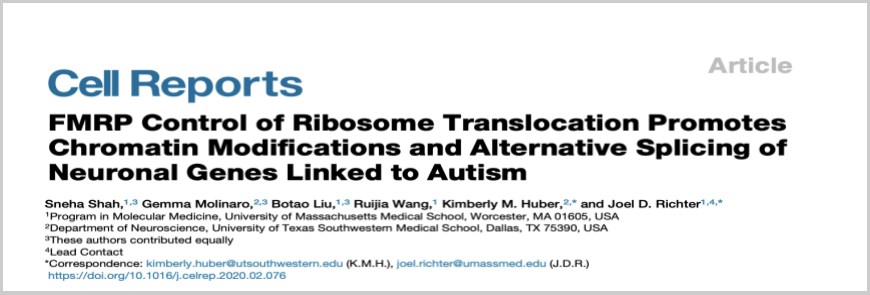
UMPA presents

Postdoc Spotlight Series

National Postdoc Appreciation Week

September 21-25

Let's celebrate us Postdocs!



Article

Cell Reports

FMRP Control of Ribosome Translocation Promotes Chromatin Modifications and Alternative Splicing of Neuronal Genes Linked to Autism

Sneha Shah,[1,3] Gemma Molinaro,[2,3] Botao Liu,[1,3] Ruijia Wang,[1] Kimberly M. Huber,[2,*] and Joel D. Richter[1,4,*]
[1]Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, MA 01605, USA
[2]Department of Neuroscience, University of Texas Southwestern Medical School, Dallas, TX 75390, USA
[3]These authors contributed equally
[4]Lead Contact
*Correspondence: kimberly.huber@utsouthwestern.edu (K.M.H.), joel.richter@umassmed.edu (J.D.R.)
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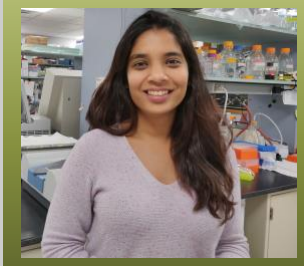
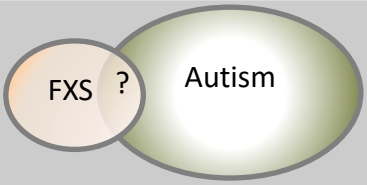


Sneha Shah, Ph.D.

Richter Lab

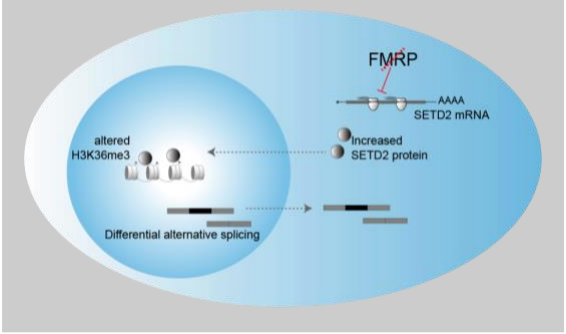
Program in Molecular Medicine



Are there common underlying mechanisms amongst intellectual disabilities?

Studying the different mechanisms by which gene expression is regulated is fascinating. During my PhD, I studied epigenetic and transcription-based mechanisms of gene expression in yeast at the University of Oxford, UK. In my postdoctoral project, I am studying the effects of dysregulated protein expression in an intellectual disability, the Fragile X Syndrome (FXS). This exciting project is funded by a generous postdoctoral grant from the FRAXA research foundation (2019-2021).

Autism Spectrum Disorder (ASD) is an intellectual disability that results in mild to severe cognitive impairments and is found to occur in 1 in 54 children. About 15% of autism cases can be attributed to genetic causes and the most prevalent amongst these is the Fragile X syndrome (FXS). In FXS, a single gene on the X chromosome called the *FMR1* gene is 'switched off 'which results in loss of the protein, FMRP. FMRP binds mRNAs and ribosomes that translate the mRNAs into protein products.



Our lab is investigating a model in which, FMRP hinders ribosome movement on mRNAs regulating protein expression. Removal of FMRP results in faster ribosome movement and more protein production. In this study we identified a number of neuronal mRNAs on which FMRP blocks ribosome movement, for example, *SETD2.* Indeed, an increase in SETD2 protein levels is found upon loss of FMRP. We further studied the downstream consequence of increasing SETD2 levels and found genome wide alteration of epigenetic marks that are deposited by SETD2. Furthermore, this change in epigenetic marks also affects the mRNAs produced from these genomic loci by leading to differential alternative splicing changes.

In a nutshell, upon deletion of the FXS causative gene, *Fmr1,* we find widespread defects in epigenetic marks and alternative splicing of mRNAs required for proper brain function. These findings align with those previously made in Autism patients. Understanding similarities and differences between FXS autism might aid in better detection and designing of therapeutics for intellectual disabilities.