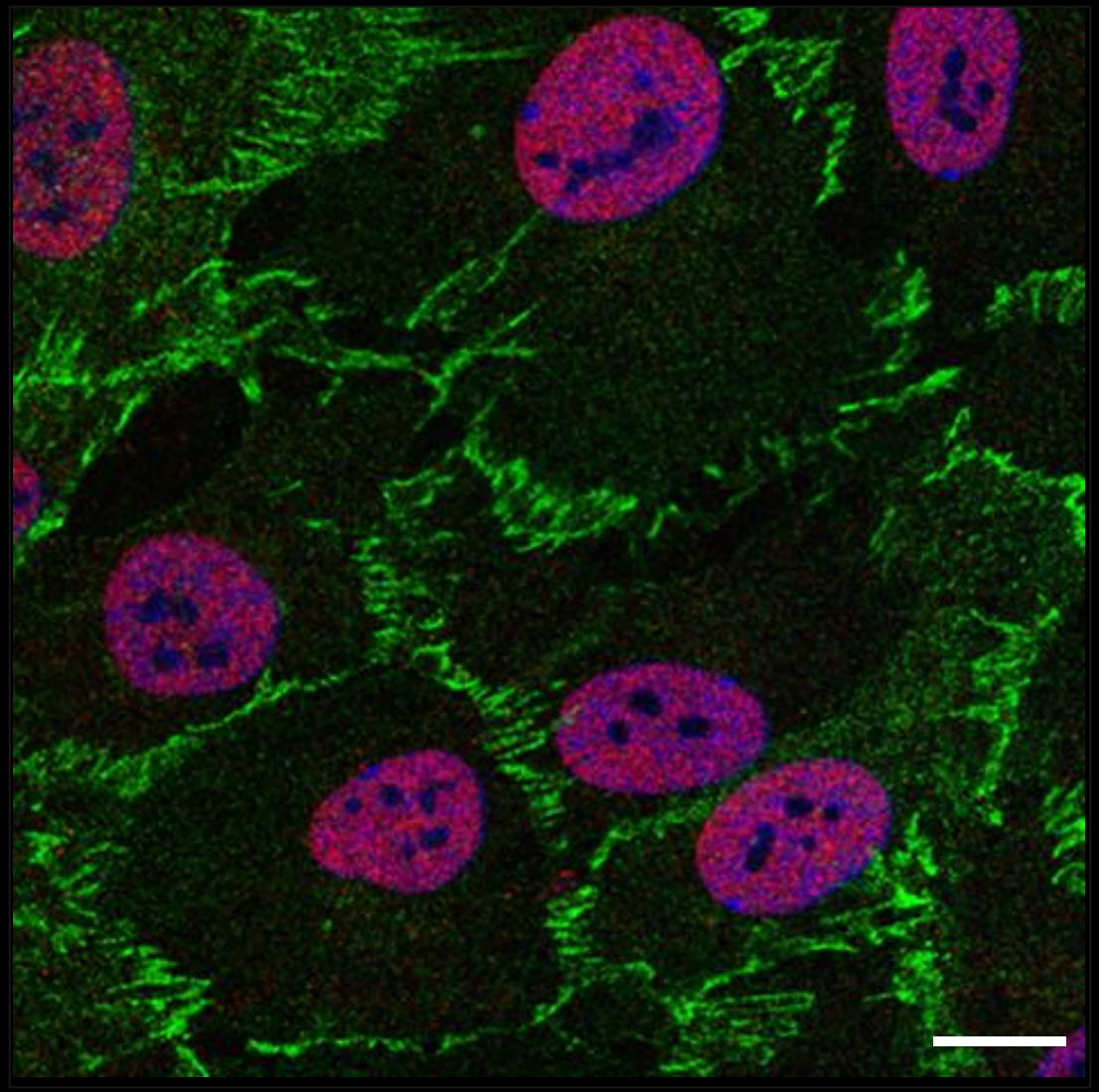


Cell consequences of loss of function of the epigenetic factor EHMT1

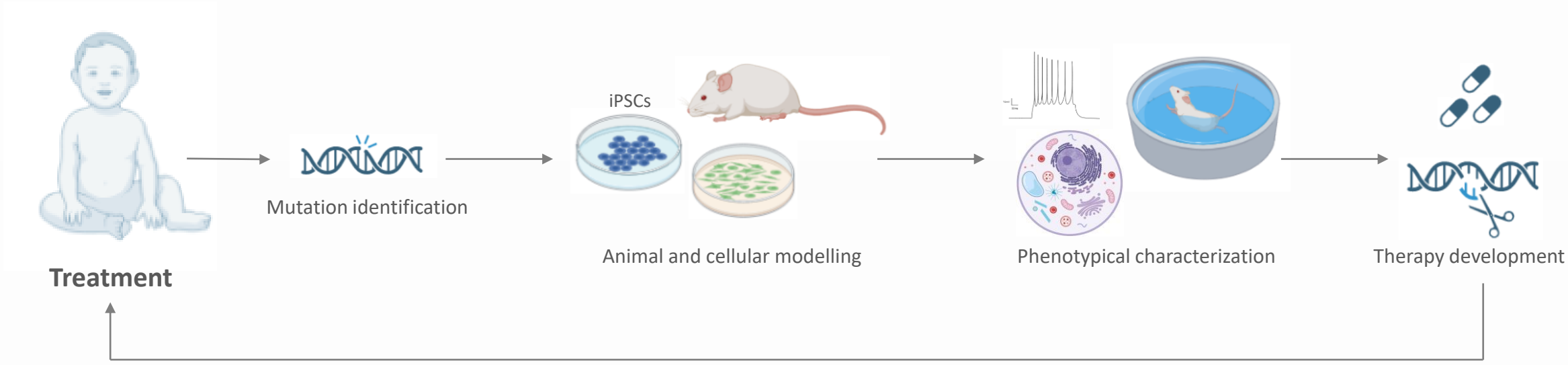
Sabrina Rivero Canalejo

Normal and Pathological Cytology and Histology Department,

University of Seville, Spain

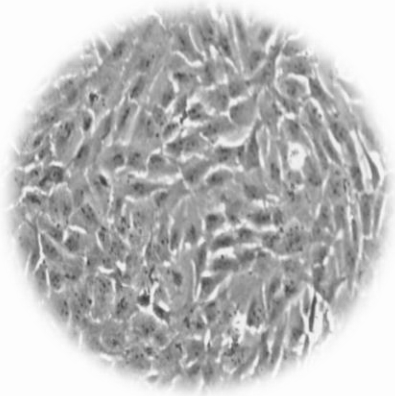
Andalusian Molecular Biology and Regenerative Medicine Centre, Seville, Spain

“From identification of NDD-related genes to therapy”



