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OMICS International is a pioneer and leading science event organizer, which publishes around 500 open access journals and conducts over 500 Medical, Clinical, Engineering, Life Sciences, Pharma scientific conferences all over the globe annually with the support of more than 1000 scientific associations and 30,000 editorial board members and 3.5 million followers to its credit.

OMICS Group has organized 500 conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.

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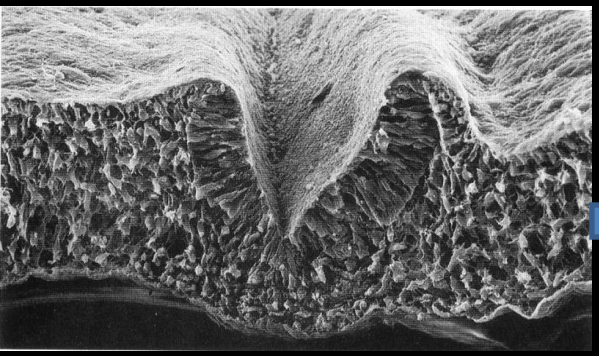
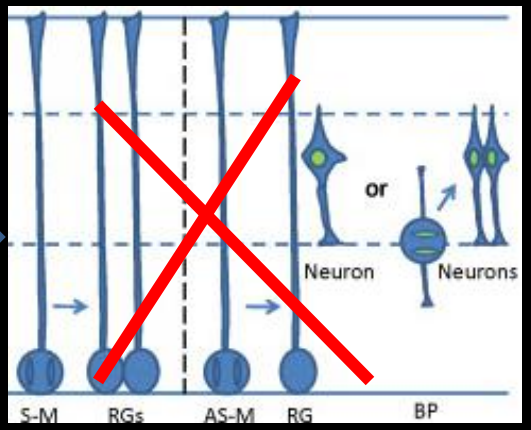
A critical role of an exon junction complex (EJC) factor in regulation of embryonic neurodevelopment and implications in neurodevelopmental disorders

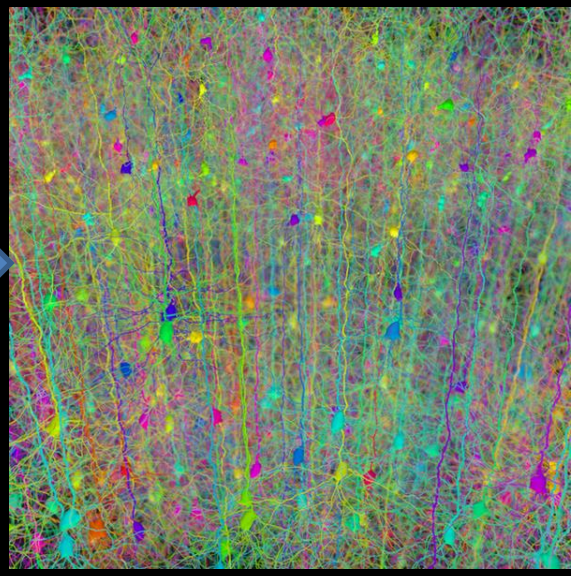
Yingwei Mao
Department of Biology
Penn State University

2015 International Conferences on Transcriptomics
July 27, 2015, Orlando, Florida

Neurodevelopment and neurological diseases



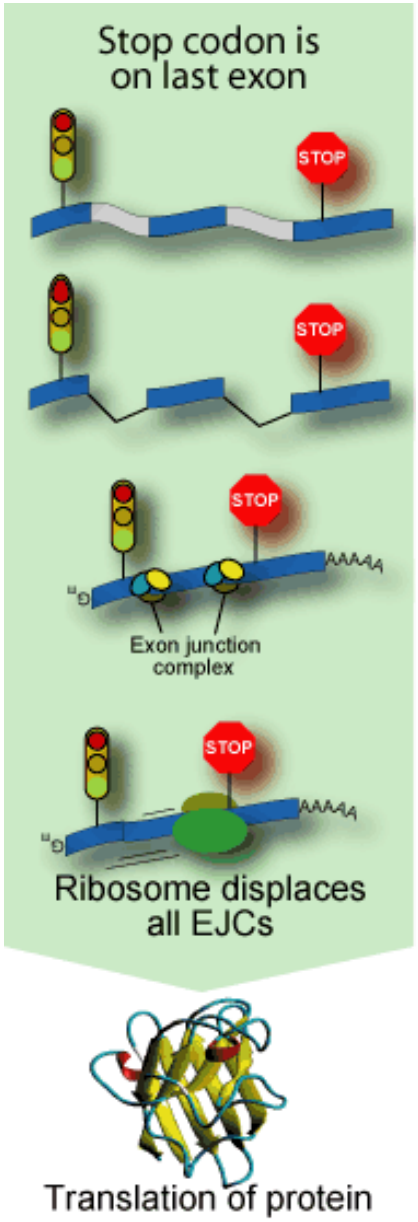




neurological disorders

Nonsense-mediated mRNA decay (NMD)

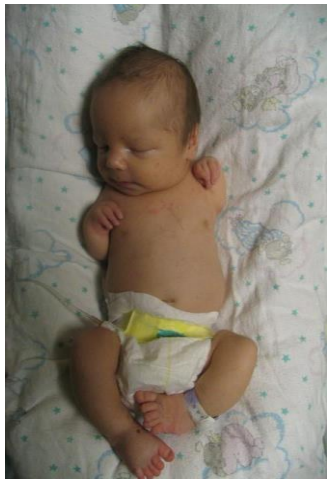
- **Nonsense mediated decay** (**NMD**) functions to detect **premature termination mutations** and prevent the expression of truncated or erroneous proteins.
- **NMD** is triggered by **exon junction complexes (EJCs)** and their associated RNPs that are deposited during pre-mRNA processing.
- The core complex includes Upf factors, **RBM8A,** eIF4AIII, MNL51/BTZ, and Magoh.



