In search of conditions for Gd-TiO_2 activation by light irradiation in photodynamic treatment of pancreatic cancer cells

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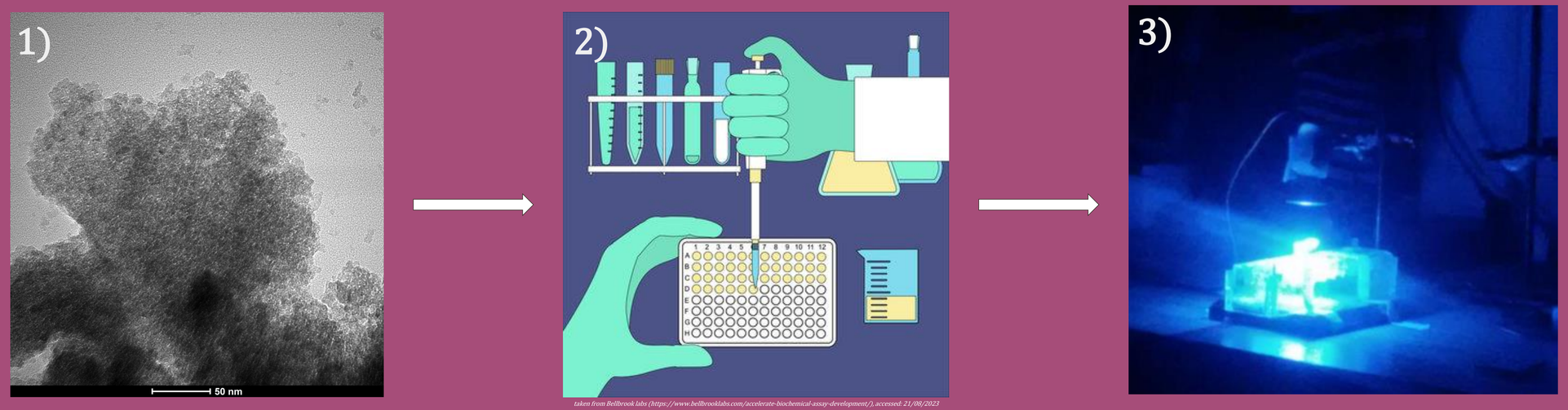
Introduction

Pancreatic cancer cells express high resistance to commonly used chemotherapies and radiotherapy[1]. The emergence of new therapeutic solutions to fight this issue is becoming essential, one of them being photodynamic therapy (PDT)[2]. By the use of photosensitizing nanoparticles and light sources, PDT focuses on tumor tissue and its size reduction by the creation of reactive oxygen species. We have synthesized Gadolinium-doped Titanium-dioxide nanoparticles (Gd-TiO_2 NPs) and tested their activation with visible light and effects on two pancreatic cancer cell lines, PANC-1 and MIA PaCa-2.

Methods

- NPs synthesis and characterization as described in our previous work [3].
- UV-VIS analysis - TiO_2 band-gap reduction - possible excitation with visible blue light
- PANC-1 and MIA PaCa-2 cells were seeded in 96 well plates, treated with different concentrations of NPs, and irradiated with a visible light source.
- Irradiation times and intensities: from 10 to 30 minutes, from 36μW to 1.3 mW
- SRB-assays - cell viability 48h after treatment



taken from Bellbrook labs (https://www.bellbrooklabs.com/accelerate-biochemical-assay-development/), accessed: 21/08/2023

Figure 1: Experimental set-up: 1) TEM image of Gd-TiO2 NPs, 2) NPs treatment of PANC-1 and MIA PaCa-2 cells, 3) Blue light irradiation of cells

Results

- UV-VIS spectra showed an increased absorbance in the visible light range, suggesting that the doping with Gd lead to a reduced band gap of Gd-TiO_2 NPs.

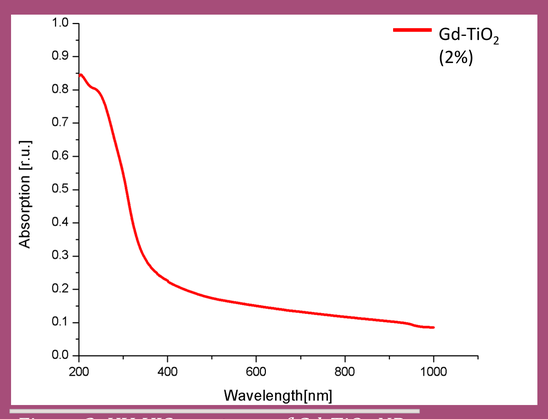


Figure 2: UV-VIS spectrum of Gd-TiO_2 NPs.

- The Tauc plot calculations indicated a band-gap of 2.7 eV, implying a possibility to excite the NPs with visible blue light.
- The cytotoxicity assays prior to irradiation showed good compatibility for concentration up to 2 mg/mL in both cell lines. [1]

Irradiation tests

- No NP treatment, 3 different irradiation powers and durations (Figure 3) → In MIA PaCa-2 cells, the cell viability increased with irradiation, compared to control.