Adapted from Iwase, S., et al. *The Journal of Neuroscience*, 2017

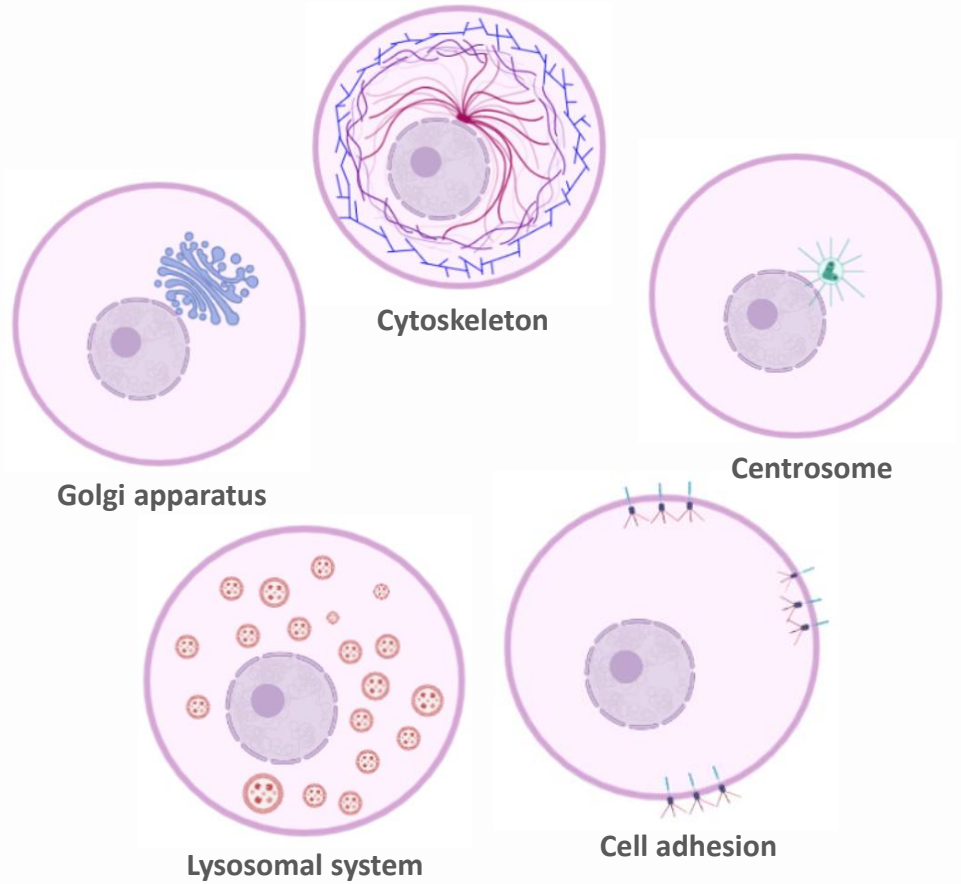
Studying EHMT1 function



RPE1 cells

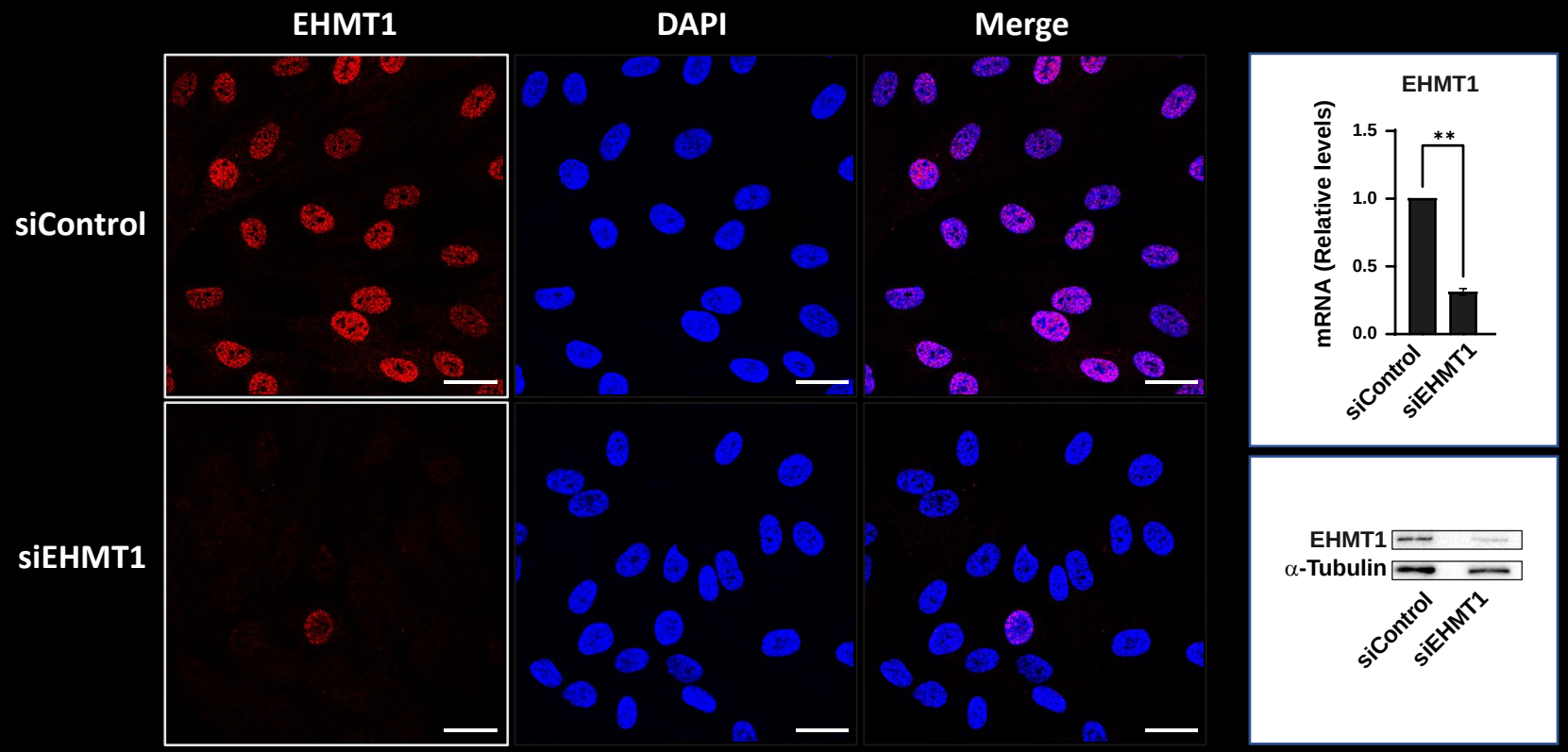
Non-tumor human epithelial cell line

EHMT1 siRNA



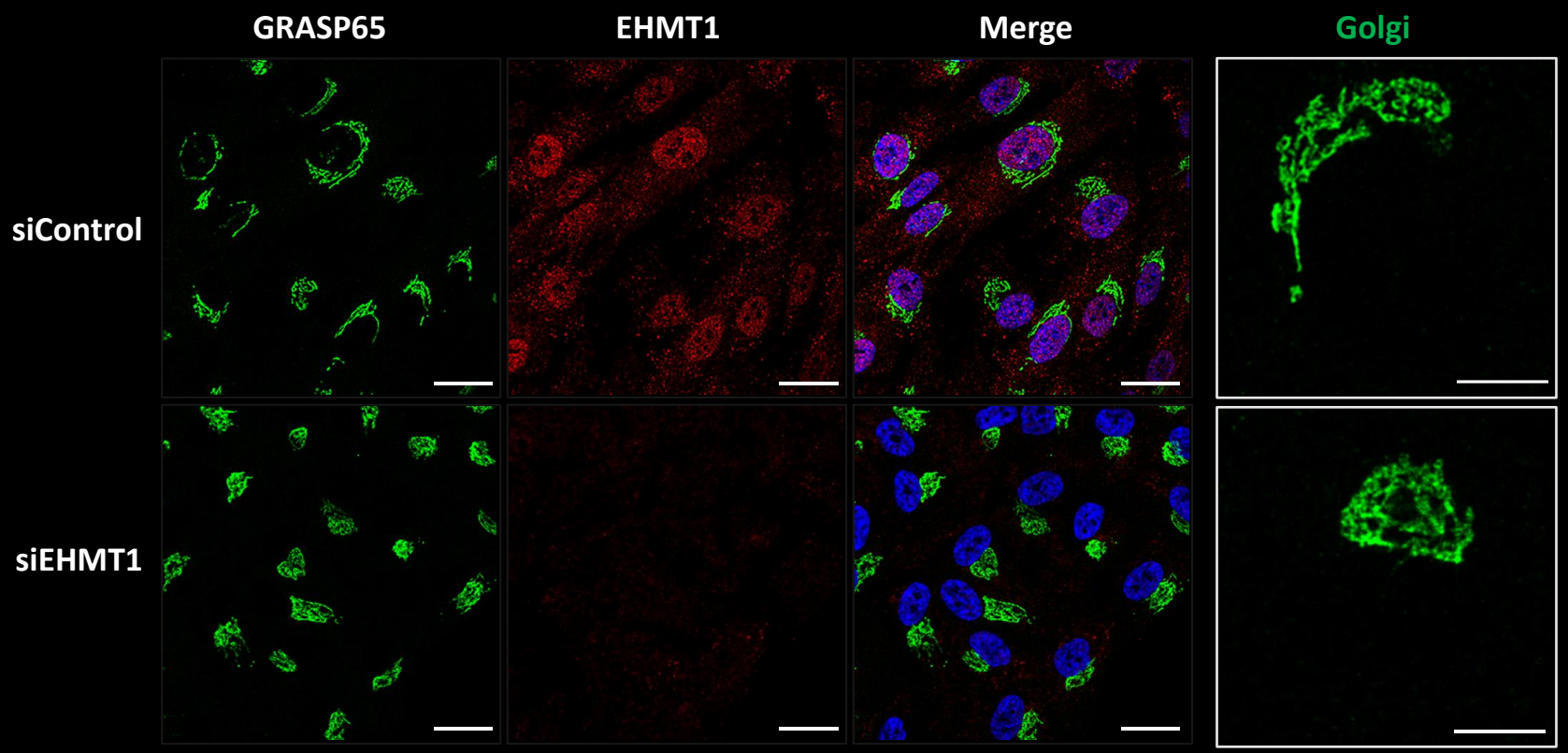
Immunofluorescence imaging analysis

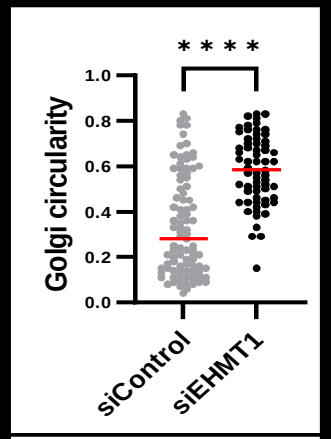
Studying EHMT1 function using siRNAs

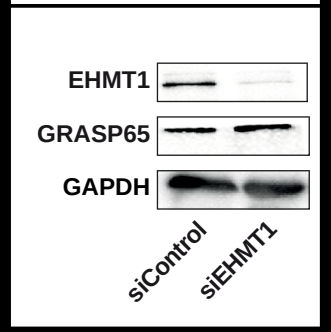


Iglesias-Ortega, L., et al. *Cellular Signalling*, 2023

EHMT1 in Golgi apparatus morphology



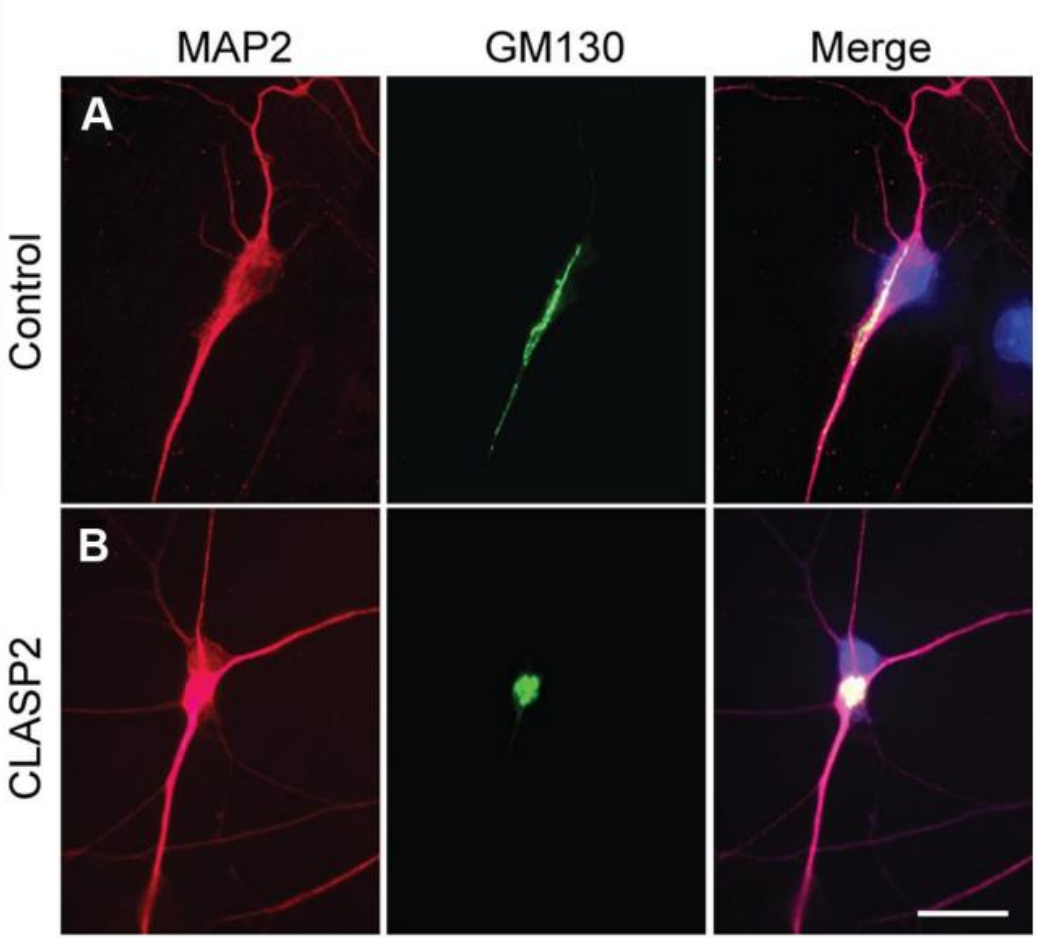


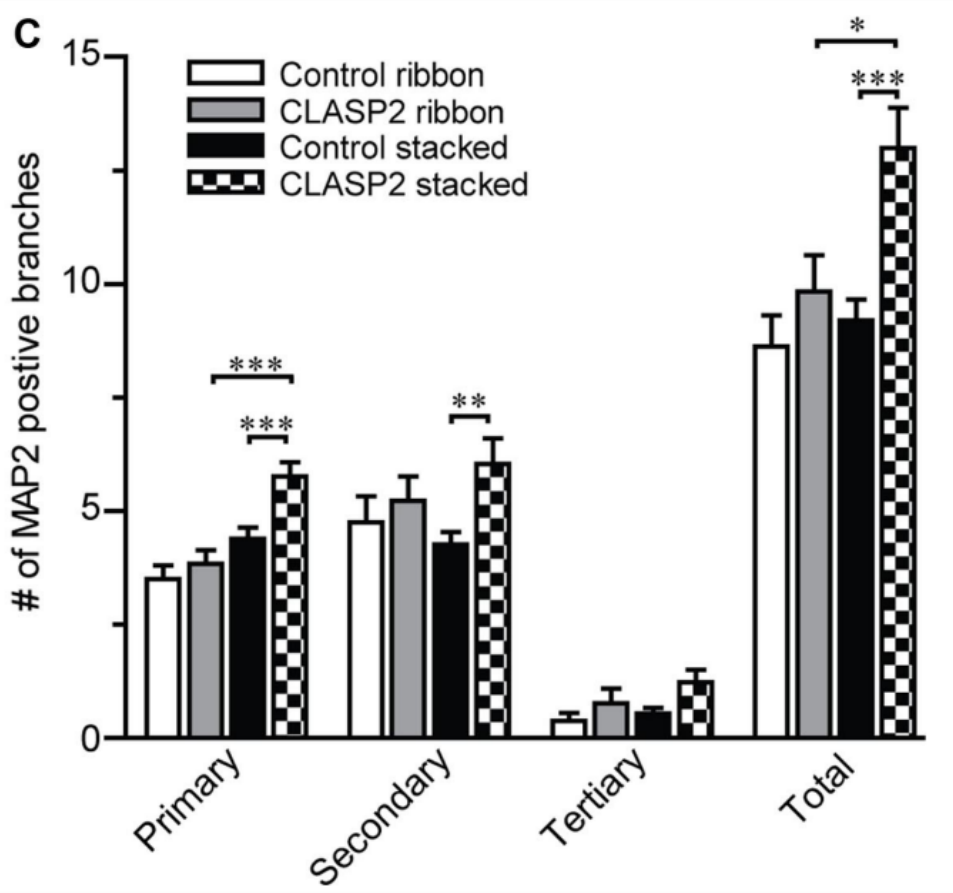


Iglesias-Ortega, L., et al. *Cellular Signalling*, 2023

