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Efficacy and Integration of a Non-viral *ABCA4* Transposon in Treating Stargardt Disease: Evidence from Mice and Primate Studies

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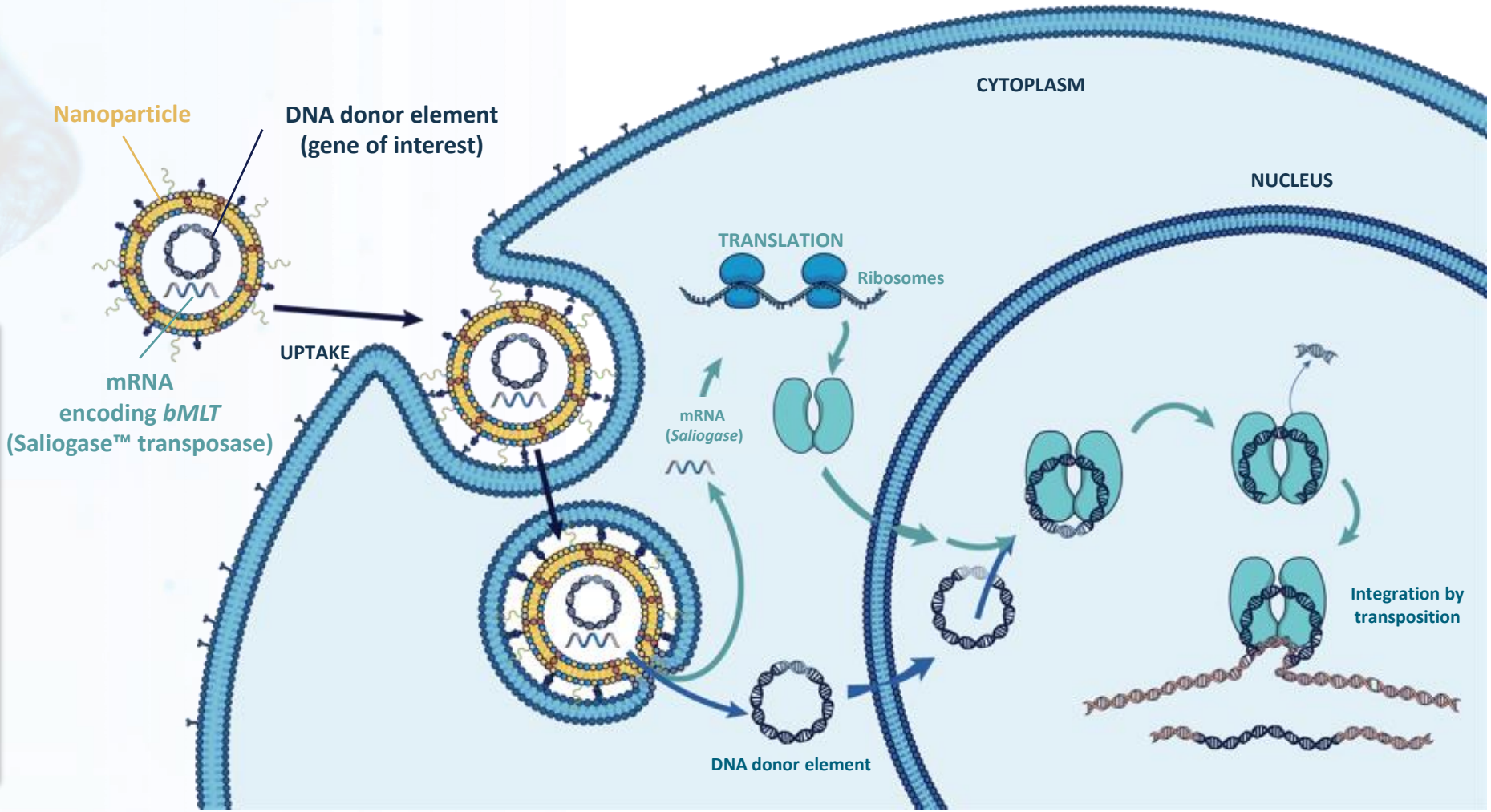
SalioGen is creating a new class of genetic medicines to improve and expand options for patients

Gene Coding™ technology employs a bioengineered mammalian transposase (*bMLT*, Saliogase™) to stably integrate large DNA constructs



