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# A single metal multifunctional nanotexaphyrin as a radiotheranostics agent for cancer imaging and therapy

Miffy H. Y. Cheng[1], Marta Overchuk[1,2], Maneesha Rajora[1,2], Juan Chen[1], and Gang Zheng[1,2]*

[1] *Princess Margaret Cancer Centre University Health Network 101 College Street, PMCRT 5-354, Toronto, Ontario M5G 1L7, Canada*

[2] *Institute of Biomaterials and Biomedical Engineering, University of Toronto, 101 College Street, Toronto, Ontario M5G 1L7, Canada*

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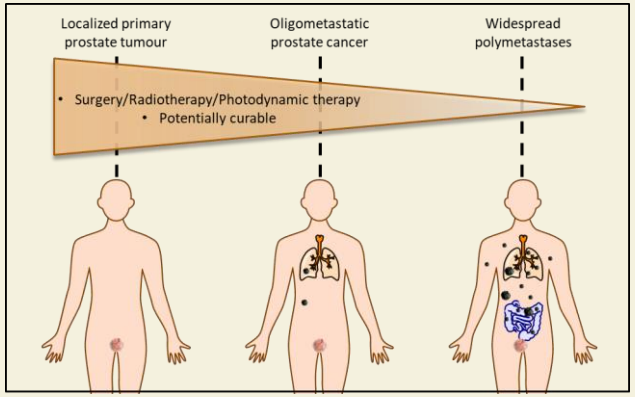
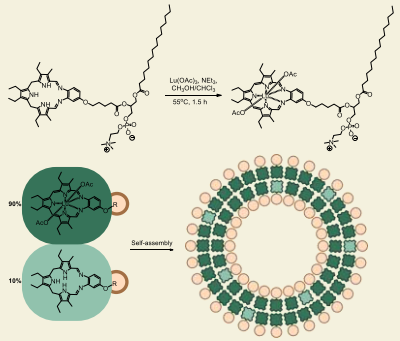
## Introduction

- Oligometastatic cancer is an intermediate disease state between localized cancer and widely disseminated metastasis. It is potentially curable with surgery and external beam radiation therapy if diagnosed and treated appropriately.[1]
- Nanoparticle improves pharmacokinetics and enables systemic delivery of the theranostic agent in a high payload to the primary disease site and distant lesions. To lower the translational hindrance, we propose a "one-for-all" the approach to develop a nanoparticle that self-assembles from a single building block (texaphyrin-lipid), that offers a multitude of intrinsic functions while minimizing formulation complexity.[2]
- This project aims to develop a dual-modality nanotexaphyrin by using a single clinically relevant metal ion (Lutetium) for radionuclide imaging and focal photodynamic therapy.

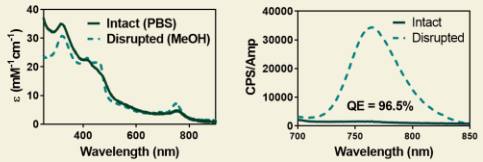



*[1] F. Bray, J. Ferlay, I. Soerjomataram, RL. Siegel, LA. Torre, A Jemal, CA Cancer J Clin. 2018; 68:394–42*
*[2] J. F. Lovell, C. S. Jin, E. Huynh, H. Jin, C. Kim, J. L. Rubinstein, W. C. Chan, W. Cao, L. V. Wang, G. Zheng, Nat. Mater. 2011, 10, 324–332332*

## Nanoparticle building block and formulation development

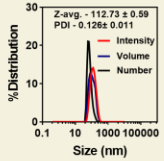


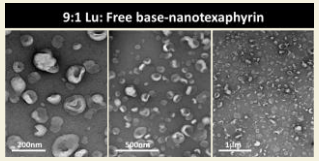

| Lipid Components | Lu/free base-nanotexaphyrin |
|---|---|
| Cholesterol | 40.0% |
| DSPE-PEG (2000) | 5.0% |
| Lu-Tex lipid | 24.75% |
| Tex lipid | 2.75% |
| DPPC | 27.5% |





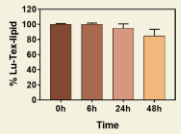


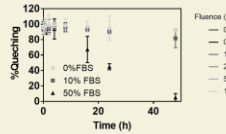


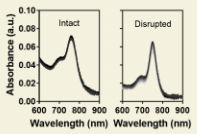




- Absorption: Soret band at 420 nm and Q band at 755 nm
- Fluorescence: 96% fluorescence quenching (FQ) at 765 nm
- DLS: hydrodynamic diameter of 112 nm with a polydispersity index (PDI) of 0.126.
- TEM: Spherical nanovesicle structures of similar sizes to DLS

## Chemical , colloidal, and optical stability




✓ **Chelation stability**

- After incubated with 50% FBS for 48 h, the nanoparticle showed 85±9% remained as Lu-texaphyrin-lipid.

