Johns Hopkins Engineering

Methods in Neurobiology

Experimental Approach to Nerve Regeneration in the CNS

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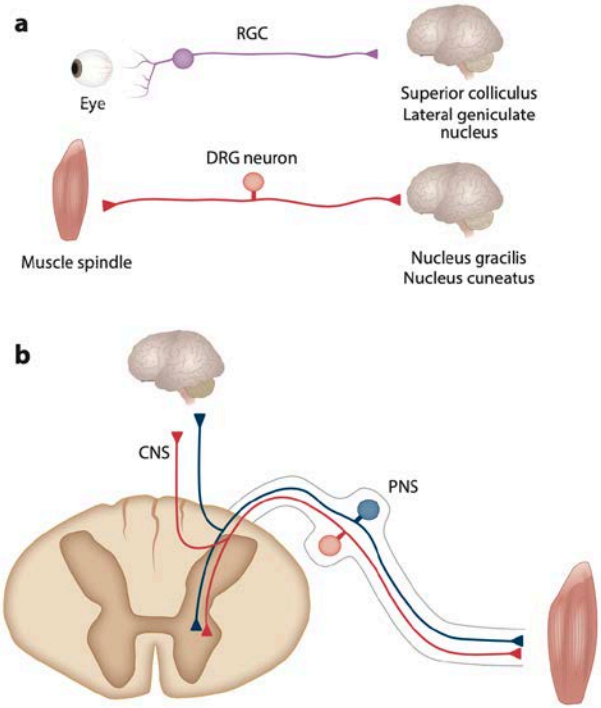
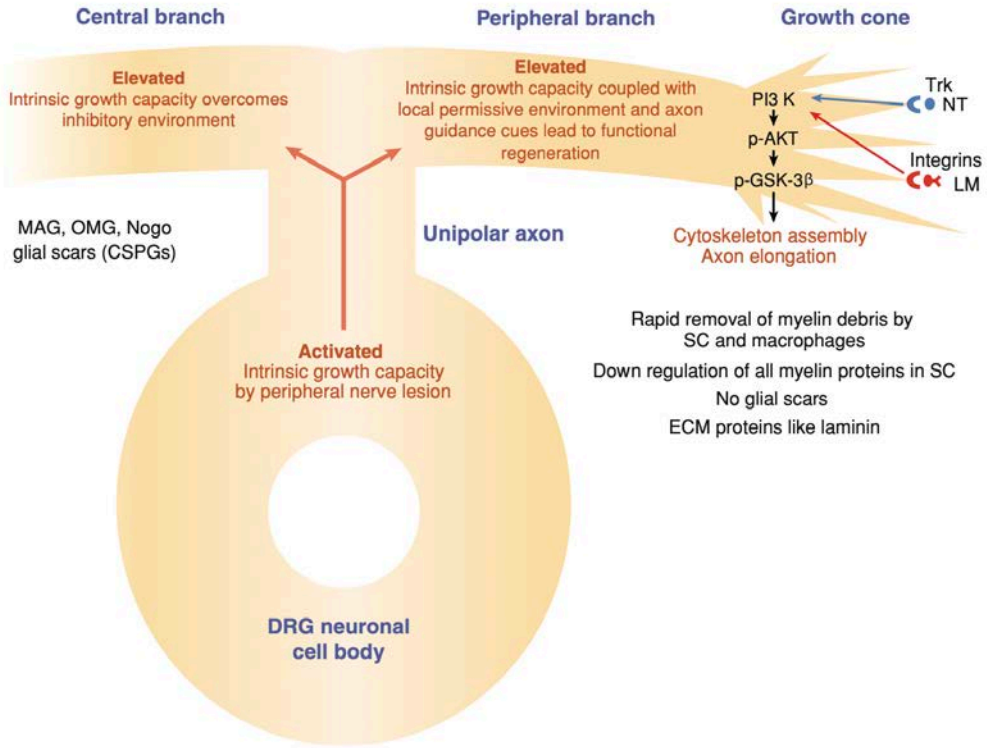
Models to study nerve regeneration in the CNS

