Photoporation of the corneal epithelium by laser-induced nanobubbles

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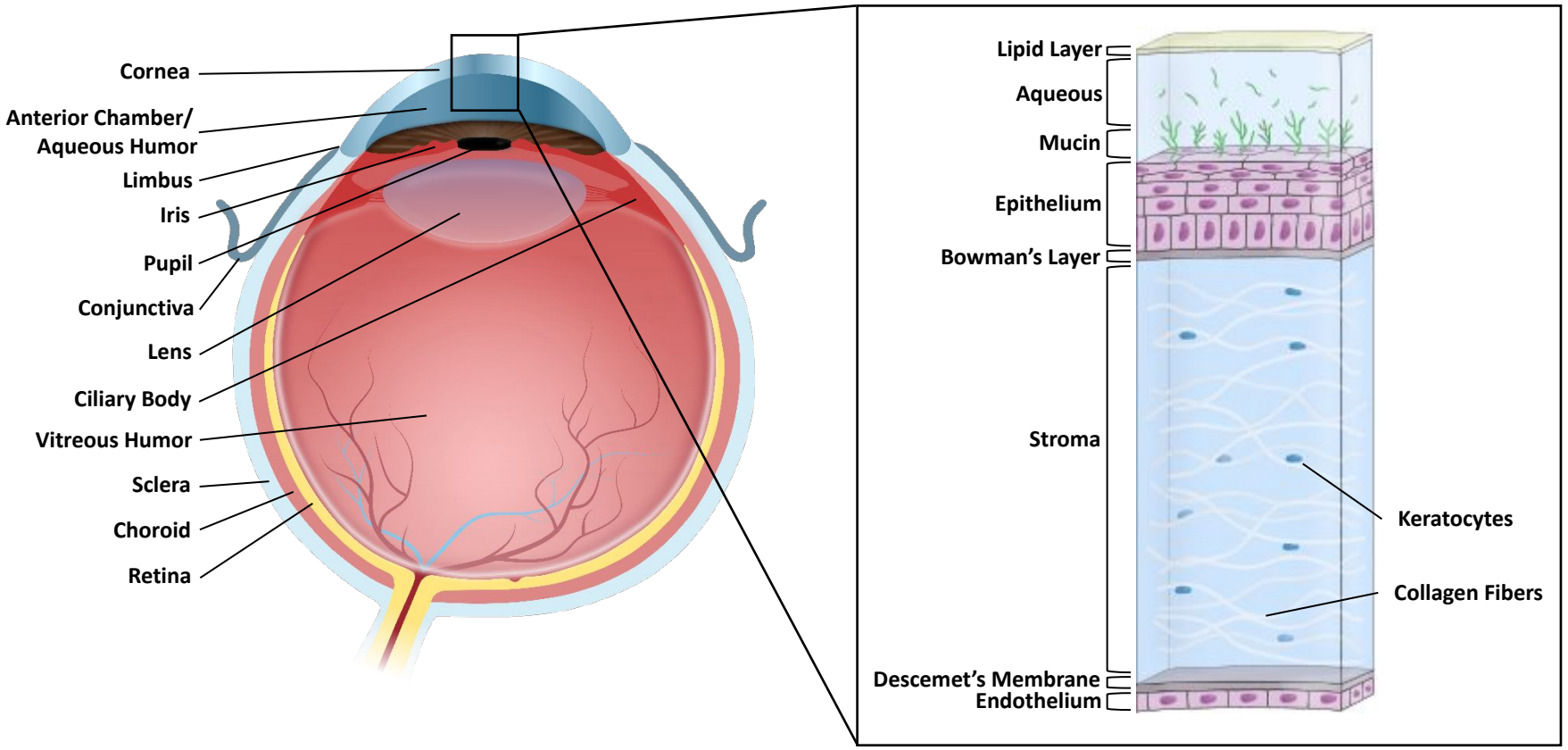
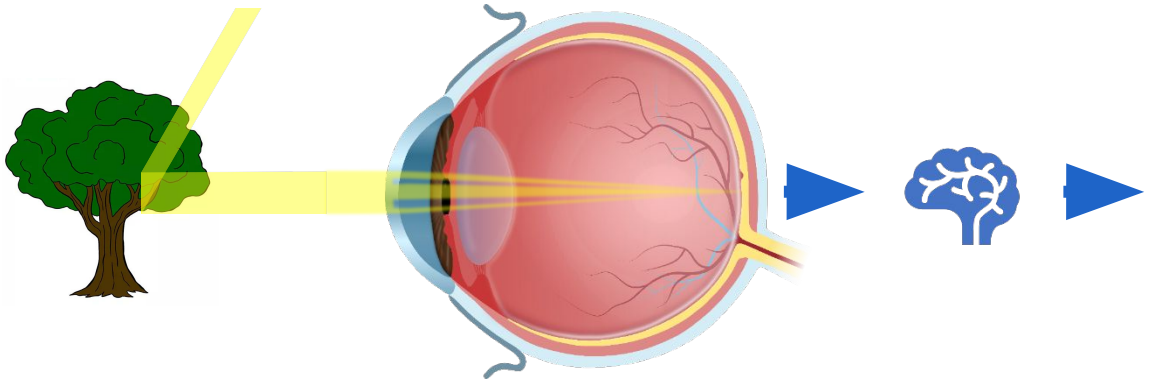
Anatomy of the eye



