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BIOMEDICAL ENGINEERING UNIVERSITY OF TORONTO

Characterisation of a murine ovarian cancer model for nanoparticle-based radiotheranostics

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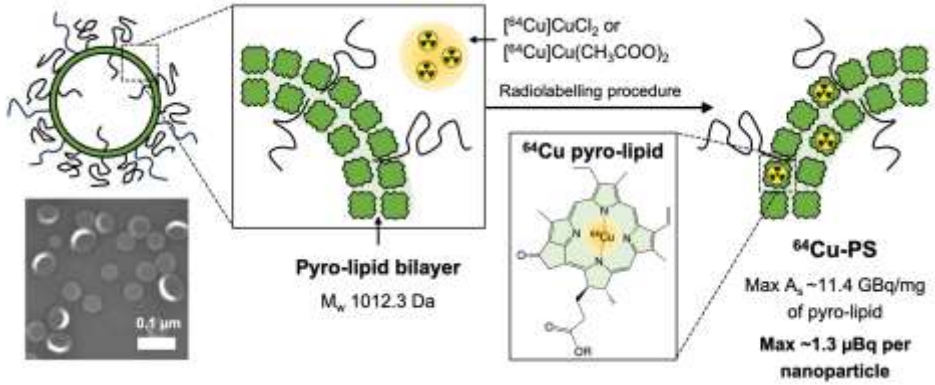
Summary of findings:

- Developed an immune competent mouse model of ovarian cancer with intra-abdominal and hepatic metastases 8 weeks post-implantation
- ^{64}Cu-labelled nanoparticles exhibited significant uptake and retention in ovarian tumours post injection:
  - *IP route*: C_{max} 25.6 %I.D./mL (T_{max} 3 h), AUC_{96h} 975 %I.D./mL*h
  - *IV route*: C_{max} 12.4 %I.D./mL (T_{max} 24 h), AUC_{96h} 927 %I.D./mL*h
- Uptake of particles in metastases and "off-target" tissues (e.g. kidneys) was similar for both administration routes

Intro to radiotheranostic porphyrin-lipid nanoparticles

PORPHYSOMES (PS) are nontargeted nanoparticles assembled from ~68,000 pyro-lipid building blocks per particle and capable of chelating Copper (Cu) radiometals: positron-emitting ^{64}Cu and β$^-$ emitting ^{67}Cu.

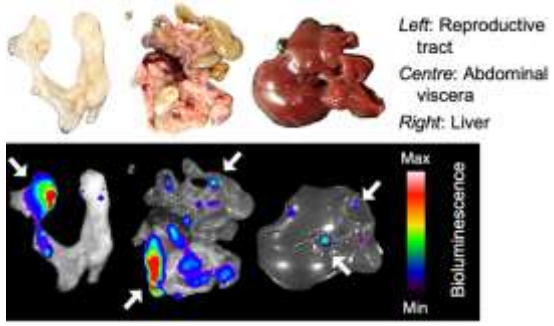


Research motivation & objective

First-in-human radiotracer imaging studies with ^{64}Cu-PS are underway at Princess Margaret in women with advance gynaecological cancers. Succeeding studies using ^{67}Cu-PS for radiopharmaceutical therapy and patient priming for immune checkpoint therapy are planned.

To enable the translational of ^{67}Cu-PS into patients, we developed an immunologically-relevant ovarian cancer model in mice and characterised the tumour uptake of ^{64}Cu-PS radiotheranostics for planning future proof-of-principle safety and efficacy studies using ^{67}Cu.

Characterisation of syngeneic orthotopic ID8-Luc$^+$ ovarian cancer model in female C57/BL6 (immune competent) mice

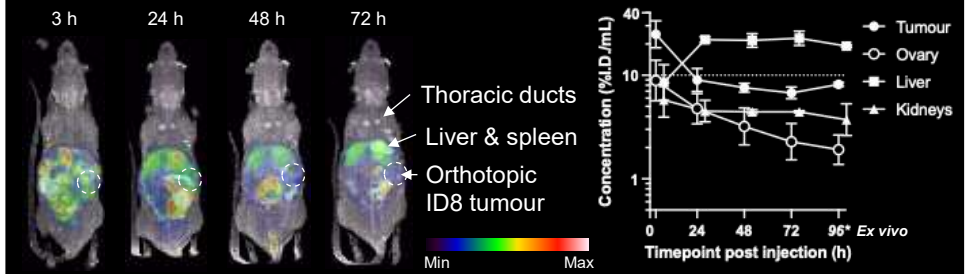


Site	Incidence rate (%)†
Primary tumour	≥ 90%
Intra-abdominal metastases	≥ 80%
Hepatic metastases	≥ 70%

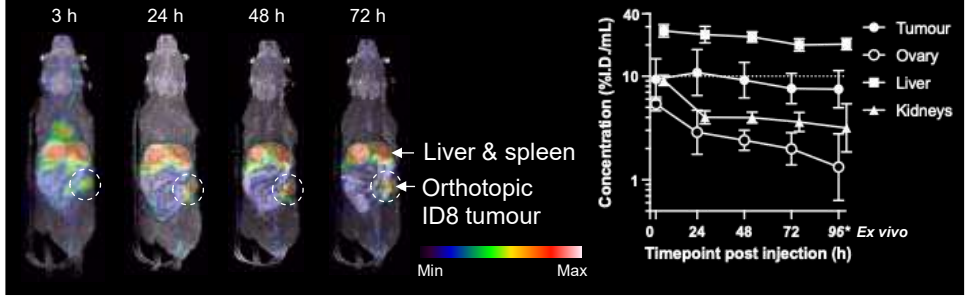
†8 weeks post-implantation.

Serial PET/MR imaging of ^{64}Cu-PS uptake in orthotopic ID8 ovarian models: IP vs. IV routes

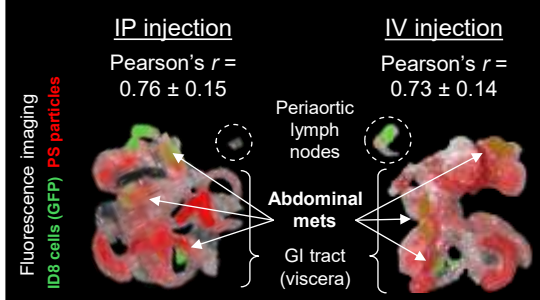
Intra-peritoneal (IP) injection: 3.8 ± 0.8 GBq ^{64}Cu/kg, 3.5 ± 0.7 mg/kg, N=3



Intra-venous (IV) injection: 4.3 ± 1.2 GBq ^{64}Cu/kg,10.7 ± 2.3 mg/kg, N=6



Ex vivo distribution of ^{64}Cu-PS to tumour metastases 96 h post-injection: IP vs. IV routes



Conc. ratio	IP	IV
Abdominal mets-to-viscera	1.55 ± 0.43	1.32 ± 0.18
Hepatic mets-to-liver	0.51 ± 0.23	0.35 ± 0.17

Mean ± 1 S.D.

Next steps

1. Estimate radiation dosimetry for planning treatments using ^{67}Cu-PS
2. Explore folate receptor (FR) targeting for improved ID8 tumour uptake