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Development of a method using retrograde neuronal tracers to neuroanatomically characterize respiratory neural circuitry

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**Sidney Kimmel
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Development of a method using retrograde neuronal tracers to neuroanatomically characterize respiratory neural circuitry

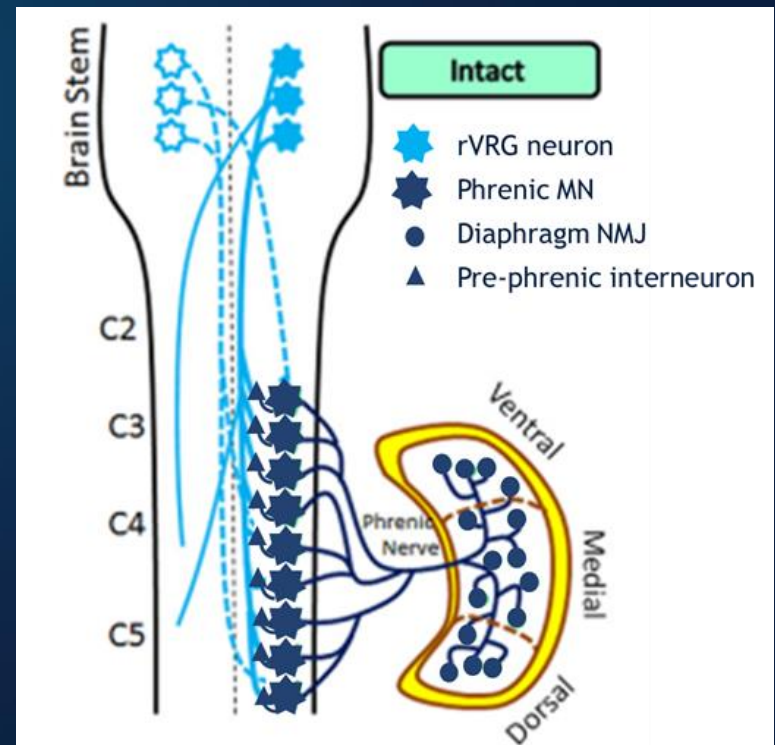
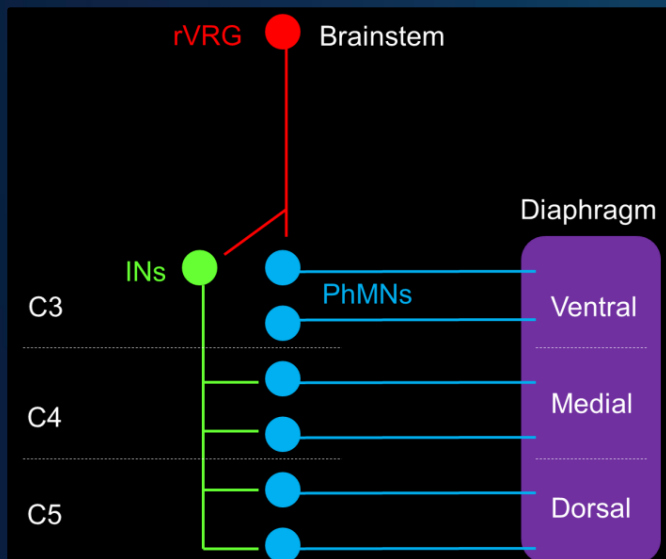
Samantha Thomas, Angelo Lepore*

(*) indicates primary project advisor

- There are over 270,000 Americans living with a spinal cord injury (SCI)
- The majority of SCI's are cervical
- Respiratory insufficiency is a common complication
 - Silencing & loss of phrenic motor neurons (PhMNs)
 - Loss of diaphragm function
- Significant contribution to morbidity & mortality
 - Increased risk of infection/pneumonia, pleural effusion, decreased cough reflex

Spinal cord has limited intrinsic capacity for recovery

- Several mechanisms
- Spinal interneurons contribute
- Little is known about pre-phrenic interneuron circuitry and remodeling