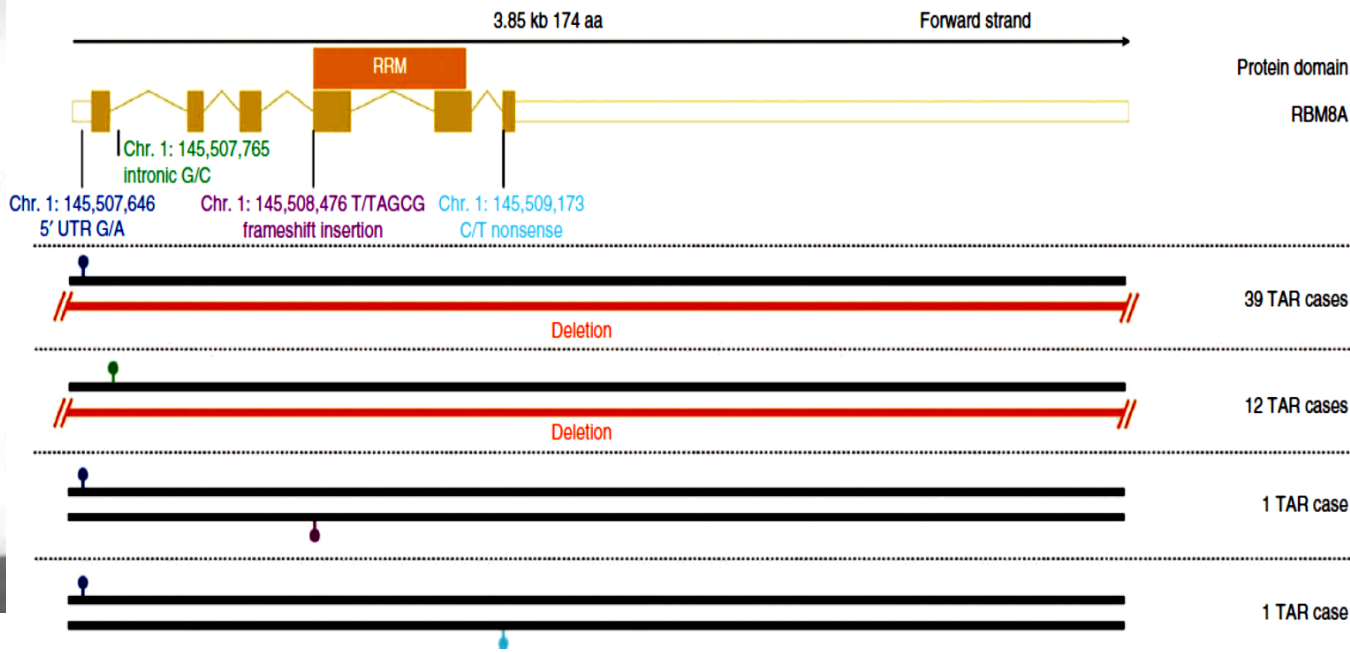
PNAS, 100:189, *2003*

RBM8A is in 1q21.1 associated with schizophrenia and TAR syndrome

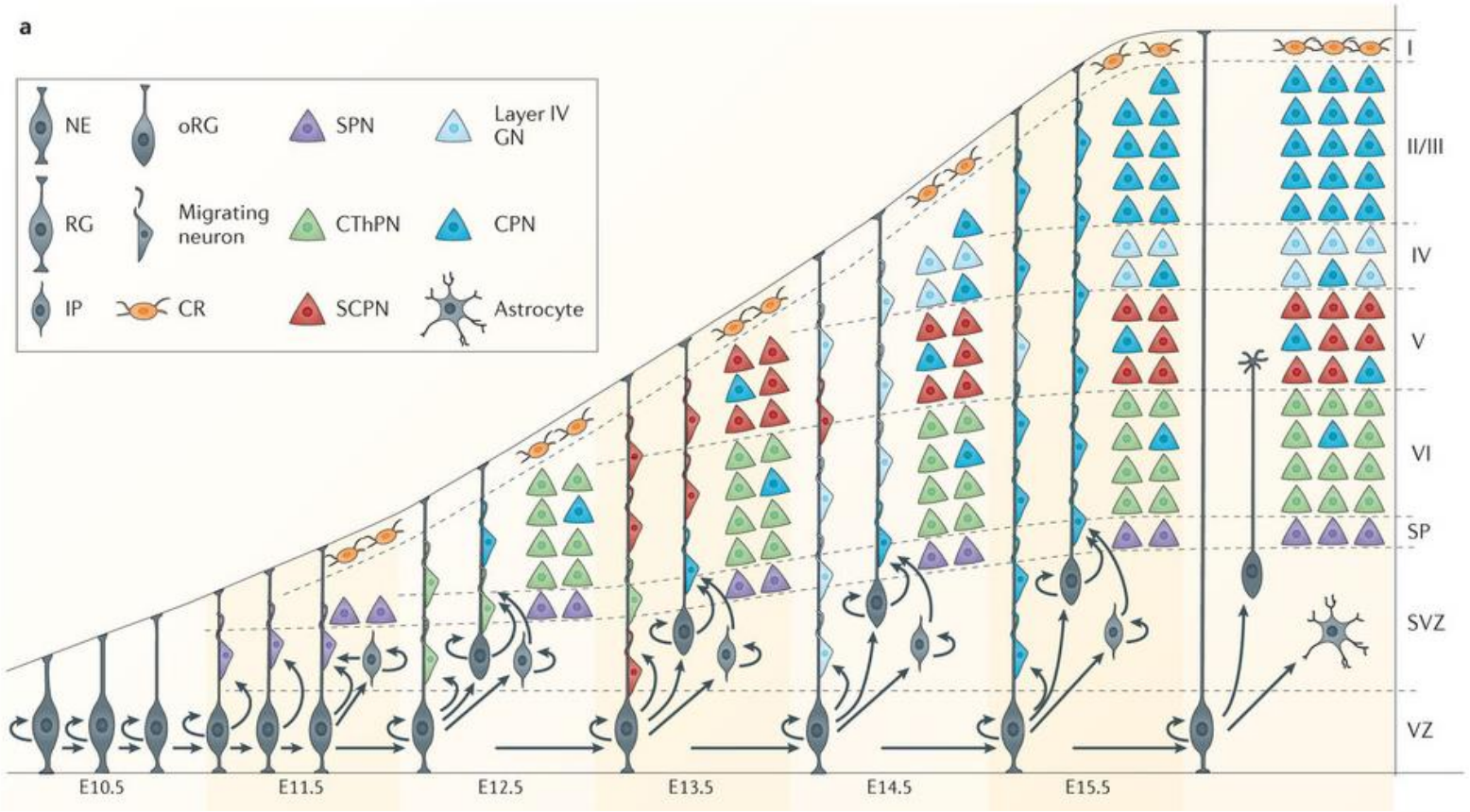
- Mutation in **RBM8a** is the cause of **Thrombocytopenia and Absent Radius syndrome (TAR)** syndrome (Nature Genetics. 2012, 44:435),
- TAR patients associate with lower limb anomalies, milk intolerance, renal anomalies, cardiac anomalies, mental retardation, abnormal brain development and psychosis (J Med Genet 2002,39:876).



TAR syndrome



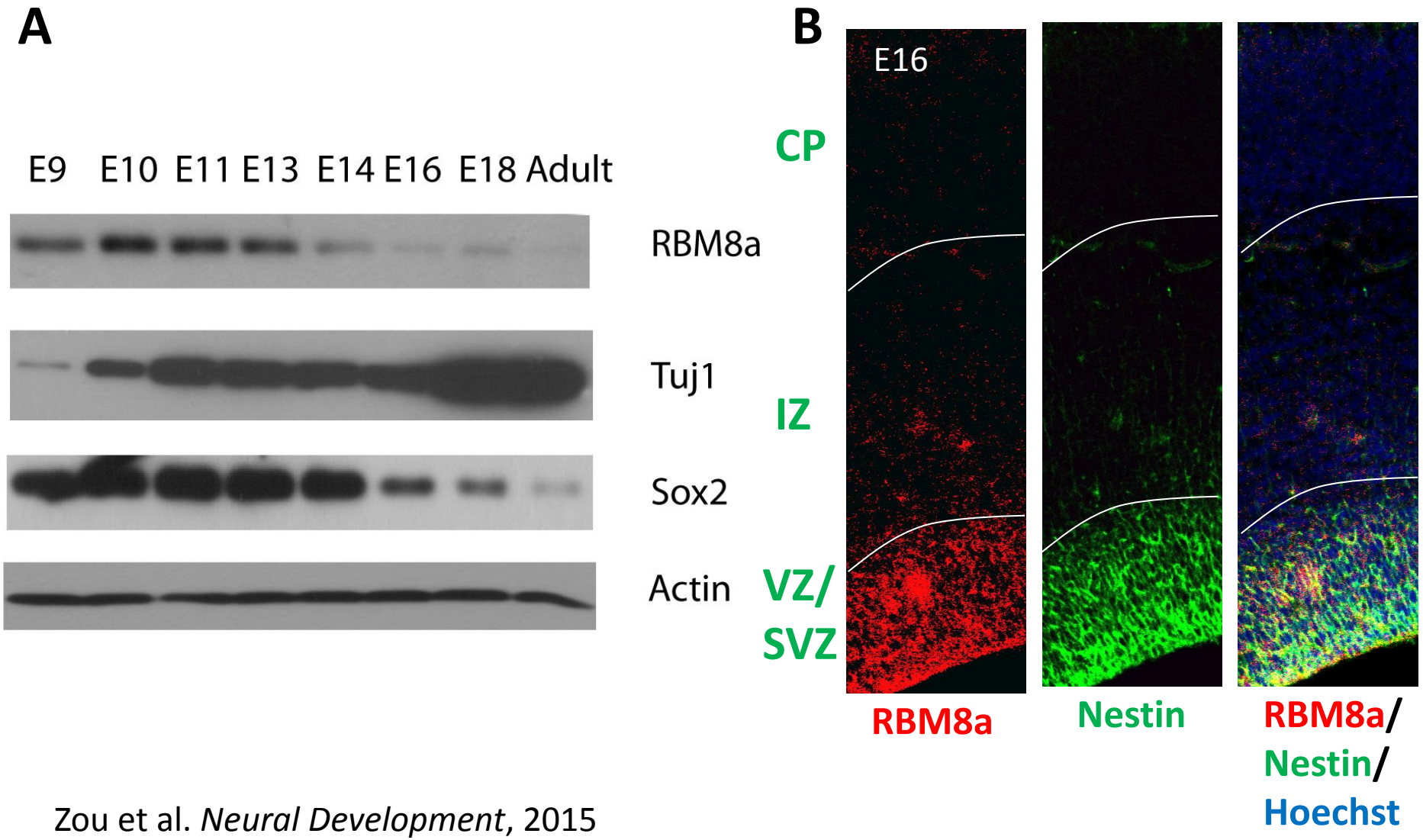
Neocortical neurogenesis and neuronal migration



Inside-out

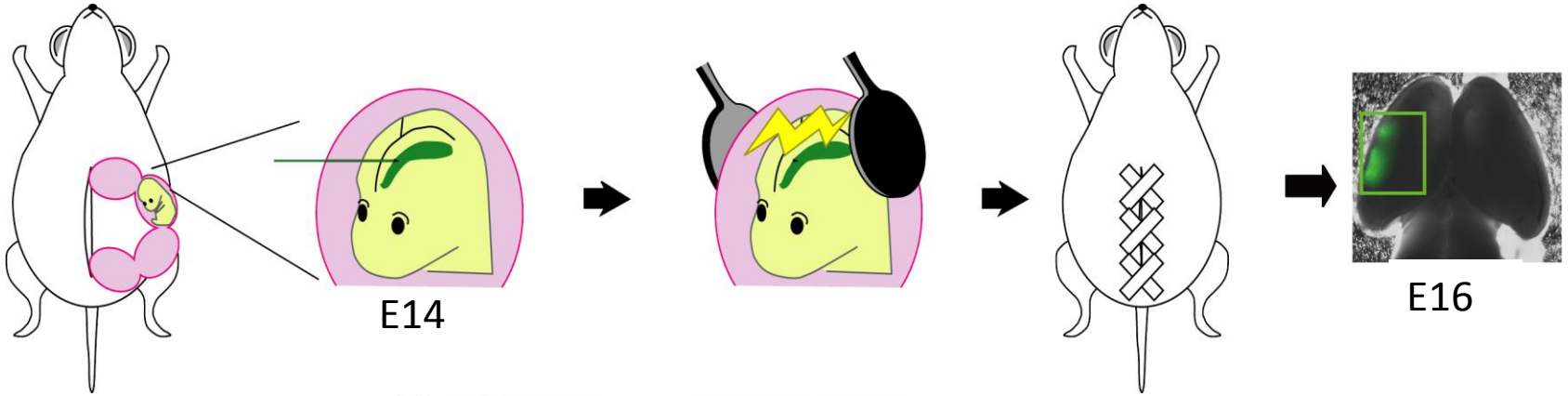
(Greig, Woodworth et al. 2013)

