ARC Centre of Excellence in
CONVERGENT
BIO-NANO SCIENCE
& TECHNOLOGY

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Signature Projects

Our CBNS Signature Projects draw on the capabilities of our expert researchers to solve the big questions in bio-nano research.

ISOLATING, INTERROGATING AND BIOENGINEERING SINGLE CIRCULATING CELLS

Leaders: Professor Justin Gooding, Professor Benjamin Thierry
Co-Leaders: Dr Stephen Parker, Dr Marnie Winter

THE PROJECT

The isolation of rare single circulating cells from biological samples, including blood, presents tremendous opportunities to not only advance the understanding of the molecular basis of diseases such as cancer, but also to develop novel diagnostic modalities. We are developing a range of technologies able to isolate, interrogate and bioengineer circulating cells, with a focus on;

- Circulating tumour cells
- Circulating fetal cells
- Immune cells that can be harnessed for anti-cancer immunotherapy

THE BIG QUESTIONS

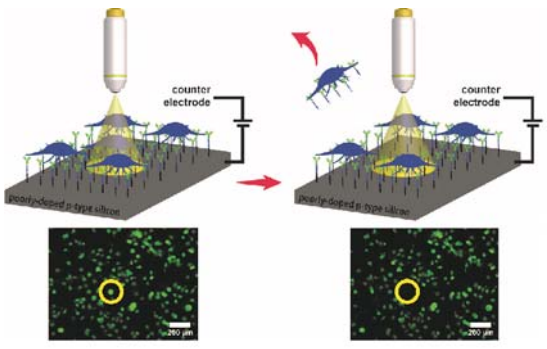
- How can we understand the heterogeneity in cell populations, and in particular, rare cells such as circulating tumour cells?
- This program aims to provide new tools for biomedical researchers to specifically capture rare cells and then be able to release individual cells of interest for further analysis such as genomic/transcriptomic/proteomic screening and cloning or single cell bioassays. Such a technology will have implications for both fundamental research in understanding cell heterogeneity and in precision medicine, where therapeutic strategies can be designed for the heterogeneity in the cells of a given patient.
- Can genomic and transcriptomic testing of circulating fetal cells isolated from maternal blood, provide a non-invasive prenatal diagnostic modality able to detect the full range of chromosomal abnomalities and single gene disorders, that are the major reason for referral to fetal medicine units?

The benefits of this research

- Efficient technologies able to isolate rare circulating cells from biological fluids such as blood, will lead to novel diagnostic and prognostics approaches, as well as provide new and significant insights into the molecular basis on diseases including, metastatic cancer and pregnancy complications such as preeclampsia, thereby guiding the development of more effective treatments.

Our goals

- We will develop a technology able to select unique rare cells from other background cells before isolating and cloning it, such that its relative contribution to the progression of diseases can be determined. We will use this unique capability to determine the molecular profile and processes that are responsible for a circulating tumour cell forming a metastatic tumour.
- We will perform genetic and transcriptomic analysis of circulating fetal cells from pregnant womens' blood, to identify biomarkers of pregnancy complications including, pre-eclampsia for improved diagnosis and treatment. In close collaboration with obstetricians, geneticists and ethicists, we will translate our technological development into a clinically relevant non-invasive prenatal diagnostic technology.



A semiconductor (such as silicon) surface is modified with antibodies that bind specifically to surface proteins that are known to be upregulated in rare cells. These antibodies are conjugated to the semiconductor surface via an electrochemically-cleavable linker molecule. This surface can capture the rare cells out of a sample such as whole human blood. Once captured, the rare cells can be interrogated both fluorescently and electrochemically (left panel) before selecting a unique rare cell. Illuminating that unique cell results in accumulation of electrons within the illuminated region, leading to that region becoming conductive when compared to neighbouring non-illuminated regions. Applying a negative bias will initiate the electrochemical cleaving reaction in the illuminated region only, and subsequent release of the cell within the illuminated region only (right panel).

