

Viral/nonviral nanoparticles as promising vectors for gene transfection to the eye

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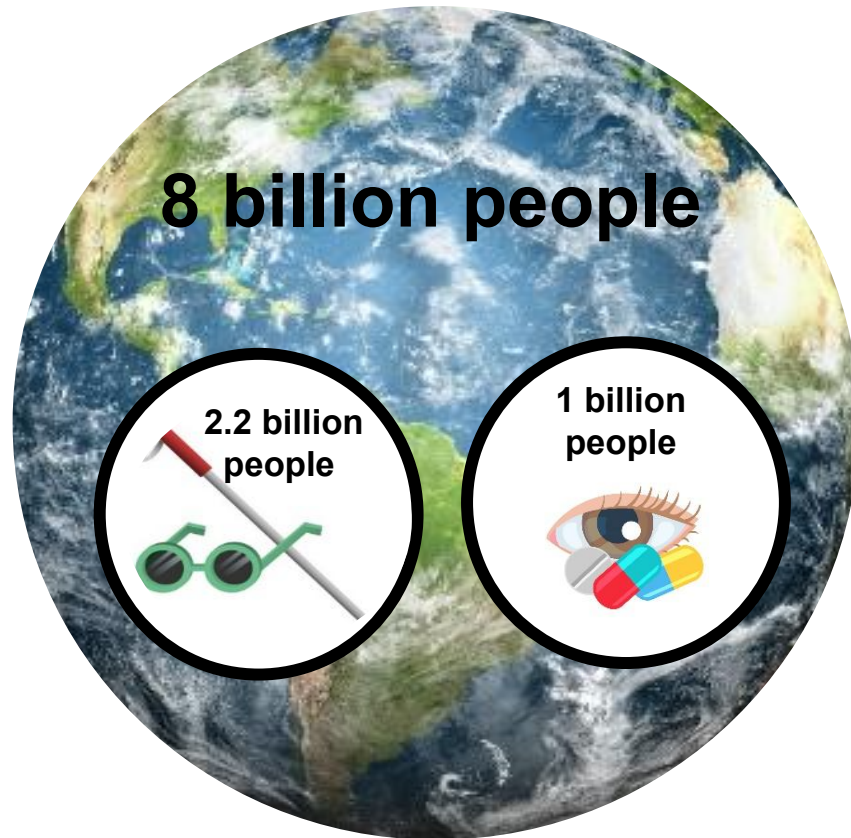


**Annual Meeting
AND Exposition**
JULY 8-12, 2024 • BOLOGNA, ITALY

INTEGRATING
Delivery Science
ACROSS DISCIPLINES



Blindness and Vision Impairment

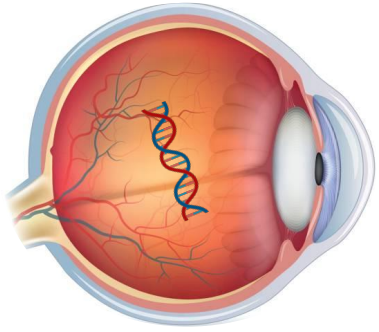


- 👁️ Refractive errors
- 👁️ Cataract
- 👁️ Diabetic retinopathy
- 👁️ Glaucoma
- 👁️ Age-related macular degeneration

- Most people with vision impairment are over 50's
- Ocular diseases: complex and multiple pathways
- 55% affects the posterior segment
- Recent treatments: adverse effects, ineffective targeting

WHO – World Health Organization. Blindness and vision impairment. Available at:
<https://www.who.int/news-room/fact-sheets/detail/blindness-and-visual-impairment>. Accessed: June/2024

Gene therapy



- Easy to access
- Immune-privileged (protected by the BRB)
- Low dosages are required
- Minimum systemic exposure



