

Neurite elongation is enhanced in cells heterozygous for BDNF Val66Met polymorphism. Claire McGregor & Arthur English, Department of Cell Biology, Emory University School of Medicine, Atlanta, GA

Introduction

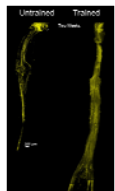
Poor Regeneration Of Axons In Peripheral Nerves Is a Major Public Health Problem

- Injuries to peripheral nerves are relatively common.
- 90% of patients never regain full function¹.
- Fewer than 20% of adult patients with transection nerve injuries (Sunderland stage 5) report *any* restoration of function over a ten year period¹.

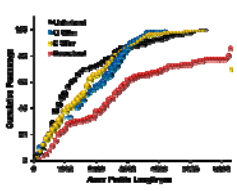
Axon regeneration is often blamed for these poor functional outcomes.

- The process is slow and inefficient.
- Some regenerating axons are not successful.

Activity-Dependent Treatments Enhance Axon Regeneration



Sabatier et al., 2008



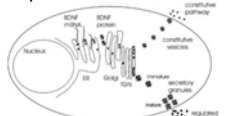
This enhancement depends on neuronal release of BDNF²

BDNF Val66Met Polymorphism



A Single Nucleotide Polymorphism in the BDNF gene, Val66Met, is present in over 25% of Americans

- This SNP results in:
- Decreased regulated release of BDNF³
 - Decreased dendritic trafficking of BDNF mRNA⁴
 - Increased p75NTR activation⁵

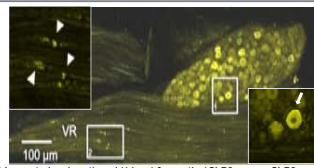


Kuczewski et al., 2009. Activity dependent release of BDNF and biological consequences. Mol Neurobiol 39(1): 37-49.

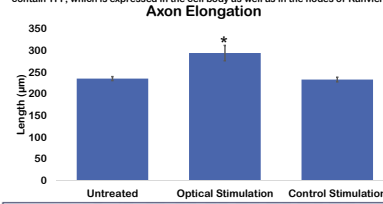
Hypothesis: Axon elongation will be greater in DRG neurons collected from V/M mice than those collected from V/V mice; optical stimulation will not enhance axon elongation in neurons from V/M mice.

Results

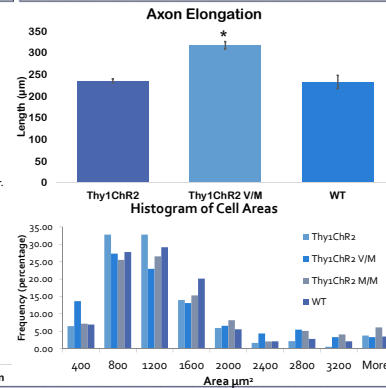
Optogenetic Stimulation Enhances Axon Elongation



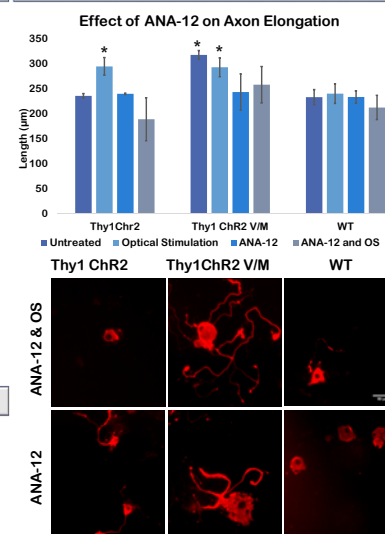
A DRG harvested and sectioned (14 μm) from a Thy1Chr2 mouse. Chr2+ cells contain YFP, which is expressed in the cell body as well as in the nodes of Ranvier.



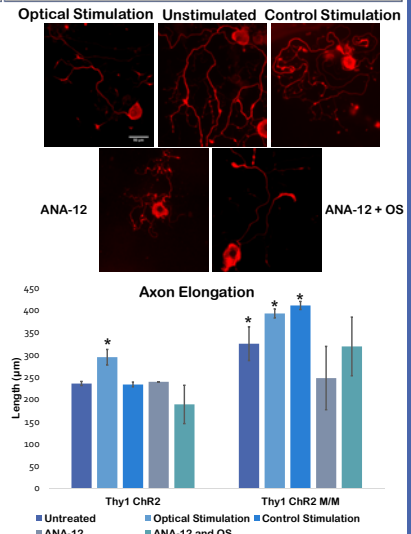
Axon Elongation is Enhanced in Neurons from V/M Mice



ANA-12 Inhibits Axon Elongation and Blocks Effect of Optical Stimulation



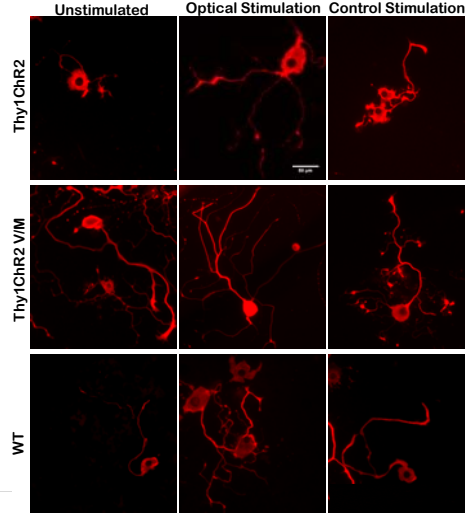
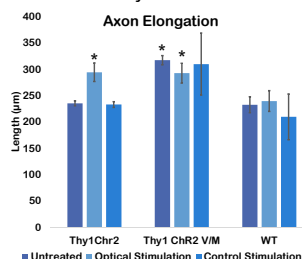
Axon Elongation is Enhanced in Neurons from M/M Mice



Optogenetic Stimulation Does Not Enhance V/M Axon Elongation



Lumos optical stimulation system (Axion BioSystems)
This study funded in part by Axion



Conclusions

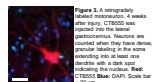
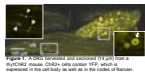
- 1 hr of optical stimulation enhances axon elongation in cultured adult sensory neurons
- Axon elongation is enhanced in cultured adult sensory neurons from V/M and M/M mice
- This enhanced growth is trkB-dependent
- Optical stimulation does not enhance growth in V/M and M/M neurons

Acknowledgements

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References

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Methods:
 Adult DRG neurons harvested from Thy1 ChR2 mice.
 48 Hours after plating treated with 1 hr of OS
 20Hz, 5ms pulse widths, 0.585 mW/mm²



