

Unipolar brush cells: investigating the role of Tbr2 in cerebellar development

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Disclosures

None



Brief Communication abstract

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Homozygous silencing of T-box transcription factor EOMES leads to microcephaly with polymicrogyria and corpus callosum agenesis

Lekbir Baala^{1,2}, Sylvain Briault^{3,8}, Heather C Etchevers², Frédéric Laumonnier³, Abdelhafid Natiq¹, Jeanne Amiel², Nathalie Boddaert⁴, Capucine Picard⁵, Aziza Sbiti¹, Abdellah Asermouh⁶, Tania Attié-Bitach^{2,7}, Féréchté Encha-Razavi^{2,7}, Arnold Munnich^{2,7}, Abdelaziz Sefiani¹ & Stanislas Lyonnet^{2,7}

The Big Picture

- Tbr2 = *EOMES*
- Question: What is the role of the Tbr2 transcription factor in cerebellar neurogenesis?



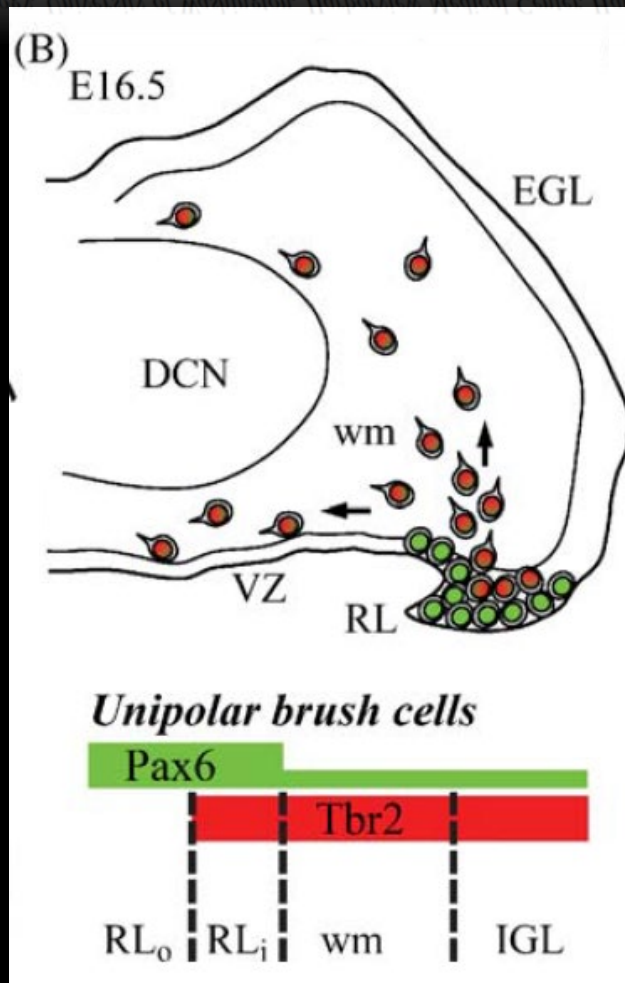
Transcription factors in glutamatergic neurogenesis: Conserved programs in neocortex, cerebellum, and adult hippocampus

