Curriculum Vitae
Shekhar Saha, PhD

Personal Data

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Citizen Indian

Education

2003-2006 Bachelor of Science in Chemistry (Hons), Maulana Azad College, University of Calcutta, West Bengal, India

2007-2009 Master of Science in Chemical Sciences, Indian Association for the Cultivation of Science, West Bengal, India

2009-2014 PhD in Molecular Cell Biology, Indian Association for the Cultivation of Science, West Bengal, India
Advisor: Prof. Siddhartha S Jana

Postdoctoral Training

2015-present Postdoctoral Fellow in Dept. of Biochemistry and Molecular Genetics, University of Virginia School of

Medicine

Academic and Professional Honors

2007	Securing 136th rank in Joint Admission test for M.Sc (JAM 2007), an all India based admission test conducted by all the IITs in India, with 3195 applicants.
2007	One among best 10 selected candidate out of 1000 Participants for pursuing Post B.Sc. Integrated PhD in Indian Association for the Cultivation of Science and S N Bose National Centre for Basic Sciences jointly Conducted integrated PhD program.
2010	Qualified All India CSIR-UGC NET for PhD Fellowship.
2012	Travel grant from Department of Science and Technology (DST), Govt. of India for attending ASCB Meeting.
2015	Travel award from ASBMB for attending ASBMB meeting.
2015	Best Poster award in IABS symposium
2020	Early Career Reviewer award from Journal of Biological Chemistry.
2020	Cancer Center Training Grant, University of Virginia, USA

Invited Presentations

2020	Invited Talk in NCCS Pune, India, January 2020
2020	Invited Talk in NIBMG, Kolkata, India, February 2020
2020	Invited Talk in IISER Kolkata, India, February 2020
2020	Invited Talk in Neuro-Oncology Dept. University of Virginia

Professional Societies

2020 Member in RNA Society

2020 The American Society for Biochemistry and Molecular Biology (ASBMB)

Editorial Board Member

2016-present Molecular Biophysics and Biochemistry

2019-present International Research Journal of Food and Nutrition

Early Career Reviewer

Early Career Reviewer for Journal of Biological Chemistry

Additional Information: Research Support and/or Scholastic Performance

1. American Society for Cell Biology Meeting 2012 at Moscone Center, San Francisco, California, USA.
2. Young Investigator Meeting, 2011, Bhubaneswar, India.
3. Indian Institute of Science Education and Research (IISER), 2011, Kolkata, India.
4. American Society for Biochemistry and Molecular Genetics meeting 2015 at Boston, USA.
5. RNA Biology Meeting, National Cancer Institute, USA, 2016.
6. RNA Biology Meeting, University of North Carolina, Chapel Hill, USA, 2017.
7. RNA Biology Meeting, National Cancer Institute, USA, 2018.
8. Poster Presentation at Regulatory and noncoding RNA meeting, May 12-15, 2020, Cold Spring Harbor

9. Poster Presentation at RNA Society meeting, May 26-31, 2020
10. Poster Presentation at FASEB meeting, September 21-22, 2020

Bioinformatics/Computational Skills

1. Basic knowledge on R programming
2. Basic Knowledge on Linux
3. Next Generation RNA-seq analysis
4. Next Generation ChIP-seq analysis

Personal Statement

My long-term research interests involve to better understanding the signaling mechanism contributing to cancer and to find out a possible cure of the disease. Specifically, I want to explore the mechanism and function of long noncoding RNAs, recently identified class of molecules that are abundantly present in the cells, and add an entirely new dimension to the mechanisms of cellular regulation, which contribute to cancer. I have a strong background in molecular and cellular cancer biology from my Master's program and doctoral program. In my under graduation degree, I have a basic knowledge of Chemistry which being a fundamental science really helped in my understanding of biological processes during my Master's research training. My doctoral research experience has broadened my knowledge in multidisciplinary subjects including molecular cell biology, cancer biology, biochemistry, microbiology, bioinformatics, and physical chemistry. During my doctoral training, I qualified in several academic and travel awards. During my postdoctoral training I gained expertise on the role of long noncoding RNAs in the progression of prostate cancer and glioblastoma and learned research skills with special importance to cancer biology. My future goal is to nurture my expertise to gain insights to the causal effects on the significant diseases prevailing in India in genomic perspective and subsequently developing new therapeutics for disease prevention.

