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PRESENTATION
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An HSV-1-Based Vector Platform for Localized Delivery to the Posterior of the Eye

Haley N. Cartwright, Ph.D.[1]; Jorge Guzman-Lepe, M.D.[1]; Trevor J. Parry, Ph.D.[1]; Suma M. Krishnan, M.S.[1]

[1]Krystal Biotech, Inc., Pittsburgh, Pennsylvania

Purpose

- Clinical use of a herpes simplex virus type 1 (HSV-1)-based gene therapy vector, beremagene geperpavec (B-VEC), has been successful in treating skin- and eye-related pathologies associated with dystrophic epidermolysis bullosa (DEB) [1-3].
- The underlying platform technology is now being explored for its potential in treating additional genetic ocular disorders, necessitating determination of feasible routes for safe transgene delivery, particularly to the posterior of the eye.

Methods: Routes of Administration to the Posterior of the Eye

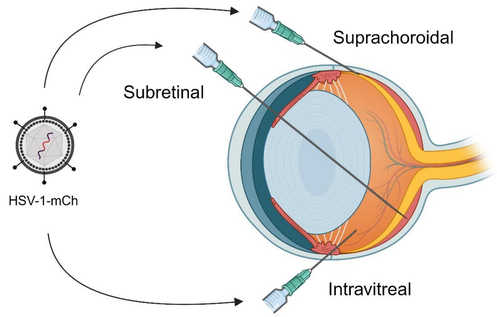

Figure 1. A single dose (1 µL) of an HSV-1-based fluorescent reporter vector was administered via subretinal, suprachoroidal, or intravitreal injection to mouse eyes. Eyes were collected after 24 hours for staining and qPCR. HSV-1-mCh = vector encoding mCherry fluorescent reporter gene. Created with BioRender.com.

Suprachoroidal and Subretinal, but Not Intravitreal, Injections Result in mCherry Expression Across the Retina

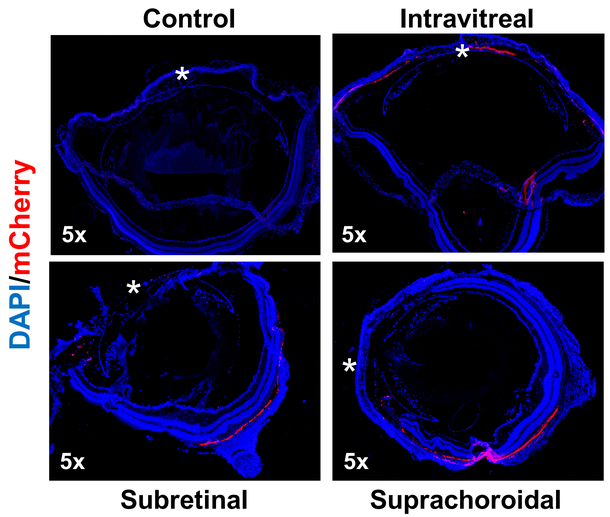

Figure 2. Suprachoroidal and subretinal injections resulted in disseminated mCherry expression across the retina, while intravitreal injection revealed mCherry signal in the cornea, iris, and ciliary body, as visualized through immunofluorescence (IF) staining. * = cornea

Vector Platform Successfully Transduces Both Photoreceptors and Retinal Pigment Epithelial Cells (RPECs) , as Visualized Through Co-IF