Microtubule Plus-End Tracking Protein CLASP2 Regulates Neuronal Polarity and Synaptic Function

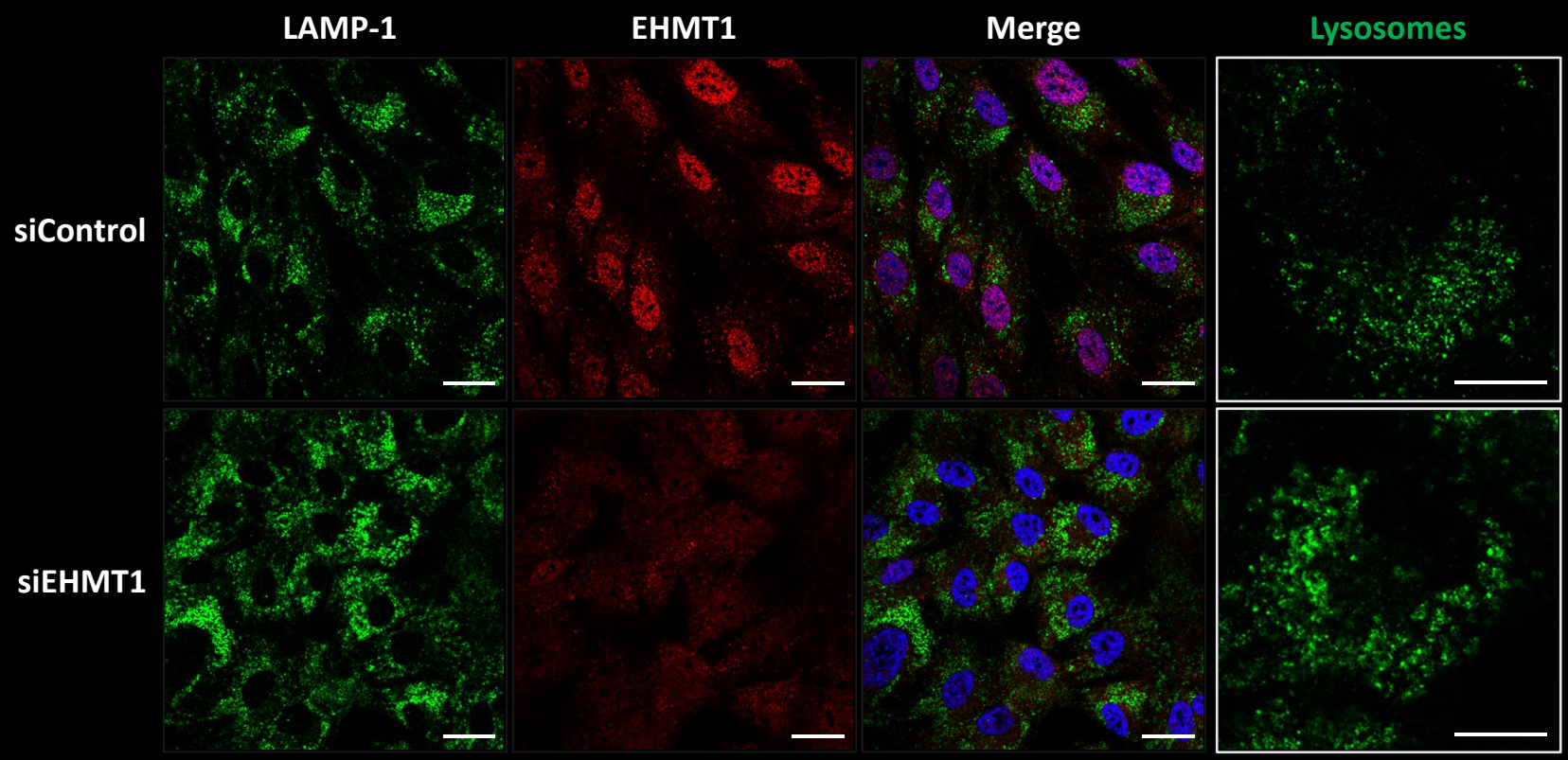
Uwe Beffert, Gregory M. Dillon,* Josefa M. Sullivan,* Christine E. Stuart, James P. Gilbert, John A. Kambouris, and Angela Ho
Department of Biology, Boston University, Boston, Massachusetts 02215

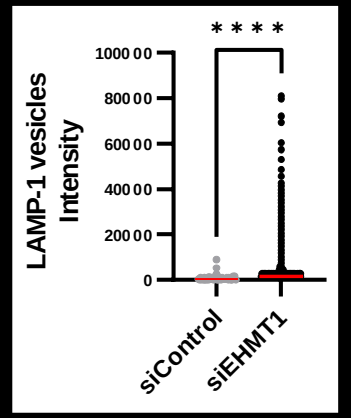


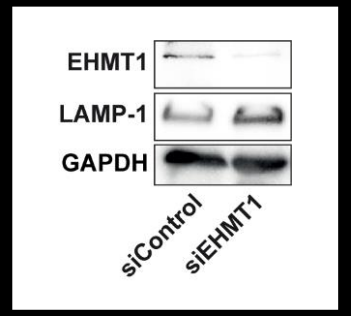


Beffert, U., et al. *The Journal of Neurosciences*, 2012

EHMT1 in lysosomal system







Iglesias-Ortega, L., et al. *Cellular Signalling*, 2023

EHMT1 in lysosomal system

AUTOPHAGY
2022, VOL. 18, NO. 2, 423–442
https://doi.org/10.1080/15548627.2021.1936777

