

# Protrudin functions from the endoplasmic reticulum to support axon regeneration in the adult CNS

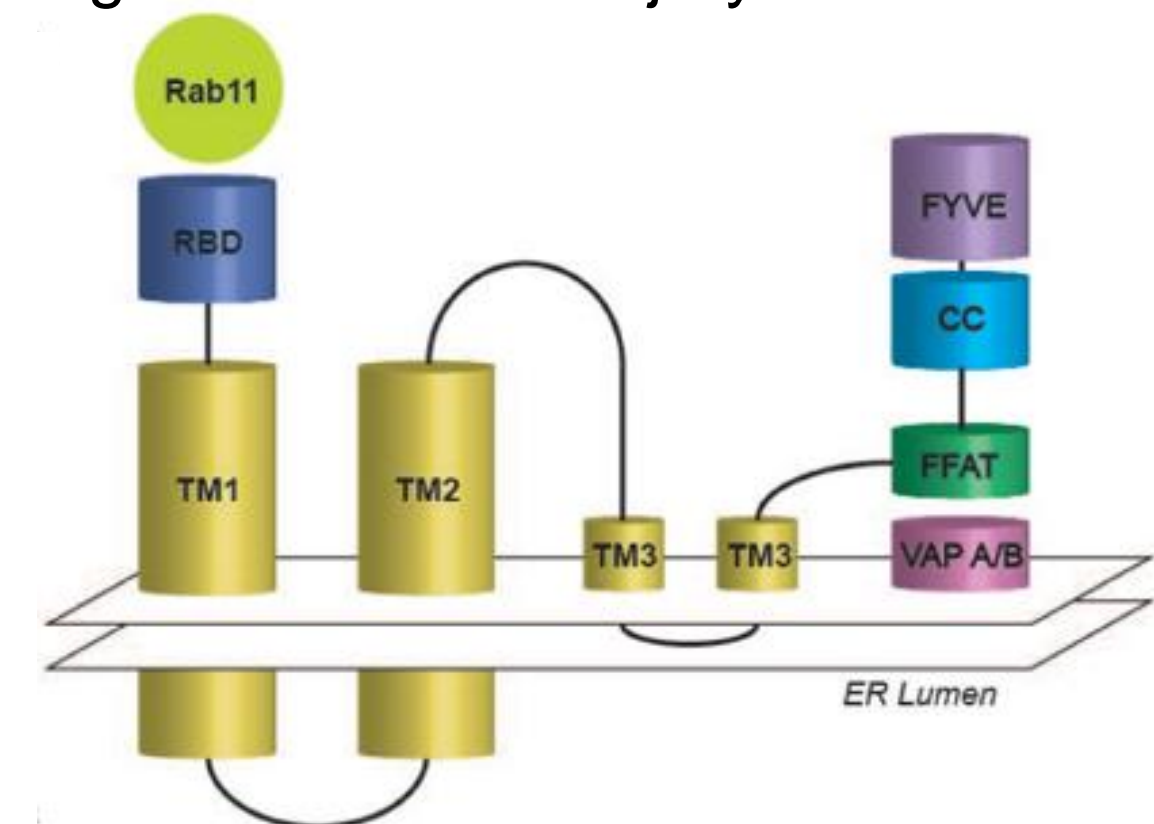
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## Introduction