Corneal epithelium defects

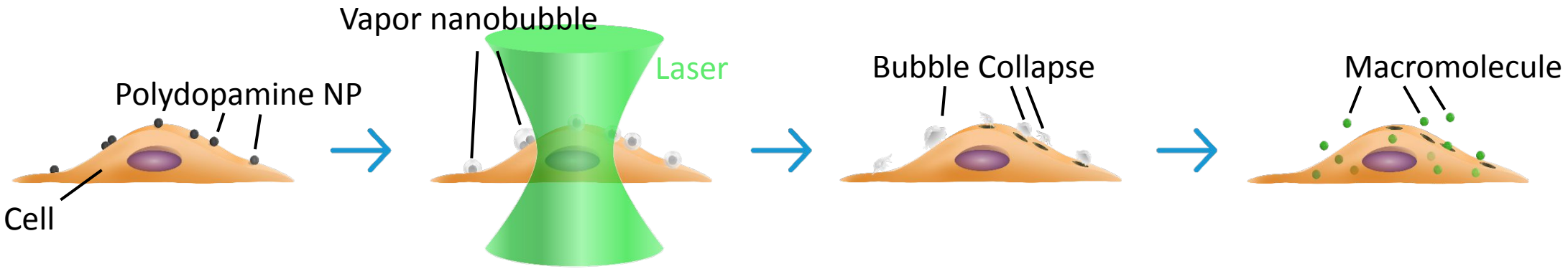
- Corneal blindness is the 4th cause of blindness worldwide
- Epithelium, stroma, endothelium
- Epithelial healing is altered with somes diseases (e.g. diabetes)
- Entry point for infections



Nucleic acids hold great promises for treating the corneal epithelium

Nucleic acids delivery at the ocular surface is hampered by several barriers (tear film, mucus…)

