ARC Centre of Excellence in
CONVERGENT
BIO-NANO SCIENCE
& TECHNOLOGY
ANNUAL REPORT 2015
Collaborating Organisations

MONASH University  THE UNIVERSITY OF MELBOURNE

THE UNIVERSITY OF QUEENSLAND  UNSW  University of South Australia

Partner Organisations

Australian Government  ANSTO  Imperial College London  Memorial Sloan-Kettering Cancer Center  The University of Warwick

University College Dublin  The University of Nottingham  The University of Wisconsin

Feature photography of CBNS staff, students and laboratories throughout this report by Joe Vittorio. Other photographs and images courtesy of CBNS members and organisations, unless otherwise attributed.
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The key scientific aim that underpins all the activities of the Centre is to fully understand, and then exploit, the interface between nanoengineered materials and biological systems. The CBNS research program is structured around the applications of understanding this interface: drug and gene delivery; vaccines; bio-imaging—both cellular and whole body imaging; and sensors and diagnostics. CBNS research is integrated by overarching research activities to understand the social dimensions of bio-nanotechnology, to visualise bio-nano interactions, and by using a systems biology approach to fully describe the complex interactions that dictate success or failure of nanotechnology for therapeutic applications.

In delivering the promise of bio-nano science the CBNS has brought together Australia’s leading scientists and engineers with expertise in nanotechnology, polymer science, cell biology, cancer biology, systems biology, chemical engineering, 3D CGI, immunology, chemistry and social science. The Centre consists of five primary nodes: Monash University; and the universities of Melbourne; Queensland; NSW; and South Australia, in addition to eight overseas partners and the Australian Nuclear Science and Technology Organisation.

The CBNS is a seven-year program of research and is funded by the ARC ($27M) and the Australian collaborating universities ($9M) over this period. The universities also contribute in-kind, as do the partner organisations. In total the in-kind support for the CBNS is valued at more than $23M over the life of the program and we thank all of the contributors for this support.

About the CBNS

The Australian Research Council Centre of Excellence in Convergent Bio–Nano Science and Technology or, as we prefer to be known, ARC Centre for Bio–Nano Science (CBNS) was established in mid–2014 as a national innovator in bio–nano sciences. We bring together a diverse team of Australia’s leading scientists with the aim of developing next generation bio-responsive nano-structured materials.

The Centre for Bio-Nano Science

- **Delivery** (delivery systems, vaccines)
- **Detection** (sensors and diagnostics, imaging technologies)
- **Understanding and exploiting the bio-nano interface**
- **Computational biology**
- **Visualisation**
- **Community outreach**
- **Health and biomedical sector engagement**
- **Education and training**
- **Social dimensions**
- **Industry and commercial engagement**

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Significant collaborations with industrial partners began in 2015
Director’s Report

Welcome to the second annual report of the ARC Centre for Bio-Nano Science, covering our activities in 2015.

The year started strongly with our sponsorship of the Australian Colloids meeting in Hobart where we provided funds for a plenary lecture from Professor Nick Abbott, our partner investigator from Wisconsin. Nick then visited the CBNS Melbourne nodes giving lectures and meeting with staff and students. Later in May we sponsored the Lowy Cancer Symposium at Coogee by supporting a plenary speaker, Prof Jason Lewis from Memorial Sloan Kettering, another of our partners. Jason then went to Brisbane to headline an extremely well-attended, one-day meeting on molecular imaging organised on behalf of the CBNS by Professor Andrew Whittaker and Associate Professor Kris Thurecht at UQ.

In July we co-hosted the International Nanomedicine Conference in Coogee and hosted our International Visiting Professor Leaf Huang from South Carolina. Leaf and Prof Paula Hammond and Prof Tariq Rana took part in our Science Advisory Board meeting held during the conference. The meeting, chaired by Prof Ian Frazer, provided us with valuable feedback and advice on our research programs. Leaf then undertook a CBNS lecture tour and took the opportunity to meet with many of the CBNS young researchers around the country.

In December we organised our first 3-day CBNS research retreat at Lorne in Victoria attended by 120 CBNS staff and students. The two days saw wide-ranging, energetic discussions and considerable networking (both social and scientific) and was thoroughly enjoyable and worthwhile—indeed in 2016 we plan to follow up with a retreat in South Australia.

In the midst of these major meetings we held a number of 1-2 day meetings—organised by CBNS investigators—including a nanosafety workshop (UniSA in April), Biomedical applications of engineered antibodies (cohosted with the AIBN, UQ in November) and a workshop on social media in research aimed at our students and postdocs (in Melbourne in December) that preceded our Lorne retreat ensuring that a plethora of tweets emerged from that meeting.

Significant collaborations involving industrial partners were instigated in 2015, with a number of new Linkage grants to CBNS researchers. Profs Justin Gooding and Maria Kavallaris were awarded $410,000, partnering with AgaMatrix Inc to develop a biosensor for detecting short sequences of RNA, called microRNA (miRNA) in blood.

Prof Nico Voelcker was awarded $322,616, partnering with Perkin Elmer and Forensic Science SA to develop fit-for-purpose mass spectrometry tools for roadside and workplace testing of illicit drugs. Associate Professor Kris Thurecht was awarded $360,000, partnering with Minomic International, to develop and optimise a novel platform technology that will assist in the development of hybrid materials consisting of nanomaterials and biomolecules, which from the basis of many commercial diagnostic devices.

CBNS researchers also received significant awards and fellowships throughout the year with Prof Justin Gooding becoming the third Laureate Fellow within the Centre. The CBNS was also well-represented in the new prestigious NHMRC-ARC Dementia Research Fellowships with awards to Dr Kristian Kempe (Monash) and Dr Adam Martin (UNSW) and the awarding of a Peter Doherty Biomedical Early Career Fellowship from the NHMRC to Dr Anna Cifuentes-Rius. I want to speciality highlight the incredible year of Prof Justin Gooding, with significant recognition of his work with not only the Laureate Fellowship, but also the RSC Faraday Medal, appointment as inaugural Editor-in-Chief of ACS Sensors, and being named as one of the Top 100 most influential analytical scientists in the world. In addition, Prof Maria Kavallaris was named in the 100 Women of Influence and Prof Mark Kendall in the Top 100 most influential engineers.

Finally I wish to welcome two new Chief Investigators to the CBNS. Dr John McGhee from UNSW Faculty of Art & Design. We originally started collaborating with John as part of our strategic activities, working on using CBNS-generated biomedical imaging data to generate visual representations of cells and whole-body imaging as part of our outreach strategy. The success of the initial work, with collaborations across the Centre, has now transitioned so that John is now a full member of the Centre and his work will be featured more comprehensively in future annual reports. We also welcome Dr Beatriz Prieto-Simón from UniSA, who replaced Prof Thomas Nann as a Chief Investigator in the CBNS. Thomas was appointed as Director of the MacDiarmid Institute in New Zealand where he remains closely affiliated with the CBNS and continues to collaborate on our research programs.

For me personally it has been a thoroughly enjoyable and productive year. The CBNS is now firmly established with a complex developing research web of collaboration in diverse areas.

The CBNS is now firmly established with a complex developing research web of collaboration in diverse areas. We have seen the recruitment of a new cohort of postdocs and PhD students across the country in collaborative projects that will become the engine room for the future of the Centre. It has been great to welcome back the Centre Manager Gaby Bright from maternity leave, and I want to say a thank you to Julia Cianci who did an excellent job as the interim Manager and we wish her well in her new role at CSL.

Tom Davis
Centre Director
CBNS at a Glance

Timeline 18 months into 84 month program

Funding
$35M over 7 years
$26M in ARC funding
$9M in Uni funding

Partners and collaborators
5 Australian universities
9 partner organisations

Key data
25 publications in journals with impact factors >10
50 talks given
247 people
5 fellowships awarded

Diverse disciplines:
- bioimaging
- cell biology
- chemistry
- engineering
- immunology
- pharmacology
- sociology
- systems biology
- visual arts

Our people

20 Chief Investigators
9 Partner Investigators
21 Research Assistants and Technical Staff
106 PhD students
3 Senior research fellows undertaking CBNS research
66 Post-doctoral researchers, 31 of whom are early career researchers*
15 Honours and Masters students
5 Management, administration and operational staff

*ECRs, <5 years post-PhD
Partner Organisations

US Partner Organisations:
- Memorial Sloan Kettering Cancer Center (New York)
- University of California, Santa Barbara
- University of Wisconsin-Madison

European Partner Organisations:
- University of Nottingham
- University of Warwick
- Imperial College, London
- University College Dublin

Asian Partner Organisation:
- Sungkyunkwan University, Korea

Australian Partner Organisation:
- ANSTO (Sydney)

Collaborating Organisations

1. Monash University
   (Administering Organisation)
   Delivery Systems, Imaging Technologies, Vaccines

2. University of Melbourne
   Delivery Systems, Computational and Systems Biology, Vaccines

3. University of Queensland
   Delivery Systems, Imaging Technologies, Sensors and Diagnostics, Vaccines

4. University of New South Wales
   Delivery Systems, Imaging Technologies, Sensors and Diagnostics, Social Dimensions

5. University of South Australia
   Delivery Systems, Sensors and Diagnostics
Research

The CBNS research program is structured around four themes: delivery systems; vaccines; sensors and diagnostics; and imaging technologies. These capture the ultimate application end points of the research. Sitting across all of these activities are three Centre-wide research programs: social dimensions of bio-nanotechnology research; systems biology; and visualisation.

CBNS research is broadly described as the engineering of nanomaterials; the study of the interactions between these materials and biological systems; the stimulation of immune responses; and the reporting of biological events. Every CBNS researcher engages in at least one of these activities or studies the system as a whole.

The research program, and expertise within the CBNS, is presented in more detail in the following pages.
Delivery Systems

The work of the Delivery Systems theme presented here is undertaken by the following CBNS Chief Investigators and their teams: Chris Porter (Theme leader, Monash); Tom Davis (Monash); Frank Caruso (Melbourne); Pall Thordarson (UNSW); Nigel Bunnett (Monash); Ben Boyd (Monash); Nico Voelcker (UniSA); Maria Kavallaris (UNSW); Angus Johnston (Monash); Kris Thurecht (UQ). The research of our themes is broad, Delivery Systems in particular, and contributions are made by others in the CBNS.

The primary focus of the Delivery Systems theme at CBNS is to examine, understand, and ultimately quantify, the nanoscale interactions between delivery systems and the cells, tissues and organs of the body that define patterns of drug activity and toxicity. Our researchers are from a range of disciplines including polymer, materials, biological and pharmaceutical sciences and they collaborate at the interface of chemistry, biology and engineering. This interdisciplinary background provides a foundation to map the relationships between nanostructure and cellular and subcellular processing pathways; to encapsulate drugs, vaccines and imaging agents in delivery systems that respond to biological stimuli to release their cargo in specific locations; to harness ligand-receptor interactions that target drugs to specific cells and organs; to promote gene silencing, turning off aberrant and potentially pathological process; and to promote delivery across mucosal or epithelial barriers, enhancing the absorption of molecules that might otherwise require injection. Our ultimate goal is to harness an understanding of the fundamental basis of these nanoscale interactions to inform the development of more selective, less toxic and more effective therapeutics.

Specifically, the major foci of research activity are:
• the evaluation of the complex map of interactions between novel nanomaterials and the biological environment, setting the framework for rational and deliberate delivery system design
• the identification of novel nanomaterials, and in particular nanomaterials that respond to specific biological stimuli, providing a means to release drug at a particular location, or in response to a particular condition
• understanding the determinants of the use of nanostructured materials as delivery systems to promote gene silencing and gene therapy
• employing the unique properties of nanomaterials, especially surface modified nanomaterials, to promote site specific delivery to organs, cells and subcellular locations that are specifically associated with disease
• the use of nanostructured materials, including microprojection arrays and microemulsions to facilitate transepithelial and transmucosal drug delivery.

Delivery Systems: Mapping Bio-Nano Interactions

Predicting the fate of nanomaterials in the body
One of the major ‘signature’ projects of the CBNS continues to be the development of simple laboratory (in vitro) assays that provide an indication of how nanomaterials interact with cells in the blood and in doing so predict cellular interactions more broadly. This assay takes advantage of our ability to fluorescently label nanoparticles and to select and sort the different cell types that interact with and take up these fluorescent particles. These studies are described in more detail in the Vaccines section of this report since cellular interactions are critical to both drug and vaccine delivery. In a recent extension to this work, however, CBNS researchers have started to investigate the interactions between cells in blood with nanostructured liquid crystalline delivery particles, so-called ‘cubosomes’. Cubosomes are, as the name suggests, cubic nanoparticles made of self-assembled structured lipids. They show great promise for controlled drug delivery, but to this point very little is known about their behaviour in the body. The current studies will provide some of the first data to describe their biological interaction and pave the way for studies in 2016 that functionalise these particles to enable ‘click’ targeting to metabolically labelled cells.
Nanoparticles to prevent amylin aggregation in diabetes

Type 2 diabetes mellitus (T2D) is a metabolic disease currently affecting 9% of the global adult population, with prevalence expected to double by 2035. The 37-residue peptide human islet amyloid polypeptide (hIAPP), co-secreted with insulin for glycemic control, aggregates in T2D patients forming amyloid plaques and fibrils. This process contributes to the death and dysfunction of insulin-producing pancreatic β-cells. Consequently, there is a need for mechanisms to target the amylin aggregation pathway and to breakdown amyloid end products.

Nanoparticles with surface chemistries similar to that of polyphenols, which are known to inhibit amyloidosis, may disrupt the steric stacking, hydrogen bonding and hydrophobic interaction of the cross-β fibril architecture, thereby preventing protein aggregation and mitigating its toxic effect. CBNS scientists have studied the off-pathway oligomer formation of amylin-polyphenols, toxicity of amylin species, and demonstrated that generation three OH-terminated dendrimers (G3 PAMAM-OH) and graphene oxide (GO) nanosheets are effective in inhibiting amylin aggregation and further mitigating its toxic effect on pancreatic β-cells. Future work will look to evaluate whether this is transferrable to other nanoparticle structures and whether the effects can be translated in vivo.


Understanding the structural determinants of blood clearance of nanomaterials

Functional nanoparticle platforms that precisely target and destroy cancer cells have the potential to revolutionise conventional cancer treatments. Nanoparticles that avoid uptake by clearance mechanisms in the liver and spleen and are not eliminated by the kidneys inherently accumulate in tumours, since the vasculature in tumours is more ‘leaky’ that elsewhere in the body. This is a process termed the enhanced permeability and retention effect or EPR effect. To take advantage of this effect, nanoparticle platforms must be stable in circulation, biocompatible and exhibit extended half lives in the blood. CBNS researchers have been investigating the interaction of a range of nanomaterials with in vivo biodistribution and clearance mechanisms to get a better feel for the relationship between nanoparticle structure and residence time in the body. These studies are being conducted alongside experiments to develop sensitive in vitro methods to predict these in vivo clearance mechanisms and the correlation of in vitro and in vivo outcomes across a broad range of nanomaterials is a significant focus of CBNS activities.

Star polymers are one such delivery platform that possesses many attractive properties for targeted drug delivery. For example, star polymers loaded with doxorubicin have been used for pH-stimulated intracellular delivery in cancer cells. However, whilst the utility of star polymers has been demonstrated in...
Understanding the protein corona on nanoengineered surfaces

Nanoengineered particles typically absorb proteins when introduced in a biological medium to form a protein corona. This plays an important role in determining the surface properties of particles and their interaction with cells and cell surface receptors. In 2015, CBNS researchers started to evaluate the impact of the protein corona on nanocapsules functionalised with a targeting moiety to promote site specific delivery. In these studies the nature of the protein corona that assembled on the surface of antibody derivatised polymer particles was evaluated and the impact of the corona on targeting properties of the particle assessed. Interestingly, although a protein corona did indeed form on the surface of the targeted particles, the targeting ability was not significantly influenced. The data suggest that the surface functionality of engineered capsules can be preserved even in the presence of protein coronas. However, this was dependent on the nature of the targeting group and the protein corona dramatically inhibited the targeting ability of similar affibody-functionalised particles. This research identifies how protein coronas influence targeting abilities and provides key insights into the importance of challenging engineered particles with multicomponten biologically relevant environments during the design phase.
Controlling nanoparticle shape

The nanometre-sized dimensions of nanomaterials are clearly critical to many of their advantageous properties and the effect of size on behaviour remains an important area of investigation. In addition, however, the shape of a nanoparticle also has a profound influence over its behaviour in a biological context. Particle shape has been shown to affect circulation time, cellular uptake, nuclear localisation, tumour inhibition, tumour accumulation, spleen accumulation, lung accumulation, and brain accumulation. \(^1\) Thus shape, along with surface chemistry, size and bulk material properties must be considered in assessing the suitability of a nanomaterial for a particular application.