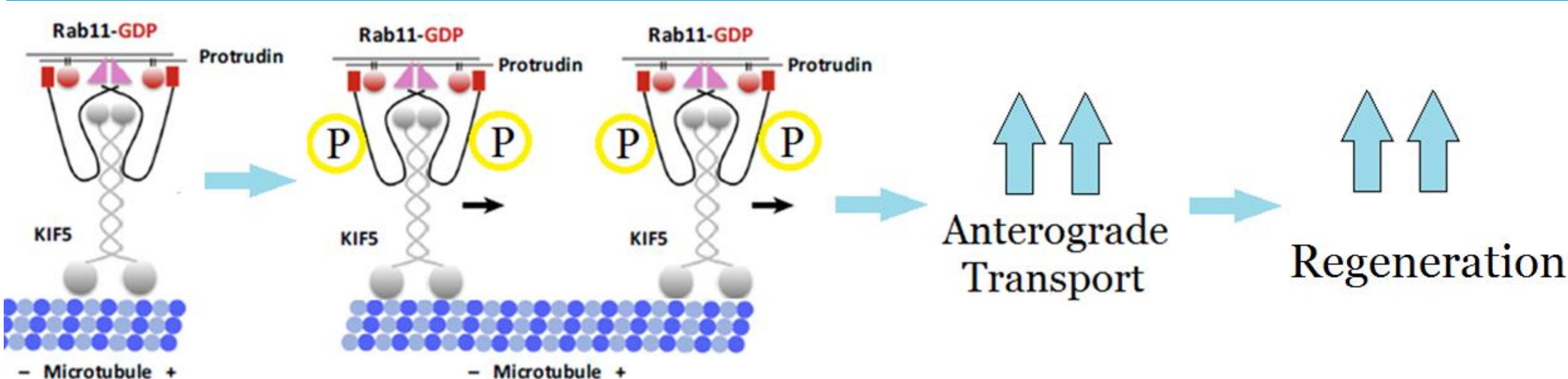
Adult CNS axons have **poor regenerative capabilities** for several reasons: 1) Decline in axon transport of growth molecules and organelles; 2) Epigenetic silencing; 3) Poor intracellular signalling and receptor activity.

Our aim is to restore the axon transport of growth molecules and organelles by manipulating components of their transport machinery in order to improve axon regeneration after injury.



**Protrudin (ZFYE27)**, a zinc-binding protein, is an ER-associated protein involved in neurite outgrowth and directional membrane trafficking. **Phospho-Protrudin** binds to **Rab11** and acts as a protein **adaptor** between **Rab11-tagged vesicles** and **kinesins**, aiding the anterograde movement of cargo.

