Ophthalmic Programs

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OMNI™ Technology Platform

Superior Performance through AI-Driven Design

AnGes

About EmendoBio

- Founded in U.S. in 2016 by scientists from the Weizmann Institute, Israel
- Founding investors: OrbiMed and Takeda Ventures
- AnGes became a majority shareholder in December 2020

Management

Naoya Satoh, PhD
President & CEO

Assaf Sarid
CFO

Idit Buch, PhD
VP, Computational Biology

Roy Sirkis, PhD
VP, Biomaterials Development and Production

Board of Directors

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AnGes

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Chief Genetic Immunotherapy, NIH

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Director Immunity and Immunotherapies, SCRI

Andrew Kung, MD PhD
Chair Dept. Peds. Sloan Kettering

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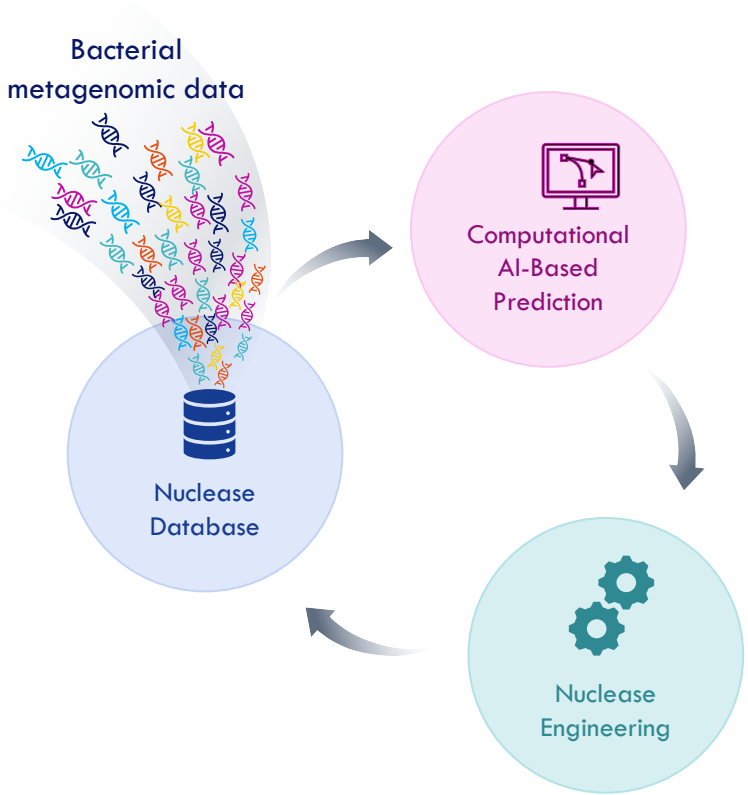
OMNI™ Platform Offers a Variety of Gene-Editing Solutions

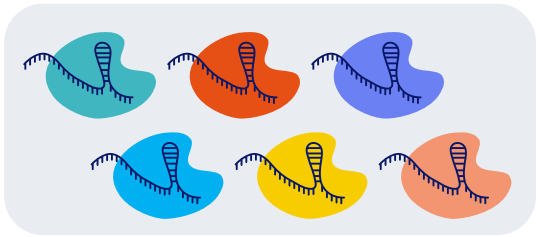
Synergistic discovery, engineering and computational technologies combine to produce a portfolio of high-performance OMNI™ nucleases