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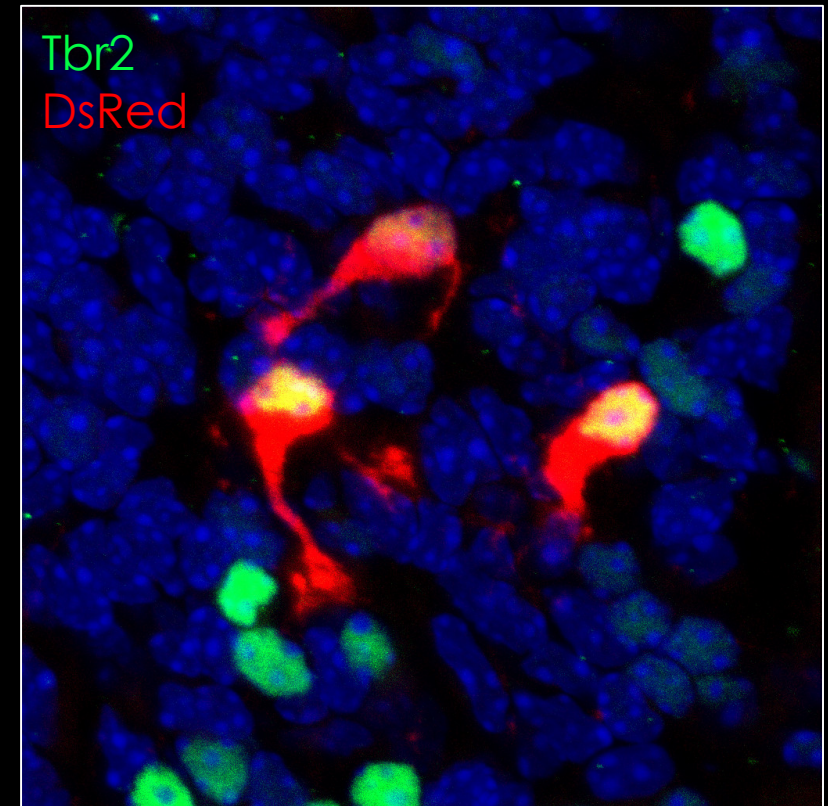
What is Tbr2?

- T-box brain protein
- Transcription factor in neurogenesis
- Tbr2 expressed transiently in 3 types of cells during development of the cerebellum:
 - DCN
 - Granule neurons
 - **Unipolar Brush Cells remain Tbr2+ into adulthood**



What are Unipolar Brush Cells (UBCs)?

- Glutamatergic interneurons with complex morphologies
- Located in the internal granular layer of the cerebellum
- Express Tbr2
- 2 types:
 - Type I: Calretinin+
 - Type II: mGluR1 α +
- Typical morphology: cell body with a single dendrite and a brush of dendrioles



Two Methods

Tbr2 cKO mouse

- Observations: No ataxia or gross cerebellar malformations



http://www.animalresearch.info/files/2014/1865/5563/mouse_white_black_background_2charwell.jpg

Tbr2 lineage tracer mouse

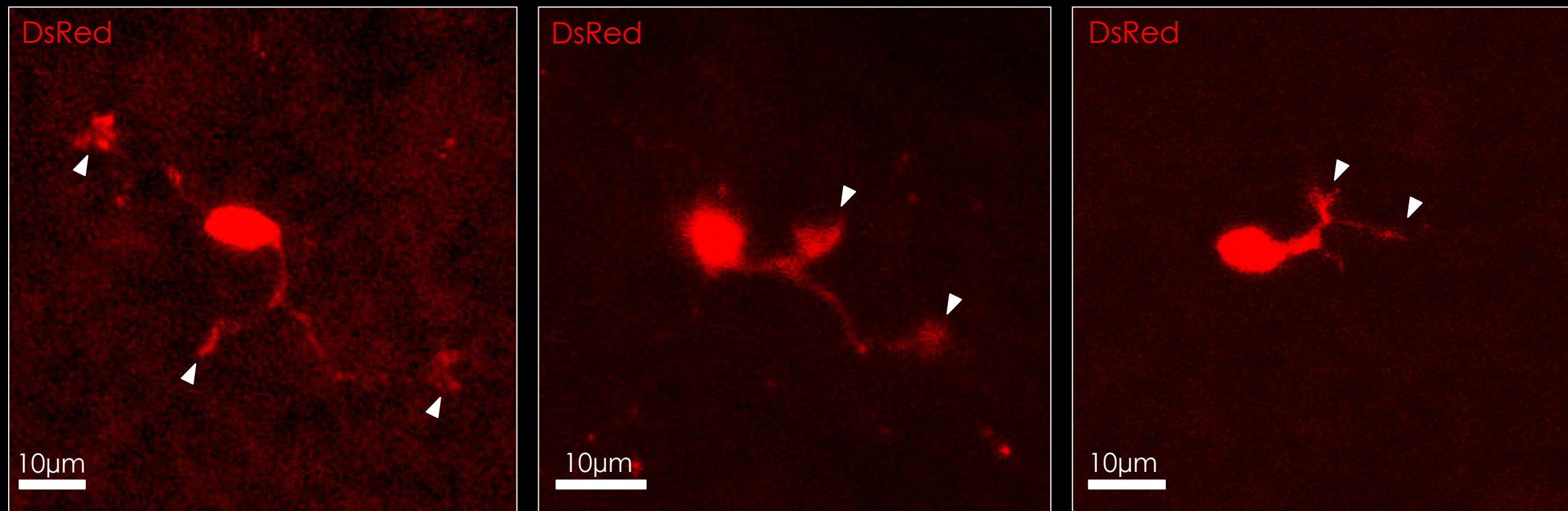
- Label all cells that come from the *Tbr2* lineage: the UBCs