One of the challenges in assessing nanomaterials of different shape is to vary the particle morphology without affecting other material properties at the same time. To this end, CBNS researchers are exploring approaches for preparing materials with different shape but comparable surface chemistry and bulk properties. Employing self-assembly from different solvents provides particles with spherical, worm-like, vesicular, large-compound micellar and flower-like morphology, each with the same bulk material and surface properties. \(^2\)

CBNS researchers have also been exploring novel hydrophilic polymers to provide biocompatible surfaces, and have examined the use of these new hydrophilic materials to prepare block copolymer-derived nanoaggregates of spherical, vesicular, worm-like and lamellar morphology (see figure below). \(^3\)

In relatively recent work, CBNS researchers have also been examining the preparation of materials with comparable size, morphology, surface chemistry and shape, but with different bulk material properties. \(^4\)

The prepared filomicelles have the same biocompatible surface, but are fabricated with cores of widely differing properties (notably flexibility as assessed by glass transition temperature). This suite of materials has allowed the research team to start to elucidate the impact of bulk material properties on cellular uptake and circulation time \(^5\) and may provide a route to novel nanomaterials with improved biological properties.


Mapping drug encapsulation in thermoresponsive polymersomes

Polymersomes are an attractive vehicle for drug delivery. They share many of the beneficial properties of nanomaterials such as liposomes, but have markedly improved stability properties. One challenge in the application of these materials as delivery vectors is in accurately mapping the location of a loaded drug cargo within the polymersome structure. To this end CBNS researchers have developed a polymersome systems capable of reporting on its cargo. This was achieved by encapsulating drugs or proteins as fluorescent acceptors in a polymersome containing a fluorescent protein donor. Fluorescence lifetime imaging microscopy and Förster resonance energy transfer (FLIM-FRET) was then employed to spatially map the interaction between donor and acceptor. \(^6\) Accurate methods to locate drug and protein cargos in polymersomes opens the pathway for new developments in combination therapy using small-molecule cancer drugs together with proteins, such as cancer-targeting antibodies, and enzymes, including asparaginase, that are already used in the fight against leukaemia.

Nanoparticles for endosomal escape

One of the advantages of nanoparticles is that many cell types inherently take these materials up into the cell using constitutive processes—thereby allowing a means of intracellular delivery. However, the uptake process usually delivers the particle not to the general intracellular environment, i.e. the cytosol, but instead to a series of interconnected membrane enclosed compartments—the endosome/lysosome network. This can have delivery benefits—indeed some of our researchers are actively seeking to target drug signalling pathways in the endosomal network—but it can also be a pathway for breakdown. For some applications, particles that ‘escape’ from the endosome into the cellular cytosol are preferred. This is especially the case for systems designed to deliver or alter genetic material where access to the cytosol or the nucleus is required. To achieve this CBNS researchers have developed a one-step assembly system to form nanoparticles that respond to being internalised into a cell and induce escape from the endosomal/lysosomal compartments. The nanoparticles were formed by the nanoprecipitation of pH-responsive poly(2-(diethylamino)ethyl methacrylate) (PDEAEMA) and poly(2-(diethylamino)ethyl methacrylate)-b-poly(ethylene glycol) (PDEAEMA-b-PEG). The particles disassemble when the pH drops below 6.8, and release their therapeutic cargo.

The ability to induce escape from the endosomes was demonstrated by the use of calcein, a membrane-impermeable fluorophore (see figure below). The modular nature of these particles combined with promising endosomal escape capabilities make dual component PDEAEMA nanoparticles useful for drug and gene delivery applications.


![Figure: Endosomal escape induced by calcein.](image)


pH responsive nanoparticles based on metal–phenolic networks (MPNs)

CBNS researchers are developing a new class of nanoparticles that respond to changes in pH—moving one step closer to delivery vehicles that allow tailored patterns of drug release. In this case the pH responsive nature is generated using metal–phenolic networks (MPNs). The goal is to engineer particles that are stable under normal pH conditions in the body (approximately neutral) but that trigger drug release when particles are taken up into cells (since the intracellular environment is slightly acidic). To this end, the fabrication of drug-loaded MPN capsules, based on the formation of coordination complexes between natural polyphenols and metal ions over a drug-coated template, represents an effective strategy to engineer robust and versatile drug delivery carriers. Moreover, the functional properties of the MPN capsules can be tailored by incorporating different metal ions to align properties with the ideal characteristics for drug delivery, positron emission tomography (PET), magnetic resonance imaging (MRI), catalysis, and oxidative stress ultrasound imaging.

Figure: Scheme of the fabrication process of DOX-loaded MPN capsules and the release mechanism of DOX from MPN capsules.

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Endosomal drug delivery: Targeting Pain at the Source

G protein-coupled receptors control most pathophysiological processes and are major drug targets. At the cell-surface, GPCRs ‘sense’ extracellular signals and receptor activation initiates intracellular signalling events that underlie complex pathophysiological processes. Activated receptors also internalise to endosomes and their role within these dynamic tubulovesicular networks remains unclear. This program aims to determine whether endosomal receptors are important for the generation of distinct pathophysiological signals and are viable therapeutic targets.

CBNS researchers have demonstrated that receptors for the neuropeptides Substance P and calcitonin gene-related peptide can internalise, generating signals from endosomes to initiate signalling events that lead to spinal neuron excitation and pain transmission. Signalling is mediated via G proteins and β-arrestins increasing local production of cAMP, protein kinase C activity and extracellular signal regulated kinases in the nucleus. The researchers hypothesise that the delivery of receptor antagonists directly to endosomes offers a unique and novel strategy for effective and selective inhibition of pain (see figure).

Two endosomal delivery strategies are currently being investigated:
1. Conjugation of inhibitors to cholestanol to promote endosomal targeting and retention;
2. pH-sensitive soft nanoparticles for delivering receptor antagonists into endosomes.

To date, the team have demonstrated for the first time that endosomal signalling of G protein-coupled receptors is critical for the complex pathophysiology of pain. As a proof of concept, inhibiting receptor endocytosis blocked these signalling events and pain transmission. In addition, cholestanol conjugated antagonists have successfully inhibited endosomal signalling and suppressed neuronal excitability and pain in mice, thus demonstrating the utility of endosomally-targeted antagonists.

A library of pH-responsive soft nanoparticles have been synthesised and these selectively disassemble within the endosomal environment, for release of an inhibitor payload. In addition, the scientists have demonstrated that they can tune the nanoparticle pH sensitivity or drug loading capacity and abrogate the potential of cellular toxicity. They are currently investigating their analgesic potential through cell signalling assays and their ability for tissue-selective release by decorating particles with targeting ligands. Together, targeted drug delivery and retention may increase selectivity or therapeutic outcomes, and consequently minimise drug dosage and associated side effects.
Nanoparticle delivery of gaseous signalling molecules (gasotransmitters)

The gasotransmitters, hydrogen sulfide (H$_2$S) and nitric oxide (NO), are biologically active gases that play fundamental roles in human biology. By influencing an array of intracellular signalling processes, they are able to exert fine, modulatory control over many cellular functions. NO is associated with diabetes, liver fibrosis, cardiovascular illness, neurodegenerative diseases, and cancer and has antimicrobial applications such as the dispersal of biofilms. H$_2$S plays a role in inhibition of leukocyte adherence in the microcirculation during vascular inflammation and provides cardioprotective, neuroprotective, gastroprotective and wound healing effects.

Exogenous delivery of H$_2$S and NO gasotransmitters may therefore be a useful strategy in the management of a number of diseases. However, the potential to deliver these gaseous signalling molecules to tissues can only be realised with a delivery system that mimics their controlled endogenous biosynthesis mechanism, with an extended time of delivery and delivery in a physiologically relevant concentration range. CBNS researchers have been investigating the controlled delivery of NO and H$_2$S using nanoparticle-based delivery systems. The initial data is promising and has shown that controlled delivery to lung cancer cells is possible (figure below). This remains an active area of investigation.

Responsive nanostructured lipids and lipid-polymer hybrids for controlled release

Nanostructured lipids have received less attention than polymeric nanoparticles as a medium for controlling drug release, and yet the flexibility and biocompatibility of these materials makes them an excellent vehicle for drug delivery. CBNS researchers are exploring the use of nanostructured lipids, and harnessing their unique ability to act as substrates for a range of lipase enzymes to modify their structure and properties. Recent studies have explored, using classical pharmacokinetic approaches and the latest imaging modalities, how enzymes can be used to form highly structured nanomaterials in situ from simple precursor systems. Lipid systems that respond to laser light to deliver a payload upon site-specific activation have also been explored. By combining strengths across the CBNS our researchers have also recently explored lipid-polymer hybrid nanomaterials as a means of generating novel lipid systems that respond to changes in environmental pH.

Quantifying drug targeting using next generation in vivo imaging and analysis

One of the major benefits of the structure of the CBNS is the ability to utilise cross-disciplinary strengths to better answer fundamental questions in nanotechnology. One recent example of this is the use of expertise in in vivo imaging to better quantify the extent of tumour targeting. Nanotechnology provides a highly effective means of increasing the local concentration of therapeutics within a tumour environment by making use of the EPR effect. However, quantification of the relative difference in efficiency of different nanomaterials, especially in a time resolved manner, is limited using traditional pharmacokinetic approaches since the number of timepoints at which tumours can be removed and assayed is small. By utilising new in vivo imaging approaches and applying mathematical modelling of the rich data sets that are available, CBNS researchers are starting to far better understand the kinetics of tumour access, egress and accumulation.

A key aspect of the Centre’s work in engineering nanoparticles with high affinity for tumours is the ability to use biologically relevant cancer models for evaluation of biodistribution and efficacy studies. To this end we have developed and evaluated clinically relevant models of lung cancer and the childhood cancer neuroblastoma. These models represent both primary and metastatic disease and serve as a valuable resource within the CBNS for the biological distribution, evaluation, and efficacy of newly developed delivery vehicles.

Figure: H$_2$S detection in live H460 lung carcinoma cells using a H$_2$S selective fluorescent probe: Significant intracellular fluorescence was detected using the fluorescent probe in cells treated with H$_2$S donating nanoparticles (right), relative to cells treated with control (no H$_2$S donor) nanoparticles (left). Bright-field images with Hoechst nuclear staining (not shown) confirmed that the cells remain viable throughout exposure to H$_2$S donating nanoparticles.

CBNS Annual Report 2015
Targeted silica microtubes for tumour specific drug delivery

Drug carriers based on silica are of particular interest due to their biosafety and tunable physicochemical properties. In particular, porous silicon fabricated by electrochemical etching is a promising material that can be tailored to obtain nano and microstructures for direct application as drug delivery systems. Combined with microfabrication techniques, monodispersed tubular microparticles can be fabricated with an extraordinary control over geometry and dimension. The unique architecture of silica microtubes allows the differential functionalisation of internal and external surfaces. The external surface can be selectively functionalised with specific antibodies to target overexpressed antigens on cancer cells and the hollow core can act as a cargo carrier for storing a substantial payload of anticancer drug. In recent studies CBNS researchers attached an antibody to the surface of silica microtubes to promote targeting to neuroblastoma cells. An anti-p75NTR antibody that binds to the p75 neurotrophin receptor on neuroblastoma cells was employed. The hollow cores of the microtubes were loaded with the anticancer drug camptothecin (CPT). The data revealed selective killing of 95% of neuroblastoma cells without harming healthy cells, a significant step forward in the targeted delivery of hydrophobic drugs. The work was selected as one of the covers in the journal Small (figure below) and has inspired further research using the reported targeting approach and the possibilities of drug encapsulation.

Figure: A stylised image showing silica microtubes releasing camptothecin at the site of neuroblastoma cancer cells. The microtubes have been coated with an antibody that enables targeting of the neuroblastoma cells.

Comparing the utility of different targeting moieties

A variety of ligands have been utilised to increase the accumulation of nanotherapeutics within tumour tissues through direct targeting of surface receptors. It is well established that different ligands will interact with cells in different ways, but to this point very few studies have examined the differential targeting effect of different targeting moieties directed to the same target. CBNS researchers have therefore developed a range of bespoke nanomaterials, engineered to target a single receptor (prostate-specific membrane antigen), but where the targeting ligand is either an antibody, a peptide or a small molecule. These materials have been utilised to establish methods for direct comparison of the impact of the size and binding affinity of the ligand on the interaction of the targeted delivery system with tumour cells. Ultimately it is hoped that these methods will provide a means of predicting the efficacy of nanotherapeutics.

1Biomacromolecules 2015 16, 3235.

Delivery Systems: Gene Silencing and Gene Therapy

Abnormal gene expression is associated with a wide range of disease states and many of these genes remain undruggable, i.e. gene expression cannot be altered by traditional drug therapies. Gene silencing or RNA interference (RNAi) is an evolutionary conserved mechanism of gene regulation. Short-interfering-RNA (siRNA) and micro-RNA (miRNA) hold promise as a class of therapeutics that can selectively silence disease-causing genes. In cancer, targeting genes that regulate cell division and/or the cytoskeleton are attractive therapeutic strategies. A major challenge with using RNAi, however, is that it cannot enter cells without a delivery vehicle. To address this challenge CBNS researchers have investigated the use of a dendrimer-based delivery system (interfering nanoparticle-7, iNOP-7) to deliver siRNA and silence polo-like kinase 1 (PLK1), a serine-threonine protein kinase which is overexpressed in cancer cells, and plays a major role in regulating tumour growth. iNOP-7 was non-toxic, and delivered siRNA with high efficiency to lung cancer cells. iNOP-7-PLK1 siRNA potently silenced PLK1 expression and reduced lung cancer growth in vitro. In vivo, iNOP-7 delivered siRNA to orthotopic lung tumours in mice, and reduced lung tumour burden. iNOP-7-PLK1 siRNA may provide a novel therapeutic strategy for the treatment of lung as well as other cancers which aberrantly express this gene.

Oncotarget 2015, 20, 6(14), 12020.

Delivery Systems: Advances in transepithelial and transmucosal drug delivery

Microneedle and nanoneedle delivery systems

One area of significant focus within CBNS is in the use of nanostructured micro- or nano-needles as a means of delivering drugs, vaccines and nucleic acids across otherwise impermeable cellular barriers. Much of this work has focussed on vaccine delivery across the skin. The Nanopatch delivery system, developed by CBNS researchers, has the ability to deliver across the skin into immune rich tissues using microneedles without penetrating far enough to cause pain.

Similar porous silicon (pSi) nanoneedle patches have also been employed to deliver DNA payloads into cells. pSi nanoneedles are fabricated by metal-assisted chemical etching (MACE), resulting in high-density arrays of projections (up to 50 million needles per cm²) with tuneable porosity.

Using these systems, transfection efficiencies of over 90% have been achieved for a range of immortalised and primary cells with retention of high cell viability. Further research in 2016 will look to translate these findings to delivering genes through skin in vivo.

1Advanced Functional Materials 2015, 25, 7215; 2ACS Applied Materials and Interfaces 2015, 7(42), 23717.
Enhancing oral drug delivery

In almost all cases, oral delivery of pharmaceuticals is preferred by patients as it is familiar and simple and tablets and capsules are readily transported. In some instances, and life threatening diseases such as cancer where patients are often treated in hospital is one good example, intravenous administration may be acceptable. In the majority of instances, however, oral products are preferred. For many traditional drug molecules absorption across the absorptive cells that line the gastrointestinal (GI) tract is possible and oral delivery is a viable means of drug delivery. For many of the new generation of drugs, molecules that have much larger molecular weights, more complex structures and often very poor water solubility, absorption across the GI tract is far more complex and often low. CBNS researchers are exploring a range of methods where nanotechnology can be employed to promote drug absorption in the GI tract. Two specific examples that have been a focus in 2015 are the use of ionic liquids and lipidic prodrugs to convert drug molecules into more lipid-like forms. The general philosophy that underpins this work is that by lipidating drug molecules they can more readily ‘piggyback’ onto natural lipid digestion and absorption pathways. These natural pathways have evolved over millennia to support the absorption of dietary fats and are extremely effective. To achieve this, CBNS researchers have paired drug molecules with highly lipophilic lipid-like counterions to form lipid-like salts or ionic liquids. These materials have very low melting points and are often liquids at room temperature. This allows them to be dissolved in lipids at much higher concentrations than is possible for the non-ionic liquid form, in turn allowing formulation in contemporary lipid based oral formulations that significant enhance oral absorption. The intellectual property that resulted from this work was acquired by the US-headquartered drug delivery company Capsugel in 2015, resulting in the first IP assignment deal for the CBNS and an ongoing research alliance to develop the technology.

The second approach that has been evaluated has been to covalently couple drug molecules to lipids to form a ‘mimic’ of a natural glyceride lipid. These prodrugs are designed to be processed in an identical way to dietary lipids. As such they are digested in the intestine, absorbed and then integrated into the natural lipid biochemical pathway. This pathway ultimately results in prodrug incorporation into endogenous lipid nanomaterials—lipoproteins—in the intestine. Importantly, association with lipoproteins changes the pathway of drug absorption and hijacks a very efficient transport pathway that completely avoids drug metabolism on ‘first pass’ through the liver. This technology has a significant potential benefit for drugs where first pass metabolism is a major limitation to absorption.

Finally, and in a slightly different application CBNS researchers have developed nanoparticle-encapsulated microcapsules to overcome some of the issues associated with oral delivery of therapeutics to the colon. These novel carriers showed that through careful design of the encapsulating material, nanoparticles incorporating a suitable chemotherapeutic could be deposited within the colon in mouse models.

