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Photothermal Cancer Therapy with Graphene-Based Materials and their Drug Conjugates

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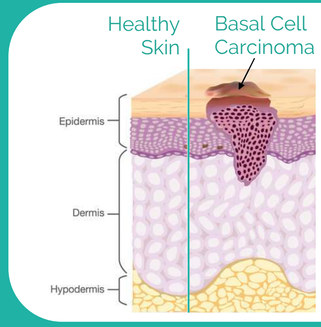
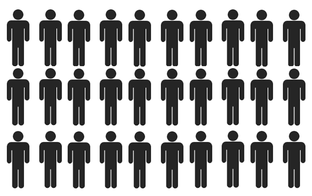




Most common cancer worldwide

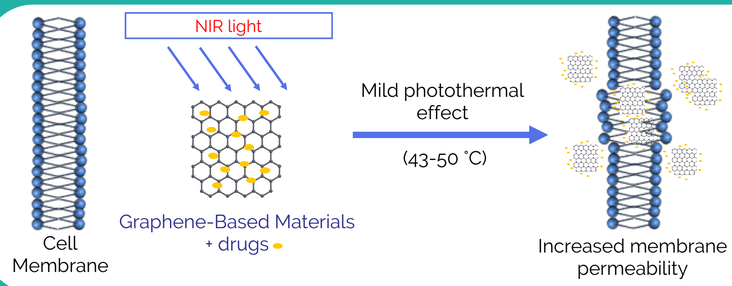
Current therapies:
- Complete surgery
- Topical therapies
- Chemo-, Immuno-, Radiotherapy

✘ Bioaccumulation of cytotoxic anti-cancer drugs

✘ Relapse following treatment discontinuation

Basal Cell Carcinoma (BCC), the most common form of cancer, requires surgical treatment. Alternatively, photothermal therapy may be an effective non-invasive treatment [1].

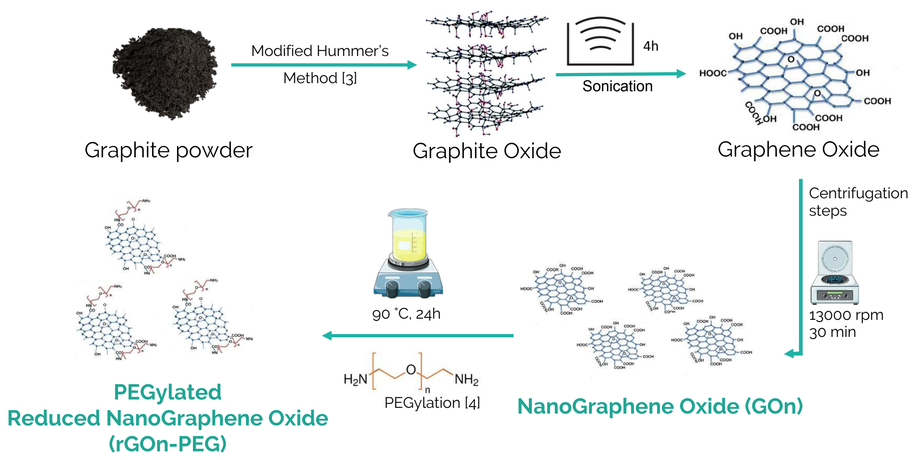
In this study, graphene-based materials (GBM), which can absorb radiation, are investigated as platforms to induce mild photothermal effects and further loaded with an anti-cancer drug envisioning a combined therapy to treat BCC, improving current clinical outcomes.



Near-infrared (NIR) light energy can induce mild temperature increases (43-50 °C), leading to the activation of apoptotic pathways on tumor cell, including enhanced membrane permeability and consequent increased cell uptake [2].

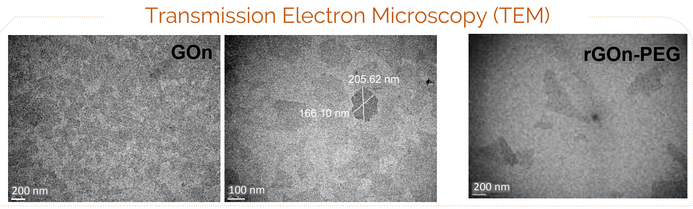
1. Graphene-Based Materials

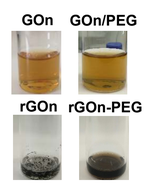
• GBM synthesis



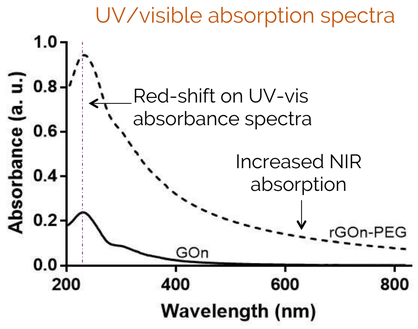
• Characterization of GOn and rGOn-PEG

Transmission Electron Microscopy (TEM)





UV/visible absorption spectra



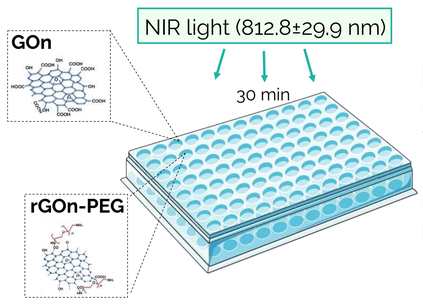
Particle size	GOn
TEM (average; range)	248 nm; 50 – 250 nm
DLS (average; range)	141 nm; 96 – 230 nm

GBM	Zeta potential (mV)
GOn	-25.6 ± 0.8
rGOn-PEG	-13.7 ± 0.7

Nano-sized GO was synthesized, successfully reduced and functionalized with PEG to obtain stable aqueous dispersions (rGOn-PEG).