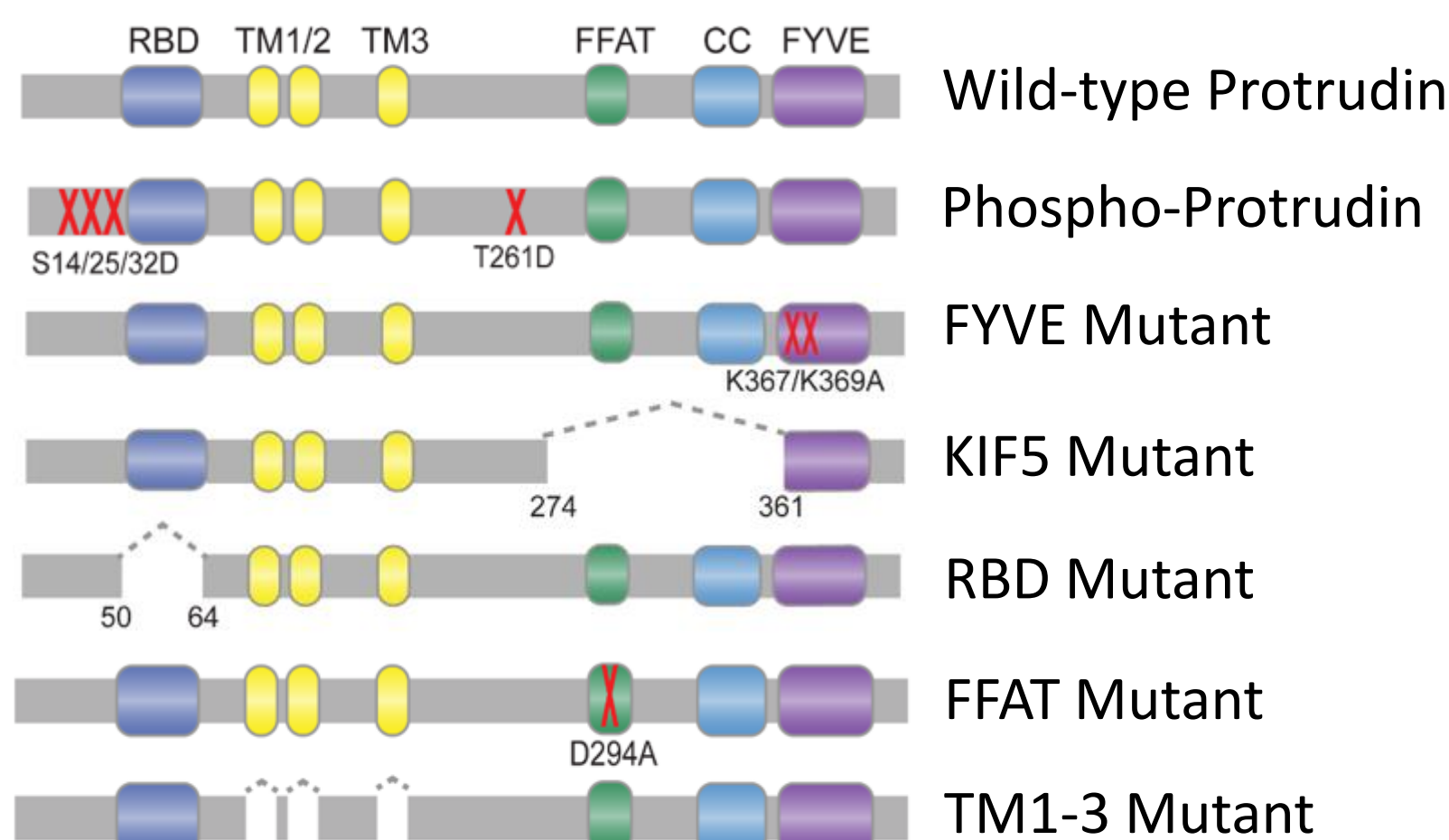
## Hypothesis



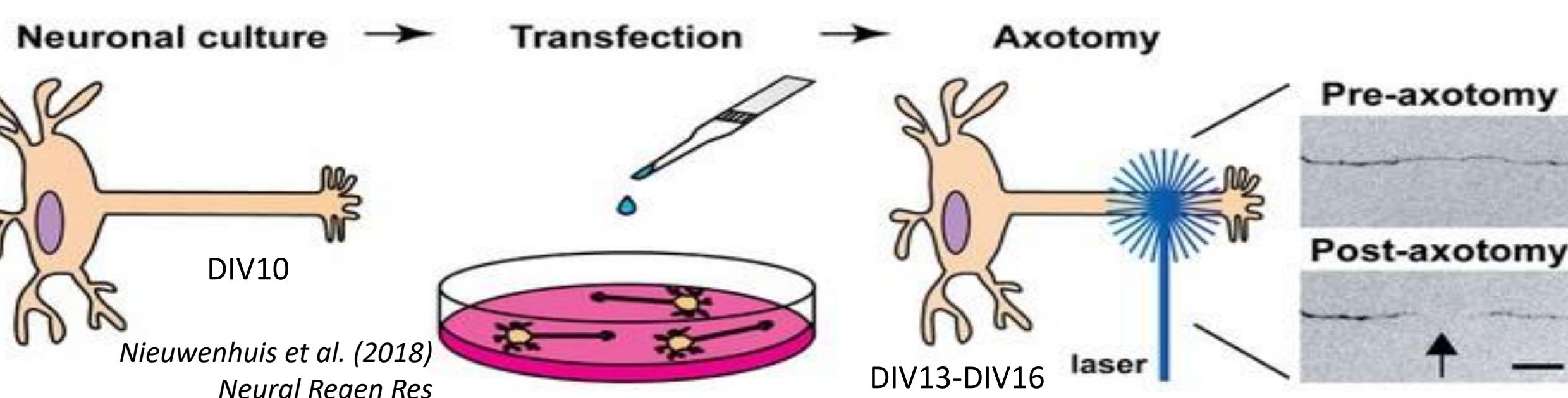
Constitutive phosphorylation of Protrudin will result in increased association with Rab11 which in turn will increase anterograde axon transport of growth-associated cargo to the tip of injured axons, subsequently resulting in improved regeneration.