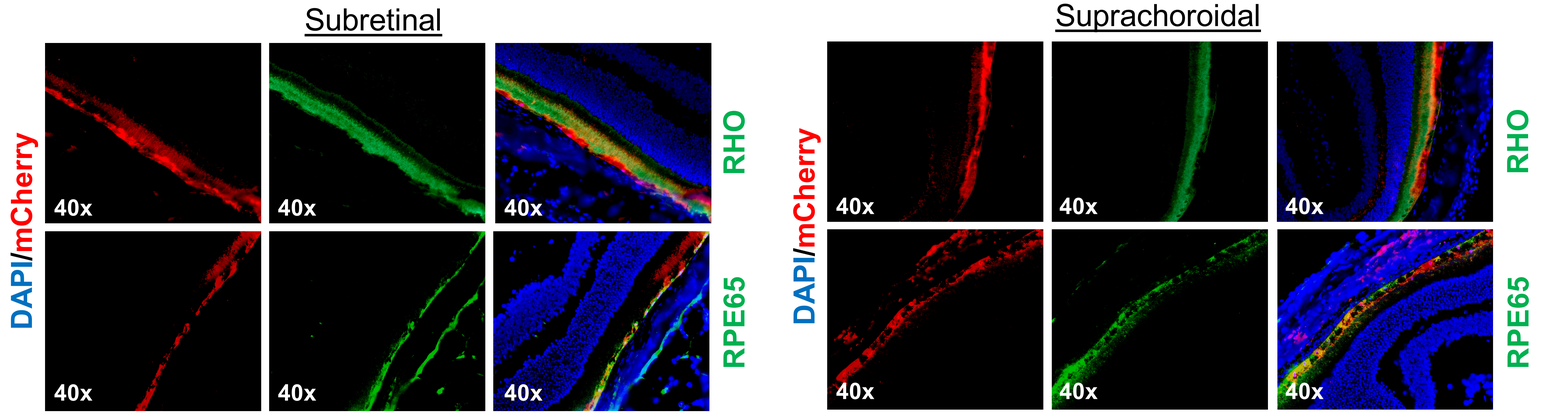

Figure 3. Vector cell-type affinity in the retina after subretinal and suprachoroidal injection was assessed by co-localization of viral mCherry expression with rhodopsin (RHO; photoreceptor marker) or RPE65 (RPEC marker) fluorescent staining. DAPI was used to visualize nuclei.

Ocular Injection Results in Minimal Inflammation in the Eye

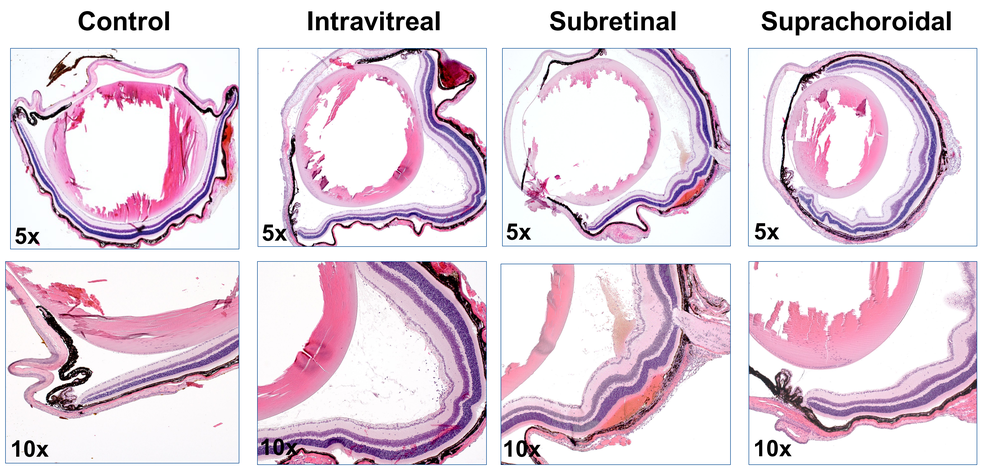

Figure 4. Very few inflammatory cells were observed in the suprachoroidal and subretinal groups, while the intravitreal group showed mild inflammatory cell infiltration by hematoxylin and eosin (H&E) staining. The upper panels are imaged at 5x, and the lower panels are imaged at 10x.

Ocular Injection Reveals Low Vector Dissemination into Circulation

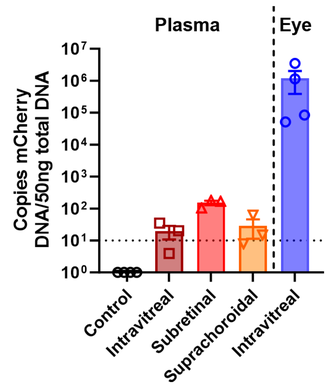

Figure 5. qPCR of murine plasma revealed low-detectable levels of vector genomes after subretinal injection; dissemination was at the limit of detection after intravitreal or suprachoroidal treatment. Vector genome copies in eye tissue after intravitreal injection in rodents (blue) is provided for comparison, demonstrating ~4-5 log-fold higher concentrations than those observed in the plasma.

Conclusions

This HSV-1-based platform technology can transduce multiple clinically-relevant cell types in the eye, including both photoreceptors and RPECs in the retina, with little-to-no inflammation. These data support further development of this technology for ocular disorders, particularly inherited retinal diseases.

Acknowledgements/Disclosures/References

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