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

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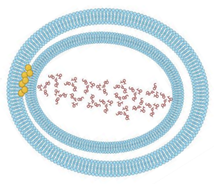
Introduction

Drawbacks:

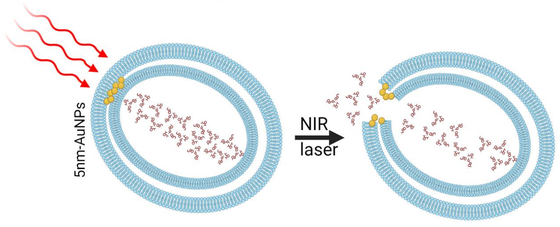
1. **Not specific** to cancer cells
2. Only **5%** of the drug reaches the tumor
3. **High toxicity** resulting in a limited amount tolerated by the body

➢ **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!

Our approach

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**

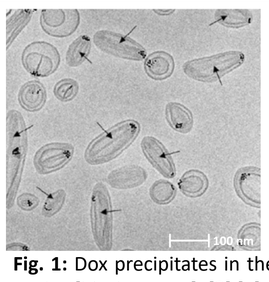
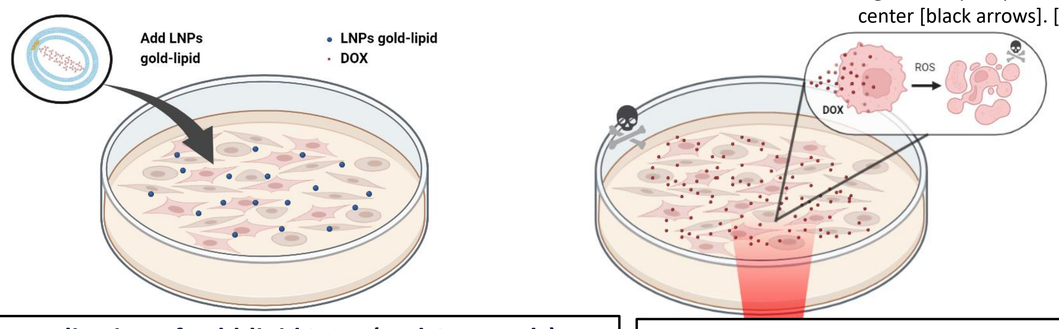


Fig. 1: Dox precipitates in the center [black arrows]. [2] [5]



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.
2. **48h incubation**
3. **LASER irradiation (different parameters)**
4. **24h incubation**
5. **Viability test (MTT test or fluorescence imaging)**

Mechanism

Trigger mechanism:

➢ **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)

➢ **Liposome opening**

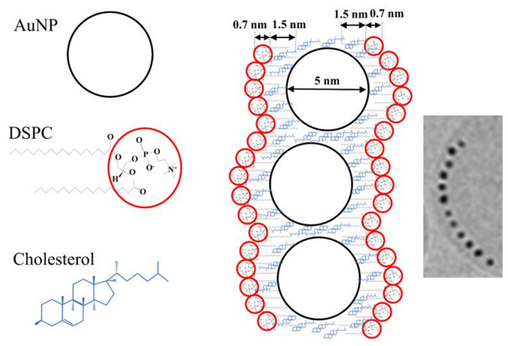


Fig. 2: Schematic diagram applied for the numerical simulations of temperature increase

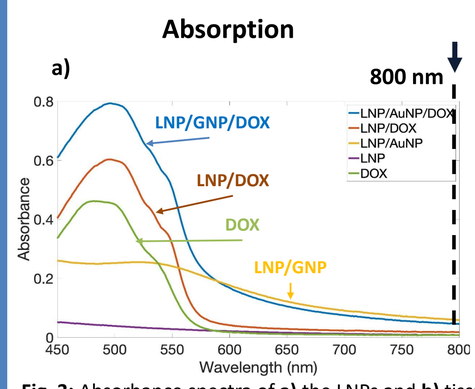
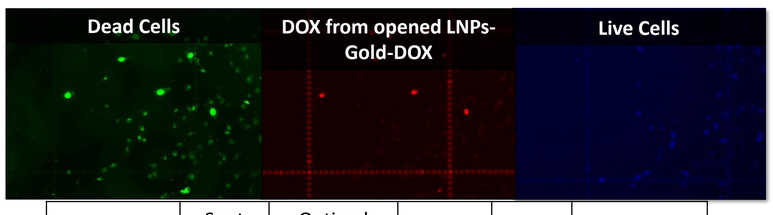


Fig. 3: Absorbance spectra of **a)** the LNPs and **b)** tissue. Adapted from [2].

Low tissue and nanoparticles absorption at 800 nm

In vitro results with MDA-MB-231 breast cancer 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) - Optimization

*Spot is 35 µm

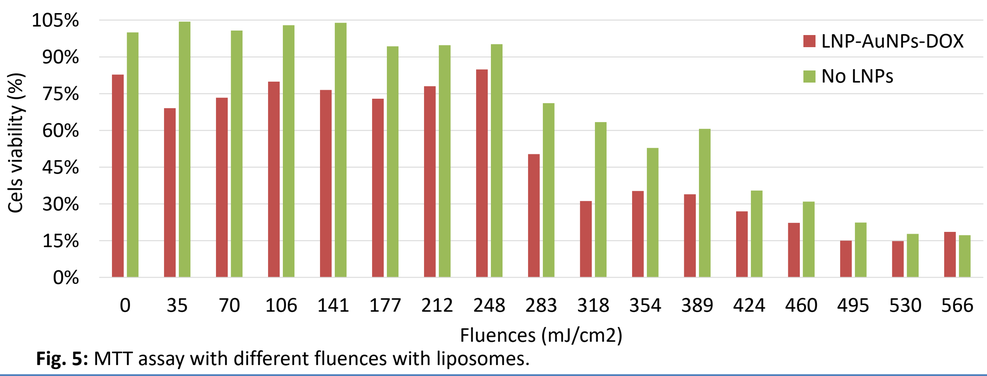


Fig. 5: MTT assay with different fluences with liposomes.

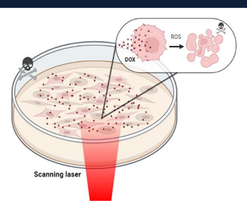
Conclusion :

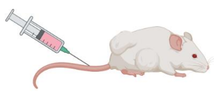
➢ **Over 95 % cells viability** for less than 248 mJ/cm^2

➢ **20-40% DOX is released** and kills cells in the optimal range after LASER irradiation

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

Conclusion





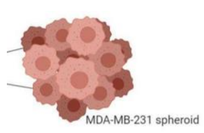


Fig. 6 : Future work processus in three steps over 5 years.

Conclusion :

➢ **Encapsulated triggered release DOX is effective** in delivering chemotherapeutic drug to cancer cells.

Expected results :

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

↑ Increased **tolerated injectable dose.**

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

Overall, this increases the chances of treating cancer!

References

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[3] Upputuri, Paul Kumar & Pramanik, Manojit. (2019). *Photoacoustic imaging in the second near-infrared window: a review*. Journal of Biomedical Optics. 24. 40901. 10.1117/1.JBO.24.4.040901.

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[5] Zhigaltsev, Igor & Tam, Yuen & Kulkarni, Jayesh & Cullis, Pieter. (2022). *Synthesis and Characterization of Hybrid Lipid Nanoparticles Containing Gold Nanoparticles and a Weak Base Drug*. Langmuir. 38. 10.1021/acs.langmuir.2c01221.

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