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RESEARCH PAPER

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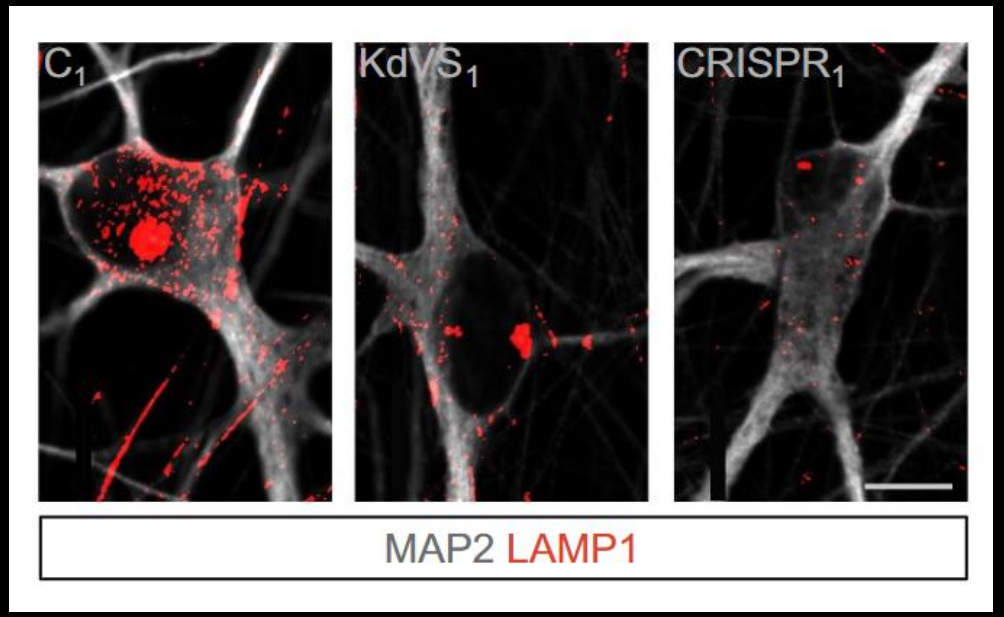
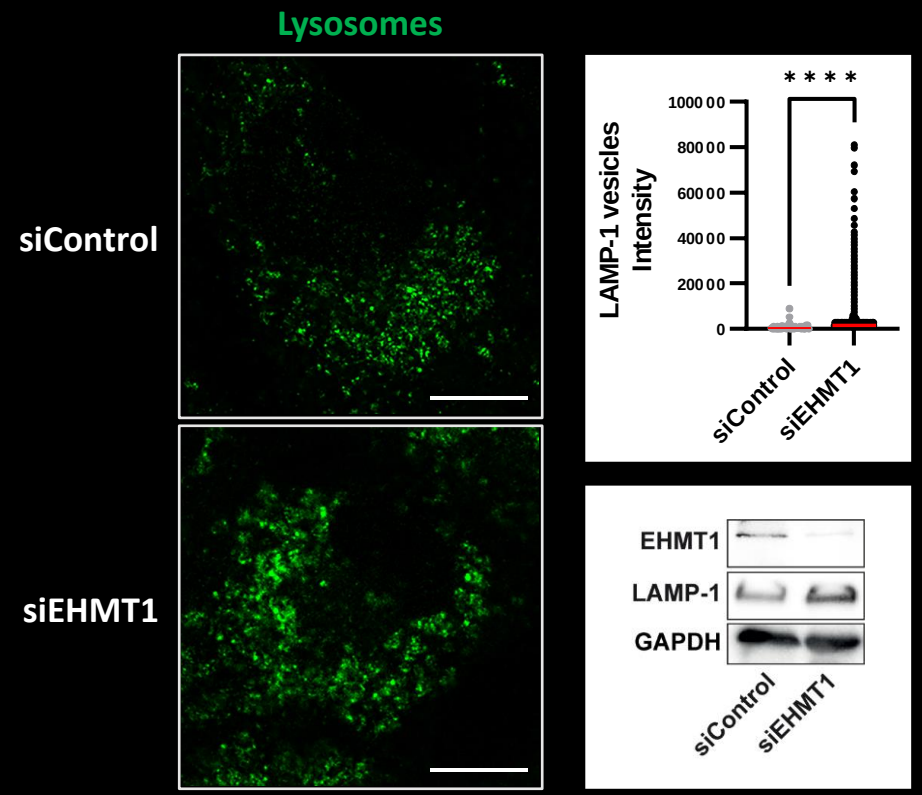
Imbalanced autophagy causes synaptic deficits in a human model for neurodevelopmental disorders

Katrin Linda[a], Elly I. Lewerissa[a], Anouk H. A. Verboven[a], Michele Gabriele[b,c,d], Monica Frega[a,e], Teun M. Klein Gunnewiek[a,f], Lynn Devilee[a], Edda Ulferts[a], Marina Hommersom[a], Astrid Oudakker[a], Chantal Schoenmaker[a], Hans van Bokhoven[a,g], Dirk Schubert[g], Giuseppe Testa[b,c], David A. Koolen[a], Bert B.A. de Vries[a], and Nael Nadif Kasri[a,g]

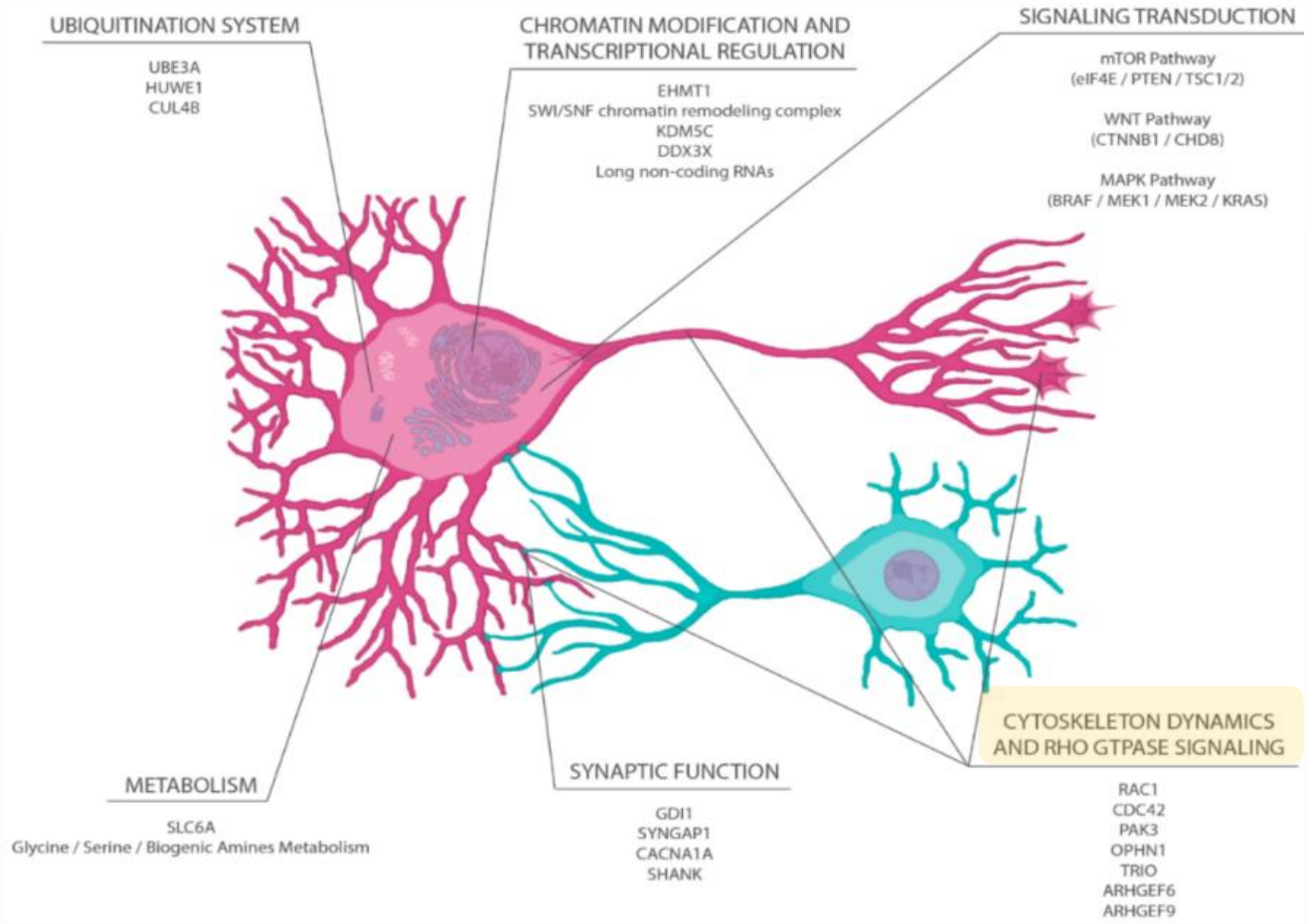




Iglesias-Ortega, L., et al. *Cellular Signalling*, 2023

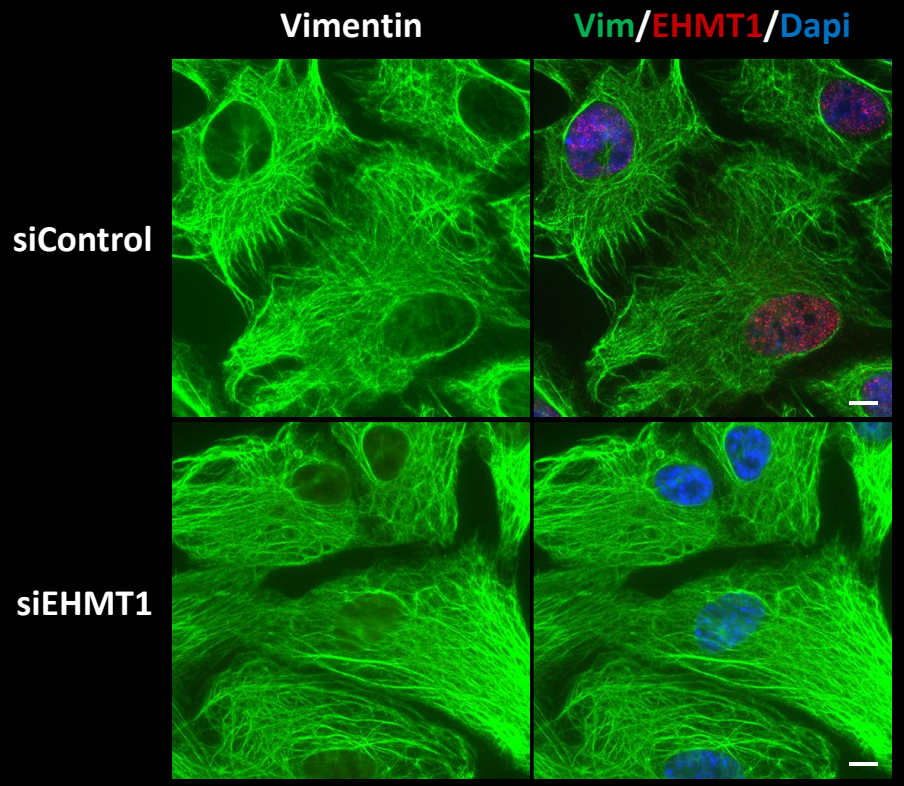
Core regulations in intellectual disability

- Most mutations affecting synaptic functioning are linked with cytoskeleton regulation
- Cytoskeleton dynamics is affected by mutations in different NDDs