Early Career

During my Master's degree, I began working in the laboratory of Dr. Siddhartha Shankar Jana in Indian Association for the Cultivation of Science, Kolkata, India where my research work focused on the role of Nonmuscle Myosin IIs (NM IIs) in 3-Methylcholanthrene (3-MC) induced sarcoma in mouse. Previous literature reports suggest that transformation of muscle cells to atypical cells is one of the causes of tumor formation. The molecular events that lead to transformation of normal cells to atypical cancerous cells are not well understood. I found an increased expression of NM II-A and II-B in sarcoma compared to normal

associated tumor by mass spectrometry, qPCR and immunobloting. Immunofluorescence confocal microscopy reveals that fibroblast cells which are sparsely distributed in normal tissue are densely populated but of atypical shape in the tumor. These observations suggest the transformation of atypical fibroblast or non-fibroblast to cancerous cells is associated with increased expression of NM II-A and II-B in 3-MC induced sarcoma in mouse. Although DNA structural changes and fibroblast transformation at the site of 3-MC injection are hypothesized to be the main causes of sarcoma, I postulated that dedifferentiation of muscle cells into mononucleated cells can further contribute to sarcoma which is experimentally demonstrated in C2C12 myotubes treated with 3-MC.

PhD Career

In my PhD, I have studied the role of Nonmuscle Myosin II-C1C2 (NM II-C1C2) in neuritogenesis of Neuro-2a cells. Nonmuscle myosin IIs (NM IIs) are ubiquitously expressed throughout the entire organism and play distinct roles in cell division, adhesion, migration etc. Till date, three types of nonmuscle myosin IIs, IIA, IIB and IIC are found in vertebrates. Recently, similar to NM II-B, it has been shown that splicing at loop1 and loop 2 of NM heavy chain II-C can produce four different isoforms of NM II- C- NM II-C0, NM II-C1, NM II-C2 and NM II-C1C2. C2 insert containing isoforms are specifically expressed in mouse and human brain, and their activities are independent of myosin light chain phosphorylation. But it is unknown which type of cells in brain express C2 containing NM II-C isoforms, and also the functional role of these proteins. In this thesis, I have studied the function of C2 insert containing isoform of NM II-C, NM II- C1C2, in Neuro-2a cells. I have shown that expression of NM II-C1C2 both at mRNA and protein level during neuritogenesis of Neuro-2a cells is detectable by RT-PCR and immunoblot analyses. Inhibition of C2 insert containing isoform (NM II-C1C2) by siRNA decreases number of neurites and number of filopodia, reduces the length of neurites, and loosens neurite's attachment with its substratum. NM II-C1C2 can colocalize and interact with β1 integrin at later stage of neuritogenesis. Ectopic expression of GFP tagged C2 containing isoforms (NM II-C2 and NM II-C1C2) in Neuro-2a cells shows puncta localization in neurites. I further investigated what make C2 insert containing molecule so unique in binding with integrin and showing puncta pattern of localization in neurites. Fluorescence intensity versus time trajectories revealed that NM II-C2-GFP displays oscillation of fluorescence intensity in neurites. Deletion of N-terminal region of C2 insert abolishes the fluctuation nature of NM II-C2 in neurites of Neuro-2a cells. Our study provides the importance of Glutamine and Lysine residues of C2 insert in the neuritogenesis of Neuro-2a cells.

Postdoctoral Career

In my postdoctoral work, I focused my research career to the better understanding and treatment of cancer. Specifically, I explored the mechanism and function of a tumor suppressive long noncoding RNA that regulates prostate and brain cancer progression. Cancer management relies heavily on predicting the invasiveness and outcome of the tumor. In spite of a number of cancer markers in clinical use, unraveling the molecular pathways by which a cancer transform to an aggressive stage is a major challenge for cancer researchers. Long noncoding RNAs (lncRNAs) are a recently identified class of molecules, which are abundantly present and add an entirely new dimension to the mechanisms of cellular regulation. Thus identifying and investigating lncRNAs involved in different cancer progression will unfold novel prognostic and therapeutic targets in cancer. My mentor's lab recently identified several lncRNAs, which might have prognostic as well as therapeutic potential for brain cancer and other different malignant tumors. I worked on an lncRNA DRAIC which has been predicted to be a good prognostic marker in 9 different malignant tumors. During my postdoctoral work, I showed that the lncRNA, DRAIC is down regulated in invasive cancer cells and its over-expression in such cells reduces their invasive and migratory properties. Mechanistically I have shown that the lncRNA, DRAIC mediates this effect through the interaction with IKK alpha and NEMO of IKK trimeric complex and thereby regulate the NF-κB pathway. Furthermore, I have narrowed down the domain of the lncRNA that is sufficient to disrupt the complex formation to inhibit tumor growth. My ongoing work is involved in getting the cryo-EM structure of DRAIC along with its interacting protein in collaboration with Dr. Edward H. Egelman, University of Virginia. I am also working on developing this lncRNA as a prognostic or/and therapeutic target for metastasis in brain cancer in collaboration with Dr. Roger Abounader, University of Virginia.