EmendoBio's Platform



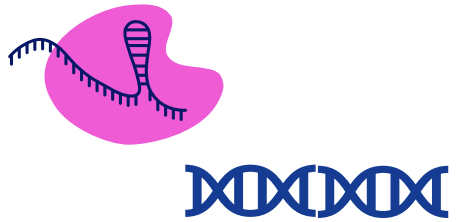
Panel of Engineered OMNI™ Nucleases

- Novel
- Highly active
- Highly specific



Optimal Therapeutic Compositions per target

- High safety profile
- Expanded range of applications
- Freedom to operate



OMNI™ Panel Genome Accessibility

Nuclease Portfolio

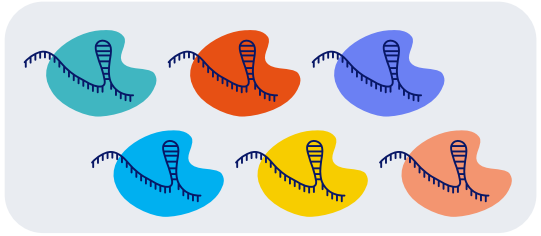
10,000 discovered nucleases

300 validated in vitro

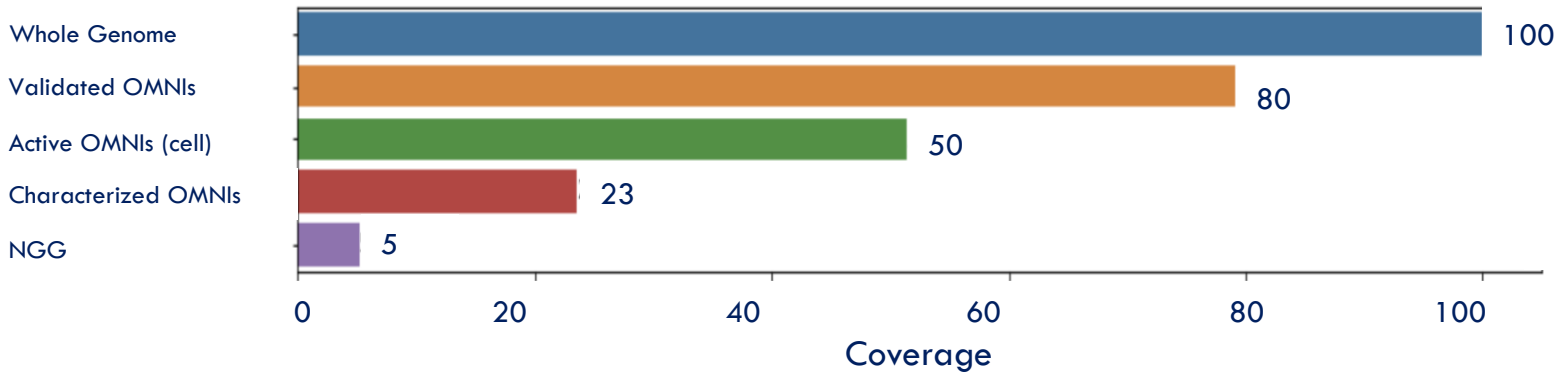
80 shown active in cells

12 characterized

2 engineered



OMNI™ Genomic PAM Coverage



The diversity of PAM sites of the OMNI™ nucleases overcomes PAM constraints and significantly widens genome accessibility, making **any gene targetable**

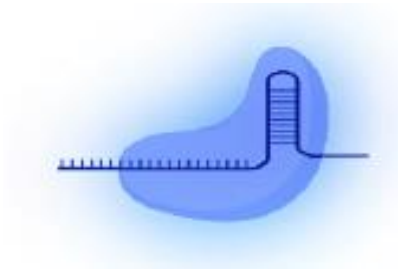
Nuclease Engineering Platform

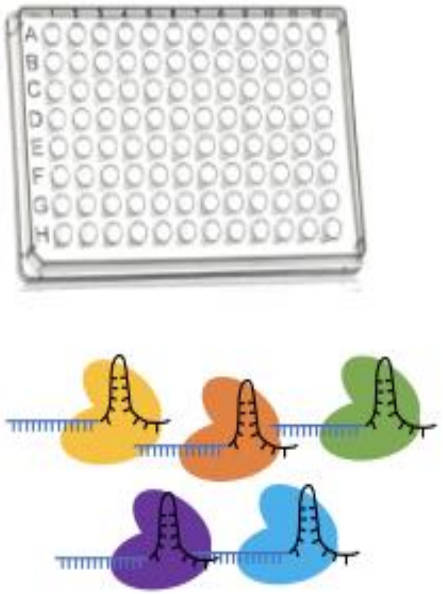
OMNI™ nuclease (from panel)

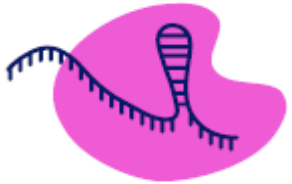
AI based engineering for variant library generation