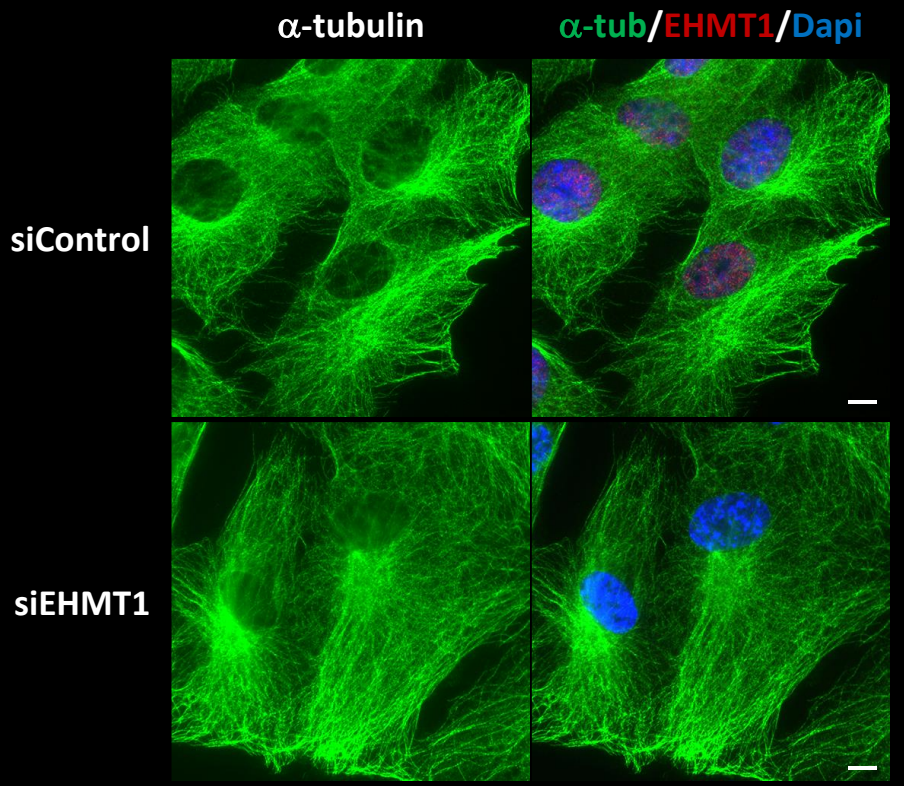


Liaci, C., et al. *International Journal of Molecular Sciences*, 2021

EHMT1 in cytoskeleton organization



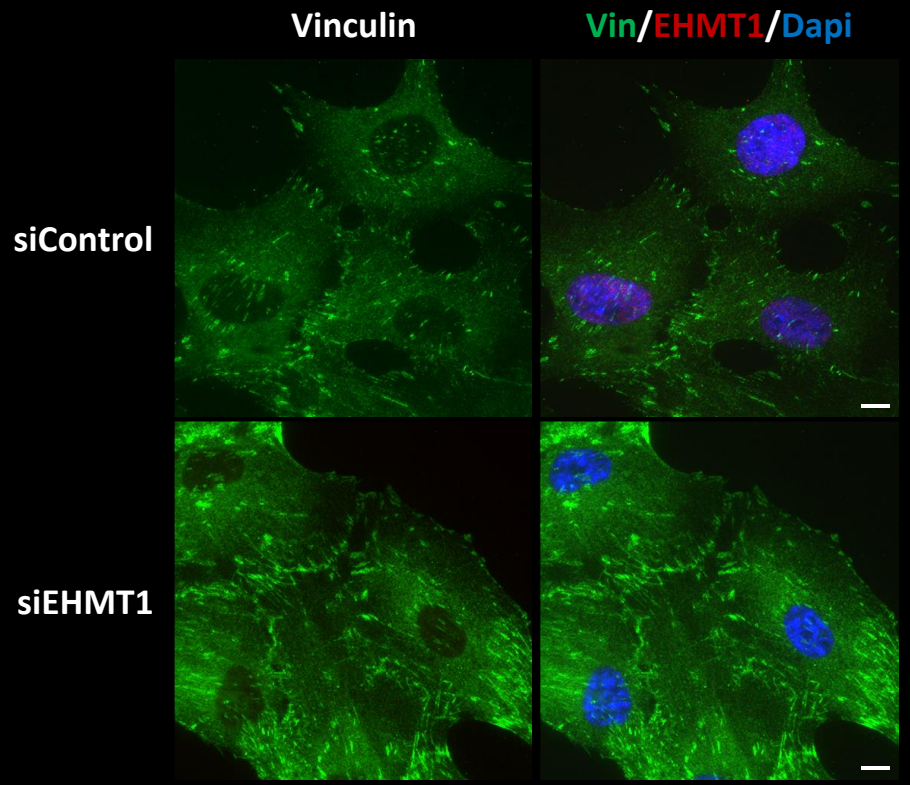
Intermediate filaments



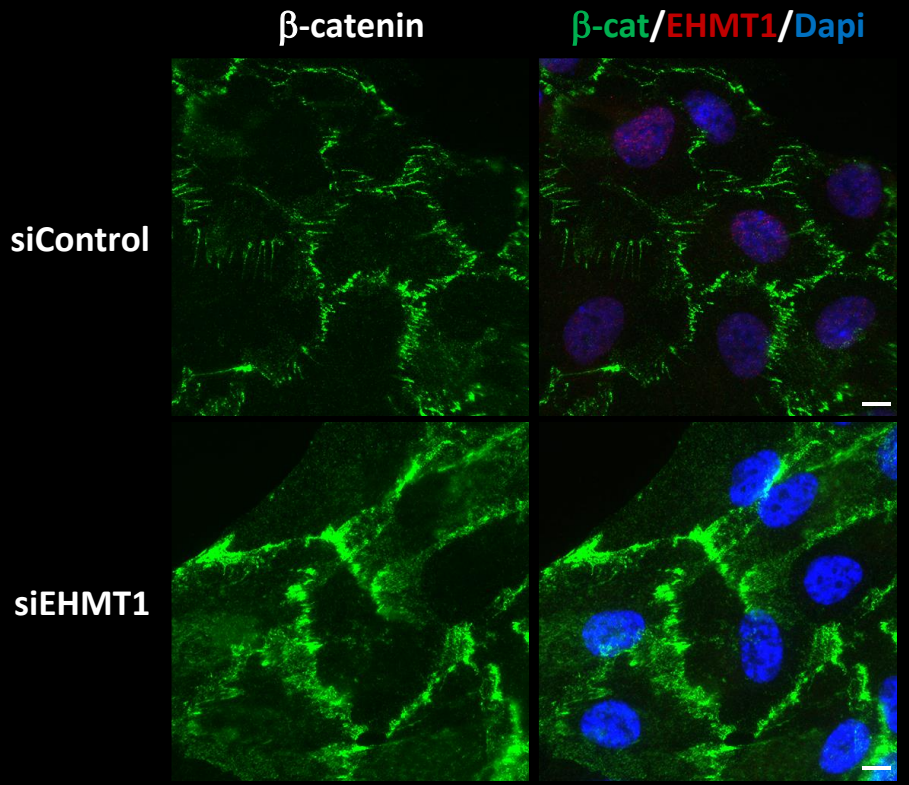
Microtubules

Iglesias-Ortega, L., et al. *Cellular Signalling*, 2023

EHMT1 role in cell adhesion



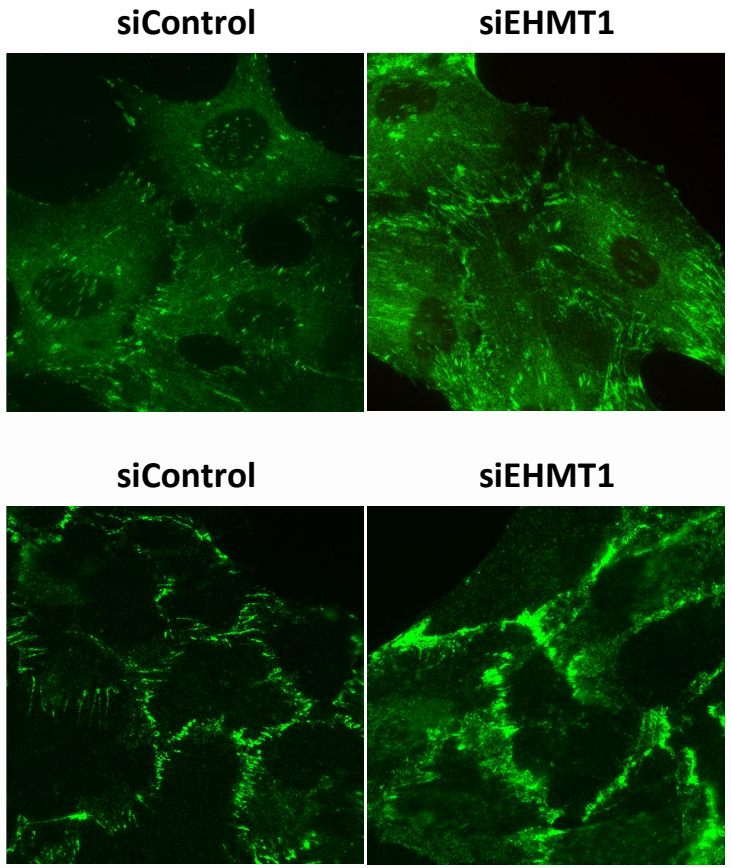
Cell-matrix adhesion

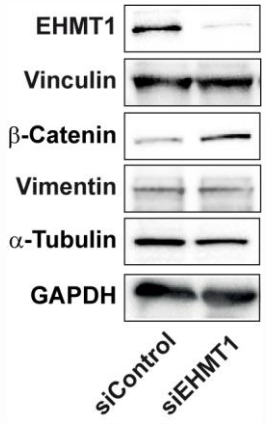


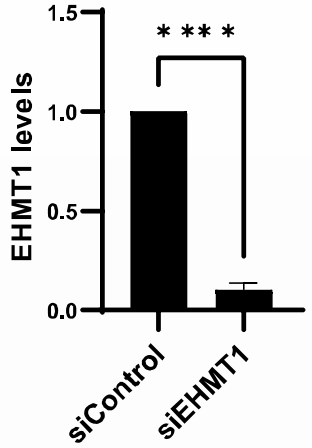
Cell-cell adhesion

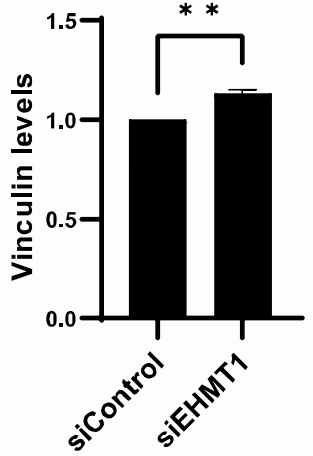
Iglesias-Ortega, L., et al. *Cellular Signalling*, 2023