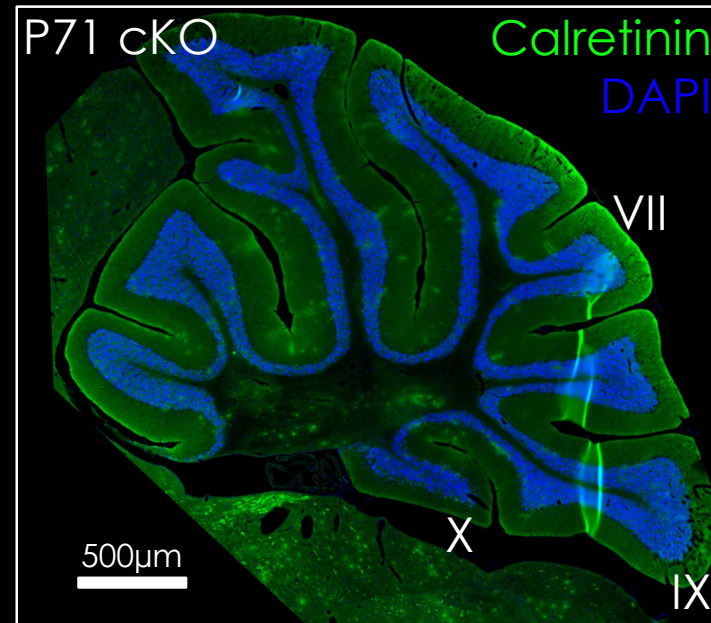
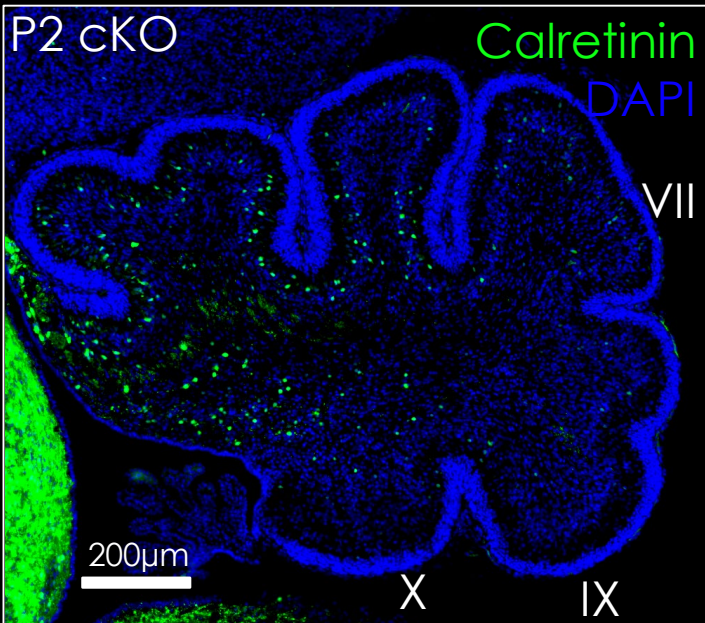
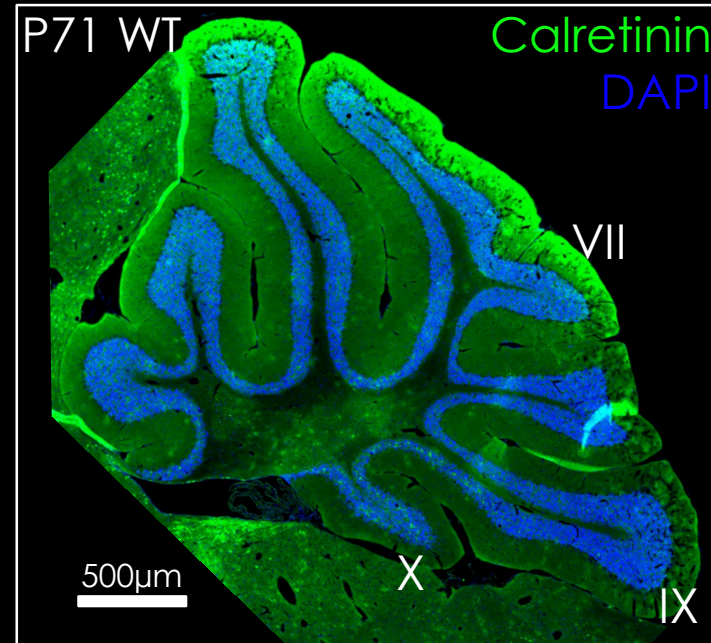
