



a place of mind

THE UNIVERSITY OF BRITISH COLUMBIA

Department of Cellular and Physiological Sciences



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University of British Columbia

12:30 PM Thursday, Nov. 15, 2018

Location: LSC3

**Hosted by Dr. Elizabeth Rideout, Dr.
Janel Kopp**

Two Gene Therapy Stories – MiniPromoters for rAAV and CRISPR for Blindness

Retinal gene therapy is leading the neurological gene therapy field, with 32 ongoing clinical trials of recombinant adeno-associated virus (rAAV)-based therapies. Promoters that restrict expression have demonstrated increased efficacy, and can limit the therapeutic to the target cells thereby reducing unwanted off-target effects. Retinal ganglion cells are a critical target in ocular gene therapy; they are involved in common diseases such as glaucoma, rare diseases such as Leber's hereditary optic neuropathy, and in revolutionary optogenetic treatments. We used computational biology and mined the human genome for the best genes from which to develop a novel minimal promoter (MiniPromoter) to improve the safety and efficacy of retinal ganglion cell gene therapy. We developed a new human-DNA MiniPromoter, Ple345 (neurofilament, light polypeptide (NEFL)), which in combination with intravitreal delivery in rAAV9 showed specific and robust expression in the retinal ganglion cells of mouse and the nonhuman-primate rhesus macaque retina.

Aniridia is a rare syndrome; best known for the iris hypoplasia visible in the child's eyes at birth. However, aniridia is actually a panocular disorder in which patients are born with poor vision that typically progresses to complete vision loss by adulthood. Currently, there is no cure or long-term successful treatment for aniridia. Aniridia is caused by mutations in the gene, paired box 6 (PAX6). We are exploring the possibility of treating aniridia with gene-editing therapy directed at correcting the causative Pax6 mutation. Towards this end, we initiated ex-vivo correction of a Pax6 mutation in mouse embryonic stem cells. Excitingly our best guide RNA and single stranded donor corrected the Pax6 mutation in 29% \pm 7% (SEM) of the cells. More recently we have successfully used this CRISPR strategy to correct the Pax6 mutation in vivo in zygotes of "aniridic" mice, repairing the germline mutation and restoring vision in the mouse model of aniridia.

Join us for coffee and cookies at Noon in LSC 1416!!!

For more information please contact [Dr.Rideout<elizabeth.rideout@ubc.ca>](mailto:elizabeth.rideout@ubc.ca), [Dr.Kopp<janel.kopp@ubc.ca>](mailto:janel.kopp@ubc.ca)