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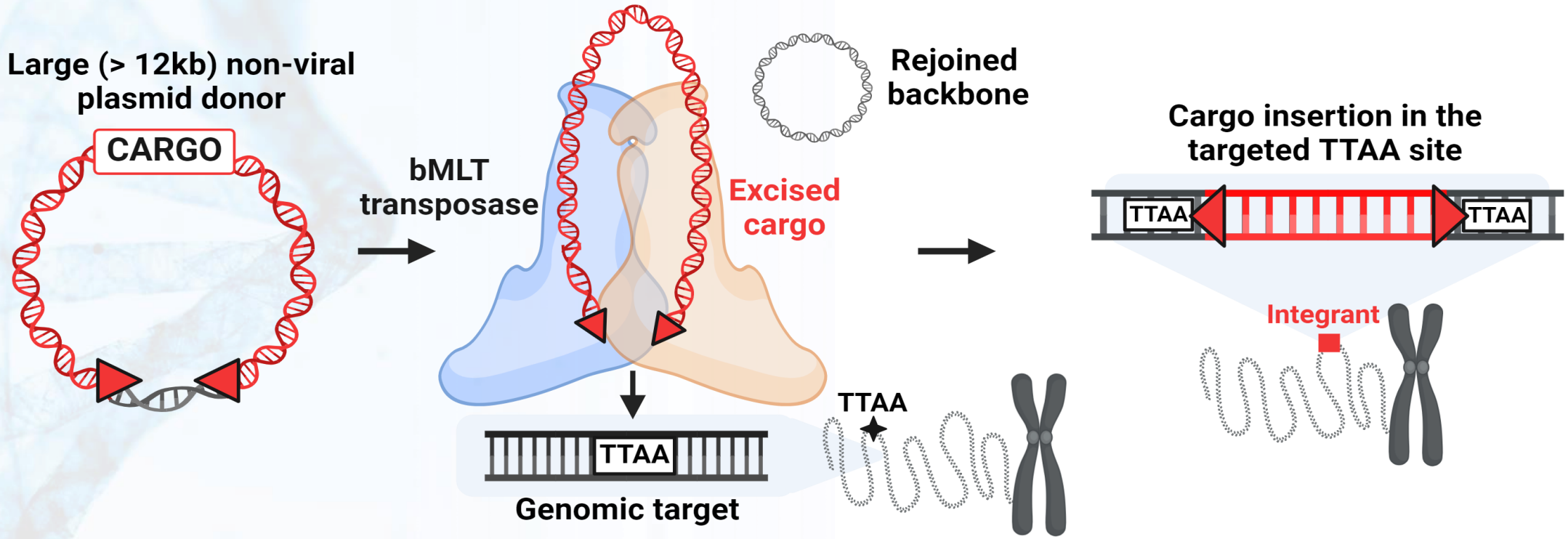
Saliogase targets defined genomic locations (TTAA sites) and seamlessly integrates via transposition,* offering significant safety advantages



- ✓ One step transposition process (targeting, excision and insertion)
- ✓ RNA delivery of Saliogase ensures transient enzyme expression
- ✓ Does not create DSBs or rely on host DNA repair pathways
- ✓ Does not require gRNA or viral vectors

*For further information see 2024 ASGCT **posters #1212** and **#1677***

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Nonviral Gene Coding technology is a one-time therapy to correct *ABCA4*-associated Stargardt disease, regardless of the mutation

Stargardt's Disease (STGD1) is the most common inherited macular dystrophy, with no approved gene therapies to date

Gene	Human *ABCA4* >2,000 ABCA4 mutations
Target Cell	Photoreceptors (PRs)
Pathogenesis	ABCA4 must "flip out" toxic byproducts or lead to A2E accumulation and PR death
Impact to Vision	 *Loss of central vision in the macula*

Obstacles

- ✕ **Exceeds AAV capacity:** *ABCA4* size is 6.8 kb
- ✕ **Mutation specific:** Limited to select genotypes
- ✕ **Photoreceptor delivery:** Traditionally low transduction/ transfection

Gene Coding technology can overcome limitations of traditional gene editing

- ✓ **Unlimited cargo size**
- ✓ **Full transgene integration:** Correct all patients regardless of genotype
- ✓ **On target delivery:** Targeted LNPs for PR delivery