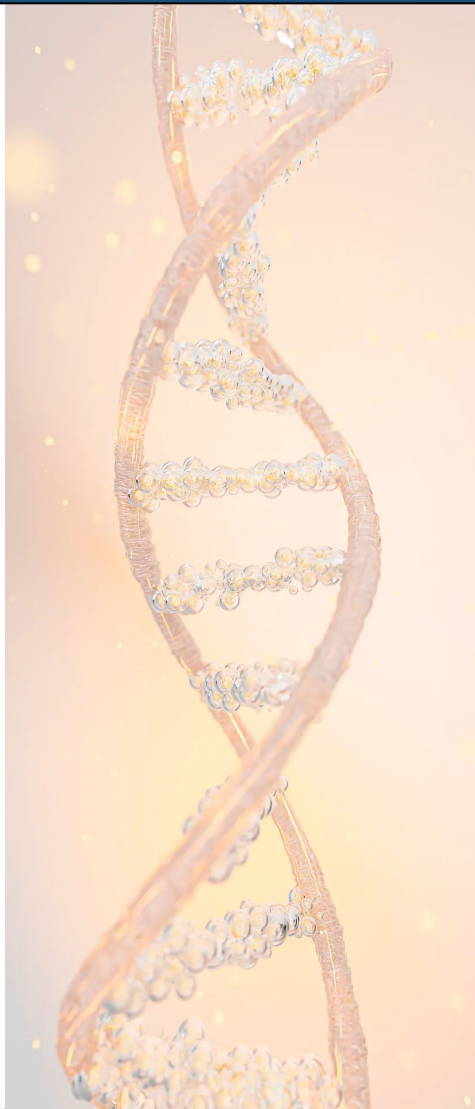
- Efficient transduction
- Reach the target tissue
- Scale-up manufacturing

- 1st FDA-approved gene therapy for ocular diseases (2017)
- Inherited retinal disease due to mutations in *RPE65* gene
- Subretinal injection
- AAV vector

LUXTRNA™
voretigene neparvovec-rzyl
for subretinal injection



> 30 clinical trials of gene therapy for ocular diseases



Viral vectors

- Good transfection
- Immune responses
- Difficulty large scale production



Non-viral vectors

- Poor transfection (*in vivo*)
- Low immunogenicity
- Easier large scale production

