Characterisation Of Axonal Injury Evolution In A Preclinical Model Of Traumatic Brain Injury.

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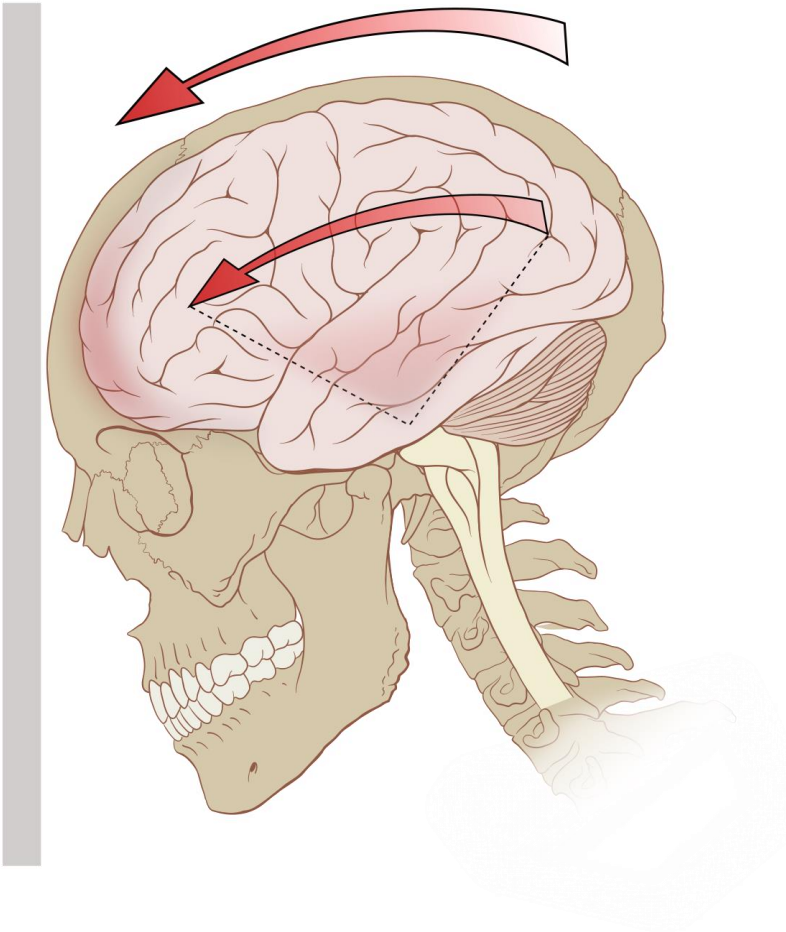
Traumatic Brain Injury

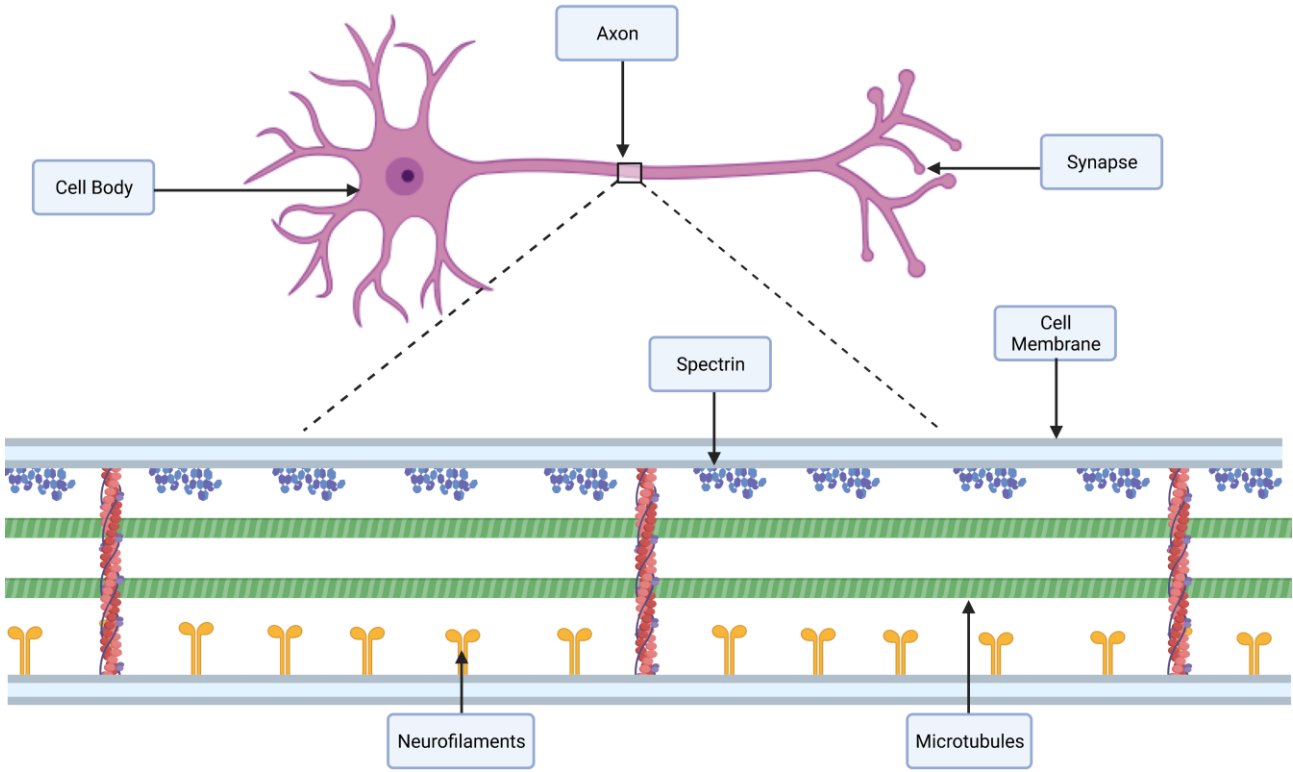
- Results from mechanical force to the brain
- Leading cause of death and disability for individuals under 45 years of age[1]
- Australian TBI Incidence: 99.1/100,000[2]
- Often results in physical, cognitive, behavioural and social deficits[3,4]
- Injury to neurons drives these deficits[4]