SGT-1001 as a one-time treatment for Stargardt disease

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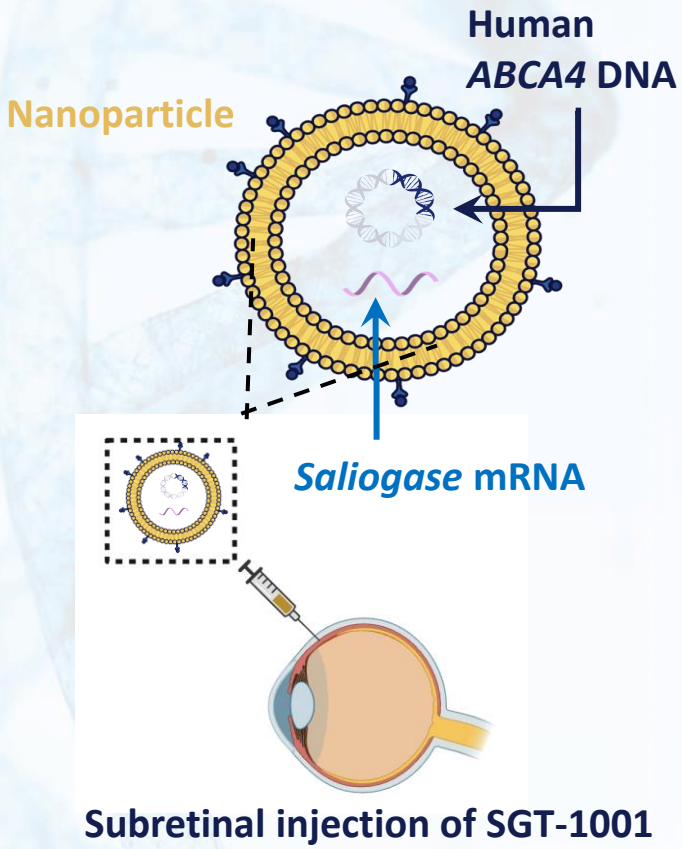
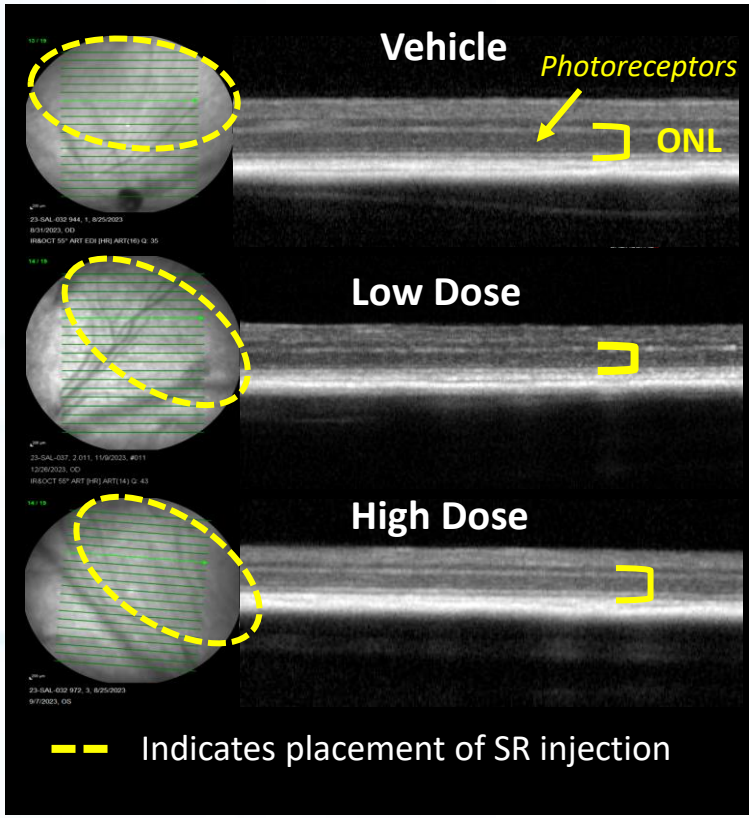
LNP/*ABCA4* & *Saliogase* mRNA shows good tolerability following subretinal injection in mice