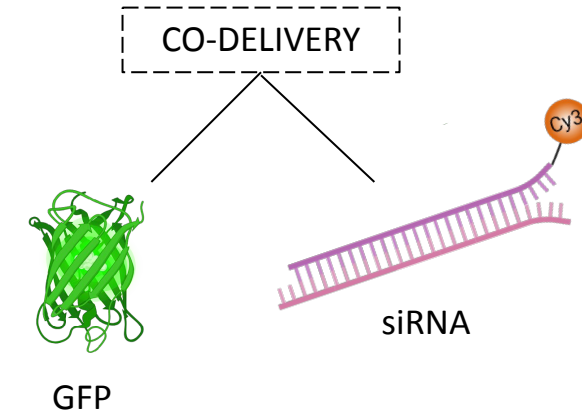


Chimeric Nanoparticles

Viral and non-viral vectors in a single nanoparticle

High transduction efficiency

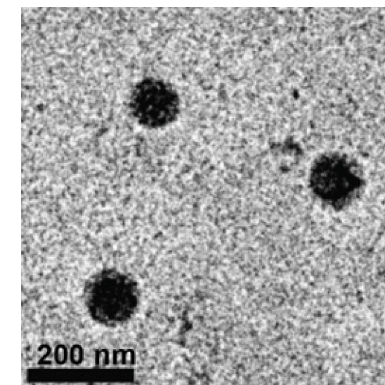
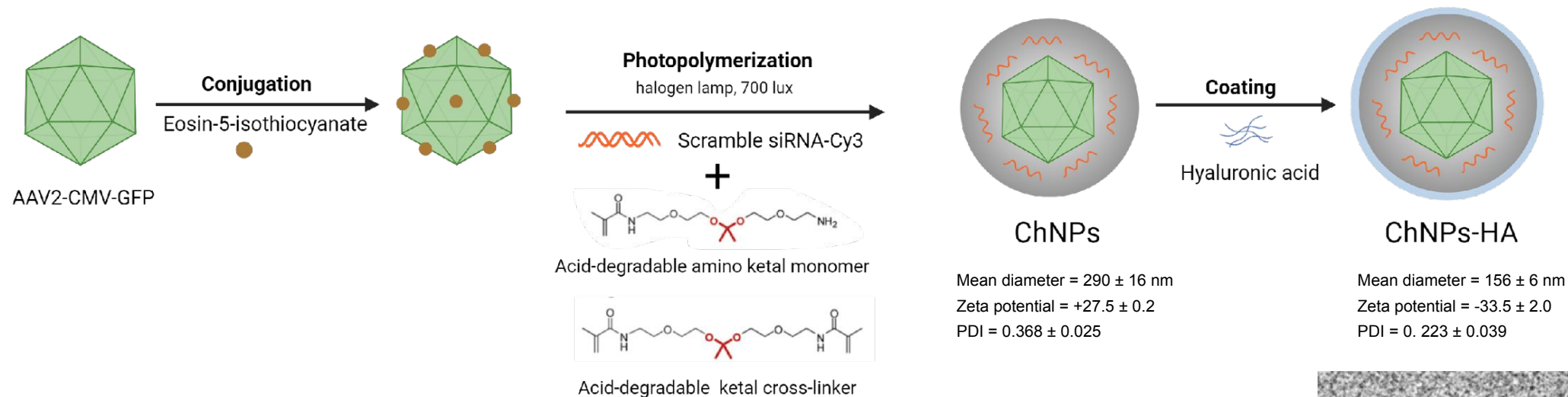
Low immunogenicity



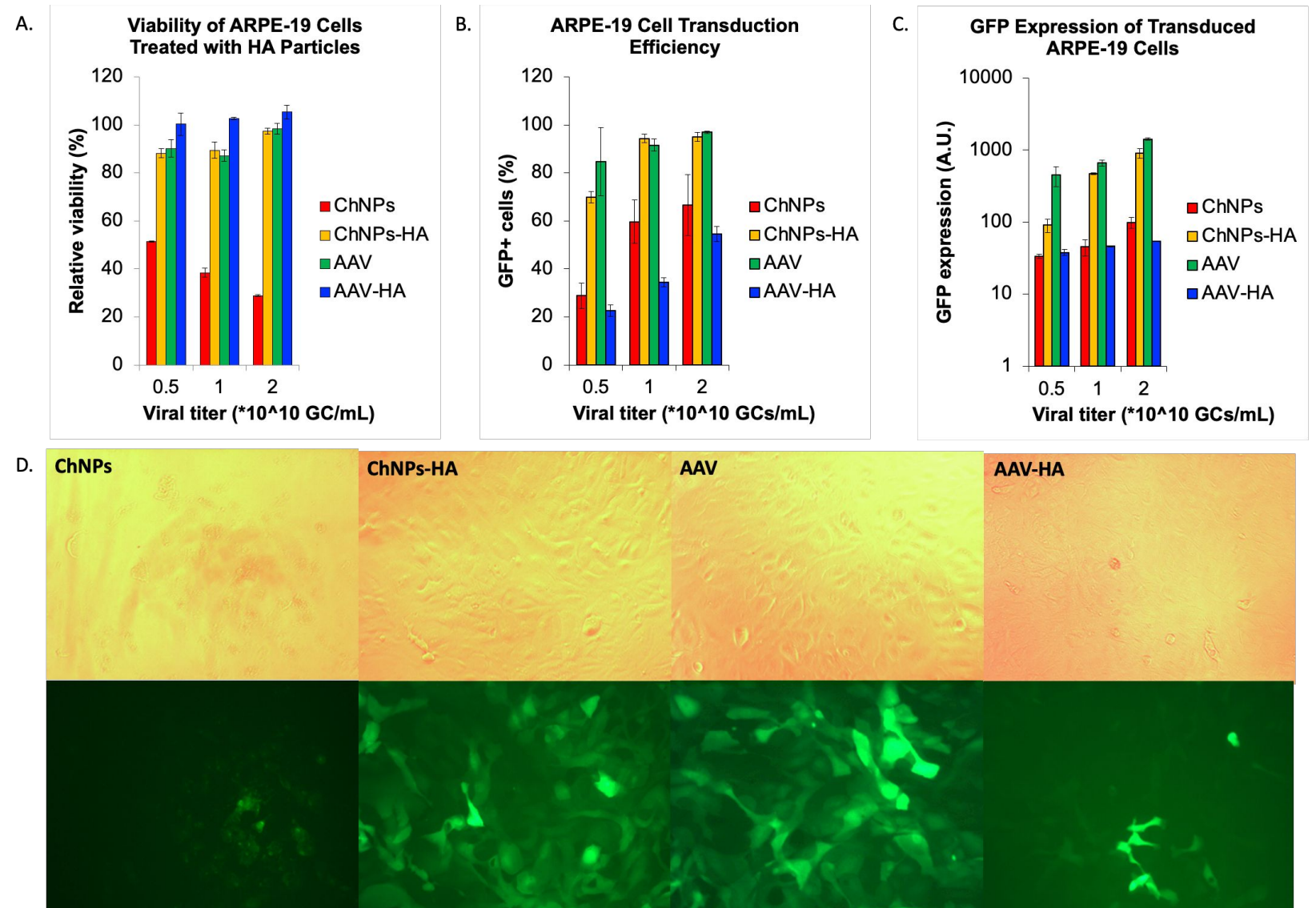
Simultaneous expression and silencing of multiple genes

