## BIOGRAPHICAL SKETCH

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NAME: **Asha Acharya**

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

POSITION TITLE: **Instructor**

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 |
|---|---|---|---|
| University of Delhi, New Delhi, India | B.Sc. | 05/1994 | Biochemistry |
| Indian Institute of Science, Bangalore, India | M.S. | 07/1997 | Biological sciences |
| Indian Institute of Science, Bangalore, India | Ph.D | 12/2002 | Molecular Biology |
| Michigan State University, East Lansing, MI | Postdoc | 07/2005 | Biochemistry |
| UT Southwestern Medical Center, Dallas, TX | Postdoc | 06/2009 | Molecular Biology |

### A. Personal Statement

I am an Instructor in the Mendell laboratory within the Department of Molecular Biology at UT Southwestern. I use RNA-based tools to decipher the roles of noncoding RNAs in cancer biology and physiology. I am currently investigating the roles of small noncoding RNAs known as microRNAs in normal vertebrate physiology and in diseases such as cancer. I utilize genetically engineered mice to model miRNA gain- and loss-of-function *in vivo*, to elucidate how conserved miRNAs modulate multiple transcriptional and signaling networks to regulate gene expression. With my prior training and experience in the areas of mouse genetics, microscopy, and cardiovascular development, I am uniquely positioned to address the roles of noncoding RNAs *in vivo*. Since joining the Mendell laboratory, I have pioneered the use of cutting-edge technologies to address some of the most pertinent and challenging questions in the field of miRNA biology. With a demonstrated record of productive research and accomplishments, I hope to continue my role as a key contributor to the NCI-funded research program within the Mendell laboratory and continue to make valuable contributions to our understanding of noncoding RNA functions in normal physiology and disease.

### B. Positions and Honors

**Academic Appointments:**

2012-Present Instructor, Department of Molecular Biology, (Joshua Mendell Laboratory)
UT Southwestern Medical Center, Dallas TX.
2009-2012 Instructor, Department of Molecular Biology, (Michelle Tallquist Laboratory)
UT Southwestern Medical Center, Dallas TX.

**Honors and Awards:**

2007-2009 Postdoctoral fellow, American Heart Association

### C. Contributions to Science

**1. *In vivo* roles of miRNAs (PI: Prof. Joshua T. Mendell)**

MicroRNAs target a vast majority of messenger RNAs and thus have widespread impact on the expression of protein coding genes. Past work has revealed a wealth of information regarding biogenesis of this small noncoding RNA species and the mechanisms by which they mediate post-transcriptional gene repression. However, the majority of functional data has been derived from studies conducted *in vitro* using cell culture.

The primary focus of my research in the Mendell laboratory has been to elucidate the *in vivo* roles of miRNAs using genetically engineered mouse models. By deriving loss- and gain-of-function alleles, we have investigated miRNA function in normal vertebrate physiology and under pathological conditions. For example, our studies of conditional depletion of miR-143/145 in mice revealed that these miRNAs are exclusively expressed in the mesenchymal compartment of the intestine and are essential for epithelial regeneration in the colon following injury [1]. On the other hand, we showed that transgenic overexpression of certain tumor suppressor miRNAs such as miR-26a potently inhibited tumorigenesis in mouse cancer models [2]. In addition, I have also explored mechanisms that regulate miRNA processing and maturation [3]. More recently, I have uncovered a new role for miR-26 in maintenance of the adipocyte progenitor cell pool by targeting the E3 ubiquitin ligase *Fbxl19* [4].

