Project Title:	Developing gene editing therapy for inherited retinal diseases 開發遺傳性致盲視網膜疾病的基因編輯治療
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To test the therapeutic effect of 5'UTR Rho KI, the team treated the RhoP23H/wt mice, which have progressive photoreceptor degeneration as human patients with the same mutation, with the dual AAV vectors on P1. Monthly retina structure examination by optical coherence tomography (OCT) revealed significant rescue of photoreceptor layer thickness from P60 to P210 in the Rho KI group in comparison to the control groups.

The ERG results showed that Rho KI eyes have significantly higher scotopic ERG a- and b-wave amplitudes under dim light conditions at late degeneration stages, suggesting the better light- sensing function of the rods. Both mixed rod-cone scotopic ERG and conedominant photopic ERG showed increased amplitude with Rho KI from P180 to P210, suggesting a rescue of the secondary cone degeneration.

Histological analysis of the P210 harvested eyes showed that Rho KI treatment preserved a thicker photoreceptor cell layer with more rods, and the remaining rods had better morphology with longer inner/outer segments. A set of animals were aged to P480 for the long-term follow-up study. At P480, the RHO staining was largely undetectable in the untreated and controltreated retinas, while it was still present across the whole retinal section of the Rho KI treated group, suggesting that the rescue effect is long-lasting.

In all assays, the control treatment without HITI Rho donor did not provide any beneficial effect or induce any toxic effect in RhoP23H/wt mice. Together, these results showed that AAV-mediated Rho KI into the 5'UTR in an allele-independent manner efficiently hampers rod degeneration and vision loss in RhoP23H/wt mice.

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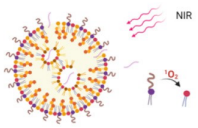
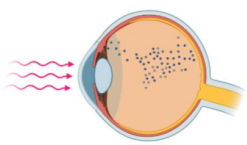
Development of A Non-viral Gene Therapy Platform for Retinal Degenerative Diseases
新型非病毒載體用於重大致盲眼病基因治療的關鍵技術研發

City University of Hong Kong, Dr Wenjun XIONG
TCFS - Category C, Platform

Innovation: Novel light-enhanced release of mRNA from LNP vectors



Light-responsive lipids can enhance membrane destabilization and mRNA escape from the endosomes.



Photodynamic therapy has been approved to treat wet Age-related Macular Degeneration (wAMD).

Patent Application