Publications

1. Saha S, Dey SK, Das P, Jana SS. Increased expression of nonmuscle myosin IIs is associated with 3MC-induced mouse tumor. **FEBS J.** 2011 Nov;278(21):4025-34. doi: 10.1111/j.1742- 4658.2011.08306.x. Epub 2011 Sep 19. PubMed PMID: 21848673 **(IF: 4.739).**

2. Saha S, Dey SK, Biswas A, Das P, Das MR, Jana SS. The effect of including the C2 insert of nonmuscle myosin II-C on neuritogenesis. **J Biol Chem**. 2013 Mar 15; 288(11):7815-28. doi: 10.1074/jbc.M112.417196. Epub 2013 Jan 25. PubMed PMID: 23355468; PubMed Central PMCID: PMC3597820 **(IF: 4.106).**

3. Saha S, Halder D, Goswami S, Jana SS. N-terminal polar amino acids of the C2 insert of nonmuscle myosin II-C2 regulate its functional properties. **FEBS Lett**. 2016 Dec;590(23):4223-4232. doi:10.1002/1873-3468.12446. Epub 2016 Oct 23 **(IF: 2.999).**

4. Dey, S. K., Dan, K., Das, M. R., **Saha, S**., Das, P., Ghosh, S., and Jana, S. S. (2013) Amphiphilic random copolymer vesicle induces differentiation of mouse C2C12 myoblasts. **Biomater. Sci**. 1, 1211- 1215 **(IF: 5.831).**

5. Sharma T, Kumari P, Pincha N, Mutukula N, **Saha S**, Jana SS, Ta M. Inhibition of non-muscle myosin II leads to G0/G1 arrest of Wharton's jelly-derived mesenchymal stromal cells. **Cytotherapy**. 2014 May;16(5):640-52. doi: 10.1016/j.jcyt.2013.09.003. Epub 2013 Nov 7. PubMed PMID: 24210786 **(IF: 3.203).**

6. Chattoraj S*, **Saha S***, Jana SS, Bhattacharyya K. Dynamics of Gene Silencing in a Live Cell: Stochastic Resonance. **J Phys Chem Lett**. 2014 Mar 20;5(6):1012-6. doi: 10.1021/jz500152m. Epub 2014 Mar 7. PubMed PMID: 26270981. (***Authors contributed equally) (IF: 7.329).**

7. Dey SK, **Saha S**, Das P, Das MR, Jana SS. Regulation of nonmuscle myosin II during 3 methylcholanthrene induced dedifferentiation of C2C12 myotubes. **Exp Cell Res**. 2014 Aug 1;326(1):68-77. doi: 10.1016/j.yexcr.2014.05.015. Epub 2014 Jun 2. PubMed PMID: 24887008 **(IF: 3.246).**

8. Pattanayak S, Khatra H, **Saha S,** Sinha S. A cationic morpholino antisense oligomer conjugate: synthesis, cellular uptake and inhibition of Gli1 in the hedgehog signalling pathway. RSC Adv. 2014, 4:1951-4. doi:10.1039/C3RA45257C **(IF: 3.049).**

9. Das P, **Saha S**, Chandra S, Das A, Dey SK, Das MR, Sen S, Sarkar DP, Jana SS. Phosphorylation of Nonmuscle myosin II-A regulatory light chain resists Sendai virus fusion with host cells. **Sci Rep**. 2015 May 20;5:10395. doi: 10.1038/srep10395. PubMed PMID: 25993465; PubMed Central PMCID: PMC4438666 **(IF: 4.122).**