Principle of laser-induced nanobubble generation



Polydopamine nanoparticle

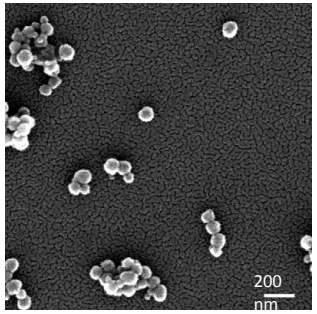
Light absorbing

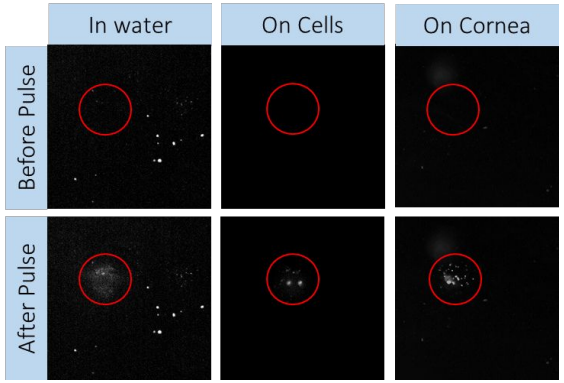
Synthetic polymer

PEI coating

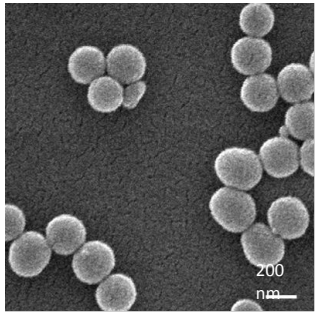
Nanobubble generation and photoporation

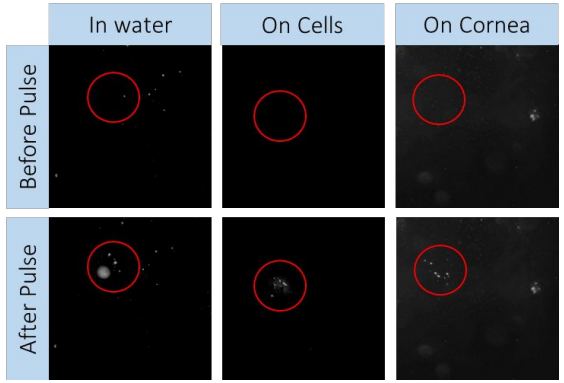
90 nm PD-PEI NPs





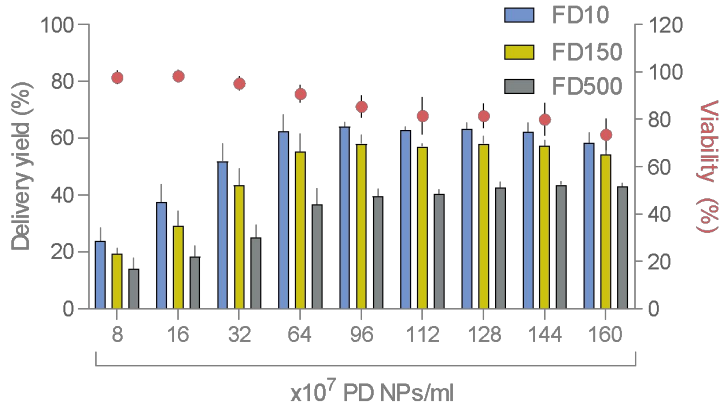
250 nm PD-PEI NPs



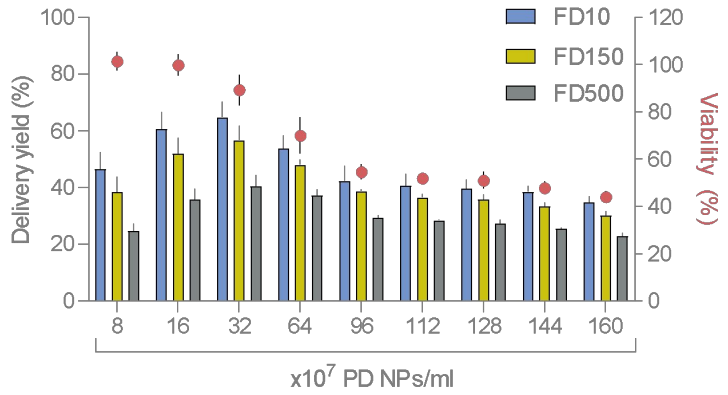


Primary bovine epithelial cells

1.8 J/cm²; 561 nm; <7ns