1 Mol Pharmaceut. 2015, 12, 1980.
2 Pharm Res. 2015 32, 1830; 3 European Journal of Pharmaceutics and Biopharmaceutics 2015, 94, 393.
Key Goals for 2016

1. To demonstrate in vivo efficacy of siRNA released from porous silicon nanoparticles.
2. To provide evidence of immunomodulation via ex vivo and in vivo targeting of antibody–functionalised porous silicon nanoparticles to dendritic cells.
3. To investigate the effect of vascularisation on nanoparticle delivery to tumours.
4. To explore the use of lipid–polymer hybrid materials for forming and controlling nanostructure where bioactive peptides are a key component.
5. To understand the role of the proinsulin C-peptide in amylin aggregation and inhibition and to develop nanomaterials that better inhibit fibril formation.
6. To develop and validate more effective delivery vehicles for RNAi/chemotherapeutic delivery to tumour cells.
7. To further evaluate the ability of nanoneedles to promote DNA delivery to cells in vivo.
8. To explore mechanisms to promote drug release from lipoprotein targeted prodrugs.
9. To employ nanotechnology solutions to improved drug absorption from the GI tract.
10. To provide in vitro and in vivo evidence of the ability of endosomally targeted nanoparticles and lipid conjugates to beneficially alter cell signalling in pain.
11. To explore the impact of passive versus active delivery of drug–loaded nanoparticles to diseased tissue.
Vaccines

The work of the Vaccines theme is undertaken by the following CBNS Chief Investigators and their teams: Stephen Kent (Theme leader, Melbourne); Rob Parton (UQ); Angus Johnston (Monash); Kris Thurecht (UQ); Frank Caruso (Melbourne); Mark Kendall (UQ). The research of our themes is broad and contributions are made by others in the CBNS.

Vaccines are a highly effective public health mechanism aimed at controlling infections and in some cases, such as the human papilloma virus, preventing cancers. Major opportunities exist for the design and delivery of more effective ‘smart’ vaccines. Such new generation vaccines should be capable of both (a) avoiding degradation and non-specific clearance, as well as (b) targeting specific immune cells such as dendritic cells capable of orchestrating the most effective immunity.

Widespread human pathogens that cause a major global burden of disease for which highly effective vaccines do not exist include HIV, tuberculosis, hepatitis C and malaria. The CBNS research work in the Vaccine theme overlaps in many respects with the Delivery systems research since reaching specific cell types while avoiding non-specific degradation is common to both applications. There is however a dearth of information about targeting immune cells with nanoengineered structures and researchers are just beginning to understand the biological ‘rules’ by which nanoparticles interact with immune cells. The most advanced concept in the Vaccine theme involves the Nanopatch™, which delivers vaccines to the dendritic-cell rich epidermal layer of the skin. Further work is now on understanding how best to achieve this. The overall goal is to deliver on the promise of nanotechnology to both improve the protective efficacy of a vaccine and at the same time reduce unwanted ‘off-target’ side effects.

How nanoengineered structures interact with immune cells is poorly understood. Chief Investigators across the CBNS have the wide range of expertise that permits them to finely tune nanoengineered structures to study their interaction with immune cells. This allows for comparison and contrast of divergent nanoparticle systems to understand the most efficient mechanisms to deliver appropriate vaccine antigens to immune cells. In future work, computational biology methods will be used to analyse the data to develop testable ‘rules’ of how physical properties such as charge and size affect interaction with human immune cells. Few if any groups worldwide have the range of skills and collaborative environment to push this forward. An over-arching understanding of these processes has become a key signature project of the CBNS. In parallel, the Centre CIs are continuing to design and test improved vaccine concepts for advanced testing through the CBNS. The team are making headway in targeting nanoparticles to immune cells using surface-tethered antibodies. Caveospheres have developed into a flexible vaccine-particle system that is being exploited in a highly productive collaboration across UQ, Melbourne and Monash University CBNS nodes. Vaccines delivered by microinjection with an array of small needles directly next to skin dendritic cells (the Nanopatch™) continue to be exploited through the CBNS. Looking forward, an additional key goal will be to understand how targeting antibodies could affect how non-specific clearance of the particles.
CBNS researchers have been developing a novel biologically derived nanoparticle system based on the formation of caveolin-induced nanovesicles in bacteria. Expression of the caveolin protein in bacteria induces budding of 50 nm diameter caveospheres from the bacterial plasma membrane. These nanoparticles can be modified to use as vaccines or to deliver drugs to specific cells of the body. Specifically, the team has engineered the caveospheres using molecular cloning techniques to incorporate vaccine components and synthetic amino acids that allows for modification of the particles in a site specific way. The purified caveospheres contain lipids from the bacterial cytoplasmic membrane and caveolin protein (approximately 150 copies per vesicle). The bacterial synthesis of the caveospheres means they are simple and economical to manufacture as the process can be easily scaled using industrial fermentation methods. In preliminary tests, the immunogenic caveospheres show significant promise as a vaccine delivery system, and the team is currently investigating the targeting and biodistribution of the caveospheres in vivo. Further experiments are underway to understand in molecular detail how caveospheres form and to use this understanding to nanoengineer the caveospheres. To further improve the caveospheres, a short polypeptide of caveolin has been identified—just 66 amino acids long—which can generate smaller ‘mini-spheres’ containing just the minimal domain of caveolin. This allows the properties of the caveospheres to be tailored for specific needs. Work is now on the investigation of the use of different versions of the caveospheres with different properties to deliver agents specifically to cells of the immune system or to target tumour cells. Preliminary work of caveospheres expressing model antigens (ovalbumin protein) shows that these particles can stimulate dendritic cells and induce potent immune responses.

*J Biol Chem* 2015, 290(41), 24875

**Vaccines: Caveolin nanospheres as a vaccine delivery agent**
Vaccines: Targeting of caveospheres to human immune cells

One version of caveospheres was developed to easily incorporate targeting antibodies onto their surface (see figure on previous page). This enabled the delivery of caveospheres to different human immune cells (CD4+ T cells and B cells). The examination of cell-targeted nanoparticles has conventionally been restricted to testing in simple cell line models (or, ‘using single cell types’). However, using this platform CBNS researchers investigated cell targeting within physiological mixtures of fresh human blood immune cells (figure below). These targeted caveospheres demonstrated enhanced binding to targeted immune cells (6.6 to 43.9-fold) within the mixed cell populations. Moreover, by targeting caveospheres to the cell protein used by HIV to enter cells (CCR5), we were able to hijack this cellular machinery to enter the CD4+ T cells normally infected by the virus—an important therapeutic target for HIV treatment. This efficient and flexible system of immune cell-targeted caveosphere nanoparticles holds promise for the development of advanced immunotherapeutics and vaccines.

![Figure: Antibody-targeted caveospheres can be delivered to human CD4+ T cells and B cells. By adding appropriate antibodies, caveospheres were targeted to human CD4+ T cells and B cells within fresh mixed blood cell populations (top). Moreover, by targeting the cell protein used by HIV to enter cells (CCR5), caveospheres can be delivered inside fresh human CD4+ T cells (bottom)—an important therapeutic target for HIV.](image-url)
Vaccines: Stealth PEG particles for improved in vivo circulation

The work described here was published in ACS Nano and led by CBNS researchers Dr. Jiwei Cui and Dr. Rob De Rose, and was awarded Most Significant CBNS Publication of 2015.

The successful delivery and accumulation of therapeutics and vaccines at the relevant sites is limited mainly by biological barriers, especially the nonspecific uptake of drug carriers by the phagocytic cells of the immune system. Modifying the surface of nanoparticle drug carriers with polyethylene glycol ("PEGylation"), has been the most widely used strategy to reduce non-specific clearance and to prolong circulating lifetimes. However, PEGylation is usually dependent on the PEG chain architecture and PEG surface density, both of which are difficult to finely control and simulate. CBNS researchers circumvented the issues relating to PEG chain architecture and PEG density on the surface of particles and instead engineered particles composed entirely of PEG by infiltrating PEG into mesoporous silica templates. They also improved in vivo circulation times of the PEG particles by modifying the molecular weight, size and rigidity of the PEG polymer. These exciting particles are now being prepared to target specific immune and cancer cells by adding targeting molecules to the surface, such as antibodies. The preliminary data using 'bispecific' antibodies (where one arm of the antibody binds to the PEG and one arm to a desired target) looks highly promising.

One of the key challenges associated with translating nanomaterials into vaccines and other therapeutics is understanding how nanomaterial characteristics interact with cellular environments. The development of predictive relationships between structure, function and subsequent physiological response will drive the rational design of novel nanomedicines. These relationships are often determined by the intrinsic characteristics of nanoparticles, such as chemical composition, size, surface charge, architecture, roughness and surface chemistry. As a model to investigate these interactions CBNS researchers are using well-defined nanomaterials known as hyperbranched polymers (HBPs).1

Size and surface charge are an initial focus of this investigation since they are the dominant physical parameters that dictate the route (absorption, distribution, metabolism and excretion) of polymeric nanocarriers in the human body and whether they can by-pass the numerous biological barriers or obstacles and take effect at the desired locations. The HBPs were evaluated for activation of human immune cells and were found to have a charge-dependent activation of dendritic cells, which are responsible for the immune response to vaccines and pathogens. Positively charged HBPs activated a major dendritic cell subset within human blood, while neutral and negatively charged HBPs had no immunostimulatory effect. Moreover, charge dictated their association with different immune cell subsets. At physiological temperatures, all cell types associated with positively charged HBPs, while negatively charged HBPs selectively associated with cells specialised for pathogen clearance and processing.

These studies provide us with strategies to predict and evaluate the fate of polymers at whole body and cellular levels, making the application of polymeric materials in vaccine delivery more time and cost effective. J Am Chem Soc 2014, 136, 2413

Figure: Flow cytometry histograms demonstrating the temperature-dependent increase in association of negative HBPs (blue) with granulocyte and monocyte populations. These observations are less so for other cell types, including B cells.

Key Goals for 2016

1. Develop a deeper understanding of the rules by which immune cells interact with a wide range of nano-engineered particle systems and physical properties.
2. Engineer next generation nanocapsule vaccines to more efficiently target dendritic cells using surface-tethered antibodies.
3. Engineering antigens into complex nanomaterials to enable effective vaccination.
4. Assess the balance between non-specific uptake by immune cells and modification of the capsule surface with targeting antibodies.
Imaging Technologies

The work of the Imaging Technologies theme presented here was undertaken by the following CBNS Chief Investigators and their teams: Andrew Whittaker (Theme leader, UQ); Kris Thurecht (UQ); Tom Davis (Monash); Rob Parton (UQ); Thomas Nann (formerly UniSA, now MacDiarmid Institute, NZ). The research of our themes is broad and contributions are made by others in the CBNS.

The CBNS is developing new, ‘intelligent’ imaging agents whose fate can be predicted and controlled, that respond to changes in local biochemical signals and that facilitate the early detection of disease progression such as metastatic spread. This CBNS research will lead to safer, more sensitive imaging agents for MRI, PET, x-ray CT and ultrasound. Imaging lies at the core of many of the research projects of the CBNS and so the Imaging Technologies research theme supports many of the activities. Importantly, the CBNS is connected to the national network of imaging capabilities, providing an outlet for commercial development and receipt of real-world feedback regarding design requirements.

Fluorescence, magnetic resonance imaging (MRI), X-ray computed tomography (CT) and positron emission tomography (PET) agents have led to major advances in our understanding of diseased tissue. Often these are blood flow agents that accumulate in the tissue of origin due to changes in the local blood flow. For example the ‘leaky vasculature’ within cancerous tissue can be taken advantage of to allow permeation and retention of imaging agents in tumours. Such simple agents however, cannot be targeted to specific diseases or even specific tumours, and are poor at detecting the early stages of disease and/or small tissue volumes.

The programs within the Imaging Technologies theme of the CBNS focus on these challenges, aiming to identify novel, safe and more effective imaging agents. The issues of selectivity, specificity, responsiveness and lifetime are tackled using polymer-based imaging agents. Using a macromolecular strategy allows, for example, superior relaxivity for paramagnetic MRI contrast agents (thereby addressing sensitivity issues) and also provides control over nanostructure and therefore in vivo lifetimes and clearance. Specificity can be achieved by modifying polymeric imaging agents with bio-recognition molecules such as antibodies in conjunction with other programs within the CBNS.

In collaboration with the Delivery Systems theme, imaging particles are made responsive using molecular beacons which can be interrogated to provide information on cell function or local metabolic processes. Simple examples of this are agents that can be designed to respond to changes in temperature, pH, redox potential, hypoxia, etc. Imaging agents responsive to oxygen tension, or specific ions, can be envisaged and polymeric architecture provides very distinct advantages in the design of these molecules.

The key scientific goals of the Imaging Technologies theme are:

1. to develop imaging agents with high specificity for particular tissue types and diseases, specifically determining the most effective targeting strategies;
2. to design imaging agents that are responsive to biological triggers, so that certain pathologies, for example hypoxia, inflammation and cancerous tissue can be identified;
3. to investigate how the structure of imaging agents influences the lifetime in vivo, so that clearance of the imaging agent can be controlled to ensure appropriate cellular uptake and removal of the agent from the body; and
4. to investigate the design requirements to optimise sensitivity of imaging agents, to allow early detection of disease and to identify the margins of diseased tissue.
In order to provide effective patient treatment, accurate imaging of disease physiology and biology is a necessity, particularly in the field of oncology. Currently, a variety of imaging modalities are available for disease staging and monitoring, including ultrasound, CT, MRI and PET. Whereas ultrasound and CT mainly focus on visualising anatomy, MRI also offers the possibility to provide physiological information. Likewise, PET is unprecedented in its ability to acquire biological information. As such, both MRI and PET—increasingly being combined into one apparatus—are emerging as multi-potent imaging modalities and offer great possibilities for medical imaging and clinical research.

To optimally benefit from the favourable features of both imaging techniques, CBNS researchers have been incorporating MRI and/or PET functionalities into novel (radio) pharmaceutical nanoparticles. In general, nanoparticles are being considered a good platform for the development of so-called ‘intelligent’ imaging agents. Intelligent imaging agents are sensitive to microenvironmental-dependent stimuli, such as subtle changes in pH or temperature, and may have tuneable properties that enable disease- or tissue-specific targeting. Advantageous properties of nanoparticles include their ability to become functionalised with one or more targeting molecules (e.g. antibodies) at a wide range of densities, their potential to enhance imaging intensity by including a large number of imaging moieties within a single nanoparticle at predetermined ratios and their tuneable size and shape which optimises biodistribution and enhances accumulation via the enhanced permeability and retention effect in tumours.1

By combining MRI contrast agents (e.g. gadolinium) and radionuclides (e.g. copper-64, iodine-124, iodine-131, fluorine-18) within nanogel star copolymers, CBNS researchers have designed novel multimodality imaging probes, which could improve sensitivity and specificity of current clinical imaging methods and enable imaging utilising hybrid PET/MRI scanners. For this work, CBNS is currently collaborating with our partner investigators at ANSTO (Sydney) and Memorial Sloan Kettering Cancer Center (New York).

Building on our previous work on polymeric MRI contrast agents and theranostic nanoparticles—in which both therapeutic and diagnostic moieties are combined—CBNS research is moving towards the development of intelligent imaging probes that enable monitoring of nanoparticle drug release via the incorporation of responsive elements.2 As a result of changes in the microenvironment (e.g. increased acidity in the tumour microenvironment), drugs are released from the nanoparticle causing an increase in MR contrast. Such systems hold great promise in the assessment of drug delivery and, ultimately, could greatly benefit personalised medicine.

In a collaboration with CSIRO and QIMR Berghofer, CBNS researchers have developed a novel imaging agent for the detection of glioblastoma multiforme (GBM).3 GBM is the most lethal of primary brain tumours and disproportionately affects younger people compared with other malignancies. The nanoparticles combine an antibody to the EphA2 receptor, which are overexpressed in a number of cancers including GBM, and a PET ligand, 64Cu. We have shown that the imaging agent delineates tumour boundaries in three different mouse models of GBM. Significantly, tumour-to-brain contrast is significantly higher using our agent compared with the current ‘gold standard’, 18F-FDOPA images, and the boundary delineation is comparable to that obtained using Gd contrast-enhanced MRI. Theranostic agents based on these nanoparticles are currently being developed.


Figure: Proposed design for a stimuli-responsive theranostic nanoparticle in which both MRI and PET imaging moieties are combined. Upon decreasing pH, which is common for the tumour microenvironment, the biochemical properties of the nanoparticle are changed. As a result, the nanoparticle becomes more accessible to water molecules, thereby increasing MR contrast.
Imaging Technologies: Responsive Imaging Agents

In recent years, the development of stimuli-responsive imaging agents has attracted significant interest from a number of scientific groups internationally, and end users of imaging agents. Imaging agents sensitive to environmental conditions (for example pH, temperature, metal concentration, etc.), termed ‘smart’ imaging agents, can be designed to be only visible (detectable) in specific circumstances. These molecules offer the prospect of non-invasively interrogating the biochemistry of tissue, using conventional imaging technology. Imaging agents that are responsive to pH are especially attractive because of the well-known variation in pH in tissue types and in diseased tissue.