Biomaterials. 2012;33(11):3316-23. doi: 10.1016/j.biomaterials.2012.01.027.

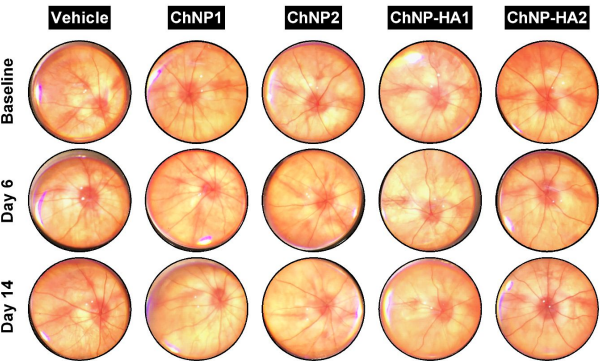
Chimeric Nanoparticles



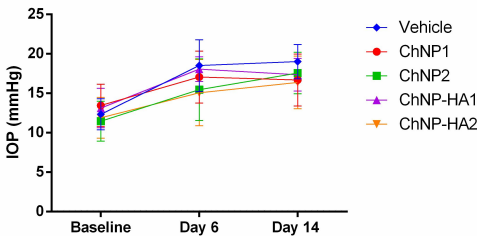
ARPE-19 cells viability and transduction