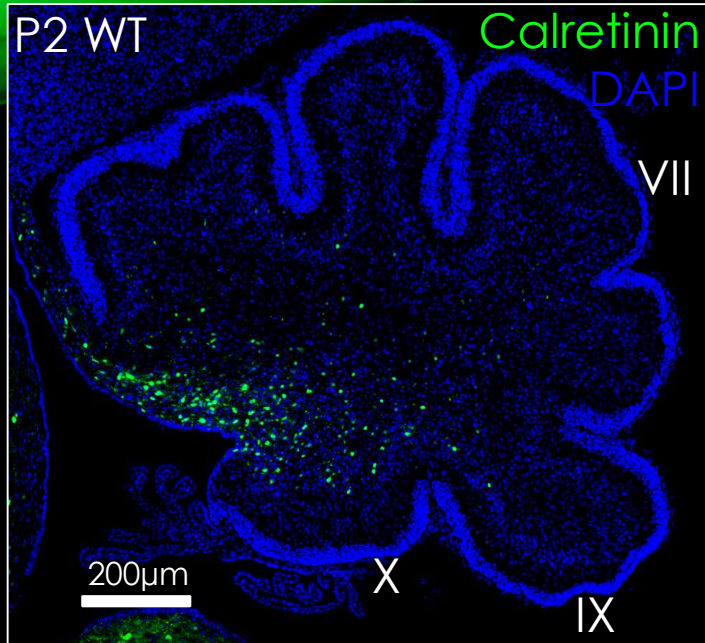
http://nightsea.com/wp-content/uploads/2011/09/mouse_composite.jpg



