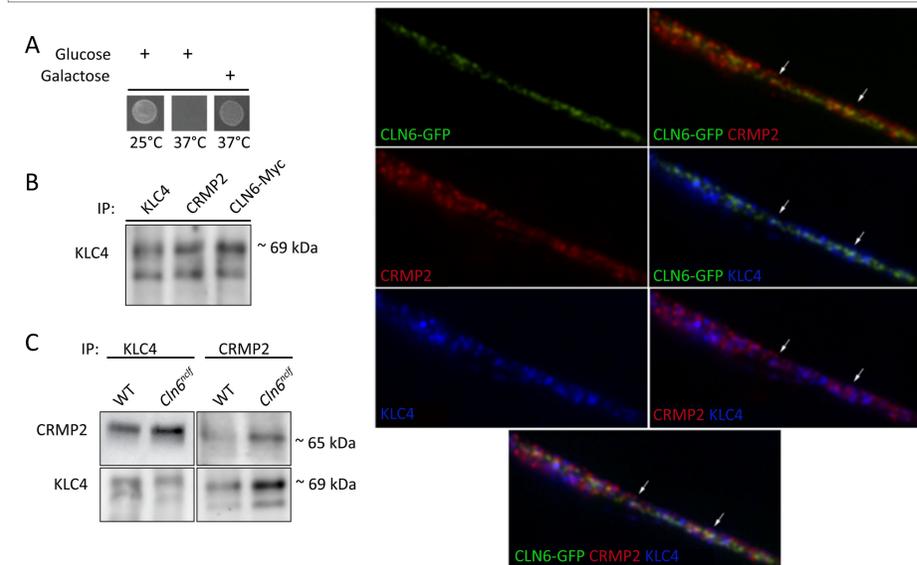


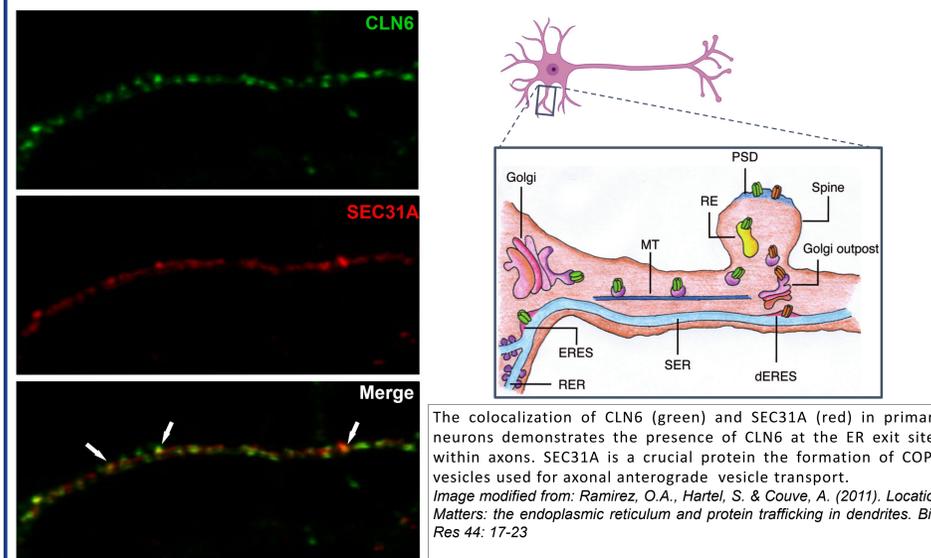
CLN6 interacts with CRMP2 and KLC4 to regulate axonal transport of ER-derived vesicles

Lay Summary: The specific vulnerability of neuronal populations in Batten disease suggests that CLN6 and other Batten proteins may have neuron-specific functions. **Here we describe a unique function of CLN6 in regulating the transport of axonal cargoes.** CLN6, together with CRMP2 and KLC4, forms a complex that regulates anterograde axonal transport in developing neurons. Our work identifies a neuron-specific function of CLN6 that has direct implications in disease pathogenesis and suggests potential avenues for treatment in Batten disease and other neurodegenerative disorders.