## Methods

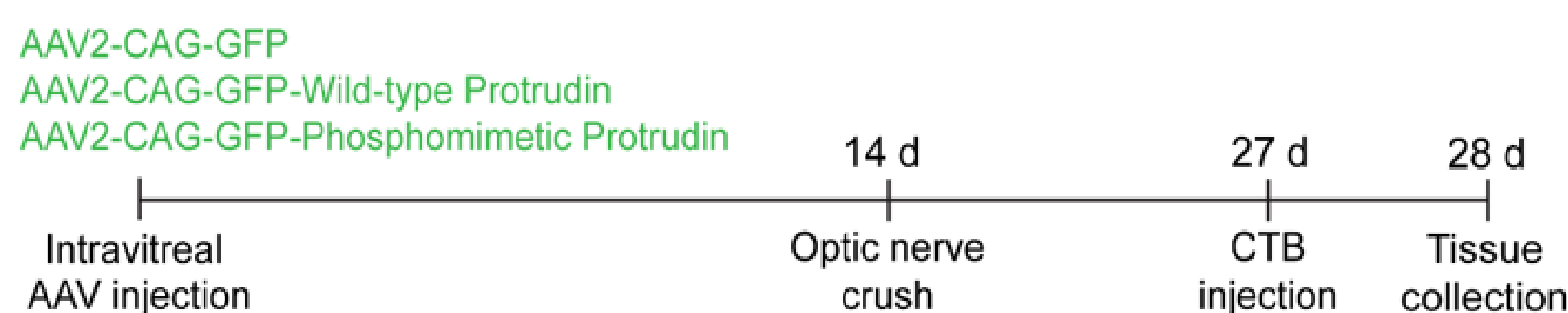
➤ **Mutagenesis of Protrudin** – two phosphomimetic forms as well as 5 domain mutant forms of protrudin were created.



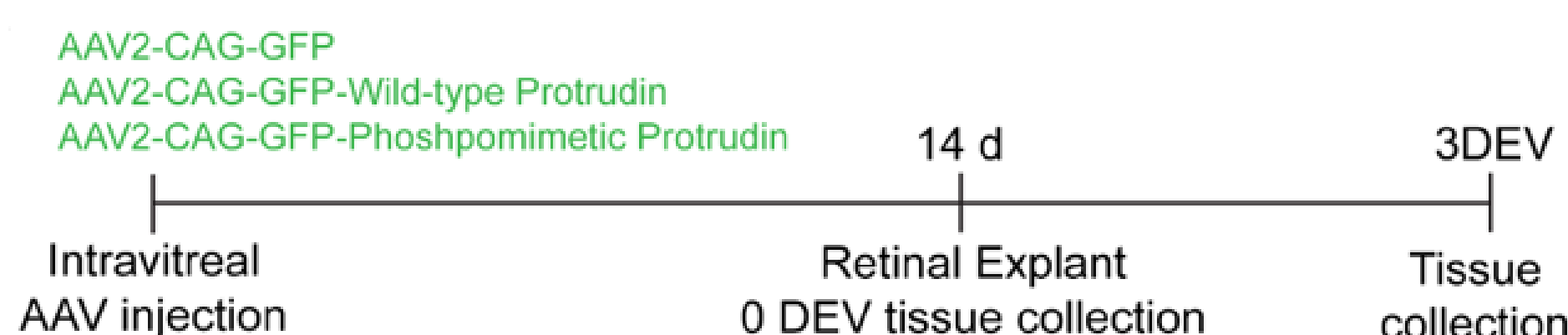
➤ **Cell Culture, transfections and laser axotomy**



