Connie Johnson Research Group

Translational Breast Cancer Research

Garvan Institute of Medical Research

UNSW SYDNEY

Challenges in Breast Cancer

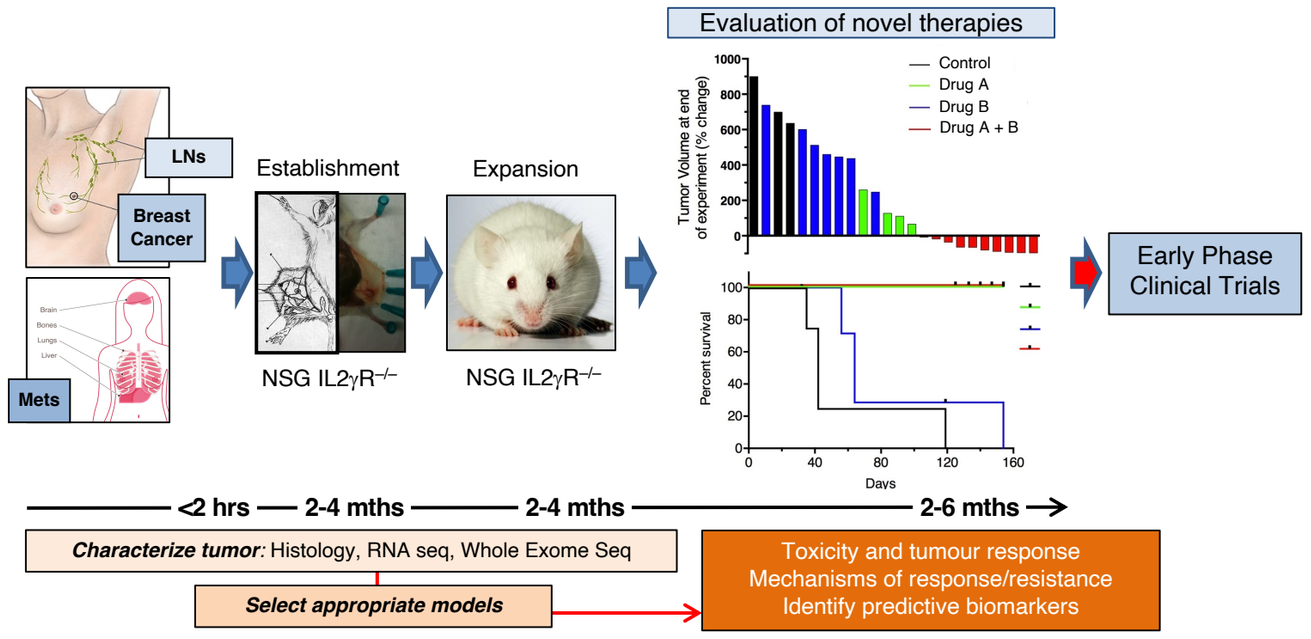
- Most common cancer affecting women
- While current therapies are effective and have changed the natural history of the disease, 20-30% of patients develop resistance to current therapies.
- We need to better understand mechanisms of resistance and identify new therapies.

Research Themes

- Patient cohorts with access to tissue through St Vincent's Hospital and clinical trials.
- Partnership with patients (Project Share) to access tissue.
- Preclinical modelling of novel therapeutics
- Overcoming endocrine resistance
- Sex steroid receptor interplay
- Oncogenic role of telomere dysfunction in drug resistance
- Translation to investigator-initiated clinical trials

Research Strategy

- Therapy sensitive, resistant and genomically modified cell line models.
- 3D tumour tissue organoid models that retain an intact tumour microenvironment for high throughput drug screening
- We are leaders in the establishment of Patient Derived Xenograft (PDX) models derived from patients and implanted into immunocompromised mice, which is the gold standard for *in vivo* study of therapeutics *(Chia et al, Current Opinion in Endocrine & Metabolic Research 2020; Portman et al, Nature Cancers 2022)*
- Bioinformatic approaches that combine biology, computer science, mathematics and statistics to analyse and interpret biological data.



Opportunities for Honours and PhD Students

New therapeutic strategies for treatment resistant Breast Cancer

- In partnership with our patients, we have access to metastatic biopsies from patients who have progressed on currently used therapies.
- We have established PDX and organoid models of treatment resistant breast cancer, allowing us to dissect the underlying mechanisms of resistance, and evaluate novel therapies in these preclinical models.
- Current and published novel therapeutic approaches include

✓ MDM2 inhibitors in ER+, p53 wildtype breast cancer *(Portman et al, Breast Cancer Research 2021; Portman et al, Frontiers Oncology 2021)*

✓ Androgen Receptor Modulators *(Chia et al, Endocrine Related Cancer 2019; Hickey et al, Nature Medicine 2021)*

✓ Progesterone Agonists *(Lim et al, British Journal Cancer 2016; Lim et al, Endocrine Related Cancer 2016)*

✓ Cyclin Dependent Kinase Inhibitors *(Tadesse et al, Drug Discovery Today 2020; Alves et al, Nature Comms 2021)*

✓ PARP inhibitors *(Johnson et al, Cell Reports 2016; Aziz et al, NPJ Breast Cancer)*

- Our current projects studying mechanisms of resistance include

✓ Senescence

✓ Telomere Dysfunction

Dissecting the cancer ecosystem in ER+ BC

- Breast cancer is a complex ecosystem that includes cancerous epithelial cells surrounded by many different types of cells including fibroblasts, immune cells, held up by a collagen matrix.
- The way in which estrogen signalling and anticancer therapies affect the cancer ecosystem is not well understood.
- In partnership with our patients, we have access to paired ER+ breast cancer tissue that are obtained pre and post endocrine therapy through our Window Preoperative Therapy trials, as well as metastatic biopsies from different sites in the body. *(Chen et al, ANZ Journal of Surgery 2020)*
- In collaboration with the Swarbrick Laboratory (Garvan Institute), we will utilise single cell sequencing and digital spatial profiling technologies to understand how Estrogen Signalling and therapies affects the cancer ecosystem. *(Wu et al, Nature Genetics 2021; Wu et al, Genome Biology 2021)*

Students & Current Lab Members

- ***PhD completed:*** Chia KeeMing *(2019, Deans Award, NHMRC Scholar)*, Sara Wahlroos *(2021, NHMRC Scholar)*
- ***PhD current:*** Allegra Freelander *(APA Scholar)*, Julia Chen *(Scientia Scholar)*
- ***Honours current:*** Chan Jae Lee
- ***Post Docs:*** Leila Eshragi, Fiona Zhou
- ***Research Assistants:*** Denise Attwater, Nimmy Geetha, Peta Somerville, Kate Saw
- ***Clinical Fellow:*** Teesha Downton

Funding Agencies

National Breast Cancer Foundation

Love Your Sister

Australian Government Cancer Australia

Australian Government National Health and Medical Research Council NHMRC

St Vincent's Curran Foundation

Cancer Council NSW

Breast Cancer Trials

The Balnaves Foundation

Garvan Institute

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