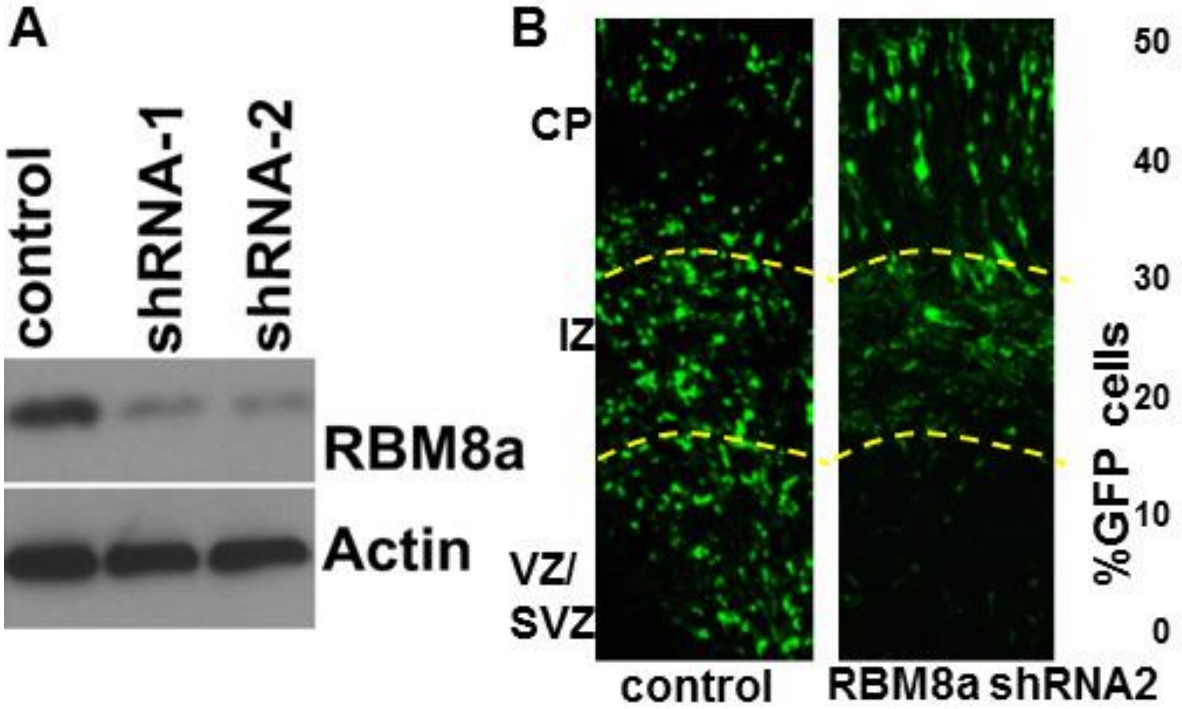
RBM8a expression during neurodevelopment



Zou et al. *Neural Development*, 2015

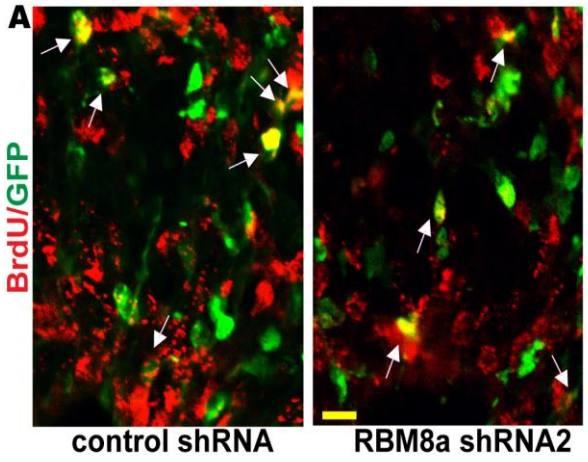
Knockdown of RBM8a increases neuronal migration

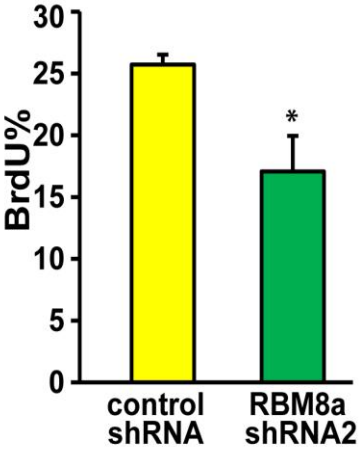


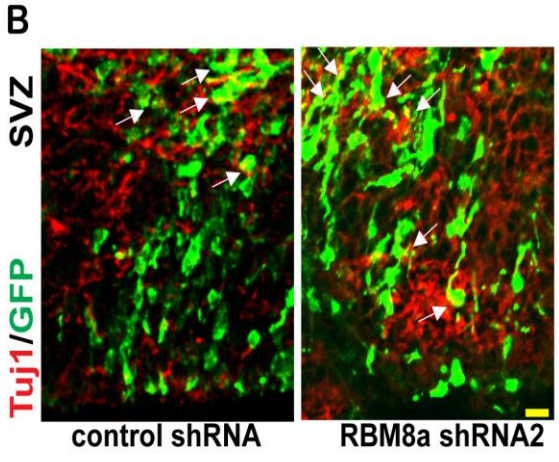


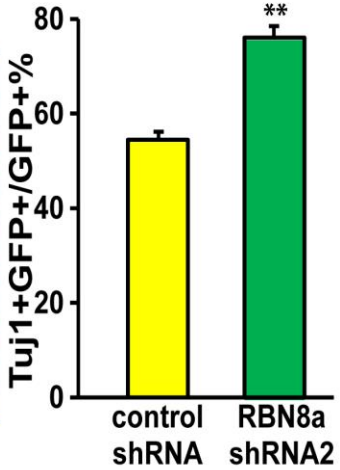
Zou et al. *Neural Development*, 2015

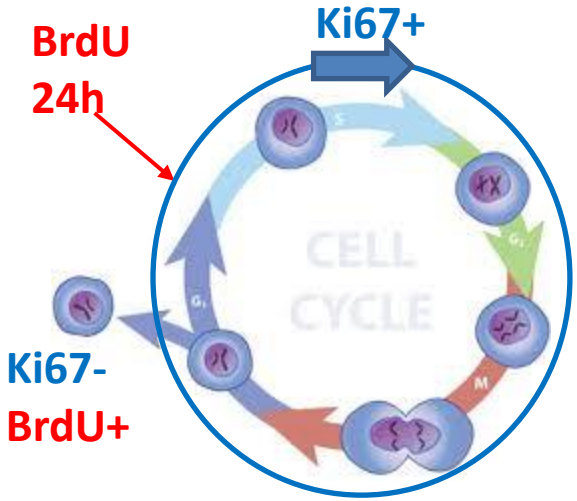
Knockdown of RBM8a decreases progenitor proliferation





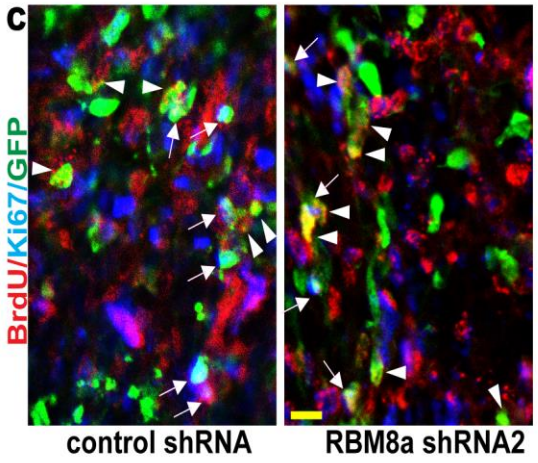


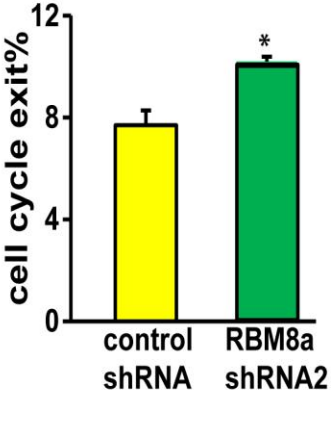




Cell cycle exit index =

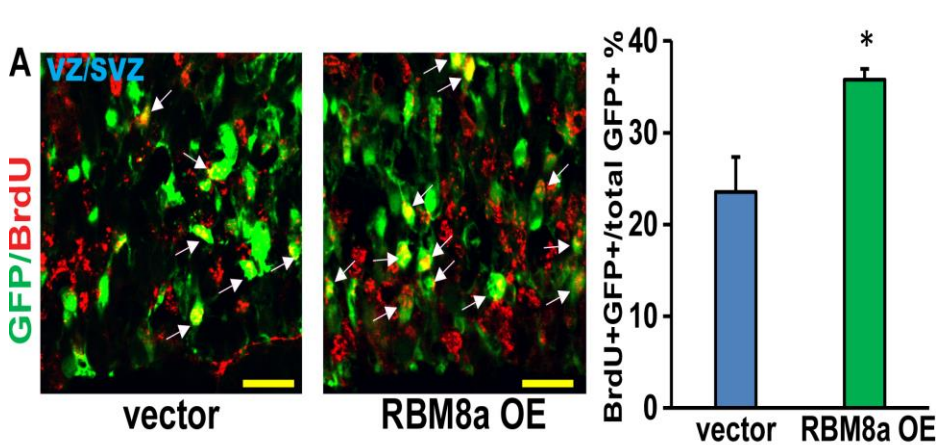
$$\frac{\text{GFP+ BrdU+ Ki67-}}{\text{GFP+ BrdU+}}$$

