Plasmonic enhanced femtosecond laser anticancer drug delivery using gold-lipid nanoparticles

Amélie Baron[1], Leonidas Agiotis[1], Igor V. Zhigaltsev[2], Antoine Uzel[1], Morteza Kafshgari[1], Pieter Cullis[2] and Michel Meunier[1]

[1]Department of Engineering Physics, Polytechnique Montreal, Montreal, QC H3C3A7, Canada [2] Department of Biochemistry and Molecular Biology, University of British Columbia, Vancouver, BC V6T 1Z3, Canada

Abstract

Chemotherapy is not specific to cancer cells as less than 5% of the administered dose targets cancer cells. **Our aim is to improve local treatment using liposomes (LNPs) containing gold nanoparticles (GNPs) and the chemotherapeutic agent, doxorubicin (DOX).** Using MDA-MB-231 breast cancer cell line, proof-of-concept is performed with a **femtosecond laser** (800 nm wavelength, 55 fs pulse duration). Optimization of laser irradiation parameters resulted in **an optimal fluence of ~100 mJ/cm 2 with ~2 pulses per spot,** leading to a reduction in cell viability of up to 30%. The method of delivery **increases the specificity of the treatment.**

Introduction

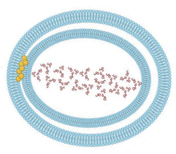
Drawbacks:

1. Not specific to cancer cells

2. Only **5%** of the drug reaches the tumor

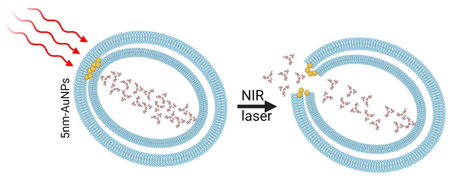
3. High toxicity resulting in a limited amount tolerated by the body

➢ **Encapsulation** of the chemotherapeutic drug



➢ **Long-lasting lipid nanoparticles (LNPs)** inside the body but still not specific to the cancer cells

➢ **Laser-triggered release** the drug using the **gold nanoparticles**



➢ **Specific delivery**

Specific release in the tumor area

Decreased drug release in **the general body**

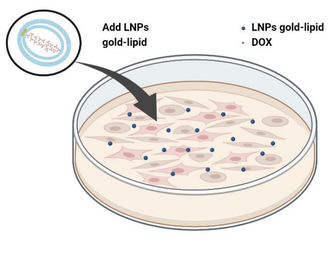
Our goal : Improving cancer drug delivery!

Methods

The formulation :

➢ **Liposome (LNPs) of 100 nm** with **gold nanoparticules (GNPs) of 5-10 nm** encapsulating chemotherapy drug **Doxorubucin (DOX) [50 μg/mL]**

➢ **LNPs** formed from **DODAP/DSPC/Chol/PEG-DSPE**



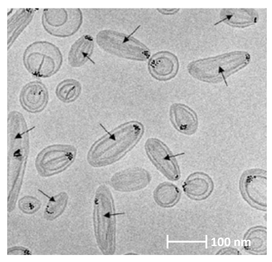


Fig. 1: Dox precipitates in the center [black arrows]. [2] [5]

1. **Internalization of gold-lipid LNPs (and 4 controls) with breast cancer cells (MDA-MB-231)** with subsequent washing of the cells
2. **Laser scanning** to trigger liposome opening
3. **Viability test after** irradiation (to ensure that DOX effectively kills cells)

Protocol

1. Seeding of cells [20,000 cells/well] in 96 wells.

48h incubation

2. LASER irradiation (different parameters)

24h incubation

3. Viability test (MTT test or fluorescence imaging)

Mechanism

Trigger mechanism:

➢ **Nanoscale interaction** of a few nanoseconds

➢ **Off resonance plasmonic** response to triggered light

➢ **Collective amplification** allowing to reach a high intensity (~2.5 × 10^{13} W/cm^2)

➢ **Ionization of the DSPC molecule** (photochemical effect) and **liposome opening**

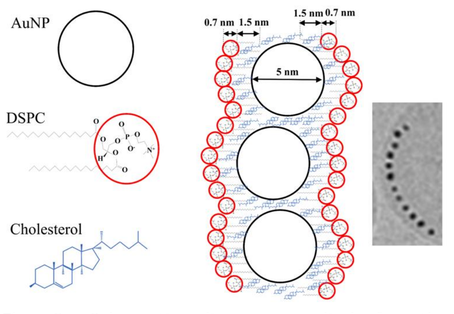


Fig. 2: Schematic diagram applied for the numerical simulations of temperature increase

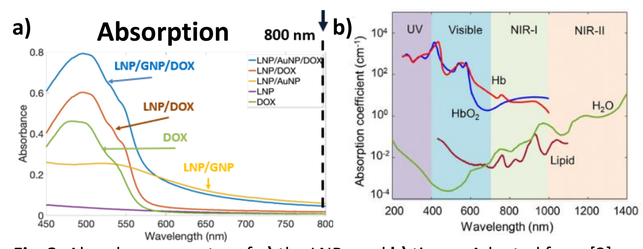
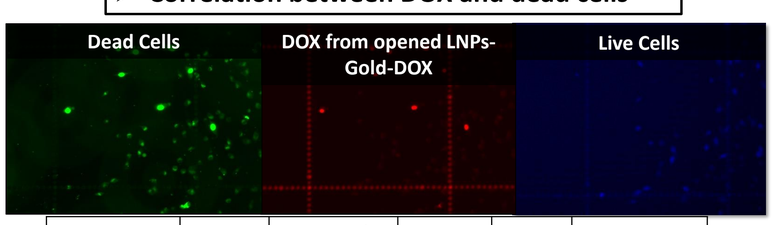


Fig. 3: Absorbance spectra of **a)** the LNPs and **b)** tissue. Adapted from [2].