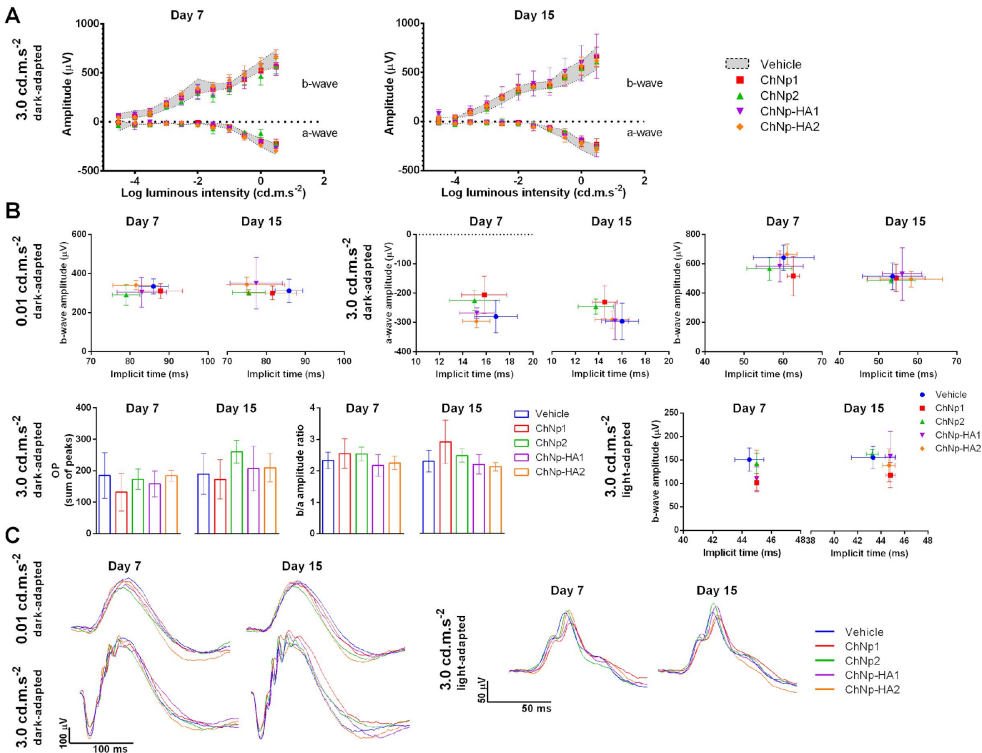
Safety evaluation in rats



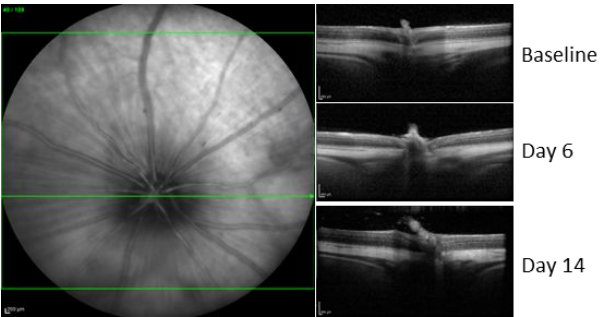
Normal fundus and IOP



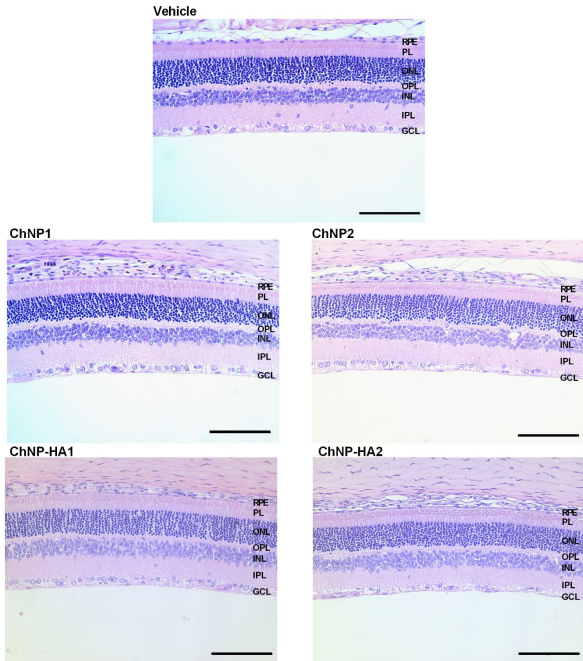
Baseline exams	Intravitreal injection	Follow-up (6 and 14 days)	Histology (14 days)
- Fundoscopy	- 5 μ L	- Fundoscopy	
- IOP	- ChNP1; ChNP-HA1 (5×10^5 GC/mL)	- IOP	
- ERG	- ChNP2; ChNP-HA2 (1×10^6 GC/mL)	- ERG	
- OCT	- Vehicle (10 mM HEPES)	- OCT	