CBNS researchers have developed new approaches to stimuli-responsive polymers based on 19F MRI, a new and potentially powerful technology. Detailed studies of the behaviour of the partly-fluorinated macromolecules in physiologically-relevant media are being supported by molecular dynamics simulations of the conformations and dynamics of the polymer chains. The combination of the experimental1-3 and computational analyses yield a unique insight into the behaviour of the molecules in solution.

In a detailed study the researchers examined the changes in conformation of copolymers of oligoethylene glycol methacrylate (OEGMA) and trifluoroethyl acrylate (TFEA) as a function of temperature across the lower critical solution temperature by NMR and molecular dynamics (MD) simulations. The results showed how as the OEGMA side-chains became hydrophobic they interacted more strongly with the polymer backbone, and the hydrophobic TFEA units.2 The figure at right shows a snapshot of the conformation of the macromolecule from the MD studies. In a similar study the CBNS examined the changes in conformation in highly novel dendronised polymers developed by our collaborators in Shanghai University.3 Both of these studies provide design rules for the next generation of stimuli-responsive polymers.


Imaging Technologies: Theranostic Devices

In a collaboration with researchers at International Medical University (IMU) Malaysia, CBNS researchers have developed novel theranostics for the treatment of colon cancer.

The theranostics were designed for oral delivery, and hence are required to traverse the harsh environment encountered along the digestive tract. In order to measure the efficacy of delivery to the colon, fluorescence imaging was utilised to monitor the biodistribution of drug-loaded nanoparticles throughout the digestive tract.

CBNS researchers have further developed new polymer theranostics for understanding and treating prostate cancer in a collaboration with researchers at Queensland University of Technology.2 The nanoparticles were targeted to prostate cancer cells using three different ligands to prostate specific membrane antigen (a protein overexpressed on most prostate cancers). The study investigated the difference in efficiency of a small molecule (glutamate urea), a peptide, and a full antibody as ligands that bind to the disease with high affinity. All variants of the agent showed good binding, with the peptide being most efficient for this particular nanoparticle.

1 European Journal of Pharmaceutics and Biopharmaceutics 2015, 94, 393; 2 Biomacromolecules 2015, 16, 3235.
Imaging Technologies: Imaging of the Cell

One goal in 2015 has been to extend the imaging technologies within the Centre to high resolution electron microscopic techniques which can be correlated with parallel light microscopy approaches. The use of green fluorescent protein (GFP) has revolutionised the study of dynamic cellular processes in cells, tissues, and whole organisms. In 2015 CBNS researchers developed a new electron microscopic method that provides rapid, simple, high resolution, and quantitative detection of GFP-tagged proteins. This method is compatible with the new 3D electron microscopic techniques now available, including electron tomography and serial blockface scanning electron microscopy, and will be used to extend the scope of the strategic project ‘Journey to the Centre of the Cell’ to the visualisation of specific proteins.

Imaging Technologies: New Hybrid Nanomaterials for Bioimaging

None of the current clinical imaging techniques offer a universal solution. For example, MRI, CT or PET are standard methods to detect and locate tumour tissue, however, they do not allow for visualisation of malignant tissue under surgery. There is therefore a need for the design of contrast agents that can be precisely engineered to offer optimal properties for the targeted cells (and disease) independent of the imaging technology.

CBNS researchers have developed new, hybrid, multi-functional nanostructures that can be detected by different modalities. The figure at right shows hetero-dimer nanoparticles made of gold and magnetite nanoparticles. The magnetite part of the structure acts as MRI contrast agent, while the gold can be detected by various optical methods. Complex nano-architectures like this can be further functionalised by coating them with targeting moieties and loading them with drugs.

Key Goals for 2016

Imaging Technologies are enabling sciences, and activities within the theme are highly complementary with both the Delivery Systems and the Sensors and Diagnostics Themes. The challenges ahead in imaging lie in two directions; development of smarter (responsive) and more sensitive agents that can be applied across multiple imaging modalities; and maximising the synergistic combination of imaging and delivery functions into a single nanoparticle system. Of course Imaging Technologies is a fundamental tool in addressing important biological challenges, such as cellular uptake, tumour penetration, etc. In 2016 our main goals are to:

1. Build a fundamental understanding of mechanism of USPIO contrast agents and design efficient relaxation agents.
2. Demonstrate MRI agents that enable high sensitivity cell tracking as applied to stem cell therapy.
3. Develop molecular imaging probes and methodologies to understand nanomedicine distribution in tumours.
4. Develop bimodal PET/MRI probes employing a range of clinically applied radioisotopes.
5. Develop an MRI probe that enables in vivo monitoring of nanoparticle drug release.
6. Develop a theranostic probe that combines radiosensitising and imaging moieties within a single nanoparticle.
7. In vitro testing and further optimisation of synthesis methods of hybrid polymer–nanoparticle imaging agents.
Sensors and Diagnostics

The work of the Sensors and Diagnostics theme presented here is undertaken by the following CBNS Chief Investigators and their teams: Justin Gooding (Theme leader, UNSW); Nico Voelcker (UniSA); Beatriz Prieto-Simón (UniSA); Simon Corrie (UQ). The research of our themes is broad and contributions are made by others in the CBNS.

Diagnosis is the key to both the prevention and treatment of diseases. Traditionally diagnoses are performed in centralised pathology laboratories which are still, and will remain, robust methodologies in biomedical diagnostics. However, increasingly there is a move towards diagnostic tools that can be used at home, in community clinics, in the hospital or even during surgery. Decentralised diagnostic devices have enormous potential for early disease diagnosis and the measurement of the efficacy of treatment strategies.

The goal of the Sensors and Diagnostics theme is to develop technologies for detecting ultralow amounts of analyte that provide robust analytical information in a reasonable response time. The main application goals of the CBNS are to develop technologies for biomarkers and methods for the isolation and measurement of single cells. The progress of the Sensors and Diagnostics theme in 2015 towards these application goals can be subdivided into the following categories:

1. new materials for sensing;
2. new measurement methodologies;
3. the rapid and accurate detection in complex samples; and
4. minimally invasive sampling and measurements performed in vivo.

Sensors and Diagnostics: New Materials for Sensing

Within the CBNS there is a strong emphasis in materials development for silicon based materials. The main reason for this is that silicon is a benign material in vivo, and when present at the nanoscale it can degrade away in the body with no reported deleterious effects. Additionally it is amenable to further functionalisation with powerful surface chemistry that is incredible robust. In 2015 the CBNS has developed a range of new silicon structures including nanopore arrays which electrochemically transduce via nanochannel blockage. This system is of interest as the channel size allows selective detection of the biomarkers over interferences. CBNS researchers have also developed silicon quantum dots (SiQDs), important because they are nontoxic, and along with microscopy methods to make these SiQDs amenable to intracellular biolabeling and intracellular sensing. The intracellular sensing is made possible by the CBNS establishing for the first time that SiQDs can act as donors in Förster resonance energy transfer (FRET).

At CBNS new antifouling coatings have been developed via a diglyme plasma polymerisation process. This method has been shown to be incredibly effective and this chemistry will serve to allow the development of technologies that work effectively in biological fluids. Most importantly production of these antifouling coatings is incredibly general—any surfaces that present the correct chemistry and the plasma approach are ideal for modifying any material at an industrial scale. Such modification layers can also be combined with new surface chemistry for coupling biorecognition molecules such as antibodies.

Figure: A strategy for making nontoxic silicon quantum dots compatible with bioimaging using advanced microscopy. Fluorescence lifetime and two photon excitation allows the SiQDs to be measured despite autofluorescence while FRET allows the colour to be easily changed.

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Sensors and Diagnostics: New Measurement Technologies

New ways of performing sensing measurements will enable new biomarkers to be measured, or for the measurement of biomarkers in concentrations or locations never previously possible. At the CBNS in 2015 there were two major advances in measurement technologies. The first relates to electrochemical sensors. As successful as traditional electrochemical devices have been, they have never been able to compete with optical devices when it came to being made in array form, where each electrode needs a wire. CBNS researchers have developed a method of connecting electrodes with light\(^1\) which will allow electrode arrays to compete with optical arrays but with all the advantages of the portability of electrochemistry. This technology is being applied to electrode arrays for profiling microRNA, important in cancer diagnostics, and to create devices that can capture and release single cells.

The second new measurement technology developed involves detecting many single molecules simultaneously using surface enhanced Raman spectroscopy\(^2\). Technologies that can detect many single molecules promise to be the next generation of diagnostic devices as they can solve issues related to calibration, specificity and multiplexing. In the CBNS-developed technology the sensor operates like a conventional sensor, where many analyte molecules interact with the surface, but upon a temperature change single molecules are captured in plasmonic hotspots. The hotspots can be measured individually to give single molecule signals.

\(^1\)Chem Sci 2015, 6, 6769; \(^2\)Nature Comm 2015, 6, 8797

Figure: A new approach to developing electrochemical arrays for multianalyte sensing electrochemistry, called light activated electrochemistry, which uses light to connect to any location on a monolithic surface so that electrochemistry is only observed at the site of illumination. This new technology allows high density electrode arrays to be formed with only a single metallic connecting wire. Illustrated here for the detection of nucleic acids such as DNA or microRNA. Image courtesy of Kate Patterson.
The developments in antifouling surface coating, new materials and new measurement methodologies have allowed the CBNS to develop a range of biosensing systems that operate in complex biological fluids. Perhaps the most dramatic successes have come through the CBNS’s world leading capabilities in porous silicon. Porous silicon is made from the electrochemical etching of single crystalline silicon. The control over the etching rate that the electrochemical method provides allows porous silicon structures to be engineered into high quality optical structures that operate in the visible and infrared regions of the electromagnetic spectrum. The challenge with porous silicon for biosensing application has always been the issue of stabilising the material long enough for the measurement. This is a challenge CBNS researchers have solved, and combined with antifouling chemistries, has the Centre poised to make a major impact with these exciting materials.

In 2015 CBNS researchers achieved a number of milestones. They have shown that the porous silicon devices can be used to monitor the health of islet cells, such that their suitability for transplantation can be assessed. This work was achieved using aptamers as the biorecognition species, which is a new development for porous silicon devices. Multiplexed detection of wound healing biomarkers was shown on porous silicon resonant microcavities with microscale spots of fluorogenic peptide substrates.

Other studies from the CBNS show the use of antibodies for the detection of endotoxin. Still further work has shown these materials can be used for the profiling of different matrix metalloproteinases from primary cell lines. This latter study is poised to allow CBNS to make cell chips with arrays of single cells, which will be ideal for understanding cell heterogeneity and profiling how cells respond to therapeutic treatments. Another exciting study has employed porous silicon for the detection of bacteriophage using antibody modified structures. Most notable here is that the detection is not optical but electrochemical. The catalogue of these studies shows how the one material can detect many different biologically important species using different readout approaches.

The CBNS has developed electrochemical sensors that employ antibodies which can operate in biological fluids. This is a major achievement as the vast majority of biomarkers that one might want to detect rely on antibodies or other affinity molecules. The advantage of using electrochemical methods is the compatibility of electrochemistry with portable analytical devices. The most notable paper from 2015 uses magnetic oxide modified carbon nanotubes as the electrode material.

Sensors and Diagnostics: Rapid and accurate detection in complex samples

Figure: Schematic of multiplexed wound biomarker detection from a porous silicon resonant microcavity (left) featuring an array of immobilized FRET substrates for Sortase A (top centre) and matrix metalloproteinases (bottom centre). Upon enzymatic cleavage (centre panels), the confinement effect of light inside the cavity layer of the porous silicon resonant microcavity where the fluorophore is embedded induces a fluorescence enhancement effect (right).
In the long term any technology developed in this theme will need to either sample biological fluids or measure directly in vivo, depending on the application.

Turning to sampling of biological fluids first. The detection of biomarkers in bodily fluids in vitro has the one drawback in that the biological fluid must be obtained. Apart from urine and tear film this means penetrating the skin with the associated pain. At the CBNS we are developing a range of microneedle projections to sample blood and other bodily fluids that are pain free. Part of the power of the microneedles is that depending on their length different bodily fluids of different composition can be sampled. In recent times advances have been made in the material the projections are composed of. Originally the microporation arrays were made of silicon but more recently polycarbonate projection arrays have been formed. A recent paper from the CBNS has illustrated this power. Using polycarbonate microneedles, proteins produced as a result of dengue fever were collected from diseased mice. This is the first time that patch based biomarker detection has been performed with a diseased animal. This is a major step towards using microneedles in commercial biosensing devices. Part of the key to achieving these results was the low nonspecific adsorption of proteins conferred by the state-of-the-art zwitterionic antifouling coatings on the microporation.

1. The world-leading capability of CBNS in developing detection technologies based on porous silicon has seen the first moves towards using this in vivo. Protease activity is detected by implanting the sensors into rabbits and mice and detecting the optical responses from outside the body using near infrared wavelength light. These exciting developments will be published in 2016.


Figure: Illustration of the preparation of the sensing platform based on the use of single walled carbon nanotubes as magnetic immunocarriers.

Sensors and Diagnostics: Minimally invasive sampling and measurements performed in vivo

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Key Goals for 2016

2015 was a year where a range of new capabilities were developed that are vital for developing diagnostic devices that operate in biological fluids. The key goals for 2016 relate to applying these technologies for diagnostics within complex biological samples. These include:

1. The demonstration of the isolation of single cells from biological fluids.

2. Development of the first diagnostics for the detection of biomarkers from single cell.

3. The first demonstration of the use of porous silicon sensing technologies for the detection of inflammatory disease markers in vivo.

4. Advancement of our understanding of how microporation patches allow the sampling of proteins and cells and integrate this sampling method with new detection technologies.
Computational and Systems Biology

The work of the Computational and Systems Biology theme is led by the CBNS Chief Investigator Edmund Crampin (Theme leader, Melbourne). It sits across the primary research themes.

A major unmet challenge to advancing bio-nano technology is the ability to predict how a biological system will respond when exposed to a particular type of nanomaterial before the material is produced, let alone introduced to the system. This understanding would create a pathway for engineering design of nanomaterials with desired and predictable biological interactions. A significant hurdle to overcome is the development of standards and approaches which will allow data from different experimental investigations to be combined and analysed in order to identify underlying patterns in the data. Such patterns reveal the properties of nanomaterials which dictate their biological interactions. CBNS researchers are developing strategies for data collection and computational approaches for modelling of data generated in the CBNS to better understand, and hence predict, how specific properties of nanoscale materials lead to specific biological responses.

Figure: Systems Biology is an approach we are pursuing in the CBNS, which uses mathematical and computational modelling to analyse high-throughput experimental data to understand and ultimately predict the interactions between nano-engineered materials and biological systems.
Computational and Systems Biology: Model-based cellular dosimetry

This project is motivated by a simple question: can we standardise cellular uptake assays between different nanoparticle materials in order to fairly assess cellular uptake? The challenge is that different physical properties of nanoparticles can obscure the true nature of cellular association in commonly used experimental assays. Our approach allows us to account for differences in diffusion and sedimentation in experimental assays, in order to accurately determine cellular dose. Mathematical modelling using partial differential equations to describe transport of particles by diffusion and sedimentation, as well as particle-cell interactions, allows standardisation between different experiments, and hence to accurately compare cellular dose between different materials.

(Manuscript submitted at the time of publication: Cui, Faria, Björnmalm et al.)

Figure: Nanoparticles with different physical characteristics (a) were prepared and assayed for cellular association in a variety of different experimental conformations (b) by computationally modelling the nanoparticles in the assay (c) the physical characteristics which otherwise obscure the true cellular associations of the particles in the assay can be accounted for. (Cui, Faria, Björnmalm et al., submitted)

Computational and Systems Biology: Nanoparticle uptake in whole blood assay

An important issue in the use of nanoparticles for vaccine delivery, for example, is to understand what determines the distribution of uptake of nanoparticles between different blood cell types in whole blood. The CBNS is pursuing experimental and modelling approaches to improve our understanding of this question, in particular to determine which properties of nanoparticles (size, charge, etc) influence the observed cellular distributions when incubated in whole blood. Preliminary work has focused on making sure that results are reproducible, and assessing and controlling sources of variability which may otherwise mask important factors.
Computational and Systems Biology: Framework for physically plausible modelling of bio-nano interactions

To model biological processes and interactions with nanomaterials, it is maintained that constraining models to obey the fundamental laws of physics will increase model fidelity and hence predictive power. Therefore CBNS researchers are developing a framework for physically-plausible modelling of biological systems, by extending the Bond Graph formalism which has been used in multi-domain engineering design and control applications for decades. This formalism allows for representation of physically realistic interactions, to combine models easily, and it ensures consistency of the modelling approach. The formalism has been extended to capture a range of biological properties, and will continue to develop the tools for model-based analysis of data for bio-nano interactions.

Proc. R. Soc. 2015 A 471: 20150642

Key Goals for 2016

1. Bond Graph formalism: extend the computational framework for modelling cellular networks to combine biochemical, electrical and mechanical aspects of biological systems.


Figure 3: Schematic showing (a) biological pathway (glycolytic pathway), (b) Bond Graph representation, and (c) physically-plausible mathematical model generated from the Bond Graph representation.

