, fellowships received.**

- International Travel Award from EMBO for attending EMBO Conference on 'Ubiquitin and SUMO: From molecular mechanisms to system-wide responses' (2017)
- International Travel Award from organizers of 'WNT meeting' (2010)
- John E. Fogarty International Visiting Fellowship (Postdoctoral, 2000-2005)
- Council of Scientific and Industrial Research-Senior Research Fellowship (1996-1999)
- Council of Scientific and Industrial Research-Junior Research Fellowship (1993-1996)
- Indian Council of Agricultural Research-Junior Research Fellowship (1991-1993)
- National Merit Scholarship (1984-1990)

## **I. Memberships**

- Elected member, Guha Research Conference (GRC), 2019

- Selected Member, Molecular Immunology Forum, 2019
- Life Member, Indian Society for Cell Biology (2008 onwards)
- Life Member, Society of Biological Chemists, India (2014 onwards)
- Life Member, Indian Society for Developmental Biologists (2017 onwards)
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J. Complete list of publications

1. Kalarikkal M, Saikia R, Oliveira L, Bhorkar Y, Lonare A, Varshney P, Dhamale P, Majumdar A, Joseph J\*. Nup358 restricts ER-mitochondria connectivity by modulating mTORC2/Akt/GSK3 $\beta$  signalling. **EMBO Rep**. 2024 Jul 18. doi: 10.1038/s44319-024-00204-8.
2. Chavan S, Khuperkar D, Lonare A, Panigrahi S, Bellare J, Rapole S, Seshadri V, Joseph J\*. RanGTPase links nucleo-cytoplasmic transport to the recruitment of cargoes into small extracellular vesicles. **Cell Mol Life Sci**. 2022 Jul 2;79(7):392.
3. Palazzo AF, Joseph J, Lim M, Thakur KT. Workshop on RanBP2/Nup358 and acute necrotizing encephalopathy. **Nucleus**. 2022 Dec;13(1):154-169.
4. Banerjee P, Markande S, Kalarikkal M, Joseph J\*. SUMOylation modulates the function of DDX19 in mRNA export. **J Cell Sci**. 2022 Jan 26;jcs.259449. (Selected for First Author interview)
5. Kalarikkal M, Saikia R, Varshney P, Dhamale P, Majumdar A, Joseph J\*. Nup358 regulates remodelling of ER-mitochondrial contact sites and autophagy. **bioRxiv** 2021.10.01.462723; doi: <https://doi.org/10.1101/2021.10.01.462723>
6. Saikia R, Joseph J\*. AMPK: a key regulator of energy stress and calcium-induced autophagy. **J Mol Med (Berl)**. 2021 Nov;99(11):1539-1551.
7. Deshmukh P, Singh A, Khuperkar D, Joseph J\*. (2021). Acute necrotizing encephalopathy-linked mutations in Nup358 impair interaction of Nup358 with TNRC6/GW182 and miRNA function. **Biochem Biophys Res Commun**. 559:230-237.
8. Deshmukh P, Markande S, Fandade V, Ramtirtha Y, Madhusudhan MS, Joseph J\*. (2021). The miRISC component AGO2 has multiple binding sites for Nup358 SUMO-interacting motif. **Biochem Biophys Res Commun**. 556:45-52.
9. Dandewad V, Vindu A, Joseph J, Seshadri V (2019). Import of human miRNA-RISC complex into Plasmodium falciparum and regulation of the parasite gene expression. **J. Biosci**. 44(2):50.
10. Magre I, Fandade V, Damle I, Banerjee P, Yadav SK, Sonawane M\*, Joseph J\* (2019). Nup358 regulates microridge length by controlling SUMOylation-dependent activity of aPKC in zebrafish epidermis. **J. Cell Sci**. pii: jcs.224501. (Cover page article) (Also selected for First Author interview).
11. Khuperkar D, Kamble A, Singh A, Ghate A, Nawadkar R, Sahu A\*, Joseph J\* (2017). Selective recruitment of nucleoporins on vaccinia virus factories and the role of Nup358 in viral infection. **Virology** 512:151-160.
12. Sahoo MR, Gaikwad S, Khuperkar D, Ashok M, Helen M, Yadav S, Singh A, Magre I, Deshmukh P, Dhanvijay S, Sahoo PK, Ramtirtha Y, Madhusudhan MS, Gayathri P,