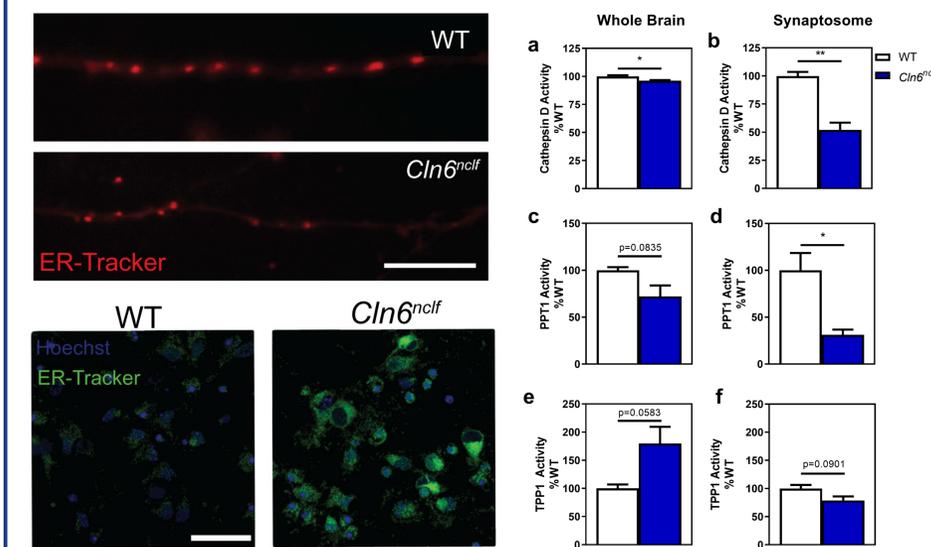


Left: A: Using the N-terminal cytosolic domain of CLN6 as a bait protein, yeast 2-hybrid screening identifies novel interaction between CLN6 and KLC4. B: KLC4 coimmunoprecipitates with CLN6-myc and CRMP2 in PC12 cells. C: Loss of CLN6 in the *Cln6^{nclf}* mouse model leads to enhanced KLC4-CRMP2 coupling, suggesting CLN6 may negatively regulate this process. **Right:** Colocalization of CRMP2, CLN6-GFP, and KLC4 in neuronal processes of cultured primary cortical neurons.

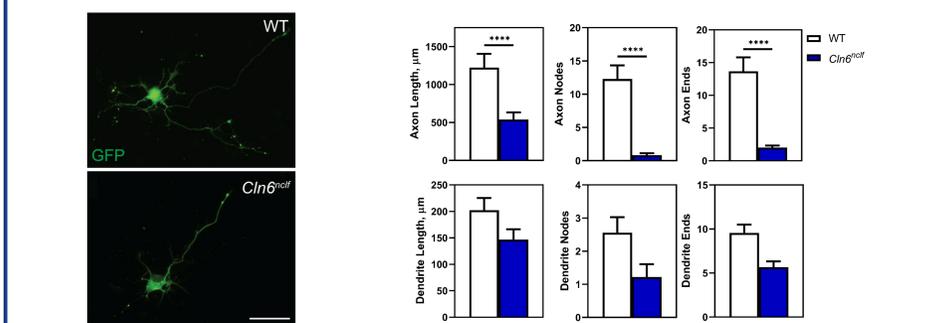
CLN6 colocalizes with COPII proteins



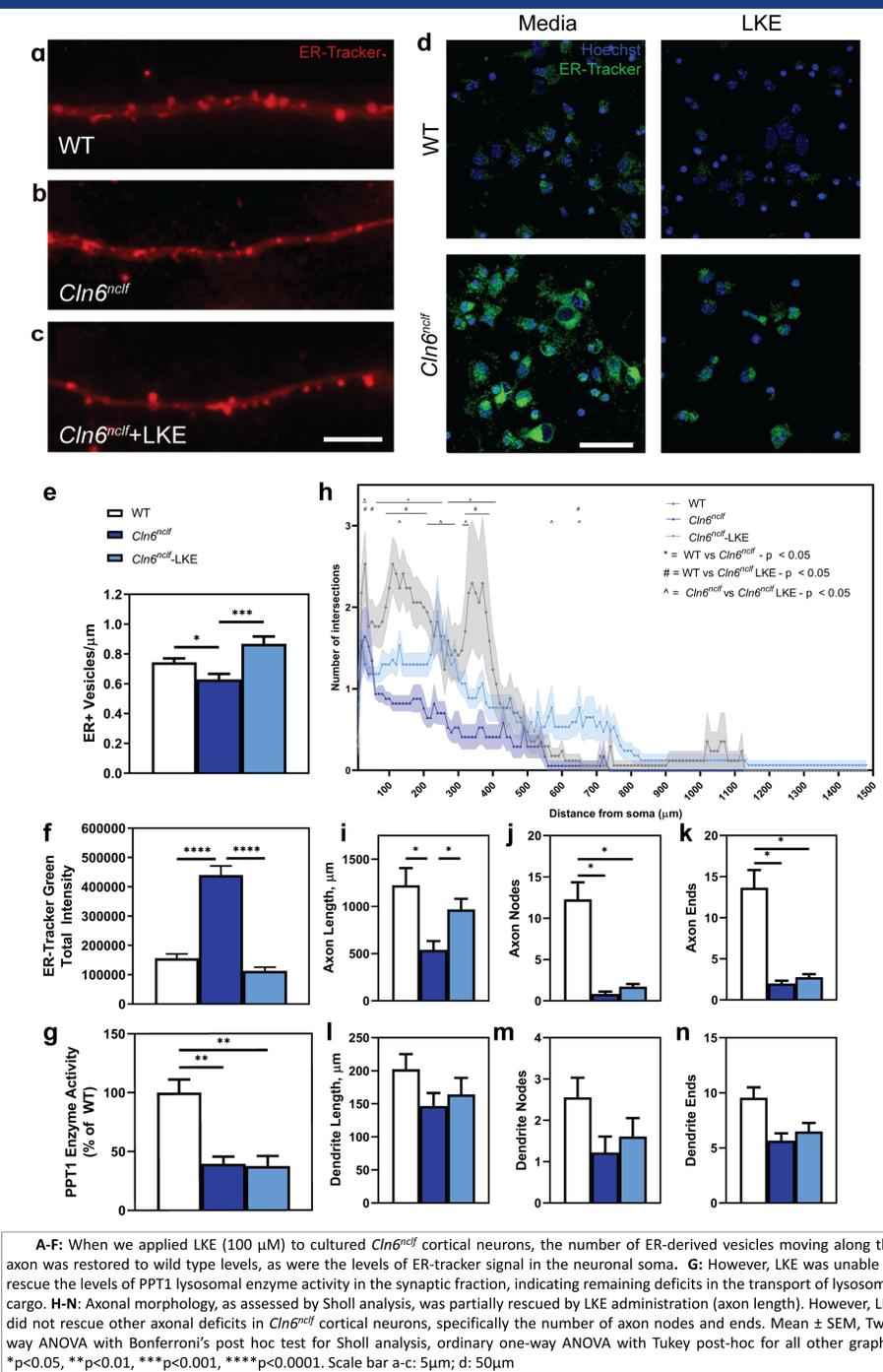
CLN6 is required for axonal vesicle entry and synaptic lysosome function