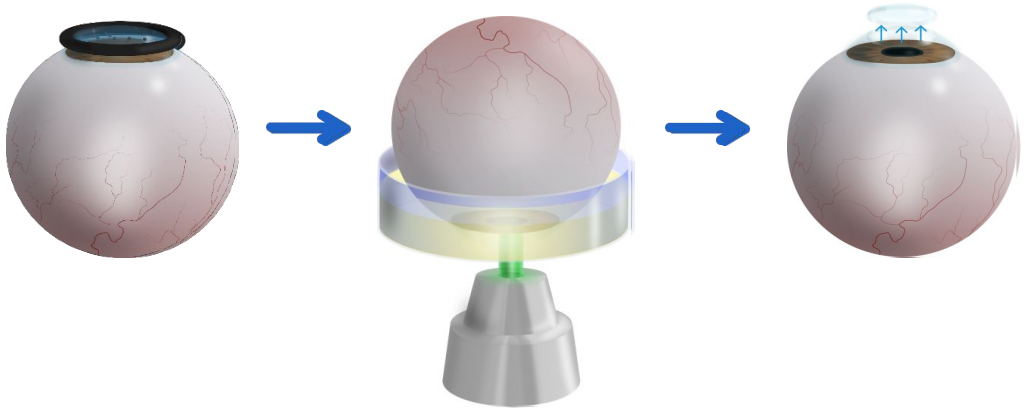


1.8 J/cm²; 561 nm; <7ns

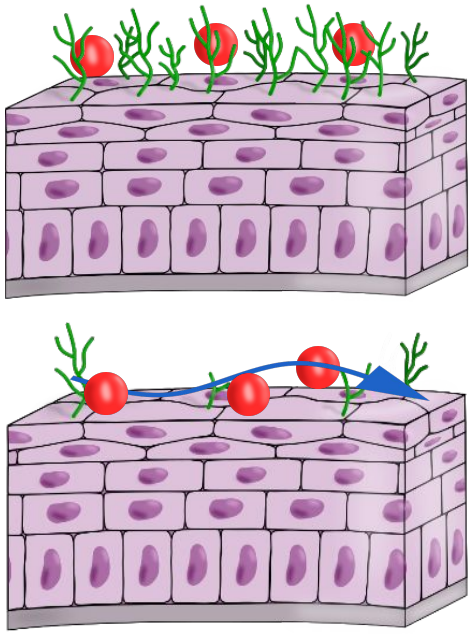


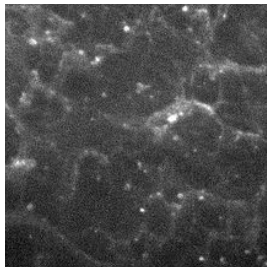
Nanobubble-mediated mucus disruption

Ex vivo model (bovine)

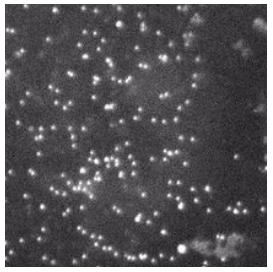


2.5 J/cm²; 561 nm; <7ns

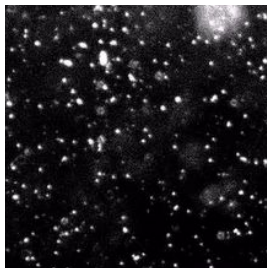




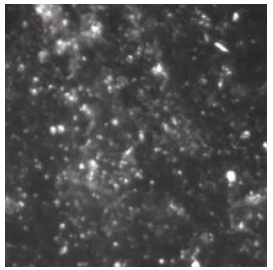
Bla



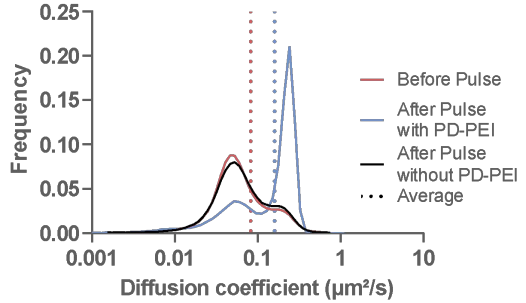
Beads



Beads with PD-PEI NPs



Beads with PD-PEI NPs



Photoporation *(ex vivo)*

Ex vivo model (bovine)