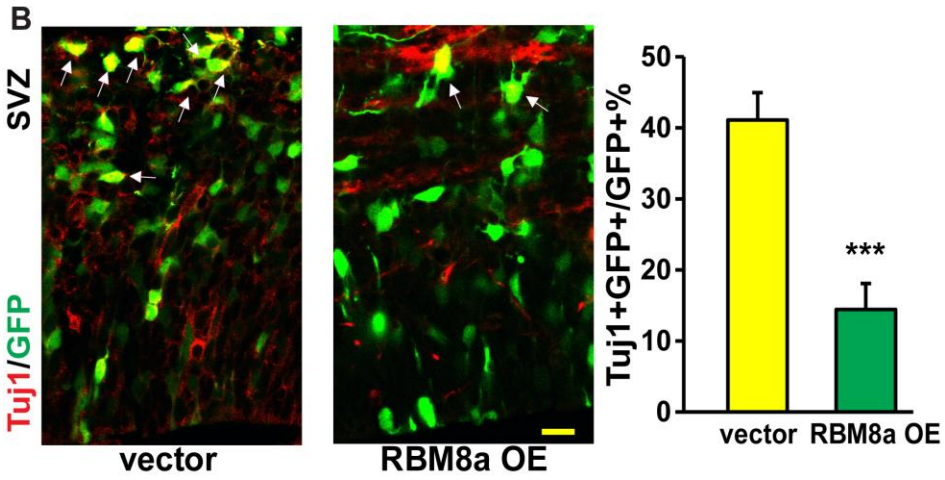


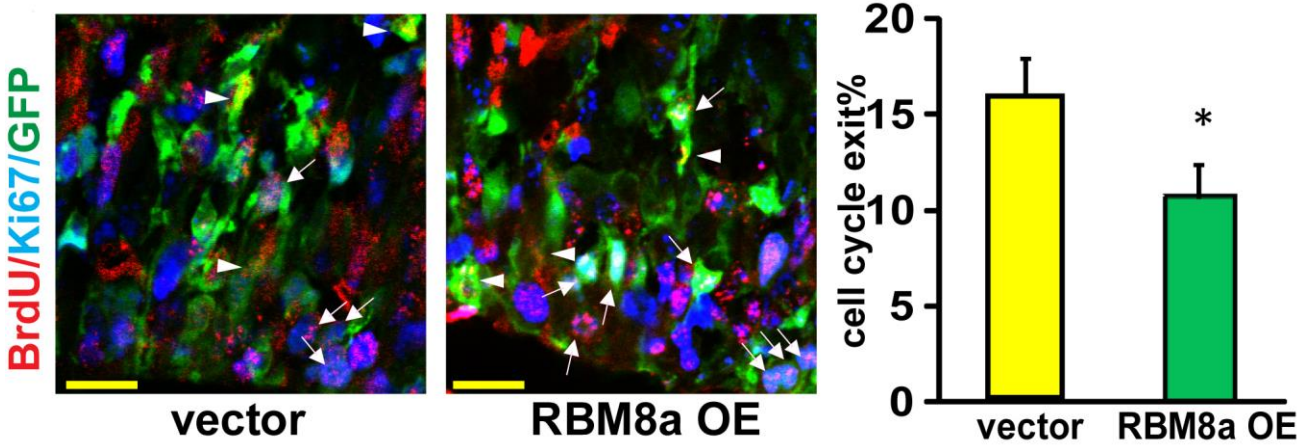


Zou et al. *Neural Development*, 2015

Overexpression of RBM8a stimulates progenitor proliferation

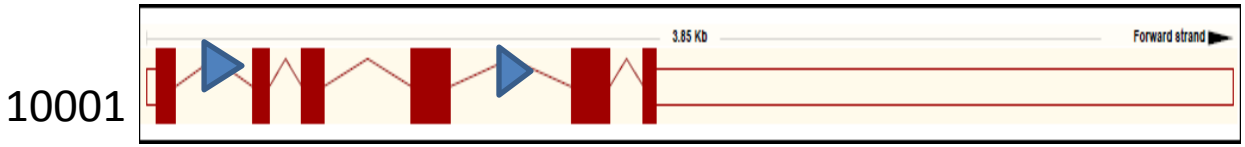


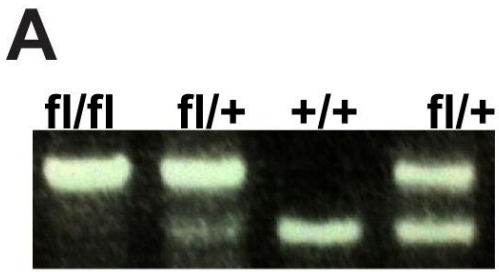


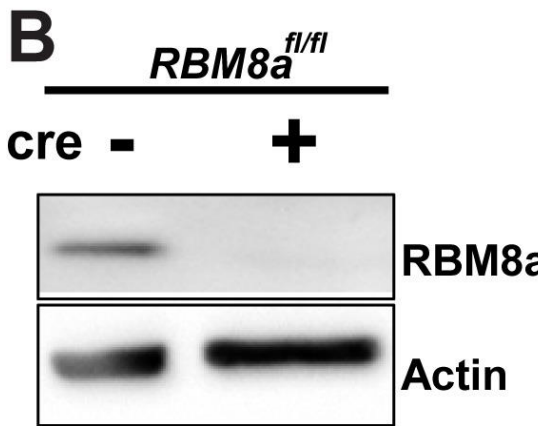


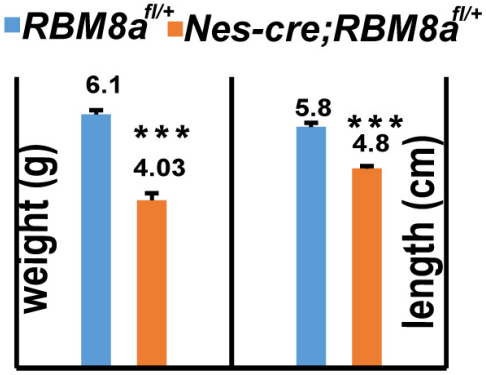
Zou et al. *Neural Development*, 2015

RBM8a conditional knockout



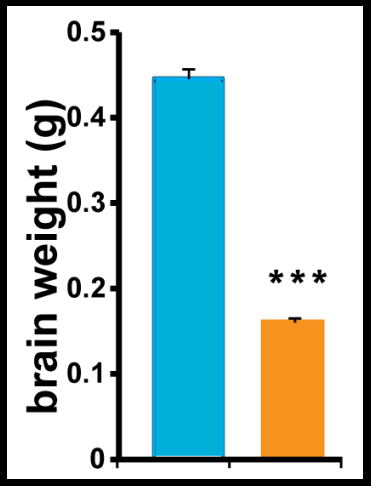


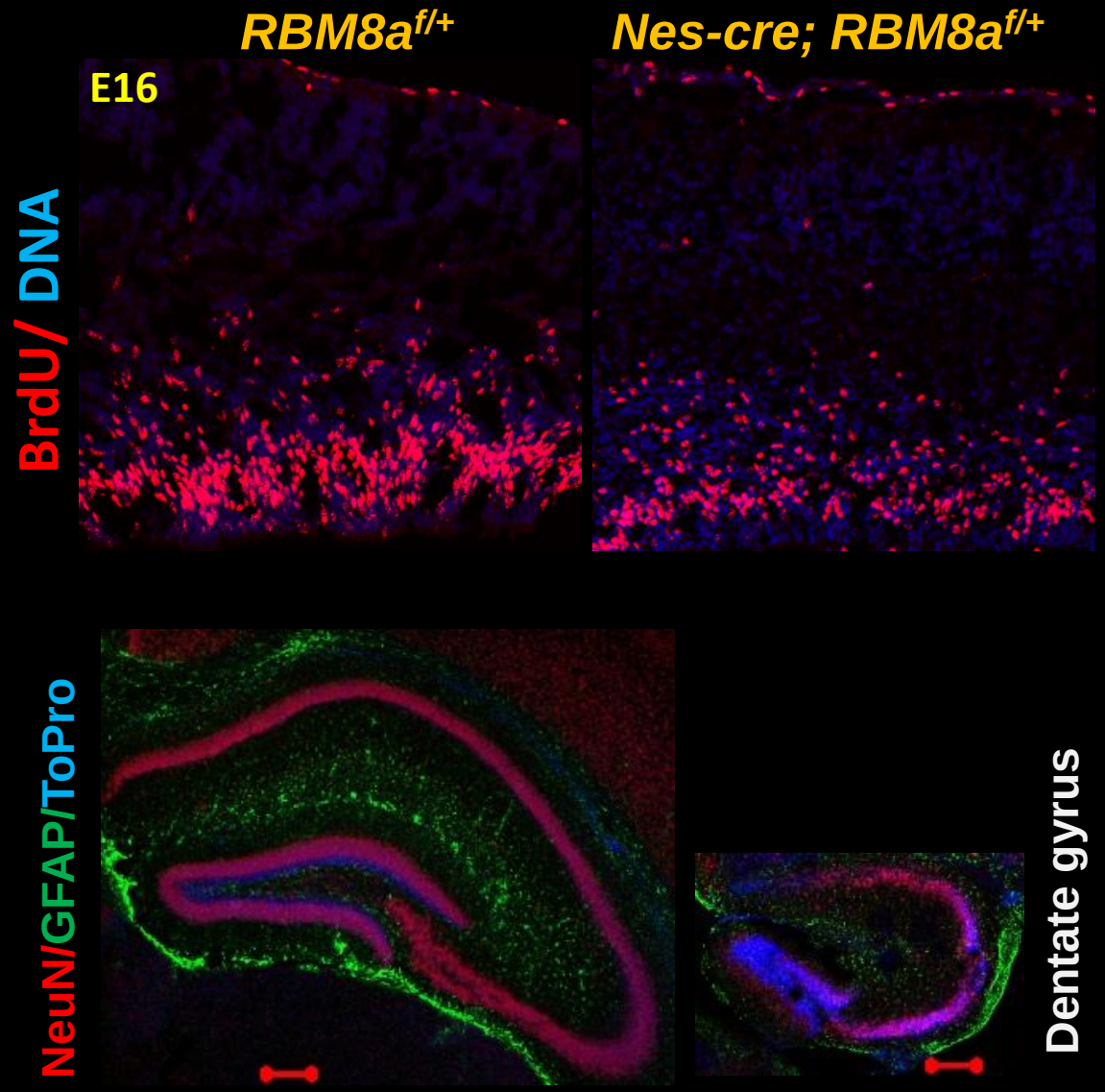