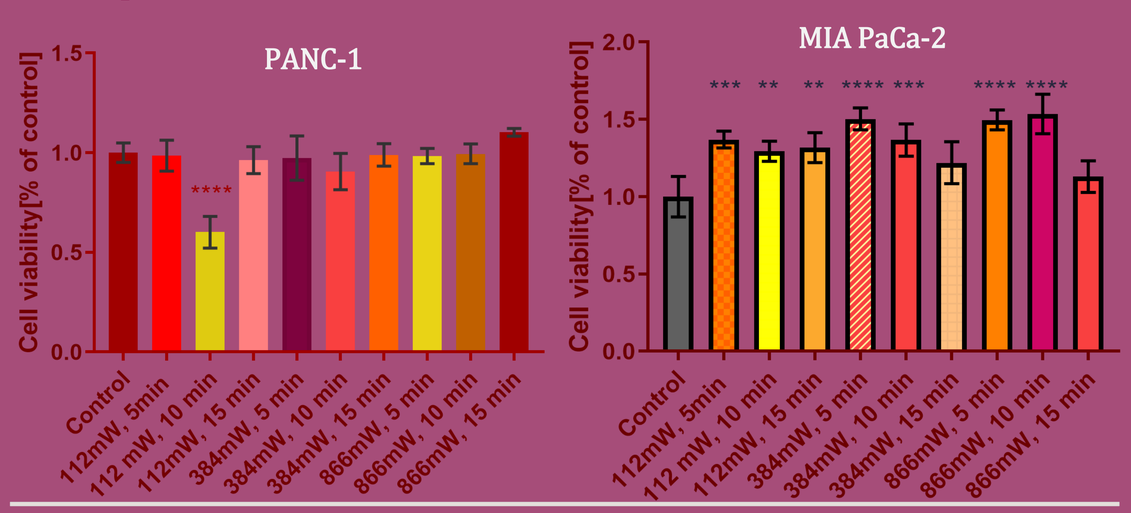


Figure 3: Irradiation with different light power, no NPs

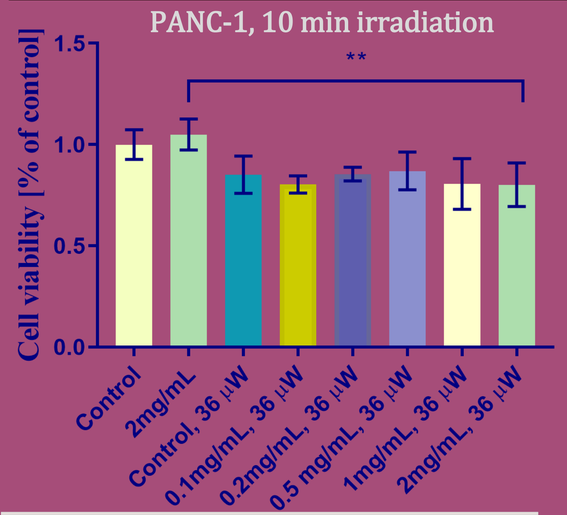


Figure 4: Low power irradiation, 4 different concentration of NP treatment.

- NP-treated, 3 concentration, lowest irradiation power of 36μW for 10 minutes (Figure 4) → Significant decrease in viability observed only for the highest concentration of 2mg/mL, comparing to non-irradiated, compared to NP-treated control.
- NP-treated, 3 concentrations, irradiation power 75μW → In both cell lines, the NP-treated and irradiated cells expressed higher viability, contrary to what was expected. Cytotoxicity of NP/light treatment of MIA PaCa-2 is given in Figure 5.

Figure 6: PANC-1, 1 mW and 1.3 mW irradiation of 1mg/mL NP-treated cells.

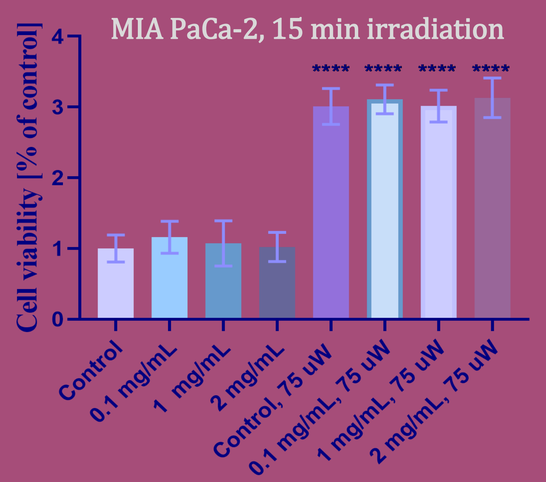


Figure 5: MIA PaCa-2, 75μW irradiation of 3 different concentrations of NP treatment.

- NP-treated, different light source, optical fiber and higher radiation power (Figure 6)
  → Treatment did not induce a significant change in viability of PANC-1 cells.

Conclusions

By using two different light sources, varying irradiation power and duration, we attempted to activate the Gd-TiO_2 NPs and induce ROS formation that would influence the viability of the two pancreatic cell lines. However, cell viability was not consistently decreased for treated and irradiated cells, while in some cases the viability increased.
A possible explanation might lie in the limited absorbance of NPs in visible light range. Doping the NPs with additional photosensitizers might lead to a better activation. Direct measurements of ROS production can be used as further assessment of the NP activation.

Acknowledgments

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Citations

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