- Seshadri V, Joseph J\* (2017). Nup358 binds to AGO proteins through its SUMO-interacting motifs and promotes the association of target mRNA with miRISC. **EMBO Rep.** 18(2):241-263.
13. Yadav SK, Magre I, Singh A, Khuperkar D, Joseph J\* (2016). Regulation of aPKC activity by Nup358 dependent SUMO modification. **Sci Rep.**, 6:34100.
  14. Chouhan S, Singh S, Athavale D, Ramteke P, Pandey V, Joseph J, Mohan R, Shetty PK, Bhat MK (2016). Glucose induced activation of canonical Wnt signaling pathway in hepatocellular carcinoma is regulated by DKK4. **Sci Rep.** 6:27558.
  15. Khuperkar D, Helen M, Magre I, Joseph J\* (2015). Inter-cellular transport of ran GTPase. **PLoS One.** 10(4):e0125506.
  16. Panda AC, Sahu I, Kulkarni SD, Martindale JL, Abdelmohsen K, Vindu A, Joseph J, Gorospe M, Seshadri V (2014). miR-196b-Mediated Translation Regulation of Mouse Insulin2 via the 5'UTR. **PLoS One.** 9(7):e101084.
  17. Zaim M, Ali A, Joseph J, Khan F. (2013). Serological and Molecular Studies of a Novel Virus Isolate Causing Yellow Mosaic of Patchouli [Pogostemon cablin (Blanco) Benth]. **PLoS One** 8(12):e83790.
  18. Vyas P, Singh A, Murawala P, Joseph J\* (2013). Nup358 interacts with Dishevelled and aPKC to regulate neuronal polarity. **Biology Open** 2:1270-1278.
  19. Sahoo, PK, Murawala P, Sawale PT, Sahoo MR, Tripathi MM, Gaikwad SR, Seshadri V, Joseph J\* (2012). Wnt signaling antagonizes stress granule assembly through a Dishevelled-dependent mechanism. **Biology Open** 1: 109-119.
  20. Hamada M, Haeger A, Jeganathan KB, van Ree JH, Malureanu L, Wälde S, Joseph J, Kehlenbach RH, van Deursen JM (2011). Ran-dependent docking of importin-beta to RanBP2/Nup358 filaments is essential for protein import and cell viability. **J. Cell Biol.** 2011, 194(4): 597-612.
  21. Notani D, Gottimukkala KP, Jayani RS, Limaye A, Damle MV, Mehta S, Purbey PK, Joseph J and Galande S (2009). Global regulator SATB1 recruits  $\beta$ -catenin and regulates T helper type 2 differentiation in Wnt/ $\beta$ -catenin-dependent manner. **PLoS Biol.** 8(1):e1000296.
  22. Atre AN, Surve SV, Shouche YS, Joseph J, Patole MS, Deopurkar RL (2009). Association of small Rho GTPases and actin ring formation in epithelial cells during the invasion by Candida albicans. **FEMS Immunol Med Microbiol.** 55(1): 74-84
  23. Murawala P, Tripathi MM, Vyas P, Salunke A and Joseph J\* (2009). Nup358 interacts with APC and plays a role in cell polarization. **J. Cell Sci.** 122(17): 3113-22.
  24. Joseph J\*, Dasso M\* (2008). The nucleoporin Nup358 associates with and regulates interphase microtubules. **FEBS Lett.** 2008. 582(2):190-6.
  25. Joseph J\* (2006). Ran at a glance. **J. Cell Sci.** 119(17):3481-4.
  26. Rundle NT, Nelson J, Flory MR, Joseph J, Th'ng J, Aebersold R, Dasso M, Andersen RJ, Roberge M (2006). An ent-kaurene that inhibits mitotic chromosome movement and binds the kinetochore protein ran-binding protein 2. **ACS Chem. Biol.** 1(7):443-50.