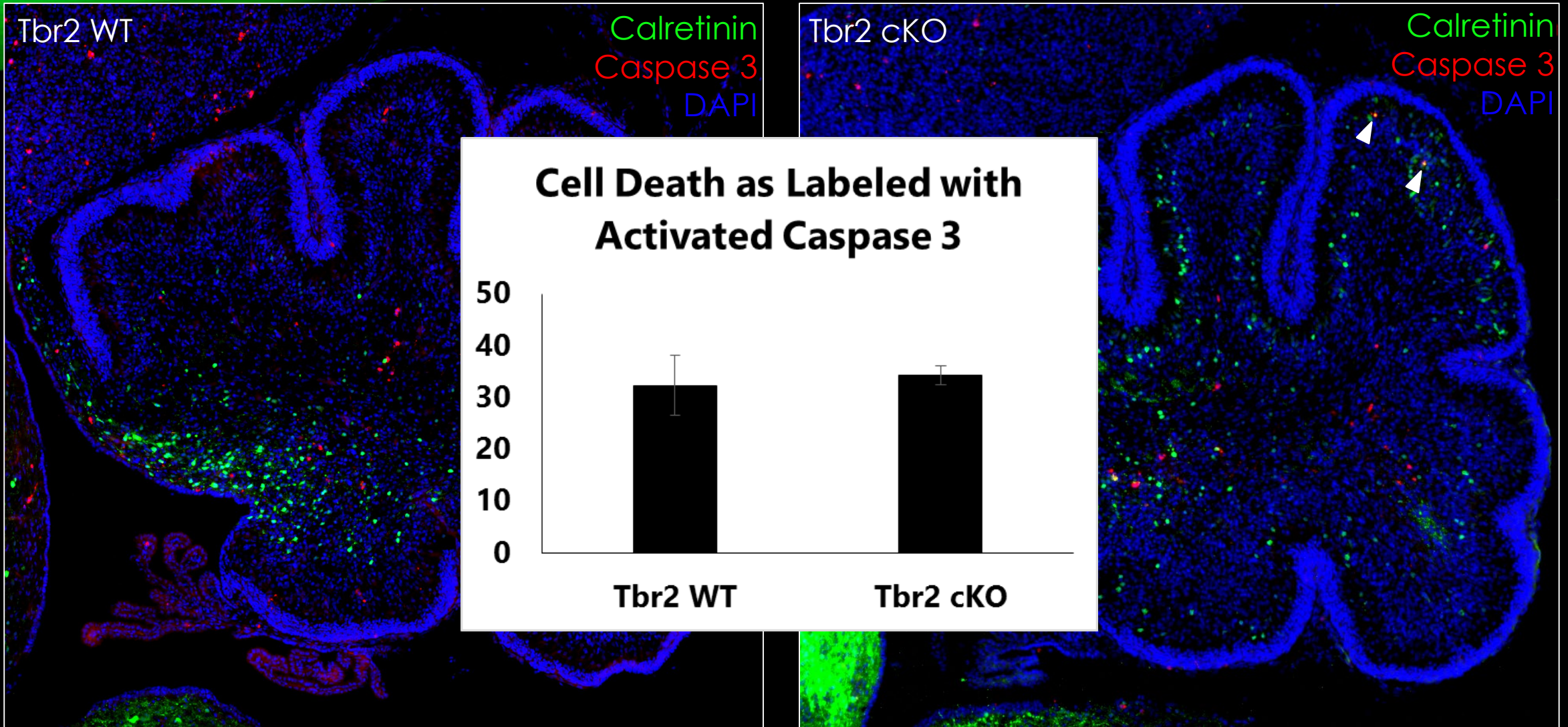
UBCs have more complex morphologies



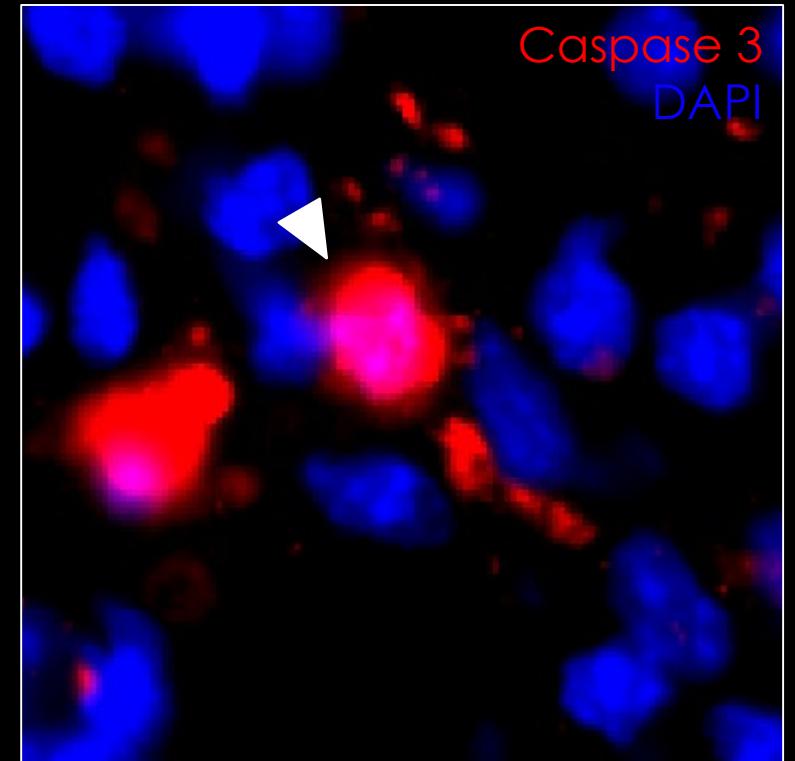