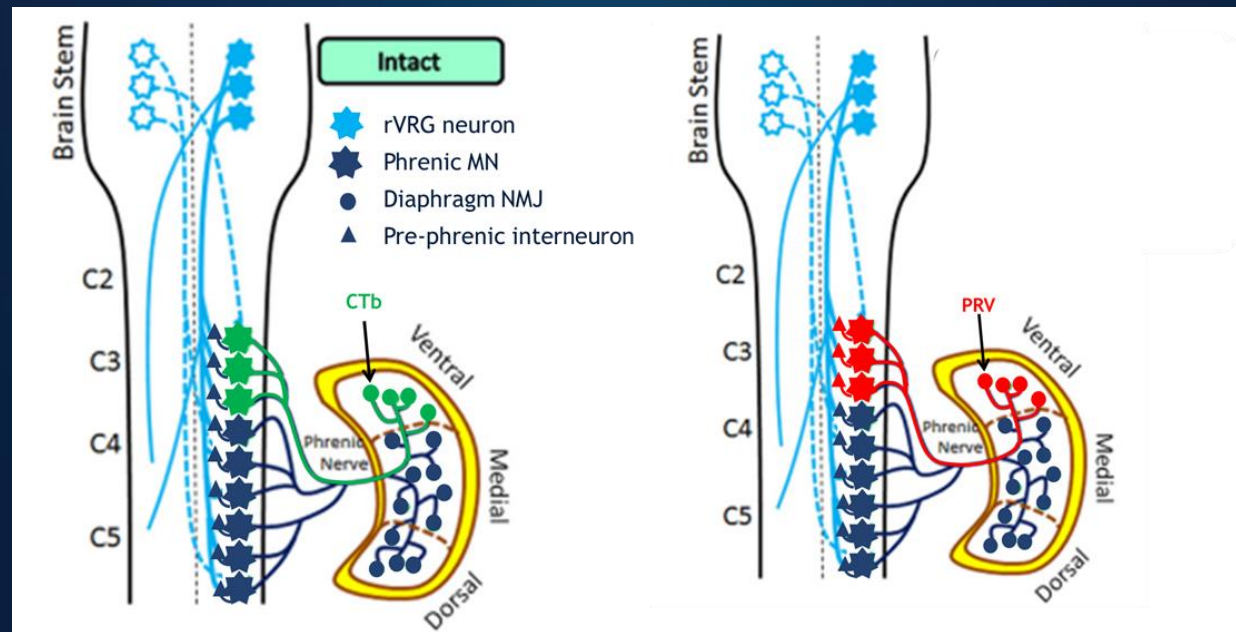


Objectives & Hypothesis

- **Research Question**
 - Short term: How can we develop a method to further investigate the role and distribution of interneurons within the respiratory circuitry?
 - Long term: How is the respiratory circuitry remodeled following cervical SCI?
- **Hypothesis**
 - Pre-phrenic interneurons undergo changes in plasticity following SCI that allow their recruitment into new circuits with damaged rVRG axons to help drive respiratory recovery

Approach: Validation of Method

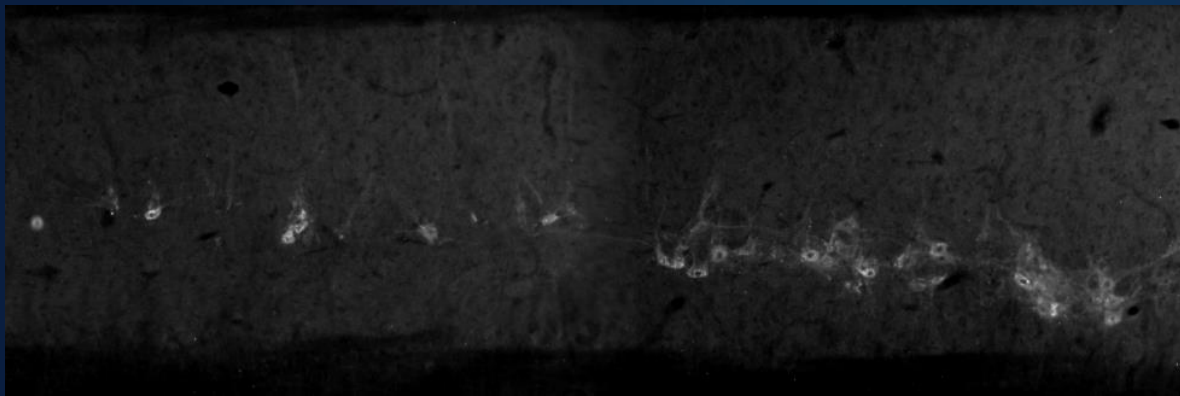
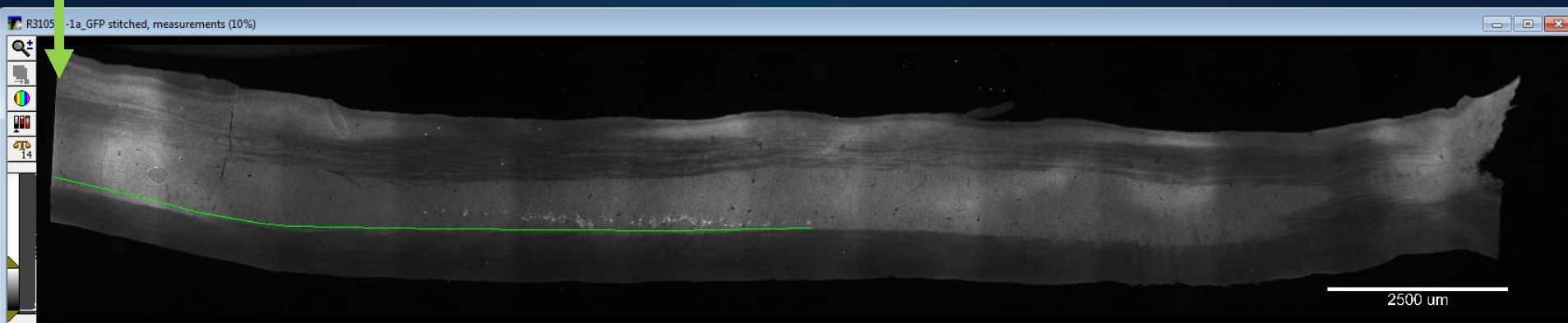
- Rat model
- Injury model: C2 hemisection
- Fluorophore-conjugated neuronal tracers
- Sagittal SC tissue cuts – microscopy & quantification
- Examine normal distribution of pre-phrenic interneurons (intact SC)