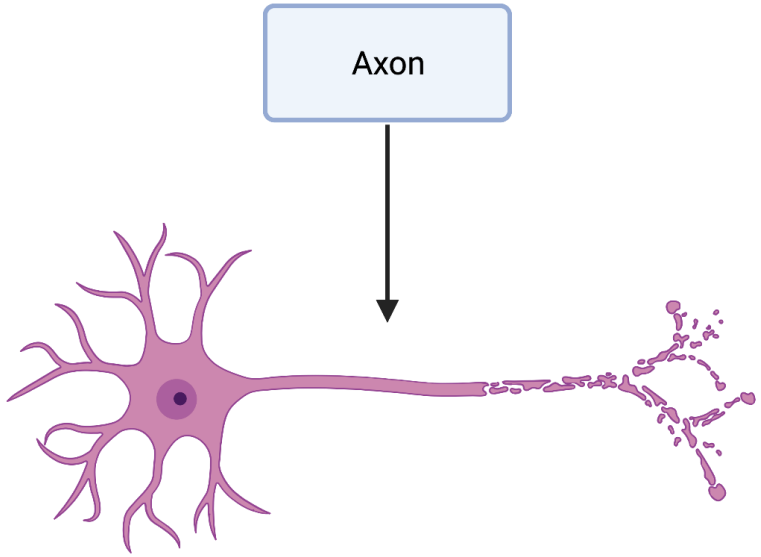
1. De Silva et al. 2009 *Int J Epidemio*
2. Gardner et al. 2015 *Mol Cell Neurosci*
3. Bierbaum et al. 2019 *Health Promot J Austr.*
4. Benedictus et al. 2010 *Arch. Phys. M.*

Neurons

- Functional cells of the brain
- Axons carry electrical signals from cell body to synapse
- Axons are vulnerable due to their elongated structure
- Supported with an internal scaffolding - cytoskeleton