Libraries of nuclease variants

Screening in mammalian cell line







Highly Active and Specific
Optimized OMNI™ Variants

Pipeline

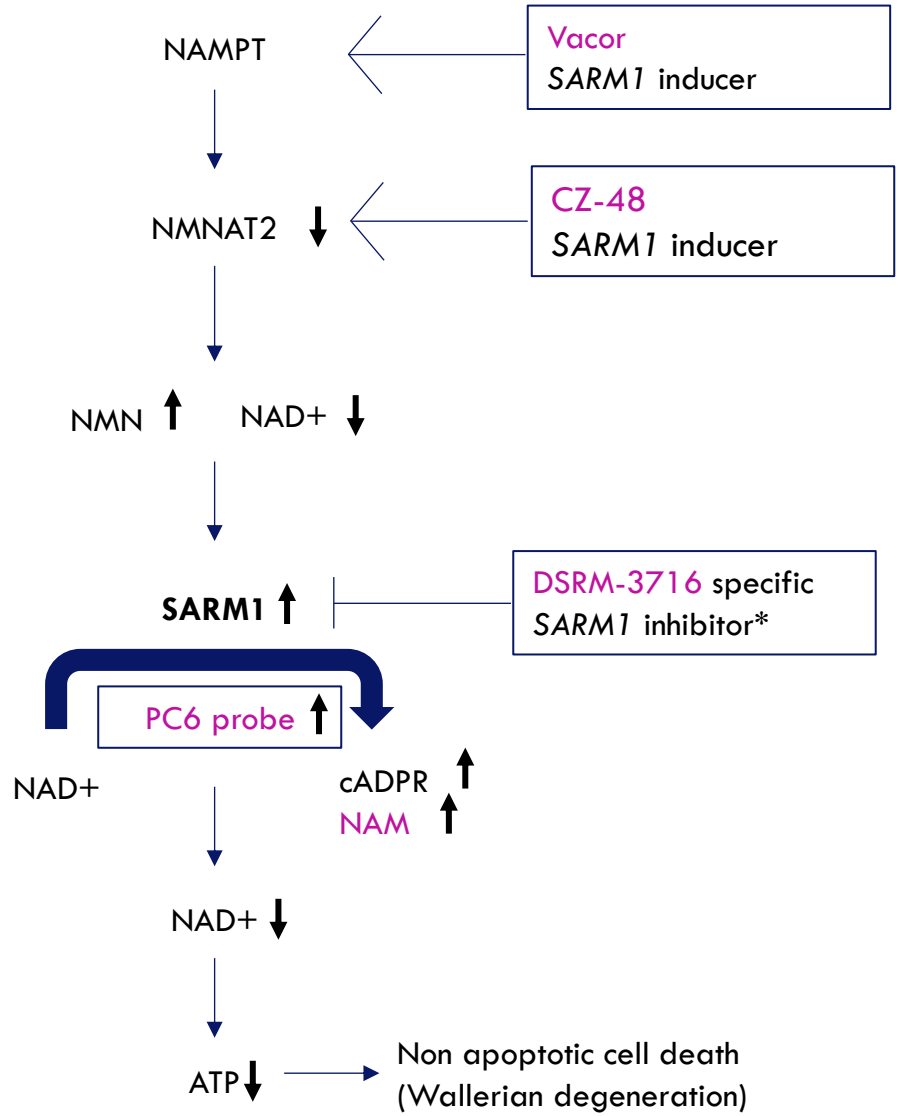
Disease Area	Program	Target	Indication	Approach	Research	Lead Optimization	IND-Enabling	Phase 1
Hematology	EMD-101	ELANE	Severe Congenital Neutropenia	Allele-specific ex vivo excision				
Cardiovascular	EMD-301	LDLR	**ASCVD not at LDL-C goal** Including Heterozygous Familial Hypercholesterolemia (HeFH)	In vivo excision				
	EMD-302	ANGPTL3	**ASCVD not at LDL-C goal** Including Homozygous Familial Hypercholesterolemia (HoFH)	In vivo KO				
Ocular	EMD-201	SARM1	Glaucoma	In vivo KO				
	EMD-202	RHO	Retinitis Pigmentosa	In vivo excision				
	EMD-203	RPE65	Retinitis Pigmentosa	In vivo excision				

EMD-201 Targeting *SARM1*

Ophthalmic Program

SARM1 KO as Neuroprotective Therapy

- SARM1 is expressed in neuronal and retinal tissues, found in an auto-inhibited state and activated under cellular stress caused by NAD+ depletion
- SARM1 acts as stress regulator and induces Wallerian degeneration upon activation (active program of axon self-destruction)
- Knockout of *SARM1* in primary neurons and in live mice reduced axon damage in models of peripheral neuropathy induced by trauma or chemotherapy
- EmendoBio's strategy: Biallelic knockout of *SARM1* to rescue/postpone Retinal Ganglion Cells (RGCs) from cell death
- Initial application is glaucoma