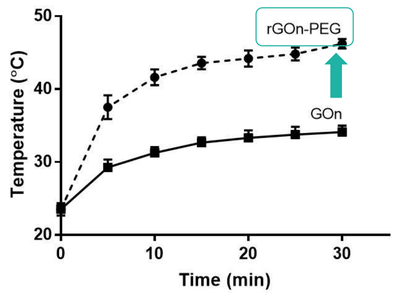
2. NIR Absorption

• NIR irradiation



Near Infrared (NIR) irradiation studies were performed using a custom-built LED based light source.

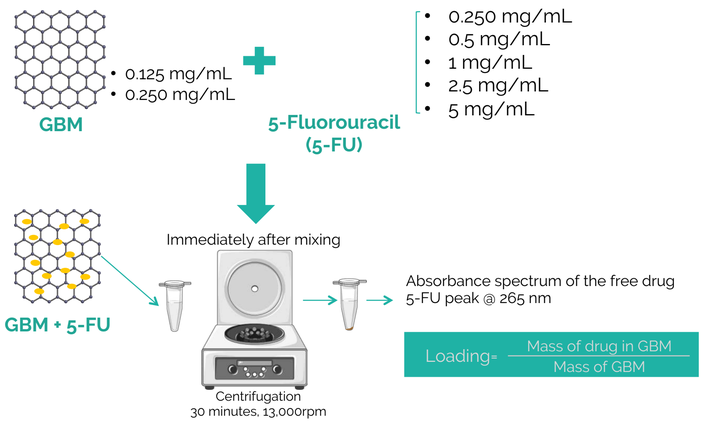
• Temperature change



NIR irradiation increased rGOn-PEG temperature, with a difference of 11.7 °C, compared to GOn. Maximum temperature reached by rGOn-PEG was 47 °C.

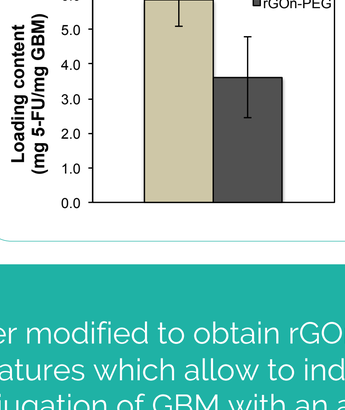
3. Drug Loading on rGOn-PEG

• Drug Adsorption



Physisorption does not inactivate drugs, as might happen when covalent functionalization is performed.

• 5-FU loading on rGOn-PEG

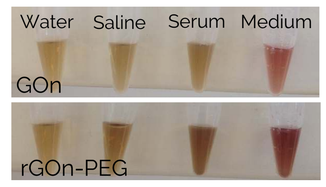


GBM	Loading
GOn	5.8 ± 0.8
rGOn-PEG	3.6 ± 1.2

5-FU was successfully loaded by simple molecular physisorption via π-stacking onto GBM.

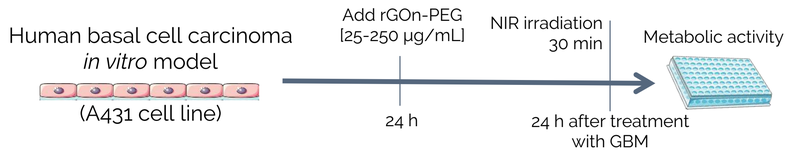
4. *In vitro* Cellular studies

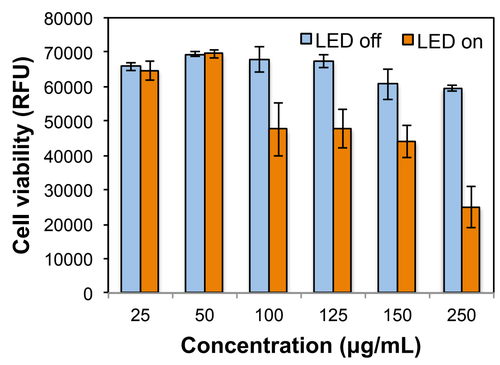
• Stability of GBM



GOn and rGOn-PEG are stable in physiological solutions, including cell culture medium.

• Cell viability after NIR irradiation





Increasing rGOn-PEG concentration in combination with NIR irradiation reduced cellular viability.

Conclusions:
- ✓ Nano-sized GO (GOn) was synthesized and further modified to obtain rGOn-PEG.
- ✓ Under NIR irradiation, rGOn-PEG reaches temperatures which allow to induce mild photothermal effects.
- ✓ Simple molecular physisorption enabled the conjugation of GBM with an anti-cancer drug, 5-Fluorouracil.
- ✓ The combination of rGOn-PEG with near-infrared light irradiation led to reduced cell viability in an *in vitro* model of basal cell carcinoma.

↳ Our study opens new avenues for the use of GBM-based nanodelivery for cancer double therapy.

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References

1. Kim J.Y. *et al.*, J Am Acad Dermatol 2018, 78:540-559;
2. 2. Zhang, B. *et al.*, Curr Med Chem, 2017, 24: 268;
3. Pinto A.M. *et al.*, Carbon, 2015, 99:318;
4. Chen J. *et al.*, Biomaterials, 2014, 35:4986-4995

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