

Exploring light for advanced drug delivery & surgery in the eye

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Delivery of – especially biological – drugs into the various compartments of the eye remains an enormous challenge. In this talk I will highlight recent work of our group in which we evaluate the potential of the combined use of pulsed laser light and ocular photosensitizers, more precisely ocular dyes packaged in nanomaterials, to cross biological barriers in the eye. The first part of my lecture will introduce photoporation of cell membranes for the intracellular delivery of macromolecular drugs; a special emphasis will be on our recent findings which show the capacity of photoporation for the delivery of nucleic acids into the epithelium and endothelium of the cornea. In the second part I will explain how pulsed laser light and packaged photosensitizers allow to safely destroy pathological collagen aggregates which appear upon aging in the vitreous of the eye and which may heavily disturb vision. Finally, I will introduce photoporation of the inner limiting membrane, a collagen rich membrane which separates the vitreous from the retina, and which severely hinders transport of macromolecules from the vitreous into the retina. I will show that locally applying photosensitizers and irradiating the inner limiting membrane with pulsed laser light might be an attractive strategy to facilitate the transport of intravitreally injected nucleic acids and nanomedicines into the retina. These findings might be of interest for further exploration to allow genetic treatments of the retina.

References

Hua, D., Harizaj, A., Wels, M., Brans, T., Stremersch, S., De Keersmaecker, H., Bolea-Fernandez, E., Vanhaecke, F., Roels, D., Braeckmans, K., Xiong, R., 2021. Bubble forming films for spatial selective cell killing. *Advanced Materials*,

33(27), 2008379.
<https://doi.org/10.1002/adma.202008379>Citations: 18
Peynshaert, K., Devoldere, J., Minnaert, A.K., De Smedt, S.C., Remaut, K., 2019. Morphology and composition of the inner limiting membrane: species-specific variations and relevance toward drug delivery research. *Current eye research*, 44(5), 465-475.
<https://doi.org/10.1080/02713683.2019.1565890>
Sauvage, F., Fraire, J.C., Remaut, K., Sebag, J., Peynshaert, K., Harrington, M., Van de Velde, F.J., Xiong, R., Tassignon, M.J., Brans, T., Braeckmans, K., 2019. Photoablation of human vitreous opacities by light-induced vapor nanobubbles. *ACS Nano*, 13(7), 8401-8416.
<https://doi.org/10.1021/acsnano.9b04050>
Sauvage, F., Nguyen, V.P., Li, Y., Harizaj, A., Sebag, J., Roels, D., Van Havere, V., Peynshaert, K., Xiong, R., Fraire, J.C., Tassignon, M.J., 2022. Laser-induced nanobubbles safely ablate vitreous opacities in vivo. *Nature nanotechnology*, 17(5), 552-559. <https://doi.org/10.1038/s41565-022-01086-4>
Sauvage, F., Schymkowitz, J., Rousseau, F., Schmidt, B.Z., Remaut, K., Braeckmans, K., De Smedt, S.C., 2020. Nanomaterials to avoid and destroy protein aggregates. *Nano Today*, 31, 100837.
<https://doi.org/10.1016/j.nantod.2019.100837>
Xiong, R., Hua, D., Van Hoeck, J., Berdecka, D., Léger, L., De Munter, S., Fraire, J.C., Raes, L., Harizaj, A., Sauvage, F., Goetgeluk, G., 2021. Photothermal nanofibres enable safe engineering of therapeutic cells. *Nature nanotechnology*, 16(11), 1281-1291. <https://doi.org/10.1038/s41565-021-00976-3>
Xiong, R., Raemdonck, K., Peynshaert, K., Lentacker, I., De Cock, I., Demeester, J., De Smedt, S.C., Skirtach, A.G., Braeckmans, K., 2014. Comparison of gold nanoparticle mediated photoporation: vapor nanobubbles outperform direct heating for delivering macromolecules in live cells. *ACS nano*, 8(6), 6288-6296.
<https://doi.org/10.1021/nn5017742>

Xiong, R., Samal, S.K., Demeester, J., Skirtach, A.G., De Smedt, S.C., Braeckmans, K., 2016. Laser-assisted photoporation: fundamentals, technological advances and applications. *Advances in Physics: X*, 1(4), 596-620. <https://doi.org/10.1080/23746149.2016.1228476>