* Licensed to Eli Lilly and is in phase 1 for neurodegenerative diseases

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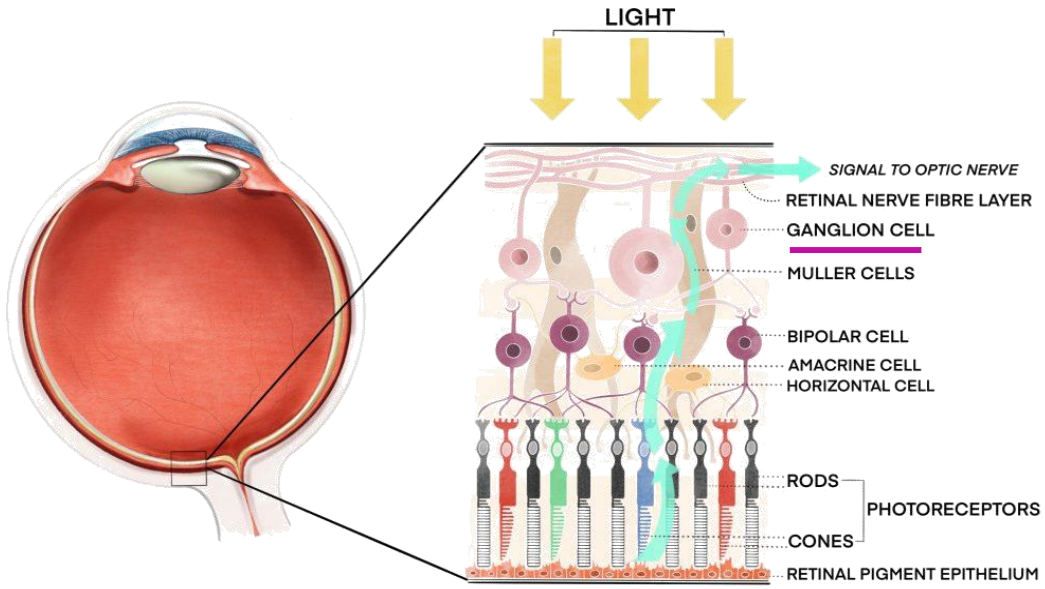
Glaucoma & Neuroprotection

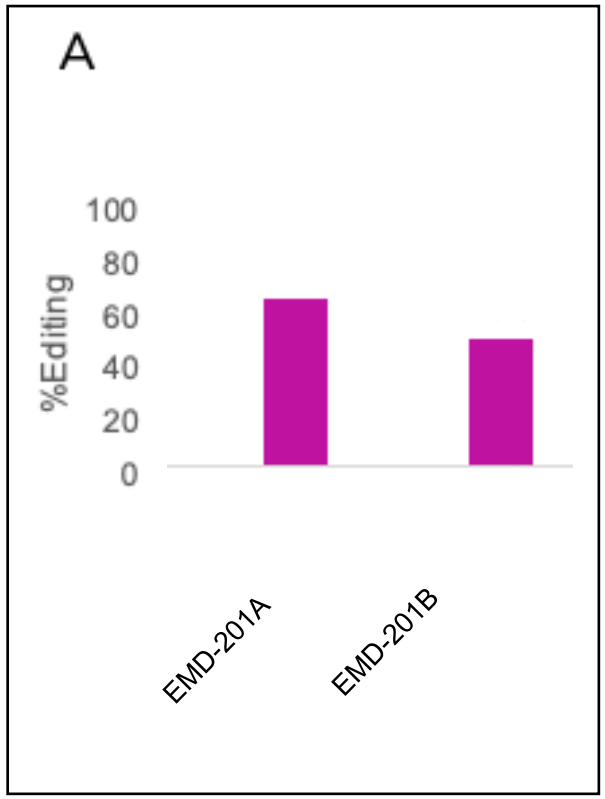
- Glaucoma is a group of optic neuropathies characterized by retinal ganglion cell (RGC) degeneration and visual field loss.
- Elevated intraocular pressure (IOP) is the main risk factor, however, IOP lowering does not always prevent disease progression due to the multifactorial nature of the glaucomatous disease.
- Therefore, neuroprotective strategies aiming at slowing down progression have been developed in recent years.