**Publications most relevant to the current application:**


1. Chivukula R.R*., Shi G*., **Acharya A.**, Mills E.W., Zeitels, L.R., Anandam, J.L., Abdelnaby A.A., Balch G.C., Mansour J.C., Yopp A.C., Maitra A., and Mendell J.T. (2014). An essential mesenchymal function for *miR-143/145* in intestinal epithelial regeneration. *Cell*, 157(5): 1104-1116. PMC4175516
2. Zeitels LR, **Acharya A**, Shi G, Chivukula D, Chivukula RR, Anandam JL, Abdelnaby AA, Balch GC, Mansour JC, Yopp AC, Richardson JA, Mendell JT. (2014). Tumor suppression by miR-26 overrides potential oncogenic activity in intestinal tumorigenesis. *Genes & Dev.,* 28(23):2565-2584. PMC4248289
3. Hunter R.W., Liu Y., Manjunath H., **Acharya A**., Jones B.T., Zhang H., Chen B., Ramalingam H., Hammer R.E., Xie Y., Richardson J.A., Rakheja, D., Carroll T.J., and Mendell J.T. (2018). Loss of *Dis3l2* partially phenocopies Perlman syndrome in mice and results in up-regulation of Igf2 in nephron progenitor cells. *Genes & Dev.,* 32(13-14):903-908. PMC6075040
4. **Acharya A**., Berry, D.C., Zhang, H., Jiang, Y., Jones, B.T., Graff, J.M., and Mendell J.T. (2019). miR-26 suppresses adipocyte progenitor differentiation and fat production by targeting *Fbxl19*. *Genes & Dev.,* 33(19-20):1367-1380. PMC Journal-in process.


***2. Tcf21* in development and disease (PI: Prof. Michelle D. Tallquist)**

A class II bHLH family member, *Tcf21* orchestrates cell-fate specification, commitment, and differentiation in multiple cell lineages during vertebrate development. To explore mechanisms through which *Tcf21* regulates cell fate specification, we generated a tamoxifen inducible *Tcf21-Cre* mouse (*Tcf21*$^{iCre}$) [1]. Using this line, I was able to establish an essential role for *Tcf21* in fate specification of cardiac fibroblasts. Our work demonstrated a unique lineage-specific requirement for *Tcf21* in epithelial to mesenchymal transition (EMT) of multipotent epicardial progenitors during development [2]. The generation of the *Tcf21*$^{iCre}$ mouse line fostered several valuable collaborations striving to identify cell-specific roles of *Tcf21* both in the heart and other tissues. For example, in the adult heart, fibrosis due to activation of cardiac fibroblasts impedes cardiac regeneration and contributes to loss of contractile function, pathological remodeling, and susceptibility to arrhythmias. Work done in collaboration with the Olson laboratory has shown that phenotypic reprogramming of cardiac fibroblasts to a myocardial cell fate is feasible by enforced expression of cardiogenic transcription factors both *in vitro* and *in vivo* [3]. Likewise, lineage tracing with *Tcf21*$^{iCre}$ in the adrenal has identified a unique contribution of *Tcf21*-expressing cells to fate specification of developing fetal cortex and establishment of a progenitor cell niche in the adult cortex [4].


1. **Acharya A.**, Baek S.T., Banfi S., Eskiocak, B., and Tallquist M.D. (2011). Efficient Inducible Cre-mediated recombination in *Tcf21* cell lineages of the heart and kidney. *Genesis*, 49(11): 870-877. PMC3279154
2. **Acharya A**., Baek S.T., Huang G., Eskiocak B., Goetsch S., Sung C.Y., Banfi S., Sauer M.F., Olsen G.S., Duffield J.S., Olson E.N., and Tallquist M.D. (2012). The bhlh transcription factor, Tcf21, is required for lineage-specific EMT of cardiac fibroblast progenitors. *Development*, 139(120: 2139-49. PMC3357908
3. Song K., Nam Y.J., Luo X., Qi X., Tan W., Huang G., **Acharya A**., Smith C.L., Tallquist M.D., Neilson E.G., Hill J.A., Bassel-Duby R., and Olson E.N. (2012). Heart repair by expression of cardiac transcription factors in non-cardiomyocytes in vivo. *Nature,* 485(7400): 599-604. PMC3367390
4. Wood M.A., **Acharya A**., Finco I., Swonger J.M., Elston M.J., Tallquist M.D., and Hammer G.D. (2013). Fetal adrenal capsular cells serve as progenitor cells for steroidogenic and stromal adrenocortical cell lineages in M. musculus. *Development*, 140(22): 4522-32. PMC3817941