➤ **Immunocytochemistry and live cell imaging**  
➤ **Optic nerve crush – survival and regeneration studies**



➤ **Retinal explant model – survival studies**

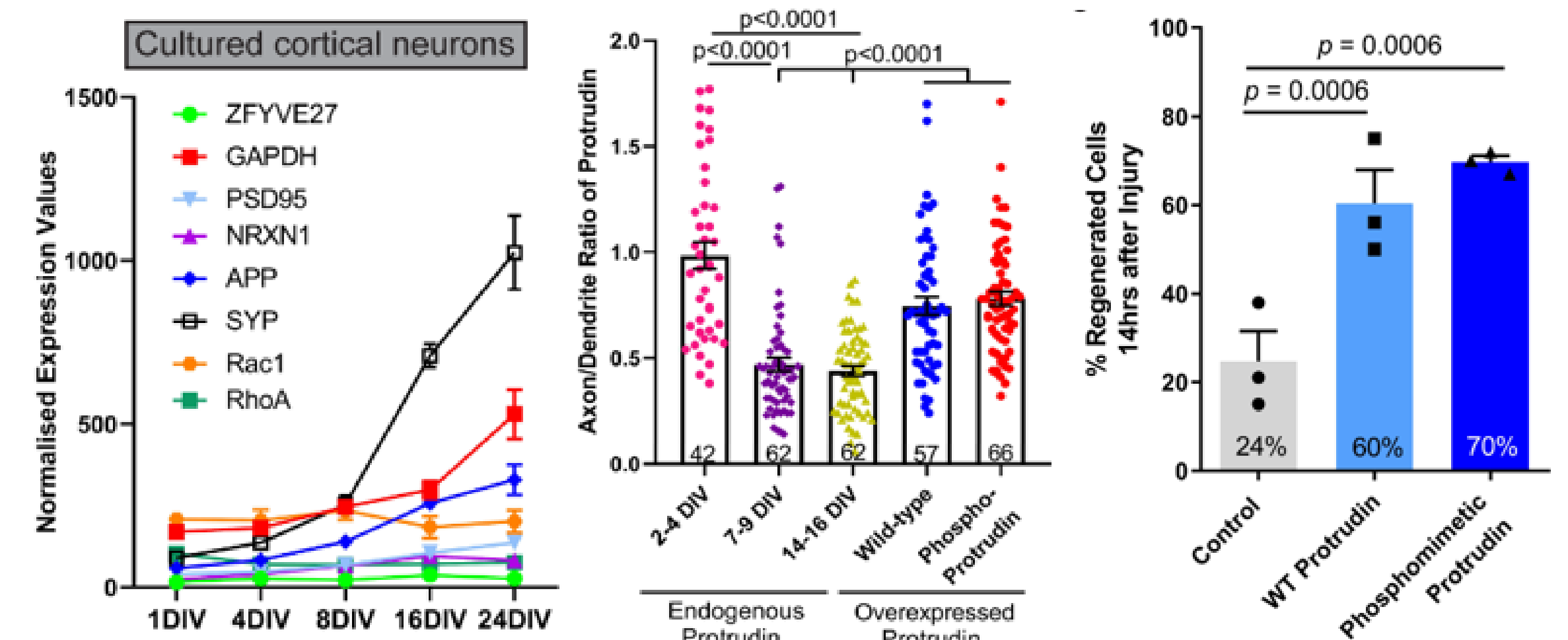


