Regulating Gene Expression Networks to Promote Neuroprotection and Repair

March 19

Tuesday, 12:30 pm

Billings Building
Rosedale Room

SPEAKER:

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Host: BNI Postdocs

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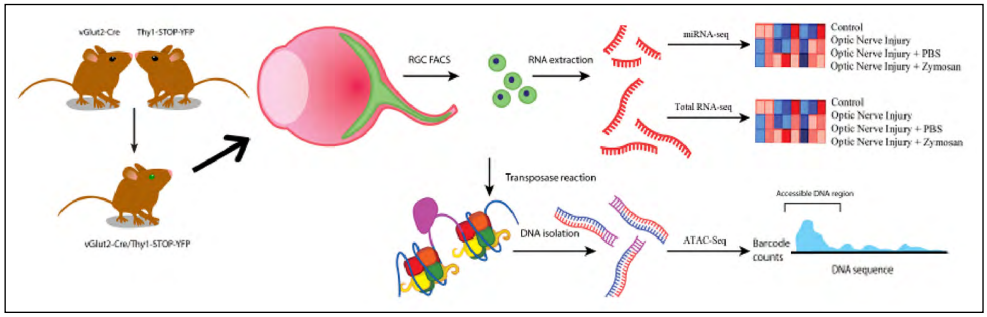
Abstract

Numerous neurological conditions and traumatic injuries disrupt connections between neurons in the adult mammalian Central Nervous System (CNS). CNS neurons have a limited capacity to regenerate axons following injury and facilitating axon regeneration could support neurological recovery and serve as an adjunct for cellular transplantation approaches. There are currently no approved treatments to stimulate CNS axon regeneration. An exciting advance in the CNS regeneration field is the demonstration that global alterations in the cell-intrinsic growth state of the neuron can trigger extensive axon regeneration even in the inhibitory CNS milieu. Genetic manipulation of oncogenes and tumor suppressors promote the most significant axon regeneration ever reported and this can be further enhanced by enhancing neuronal activity. Unfortunately, therapeutic translation of these experiments is limited because of the likely off-target consequences of targeting tumor suppressors and oncogenes. An alternative strategy to positively regulate the intrinsic growth state of the neuron is through trans-acting gene regulatory molecules such as miRNAs. Epigenetic mechanisms such as miRNA regulation can affect broad programs of gene expression, and this is a promising strategy to promote axon repair. We have conducted multi-modal sequencing of Retinal Ganglion Cell neurons subjected to pro-regenerative inflammatory stimuli. We have harnessed multi-modal sequencing information to identify pro-survival and pro-regenerative interventions based on miRNA regulation in in vitro cell culture and mouse optic nerve injury models. Regulating the intrinsic growth state of the neuron through trans-acting gene regulatory molecules such as miRNAs can positively influence neuronal cell survival and regeneration following CNS injury.



Publications

1. *Cellular rejuvenation protects neurons from inflammation mediated cell death.* Drake SS, Mohammadnia A, Heale K, Groh AMR, Hua EM, Zaman A, Hintermayer MA, Zandee S, Gosselin D, Stratton JA, Sinclair DA, Fournier AE. bioRxiv. 2023 Oct 2:2023.09.30.560301. doi: 10.1101/2023.09.30.560301. Preprint.

2. *Polypharmacological Perturbation of the 14-3-3 Adaptor Protein Interactome Stimulates Neurite Outgrowth.* Kaplan A, Andrei SA, van Regteren Altena A, Simas T, Banerjee SL, Kato N, Bisson N, Higuchi Y, Ottmann C, Fournier AE. Cell Chem Biol. 2020 Jun 18;27(6):657-667.e6. doi: 10.1016/j.chembiol.2020.02.010. Epub 2020 Mar 26. PMID: 32220335