While social scientific and humanities engagement with the bio and life sciences has a long history, the first large-scale coordinated programme of research in this area was the Ethical, Legal and Social Implications (ELSI) programme of the Human Genome Programme (HGP), designed to explore these aspects of gene research. Set in the context of social conflicts over the risks associated with science and technology (for example around pesticides and nuclear technologies) and a concern that the HGP would generate similar controversies the primary aims of the ELSI programme were to:

1. “Anticipate and address the implications for individuals and society of mapping and sequencing the human genome;”
2. Examine the ethical, legal and social consequences of mapping and sequencing the human genome;
3. Stimulate public discussion of the issues; and
4. Develop policy options that would assure that the information be used to benefit individuals and society.1

Critically, the ELSI programme also acted as a funding mechanism for dedicated research on societal dimensions of biotechnology with between 3–5% of HGP research funding dedicated to ELSI initiatives. More broadly, this approach to integrated research funding for social science and humanities research was situated in the context of broad shifts in the social and political expectations associated with novel areas of science—with an increasing emphasis on the economic and commercial value of research, social impact and public engagement.

Since the inauguration of the ELSI programme, research in this area has developed in a number of significant directions. While the ELSI programme constituted a standalone field of enquiry more recent approaches have shifted focus to encourage active integration and collaboration between social science and the advanced life sciences. Practically, this has meant building collaborative teams to explore the social dimensions of novel areas of technological development in ‘real-time’ by engaging with those affected by science and technology during the research—rather than simply afterwards. Internationally, social science researchers have pioneered such concepts as ‘upstream public engagement’, ‘anticipatory governance’ and ‘responsible innovation’ to capture this need to integrate social concerns into the scientific research design and process.

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1.1 https://www.genome.gov/10001754

The Social Dimensions theme spans all four of the core research themes of the Centre. 2015 has been an exciting year, with researchers commencing a phase of ethnographic research with CBNS research nodes—attending lab meetings and the inaugural retreat. Initial findings from these meetings between social researchers and ‘bench’ scientists has emphasised the value of making societal perspectives visible in the laboratory. In this context the team has been particularly struck, not only by inventiveness of experiments undertaken, but their profound implications for medicine, care and health. Research across this field is likely to contribute to changing notions of health and wellness and shifts in the everyday experience of healthcare. Through 2016 the social dimensions programme will continue to explore how the promises of research in this area are shaped by an evolving medical system, which is often subjected to broader economic and social shifts away from collective ownership and responsibility. In addition the social dimensions researchers will collaborate with node researchers to delve beyond the important questions of risk (associated with nanoparticles, in particular) and investigate how nanotechnology research will impact care-giving, medical treatment, the patient experience and wider concerns of public health. The team expect node researchers who are applying nanotechnological research to such health care innovations as cancer drug delivery, sensing cancer cells, and post-operative skin treatment to benefit from collaboration.

In addition to this ongoing research effort, CBNS social science researchers released the landmark volume Remaking Participation: Science, Environment and Emergent Publics (Routledge), with launch events in Denver, Paris and Oxford. Including contributions from leading figures across the social studies of science from Europe, the UK and the USA the volume charts how the changing relations between science and democracy have led to a proliferation of new spaces of public participation and engagement. The volume develops a new approach to public participation with science and technology, which will form the basis for CBNS engagement activities and projects over the coming year.

Key Goals for 2016

1. Continue the programme of integrated and ethnographic analyses of CBNS research, and in-depth research engagement across CBNS nodes.
2. Coordinate a series of cross-node workshops with key CBNS projects and outreach activities.
3. Collaborate with researchers working on the legal and regulatory aspects of bio-nanotechnology on a public workshop on these issues.
4. Develop proposals for CBNS public engagement initiatives.
Strategic Projects

In addition to the core research undertaken in the four primary themes and the Centre-wide research, detailed in the previous pages, the CBNS provides funding for activities that meet the strategic objective of the CBNS to increase collaboration whilst extending the research capabilities.

Strategic Projects are assessed by all Chief Investigators and are supported through a dedicated fund. The strategic funding is managed centrally and all collaborating organisations contribute part of their ARC funding each year.

When assessing proposals for strategic funding the CBNS Management Committee consider whether the projects:

- Involve collaboration between at least two CIs, or members of their research groups;
- Involve collaboration between at least two nodes;
- Introduce skills, expertise or activities not presently available within the Centre;
- Have a duration no longer than two years (although after two years successful projects can apply for additional funding to continue the project);
- Address at least one non-research KPI (such as media, public or industry engagement, visitors, training etc.); and
- Not exceed an annual cost of $100,000.

In addition to small amounts of funding supporting student attendance at workshop, two major projects were funded in 2015. They are detailed following.
Journey to the Centre of the Cell

The therapeutic effect of most drugs occurs in specific locations within the cell so an understanding of the intracellular fate of the drug is vital. The processes by which a particle carrying a drug is internalised to, and trafficked within, a cell are extremely complex. Describing such processes, even to scientifically literate audiences, presents a significant challenge to researchers as the visualisation tools available to assist in describing the processes are quite limited.

Dr Angus Johnston (Monash) is collaborating with Dr John McGhee from the 3D Visualisation Aesthetics Lab (UNSW) to create high quality 3D animations to visualise the complex processes that occur in cells. With electron microscopy data from Prof Rob Parton (UQ) the research team have recreated a cell. By donning a virtual reality headset a researcher can take a ‘journey to the centre of the cell’, moving around the structures within it and even poking their head into endosomes. They share the same experience as a particle delivering drugs within a cell. This virtual reality and the 3D animations will be used not only in research seminars, but also to engage the broader public.

The project is part way through, with pre-render complete on the animated cell. The immersive virtual reality experience is in progress. When complete an exhibition is planned, before expansion to include 3D fluorescence microscopy data from Prof Nigel Bunnett (Monash) to understand ‘pathways to pain’, and immunofluorescence data on cancer therapeutics from Prof Maria Kavallaris (UNSW).

This project has been so successful that Dr John McGhee has joined the CBNS as a Chief Investigator in 2015.
Open Data Fit

The **Open Data Fit** project is creating a portfolio of websites that bring together tools and information of relevance to the CBNS as well as the wider international research community. The final suite of sites will embrace the open access approach by providing tools to enable the collection and analysis of data in bio-nano science. Each site will host calculators, simulators, video and text experiment guides and cloud based storage. Unique URLs will be created for data stored via the site, and provide a persistent link that researchers can submit with publications so that anyone can access the data to verify their analysis.

The first site, [supramolecular.org](http://supramolecular.org), went live late in 2015 and provides calculators that enable a user to determine binding constants from NMR, UV-Vis or fluorescence titration data. The simulator section of the site allows for comparison between different binding models and first and second order kinetics.

[**supramolecular.org**](http://supramolecular.org) has been cited in publications and already proved useful to scientists external to the CBNS—during a presentation of the site capabilities at the Pacificchem conference in December 2015, an audience member uploaded data and managed to fit it to a model, despite no success with other methodologies.

Under the parent website, [opendatafit.org](http://opendatafit.org), the project aims to eventually provide a subsite for each of the subjects of reaction kinetics, cytotoxicity measurement and spectroscopy.

**Screen capture of the site, [http://supramolecular.org](http://supramolecular.org)**

**Screen capture of the Bindsim app on the supramolecular site. Bindsim helps estimate the best concentrations to aim for when planning titration experiments.**
Professor Ben Boyd using the small angle X-ray scattering (SAXS) beam line at the Australian Synchrotron, where he is undertaking research into a drug delivery system for macular degeneration. Image: Simon Schluter/Fairfax Syndication
Cánsis, researchers are dedicated to reaching out beyond the academic community and have engaged in various media briefings, radio and online interviews and contributed to newspaper and magazine articles to share Centre research and expertise. The following captures key media engagements for the CBNS in 2015.

**Radio interviews**
- **Professor Maria Kavallaris** “NanoMedicine — big blue sky visions for tiny technology” ABC Radio National, Life matters, July
- **Professor Maria Kavallaris**, 2MM Greek Radio, 2015
- **Dr Simon Corrie**, 3AW, September
- **Professor Mark Kendall** “How to get innovation right” ABC Radio National, Drive, November

**Newspaper, magazine, newsletter, online and other print articles**
- **Professor Mark Kendall** “Vaccin: un nanopatch qui pourrait tout changer” Le Monde (France), January
- **Professor Maria Kavallaris** “Surviving cancer: four tales of beating the odds” Sydney Morning Herald, February
- **Professor Mark Kendall** “Needles-less Nanopath vaccine ready for human trials” Brisbane Times, February
- **Professor Mark Kendall** “We must value research more than football” Brisbane Times, February
- **Professor Mark Kendall** “Vaccinations without the pain of a needle prick are on the way” Herald Sun, February
- **Professor Maria Kavallaris** and **Associate Professor Matthew Kearnes** “The nanoscientist and the sociologist” Uniken, UNSW magazine, June
- **Professor Mark Kendall** “Meet Queensland’s other State of Origin Team” Brisbane Times, July
- **Professor Frank Caruso** “Redox-Sensitive PEG–Polypeptide Nanoporous Particles for Survivin Silencing in Prostate Cancer Cells” Prostate Cell News, July
- **Professor Nico Voelcker** “Hi-tech bandage can heal wounds and call the doc” Herald Sun, August
- **Professor Frank Caruso** “Scientists develop ‘immediate’ nano-capsule to treat heart attacks and strokes” ABC News, August
- **Professor Frank Caruso** “Blood-clot busting treatment ‘promising’”, Sydney Morning Herald, August
- **Dr John McGhee** “Nano cell project: art meets science to make the invisible visible” The Australian, August
- **Professor Ben Boyd** “Macular degeneration: nanotech drug treatment could replace eyeball injections” The Age, September
- **Professor Justin Gooding** “American Chemical Society Ask Me Anything; sensors, what’s happening scientifically, and their applications in health, environmental and food monitoring.” The New Reddit Journal of Science, September
- **Dr Simon Corrie** and **Professor Mark Kendall** “UQ team develops needle-free disease detection through nanotechnology patch” Sydney Morning Herald, September
- **Dr Simon Corrie** “Could this be the end of the blood test” The Age, September
- **Dr Simon Corrie** “Needle-free blood screening ahead” Brisbane Times, September
- **Dr Simon Corrie** “Tech talk: ‘Micropatch’ could see end of needlephobia” Australian Doctor, September
- **Dr Simon Corrie** “New painless nanopatch can detect diseases in the blood” Science Alert, September
- **Professor Mark Kendall** “Four things Malcolm Turnbull needs to know about innovation” Australian Financial Review, October
- **Professor Nico Voelcker** “Could genetically engineered algae be the key to fighting cancer?” The Mirror, UK, November
- **Professor Justin Gooding** “Electronics, but not as we know it.” The Australian, December
- **Associate Professor Matthew Kearnes** “Public participation in science and technology: why the failure to launch?” The Guardian, UK, December
- **Professor Nico Voelcker** “Algae blooms as a cancer killer” The Age, December
- **Professor Nico Voelcker** “The little green robots waging war on cancer” Canberra Times, December
- **Professor Tom Davis** “Nanotechnology: fantastic voyage led by Australian scientists” The Australian, December

**Media releases**
- **Professor Chris Porter** “New drug delivery technology from MIPS acquired by Capsugel” January
- **Professor Frank Caruso** “Nanoscale tech for better drug delivery” January
- **Professor Mark Kendall** “Nanopath vaccine technology company attracts $25 million” February
- **Professor Ben Boyd** “Digestive brilliance of breast milk unravelled” March
- **Professor Justin Gooding** “Three scientists awarded Laureate Fellowships” June
- **Professor Justin Gooding** “American Chemical Society expands reach to include rapidly emerging area of sensor science” July
- **Professor Mark Kendall** “UQ a top incubator of influential engineers” July
- **Professor Frank Caruso** “National bio-nano science centre develops world first miniature drug delivery system” July
- **Professor Justin Gooding** “International honour for UNSW chemist” August
- **Professor Nico Voelcker** “Smart bandages monitor healing and provide instant medication” August
- **Professor Frank Caruso** “New clot-busting treatment targets number one killer” August
- **Professor Ben Boyd** “Developing a light-activated drug delivery treatment for macular degeneration” September
- **Professor Justin Gooding** “Australian researchers revolutionise electronics—replacing wires with light beams” October
- **Professor Nico Voelcker** “ARC funding boost for UniSA Future Industries” October
- **Professor Nico Voelcker** “Genetically engineering algae to kill cancer cells” November
- **Professor Stephen Kent** “HIV scientists launch $30 million global project to develop a vaccine” November
- **Professor Chris Porter** “MIPS collaboration helps Starpharma seal deal with Astra Zeneca” November
- **Professor Stephen Kent** “HIV scientists launch $30 million global project to develop a vaccine” November
- **Professor Chris Porter** “Monash academics achieve international recognition as ‘highly cited’ researchers” December
- **Professor Edmund Crampin** “Mathematics adds to understanding human disease” December
Events

First annual CBNS Research Workshop

The first Centre-wide CBNS Research Workshop was held in the Victorian coastal town of Lorne in December. The three-day event provided an overview of the full spectrum of research at the CBNS and was the first chance for many of the Centre researchers to meet.

Research theme leaders and lab heads provided summaries of their work before postdoctoral researchers and postgraduate students provided more detail. A session on CBNS capabilities was presented to raise awareness of the huge range of expertise and instrumentation available across the Centre.

The poster session gave CBNS researchers the opportunity to expand on research presented in talks with some excellent work, particularly from the students. Anna Gemmell (UQ PhD student) received the prize for the Best Poster and Dr Nick Ariotti (UQ) gave the Best Presentation at the workshop. Further details of these awards is provided on page 51.

Other highlights of the workshop included a careers panel discussion, facilitated by Dr Sarah Meachem, President of the Australian Society for Medical Research. The panel provided perspectives on career alternatives to academic research. CBNS researchers heard from those who had worked in a range of areas including the explosives industry, scientific writing and government. Our thanks to Sarah, and to Dr Meg Woolfit from the Eliminate Dengue Program, who came to Lorne to contribute to this session.

Overall the workshop was a success with lots of interest in the research challenges we face and the collaborative opportunities to address them.

“The centre wide and strategic projects sessions were fantastic for providing an understanding of what exactly will drive the aims and scope of the research of the centre.”

“The poster session was a great opportunity to get to know what PhD students and ECRs do, and have a face-to-face and a more active discussion with them, interacting more closely and promoting collaboration.”

Workshop photos by Warwick Tucker, Red Bowler Hat Photography.
**CBNS Visiting Professor – Leaf Huang**

Professor Leaf Huang, a biophysicist at the Eshelman School of Pharmacy at the University of North Carolina, was the 2015 CBNS Visiting Professor. In his Laboratory of Drug Targeting, his research focuses on liposomes and immunoliposomes for drug delivery.

Current activities are focused in the development of nonviral vectors for gene (including siRNA) therapy, and receptor mediated drug and vaccine targeting using self-assembled nanoparticles. The technologies are tested for therapy of cancer and liver diseases in animal models.

During his visit to Australia Professor Huang gave the opening plenary of the International Nanomedicine Conference in Sydney. He visited CBNS researchers and gave seminars at the Children’s Cancer Centre of Australia, the University of Queensland and the Monash Institute of Pharmaceutical Sciences.

The CBNS Visiting Professor Program was established to promote the potential of nanotechnology in medicine and build new international collaborative opportunities. In addition to visiting labs and giving seminars in Australia, the Visiting Professor is a temporary member of the Scientific Advisory Board.

In 2016 the CBNS Visiting Professor will be Vince Rotello from the University of Massachuestts Amherst.

**Imaging Symposium**

On 7 May, the CBNS and the Australian Institute for Bioengineering and Nanotechnology (AIBN) organised a one-day symposium hosted at the University of Queensland highlighting the advances in molecular imaging.

Molecular imaging aims to non-invasively visualise, characterise and quantify normal and pathologic processes within the living organism and can be performed using a range of imaging modalities including MRI, CT and PET. Molecular imaging is a rapidly growing, wide-ranging field of study that has tremendous potential to diagnose diseases at its earliest stages, monitor response to treatment, and allow simultaneous imaging and drug delivery by theranostics. This will also lead to the development of individualised therapies tailored to a patient’s genetic makeup, resulting in improved patient outcomes.

The symposium was opened by Prof Andrew Whittaker, group leader at AIBN and CBNS Chief Investigator. 13 presentations were given in three themes: clinical aspects of PET and MRI; materials and microscopy; and advanced materials for imaging and theranostics. Delegates were also fortunate to receive a tour of the imaging facilities at the Centre of Advanced Imaging, including the radiochemistry labs and the world’s first Bruker ClinScan MR/PET scanner.

One of the highlights of the symposium was a plenary presentation by CBNS Partner Investigator Professor Jason Lewis of the Memorial Sloan Kettering Cancer Center. Professor Lewis reviewed current state-of-the-art molecular imaging agents in the context of precision medicine and companion diagnostics in clinical research. He highlighted the integration of new technologies, such as biomarker microchips, molecular whole body imaging, micro-NMR for cancer diagnosis, and multimodal contrast agents.

**Nanomedicine Conference**

The Australian Centre for Nanomedicine has run the International Nanomedicine Conference annually at Coogee for six years and in the last two years the CBNS has been the co-host.