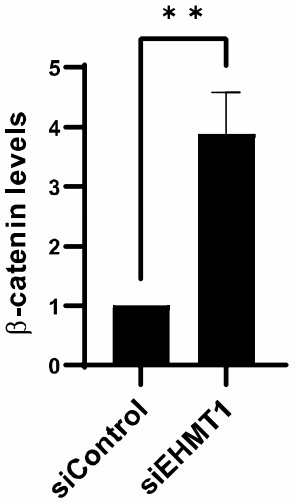
EHMT1 role in cell adhesion











Iglesias-Ortega, L., et al. *Cellular Signalling*, 2023

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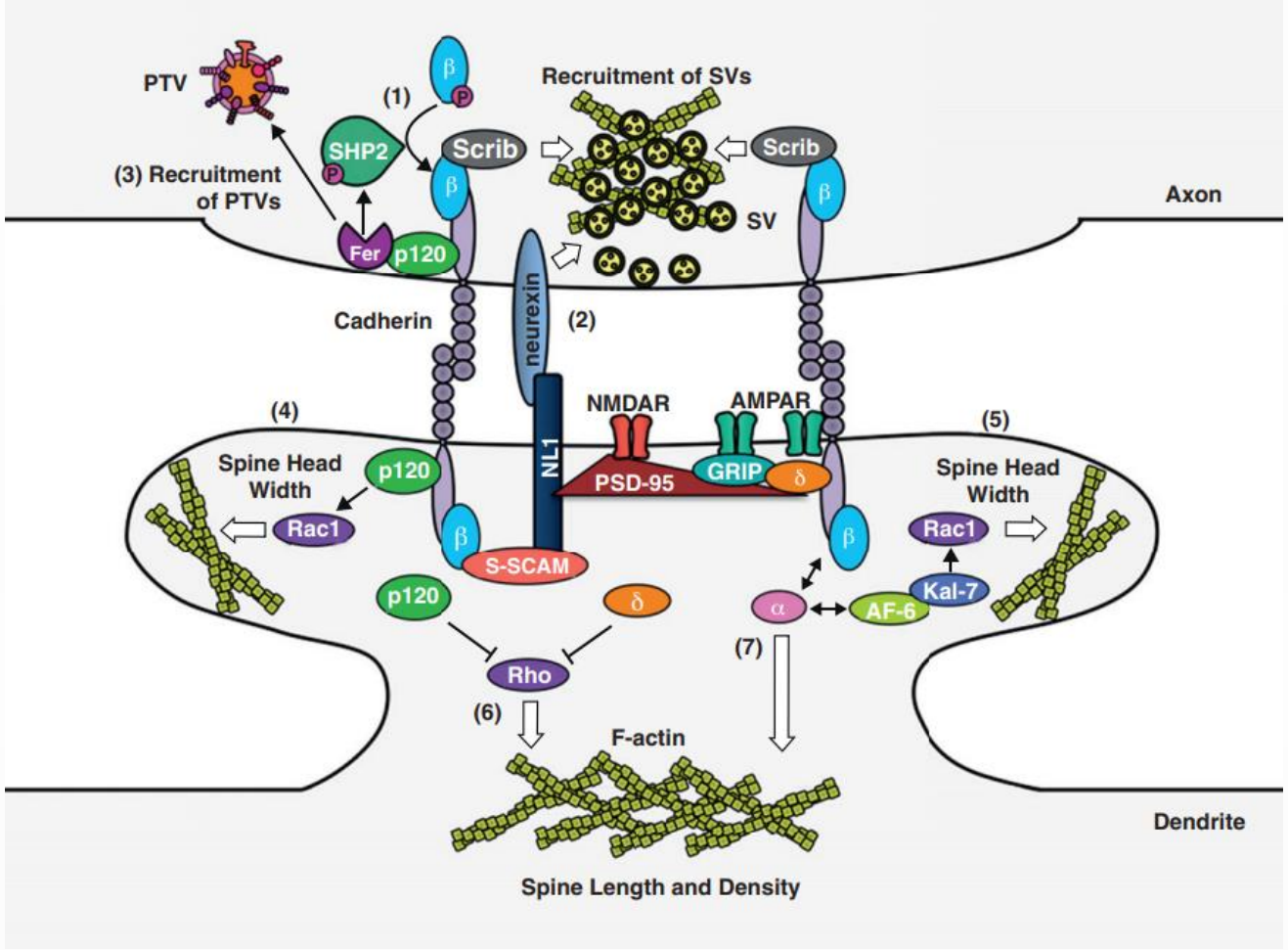
Current Opinion in Neurobiology

Cadherin-catenin adhesion complexes at the synapse

G Stefano Brigidi and Shernaz X Bamji

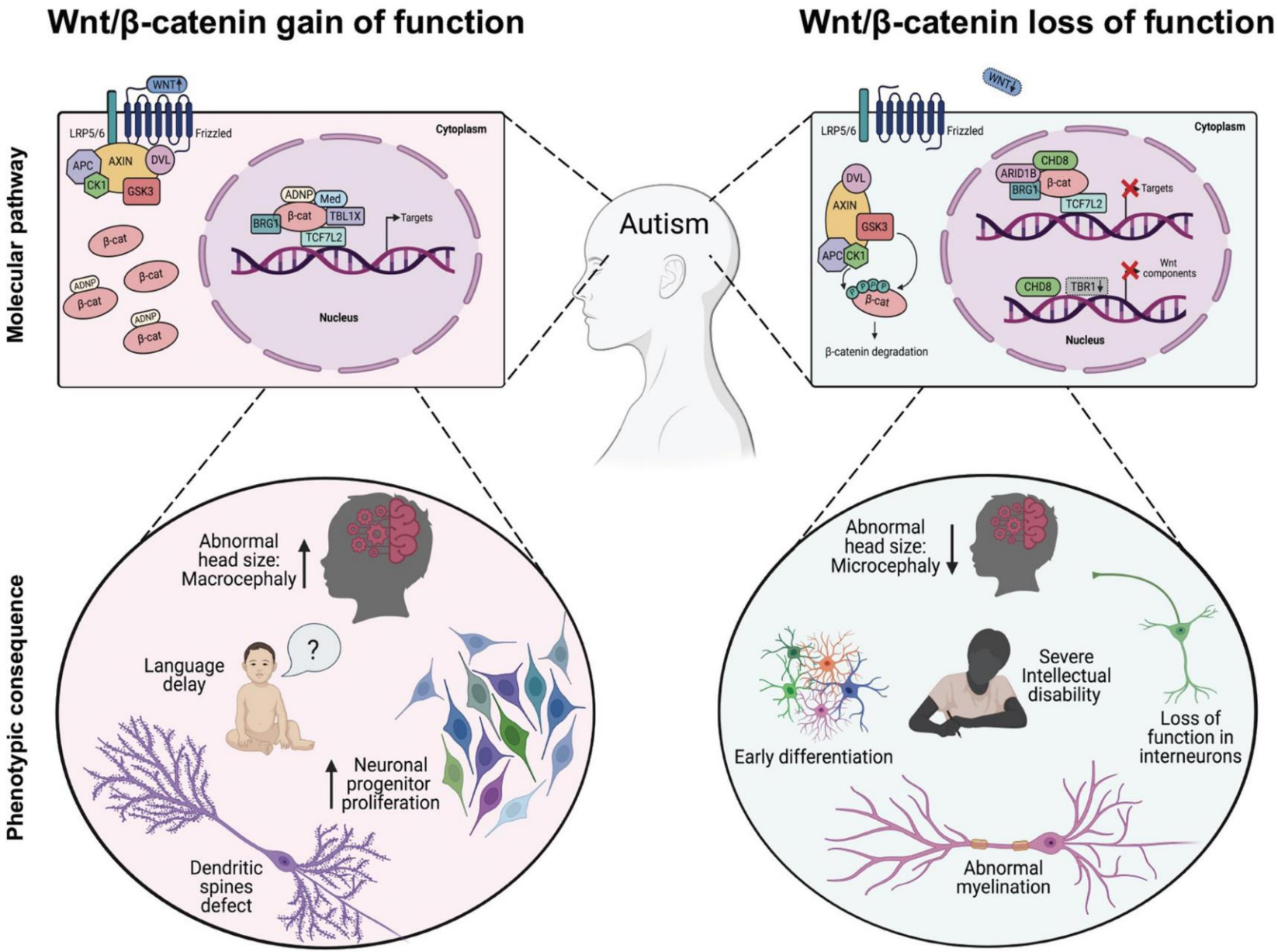


Brigidi, G.S., et al. *Current Opinion in Neurobiology*, 2011

frontiers
in Molecular Neuroscience

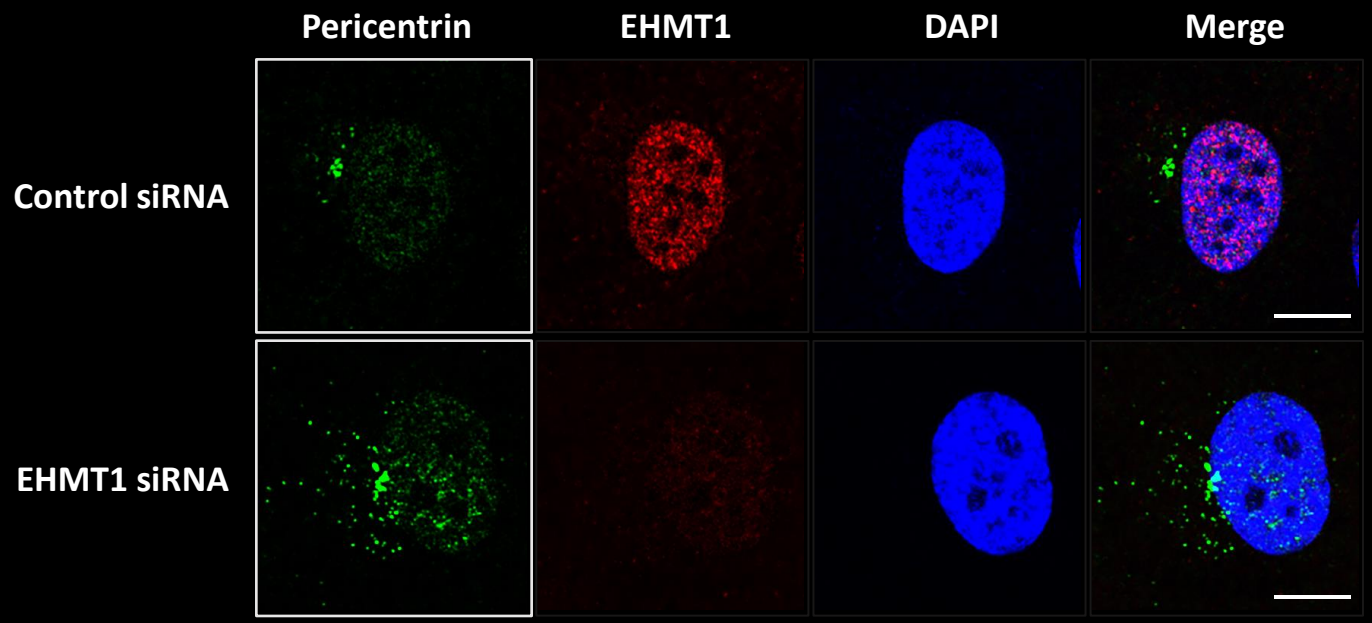
Wnt/β-Catenin-Dependent Transcription in Autism Spectrum Disorders