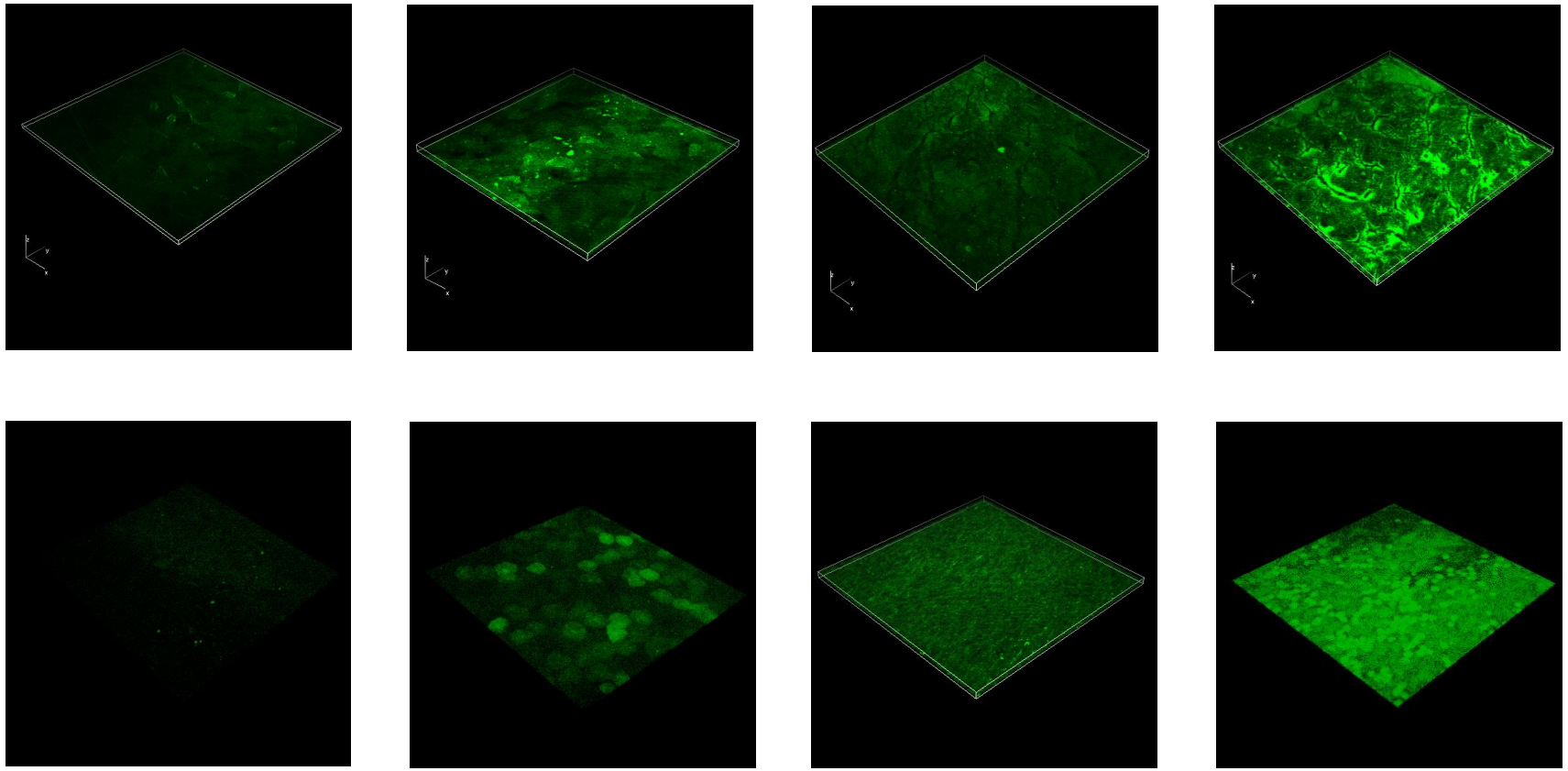
250 nm PD-PEI NPs 1.8 J/cm²; 561 nm; <7ns