The conference brings together Australian nanomedicine researchers from medicine, chemistry, engineering and sociology, with international experts. The CBNS Visiting Professor is a fixture at the conference annually, as a plenary speaker. In 2015 Leaf Huang was joined by the other plenary speakers, Prof Tariq Rana (UCSD), Prof Paula Hammond (MIT), Prof Gordon Wallace (Wollongong), and A/Prof Stephen Rose (CSIRO).

In addition to the talks and poster sessions, the conference is a confluence of national expertise and most CBNS researchers attend. There is such a critical mass at the conference that the CBNS Scientific Advisory Board meets during it, with expert input and advice from the plenary speakers each year.

**Nanosafety Workshop**

The CBNS held its first research workshop in Adelaide at the end of April.

Organised by Professor Nico Voelcker, from UniSA, the two-day workshop brought together 68 international experts on aspects of nanosafety: human toxicologists; ecotoxicologists; nanotechnologists; sociologists; regulators; and policymakers. The aim of the workshop was to develop a priority list of issues and the cross-disciplinary collaborations necessary to solve them.
BioBriefing – Seeing is believing

The BioMelbourne Network is a membership based, industry forum representing business leaders in biotechnology, medical technology and innovation industries in Victoria. Their regular BioBriefings provide opportunities for discussion and interaction between network members and researchers.

In October the Australian Synchrotron presented a BioBriefing on advances in imaging technology research and development. The CBNS, along with two other Centres of Excellence at Monash University, outlined next-generation technologies in cellular and whole-body imaging.

Following presentations at the Synchrotron, audience members were able to engage with other network members and the speakers, providing an opportunity for new collaborations.

Portable diagnostics devices – the new world of disease diagnostics

Diagnosing illness and disease can be an expensive and time consuming endeavour. For the patient it is often a painful and invasive procedure. Chemists and engineers are the new innovators in disease identification, developing technologies to improve diagnosis—reducing cost, speeding up the turn-around time for results and allowing for diagnosis ‘on the go’.

In August the CBNS co-hosted with the Convergence Science Network a panel discussion on the current advances in portable devices for diagnosis of diseases. Centre researchers, Dr Simon Corrie and Prof Nico Voelcker spoke about their work in using microneedle arrays for biomarker detection, and smart bandages, respectively. They were joined by Dr Alastair Hodges, Chief Scientist at Universal Biosensors, who develop point-of-care blood glucose monitoring devices. Audience discussion was moderated by Dr Simon Tucker, previously Vice-President of Research at Biota.

The Convergence Science Network in Melbourne was established in 2008 to promote an understanding of convergence science and how it is delivery improved health and well-being. In 2015 the CBNS has been a sponsor of the Network.

Biomedical applications of engineered antibodies and proteins

In November the CBNS co-hosted, with the Australian Institute for Bioengineering and Nanotechnology, a workshop focussed on the latest developments in antibody engineering.

The workshop provided a day of seminars from invited local and international experts focused on key techniques in antibody engineering, cloning and expression, sequence design and mutation, and scale-up. With speakers from medical research institutes (Queensland Brain Institute, Garvan Institute, Baker IDI Heart and Diabetes Institute) and industry (affinity BIO, Minomic, CSL, Avipep) the workshop provided a broad representation of the field. Covering a wide variety of applications—from diagnostic and bioanalytical reagents, imaging and theranostics, to biologic medicines and targeted nanomedicines—the workshop was a success.

Prof Nico Voelcker (UniSA, CBNS), Dr Debra Yin Foo (Phillips Ormonde Fitzpatrick), Dr Simon Corrie (UQ, CBNS), Dr Alastair Hodges (Universal Biosensors). Credit: Convergence Science Network.
Awards and Achievements

In 2015 there have been a number of significant achievements by CBNS researchers, summarised here. A full list of awards to CBNS staff and students is on page 65.

The Victorian Endowment for Science, Knowledge and Innovation, veski, awards the Victoria Prize for Science and Innovation each year. Whilst the Prize recognises a scientific discovery or innovation, or a series of such achievements, work that has a clear potential to produce a commercial or community outcome is highly regarded. Two awards are given annually, one in the physical sciences and the other in the life sciences. In 2015 the Victoria Prize (Physical Sciences) was awarded to Professor Calum Drummond, a member of the CBNS Governance Board. Calum is the Deputy Vice-Chancellor Research and Innovation, and Vice-President, at RMIT and was awarded the prize for his work in molecular assembly and particle and surface interactions in liquids.

Professor Mark Kendall features in the Engineers Australia list of the Top 100 Most Influential Engineers in Australia. This is the second year in a row that Mark has made the list, and his work and achievements place him in the Entrepreneurs and Experts category. Professor Justin Gooding featured for the second time in The Analytical Scientist’s list of Top 100 most influential analytical scientists.

Many of the CBNS Chief and Partner Investigators are members of the Editorial Boards of academic journals. In 2015 Professor Justin Gooding became the inaugural Editor in Chief of the new American Chemical Society journal ACS Sensors. Appropriately, Justin is the leader of the CBNS Sensors and Diagnostics research theme. Justin’s expertise was further recognised in 2015 when he was awarded an ARC Laureate Fellowship, the most prestigious of all ARC fellowships. Justin will expand on his CBNS research through this fellowship, to develop a diagnostic device that can measure single molecules or cells.

CBNS Chief Investigators have featured in a number of Top 100 lists this year—Professor Maria Kavallaris featured in not one, but two. The 100 Women of Influence Awards, sponsored by the Australian Financial Review and Westpac, recognises the contribution women make in Australia and aims to increase the visibility of women in leadership roles. Maria’s work as head of the Tumour biology and targeting program at the CCIA and co-Director of the Australian Centre for Nanomedicine was recognised in the Innovation category.

Maria was also selected as part of the Knowledge Nation 100. This group, selected by the Office of the Chief Scientist and Knowledge Society, are the ‘visionaries, intellects, founders and game changers building the industries and institutions to underwrite Australia’s future prosperity’. Maria was one of the ‘STEM Heroes’ and the Knowledge Nation 100 was featured in The Australian in December.

Professor Maria Kavallaris. Image courtesy of the CCIA
CBNS Awards

Each year the CBNS Scientific Management Group (SMG) awards the Most Significant Publication prize to a CBNS researcher. When determining the winner the SMG consider:

- the quality and importance of the research;
- the impact of the journal;
- the involvement of multiple Chief Investigators and nodes, indicating collaboration across the CBNS; and
- whether the nominated CBNS author of the paper is the lead author on the paper (rather than a contributor).

The inaugural Most Significant CBNS Publication award was presented to Dr. Jiwei Cui and Dr. Rob De Rose from the University of Melbourne, for their paper Engineering Poly(ethylene glycol) Particles for Improved Biodistribution, published in ACS Nano (DOI: 10.1021/nn5061578). Jiwei and Rob were joint first authors on this publication and were presented with the award at the annual CBNS Research Workshop in December. The research is presented in more detail in the Vaccines section of this report but fits equally well within the Delivery Systems research theme. This multi-theme research, and the involvement of two CBNS research groups (those of Frank Caruso and Stephen Kent), is an indication of the collaboration that is enabled through a large and long-term activity like the CBNS.

Other CBNS awards that are presented annually at the Research Workshop are for the best presentation and best poster of the workshop.

Anna Gemmell (UQ PhD student) won the Best Poster award for her work Investigating the role of micelle size for enhanced tumour delivery (above).

Dr. Nick Ariotti (UQ) received the Best Presentation of the Workshop award, for his work 3View scanning electron microscopy for the three dimensional imaging of cells and animals.

Congratulations to the winners but also to the shortlisted applications. The Senior Management Group had much discussion in reaching their decision.

Dr. Jiwei Cui and Rob De Rose being presented with their award by CBNS Director, Prof Tom Davis.
Outreach and Education

In addition to running research events, such as CBNS workshops and symposia, and holding outreach events, such as the Convergence Science Network Diagnostic device panel, the CBNS runs a program of education and training events for CBNS students and staff.

The CBNS Education Committee, established in the second half of 2015, coordinates the program and is composed of a postgraduate and postdoctoral representative from each node. Meeting monthly by teleconference the Committee discuss and coordinate their own ideas for the education and training needs of CBNS members, as well as ideas that have been contributed by their node colleagues. To fully canvass the education and training needs of CBNS staff and students a forum was held at the CBNS Annual Research Workshop in Lorne.

The CBNS held two education events in 2015. The first was a briefing by the Science Media Centre on how scientific researchers can build their media profile. Following the session, there was an increase in the number of CBNS expert profiles on the SMC site Scimex, the portal for science news in Australia and New Zealand. Scimex provides journalists with early access to embargoed science news stories, with controlled access to subject matter experts.

The second event, a workshop on social media for researchers called The Connected Academic, was aimed at CBNS researchers at all levels. It covered how researchers can build a profile on ResearchGate, LinkedIn and Twitter as well as how to increase citations using these platforms. In a world where an active social media presence can increase citations, understanding and effectively using social media is key. Workshop participants utilised their new-found skills at the Annual Research Workshop, tweeting with the hashtag #CBNSWorkshop. The connections formed via Twitter provide a further opportunity for collaboration and information sharing between CBNS members.

Illustrator training for scientific drawing

CBNS researchers are keen to effectively communicate their research in journal publications, posters and more broadly. Diagrams such as the one at right which shows nanoparticle formation, absorption into a cell and degradation, for instance, help explain the processes that are occurring at the nanoscale.

This year the CBNS strategic fund was used to run training sessions in Adobe Illustrator, a common editor for generating these types of images. (See pages 41-43 for other activities funded through the fund.) The training was developed specifically for CBNS staff and students by a professional designer who also delivered the courses. In 2015 the courses were held at Monash, and the universities of South Australia and Melbourne. In 2016 the training will be continued at the Universities of Queensland and New South Wales.

Through the two-day course, CBNS staff and students have learned to use basic tools in Illustrator, how to draw scientific schemes such as nanoparticle assembly, internalisation and trafficking. They have also developed libraries of common objects, for example polymers and particles, for re-use.

The training has gone very well, with one postdoc saying:

“Illustrator for Scientists: the most fruitful workshop I’ve been to”.

Illustration: Laura Selby, Monash CBNS PhD student
External Engagement

CBNS researchers have a range of collaborations with organisations in the health and medical sectors as well as industry and commercial organisations. These relationships are typically led by one of the CBNS Chief Investigators, and link with hospitals and medical research institutes, as well as Australian and international biotech experts. The collaborations provide an opportunity for bio-nano research to be informed by end user needs and to be translated by external partners into product development, application and use.

Industry and commercial engagement

Current collaborations between CBNS researchers and industry and commercial partners cover a wide range of activities in the bio-nano space. In areas such as biosensors and drug delivery CBNS researchers are engaging with local, national and international companies. These collaborations are in some cases just beginning and in others are long-standing relationships. In all cases CBNS researchers are working to translate knowledge generated in universities into products and other applied solutions.

Melbourne biotech company Starpharma has a long history of collaboration with CBNS researchers, Professors Chris Porter and Ben Boyd, and investigators at Monash University including Dr Lisa Kaminskas to explore dendrimers as improved drug delivery systems. The DEP™ delivery platform that emerged from this collaboration is now in Phase 1 clinical trial and in 2015 formed the basis of a significant licensing deal between Starpharma and the multinational Pharmaceutical company AstraZeneca to apply the DEP platform to the Astra Zeneca oncology drug pipeline.

By collaborating with the health and medical sector CBNS researchers can see the application of their research in a working environment and get vital feedback that further informs their research.

Industry and commercial engagement

The Australian Research Council supports industry research collaborations through the Linkage program of grants. Over the years CBNS researchers have received Linkage funding and in 2015 two projects were awarded to CBNS Chief Investigators: Professor Justin Gooding (UNSW) has received ARC Linkage funding for his collaboration with AgaMatrix to develop a biosensor for detecting short sequences of RNA, microRNA (miRNA) in blood. Changes in the levels of some miRNA sequences can serve as a biomarker for many diseases including cancers. If successful, the expected outcome of the collaboration is a commercialisable biosensor for miRNA both as a diagnostic early detection device and a prognostic device for a range of miRNA biomarkers.

Associate Professor Kris Thurecht (UQ) is collaborating with Australian company Minomic International to use MIL38, a novel antibody, as a testbed for development of hybrid biomolecules and nanomaterials for commercial diagnostic devices. The platform under development needs to be stable under physiological conditions and enable conjugation of nanomaterials with biologics. If successful it would lead to more efficient synthesis of targeted diagnostics and a significant commercial advantage for related nanomaterials.

Health and medical sector engagement

By collaborating with the health and medical sector CBNS researchers can see the application of their research in a working environment and get vital feedback that further informs their research.

Professor Edmund Crampin (University of Melbourne) is collaborating with clinicians at the Royal Children’s Hospital and the Murdoch Children’s Research Institute to undertake mathematical modelling of age-related differences in blood clotting in neonates and children. This work will inform quality of care for sick children and strategies for prevention of thrombosis in children and adults.

Also at the University of Melbourne, but collaborating much further afield is Professor Stephen Kent. Stephen is working with the National AIDS Research Institute of India and the International AIDS Vaccine Initiative to develop improved measurements of HIV immunity across different population groups. The work is funded by an Australian-India Strategic Research Fund award from the Department of Industry, Innovation and Science.

Some engagements with the health sector are enabled through funding from the NHMRC, ARC or the organisations themselves. In the case of Professor Nico Voelcker’s work with the Women’s and Children’s Hospital in Adelaide funding is provided by the Cell Therapy Manufacturing Cooperative Research Centre (CTMCRC). Associate Professor Simon Barry, from the hospital’s Gastroenterology Department, is working with Nico to develop scaffolds for regulatory T cell expansion. Regulatory T cell infusion is being used as a cell therapy in place of immunosuppression to prevent transplant rejection in organ and bone marrow transplants. The project will develop a set of functionalised surfaces and devices that allow for the rapid isolation and scalable expansion of human regulatory T cells for human therapy. Cells expanded in the CTMCRC’s GMP facility will be investigated in human clinical trials for the prevention of rejection associated with bone marrow transplants.

CBNS Intellectual Property and Commercialisation

The CBNS has an IP & Commercialisation Committee (IPCC) to provide advice for IP management to CBNS Chief Investigators as needed. The CBNS IP & Commercialisation Policy informs how the CBNS manages IP and commercialisation. The CBNS does not own intellectual property resulting from CBNS activities. Rather, the project IP is owned by the organisation or individual making the major inventive contribution, although the CBNS maintains an IP register. The Scientific Advisory Board provide advice to the CBNS on commercialisation strategy and licensing opportunities.
Governance
Governance and Management

The CBNS Governance Board has an independent advisory role to the Centre Director, Executive and Management Committee, providing guidance on governance, strategy and stakeholder engagement. The Scientific Advisory Board provides strategic scientific insight and commercial direction to the Centre.

The CBNS Executive meets regularly to discuss the research program and operational matters, referring items to the Management Committee for ultimate decision-making about the structure of the research program and Centre finances.

Governance Board

Members of the CBNS Governance Board are all research leaders and governance experts in scientific, research-based organisations. The Board monitors progress towards delivery of Key Performance Indicators and approves research, operational and financial plans. The Governance Board met twice in 2015: 23 June; and 25 November.

Professor Peter C Doherty AC FAA FRS

Chair

Professor Doherty shared the 1996 Nobel Medicine Prize for discovering the nature of the cellular immune defence. Based at the University of Melbourne and also spending part of his year at St. Jude Children's Research Hospital, Memphis, he continues to be involved in research directed at understanding and preventing the severe consequences of influenza virus infection. In addition, he goes in to bat for evidence-based reality, relating to areas as diverse as childhood vaccination, global hunger and anthropogenic climate change. In an effort to communicate more broadly, he has published four 'lay' books, and has another in progress.
Dr Tong is currently CEO of the Cancer Therapeutics Cooperative Research Centre headquartered in Melbourne. In 2013 he led the CRC through a successful extension application receiving another six years of funding until 2020. Formerly a director of Primcare Medical Ltd (NZ) and MedInnovate Ltd (UK) he is currently a member of the Advisory Board for Cortex Health. He has spent more than 20 years in executive management in drug development and commercial roles in both the major pharmaceutical and biotech industry. After graduating as Senior Scholar in Medicine from Auckland University and working in General Practice in London, he moved to New Zealand and subsequently worked in Singapore and London, in regional and global business development and commercial roles for Glaxo. Prior to coming to Melbourne Warwick spent five years in Boston as SVP, Development, for Surface Logix Inc.

Professor Gordon Wallace FAA FTSE FIOP FRACI

Professor Wallace is currently the Executive Research Director at the ARC Centre of Excellence for Electromaterials Science and Director of the Intelligent Polymer Research Institute. He is Director of the ANFF Materials node. He previously held an ARC Federation Fellowship and currently holds an ARC Laureate Fellowship.