## References

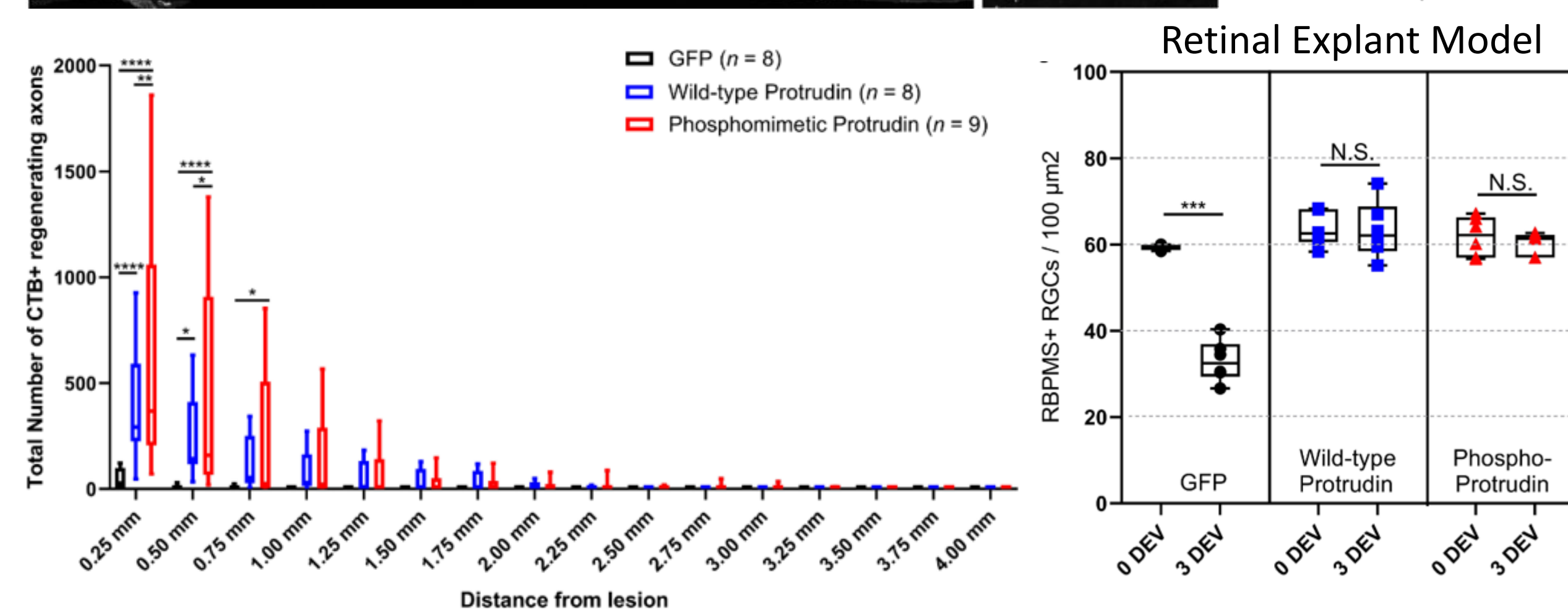
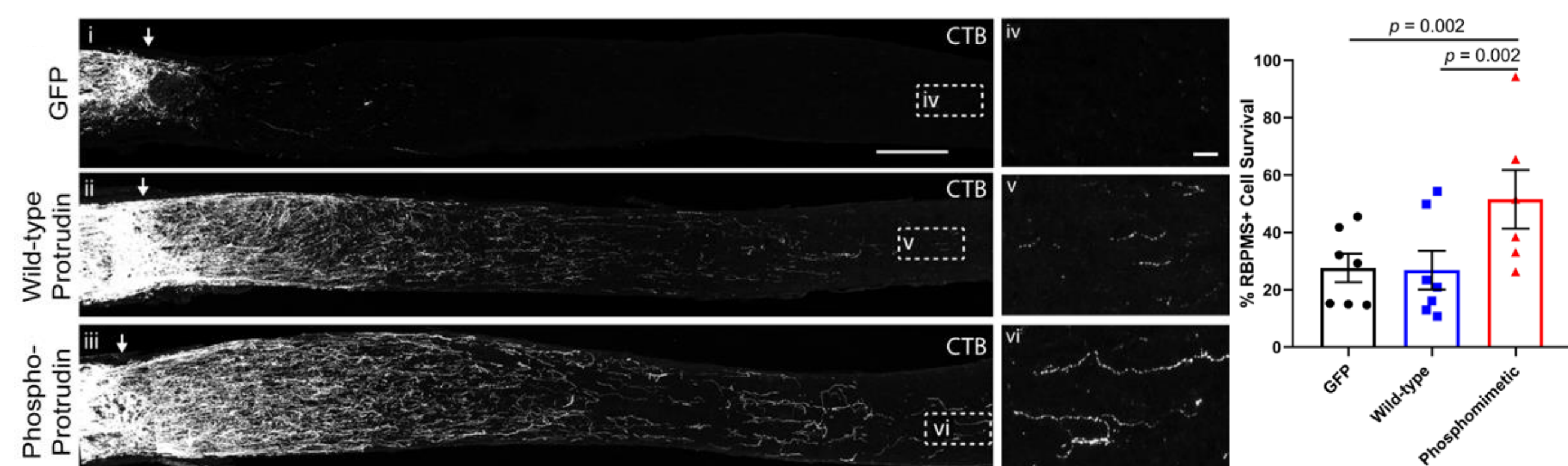
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## Results