With mucus intact

With mucus removed

500 kDa FD

eGFP mRNA



Cornea with cargo and PD-PEI NPs
But not laser treated

Fully treated

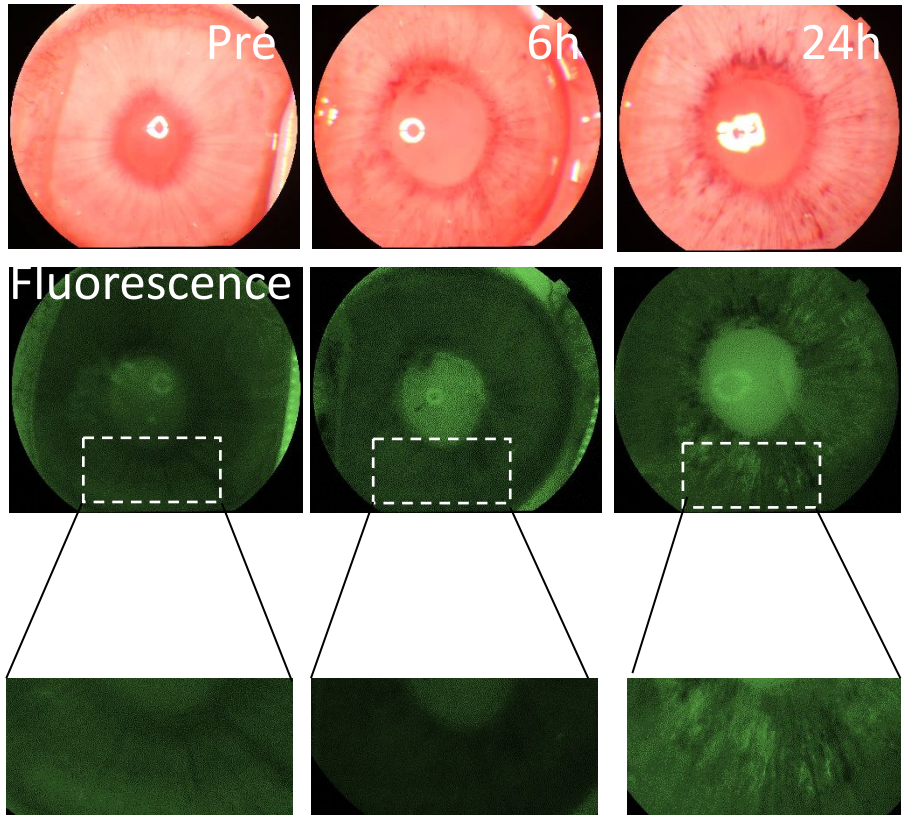
Cornea with cargo and PD-PEI NPs
But not laser treated

Fully treated

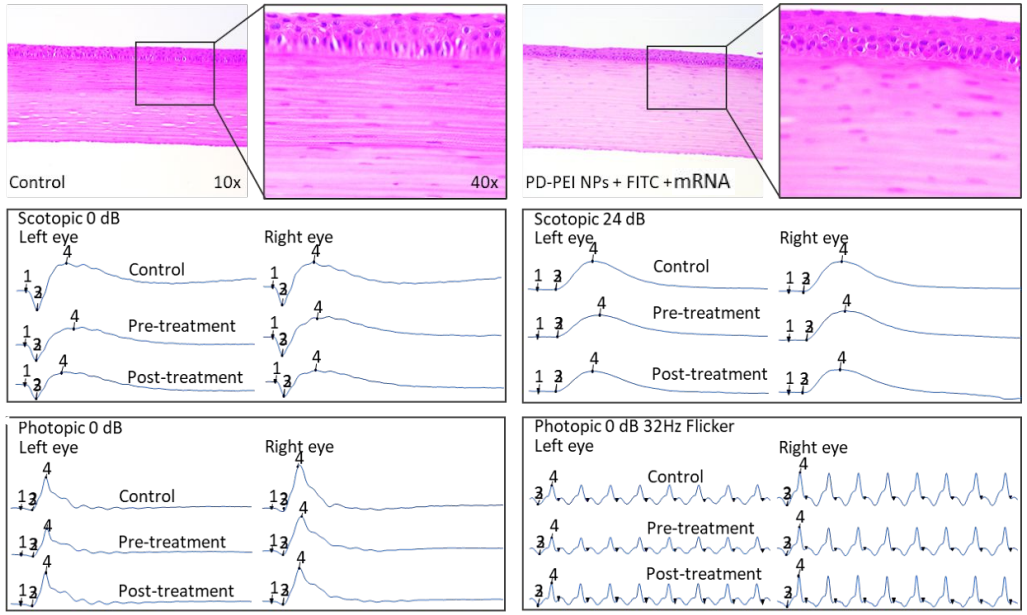
Safety & efficacy in vivo

Prof. Y. Paulus
Dr. VP. Nguyen

eGFP mRNA 1.8 J/cm²; 532 nm; <7ns



H&E and ERG



Post treatment: 7 days

Conclusion

- Laser-induced nanobubbles can disrupt the mucus
- Laser-induced nanobubbles can deliver molecular compounds in corneal epithelial cells
- eGFP expression could be seen on the corneal surface of rabbits
- Photoporation did not show toxicity in rabbits, 7 days post-treatment

Thanks for your attention!

Acknowledgement

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