Characterizing AAVrg Infection in Peripheral Nervous Tissue Following Injection of Constructs to Mouse Sciatic Nerve Dartmouth GEISEL SCHOOL OF MEDICINE



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Conclusions

AAVrg hSyn eGFP had a significantly higher rate of Schwann cell specific infection than AAVrg CAG tdTomato in the mouse sciatic nerve. The hSyn promoter confers greater transduction of gene targets.

AAVrg hSyn eGFP had minimal infection of axons and AAVrg CAG tdTomato does not infect neurons at all when injected into the sciatic

Signs of degeneration in the right sciatic nerve tissue were appreciable in tissue sections. This did not appear to have any effect on nerve

• There were significant differences in infection rate across left vs. right nerves in the AAV hSyn eGFP group.

• No significant differences in infection rates across sex, proximal vs. distal, left vs. right nerves within AAV CAG eGFP group.

Future Directions

• Test other serotypes and constructs of the AAVs.

The overall goal will be to apply these AAVs in mice to deliver gene manipulations that may promote axonal regeneration in peripheral nerves. Concurrent studies are being conducted to describe the effect of *Pten* knockout in the peripheral nervous system using this delivery

References

[1] D. Grinsell, C. P. Keating, "Peripheral Nerve Reconstruction after Injury: A Review of Clinical and Experimental Therapies", *BioMed Research* International, vol. 2014, Article ID 698256, 13 pages, 2014.

[2] Chan, Ken Y et al. "Engineered AAVs for efficient noninvasive gene delivery to the central and peripheral nervous systems." Nature neuroscience vol. 20,8 (2017): 1172-1179. doi:10.1038/nn.4593

[3] Kügler S, Kilic E, Bähr M. Human synapsin 1 gene promoter confers highly neuron-specific long-term transgene expression from an adenoviral vector in the adult rat brain depending on the transduced area. Gene Ther. 2003 Feb;10(4):337-47. doi: 10.1038/sj.gt.3301905. PMID: 12595892.

[4] Dou Y, Lin Y, Wang TY, Wang XY, Jia YL, Zhao CP. The CAG promoter maintains high-level transgene expression in HEK293 cells. FEBS Open Bio. 2021;11(1):95-104. doi:10.1002/2211-5463.13029