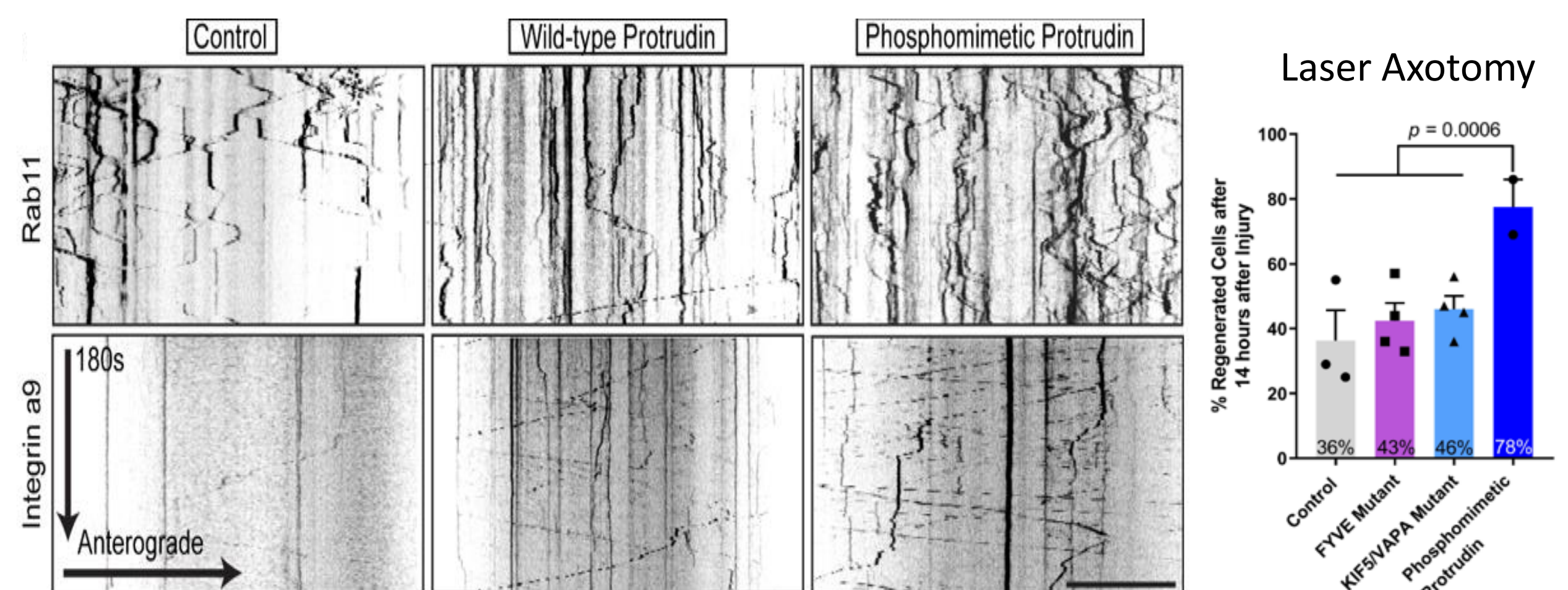
1. **Protrudin is found at low levels in axons and overexpression of wild-type and Phospho-Protrudin enhances axon regeneration after laser axotomy**



