Characterization of Immune Cells and Molecules that Promote and Suppress CNS Axon Regeneration

October 1

Tuesday, 12:30 pm

Billings Building—Rosedale Room

SPEAKER:

Roman J. Giger, Ph.D.

Richard Mark Newman Research Professor

Professor Cell and Developmental Biology

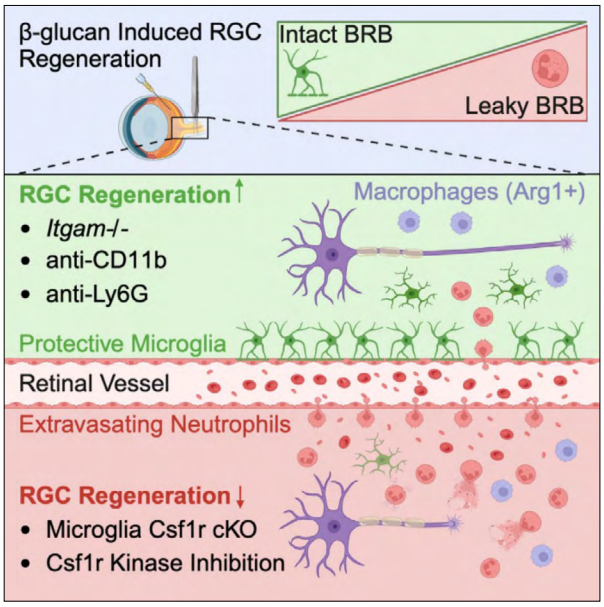
Professor Neurology

University of Michigan Medical School Ann Arbor, MI

Host: Rajiv R. Ratan, M.D., Ph.D.

For more information contact
Darlene White
daw9085@med.cornell.edu

Abstract



In adult mammals, injured retinal ganglion cells (RGCs) fail to spontaneously regrow severed axons, resulting in permanent visual deficits. Robust axon growth, however, is observed after intra-ocular injection of particulate β-glucan isolated from yeast. Blood-borne myeloid cells rapidly respond to β-glucan, releasing numerous pro-regenerative factors. Unfortunately, the pro-regenerative effects are undermined by retinal damage inflicted by an overactive immune system. In my presentation I will show that protection of the inflamed vasculature promotes immune-mediated RGC regeneration. In the absence of microglia, leakiness of the blood-retina barrier increases, pro-inflammatory neutrophils are elevated, and RGC regeneration is reduced. Functional ablation of the complement receptor 3 (CD11b/integrin-αM), but not the complement components C1q-/- or C3-/-, reduces ocular inflammation, protects the blood-retina barrier, and enhances RGC regeneration. Selective targeting of neutrophils with anti-Ly6G does not increase axogenic neutrophils but protects the blood-retina barrier and enhances RGC regeneration. Selective blocking of blood-borne monocytes from entering the eye upon ocular β-glucan administration resulted in significantly reduced RGC axon regeneration. Together, these findings reveal pro-regenerative and detrimental activities of specific myeloid cell populations toward injured CNS neurons and show that protection of the inflamed vasculature promotes neuronal regeneration.

Publications

1. Passino R, Finneran MC, Hafner H, Feng Q, Huffman LD, Zhao XF, Johnson CN, Kawaguchi R, Oses-Prieto JA, Burlingame AL, Geschwind DH, Benowitz LI, Giger RJ. *Neutrophil-inflicted vasculature damage suppresses immune-mediated optic nerve regeneration.* 2024 Mar 26;43(3):113931. doi: 10.1016/j.c elrep.2024.113931. Epub 2024 Mar 15.PMID: 38492223

2. Schmitd LB, Hafner H, Ward A, Asghari Adib E, Biscola NP, Kohen R, Patel M, Williamson RE, Desai E, Bennett J, Saxman G, Athaiya M, Wilborn D, Shumpert J, Zhao XF, Kawaguchi R, Geschwind DH, Hoke A, Shrager P, Collins CA, Havton LA, Kalinski AL, Giger RJ. *Sarm1 is not necessary for activation of neuron-intrinsic growth programs yet required for the Schwann cell repair response and peripheral nerve regeneration.* bioRxiv 2024 Apr 17:2024.03.04.583374. doi: 10.1101/2024.03.04.583374. PMID: 38496662.

3. Zhao XF, Huffman LD, Hafner H, Athaiya M, Finneran MC, Kalinski AL, Kohen R, Flynn C, Passino R, Johnson CN, Kohrman D, Kawaguchi R, Yang LJS, Twiss JL, Geschwind DH, Corfas G, Giger RJ. *The injured sciatic nerve atlas (iSNAT), insights into the cellular and molecular basis of neural tissue degeneration and regeneration.* Elife. 2022 Dec 14;11:e80881. doi: 10.7554/eLife.80881.PMID: 36515985

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Academic Affiliate of Weill Cornell Medicine
785 Mamaroneck Avenue, White Plains, NY 10605
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