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.

DEVELOPMENT OF COMPLEX CELLULAR SYSTEMS FOR THE EVALUATION AND CHARACTERISATION OF BIO-NANO INTERACTIONS

Leaders: Professor Maria Kavallaris, Professor Benjamin Thierry
Co-Leaders: Dr Frieda Mansfeld, Dr Fran Ercole

THE PROJECT

A major challenge in the development and implementation of effective nanomedicine, is the lack of preclinical models that recapitulate the complexity of the complex cellular systems and microenvironments. Towards accelerating the development of nanotechnology strategies that target specific organ and cellular systems, we are developing the next generation of *in vitro* models designed to replicate physiological and biological systems relevant to the characterization and evaluation of bio-nano-interactions. Ultimately, these advanced models will guide the development of nano-based therapeutic and diagnostic strategies better tailored to specific diseases.

THE BIG QUESTIONS

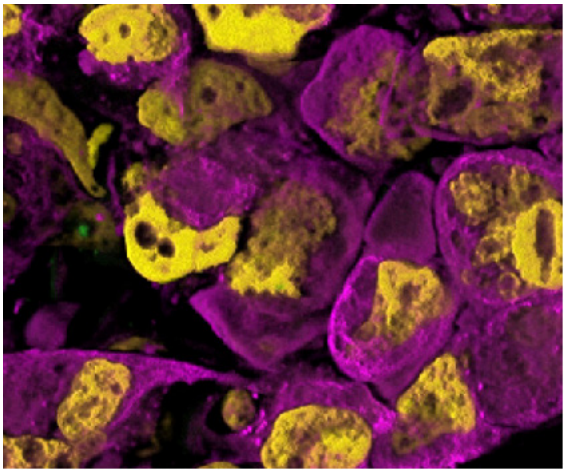
- How do we model multi cellular systems *in vitro* and *in vivo* to use in the development of effective nano-based delivery and targeting of specific cell types?
- How do we design *in vitro* models that recapitulate the complex microenvironment of both healthy and pathological tissues so that we can better model and predict the design and bioactivity of nanomaterials?
- How do we determine the key requirements for *in vitro* and *in vivo* models that replicate multicellular systems and environments that will form the basis of testing platforms for novel nanoparticles for detection and delivery to target organs, tissues and cells?

The benefits of this research

- Advanced models that recapitulate the key biological and physiological features of tissues will provide important understanding into the cellular complexity of tissues and their interactions with nanomaterials, and consequently will improve the predictive power of *in vitro* models with regards to ultimate clinical translation of novel therapeutics and diagnostic nanomaterials and devices.

Our goals

- We will development multicellular models using advanced technologies that represent the complex tissue micro-environments in order to accurately develop diagnostic devices and effective and versatile nanoparticle-based delivery systems.



An "intestinal epithelium on a chip" *in vitro* model to study the uptake of nanoparticulate carriers (green in the image) and prodrugs in the small intestine: Exposed to microfluidic fluid shear, intestinal cells (nuclei in yellow) undergo rapid differentiation and spontaneously produce a protective layer of mucus (magenta).

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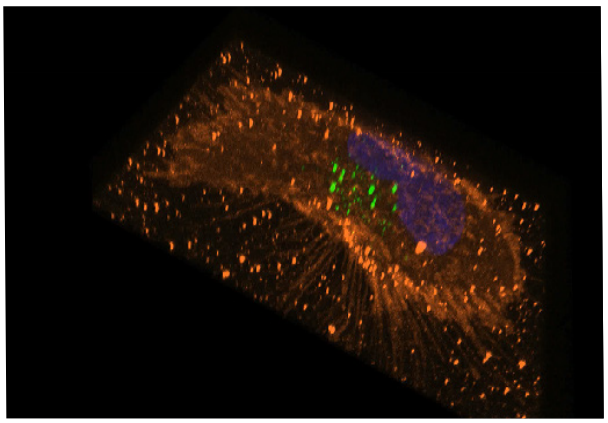
Media highlights

- The Conversation, Explainer: what is nanomedicine and how can it improve childhood cancer treatment? Published online, 2017.
- Meet three scientists finding cures for childhood cancer at the Children's Cancer Institute. ABC Radio News, 2017.
- Pancreatic cancer breakthrough using nanoparticle delivery. Channel 9, ABC radio, 96FM Perth; 2GB, Daily Telegraph (broadcast reached 2.8 million Australians), 2016.
- The age of programmable cancer drugs. Medical Republic magazine, 2016.



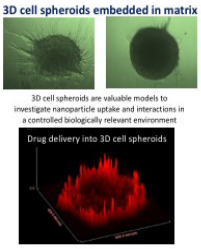
Childhood brain cancer cell showing Star-polymer nanoparticles (green) in the cell cytoplasm. Nucleus is blue and cell membrane is orange. (Image Helen Forgham)

Recent publications

- Intestine-on-a-chip microfluidic model for efficient *in-Vitro* screening of oral chemotherapeutic uptake; ACS Biomaterials Science and Engineering; Doi:10.1021/acsbiomaterials 7b00023; 2017.
- Choice of Capping Group in Tripeptide Hydrogels Influences Viability in the Three-Dimensional Cell Culture of Tumor Spheroids; ChemPlusChem; 82 (3) 383–389; 2017.
- Stathmin mediates neuroblastoma metastasis in a tubulin-independent manner via RhoA/ROCK signaling and enhanced transendothelial migration; Oncogene; 36 (4) 501-511; 2017.
- A rationally optimized nanoparticle system for the delivery of RNA interference therapeutics into pancreatic tumors *in vivo*; Biomacromolecules; 17 (7) 2337-2351; 2016.
- Overcoming instability of antibody-nanomaterial conjugates: Next generation targeted nanomedicines using bispecific antibodies; Advanced Healthcare Materials; 5 (16) 2055-2068; 2016.

Signature Project collaborations: Development of complex cellular systems for the evaluation and characterisation of bio-nano interactions

Institution	Collaborator
Memorial Sloan Kettering Cancer Centre	Professor Jason Lewis
University of Nottingham	Professor Cameron Alexander
Children's Cancer Institute	Professor Richard Lock



Metastatic neuroblastoma in lungs. Bioluminescence imaging of tumour burden on left hand side panels with red indicating large tumour burden while blue represents lower tumour burden. On the right hand side, lungs are stained with H&E and immunohistochemically for luciferase expression to reveal tumours (brown). Lower panel shows that silencing a cancer-associated gene stathmin (STMN) reduces the metastatic tumour burden.

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