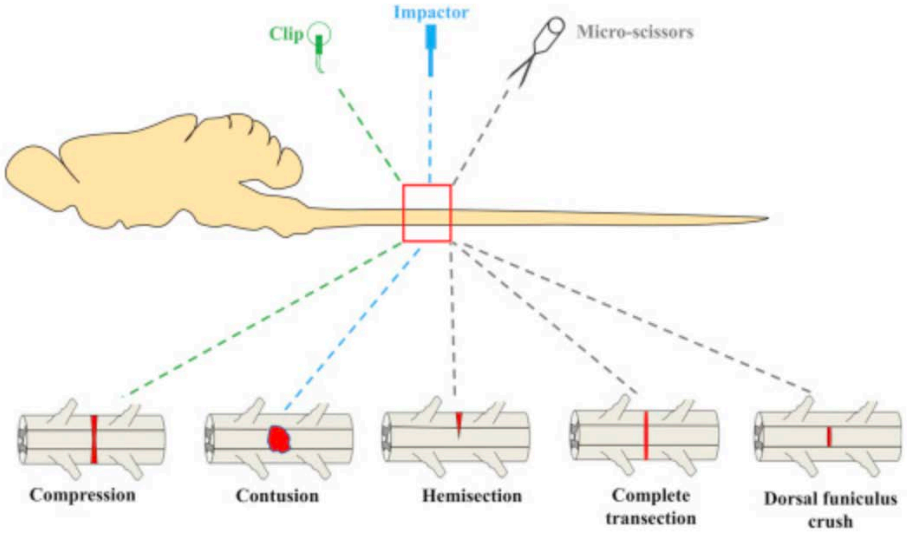


Animal models
Rats, mice (GEM)
Cats, dogs
Lower vertebrates (fish, frogs)
Invertebrates (C. Elegans)

Conditioning lesion paradigm



Models for Spinal Cord Injury



Contusion	Compression	Transection
• The model is useful for neuroprotective mechanism study [114]. • Ideal injury model for studying pathology and secondary injury mechanism [7]. • Difficult method with high variability [115]. • Recommended for translational research.	• Simple and reliable method [116]. • Suitable method to study secondary injury mechanism [16]. • Useful for cell transplantation therapy • Difficult to control the variability between subjects. • Suitable model for translational research [20].	• To study specific pathway function and regeneration [34]. • Easy to trace the axonal tract [34]. • Precise control over the injury. • Least variability between subjects. • Suitable model for neuroscience research.

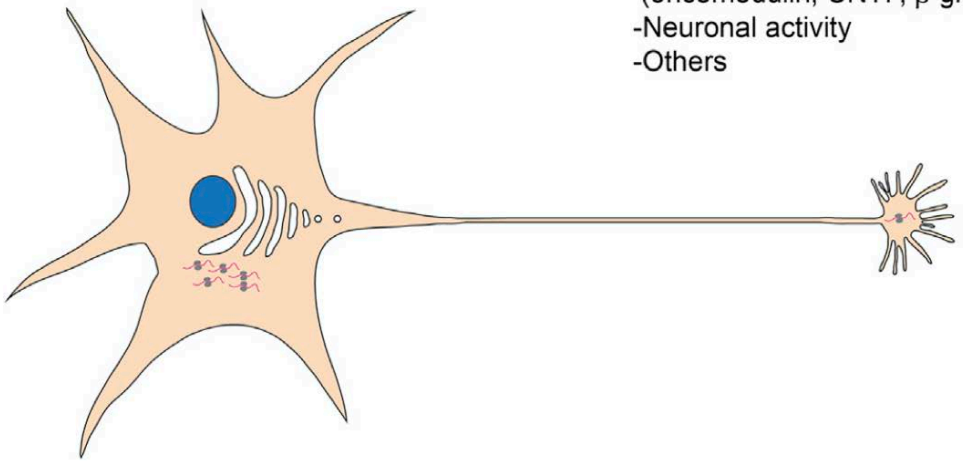
Strategies to improve nerve regeneration in the CNS

Enhancing intrinsic axon regenerative ability

cAMP production/signaling
Modulate PTEN/mTOR
Modulate SOCS3/STAT
Modulate MAPK
Transcription factors (KLFs, c-myc)
Osteopontin-based strategies

Modulate cytoskeleton
- -Taxol & epothilone B
- -DLK, EFA-6 & DCLKs

Augment pro-regenerative injury signals
- -Cytokine signaling
- -Inflammation based strategies (oncomodulin, CNTF, β-glucan)
- -Neuronal activity
- -Others



Strategies to improve nerve regeneration in the CNS

Strategy	Target	Methods/Drugs
Reactivating development	Degradation of ECM	chondroitinase-ABC
Blocking Inhibitory guidance cues	Blocking Wnt/Ryk signaling	Gene therapy
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Delivery of neurotrophic factors	Increased neurogenesis	BDNF
Cell replacement therapy	Fetal tissue or pluripotent stem cells	Surgery/injections

References

Slide	Reference
2	Curcio M, Bradke F. Axon Regeneration in the Central Nervous System: Facing the Challenges from the Inside. *Annu Rev Cell Dev Biol*. 2018;34:495-521.
3	Yu, W-M., Chen, Z-L., Strickland, S. 2007 Peripheral Regeneration Annu. Rev. Neurosci. 30:209–33.
4	Ahmed RU, Alam M, Zheng YP. Experimental spinal cord injury and behavioral tests in laboratory rats. *Heliyon*. 2019;5(3):e01324. Published 2019 Mar 8
5	He Z, Jin Y. Intrinsic Control of Axon Regeneration. *Neuron*. 2016;90(3):437-451