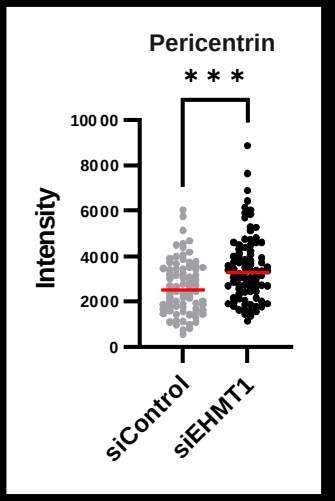
*Mario O. Caracci[1,2], Miguel E. Avila[3], Francisca A. Espinoza-Cavieres[1,2], Héctor R. López[1,2], Giorgia D. Ugarte[1,2] and Giancarlo V. De Ferrari[1,2]**



Caracci, M.O., et al. *Frontiers in Molecular Neurosciences*, 2021

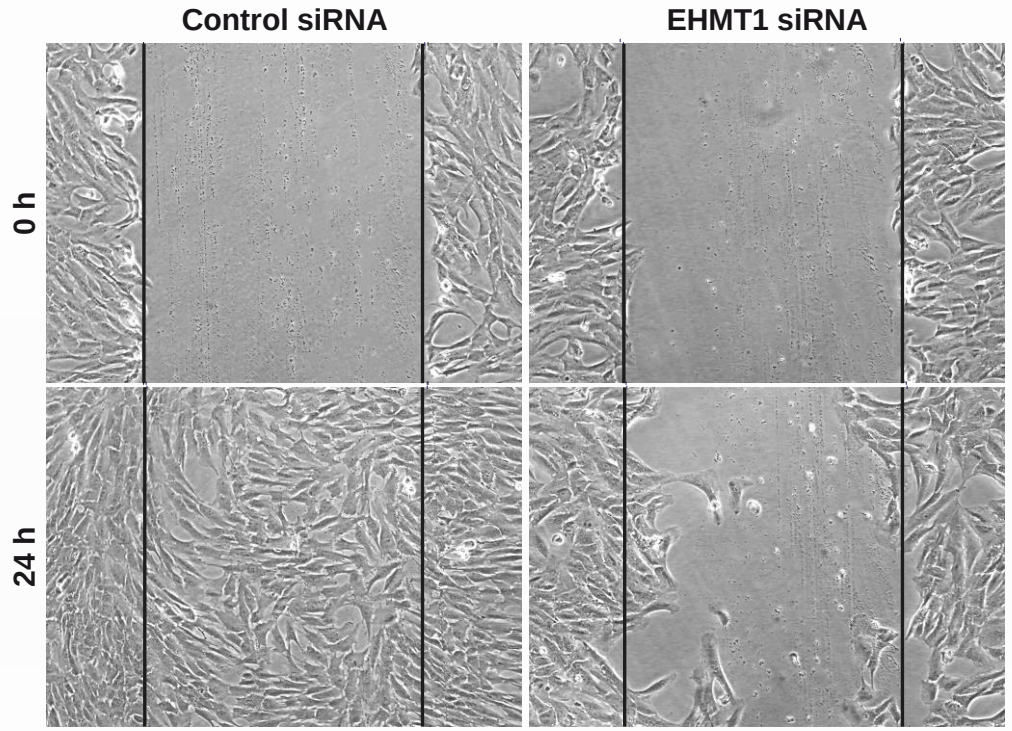
EHMT1 in centrosome functioning

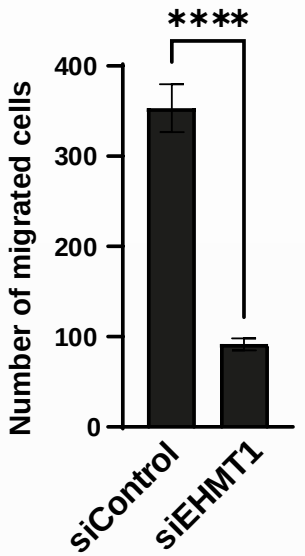




Iglesias-Ortega, L., et al. *Cellular Signalling*, 2023

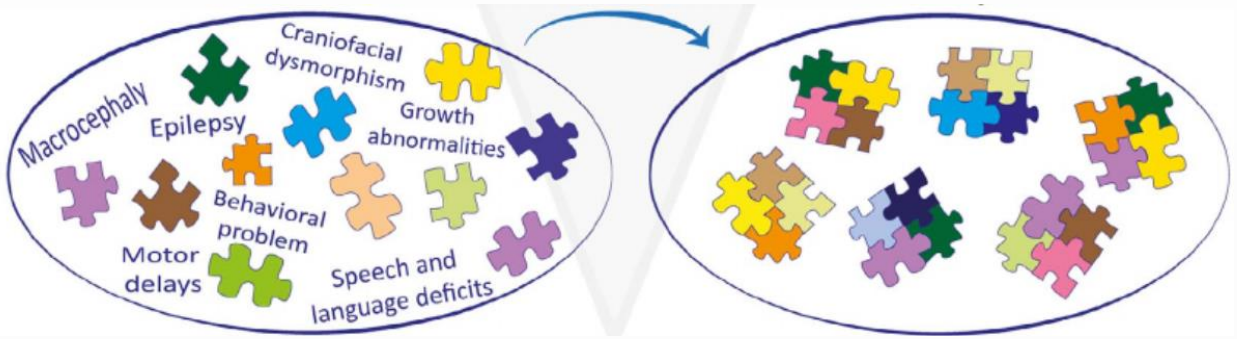
EHMT1 is required for migration





Iglesias-Ortega, L., et al. *Cellular Signalling*, 2023

Molecular Convergence of Neurodevelopmental Disorders



"Similar Cognitive Disorders phenotypes reflect functional relationships between epigenetic cognitive genes"

ARTICLE

Molecular Convergence of Neurodevelopmental Disorders

Elizabeth S. Chen,[1,2,7] Carolina O. Gigek,[1,2,7] Jill A. Rosenfeld,[3] Alpha B. Diallo,[1,2] Gilles Maussion,[1,2] Gary G. Chen,[1,2] Kathryn Vaillancourt,[1,2] Juan P. Lopez,[2,4] Liam Crapper,[1,2] Raphaël Poujol,[1,2] Lisa G. Shaffer,[5] Guillaume Bourque,[4,6] and Carl Ernst[1,2,4,*]

Cell Reports
Article

Distinct Pathogenic Genes Causing Intellectual Disability and Autism Exhibit a Common Neuronal Network Hyperactivity Phenotype

Monica Frega,[1,2,4] Martijn Selten,[1,4] Britt Mossink,[2,4] Jason M. Keller,[2] Katrin Linda,[2] Rebecca Moerschen,[2] Jieqiong Qu,[3] Pierre Koerner,[3] Sophie Jansen,[1] Astrid Oudakker,[1,2] Tjitske Kleefstra,[2] Hans van Bokhoven,[1,2] Huiqing Zhou,[2,3] Dirk Schubert,[1,5] and Nael Nadif Kasri[1,2,5,6,*]

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journal homepage: www.elsevier.com/locate/neuropharm

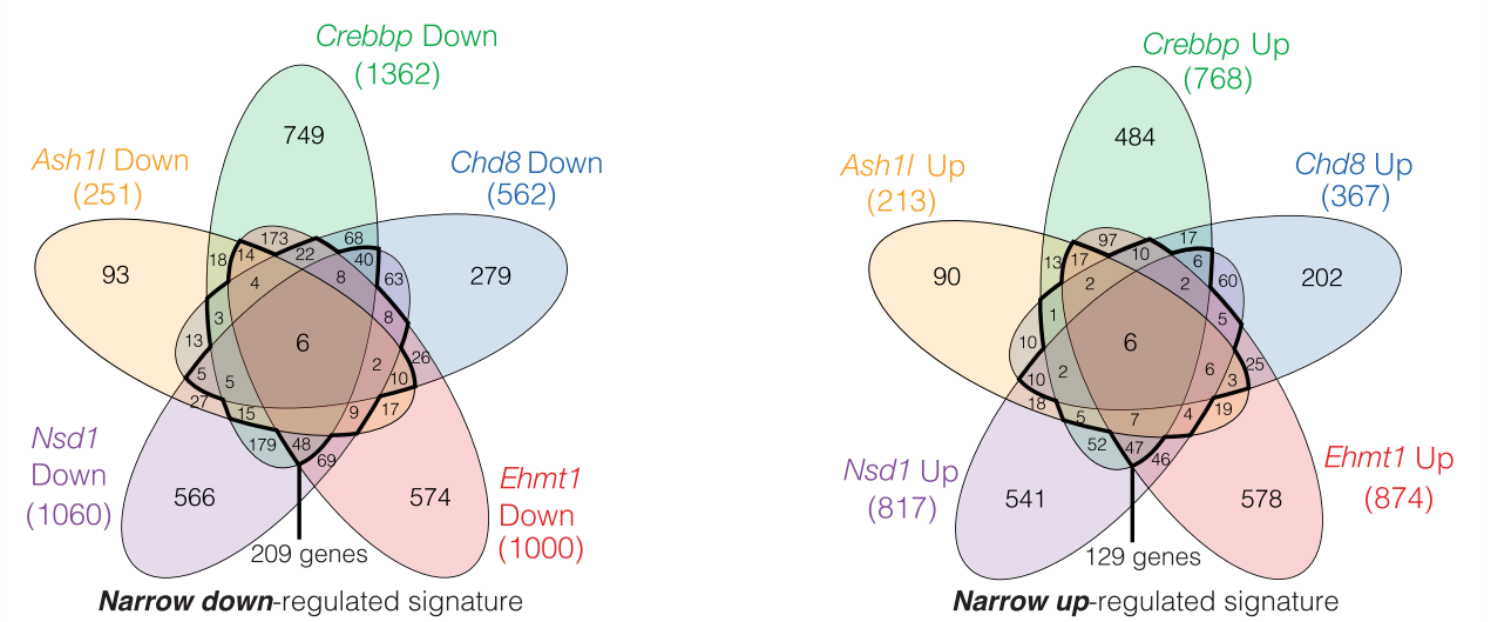
Invited review

The genetics of cognitive epigenetics

Tjitske Kleefstra [a], Annette Schenck [a], Jamie M. Kramer [a], Hans van Bokhoven [a,b,*]

