

# 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

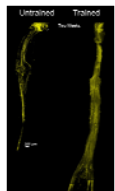
### Poor Regeneration Of Axons In Peripheral Nerves Is a Major Public Health Problem

- Injuries to peripheral nerves are relatively common.
- 90% of patients never regain full function<sup>1</sup>.
- Fewer than 20% of adult patients with transection nerve injuries (Sunderland stage 5) report *any* restoration of function over a ten year period<sup>1</sup>.

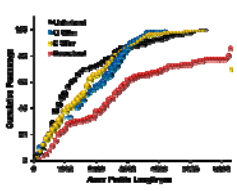
Axon regeneration is often blamed for these poor functional outcomes.

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

### Activity-Dependent Treatments Enhance Axon Regeneration



Sabatier et al., 2008



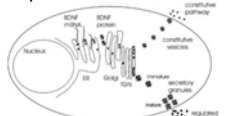
This enhancement depends on neuronal release of BDNF<sup>2</sup>

### 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 BDNF<sup>3</sup>
  - Decreased dendritic trafficking of BDNF mRNA<sup>4</sup>
  - Increased p75NTR activation<sup>5</sup>

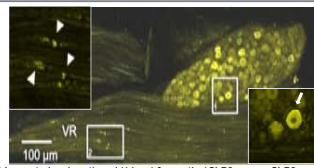


Kuczewski et al., 2009. Activity dependent release of BDNF and biological consequences. Mol Neurobiol 39(1): 37-49.

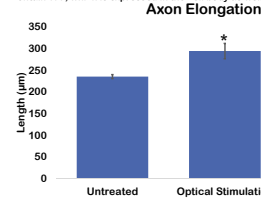
**Hypothesis: Axon elongation will be greater in DRG neurons collected from V/M mice than those collected from V/V mice; optical stimulation will not enhance axon elongation in neurons from V/M mice.**

## Results

### Optogenetic Stimulation Enhances Axon Elongation



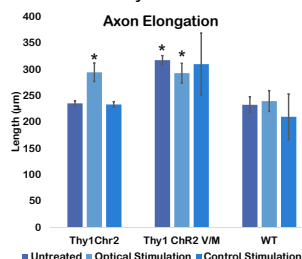
A DRG harvested and sectioned (14 μm) from a Thy1Chr2 mouse. Chr2+ cells contain YFP, which is expressed in the cell body as well as in the nodes of Ranvier.



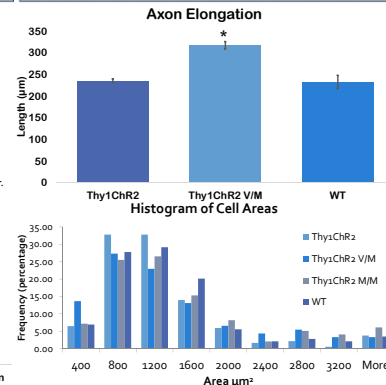
### Optogenetic Stimulation Does Not Enhance V/M Axon Elongation



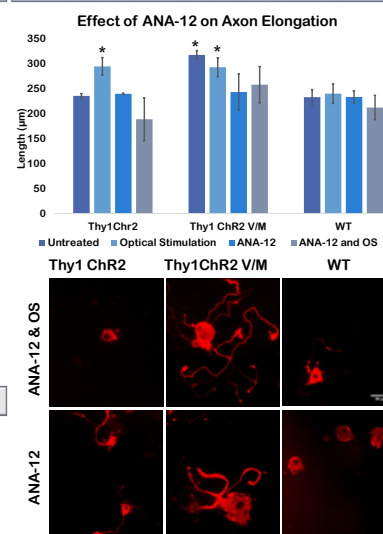
Lumos optical stimulation system (Axion BioSystems)  
This study funded in part by Axion



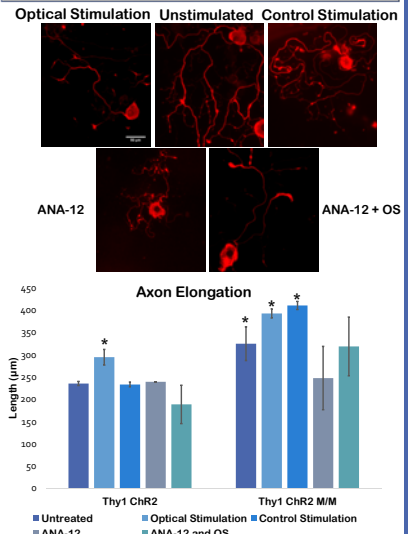
### Axon Elongation is Enhanced in Neurons from V/M Mice



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



### Axon Elongation is Enhanced in Neurons from M/M Mice



## Conclusions

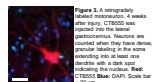
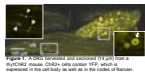
- 1 hr of optical stimulation enhances axon elongation in cultured adult sensory neurons
- Axon elongation is enhanced in cultured adult sensory neurons from V/M and M/M mice
- This enhanced growth is trkB-dependent
- Optical stimulation does not enhance growth in V/M and M/M neurons

## Acknowledgements

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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/mm<sup>2</sup>