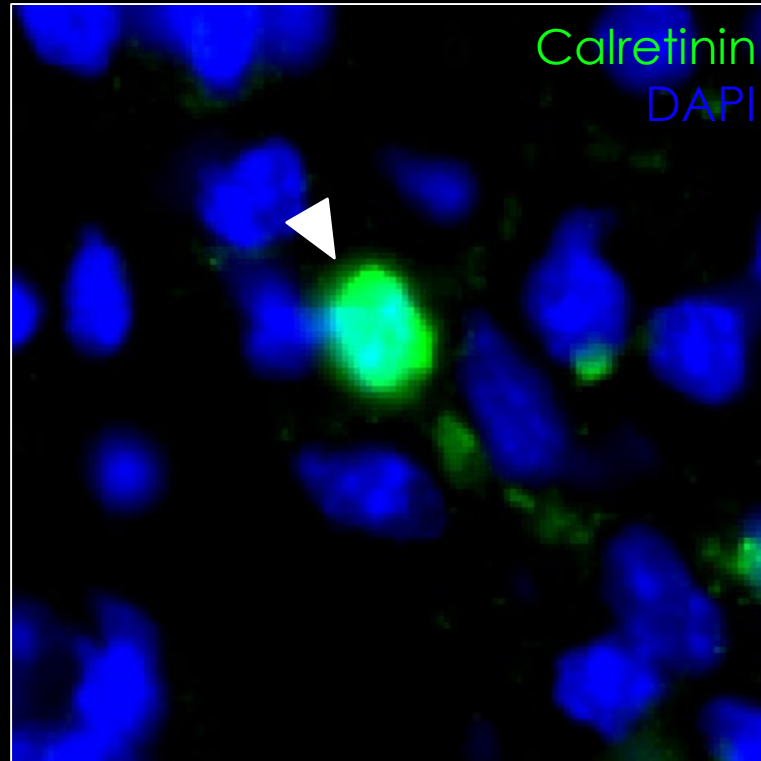
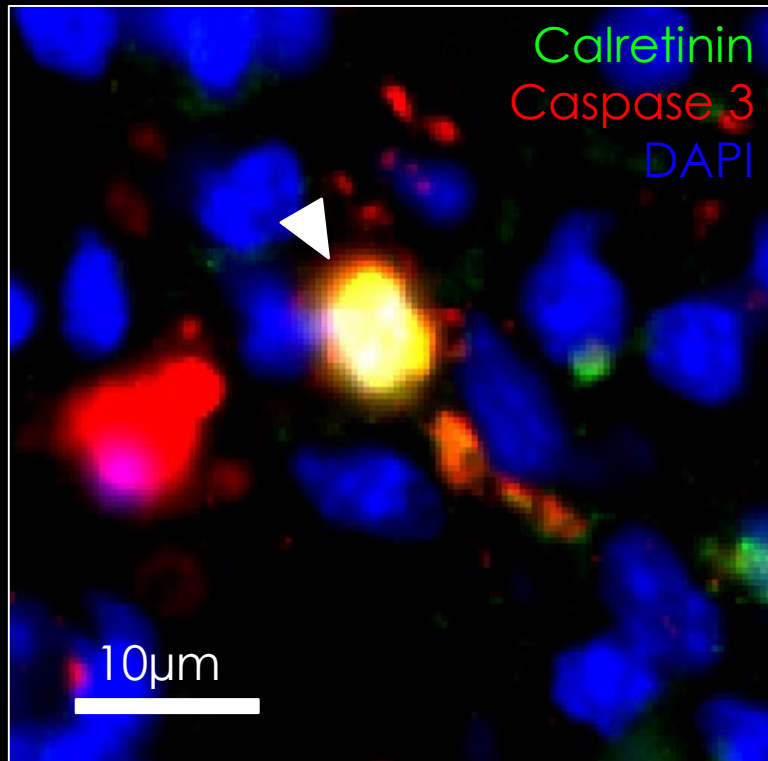
Calretinin (Type I UBCs) in *Tbr2* cKO



