Preclinical evaluation of IKAR-001: A Bicistronic gene therapy with neuroprotective and complement-modulatory activity for the treatment of Geographic Atrophy

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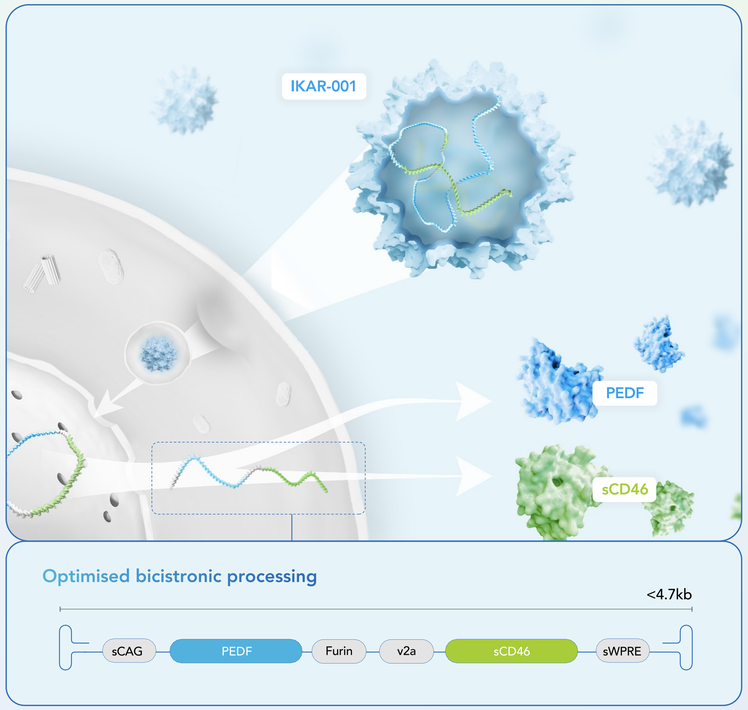
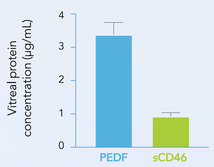
Geographic atrophy (GA), an advanced form of age-related macular degeneration (AMD), arises from multiple pathological mechanisms that are poorly addressed by current therapies. To build on the current complement targeted strategies, IKAR-001 (formerly IKC159V) was developed as a bicistronic AAV gene therapy designed to co-express a neuroprotectant (pigment epithelium-derived factor, PEDF) and a complement modulator (soluble CD46, sCD46). Here, we present preclinical data demonstrating that IKAR-001 provides both retinal protection and complement modulation across relevant disease models.

1 Single-Vector bicistronic AAV platform for dual protein delivery

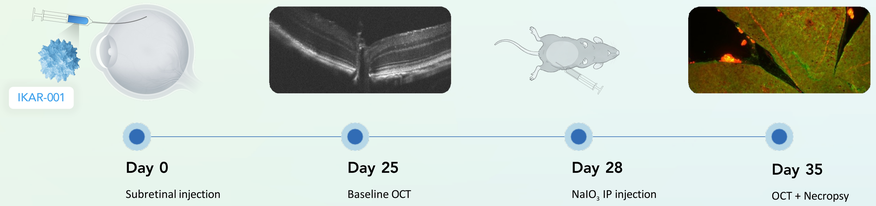


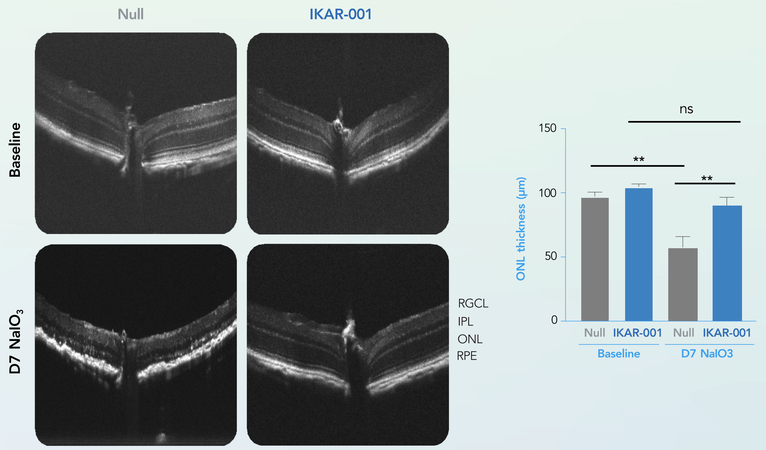
IKAR-001: Efficient processing, secretion and expression of PEDF & sCD46 in the vitreous