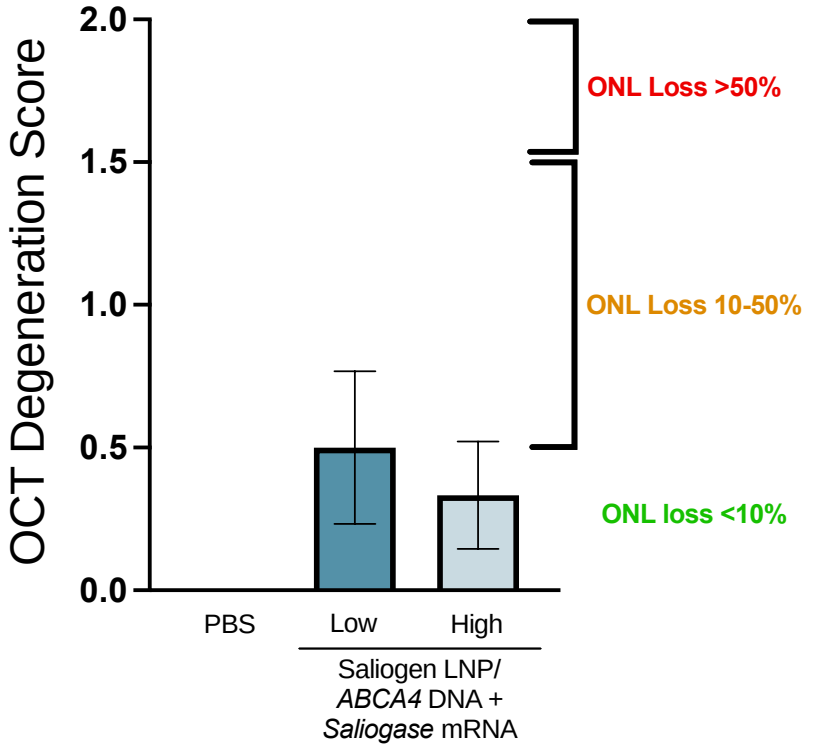
In life tolerability is assessed using OCT with a semi-quantitative scoring system