Professor Wallace is an elected Fellow at the Australian Academy of Science, the Australian Academy of Technological Sciences and Engineering, the Institute of Physics (UK) and the Royal Australian Chemical Institute. In addition to being named NSW Scientist of the Year in the chemistry category in 2008, he was also appointed to the Korean World Class University System, and received the Royal Australian Chemical Institute HG Smith Prize. In 2004, Professor Wallace received the Royal Australian Chemical Institute Stokes Medal for research in Electrochemistry, after being awarded an ETS Walton Fellowship by Science Foundation Ireland in 2003. The Royal Australian Chemical Institute awarded him the Inaugural Polymer Science and Technology Award in 1992.
Internationally renowned for the co-creation of the technology for the cervical cancer vaccines, Professor Frazer began his career as a renal physician and clinical immunologist in Edinburgh, Scotland before emigrating in 1981 to Melbourne, Australia. He continued his clinical training and pursued studies in viral immunology and autoimmunity at the Walter and Eliza Hall Institute of Medical Research with Professor Ian Mackay. In 1985, Professor Frazer accepted a teaching post with The University of Queensland and was appointed Director of The University of Queensland Diamantina Institute in 1991. In early 2011, Professor Frazer commenced as CEO of the Translational Research Institute. He retains an active research program at the Institute in immune responses to cancer and cancer immunotherapy. Professor Frazer was awarded the 2005 CSIRO Eureka Prize for Leadership in Science and was selected as Queenslander of the Year, and Australian of the Year in 2006. He was also awarded the 2008 Prime Minister’s Prize for Science, the 2008 Balzan Prize for Preventive Medicine, the 2009 Honda Prize and in 2011, was elected as a Fellow of the esteemed Royal Society of London. In 2012, Professor Frazer was appointed a Companion of the Order of Australia (AC) in the Queen’s Birthday Honours.

CBNS Scientific Advisory Board

The Scientific Advisory Board (SAB) has an independent mentoring and advisory role to the Scientific Management Group, providing strategic insight and commercial direction to the Centre. The SAB plays a key role in advising the Centre on the development of the strategic and commercialisation plans. The Board advises on patent versus publication strategy, and commercialisation and spin-out strategy, as required. They assist in identifying intellectual property partnering and licensing opportunities and organisations with which the CBNS can ally.

In addition to the core members of the SAB, there are temporary international members, including the CBNS Visiting Professor, who provide variation to the scientific mix of the SAB.

Professor Ian Frazer  AC  Chair
Internationally renowned for the co-creation of the technology for the cervical cancer vaccines, Professor Frazer began his career as a renal physician and clinical immunologist in Edinburgh, Scotland before emigrating in 1981 to Melbourne, Australia. He continued his clinical training and pursued studies in viral immunology and autoimmunity at the Walter and Eliza Hall Institute of Medical Research with Professor Ian Mackay. In 1985, Professor Frazer accepted a teaching post with The University of Queensland and was appointed Director of The University of Queensland Diamantina Institute in 1991. In early 2011, Professor Frazer commenced as CEO of the Translational Research Institute. He retains an active research program at the Institute in immune responses to cancer and cancer immunotherapy. Professor Frazer was awarded the 2005 CSIRO Eureka Prize for Leadership in Science and was selected as Queenslander of the Year, and Australian of the Year in 2006. He was also awarded the 2008 Prime Minister’s Prize for Science, the 2008 Balzan Prize for Preventive Medicine, the 2009 Honda Prize and in 2011, was elected as a Fellow of the esteemed Royal Society of London. In 2012, Professor Frazer was appointed a Companion of the Order of Australia (AC) in the Queen’s Birthday Honours.

Peter French  BSc  MSc  MBA  PhD  FRSM
Dr French is currently an Executive Director of BCAL Diagnostics, an Australian company developing a novel blood-based screening test for breast cancer. He is a Past President of the Australia and New Zealand Society for Cell and Developmental Biology and served as a member of the Board of the International Society of Differentiation from 1998-2014. He served as CEO and Managing Director of ASX- and NASDAQ-listed gene therapy company Benitec Biopharma Limited from June 2010 to December 2015. He is an Adjunct Senior Lecturer at UNSW and an Honorary Fellow at Macquarie University.

Dr French is a cell and molecular biologist who has extensive experience in both basic and clinical medical research and biotechnology. His research areas of expertise include cell biology, immunology, infectious disease, neurobiology, oncology and gene therapy. He was awarded a PhD for elucidating the molecular composition of keratin proteins in the developing hair follicle. Following a postdoctoral position studying neuronal development he was appointed Principal Scientific Officer in the Centre for Immunology, St Vincent’s Hospital Sydney. Whilst at St Vincent’s, he completed a MBA in Technology Management.

Dr Sridhar Iyengar  PhD
Dr Iyengar is a founder and director of Misfit Wearables, makers of highly wearable computing products, including the award-winning Shine, an elegant activity monitor. Dr Iyengar also founded and served as CTO of AgaMatrix, a blood glucose monitoring company that made the world’s first hardware medical device to connect directly to the iPhone, winning both the Red Dot and the GOOD Design Awards. He built AgaMatrix from a two-person start-up to shipping 15+ FDA-cleared medical device products, 3B+ biosensors, 3M+ glucose meters for diabetics, with partnerships with Apple, Sanofi, and Walgreens. Dr Iyengar holds over 20 US and international patents and received his PhD from Cambridge University as a Marshall Scholar.

Dr David Owen  BSc (Hons)  PhD
Dr Owen is the Vice President of Research at Starpharma and has extensive experience in medicinal chemistry and biochemistry, and in managing teams focused on commercially directed drug discovery. He has held several positions in the biotech industry including Mimotopes, Cerylid and Glykoz and gathered extensive international experience in biotechnology and pharmaceutical research and development. Since joining Starpharma Dr Owen has driven the drug delivery programs by developing and executing a number of successful proof-of-concept studies. The results from these studies have led to a number of commercial partnerships such as Stiebel a GSK company, Lilly and AstraZeneca, as well as driving Starpharma’s own internal drug delivery program focused on an improved dendrimer-docetaxel formulation.
Dr Leanna Read FTSE FAICD

Dr Leanna Read is the Chief Scientist for South Australia and chairs the South Australian Science Council. She is a renowned biotechnology expert and brings a wealth of executive, board and investment experience in technology-based businesses. In addition to her role as Chief Scientist, Leanna chairs the Cooperative Research Centre for Cell Therapy Manufacturing and is a member of the SA Economic Development Board and the Council for the University of South Australia. Prior roles included CEO of the Cooperative Research Centre for Tissue Growth and Repair and the founding managing director of Adelaide biotechnology company, TGR BioSciences Pty Ltd. She has received a number of awards, including an Honorary Doctorate from the University of South Australia, the 2006 South Australian of the Year (Science and Technology) and the 2011 Central Region winner of the Ernst & Young Entrepreneur of the Year in the Technology Category.

2015 temporary members

Professor Leaf Huang

Professor Huang received his PhD in Biophysics at Michigan State University. He was previously at the University of Tennessee, Knoxville (1976–1991) and at the University of Pittsburgh (1991–2005) as a faculty member. In July 2005, he was appointed Fred Eshelman Distinguished Professor and Chair, Division of Molecular Pharmaceutics at UNC Eshelman School of Pharmacy. He has published over 320 peer-reviewed articles, over 120 invited reviews/book chapters, and has co-edited two books. The Laboratory of Drug Targeting has been working on liposomes and immunoliposomes for drug delivery. Current activities are focused in the development of non-viral vectors for gene (including siRNA) therapy, and receptor mediated drug and vaccine targeting using self-assembled nanoparticles. The technologies are tested for therapy of cancer and liver diseases in animal models.

Professor Paula Hammond

Professor Hammond is the David H. Koch Professor in Engineering at MIT. She received her SB in Chemical Engineering from MIT in 1984, her MS from Georgia Tech in 1988, and earned her PhD from MIT in 1993. In 1994, she was awarded the NSF Postdoctoral Fellowship in Chemistry while performing postdoctoral research in the Harvard University Chemistry Department as a member of the Whitesides research group. In 2000, she was awarded the Junior Bose Faculty Award, and the GenCorp Signature University Award. She has also received the NSF Career Award, the EPA Early Career Award, the DuPont Young Faculty Award, and the 3M Innovation Fund Award. Recently, The Harvard Foundation presented Professor Hammond the 2010 Scientist of the Year Award as part of its annual Albert Einstein Science Conference: Advancing Minorities and Women in Science, Engineering, and Mathematics. Also, Professor Hammond was one of a group of key faculty members involved in starting the Institute for Soldier Nanotechnologies.

Professor Tariq Rana

Professor Rana received his PhD from the University of California at Davis and he was an American Cancer Society fellow at the University of California at Berkeley. He is a recipient of numerous awards including a Research Career Award from the National Institutes of Health in 1996. Professor Rana has advised a number of biotechnology companies and has served as a member of several Scientific Advisory Boards. He was a Professor of Biochemistry and Molecular Pharmacology and founding Director of the Program in Chemical Biology at the University of Massachusetts Medical School, Worcester, Massachusetts, prior to joining the Sanford–Burnham Medical Research Institute in 2008. He held Sanford–Burnham Professorship and served as the founding director for the RNA Biology Program from 2008 to 2014. Currently, he is a Professor of Pediatrics and V/C for Innovation in Therapeutics at the University of California San Diego School of Medicine, where his laboratory studies RNA regulation of development and disease.
Performance and KPIs

The CBNS achievements are evaluated by the Australian Research Council on an annual basis with a formal review in the third year (2017). CBNS performance is assessed against key performance indicators that were set at the commencement of the Centre. These cover the traditional research metrics of outputs like journal publications, and conference presentations. There are also metrics that cover the interdisciplinarity of CBNS research, new research partnerships, measures of esteem, public awareness and student and ECR mentoring.

The CBNS is progressing well and has reached almost all of the targets for 2015. Of particular note is the number of publications in high-impact journals. We achieved more than 20 publications in journals with an impact factor greater than 10. This is more than four times greater than the target for the year. We are also very pleased about the media coverage of CBNS research, demonstrating that the work is of interest and more importantly, relevance, to the wider public.

The KPIs for 2015 are summarised in this infographic. It shows the targets for each of the KPI areas, as well as our actual achievements.

Number of research outputs:

- Journal publications:
  - Target: 40
  - Actual: 200

- Patents (filed):
  - Target: 0
  - Actual: 1

- Books:
  - Target: 0
  - Actual: 9

- Books (chapters):
  - Target: 0
  - Actual: 1

- Patents (filed):
  - Target: 0
  - Actual: 2

- Publications in journals with impact factors >2:
  - Target: 5
  - Actual: 25

Quality of research outputs:

- Publications in journals with impact factors >10:
  - Target: 20
  - Actual: 45

- Publications in journals with impact factors >2:
  - Target: 50%
  - Actual: 92%

Number of operational interdisciplinary research projects:

- Target: 2
- Actual: 4

Number of invited talks / papers / keynote lectures at major international meetings (incl. those held in Australia):

- Target: 20
- Actual: 45

Number of new research fellowships:

- Target: 1
- Actual: 5

Membership on editorial boards:

- Target: 4
- Actual: 49
<table>
<thead>
<tr>
<th>Category</th>
<th>Target</th>
<th>Actual</th>
</tr>
</thead>
<tbody>
<tr>
<td>Media releases</td>
<td>6</td>
<td>18</td>
</tr>
<tr>
<td>Number of professional training courses attended</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>Number of attendees at professional training courses offered by the CBNS</td>
<td>15</td>
<td>56</td>
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<tr>
<td>Number of international visitors and visiting fellows</td>
<td>12</td>
<td>52</td>
</tr>
<tr>
<td>Number of professional training courses attended</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>New postgraduate students (PhD and Masters) working on core CBNS research</td>
<td>6</td>
<td>26</td>
</tr>
<tr>
<td>New honours students working on core CBNS research</td>
<td>10</td>
<td>17</td>
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<tr>
<td>Number of early career researchers* working on core CBNS research</td>
<td>10</td>
<td>31</td>
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<tr>
<td>New postdoctoral researchers working on core CBNS research</td>
<td>8</td>
<td>13</td>
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<tr>
<td>Number of postgraduate completions</td>
<td>6</td>
<td>12</td>
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<tr>
<td>New students mentored</td>
<td>20</td>
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<tr>
<td>New postdoctoral researchers working on core CBNS research</td>
<td>20</td>
<td>205</td>
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<tr>
<td>Number of government, industry and business community briefings</td>
<td>4</td>
<td>17</td>
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<tr>
<td>Number of overseas laboratories and facilities</td>
<td>30</td>
<td>44</td>
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<tr>
<td>Number of website hits</td>
<td>15,000</td>
<td>45,963</td>
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<tr>
<td>Number of talks given by CBNS staff open to the public</td>
<td>5</td>
<td>5</td>
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<tr>
<td>Number of new organisations collaborating within the CBNS</td>
<td>5</td>
<td>28</td>
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</tbody>
</table>

*ECR = within 5 years of completing PhD
## Financial Report 2015

### Income and Expenditure

<table>
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<tr>
<th>Income</th>
<th>2015 ($)</th>
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</thead>
<tbody>
<tr>
<td>ARC grant income</td>
<td>3,899,882</td>
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<tr>
<td>Collaborating organisation contribution</td>
<td>1,287,321</td>
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<tr>
<td><strong>Total income</strong></td>
<td><strong>5,187,203</strong></td>
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<table>
<thead>
<tr>
<th>Expenditure</th>
<th>2015 ($)</th>
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<tbody>
<tr>
<td>Salaries</td>
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<tr>
<td>Equipment</td>
<td>326,226</td>
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<td>Consumables and maintenance</td>
<td>715,107</td>
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<tr>
<td>Travel*</td>
<td>260,178</td>
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<tr>
<td>Scholarships and student support</td>
<td>218,297</td>
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<tr>
<td>Administration</td>
<td>38,677</td>
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<tr>
<td>Other #</td>
<td>109,490</td>
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<tr>
<td><strong>Total expenditure</strong></td>
<td><strong>5,083,157</strong></td>
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<tr>
<td><strong>Carry forward</strong></td>
<td><strong>4,137,448</strong></td>
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<tr>
<td><strong>Balance</strong></td>
<td><strong>4,241,494</strong></td>
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</table>

* includes accommodation and conference expenses
*# includes media consultant, website development, training courses

### In-kind contributions

<table>
<thead>
<tr>
<th>Institution</th>
<th>2015 ($)</th>
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<tbody>
<tr>
<td>Monash University</td>
<td>974,960</td>
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<tr>
<td>University of Melbourne</td>
<td>1,085,939</td>
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<tr>
<td>University of New South Wales</td>
<td>783,564</td>
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<td>University of Queensland</td>
<td>531,623</td>
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<td>University of South Australia</td>
<td>285,447</td>
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<td>Australian Synchrotron</td>
<td>422,400</td>
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<td>Australian Nuclear Science and Technology Organisation</td>
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<tr>
<td>Sungkyunkwan University</td>
<td>46,000</td>
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<tr>
<td>University of Warwick</td>
<td>NA*</td>
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<td>University of Nottingham</td>
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<tr>
<td>Imperial College London</td>
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<tr>
<td>Memorial Sloan Kettering Cancer Center</td>
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<td>University College Dublin</td>
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<tr>
<td>University of Wisconsin-Madison</td>
<td>NA*</td>
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<tr>
<td>University of California, Santa Barbara</td>
<td>26,000</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>3,324,579</strong></td>
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*these in-kind contributions were not available at the time of printing
Awards, Honours and Memberships

CBNS Governance
Board member

Professor Calum Drummond
2015 Victoria Prize (Physical Sciences) – Molecular assembly and chemistry

CBNS Chief Investigators & Staff

Dr Nick Ariotti
Best presentation, CBNS Research Workshop

Professor Frank Caruso
Melbourne Laureate Professor
Executive Member, ARC SRC Particulate Fluids Processing Research Centre
13th Professor J.W. McBain Memorial Lecture

Dr Anna Cifuentes-Rius
NHMRC Peter Doherty ECR Fellowship

Dr Jiwei Cui
Honourable Mention for Oral Presentation by an Early Career Researcher at the 6th International Nanomedicine Conference
Most significant CBNS publication of 2015 (joint with Dr Robert de Rose)

Dr Robert De Rose
Most significant CBNS publication of 2015 (joint with Dr Jiwei Cui)

Professor Justin Gooding
ARC Laureate Fellowship
Appointed Inaugural Editor-in-Chief, of the American Chemical Society journal, ACS Sensors
Top 100 Most Influential Analytical Scientists worldwide for 2015 – the Analytical Scientist

Professor Maria Kavallaris
The Australian Financial Review and Westpac’s 100 Women of Influence 2015
Knowledge Nation 100 – “Australia’s top 100 visionaries, intellects, founders and game changers who help shape the country’s future prosperity”
Appointed to NHMRC Research Committee (2015-2018)
NHMRC Research Fellowship Peer Review Panel, 2015
Chair, Australian Institute of Policy & Science
Judge, Australian Museum Eureka Awards 2015
Australian Society for Medical Research, Research Fund Executive Committee
Member of the Migration and Invasion Section of the Tumor Biology Subcommittee of the 2016 Program Committee, American Association Cancer Research

Professor Mark Kendall
Top 100 Most Influential Engineers 2015, Engineers Australia
Invotech and Vaxxas named recipients of the 2015 Good Design Award for development of the Nanopatch Jet Coating Instrument for needle-free drug delivery
Queensland State Government Innovation Ambassador award
World Economic Forum Technology Pioneer Award