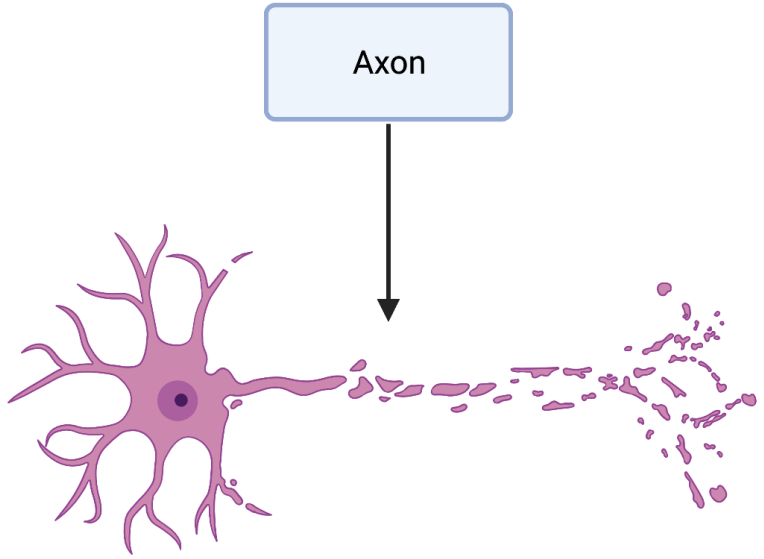
Axonal Injury Evolution



Primary

Result of mechanical insult

- Damages internal scaffolding of axons
- Irreversible

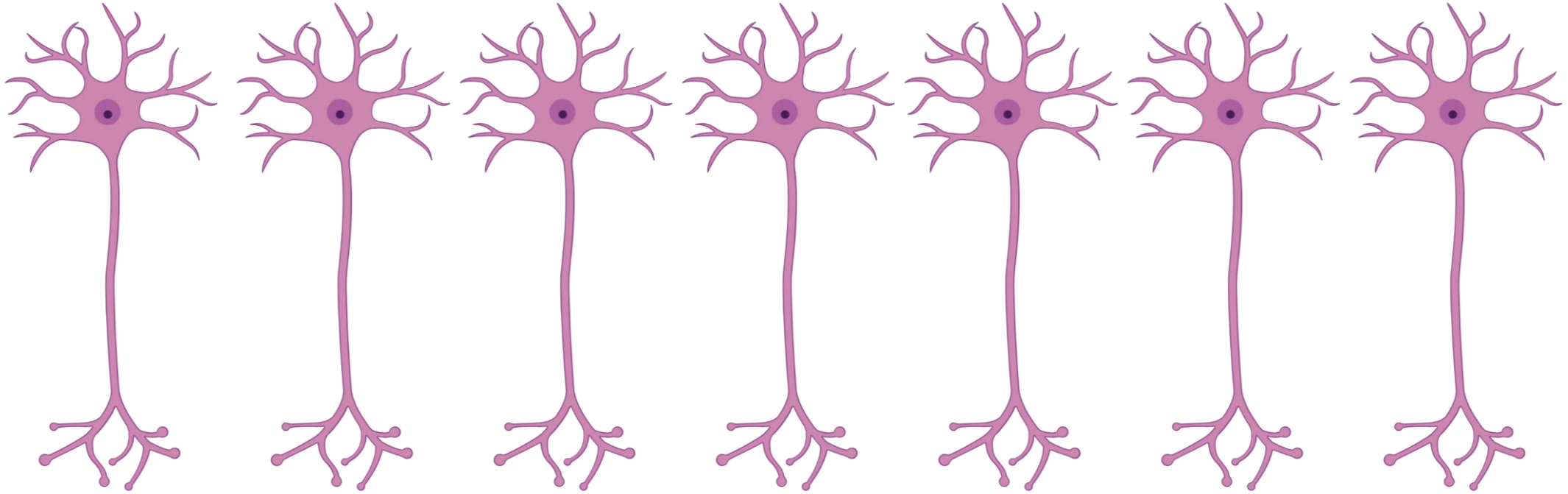


Secondary

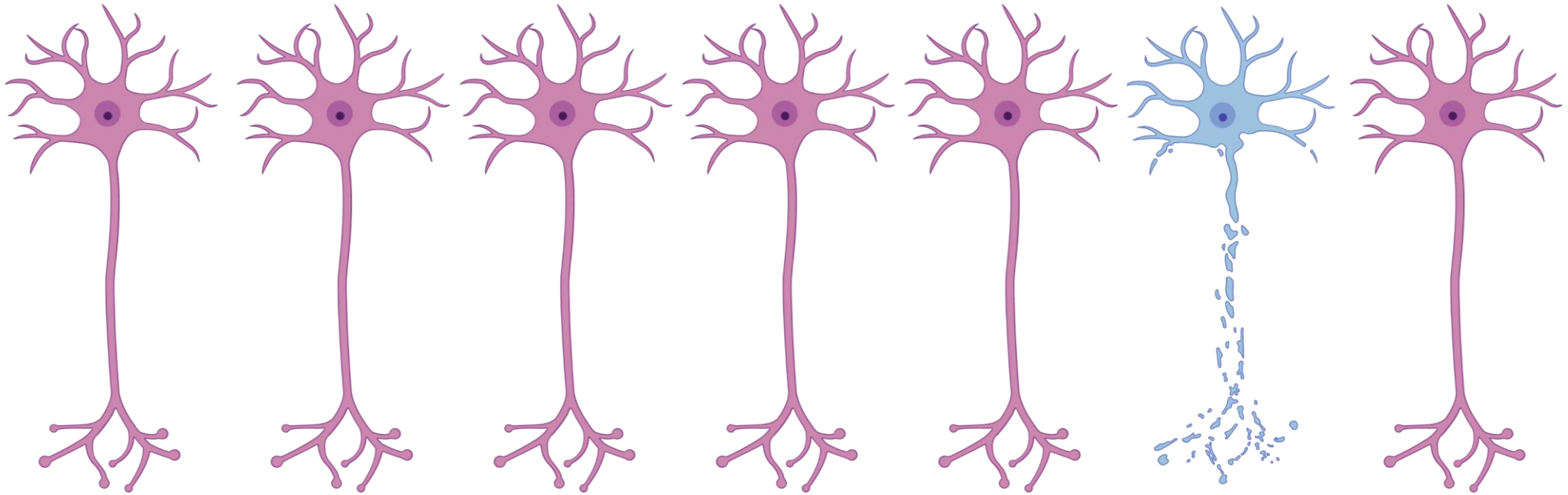
Biochemical response to the primary injury

- Dysfunction to axons, potentially causing cell death
- Potentially amenable to treatment