Subretinal injection of SGT-1001

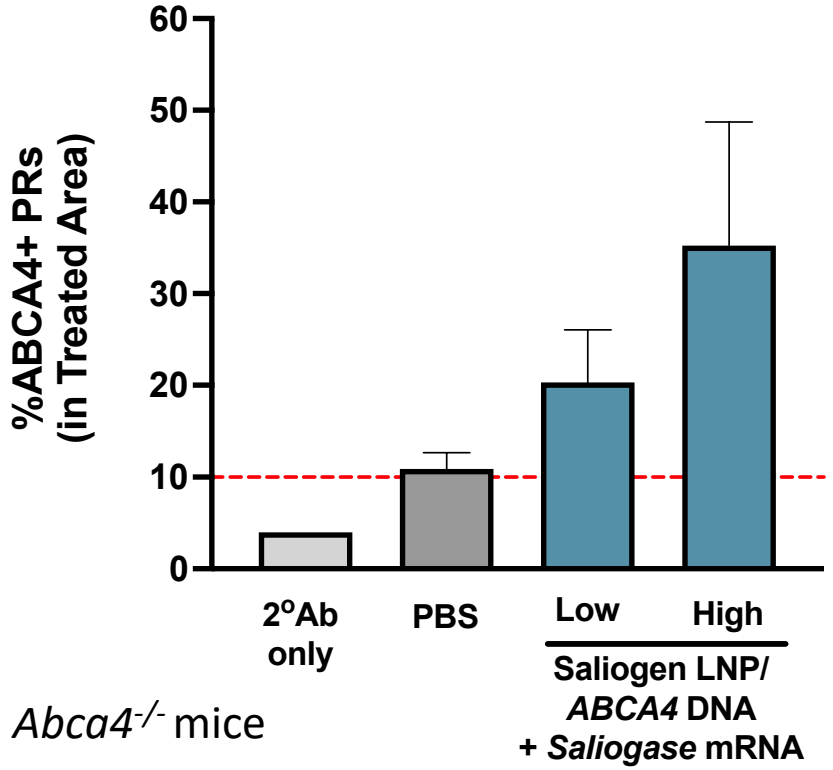


Abca4$^{-/-}$ *Rdh8*$^{-/-}$ double KO mouse model



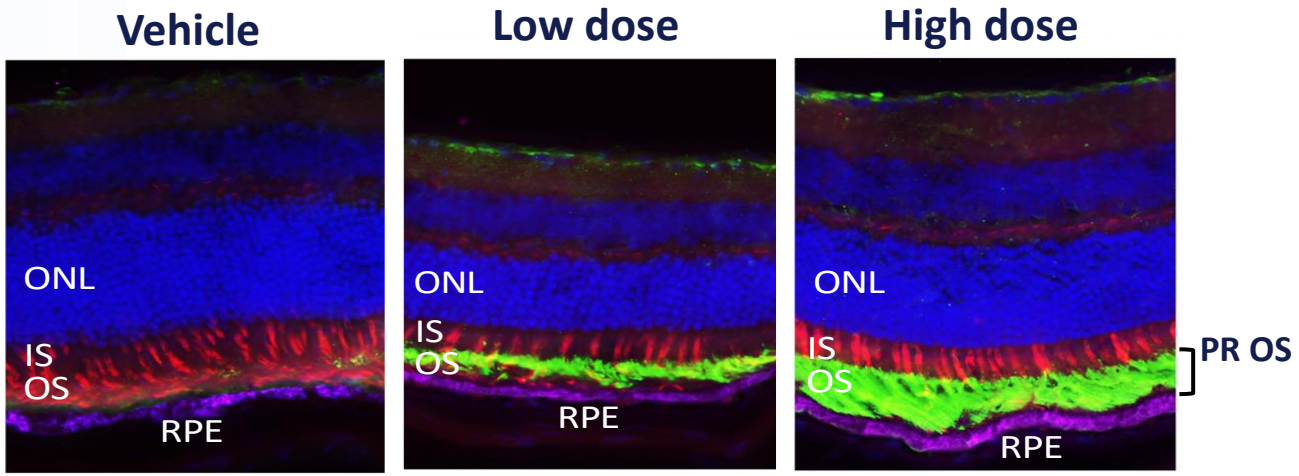
Human ABCA4 protein is detected in mouse photoreceptors following LNP delivery of Gene Coding technology

Human ABCA4 expresses in ~40% of photoreceptors within the treated region



Abca4$^{-/-}$ mice

Human ABCA4 protein is properly localized to the outer segment of mouse photoreceptors



DAPI
RPE65
PNA Lectin- IS/OS
ABCA4

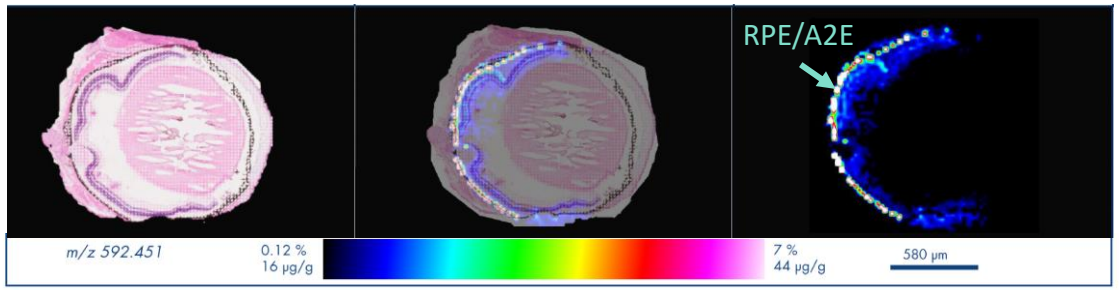
LNP/*ABCA4* DNA & *Saliogase* mRNA

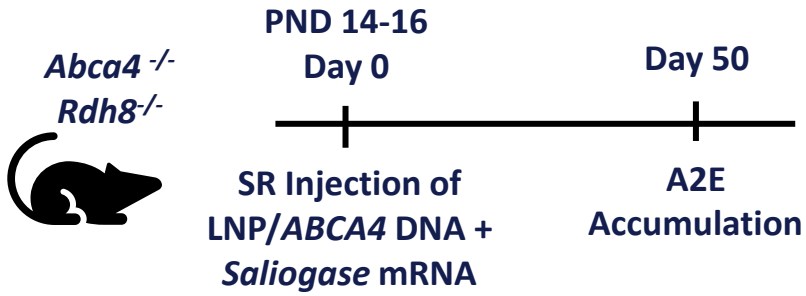
ABCA4 protein expression and localization support evaluating efficacy in a Stargardt mouse model

Non-viral delivery of *ABCA4* DNA & *Saliogase* mRNA reduces A2E accumulation in an accelerated Stargardt mouse model