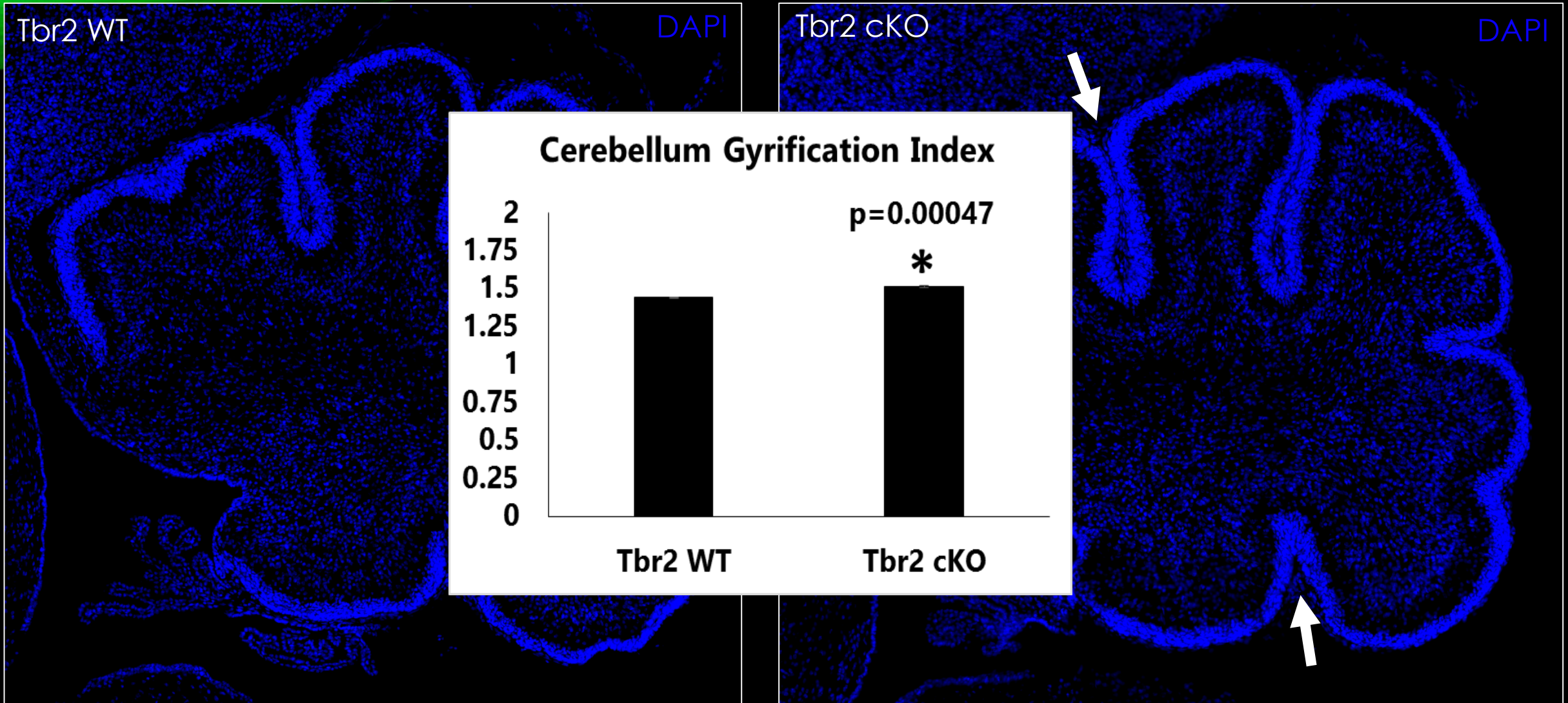
Cell death in the *Tbr2* cKO



Cell death in the *Tbr2* cKO



Cerebellar foliation in the *Tbr2* cKO



Conclusions

- Unlike previously thought, UBCs have more complex morphologies
- Type I UBCs are formed during development but die into adulthood, timing unknown
- Gross cerebellar morphology is not affected in the Tbr2 cKO, but increased foliation is apparent



Future Directions

- Exploration of UBCs and their interactions
- Timing and quantification of Type I Calretinin+ and Type II UBC death into adulthood in the *Tbr2* cKO
- Further quantification of cerebellar foliation in the *Tbr2* cKO



Thank You

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- Jim Pridgeon & Christina Buckman

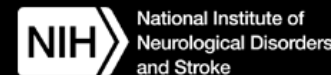


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