Characterizaiton of Y-Nanotexaphyrin for Applications in Cancer Therapy

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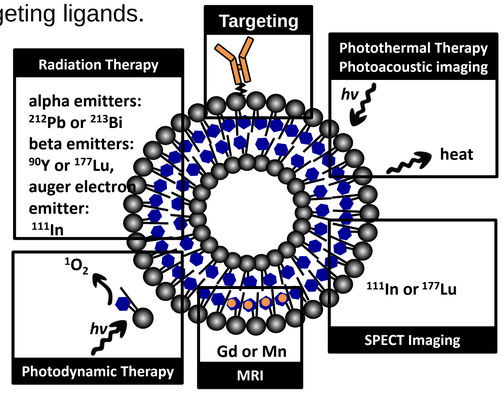
Background

Nanomedicines offer promising advantages in the development of novel radiopharmaceuticals, due to their ability utilize several radioisotopes concurrently, enabling combination therapies or theranostic modalities

Despite promising developments, issues regarding low radiochemical stability and clearance efficiency of radiolabeled nanomaterials need to be addressed in order to minimize radiation exposure to normal tissues.

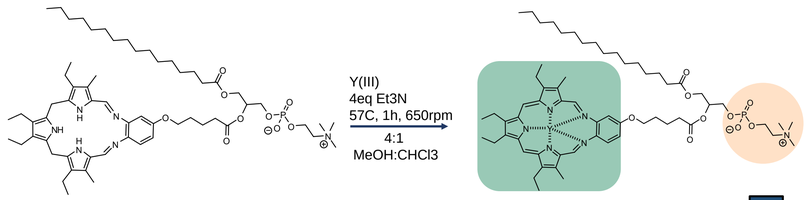
Nanotexaphyrins are one such potential multifunctional organic nanoparticle to explore for radiotherapeutic application, due to their demonstrated ability to encompass diagnostic and therapeutic isotopes as well as targeting ligands.



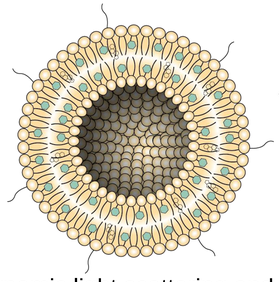
Research Objective

Design and evaluate nanotexaphyrin as a promising radiopharmaceutical candidate, by characterizing the nanoparticle in complex with yttrium, an isotope of interest in radiation therapy; and a PSMA-ligand for targeting affinity to prostate cancer cells.

Methods



Component	mol %
Y-Texaphyrin-lipid	20
DPPC	30
Cholesterol	40
DSPE-2KPEG	5
PSMA-ligand-lipid	5

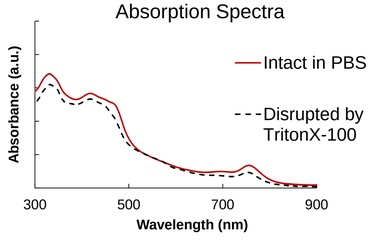


Microfluidic mixing

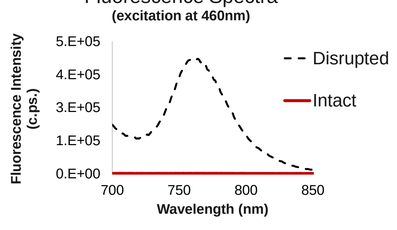
- Optical properties: absorption and fluorescence spectroscopy
- Size & morphology: Dynamic light scattering and transmission electron microscopy
- Colloidal Stability: Measured change in fluorescence quenching of particle in 10% and 50% fetal bovine serum (t = 64h, 37ºC, n=3)
- Chelation Stability: Measured change in presence of chelated Y-Texaphyrin-lipid by UPLC-Mass-Spectrometry (t=64h, 37ºC, n=3)
- Cellular Uptake assessed by fluorescence microscopy

Results

Absorption Spectra

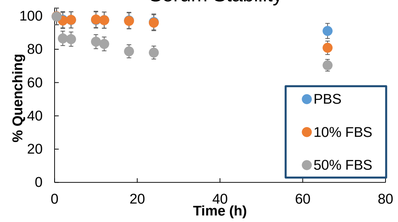


Fluorescence Spectra
(excitation at 460nm)



Results

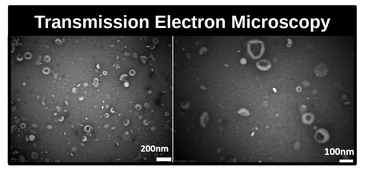
Serum Stability



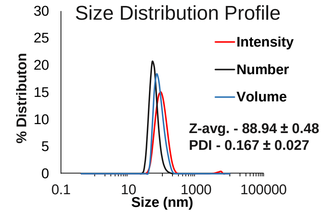
Chelation Stability

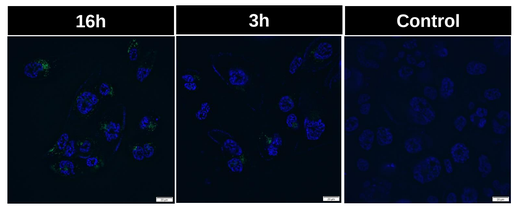
Time (h)	% Y-Texaphyrin-lipid	Standard Deviation
0	99	±0.46
24	93	±3.98
48	88	±5.44
64	86	±5.89

Transmission Electron Microscopy



Size Distribution Profile





Fluorescence microscopy images following incubation of Y-nanotexaphyrin on PC3 cells for 16h and 3h. Images suggests time-dependent uptake of the nanoparticle

Conclusions & Future Work

- The Y-nanotexaphyrin formulation demonstrated favorable colloidal and chelation stability.
- Given that chelation conditions simulated a radiolabeling protocol, we believe this synthesis approach could be easily applied for ^{90}Y radiolabeling to allow for a high energy beta-emitter nanoplatform.
- Further development will aim to acquire comprehensive cellular uptake characterization and proof-of-concept therapeutic data for ^{90}Y-nanotexaphyrin in-vivo.

References

1. Keca JM et al. A*dv. Healthcare Mater.* 2019, **8**:1800857
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3. Preihs C et al. *Inorg. Chem.* 2013, **52**: 12184−12192

Acknowledgements

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