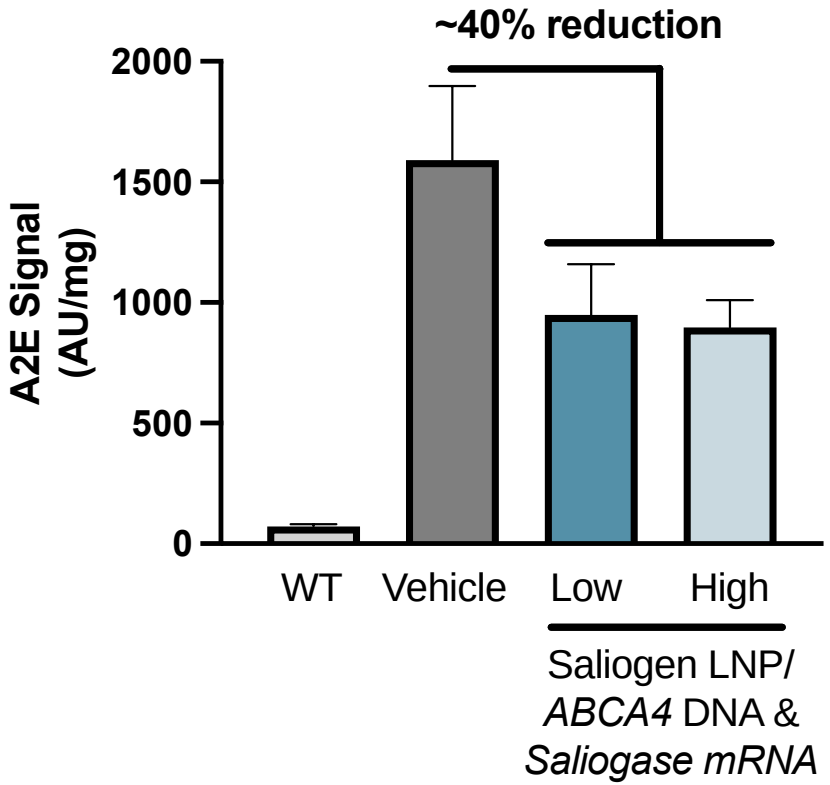
Bis-retinoid (A2E accumulation) is believed to be core to pathogenesis in STGD1

A2E Deposits in the RPE/eye cup and leads to PR death





Efficacy defined as a reduction in A2E



Abca4-/- *Rdh8*-/- double KO mouse model

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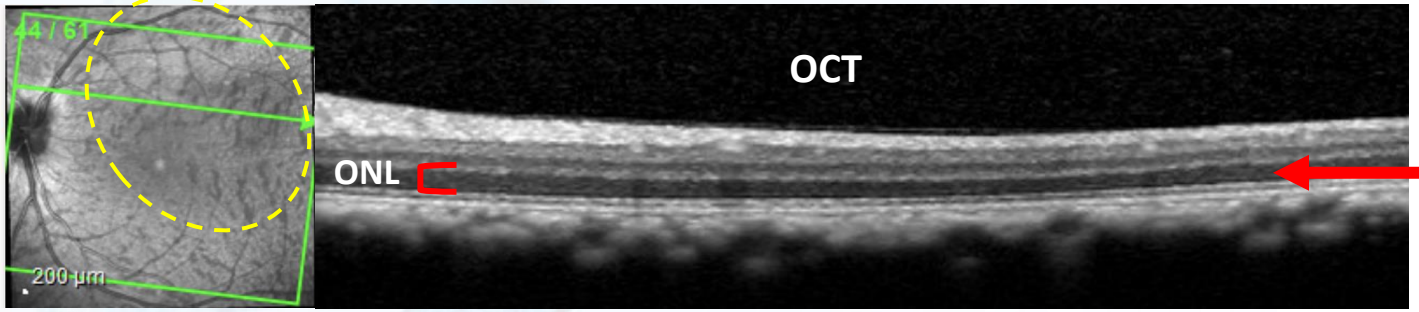
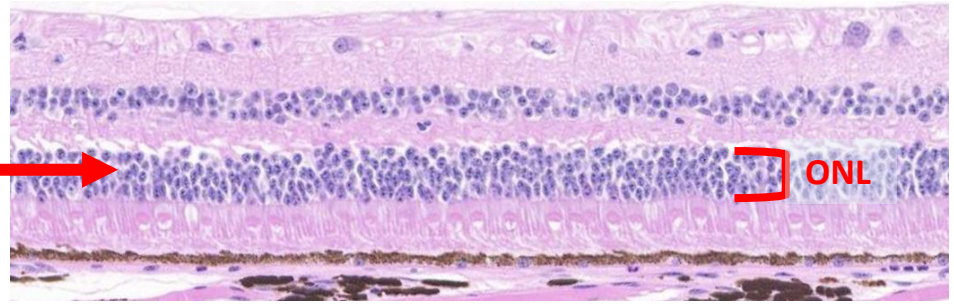
A proprietary LNP is tolerated in the NHP photoreceptor retinal layer