Colleen McSweeney

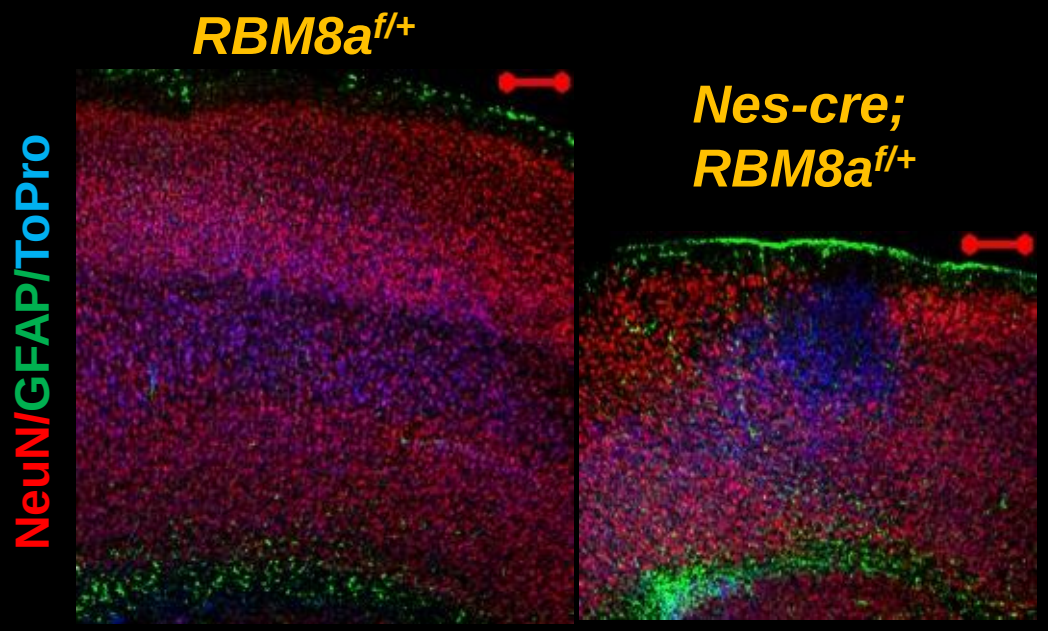
The brain deficits of RBM8a cKO mice

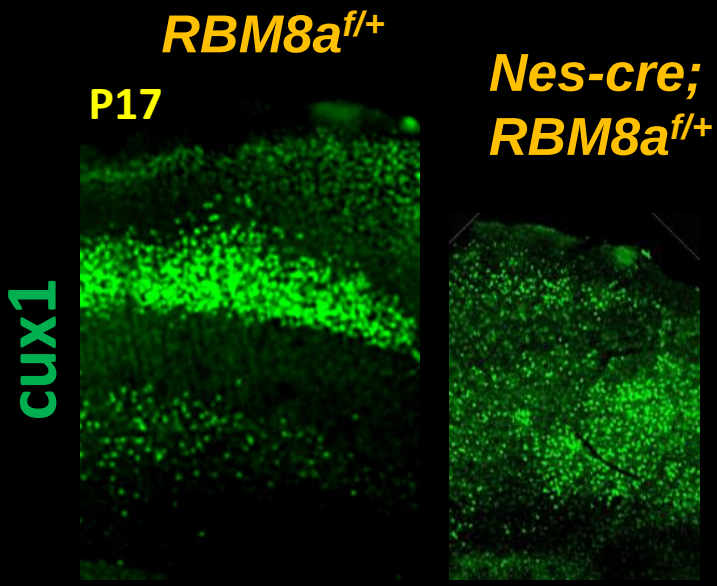




Colleen McSweeney

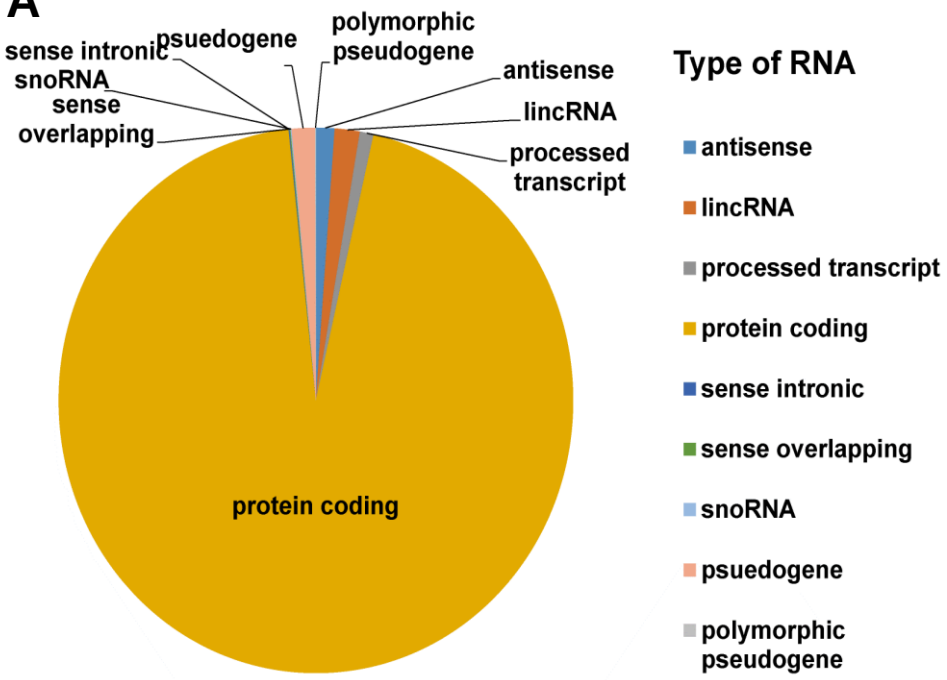
Neuronal layer defects in RBM8a cKO brain





RBM8a downstream genes are enriched for risks of neurological diseases

A

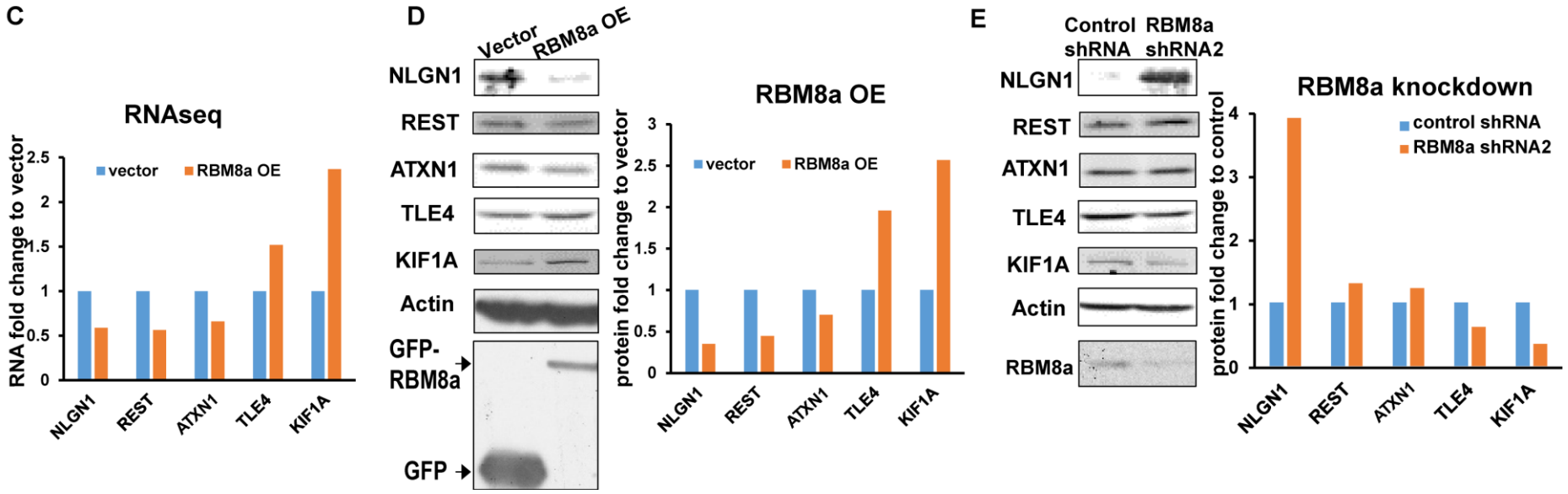


B

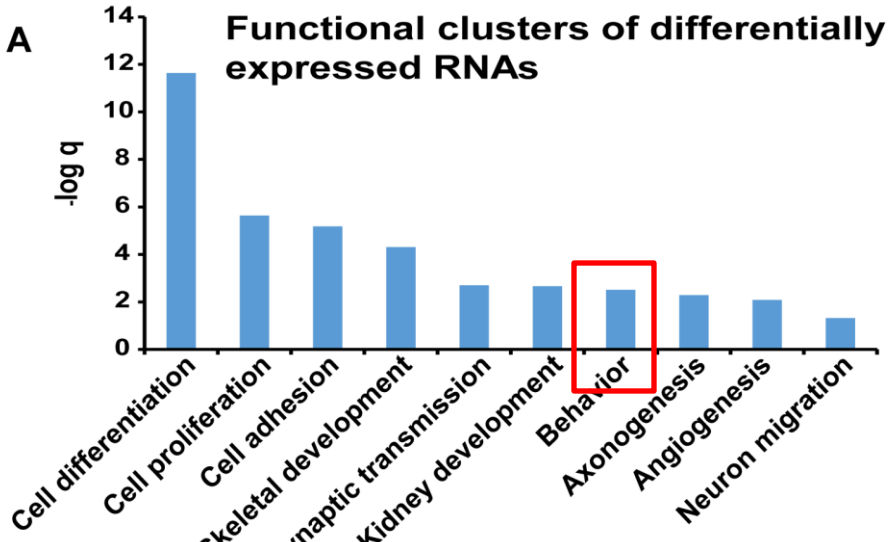
Disease	*p*-value
ASD	2.53×10^{-11}
SCZ	1.35×10^{-5}
AD	4.35×10^{-4}
ID	8.17×10^{-3}
Crohn's Disease	0.736