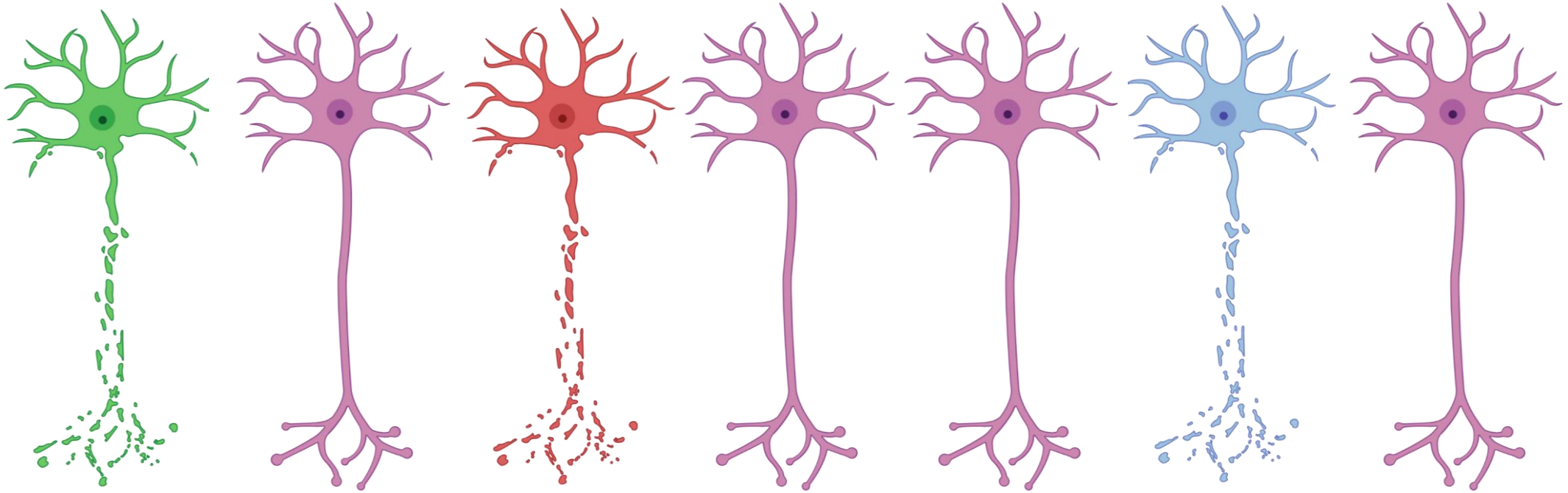
Diffuse Axonal Injury - Distribution



Diffuse Axonal Injury - Distribution

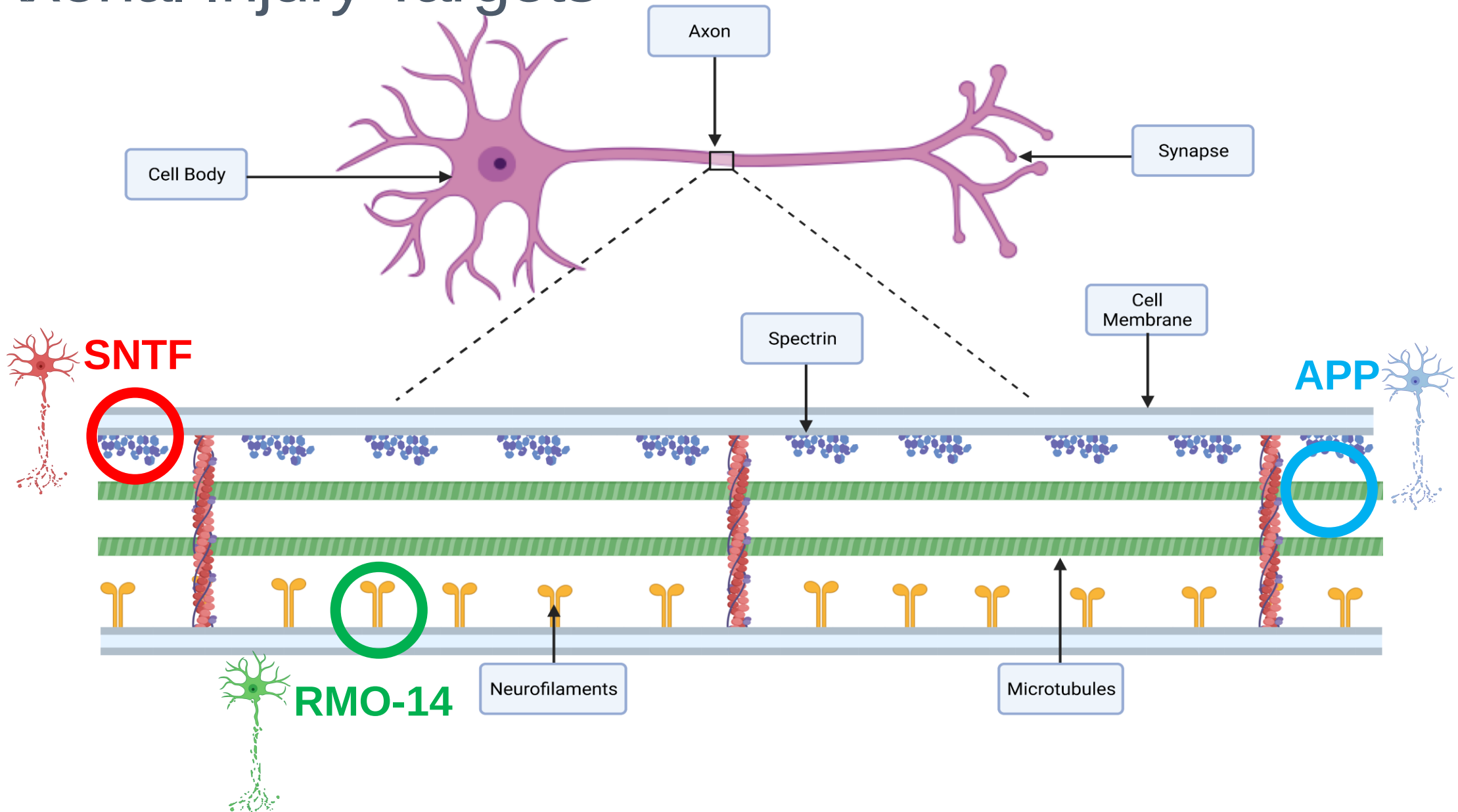


Diffuse Axonal Injury - Distribution