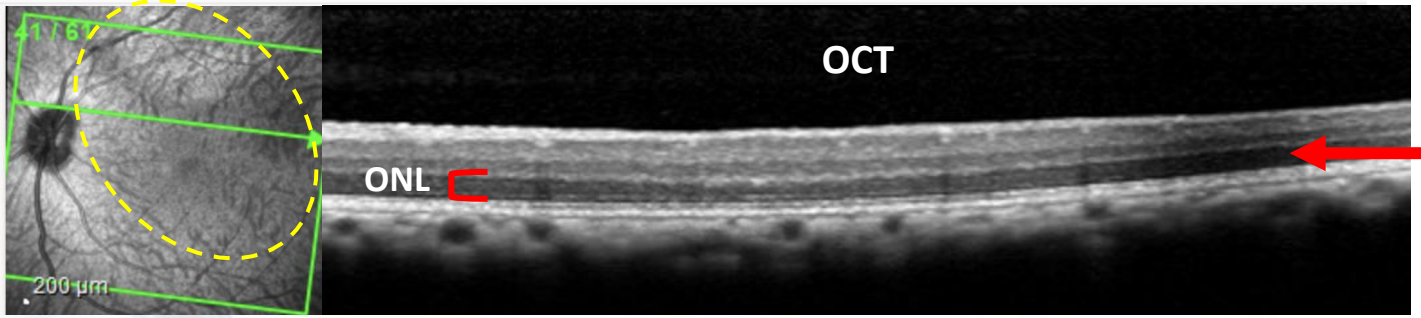
Vehicle



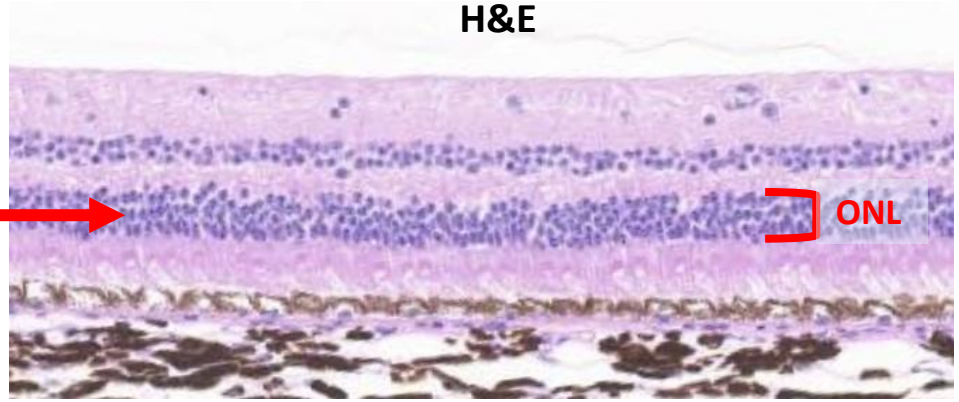
H&E



SalioGen LNP



H&E



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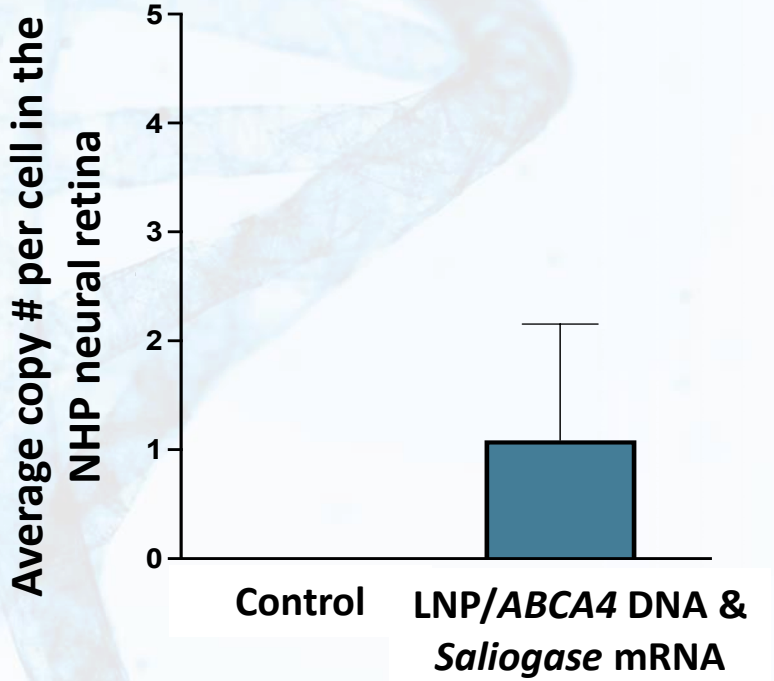
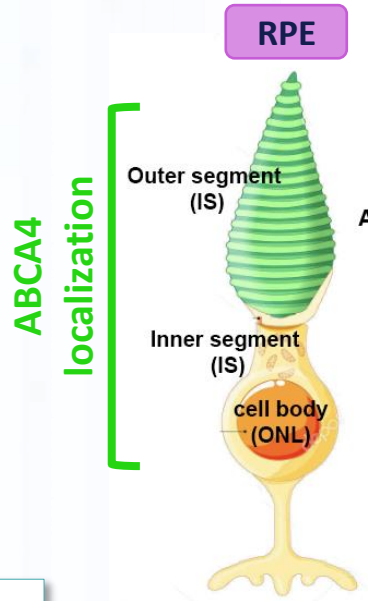
Evidence of expression and integration in the NHP following LNP/*ABCA4* DNA + *Saliogase* mRNA