10. Arora S, **Saha S**, Roy S, Das M, Jana SS, Ta M. Role of Nonmuscle Myosin II in Migration of Wharton's Jelly-Derived Mesenchymal Stem Cells. **Stem Cells Dev**. 2015 Sep 1;24(17):2065-77. doi: 10.1089/scd.2015.0095. Epub 2015 Jun 4. PubMed PMID: 25923805; PubMed Central PMCID: PMC4544822 **(IF: 3.147).**

11. Ghosal S*, **Saha S***, Das S, Sen R, Goswami S, Jana SS, Chakrabarti J. miRepress: modelling gene expression regulation by microRNA with non-conventional binding sites. **Sci Rep**. 2016 Feb 29;6:22334. doi: 10.1038/srep22334. PubMed PMID: 26923536; PubMed Central PMCID: PMC4770313. (* **Authors contributed equally) (IF: 4.122).**

12. Das MR, Bag AK, **Saha S**, Ghosh A, Dey SK, Das P, Mandal C, Ray S, Chakrabarti S, Ray M, Jana SS.Molecular association of glucose-6-phosphate isomerase and pyruvate kinase M2 with glyceraldehyde-3-phosphate dehydrogenase in cancer cells. **BMC Cancer**. 2016 Feb 24;16:152. doi: 10.1186/s12885-016-2172-x. PubMed PMID: 26911935; PubMed Central PMCID: PMC4766697 **(IF: 3.288).**

13. Dey SK, Singh RK, Chattoraj S, **Saha S**, Das A, Bhattacharyya K, Sengupta K, Sen S, Jana SS Differential role of nonmuscle myosin II isoforms during blebbing of MCF-7 cells. **Mol Biol Cell**. 2017 Apr 15;28(8):1034-1042. doi: 10.1091/mbc.E16-07-0524. Epub 2017 Mar 1 **(IF: 3.512).**

14. Chattoraj S*, **Saha S***, Halder, D*, Jana SS, Bhattacharyya K. Structural Oscillations of Non–muscle Myosin II–C2: Time Resolved Confocal Microscopy. **ChemistrySelect, 2017**, DOI: 10.1002/slct.201601963. (* Authors contributed equally) **(IF: 1.716).**

15. Halder D, **Saha S,** Singh R, Ghosh I, Mallick D, Dey SK, Ghosh A, Das B and Jana SS. Non-muscle myosin IIA and IIB differentially modulate migration and alter gene expression in primary mouse tumorigenic cells **(2018). Mol Biol Cell, 2019 Jun 1;30(12):1463-1476. Doi:10.1091/mbc.E18-12-0790 (IF: 3.512).**

16. Shekhar Saha, Manjari Kiran, Canan Kuscu, Ajay Chatrath, David Wotton, Marty W. Mayo and Anindya Dutta. Long noncoding RNA DRAIC inhibits prostate

cancer progression by interacting with IKK to inhibit NF-κB activation. **Cancer Res 2020; 80:950–63 (IF: 9.130).**

17. Ajay Chatrath, Roza Przanowska, Shashi Kiran, Zhangli Su, **Shekhar Saha**, Briana Wilson, Takaaki Tsunematsu, Ji-Hye Ahn, Kyung Yong Lee, Teressa Paulsen, Ewelina Sobierajska, Manjari Kiran, Xiwei Tang, Tianxi Li, Pankaj Kumar, Aakrosh Ratan, and Anindya Dutta. The Pan-Cancer Landscape of Prognostic Germline Variants in 10,582 Patients. **Genome Medicine, 12:15 (IF: 8.898).**

18. Pankaj Kumar, Shashi Kiran, **Shekhar Saha**, Zhangli Su, Teressa Paulsen, Ajay Chatrath, Yoshiyuki Shibata, Anindya Dutta . ATAC-seq identifies thousands of extrachromosomal circular DNA in cancers and cell lines **Science Advances Vol. 6, no. 20, eaba2489 (IF: 12.804).**

19. Zhangli Su [#], **Shekhar Saha** [#], Teressa Paulsen, Pankaj Kumar * and Anindya Dutta. ATAC-Seq-based Identification of Extrachromosomal Circular DNA in Mammalian Cells and its Validation using Inverse PCR and FISH. **Bio-Protocol (IF: 5.78). (#** Authors contributed equally**) (Accepted)**

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