Low tissue and nanoparticles absorption at 800 nm

Results

➢ **Correlation between DOX and dead cells**



Condition	Spot size	Optimal Fluence	Speed	Step	Frequency
LNPs-GNPs-DOX	23 μm	100 mJ/cm^2	15 mm/s	40 μm	1 kHz

Fig. 4 : Fluorescence imaging by LASER irradiation on MDA-MB-231 cells with LNPs-GNPs-DOX and LASER parameters.

Femtosecond laser (λ = 800 nm)

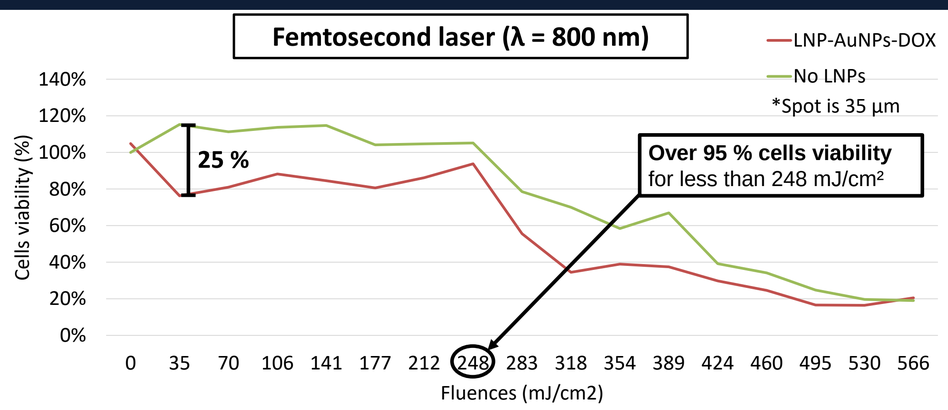


Fig. 5: MTT assay with different fluences with liposomes.

Conditions	Mean	SD
No laser and **no** LNPs-AuNPs-DOX	100.0%	9.15 %
No laser and LNPs-AuNPs-DOX	104.8%	7.27%
Laser and **no** LNPs-AuNPs-DOX	115.2%	7.50%
Laser and LNPs-AuNPs-DOX	**76.3%**	0.35%

Conclusion

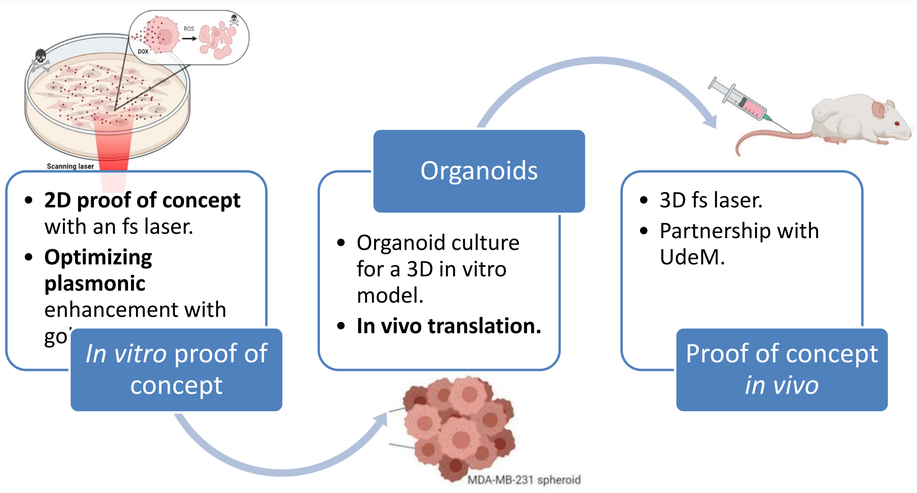


Fig. 6 : Future work processus in three steps over 5 years.

Conclusion :

➢ **Over 95 % cells viability** for less than 248 mJ/cm^2

➢ **20-30% DOX is released** and kills cells in the optimal range after laser irradiation

➢ **Femtosecond laser at 800 nm → Translation** to *in vivo* study

↑ Increased **tumor site-specific** release and ↓ decreased healthy cell death.

↓ Decreased **number of cycles** of chemotherapy to overcome cancer.

Overall, this increases the chances of treating cancer!

References

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POLYTECHNIQUE MONTRÉAL UNIVERSITÉ D'INGÉNIERIE
THE UNIVERSITY OF BRITISH COLUMBIA
NMIN NANOMEDICINES INNOVATION NETWORK RÉSEAU D'INNOVATION NANOMÉDECINES
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