Identification of a transcriptional signature found in multiple models of ASD and related disorders

Samuel Thudium,[1,2] Katherine Palozola,[1,2] Éloïse L'Her,[1,2] and Erica Korb[1,2]



EHMT1, Kleefstra syndrome

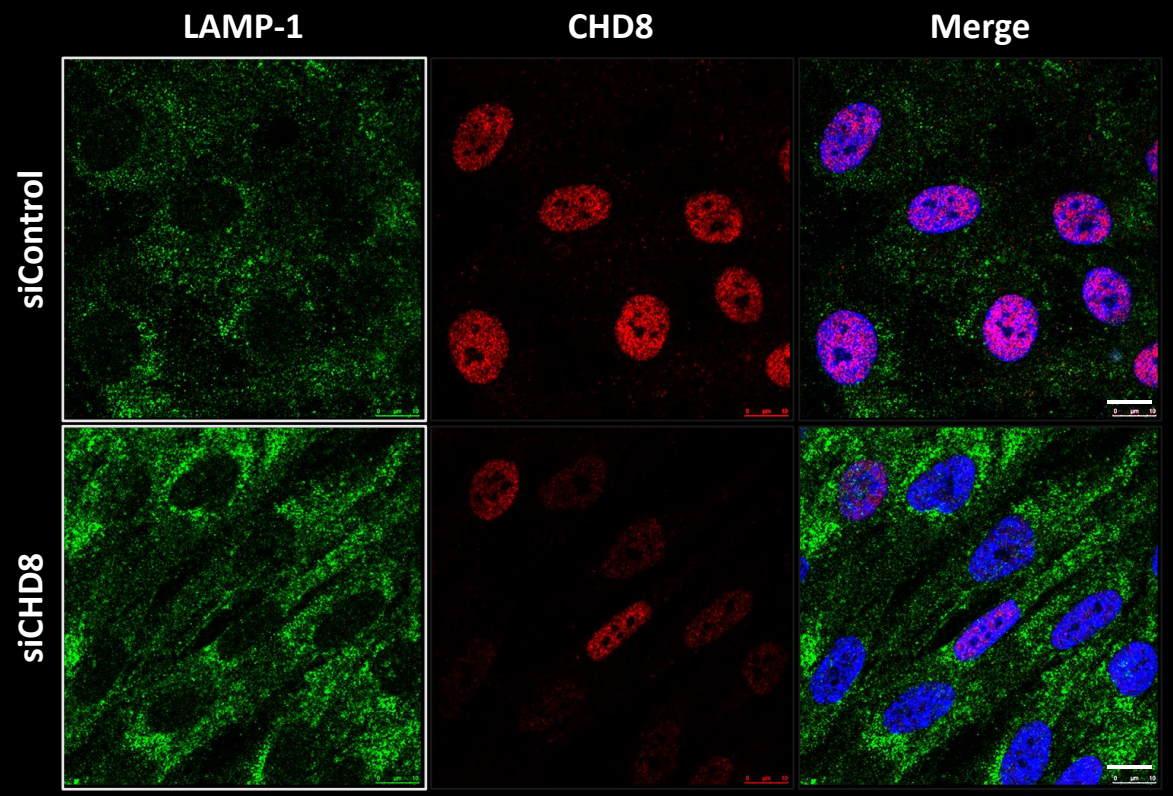
CREBBP, Rubinstein-Taiby syndrome

NSD1, Sotos syndrome

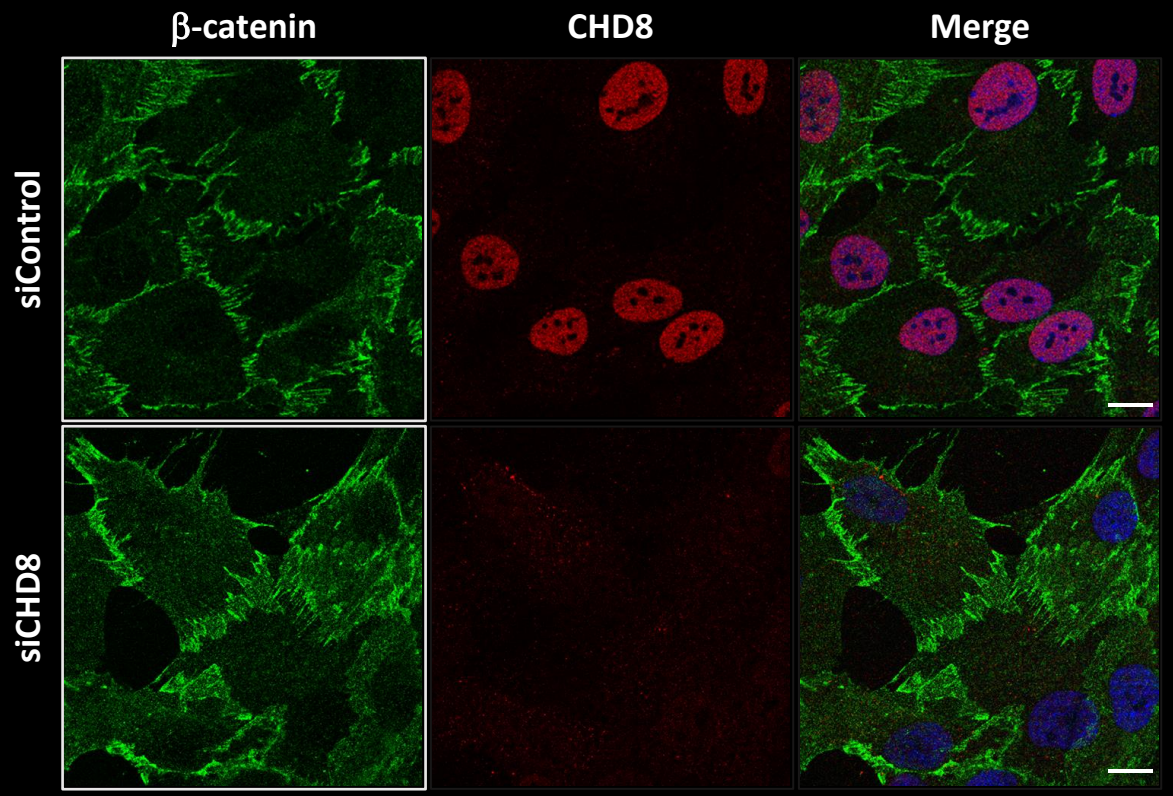
CHD8, Autism 18

Thudium, S., et al. *Genome Research*, 2022

Common cellular disruptions



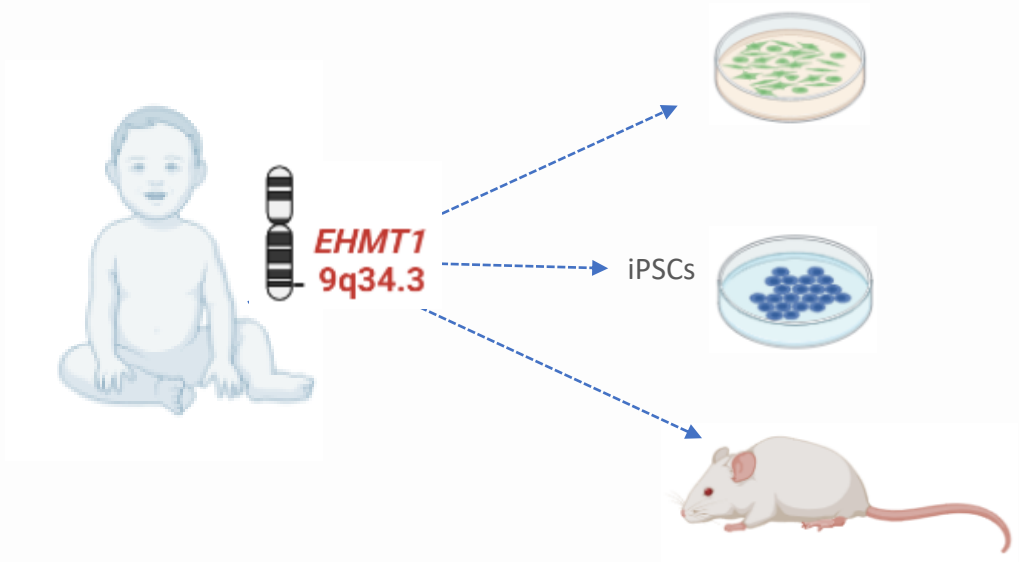
Lysosomal system



CHD8 and β-catenin

Conclusions and future direction

- EHMT1 is necessary for **Golgi structure**
- Downregulation of EHMT1 leads to **lysosomes accumulation**
- Reduced levels of EHMT1 induce **changes in cell adhesion**
- EHMT1 could has a role in **centrosome functioning**
- EHMT1 depleted cells show **reduced migration capacity**
- **EHMT1 and CHD8** could participe in **common cellular processes**



GRACIAS

THANK YOU

Colaborators:

Dra. Silvia Jimeno González

Clara Megías Fernández

Dra. Paloma Domínguez Giménez

Dra. Inés Fernández Ulibarri

http://inesfernandezulibarri.com