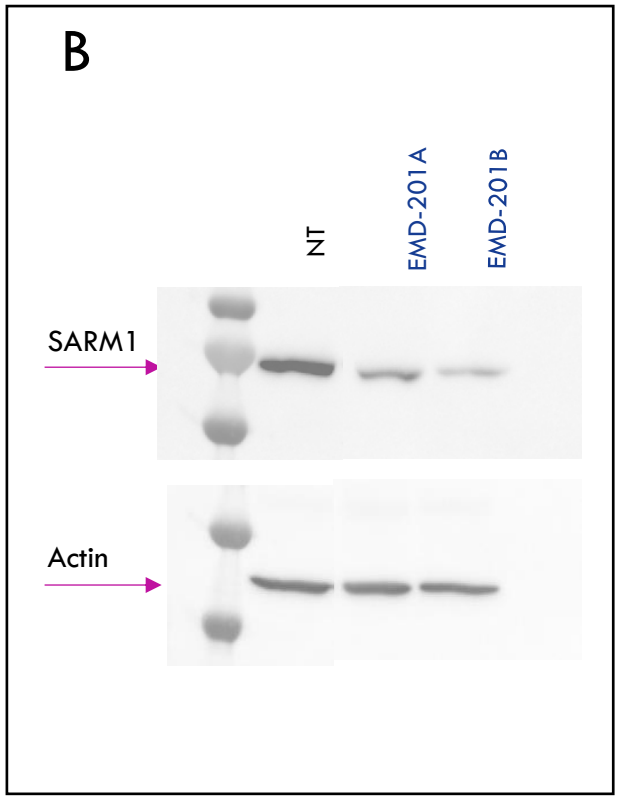


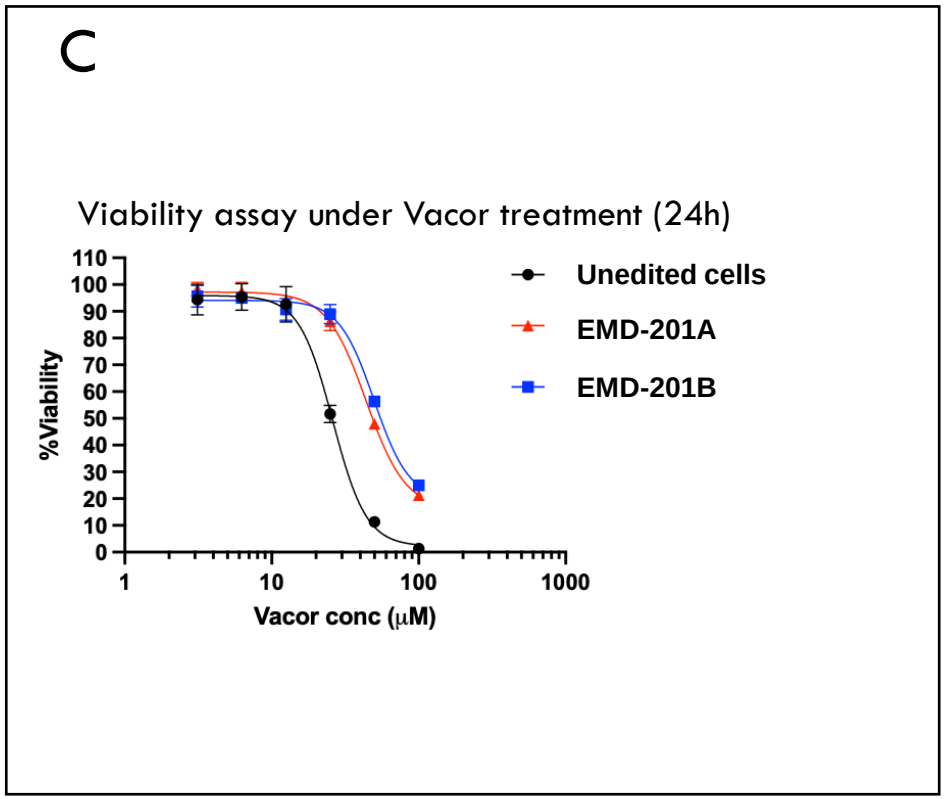
SARM1 Knock-Out Is Neuroprotective

Vacor-induced cell death

- *SARM1* KO SHSY5Y cells show improved survival to Vacor-induced toxicity







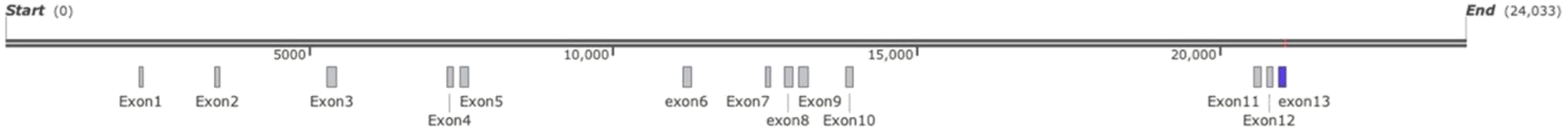
A. Editing levels of SARM by OMNI nucleases evaluated by NGS
B. Western blot analysis of reduction in SARM1 protein following KO compared to non-edited cells