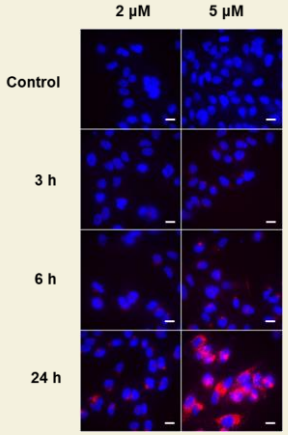
✓ **Serum stability**

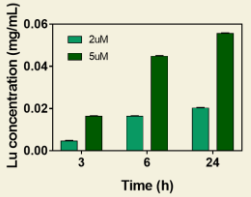
- FQ remained above 80% after incubated with 0% and 10% FBS .
- A rapid delice in FQ over 48h in 50% FBS.

✓ **Photostability**

- Both intact and disrupted nanoparticles showed excellent photostability under 1-10 Jcm$^{-2}$ of laser irradiation (750 nm).

## Cellular uptakes



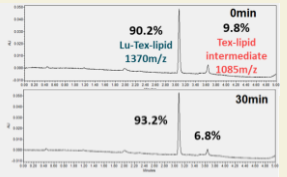




- Fluorescence microscopy imaging of PC3-luc-6 cells revealed time dependent cell uptake of the nanoparticle (2 μM and 5 μM) at 3, 6, and 24 hours (scale bar = 20 μm).
- This was confirmed by ICP-MS through increase Lu metal ion concentration (mg/mL) in cells over time (mean±S.D., n=3).

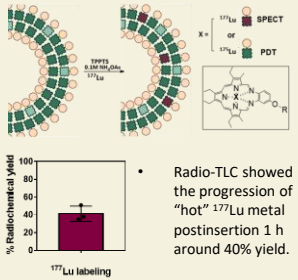
## Conclusion and Future work

- The current results highlight the utility of metallo-nanotexaphyrins as a potential theranostics agent for prostatic cancers.
- Future works involve the evaluation of the in vivo pharmacokinetic profiles and radiation dispositions of the radiolabelled Lu-nanotexphyrin.
- This work aims to demonstrate the utility of the metallo-nanotexaphyrin as a customizable and multifunctional nanomedicine platform for non-invasive SPECT imaging guided photodynamic therapy.

## "Cold" and "Hot" lutetium chelation

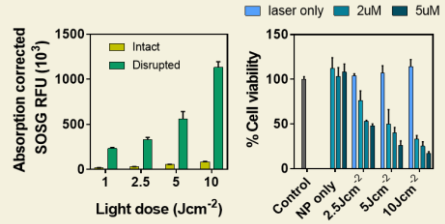


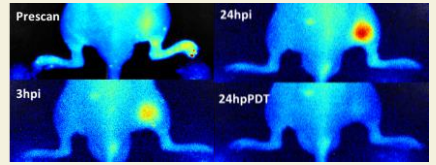

- UPLC-MS showed the progression of "cold" $^{175}$Lu metal postinsertion 30 min around 32% yield.




- Radio-TLC showed the progression of "hot" $^{177}$Lu metal postinsertion 1 h around 40% yield.

## *In vitro* PDT potency and *in vivo* accumulation




- High level of singlet oxygen can be produced under light irradiation when nanoparticles disrupt.
- *In vitro* PDT of PC3-luc-6 cells under different light doses and nanoparticle concentration showed no cytotoxicity in the controls. Whereas, the combination treatment showed potent PDT induces cytotoxic effects (up to 83±2 % cell death).
- *In vivo* fluorescence imaging showed tumour accumulations at 24 h post *i.v.* injection and photobleaching post PDT treatment.

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