Non-invasive cornea nanosurgery using plasmonic nanoparticles and femtosecond laser

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NANOMEDICINES INNOVATION NETWORK
RÉSEAU D'INNOVATION NANOMÉDECINES

Problematic

Corneal endothelial dystrophies

Major causes of blindness

40% of corneal transplantations (North America)

Current solutions

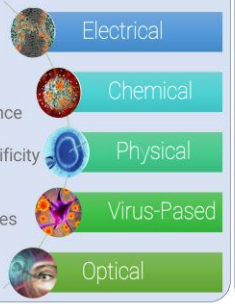
Corneal transplantation

Disadvantages of the current techniques:

- Cellular degeneration
- Graft failure
- Rejection

Gene therapy

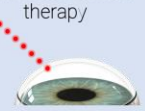
- Toxicity
- Disease persistence
- Low specificity
- Invasive techniques



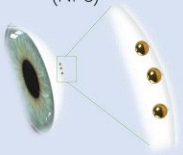
Our proposal

The use of combined tools:

Femtosecond laser therapy



Plasmonic nanoparticles (NPs)



This project collects different expertise domains such as ophthalmology and nanophotonics, opening a great opportunity to collaborate with different universities, hospitals and instances

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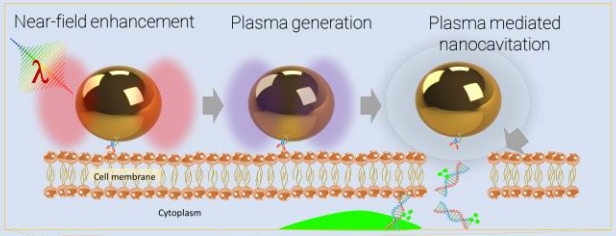
Advantages

- Well-known technique: already in use
- Optoporation / transfection
- High precision laser beam
- Non invasive technique
- Therapeutic window

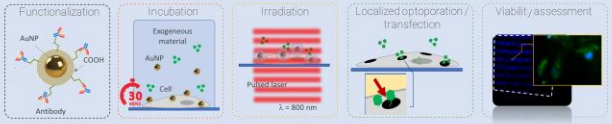
- Photostability
- Biocompatibility
- Gold surface markers
- Plasma-mediated nanocavitation
- Less energy = reduction of side effects

The principle



Gold nanoparticles (AuNPs) are attached to the cell membrane to subsequently irradiate them with a femtosecond laser (800 nm @ 1 kHz). The absorption of the energy leads to a near-field enhancement and subsequently to a plasma generation that produces a plasma mediated nanocavitation. The rupture of the cellular membrane is induced and exogenous molecules can be delivered to the nuclei or cytoplasm.

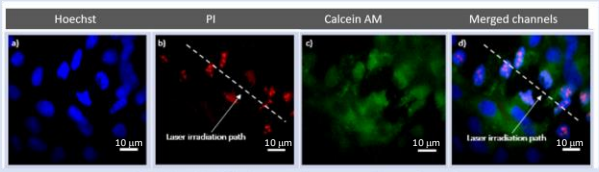
Methodology



NPs are functionalized to subsequently incubate them and irradiate the cells. The fluorescence imaging allows to provide a ratio of viability vs optoporated cells.

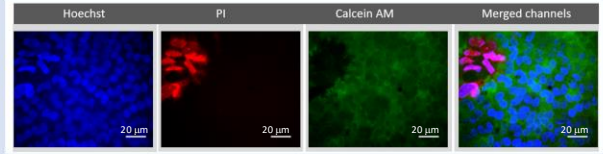
Preliminary results

In vitro tests: Irradiation of human ocular cells



~70 % of efficiency for small molecules

Ex vivo tests: Irradiation of animal model endothelium



Cell nuclei · *Optoporated cells* · *Live cells*

The proof of principle has been successfully achieved in vitro with human ocular cells.

A 70 % of internalization was achieved using small dyes in human ocular cells.

Several toxicity tests were performed in order to discard cellular death associated with the use of laser or nanoparticles correspondingly.

Nowadays we focus on ex vivo animal models to subsequently apply our technique on in vivo models.

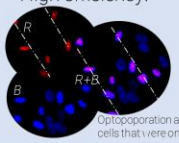
Conclusions

Proof of principle done with cells

- The treatment offers negligible toxicity.
- Less invasive than the currently available techniques.
- Safe and approved techniques are now combined to enhance the effect of laser therapy.

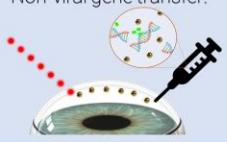
In terms of novelty, we offer a combined effect of the laser and the functionalized NPs, highlighting

- High efficiency.



Optopoporation achieved on cells that were on the laser path

- Non-viral gene transfer.



- Double specificity.

References

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