C. Cell viability assay of neuroblastoma cell line – results demonstrate KO of SARM1 slows cell death

EMD-202 Targeting *RPE65*

Ophthalmic Program

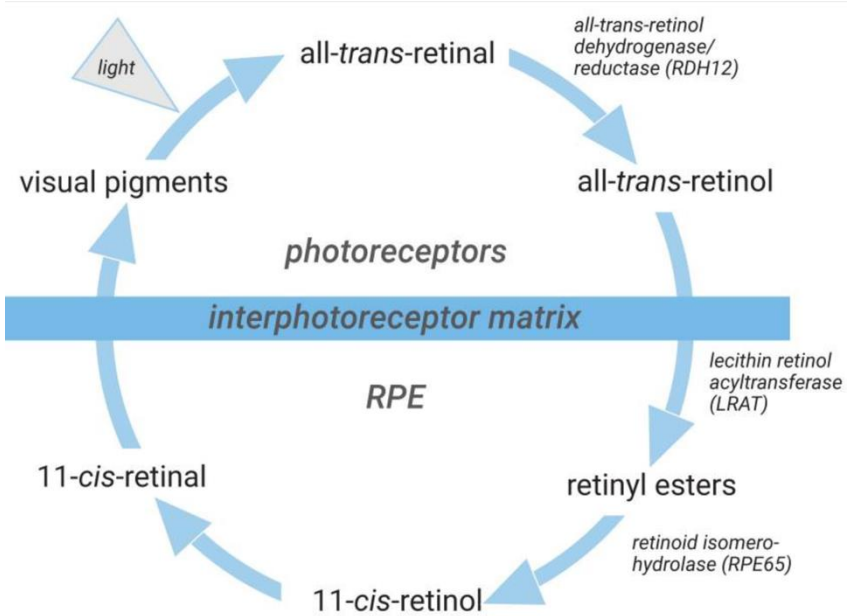
SNP-Based Mono Allelic Excision Strategies for Retinitis Pigmentosa

RPE65 gene



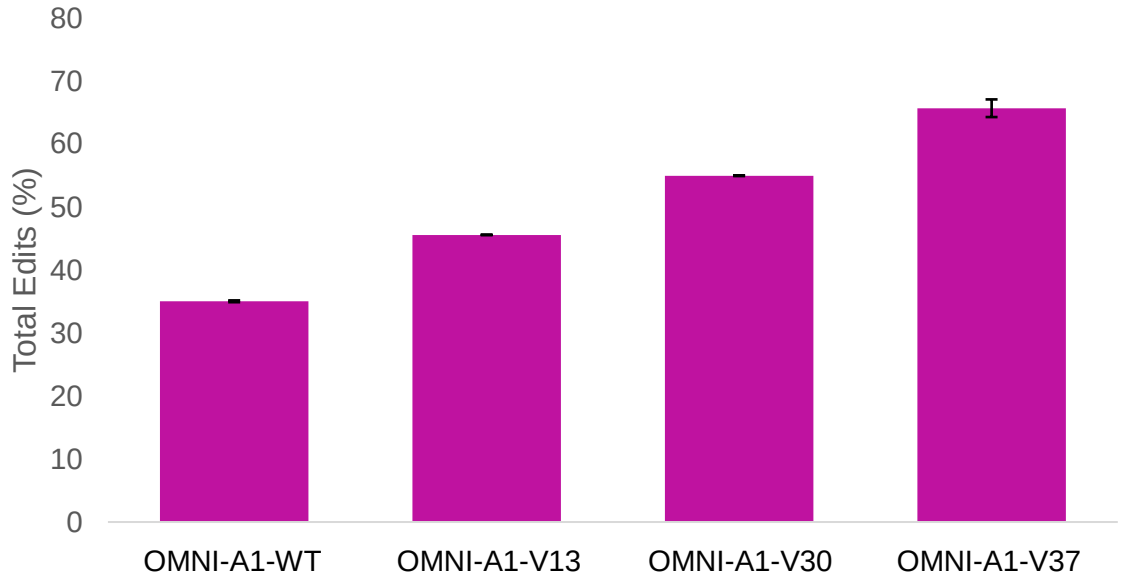
Target gene: Retinoid Isomerohydrolase RPE65, chr1:68,428,822-68,450,322(GRCh38/hg38), NC_000001.11, 21,501 bp/ 533 aa, 65kDa