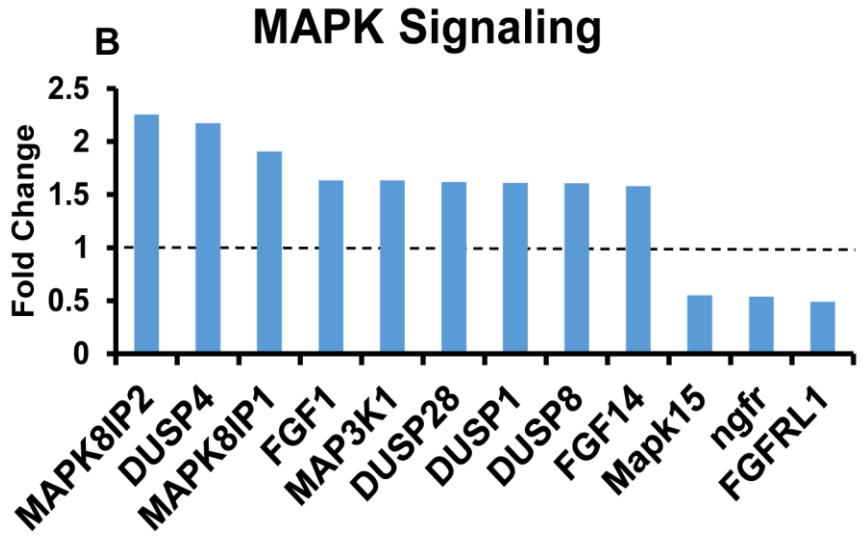
Zou et al. *Neural Development*, 2015

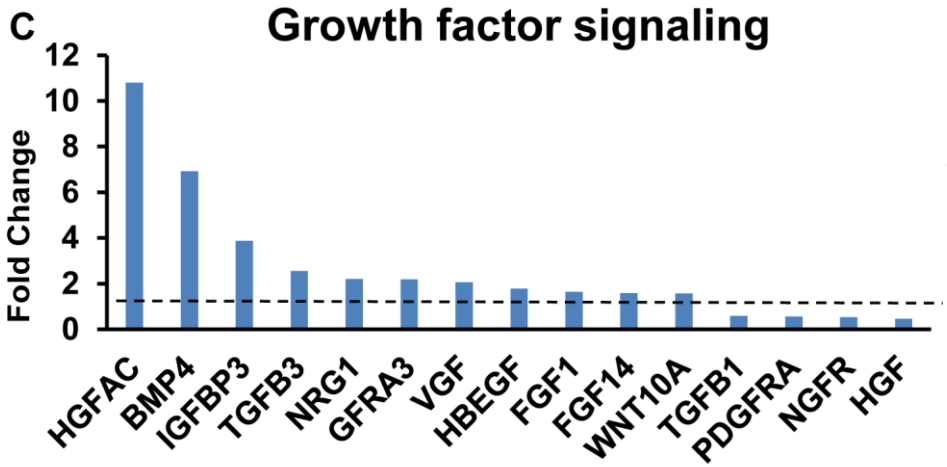
Confirmation of RNAseq data at protein level