**3. Notch signaling in calcific aortic valve disease (PI: Prof. Vidu Garg)**

As a postdoctoral fellow in Dr. Vidu Garg's lab, my studies were focused on adult cardiac valve function. Aortic valve calcification is the most common form of valvular heart disease, but the mechanisms of calcific aortic valve disease (CAVD) remain largely unknown. Published work from Dr. Garg's postdoctoral work had described association of NOTCH1 mutations with aortic valve malformations and adult-onset calcification in families with inherited disease. We found that calcified areas of human aortic valves showed reduced expression of Notch signaling pathway members and likewise inhibition of Notch signaling in porcine aortic valve interstitial cells (AVICs) accelerated calcification. Using gene expression and knockdown studies, I was able to demonstrate that loss of Notch signaling contributes to aortic valve calcification via a Sox9-dependent mechanism. This study was supported by a postdoctoral fellowship from AHA.

1. **Acharya A.**, Hans C.P*., Koenig, S.N., Nichols, H.A., Galindo, C., Garner, H.R., Merrill W.H., Hinton R.B., and Garg V (2011). Inhibitory role of Notch1 in calcific aortic valve disease*. PLoS One*, 6:e27743. PMC3218038

**4. Tethered catalysis and novel protein-protein interactions (PI: Prof. Min-Hao Kuo)**

During my post-doctoral training in Dr. Kuo's lab at Michigan State University, I studied post-translational modification (PTM) dependent protein-protein interactions. PTMs are a dynamic way of generating new protein-protein interaction interfaces that are critical for signaling networks in diverse cellular functions. However, purified recombinant proteins frequently lack these signature modifications. Using the tumor suppressor p53 as the model protein, we developed and characterized a tethered catalysis approach for the production of acetylated p53 in yeast and *E.coli* [1]. The approach has proven successful in identifying novel PTM-based interactions of p53 and histone proteins and this technology offers widespread application in the fields of signal transduction and proteomic research [2].

1. **Acharya, A**., Xu, X-J., Husain-Ponnampalam, R.D., Hoffmann-Benning, S., and Kuo, M-H. (2005). Production of constitutively acetylated recombinant p53 from yeast and *Escherichia coli* by tethered catalysis. *Protein Expr Purif.* 41:417-425.
2. **Acharya, A**. and Kuo, M-H. (2006). Signaling through chromatin modifications and protein-protein interactions. *Biotechnol. Genet. Eng. Rev.* 23:105-127.

**5. Trancriptional regulation in Bombyx mori nucleopolyhedrovirus (Mentor: Prof. K. P. Gopinathan)**

My graduate studies in the department of Cell and Molecular Biology at Indian Institute of Science focused on transcriptional regulation in baculoviruses. Hyper-transcription from the late baculoviral promoters has led to their widespread use as eukaryotic expression vector systems. The baculovirus *Bombyx mori nucleopolyhedrosis* virus (BmNPV) is a natural pathogen of the mulberry silkworm and the transition from early to late phase of gene expression in these viruses is primarily executed at the level of viral gene transcription. I therefore sought to identify the *cis* regulatory elements and *trans* factors that govern *BmNPV* late gene expression. The work identified a novel enhancer-like element upstream of the BmNPV polyhedrin gene [1]. Additionally, I performed detailed transcriptional analysis of two key viral proteins that constitute the late viral $\alpha$-amanitin resistant RNA polymerase [2] and identified a unique mode of transcriptional regulation for a gene cluster that encoded the viral structural protein Bm42 [3].

1. **Acharya, A**., and Gopinathan, K.P. (2001). Identification of an enhancer-like element in the *polyhedrin* gene upstream region of *Bombyx mori* nucleopolyhedrovirus*. J Gen Virol*. 82: 2811-2819
2. **Acharya, A**., and Gopinathan, K.P. (2002). Characterization of late gene expression factors *lef-9* and *lef-8* from *Bombyx mori* nucleopolyhedrovirus. *J Gen Virol*. 83: 2015 -2023.
3. **Acharya, A**., and Gopinathan, K.P. (2002). Transcriptional analysis and preliminary characterization of ORF Bm42 from *Bombyx mori* nucleopolyhedrovirus. *Virology* 299:213-224.

**For a complete list, please visit https://scholar.google.com/citations?user=Gp_2pGkAAAAJ&hl=en**

**D. Current Research Support**

` None