No change in retinal function

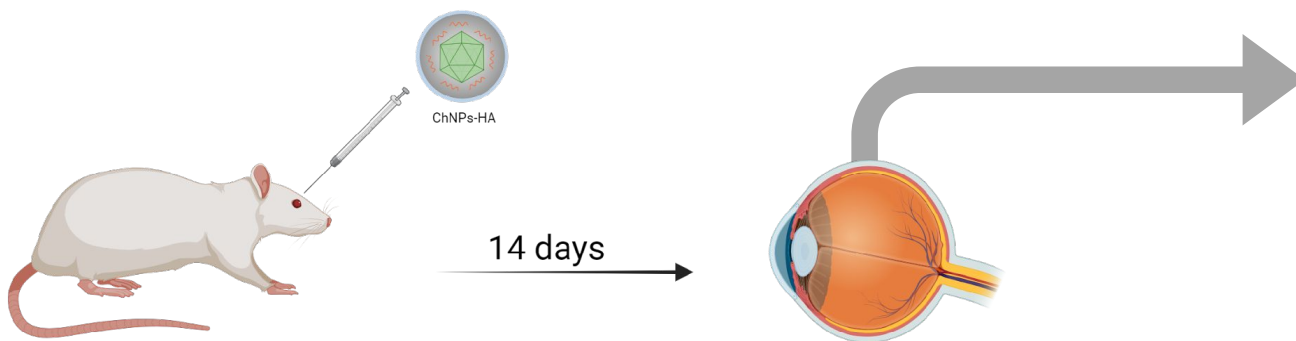


Normal thickness and morphology

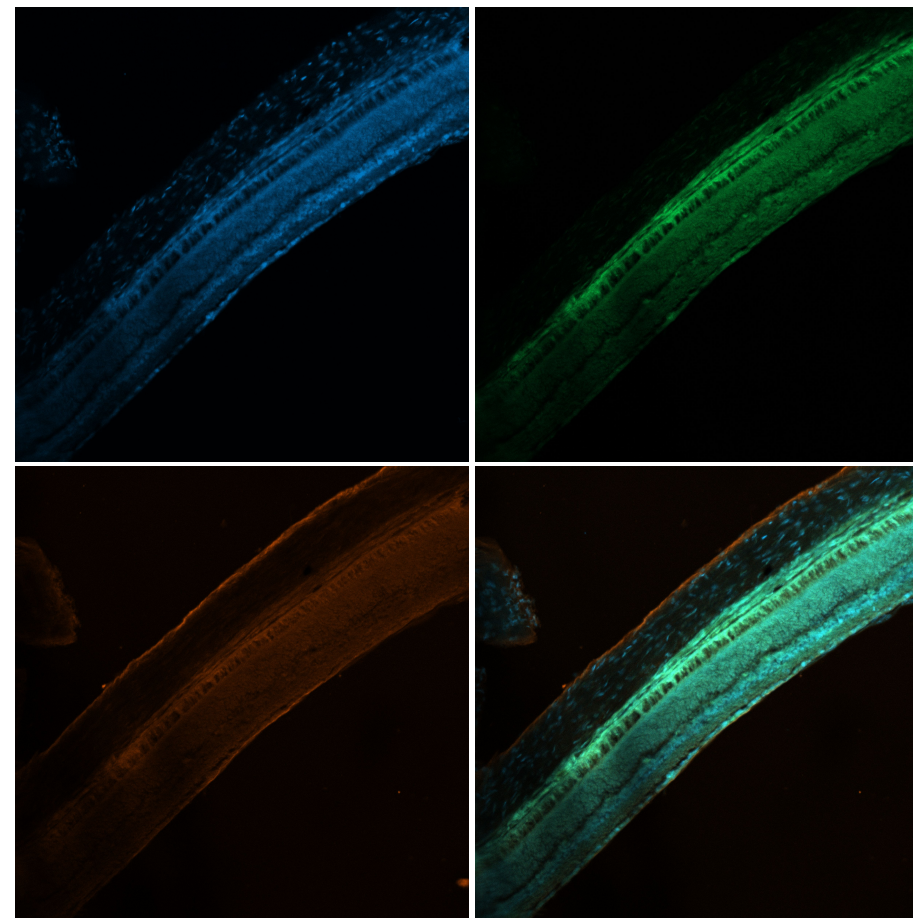


Retinal transduction in rats

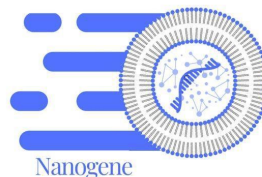
(Preliminary results)



Hoescht/GFP/Cy3



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Thank You!

For Connection!



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