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Sustainable healthcare: A future for all

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Establishing an *ex vivo* precision medicine pipeline using bladder cancer patient-derived explants

Abby R. Templeton[1,2,3,4], Penny L. Jeffery[1,2,3,4], Patrick B. Thomas[1,2,3,4], Alex Ngoo[1,2,3,4,5], Mahasha Perera[1,2,3,4,5], Gary Ng[2,6], Laura J. Bray[2,7,8], Erik W. Thompson[1,2], Ian Vela[1,2,3,4,5], Elizabeth D. Williams[1,2,3,4]

[1]Queensland University of Technology (QUT), School of Biomedical Sciences at Translational Research Institute (TRI), Brisbane, Queensland, 4102, Australia. [2]Centre for Personalised Analysis of Cancers (CPAC), Brisbane, Queensland, Australia. [3]Queensland Bladder Cancer Initiative (QBCI), Brisbane, Queensland, 4102, Australia. [4]Australian Prostate Cancer Research Centre – Queensland, Brisbane, Queensland, 4102, Australia. [5]Department of Urology, Princess Alexandra Hospital, Woolloongabba, Queensland, 4102, Australia. [6]Department of Medical Oncology, Princess Alexandra Hospital, Woolloongabba, Queensland, 4102, Australia. [7]School of Mechanical, Medical and Process Engineering, QUT, Brisbane, Queensland, 4059, Australia. [8]ARC Training Centre for Cell and Tissue Engineering Technologies, QUT, Brisbane, Queensland, 4059, Australia.

Introduction

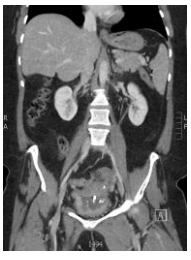
Precision medicine continues to advance, and the role of functional testing approaches are being explored. Patient-derived explants (PDEs) could be used as a patient proximal model to assess response to standard of care (SOC) therapies. PDEs maintain cellular phenotypes and the tissue microenvironment of each patient's tumour, providing a unique platform to test therapeutics.

Here we examine the viability of bladder cancer PDEs and their response to treatment with chemotherapeutic agents.

Clinical Background

Bladder Cancer PDE Viability:

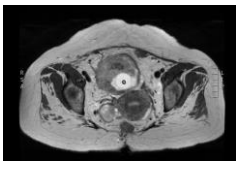
- Compared transurethral resection of bladder tumour (TURBT) and cystectomy samples.
- All samples were collected from consenting patients at the Princess Alexandra Hospital.



Contrast Enhanced CT Abdomen/Pelvis – Coronal View

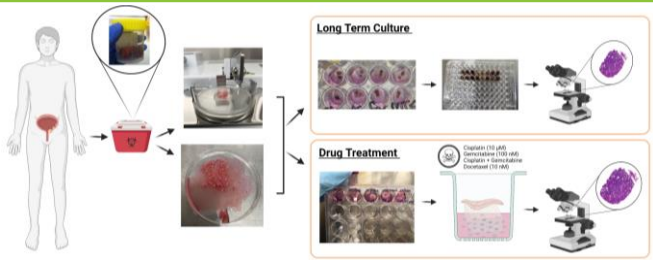
Bladder Cancer PDE Drug Treatment Case Study:

- Female patient (39 years)
- Cystectomy
- cT4 squamous cell carcinoma



MRI Pelvis (T2 Weighted) – Axial View

Methodology



Precision medicine pipeline used for processing and culturing bladder cancer samples consented at the PAH. Figure made with Biorender (2022).

Receive sample from surgery and sliced via manual dissection or using the McIlwain Tissue Chopper

↓

Use MTS Tetrazolium Assay (biochemical assay) to assess metabolic activity over 12-days

OR

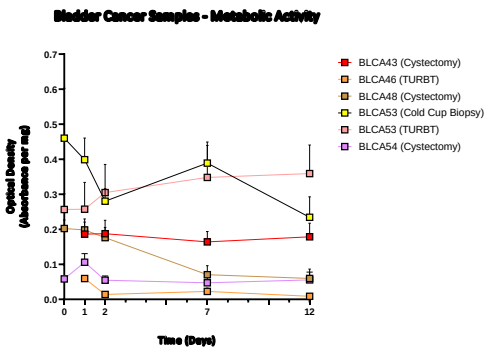
Treat PDEs with standard of care chemotherapies for 5 days. Quantitative results shown as mean ± SEM.

Conclusions

- MTS assay showed the heterogeneity between patient specimens and will be further investigated for how effective it is at assessing viability (in combination with Ki67 staining)
- Bladder cancer PDEs may pose a useful model for drug sensitivity testing. Analysis will be expanded to additional patient samples and *ex vivo* results compared to patient responses to therapy.

Results

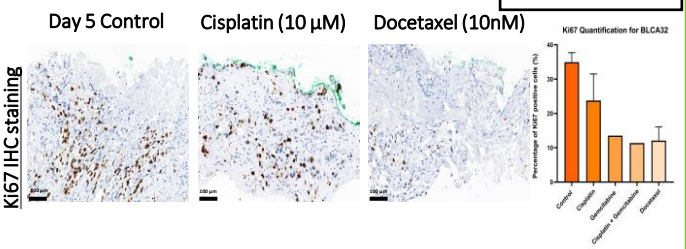
Establish viability of bladder cancer PDEs



- Heterogeneity between patients' tumours is observed
- Cold cup biopsy had higher metabolic activity in the short-term
- No clear pattern in PDE viability between TURBT and cystectomy samples

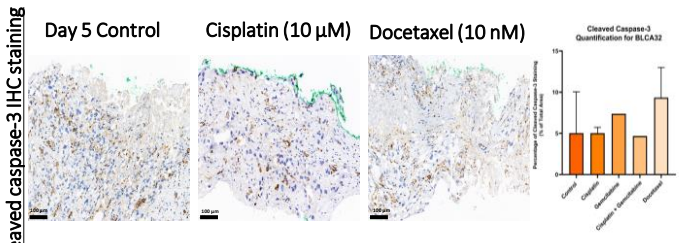
Treat bladder cancer PDEs with SOC chemotherapies

Key: ✓ Clear change in staining; – Some change in staining; ✗ Little change in staining



Decrease in Ki67 staining compared to Day 5 Control

Cisplatin – Gemcitabine ✓ Cisplatin and Gemcitabine ✓ Docetaxel ✓



Increase in cleaved caspase-3 staining compared to Day 5 Control

Cisplatin ✗ Gemcitabine ✓ Cisplatin and Gemcitabine ✗ Docetaxel ✓