Rostral
C2

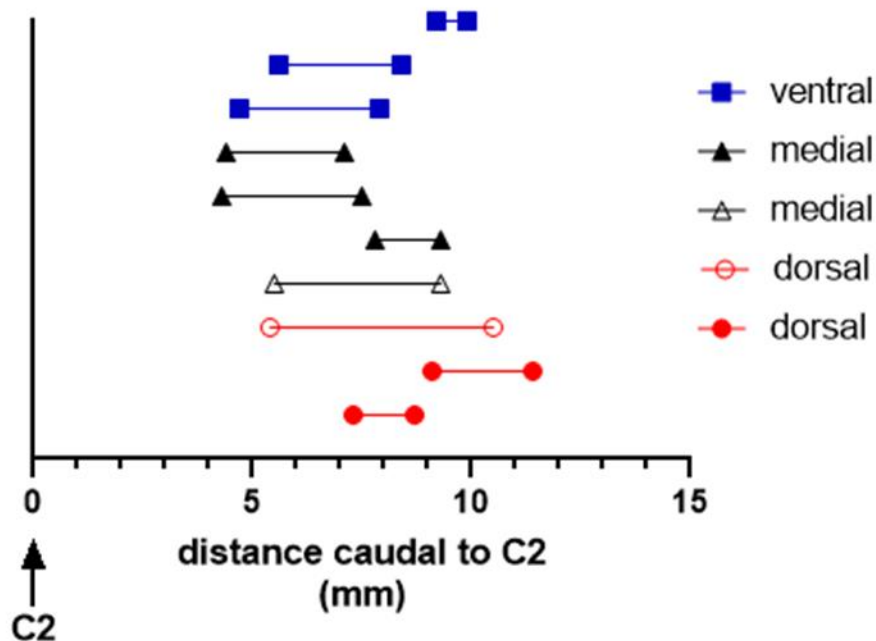
Caudal

Example of distance measurements: C2 to last labeled cell
(also recorded C2 to first labeled cell)



Higher resolution of CtB
labeled cells

Spread of cells labeled with CtB after application to individual hemidiaphragm subregions



- Each line is from one sagittal section
- Some animals had more than one section with labeled cells

Animals:

Ventral n=1 → C3

Medial n=2 → C4

Dorsal n=2 → C5

Conclusions

- Retrograde neuronal tracers can be successfully used to label and characterize the neurons involved in the respiratory circuitry
- Innervation of the hemidiaphragm is distributed topographically
- Issues with keeping tracers within the borders of each subregion can be addressed by ensuring the diaphragm is dry before application

Future Directions

- Apply method to SCI model
- Examine changes following injury
- Compare number of interneurons involved in the circuitry of each hemidiaphragm subregion in injured vs. uninjured animals
- Can this process be augmented?

Acknowledgements

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