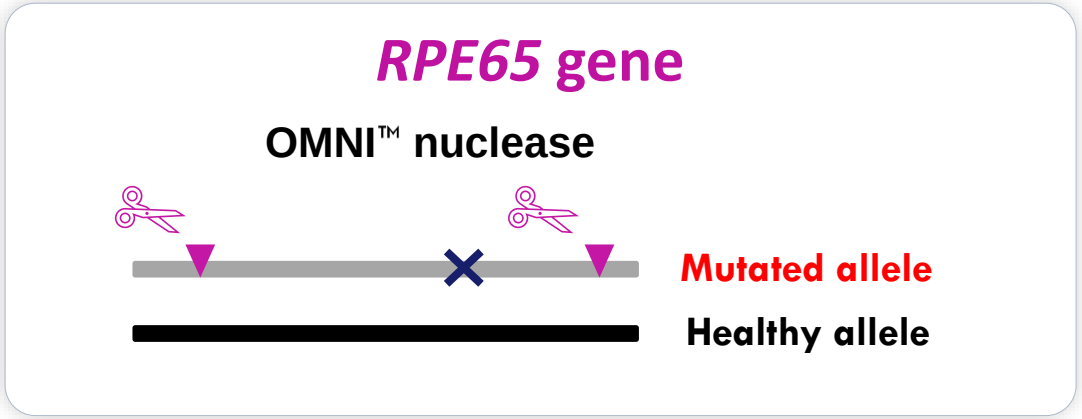
- RPE65 is expressed in the retinal pigment epithelium (RPE). RPE65 is also expressed in cone photoreceptors, where it may have a role in maintaining homeostasis of retinoid pools rather than in chromophore regeneration.
- Localized in cytoplasm.
- RPE65, all-trans retinyl ester isomerase, an enzyme crucial to the retinoid cycle.



Mechanism of Action

Mono allelic excision of mutated *RPE65* gene



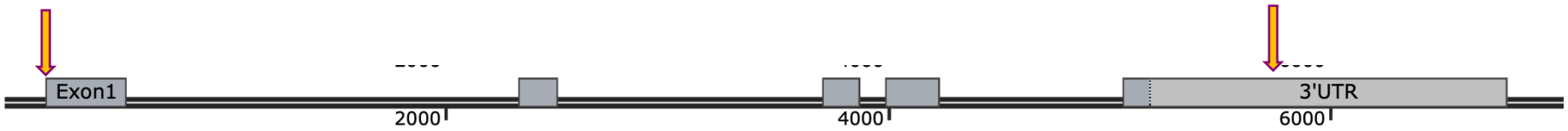


- EmendoBio is evaluating other promising editing compositions that utilize proprietary OMNI nucleases and guides
- Approximately 70% editing was observed in vitro for certain editing compositions