Dr Adam Martin
NHMRC-ARC Dementia Research Development Fellowship

Professor Chris Porter
Thomson Reuters Highly Cited Researcher 2015

Dr Roya Tavallaie
Best poster award at the 6th International Nanomedicine Conference

Associate Professor Pall Thordarson
ARC College of Experts

Associate Professor Kris Thurecht
RACI Polymer Division Sangster Polymer Science and Technology Achievement Award

Professor Nico Voelcker
South Australian Scientist of the year (Finalist)
Australian Innovation Challenge (Finalist)
ARC College of Experts

Professor Andrew Whittaker
Chinese Academy of Sciences President’s International Fellowship (Visiting Scientist)
Director of the Brisbane node of “Wuhan/Brisbane Research Alliance in Functional Polymeric Materials”

CBNS Students

Mr Nicolas Alcaraz
Rideal Travel Bursary Winner

Ms Angela Babi
Andrew McCamley Prize for an outstanding 4th Year Research Project

Mr Mattias Björnholm
Best Student Presenter at the 6th Australia and New Zealand Nano-Microfluidics Symposium

Ms Qiong Dai
Best Oral Presentation by a PhD Student at the 6th International Nanomedicine Conference

Mr Lars Esser
PolymerVic 2015 Best Poster presentation

Ms Anna Gemmell
Best poster, CBNS Research Workshop

Mr Joshua Glass
Major Bartlett Travel Scholarship, University of Melbourne

Mr Joshua Glass
Best poster award at the 6th International Nanomedicine Conference

Ms Amelia Parker
Selected to attend 65th Lindau Nobel Laureate Meeting

Ms Emily Pilkington
PolymerVic 2015 Best Poster presentation
CBNS Personnel

Chief Investigators

Professor Tom Davis
ARC Australian Laureate Fellow
CBNS Director
Delivery Systems, Imaging Technologies
Monash University

Professor Andrew Whittaker
ARC Australian Professorial Fellow
Imaging Technologies Theme Leader
University of Queensland

Dr Angus Johnston
ARC Future Fellow
Monash University Node Leader
(from October 2015)
Delivery Systems, Vaccines
Monash University

Professor Frank Caruso
ARC Australian Laureate Fellow
CBNS Deputy Director
University of Melbourne CBNS
Node Leader
Delivery Systems, Imaging Technologies, Vaccines
University of Melbourne

Professor Edmund Crampin
Systems Biology and Computational Modelling Leader
Delivery Systems
University of Melbourne

Professor Benjamin Boyd
ARC Future Fellow
Delivery Systems, Sensors and Diagnostics, Vaccines
Monash University

Associate Professor Matthew Kearnes
ARC Future Fellow
Social Dimensions of Bio-Nano Science and Technology Leader
University of New South Wales

Professor Mark Kendall
University of Queensland CBNS Node Leader
Vaccines
University of Queensland

Professor Nigel Bunnett
Delivery Systems
Monash University

Professor Maria Kavallaris
Delivery Systems, Sensors and Diagnostics
University of New South Wales

Professor Thomas Nann
ARC Future Fellow
Imaging Technologies
University of South Australia CBNS Node Leader
Delivery Systems, Sensors and Diagnostics
University of South Australia

Professor Nicolas Voelcker
University of South Australia
Professor Nann became the Director of the MacDiarmid Institute, New Zealand

Professor Rob Parton
Delivery Systems, Vaccines
University of Queensland
Partner Investigators

**Associate Professor Pall Thordarson**
ARC Future Fellow
Delivery Systems, Imaging Technologies
University of New South Wales

**Associate Professor Kristofer Thurecht**
ARC Future Fellow
Delivery Systems, Imaging Technologies, Vaccines
University of Queensland

**Dr Simon Corrie**
ARC DECRA Fellow
Sensors and Diagnostics
University of Queensland

**Dr John McGhee**
Visualisation
University of New South Wales

**Dr Beatriz Prieto-Simón**
Sensors and Diagnostics
University of South Australia
(Joining the CBNS following Professor Nann’s departure from UniSA)

**Professor Nicholas Abbott**
John T. and Magdalen L. Sobota Professor, Hilldale Professor, and Director, Materials Research and Engineering Center, Chemical and Biological Engineering
University of Wisconsin, Madison

**Professor Cameron Alexander**
Head of Division of Drug Delivery and Tissue Engineering, Faculty of Science
University of Nottingham, UK

**Professor Kenneth Dawson**
Director of the Centre for BioNano Interactions, Chair of Physical Chemistry
University College Dublin, Ireland

**Professor Craig Hawker**
Director of the California Nanosystems Institute, Dow Materials Institute, Co-Director of the Materials Research Lab
University of California, Santa Barbara, USA

**Professor Doo Sung Lee**
Director Theranostic Macromolecules Research Center, Dean of College of Engineering
Sungkyunkwan University, South Korea

**Professor Jason Lewis**
Vice Chair for Research, Chief of the Radiochemistry and Imaging Sciences Service
Memorial Sloan Kettering Cancer Center, USA

**Professor Molly Stevens**
Research Director for Biomedical Material Sciences, Institute of Biomedical Engineering
Imperial College London, UK

**Dr Ivan Greguric**
Head of Radiochemistry
Australian Nuclear Science and Technology Organisation, Australia

**Professor David Haddleton**
Head of Inorganic and Materials Section, Department of Chemistry
University of Warwick, UK
Research Staff

Postdoctoral and other Research Staff

Dr Maria Alba-Martin
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Dr Sheilajen (Vinca) Alcantara
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University of Melbourne

Dr Nicholas Ariotti
Research Officer
University of Queensland

Dr Abbas Barfidokht
Postdoctoral Researcher – ECR
University of New South Wales

Dr Michele Bastiani
Research Officer
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Dr Nadja Bertleff-Zieschang
Postdoctoral Researcher
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Dr Thomas Blin
Research Fellow
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Dr Julia Braunger
Postdoctoral Researcher
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Dr Meribell Canals
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Dr Xiaoyu Cheng
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Dr Kylooon Chua
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Dr Anna Cifuentes-Rius
Research Associate
University of South Australia

Dr Jacob Coffey
Postdoctoral Researcher
University of Queensland

Dr Christina Cortez-Jugo
Research Fellow
Monash University

Dr Michael Crichton
Postdoctoral Researcher – ECR
University of Queensland

Dr Jiwei Cui
Postdoctoral Researcher
University of Melbourne

Dr Joseph Cursons
Postdoctoral Researcher
University of Melbourne

Dr Yunlu Dai
Postdoctoral Researcher
University of Melbourne

Dr Robert De Rose
Postdoctoral Researcher
University of Melbourne

Dr Alexandra Depelsenaire
Postdoctoral Researcher
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Dr Melissa Dewi
Research Associate
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Dr Germain Fernando
Senior Research Fellow
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Dr Adrian Fuchs
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Dr Yi Guo
Postdoctoral Researcher
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Dr Keying Guo
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Dr Bakul Gupta
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Dr Pu Chun Ke
Senior Research Fellow
Monash University

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Postdoctoral Researcher
University of Melbourne

Dr Declan Kuch
Postdoctoral Researcher
University of New South Wales

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Dr Adam Martin
Postdoctoral Researcher
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Dr Joshua McCarroll
Project Leader
Children’s Cancer Institute Australia

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Mr Jin Zhang  
Research Assistant  
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Students

PhD Students

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Ian Cartmell  
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Ao Chen  
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Jiang (Johnson) Cheng  
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University of South Australia

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Swahnnya de Almedia
University of New South Wales

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Katelyn Gause
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Anna Gemmell
University of Queensland

Joshua Glass
University of Melbourne

Stephen Goodall
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James Grace
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Felicity Han
University of Queensland

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Tomoya Suma
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Jonathan Wei  
University of Queensland

Alessia Weiss  
University of Melbourne

Jonathan Wojciechowski  
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Adelene Wong  
Monash University

Chin (Ken) Wong  
University of New South Wales

Yanfang Wu  
University of New South Wales

Ken Yong  
Monash University

Sul Hwa Yu  
Monash University

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Cheng Zhang  
University of Queensland

Jing Zhang  
University of Queensland

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Manchen Zhao  
University of New South Wales

Jiang Zhen  
University of Queensland

Kelly Zong  
University of New South Wales

Masters Students
Luka Donje  
University of New South Wales
Beck Hodgetts  
Monash University
Nachnicha Kongkatigumjorn  
Monash University
Martin van Koeverden  
University of Melbourne

Honours Students
Tara Albarez  
Monash University
Jessica Casey  
Monash University
Jessie Crowe  
Monash University
Jason De la Harpe  
Monash University
Eric Du  
University of New South Wales
Hilary Huynh  
University of New South Wales
May Lai  
Monash University
Andrea Leong  
Monash University
Kellie May  
Monash University
Duyen Nguyen  
University of New South Wales
Zachary Schuurs  
University of Queensland

Benjamin Sebastian  
Monash University
Estafania Tchung  
Monash University
Ann Huu Tran-doan  
Monash University
Juan (Paula) Wang  
University of South Australia
Nicholas Westra van Holthe  
University of Queensland
Mareeha Zaki  
Monash University

Administration
Ms Gaby Bright  
Centre Manager, Chief Operations Officer  
(On maternity leave until June 2015)  
Monash University
Dr Julia Cianci  
Operations Manager  
(Until June 2015)  
Monash University
Mr Marc Reimer  
Centre Node Coordinator  
University of Melbourne
Ms Andrea Clare  
Academic Services Officer  
University of South Australia
Ms Anne Ewing  
Senior Research Administrator  
(Until September 2015)  
University of Queensland
Ms Katrina Sewell  
Centre Administrator  
Monash University
Visitors to the CBNS

The CBNS has hosted a diverse range of visitors from academia and industry during 2015. CBNS visitors have presented seminars and met with research staff and students to establish collaborations and to investigate potential commercialisation opportunities. The Centre has also hosted students visiting from institutes within Australia and around the world.

The following presents a list of academic, industry and student visitors to one or more of the five Australian University nodes of the CBNS during 2015.

Academic and Industry Visitors

Professor Nick Abbott  
University of Wisconsin-Madison, USA

Associate Professor Stefania Baldusdottir  
Department of Pharmacy, Copenhagen University, Denmark

Professor Vipul Bansal  
RMIT University

Professor Thomas Bein  
University of Munich, Germany

Dr David Cheng  
Wesley Research Institute

Dr Pavel Cherepanov  
University of Bayreuth, Germany

Professor I-Ming Chu  
National Tsinghua University, Taiwan

Professor Mark Dawson  
Peter MacCallum Cancer Centre

Professor Alison Downard  
University of Canterbury, New Zealand

Associate Professor Chris Fellows  
University of New England

Professor Ian Frazer  
University of Queensland

Dr Jess Frith  
Monash University

Dr Manisha Ghate  
National AIDS Research Institute, India

Professor Andy Giraud  
Murdoch Childrens Research Institute

Dr Ernawati A Giri-Rachman  
Bandung Institute, Indonesia

Dr Vinicius Goncalves  
University of Sao Paulo, Brazil

Professor Christoph Hagemeier  
Baker IDI Heart and Diabetes Institute

Professor Paula Hammond  
Massachusetts Institute of Technology, USA

Dr Philippe Hapiot  
University of Renne, France

Associate Professor Michael Higgins  
University of Wollongong

Associate Professor Benjamin Hogan  
University of Queensland

Professor Leaf Huang  
Division of Molecular Pharmaceutics in the Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, USA

Assistant Professor Sanyog Jain  
National Institute of Pharmaceutical Education & Research, India

Professor Lei Jiang  
Institute of Chemistry, Chinese Academy of Sciences, China

Dr Tobias Kraus  
Liebig Institute for New Materials, Germany

Professor David Lewis  
Flinders University

Dr Paul Lai  
Chang Gung Hospital, Taiwan

Professor Zhibo Li  
Chinese Academy of Sciences, China

Professor Lluis Marsal  
University Rovira I Virgili, Spain

Dr Tetsuyuki Maruyama and team  
Takeda Pharmaceutical Company, Japan

Professor Helmuth Möhwald  
Max Planck Institute for Colloids and Interfaces, Germany

Professor Nancy Monteiro-Riviere  
Kansas State University, USA

Professor Simon Moulton  
Swinburne University of Technology

Associate Professor Takashi Nakakuki  
Kyushu Institute of Technology, Japan

Professor Yvonne Perrie  
Aston University, UK

Professor Thomas Preiss  
Australian National University

Professor Addy Pross  
Ben Gurion University of the Negev, Israel

Dr Heni Rachmawati  
Bandung Institute, Indonesia

Professor Tariq Rana  
University of California San Diego School of Medicine, USA

Associate Professor Glen Reid  
Asbestos Disease Research Institute, University of Sydney

Professor Jim E. Riviere  
Kansas State University, USA

Professor Pam Russell  
Translational Research Institute

Dr Ashwini Shete  
National AIDS Research Institute, India

Dr Madhuri Thakar  
National AIDS Research Institute, India
Professor Jean Paul Thiery  
National University of Singapore

Professor Patrick Unwin  
University of Warwick, UK

Professor Stephen Vanner  
Department of Medicine, Queen’s University, Canada

Dr Majid Ebrahimi Warkiani  
University of NSW

Professor Linda Williams  
University of Aberdeen, UK

Professor Alpha Yap  
The University of Queensland

Professor Heather Young  
University of Melbourne

Professor Yanlei Yu  
Fudan University, China

Student Visitors

Altunzeli Altangerel  
National University of Mongolia  
Ulaanbaatar, Mongolia

Ms Stella Aslanoglou  
University of Crete, Greece

Ms Yasmin Assan  
University of Bath, UK

Mr Gwan-Hyun Choi  
Sungkyunkwan University, Korea

Mr Ignacio Insua Lopez  
University of Birmingham, UK

Ms Stella Koestner  
Reutlingen University, Germany

Ms Simone Kweidor  
Reutlingen University, Germany

Mr Edmund Lock  
Nanyang Polytechnic, Singapore

Padmavarthy  
Institute of Microbial Technology, Chandigarh, India

Mr Ryan Price  
University of Southern California, USA

Ms Jiaying Song  
Fudan University, China

Ms Ester Sporleder  
Fudan University, China

Ms Ruidie Tang  
Fudan University, China

Mr Sanahan Vijayakumar  
McGill University, Canada

Ms Pi Wang  
Zhejiang University, China

Ms Danyu Xia  
Zhejiang University, China

Ms Yunti Zhang  
Wuhan University, China
Publications

Books and/or book chapters
Rizwan, S.B; Boyd, B.J. Cubosomes: Structure, Preparation and Use as an Antigen Delivery System, Subunit Vaccine Delivery, 7, 125-140, 2015

Journal articles
Al-Shereiqi, A. S.; Boyd, B. J.; Saito, K. Photo-responsive self-assemblies based on bio-inspired DNA-base containing bolaamphiphiles. Chemical Communications 2015, 51, 25460-25462
Fuchs, A. V.; Gemmell, A.; Thurecht, K. J. Utilising polymers to understand diseases: advanced molecular imaging agents. Polymer Chemistry. 2015, 6, 868-880.


Ge, X.; Ke, P. C.; Davis, T. P.; Ding, F. A Thermodynamics Model for the Emergence of a Stripe-like Binary SAM on a Nanoparticle Surface. Small. 2015, 11, 37, 4894-4899.


Gooneratne, S. L.; Center, R. J.; Kent, S. J.; Parsons, M. S. Functional advantage of educated KIR2DL1+ natural killer cells for anti-HIV-1 antibody-dependent activation. Clinical and Experimental Immunology. 2015.


Hasanazadeh, Kafshgari, Morteza; Alnahki, M; Delalat, Bahman; Apostolou, S; Harding, Frances Jane; Makila, E; Salonen, Jarno; Kuss, B; Voelcker, N; Small interfering RNA delivery by polyethylenimine-functionalised porous silicon nanoparticles. Biomaterials Science 2015, 3, 12, 1555-1565.


Hong, L; Salentign, S; Hawley, A; Boyd, B. J. Understanding the Mechanism of Enzyme-Induced Formation of Lyotropic Liquid Crystalline Nanoparticles. Langmuir 2015, 31, 24, 6933-6941.

Howe, E. N. W.; Ball, G. E.; Thordarson, P. Step-by-step DFT analysis of the cooperativity in the binding of cations and anions to a tetratopic ion-pairing host Supramolecular Chemistry 2015, 27, 829-839.


Hu, J.; Whitaker, M. R.; Li, Y.; Quinn, J. F.; Davis, T. P. The use of endogenous gaseous molecules (NO and CO2) to regulate the self-assembly of a dual-responsive triblock copolymer. Polymer Chemistry 2015, 6, 13, 2407-2415.


Molecular insights for targeting protein–coupled receptor–transient
P.; McIntyre, P.; Bunnett, N. W. The g
Veldhuis, N. A.; Poole, D. P.; Poole, D.
Journal of Physical Chemistry C
2015, 6, 20, 3865-3874.
Veldhuis, N. A.; Poole, D. P.; Poole, D. P.; McIntyre, P.; Bunnett, N. W. The g protein–coupled receptor–transient receptor potential channel axis: Molecular insights for targeting disorders of sensation and inflammation. Pharmacological Reviews 2015, 67, 1, 36-73.