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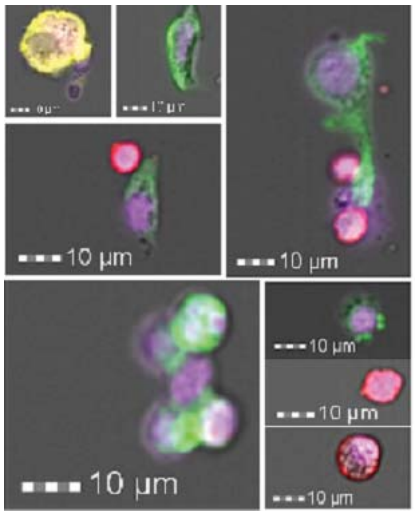
Media highlights

- Fetal Cell isolation for prenatal diagnostics, http://freshscience.org.au/2015/check-baby-with-a-chip; http://www.theleadsouthaustralia.com.au/industries/health/prenatal-test-finds-one-cell-in-a-million
- Capturing cancer cells with Nano-Plastics, http://www.labonline.com.au/content/life-science-clinical-diagnostics-instruments/news/capturing-circulating-cancer-cells-987459056
- Tumour detecting sensors to reduce follow-up cancer surgery - PhysOrg: https://phys.org/news/2016-02-tumour-sensors-follow-up-cancer-surgery.html

Recent publications

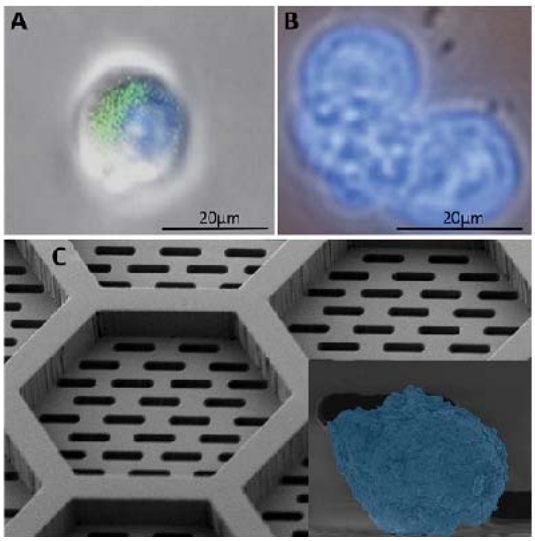
- Simultaneous impedance spectroscopy and fluorescence microscopy for the real-time monitoring of the response of cells to drugs; Chemical Science; 8, 1831-1840; 2017.
- Toward intraoperative detection of disseminated tumor cells in lymph nodes with silicon nanowire field effect transistors; ACS Nano; 10 (2) 2357-2364; 2016.
- Detection and clinical significance of circulating tumor cells in colorectal cancer – 20 years of progress; Molecular Medicine; 21(suppl 1) S25-S31; 2015.
- Connecting electrodes with light: one wire, many electrodes; Chemical Science; 6, 6769-6776: 2015.
- Nanostructured polystyrene well plates allow unbiased high-throughput characterization of circulating tumor cells; ACS Applied Matererials & Interfaces; 6 (23) 20828–20836; 2014.



The many faces of cancer: Disseminated tumor cells isolated from Cancer patients' blood and lymph nodes.

Signature Project collaborations: Isolating, interrogating and bioengineering single circulating cells

Institution	Collaborator
Ingham Institute for Applied Medical Research	Associate Professor Therese Becker
EMBL Australia Node in Single Molecule Science	Professor Katharina Gaus
Children's Cancer Institute	Professor Maria Kavallaris
Bionomics Ltd	Dr Dan Inglis
Repromed SA	Dr Deirdre Zander Fox
University of Adelaide	Professor Wayne Tilley Dr Luke Selth
Adelaide Oncology and Haematology, The Queen Elizabeth Hospital	Professor Tim Price Dr Jenny Hardingham



Circulating Fetal Cells Isolated from Maternal Blood: (A) Cytotrophoblast and (B) Syncytial Nuclear Aggregate. (C) Scanning electron microscope images of a trophoblastic cell isolated on a microfabricated honeycomb filter.

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