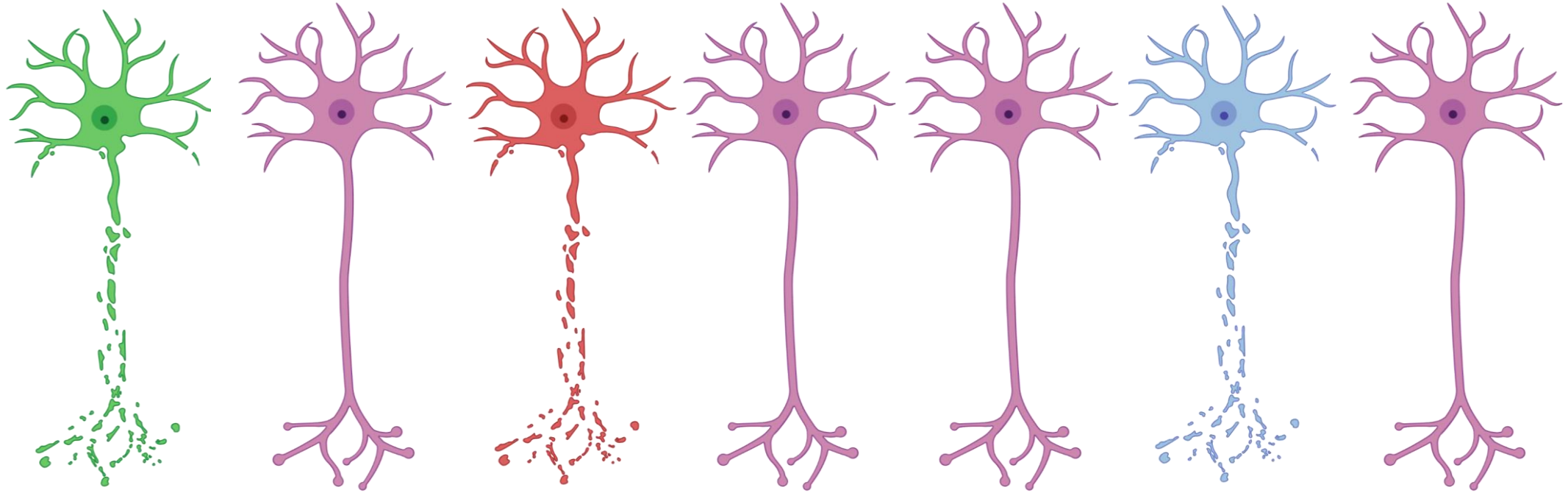


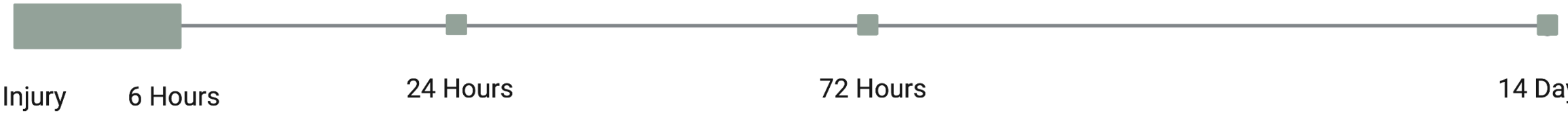
RMO-14 **SNTF** **APP**

Axonal Injury Targets

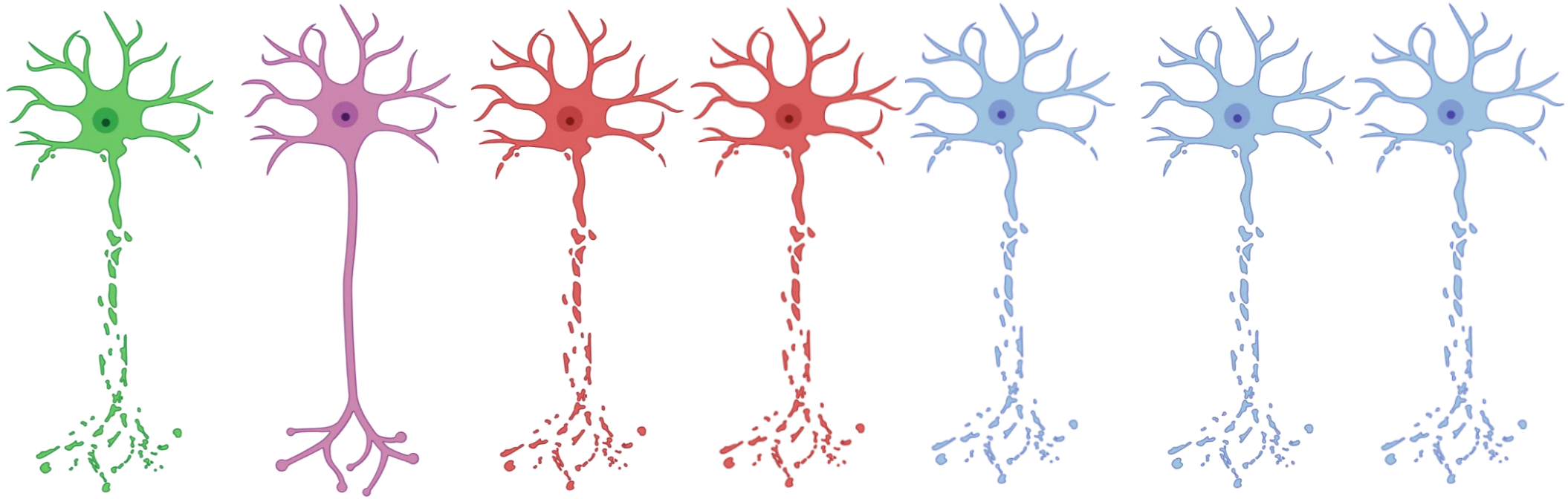