EMD-203 Targeting *RHO*

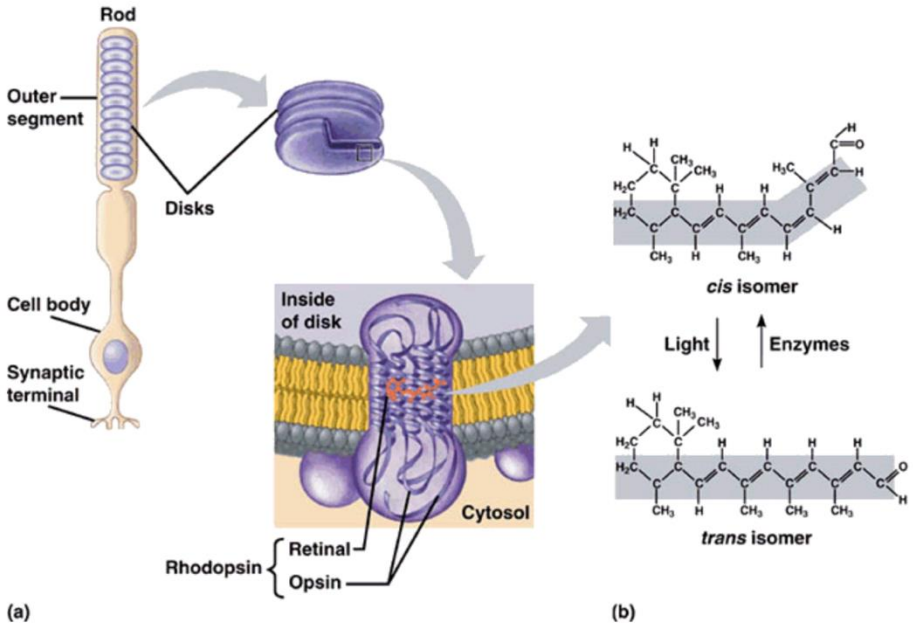
Ophthalmic Program

SNP-Based Mono Allelic Excision Strategies for Retinitis Pigmentosa



Target gene: RHO (Rhodopsin) chr3: 129,527,968 - 129,536,015(GRCh38.p13), NC_000003.12 (NC_000003.11 previous assembly), protein 348aa, 5.0 kb, 5 exons

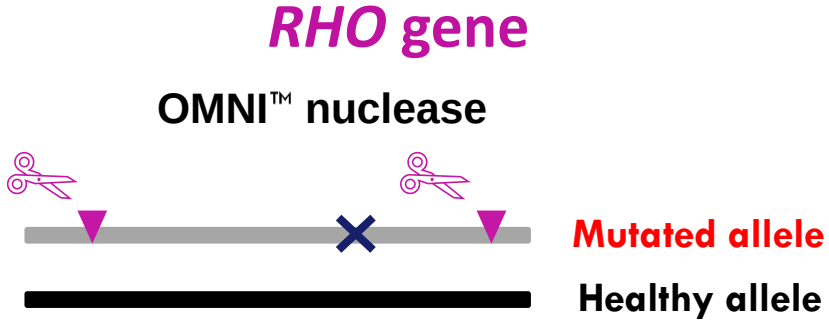
- Rhodopsin (RHO) is a light absorbing pigment, at 500nm max.
- Rhodopsin consists of the protein opsin linked to 11-cis retinal a prosthetic group. Retinal is the light absorbing pigment molecule and is a derivative of vitamin A. Opsin is a member of the 7TM receptor family.
- RHO gene mutations account for 20 to 30 percent of all cases of autosomal dominant retinitis pigmentosa, which is thought to be the most common form of the disorder
- **C110R mutation (3q22.1)** is a replacement of a single nucleotide that causes a change in Rho protein from the amino acid cysteine to arginine. As a result, the protein is retained in the ER, misfolding and instability. This change has been observed in patients with autosomal dominant retinitis pigmentosa and congenital stationary night blindness.



Mechanism of Action

Mono allelic knockout of mutated *RHO* gene

- EmendoBio is testing a several editing composition's which include a combinations of proprietary OMNI's and guides
- EmendoBio achieved as high as 80% editing in vitro
- In vivo studies were performed to evaluate mono-allelic excision levels of a mutated RHO gene.



Summary

Ophthalmic programs

- Program for SARM1 has demonstrated proof of concept with optimized OMNI™ nuclease
  - Proprietary approach for deactivating SARM1 in cells
  - Knock out (KO) of *SARM1* has potential for neuroprotection in indications such as glaucoma
  - Initial PoC in neuroblastoma cell line demonstrates KO of *SARM1* inhibits neuronal death
  - These results suggest that KO of *SARM1* using OMNI™ nucleases can be used for neurodegenerative disease treatments
- Programs targeting *RPE65* and *RHO* are ready for preclinical evaluation