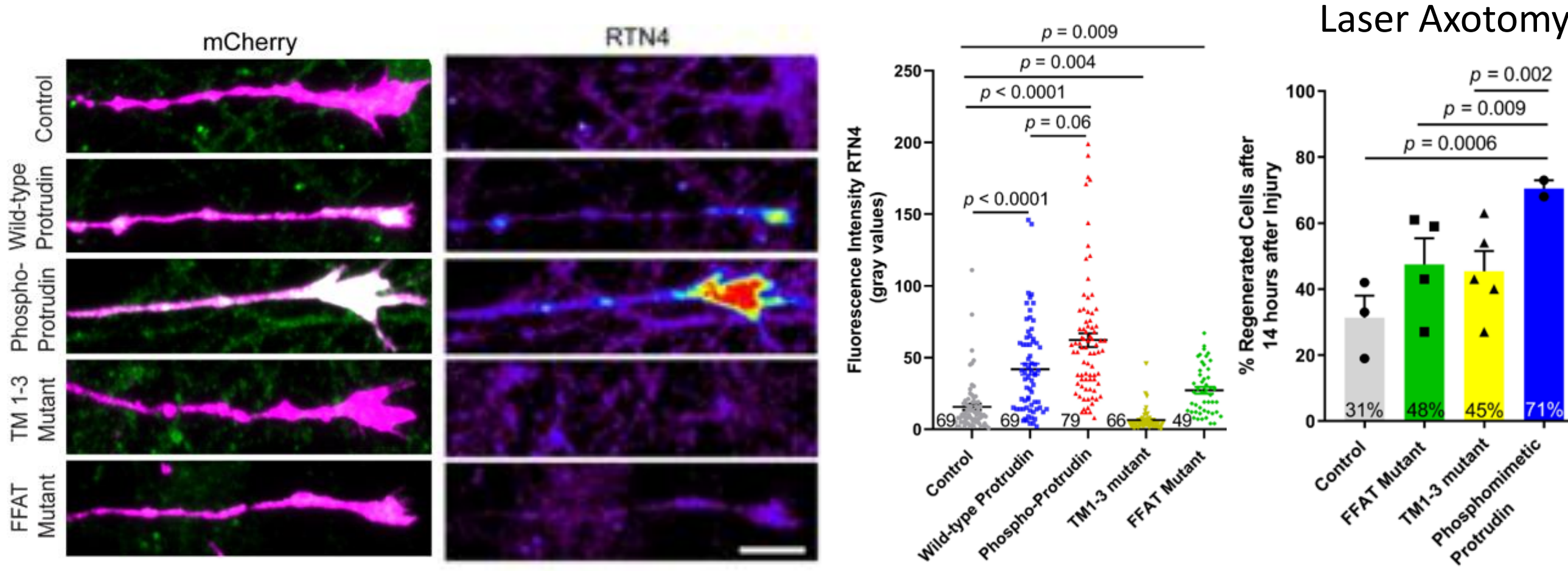
2. **Overexpression of wild-type or Phospho-Protrudin enhances axon regeneration and survival after optic nerve crush and retinal explant**



3. **Overexpression of Protrudin results in more Rab11- and integrin-associated vesicles in the distal axons and Protrudin's regenerative properties are aided by its involvement in axon transport**



4. **Protrudin's effect on axon regeneration is in part modulated by its interaction with the endoplasmic reticulum**



## Conclusion

**Protrudin acts as a scaffold protein bringing other molecules, cellular components and organelles in proximity at the tip of growing and injured axons.**