AIBN Master Projects | Prof. Kris Thurecht

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Project-1: Development of novel theranostics

Lead Investigators: Prof. Kris Thurecht, Dr Nick Fletcher, Dr Craig Bell and Dr Pie Huda

The field of nanomedicine has revolutionised modern medicine. One area of nanomedicine where this holds particular import is theranostics; this is where materials are tailored to provide a diagnostic response to targeted drug delivery *in vivo*. In theranostics, utilising the advantages of multiple molecular imaging modalities within a single device is key to understanding the therapeutic benefit of the agent, where the release of the drug and the subsequent effect on a particular disease state can be directly observed. The development of novel theranostics requires advances in both fundamental science (physics, chemistry and biology), as well as the applied sciences (nanotechnology, (pre)clinical imaging) and this research program builds upon developing a fundamental understanding of how material properties affects function of the theranostic, and then translating the device into preclinical and clinical models. This project includes aspects of materials/biologics development, biological assessment and imaging in cell and mouse models.

Project-2: Smart polymer membranes for separation of high value proteins

Lead Investigators: Prof. Kris Thurecht, Dr Craig Bell, Dr Pie Huda

The aim of this project is to develop next generation membrane technology for separation of high value proteins from serum. The project looks to explore how both physical properties (e.g. porosity) and molecular capture (e.g. using antibodies) can increase the selectivity and sensitivity of the membranes. The project will involve aspects of chemistry and bioengineering and is in collaboration with Aegros International, and Australian biotechnology company.

Project-3: Preclinical evaluation of 18F- and 11C-PET probes for imaging neuroinflammation

Lead Investigators: Dr Muneer Ahmad, Prof. Kris Thurecht

Imaging of brain cannabinoid 2 receptors (CB_2) receptors with PET has a promising role in identifying neuropathological changes. Upregulation of CB2 expression is predominantly observed in activated microglia in brain and hence it has great potential in diagnosis and treatment follow-up of neurodegenerative disorders such as Alzheimer's, Parkinson's and Huntington's disease, multiple sclerosis and amyotrophic lateral sclerosis, in which overexpression of CB_2 receptors has been documented.

Non-invasive *in vivo* imaging of cannabinoid CB_2 receptors using PET-MR will be pursued to study neuroinflammation. The purpose of this study is to evaluate the brain penetrance, *in vivo* binding

specificity of novel ^{18}F- and ^{11}C-PET ligands having picomolar affinity towards *h*CB2. Advanced radiochemistry methodology, high resolution autoradiography, and neuroinflammatory animal models with overexpression of CB_2 receptors will be used. This study will be done in collaboration with Centre for Brain Research, School of Medical Sciences, University of Auckland.

Project-4: Aptamer-targeted radiotherapeutic nanomedicines for breast cancer

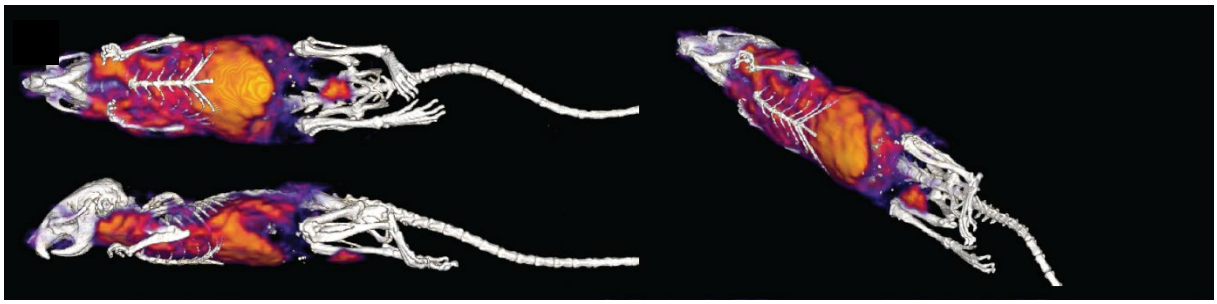
Lead Investigators: Dr Nick Fletcher, Prof. Kris Thurecht

Nanomedicine is the use of nanomaterials in medical approaches and offers the opportunity for a step-change in cancer treatment and diagnosis. Nanomedicines can be loaded with therapeutics such as chemotherapy and radiotherapies, and then targeted to selectively deliver their payload to the tumour site. This provides both enhanced efficacy as well as reduced side effects to the rest of the body by providing site specific delivery.

One promising approach to enhance nanomedicine therapeutic efficacy is to include a targeting agent, such as an antibody or other ligand for a disease specific marker, to increase accumulation at the tumour site. Recent work in our group has demonstrated the use of an oligonucleotide aptamer as a targeting ligand for polymeric nanomedicines to improve tumour localization in breast cancer (Figure).

This current project now aims to further expand on this by developing a radiotherapeutic nanomedicine platform able to be functionalized with oligonucleotide aptamer for selective delivery of therapy to the tumour site. This work will involve polymerization and modification of polymeric nanomedicines materials and will then utilize cutting edge preclinical molecular imaging available through the Centre for Advanced Imaging to determine behaviours in the body.

The project would be well suited to a student with some background in chemistry and analytical techniques, with experience in in vitro assays and animal handling experience beneficial.



Fletcher et al. **Chem. Commun.**, 2018,**54**, 11538-11541

Project-5: Development of Degradable Hyperbranched Polymers for Tuning of the Biological Clearance Half-life

Lead Investigators: Dr Craig Bell and Prof. Kristofer Thurecht

Hyperbranched polymeric nanomedicines allow for a non-invasive way to diagnose and track disease. However, these constructs are typically derived from synthetic monomers, which are inherently non-degradable and so rely on the body's natural clearance mechanisms for complete removal. However, polymers obtained by radical ring-opening polymerisation (rROP) of cyclic ketene acetals (CKAs) allow for the construction of degradable vinyl polymers as they can be copolymerised with commercially available synthetic vinyl monomers, and the incorporation of degradable ester units into the polymer backbone allows for enzymatic and hydrolytic degradation. This project aims to develop a series of

synthetic hyperbranched polymers of PEG methacrylate that also incorporates 5,6-benzyl-2-methylene-1,3-dioxepane (BMDO), a CKA that can be copolymerised with methacrylates using RAFT polymerisation chemistry. The level of incorporation of BMDO will allow for tuning of the degradation rate *in vivo*, thereby modulating the biological clearance half-life of these constructs and expediting the natural clearance of these constructs.

Contact the project advisor directly to discuss the project and arrange a meeting or AIBN Events (aibn.events@uq.edu.au) to arrange a visit to the AIBN lab.

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