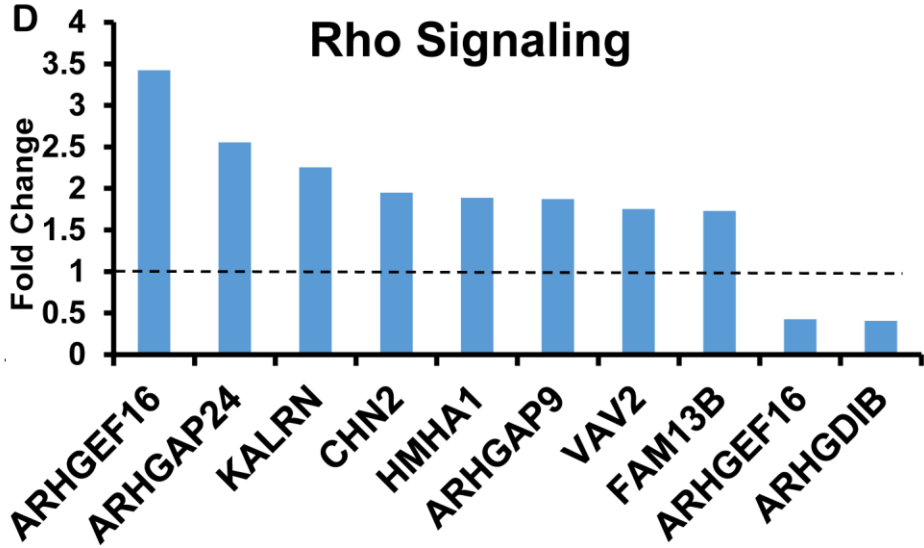


Pathways of RBM8a downstream genes





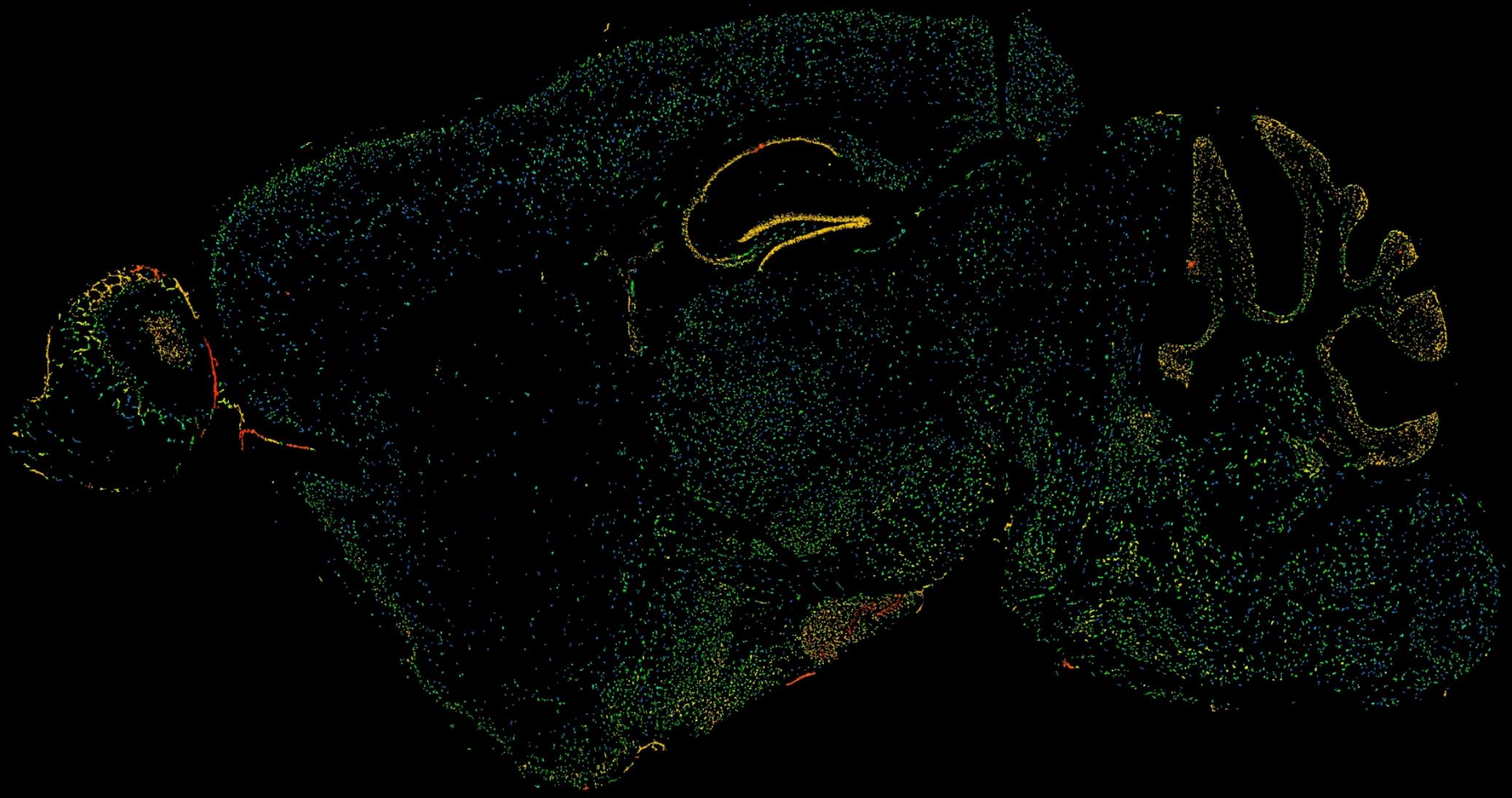




Zou et al. *Neural Development*, 2015

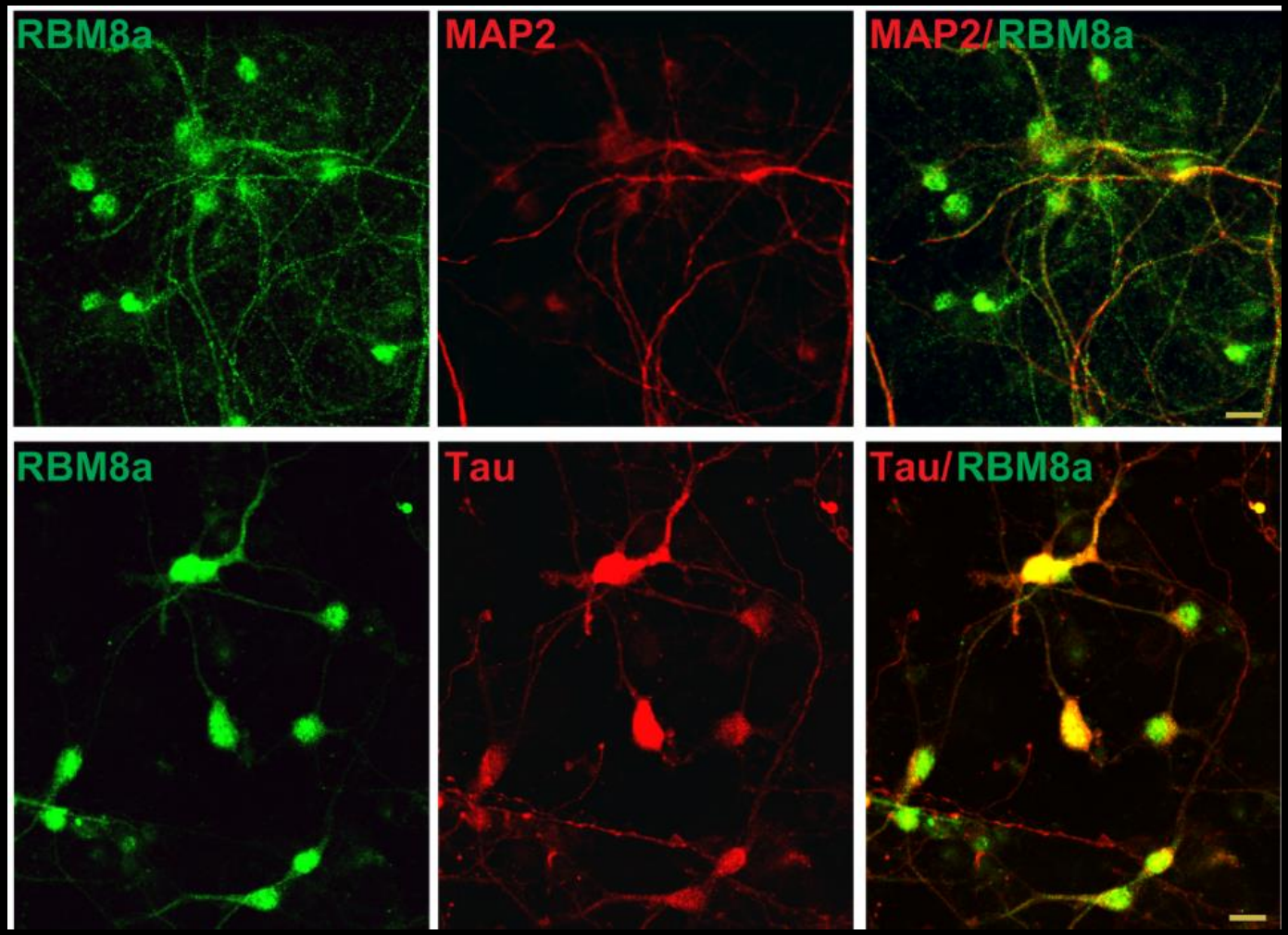
Functions of RBM8a in behaviors

RBM8A expression in adult brain



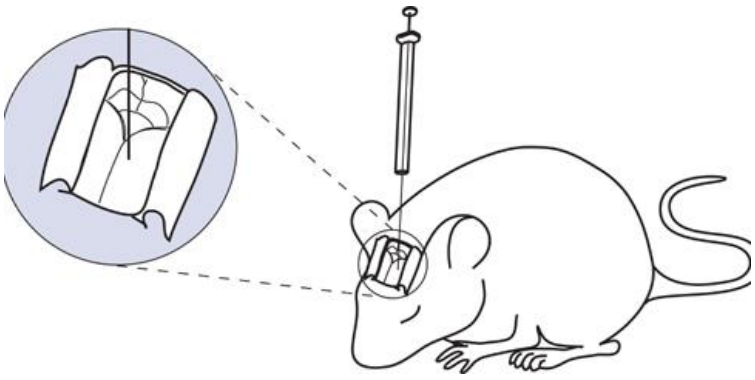
Allen Brain atlas

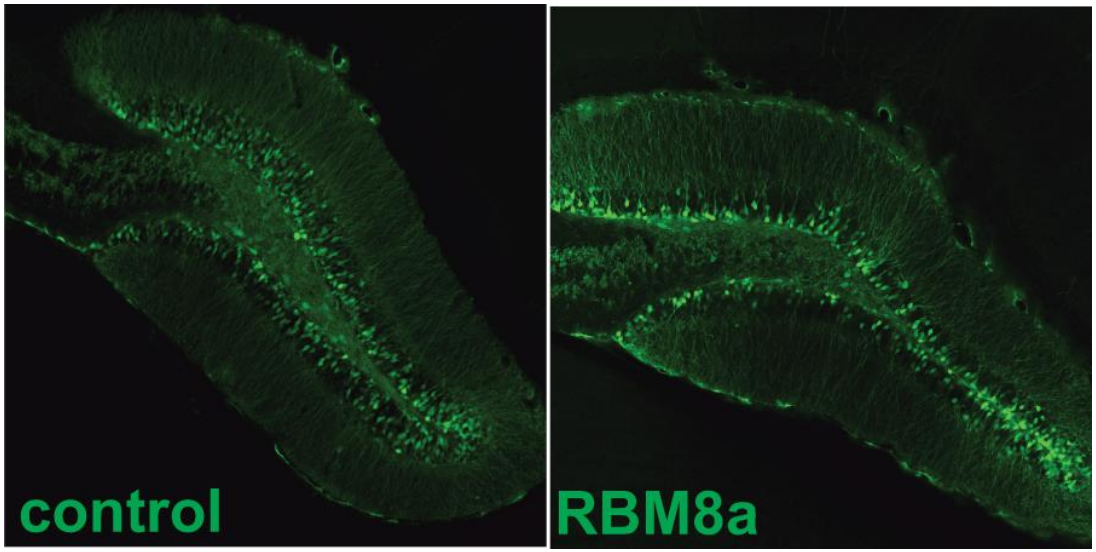
RBM8a is localized in axons and dendrites



(Alachkar et. al. *Current Molecular Medicine*, 2013)

Lentiviral stereotaxic injection

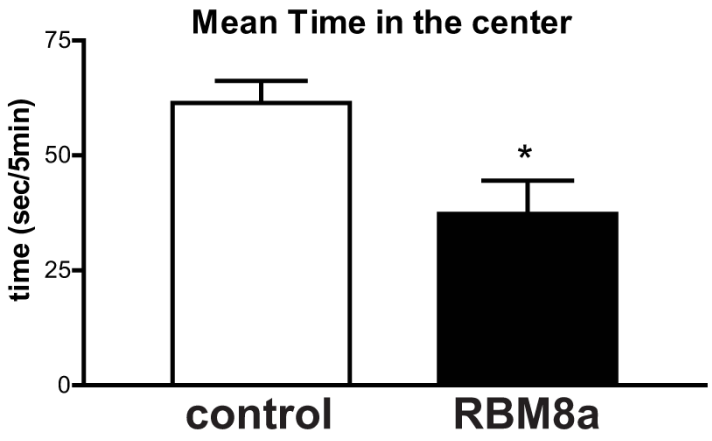




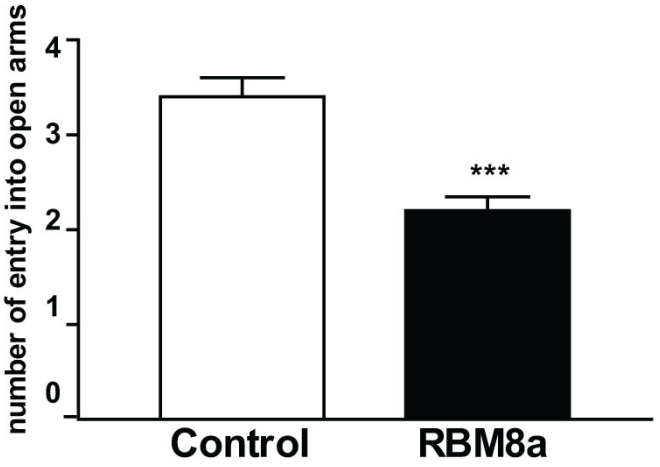
(Alachkar et. al. *Current Molecular Medicine*, 2013)

Mice expressing RBM8a show increased anxious behaviors

- Open field test



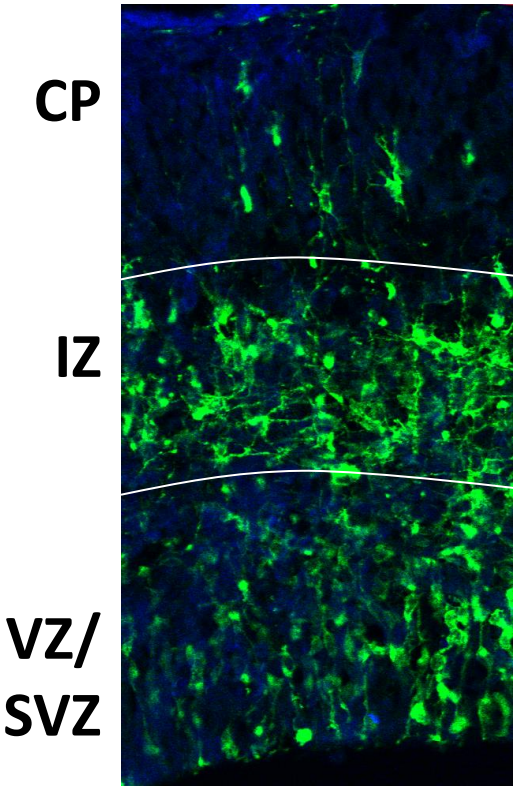
- Elevated plus maze



(Alachkar et. al. *Current Molecular Medicine*, 2013)

Summary

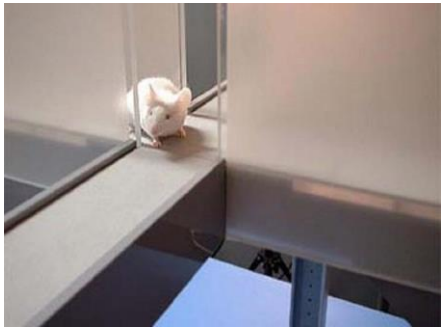
- **Embryonic brain**



Neuronal maturation

RBM8a

NSC proliferation



behavior

Acknowledgements

Mao lab

Colleen McSweeney,
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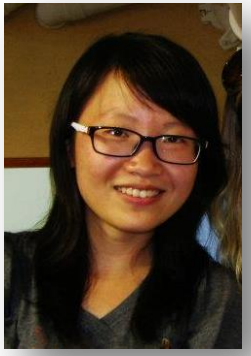
Amal Alachkar
Visiting scholar