CLN6 is required for neurite morphogenesis



Stabilization of CRMP2 via LKE rescues some CLN6-related deficits



Summary

- CLN6 is a critical regulator of axonal entry of ER-derived vesicles in cortical neurons, likely through interactions with key mediators of vesicle trafficking such as KLC4 and CRMP2.
- Disruption of the CCK complex leads to impaired neuronal health and alters CRMP2's interactions with other proteins.
- Stabilization of CRMP2 via LKE corrects some *Cln6^{nclf}* phenotypic deficits.
- The CLN6-CRMP2 interaction is important in a neurodegenerative disease and is a potential new therapeutic target for CLN6-Batten disease.

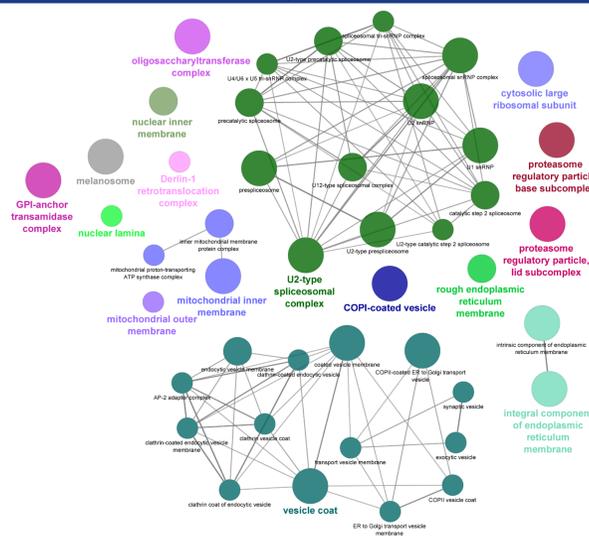
Acknowledgements

This work was supported through the National Institutes of Health (R01NS082283, P20GM103620, and P20GM103548)

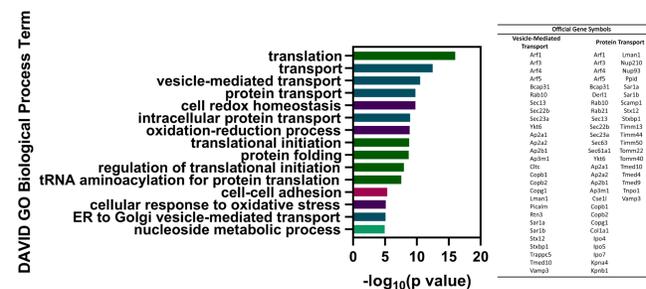
Find more information about our work:



Network Analysis of CLN6 BioID



DAVID GO Biological Process analysis of CLN6 BioID screen highlighted the role of CLN6 in transport processes (blue) throughout the cell. Table displays the gene symbols that contributed to the terms "vesicle-mediated transport" and "protein transport".



Check out Meyerink *et al.* "Interactor and pathway analysis of CLN3, CLN6, and CLN8 using proximal biotinylation" for more BioID results (NCL Congress Poster).