Diffuse Axonal Injury – 6 Hours





Diffuse Axonal Injury – 24 Hours



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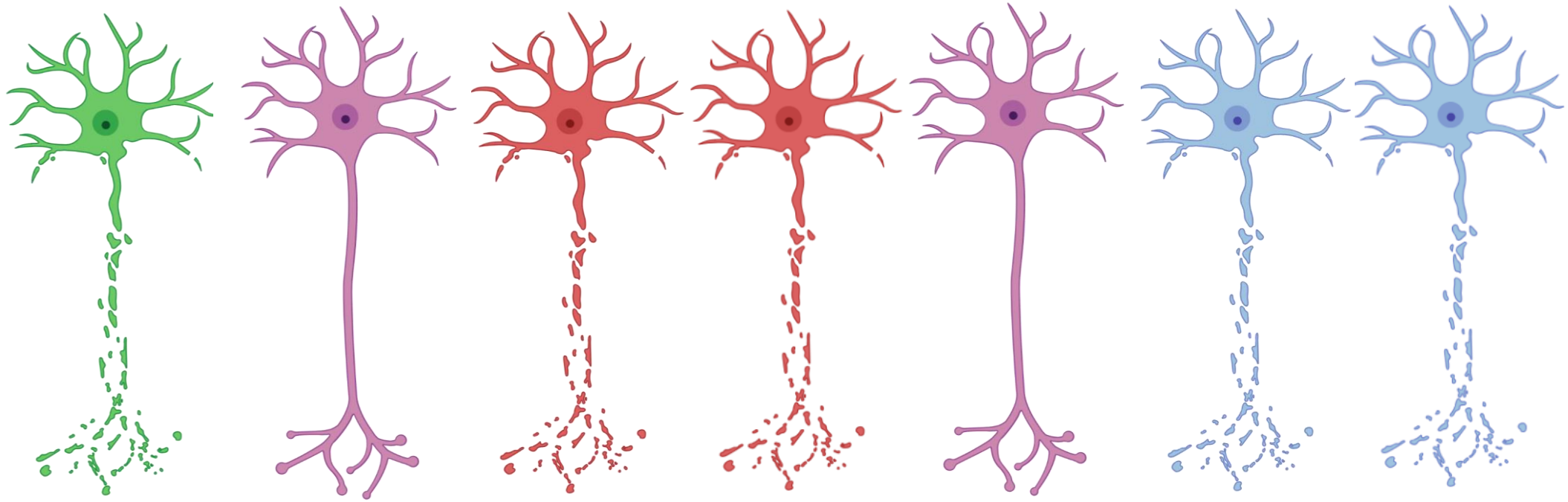
Injury 6 Hours 24 Hours 72 Hours 14 Days