ABCA4 protein is expressed in NHP cone photoreceptors with evidence of DNA integration

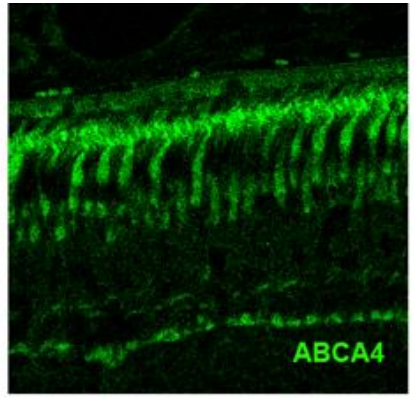
Evidence of human *ABCA4* DNA integration into the NHP genome

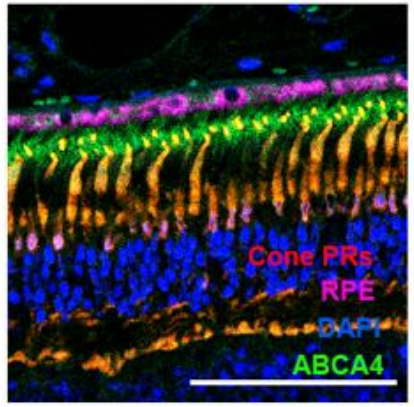


Schematic of cone photoreceptor with RPE

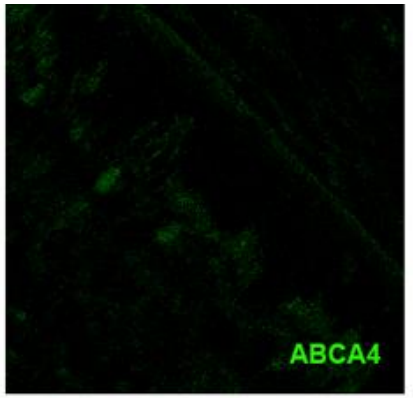


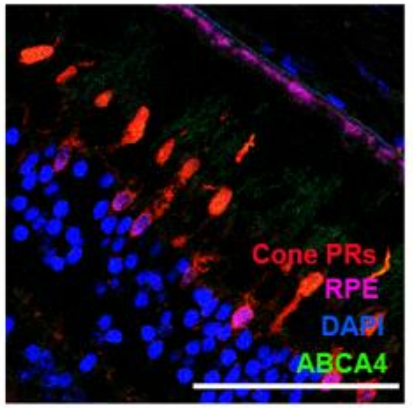
LNP/*ABCA4* DNA & *Saliogase* mRNA





Control





Cone PRs: Arrestin-C ; RPE: RPE65 ; DAPI: cell nuclei

Supporting interspecies translatability of the Gene Coding technology transposition process

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Nonviral delivery and stable integration of *ABCA4* in both rodent and NHP supports initiation of IND-enabling studies

Mouse Summary

- ✓ Subretinal injection of SalioGen LNP/*ABCA4* DNA + *Saliogase* mRNA is well tolerated and comparable to AAV
- ✓ ABCA4 expresses in 40% of photoreceptor outer segments
- ✓ LNP delivery of *ABCA4* DNA & *Saliogase* mRNA reduces A2E in an *Abca4*$^{-/-}$ *Rdh8*$^{-/-}$ mouse model

NHP Summary

- ✓ SalioGen LNP is tolerated in the photoreceptor layer of the NHP retina
- ✓ ABCA4 expresses in NHP cone photoreceptors using Saliogen LNP
- ✓ Evidence of integration in the NHP following LNP/*ABCA4* DNA + *Saliogase* mRNA

SGT-1001 is being developed as a one-time treatment to arrest progression of *ABCA4*-associated Stargardt disease and to preserve patients' vision

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Thank you!