Fengping Dong MS
Graduate Student

Donghua Zou MD
Visiting Scholar



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Dazhi Deng MD
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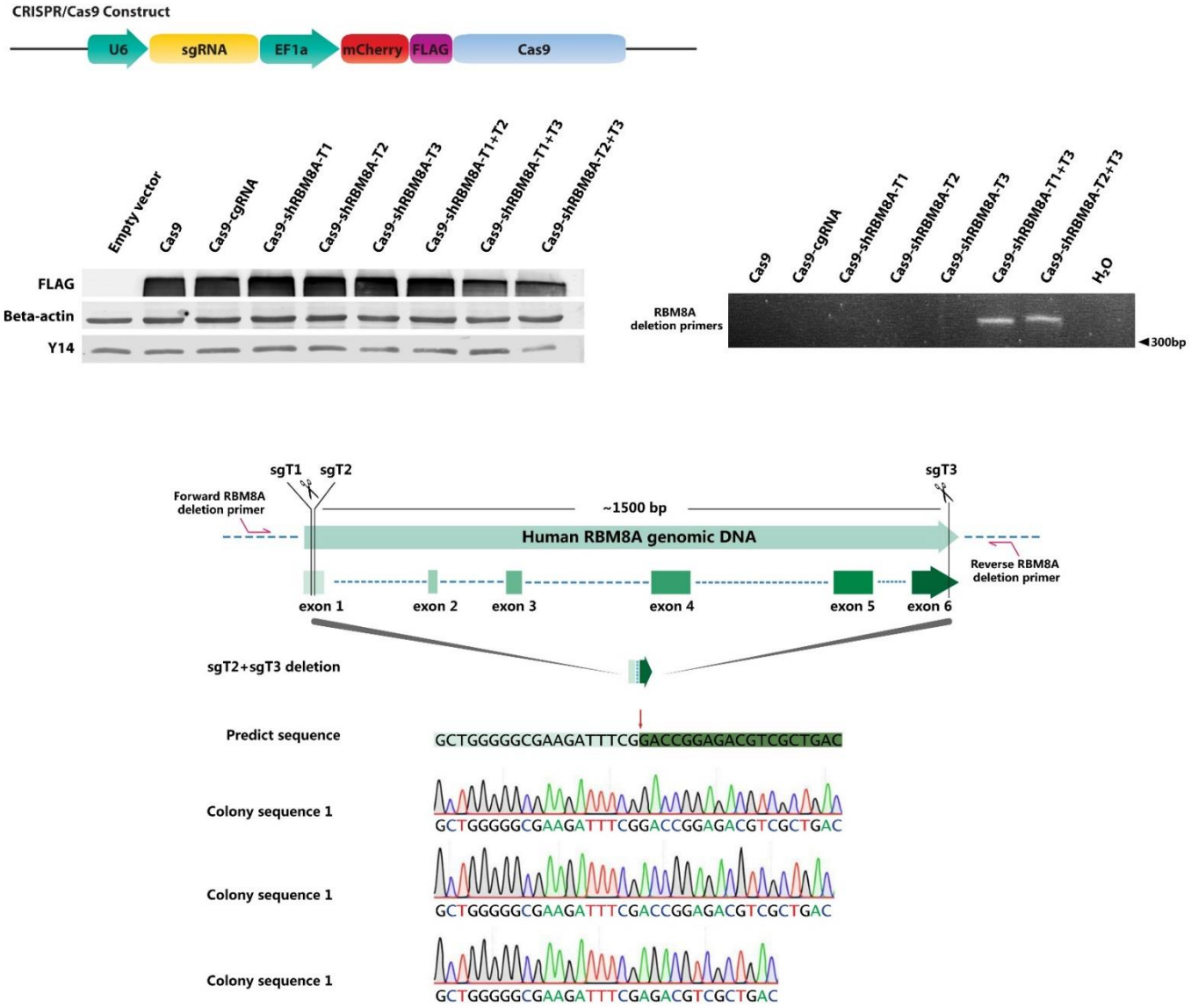
Dr. Gong Chen, PSU
Dr. Benhard Luscher, PSU
Dr. Yongshen Shi, UC Irvine
Dr. Jizhong Zou, NIH

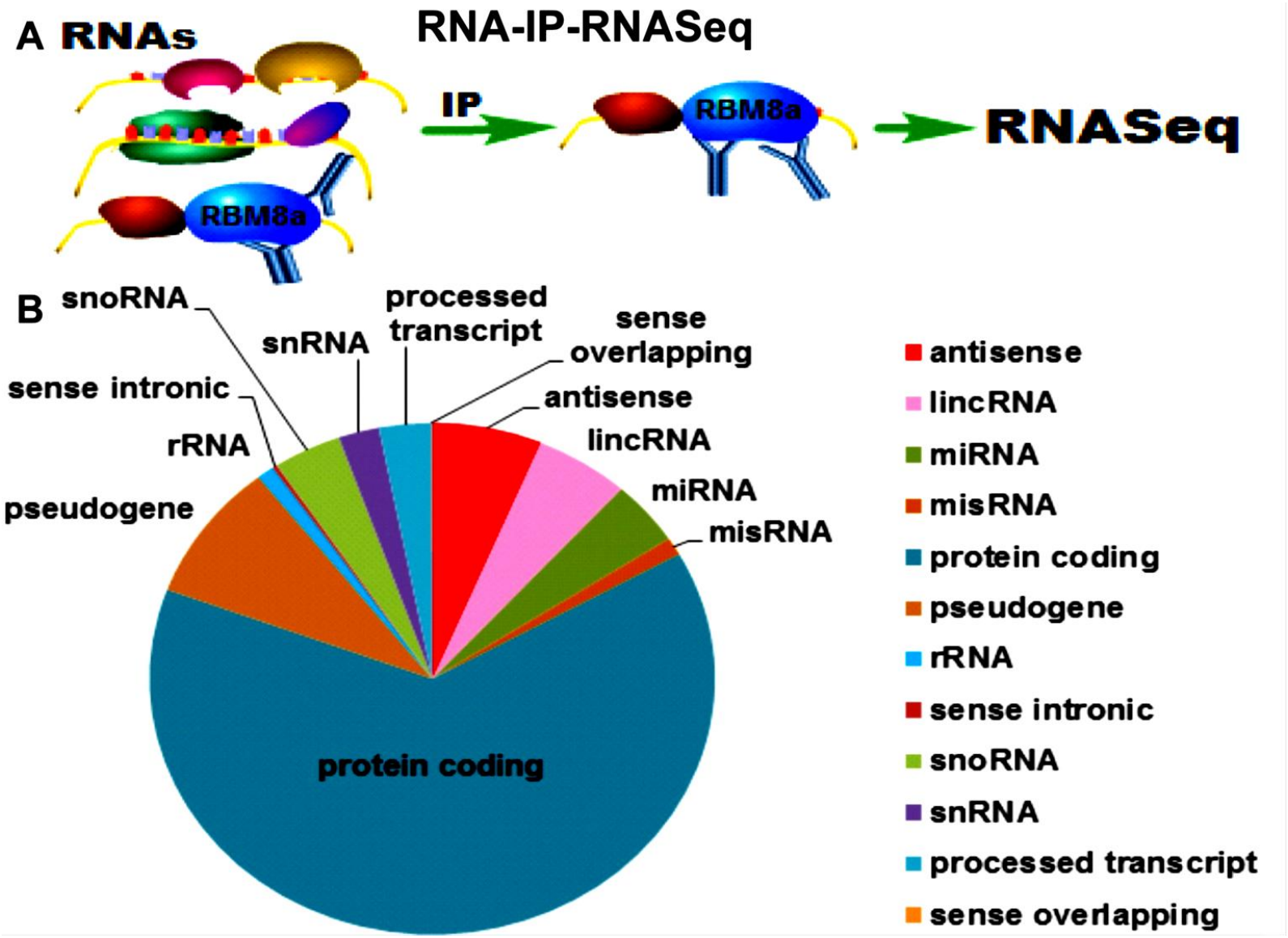
Funding: AHA, NARSAD

Genome editing on RBM8a



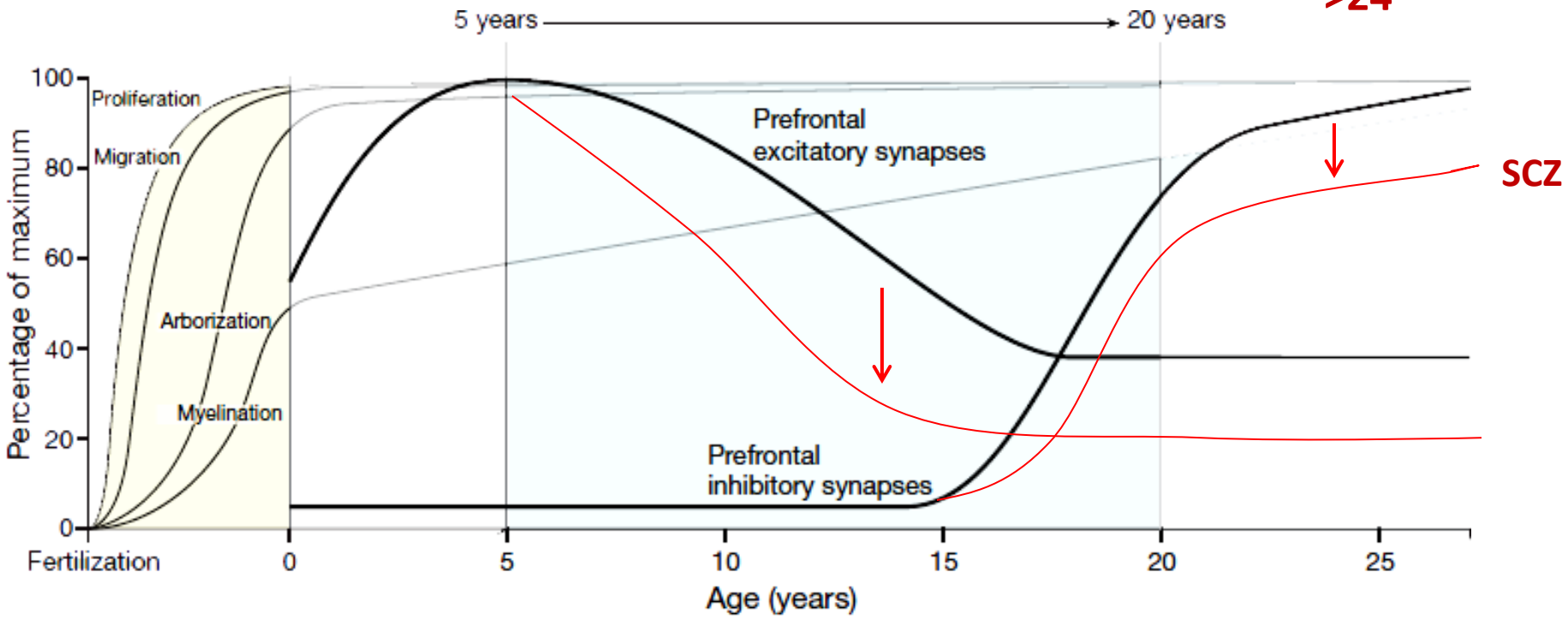
Fengping Dong

RNA-immunoprecipitation analysis



Possibility for novel therapy/early intervention

risk **<12** | **prodrome** **12-16** | **psychosis** **16-24** | **Chronic disability >24**



Early intervention /prevention

Nature (2010), 486:187-193

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