27. Prunuske AJ, Liu J, Elgort S, Joseph J, Dasso M, Ullman KS (2006). Nuclear envelope breakdown is coordinated by both Nup358/RanBP2 and Nup153, two nucleoporins with zinc finger modules. **Mol. Biol. Cell.** 17(2):760-9.
28. Arnaoutov A, Azuma Y, Ribbeck K, Joseph J, Boyarchuk Y, Karpova T, McNally J, Dasso M (2005). Crm1 is a mitotic effector of Ran-GTP in somatic cells. **Nat. Cell Biol.** 7(6):626-32.
29. Jeong SY, Rose A, Joseph J, Dasso M, Meier I (2005). Plant-specific mitotic targeting of RanGAP requires a functional WPP domain. **Plant J.** 42(2):270-82.
30. Anindya R, Joseph J, Gowri TDS and Savithri HS (2004). Complete genomic sequence of Pepper vein banding virus (PVBV): a distinct member of the genus Potyvirus. **Arch. Virol.** 149(3):625-32.
31. Joseph J, Liu ST, Jablonski SA, Yen TJ, Dasso M (2004). The RanGAP1-RanBP2 complex is essential for microtubule-kinetochore interactions in vivo. **Curr. Biol.** 2004.14(7):611-7.
32. Joseph J and Dasso M (2003). Cellular roles of the Ran GTPase. Review in **Handbook of cellular signaling**, 2: 695-699. H. Hamm ed. San Diego, Academic Press.
33. Joseph J, Tan SH, Karpova TS, McNally JG, Dasso M (2002). SUMO-1 targets RanGAP1 to kinetochores and mitotic spindles. **J. Cell Biol.** 156(4):595-602. [Significance of this paper has been highlighted in the Editor's Choice section of **Science** 295(5561): 1795 (2002)].
34. Joseph J and Savithri HS (2000). Mutational analysis of the NIa protease from pepper vein banding potyvirus. **Arch. Virol.** 145: 2493-2502.
35. Joseph J and Savithri HS (1999). Determination of 3'-terminal nucleotide sequence of pepper vein banding virus RNA and expression of its coat protein in Escherichia coli. **Arch. Virol.** 144: 1679-1687.
36. Hema M, Joseph J, Gopinath K, Sreenivasulu K and Savithri HS (1999). Molecular characterization and intervirial relationships of a flexuous filamentous virus causing mosaic disease of sugarcane (Saccharum officinarum L.) in India. **Arch. Virol.** 144: 479-490.
37. Ravi KS, Joseph J, Nagaraju N, Parasad SK Reddy HR and Savithri HS (1997). Characterization of a pepper vein banding virus from chili pepper in India. **Plant Disease** 81: 673-676.

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J. Details of Research Projects being implemented/ completed/

## **COMPLETED PROJECTS:**

### **Grants**

Principal Investigator, Regulation of  $\beta$ -catenin function by the nucleoporin Nup358 in Wnt signaling, 2008-2011, Department of Biotechnology, India (Total Support, Rs. 16.144 lakhs).

Principal Investigator, Molecular characterization of the interaction between the tumor suppressor Adenomatous polyposis coli and the nucleoporin Nup358, 2008-2012, Department of Biotechnology, India (Total Support, Rs. 28.24 lakhs).

Principal Investigator, Regulation of RNA metabolism by Dishevelled, a critical player of Wnt signalling, 2011-2015, Department of Biotechnology, India (Total Support, Rs. 55.05 lakhs).

Principal Investigator, Exploring the functional connection between Par polarity proteins and Nup358 in cell polarity, 2012-2016, Department of Biotechnology, India (Total Support, Rs. 48.948 lakhs).

Principal Investigator, Role of Nup358 in the regulation of cytoplasmic mRNP granules, 2016-2019, Department of Science and Technology, India (Total Support, Rs. 41.26 lakhs).

## **ONGOING PROJECTS:**

### **Grants**

Principal Investigator, Understanding the functions of Annulate Lamellae, an underexplored cell organelle, 2022-2025, SERB (SUPRA), Department of Science and Technology, India (Total Support; 79.24 lakhs)

Principal Investigator, Characterization of inter-cellular transport of Ran GTPase, 2020-23, Department of Biotechnology, India (Total Support, Rs. 79.86 lakhs).

Principal Investigator, Characterization of acute necrotizing encephalopathy-1 (ANE1)-associated mutations in Nup358, 2019-22, Department of Biotechnology, India (Total Support, Rs. 69.93 lakhs)