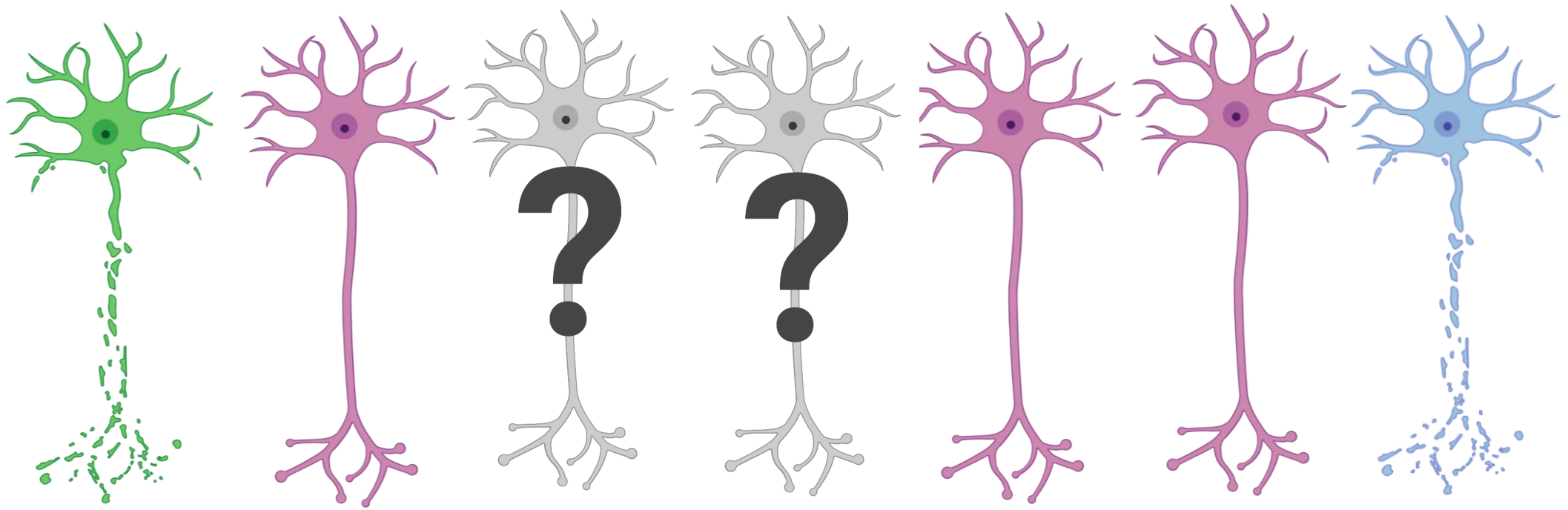
Diffuse Axonal Injury – 3 Days



RMO-14 SNTF APP

Injury 6 Hours 24 Hours 72 Hours 14 Days

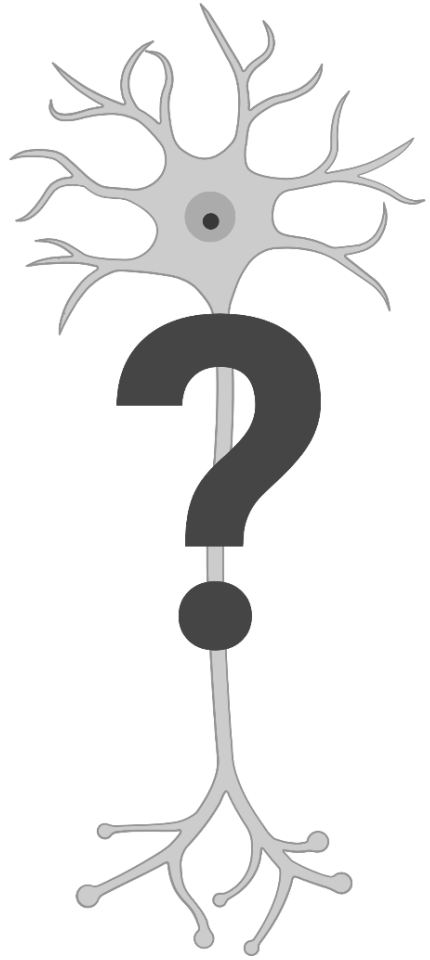
Diffuse Axonal Injury – 14 days



Injury 6 Hours 24 Hours 72 Hours 14 Days

Research Questions

- What is the spatial distribution of axonal injury following TBI in a pre-clinical model?
- How does this axonal injury evolve over time?
- How does an axonal injury treatment affect other markers of axonal injury?



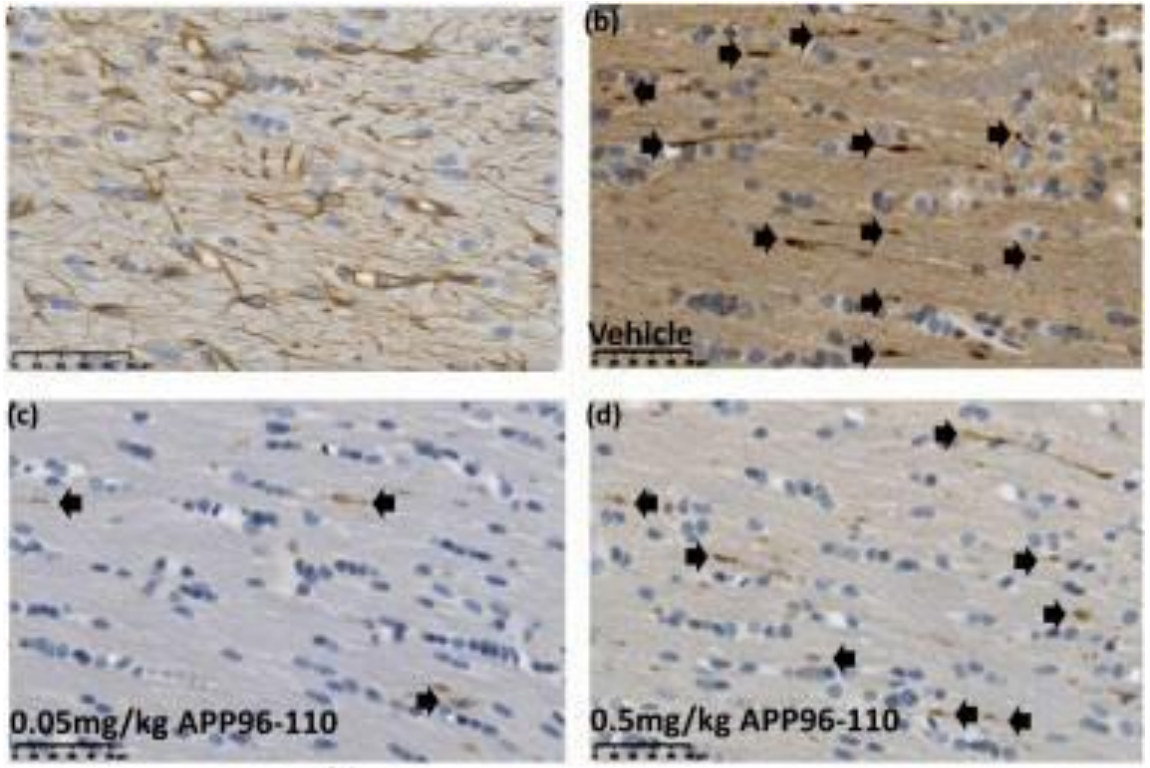
Treatment

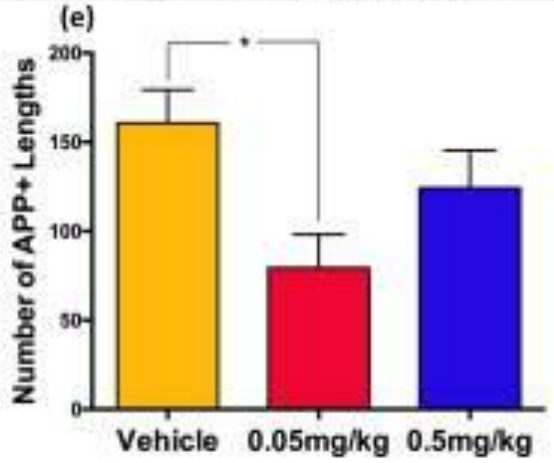
Tested within our lab:

- Attenuated axonal injury[14]
- Improved motor outcomes[14]

Drug targets:

- Stabilising the cytoskeleton





14. Plummer et al. 2018. *PLOS One*

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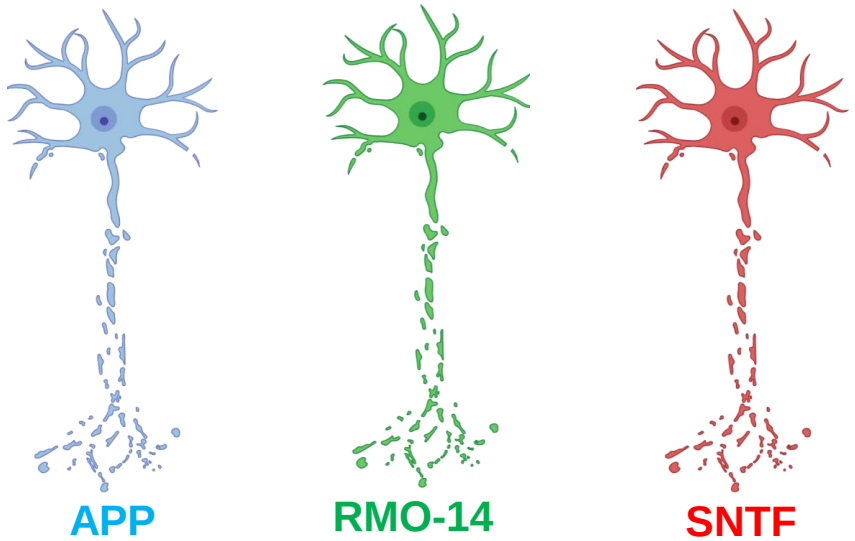

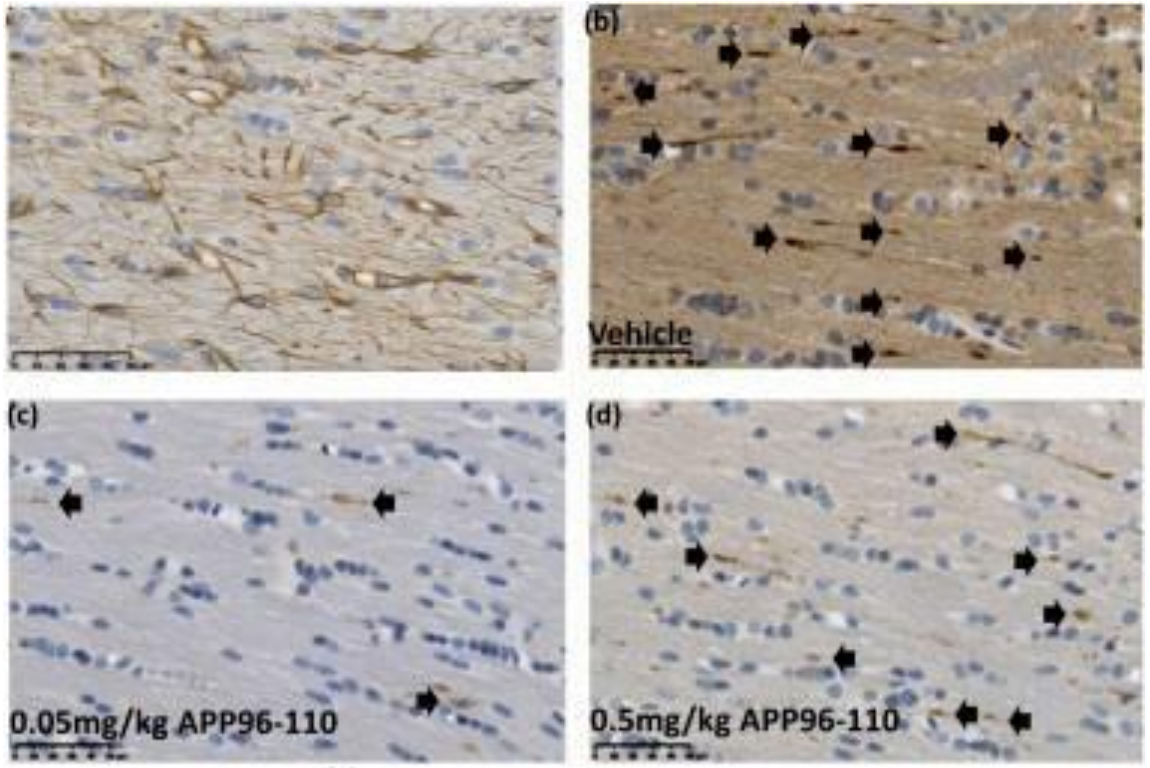

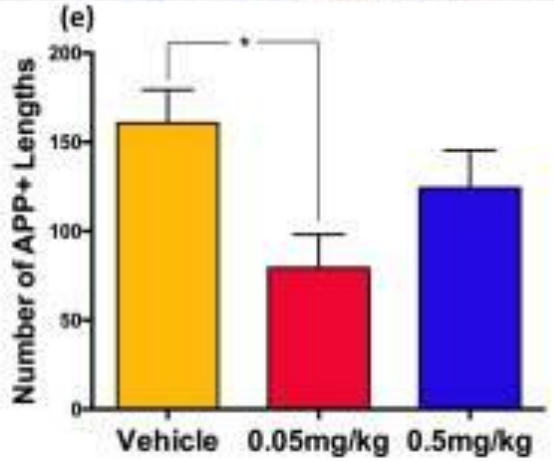

14. Plummer et al. 2018. *PLOS One*

Research Significance

- Extends our understanding of axonal injury evolution – potentially leading to more appropriate treatments and time courses

- Redefines how we evaluate axonal injury for drug treatments – helping to improve clinical translatability

Acknowledgments

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