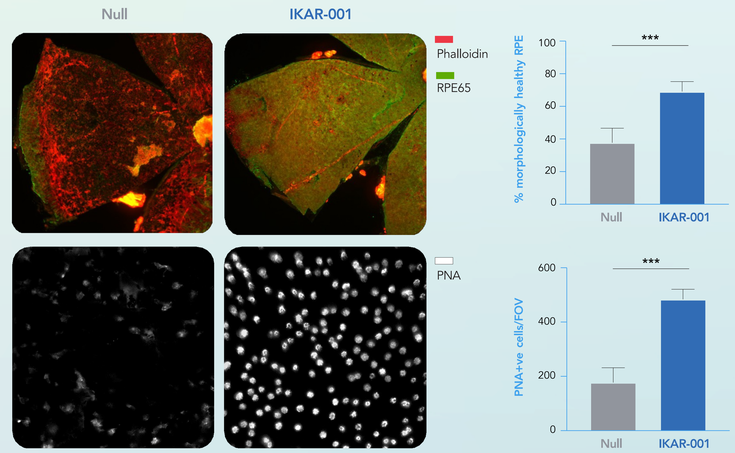
2 Preservation of RPE and Photoreceptors in a Rodent GA Model

Retinoprotection was evaluated in a murine sodium iodate ($NaIO_3$)-induced injury model, which leads to the degeneration of retinal pigment epithelium (RPE) cells and photoreceptors, the same cell layers most affected in GA. IKAR-001 or control vector was delivered subretinally. Retinal structure and survival were assessed using optical coherence tomography (OCT) and histological analysis.





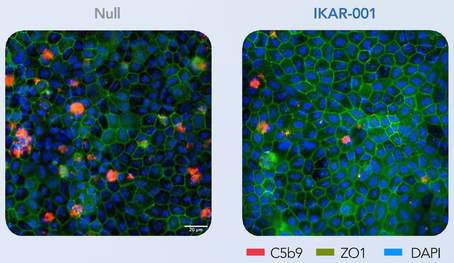
IKAR-001 preserves retinal structure following sodium iodate-induced injury, as demonstrated by maintenance of outer nuclear layer (ONL) retinal thickness on OCT.



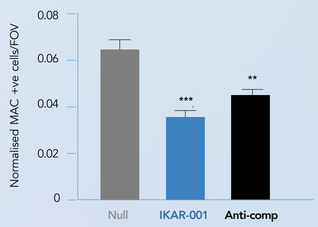
Histological analysis demonstrates preservation of RPE morphology and increased cone photoreceptor survival with IKAR-001 treatment.

3 IKAR-001 Reduces Complement-Mediated Damage in Human iPSC-RPE Cells

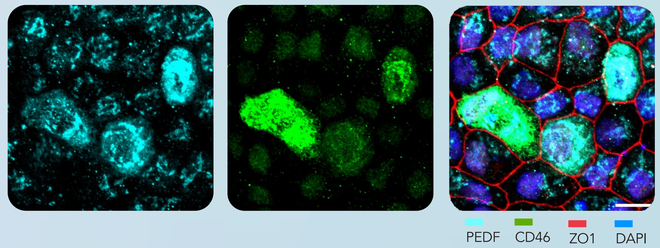
To evaluate complement modulation, human induced pluripotent stem cell-derived RPE (iPSC-RPE) cells were transduced in vitro and used to assess the ability of IKAR-001 to reduce complement-driven membrane attack complex (MAC) formation following normal human serum (NHS) challenge.



IKAR-001 reduces complement-mediated damage in human RPE cells, demonstrated by decreased MAC deposition following serum challenge.



Greater reduction observed vs comparator anti-complement, supporting enhanced efficacy.



Confocal imaging demonstrates efficient transduction of iPSC-RPE cells, with co-localised expression of PEDF and sCD46

4 Conclusions

- IKAR-001 protects retinal structure and key cell populations in a model of GA
- Complement-driven RPE damage is significantly reduced in human cell models
- Dual-pathway gene therapy enables combined neuroprotection and complement regulation
- These data support IKAR-001 as a differentiated therapeutic approach for GA

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