



Medicinal Chemistry and Chemical Biology Symposium

Online Symposium hosted by the
RACI Medicinal Chemistry and Chemical Biology Division

Tuesday 17th November 2026

3:00 - 5:00 pm (Vic, NSW, Tas, ACT) AEDT 2:00 - 4:00 pm (Qld) AEST

2:30 – 4:30 pm (SA) ACDT 1:30 – 3:30 pm (NT) ACST

12 noon – 2:00 pm (WA) AWST

Chair: Dr Shane Hickey

Program

Keynote: Dr Andrea North CSIRO

Invited:

Dr Angus Muller Monash University

Anne Sophie Braun Griffith University

Dr Luke Darveniza SAHMRI

Imesha Hettige Monash University

Dr Kayla Williams University of Sydney

Free registration

Registration closes on Monday 16th November 2026

Bioconjugation at CSIRO

Andrea North

CSIRO Clayton, Victoria

Abstract

This presentation will provide an overview of conjugation and targeted drug-delivery projects undertaken by CSIRO's Biotherapeutics Program, including antibody-drug conjugate (ADC) synthesis and design campaigns, and the development and characterisation of polymer-, nanoparticle-, peptide-, and nucleotide-based delivery systems, with a focus on advancing complex therapeutic products from early-stage research towards clinical trial readiness.

Biography

Dr Andrea North leads the Bioconjugation Team within CSIRO's Chemical Biology and Botanicals Group. She combines a great passion for synthetic chemistry and protein science, with expertise in analytical and process development to progress new biotherapeutic products in the bioconjugation space.



Towards the development of selective LIMK degraders for the treatment of pathological actin dynamic dysfunction

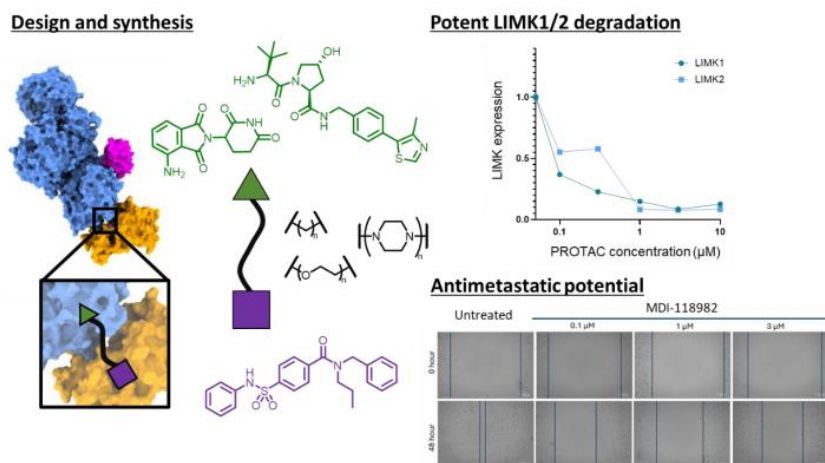
Angus Muller^a, Alex Baldwin^b, Simon Ward^b, Christopher Hyland^a

^a School of Science, University of Wollongong, NSW, Australia

^b Medicines Discovery Institute, Cardiff University, Wales, United Kingdom

Abstract

Abnormal regulation of actin remodelling has been identified as a key driving force in both neurological and oncological disorders, being particularly prevalent in various metastatic cancers.¹ A common mediator of this dysfunction is the hyperactivity of LIM kinases (LIMKs) which manifests as altered cell morphology and increased propensity for invasion and migration. Despite significant work investigating LIMK inhibitors, identification of an effective antagonist remains elusive.² Application of targeted protein degrader technology to LIMK represents a promising strategy to utilise this target where traditional inhibition has proven ineffective.³ This presentation will describe the design, synthesis and analysis cycle of selective LIMK degraders over multiple generations. A click-reaction-based synthetic strategy has been developed to efficiently prepare a diverse series of degraders containing a highly selective allosteric LIMK ligand. The lead compound potently impedes migration and invasion in metastatic breast cancer through selective LIMK knockdown. Promising results from early biochemical characterisation of the candidate supports the in vivo assessment of both the DMPK profile and efficacy against metastatic disease.



1. Villalonga et al. Cells, 2023, 12(5), 805
2. Berabez et al. Cells, 2022, 11(13), 2090
3. Békés et al. Nat Rev Drug Discov, 2022, 21, 181-200

Biography

Angus completed his PhD at the University of Wollongong, where his research focused on developing PROTACs to address cytoskeletal dysfunction in metastatic cancer. He has since joined MedChem Australia and the Australian Translational Medicinal Chemistry Facility at MIPS, where he works across multiple drug discovery projects with a focus on translating research towards commercialisation.



Development of Novel Solid-Phase Synthesis for Nucleoside Mono-, Di- and Triphosphates and their Use to Detect DNA Replication in Plasmodium Parasites

Anne-Sophie C. Braun, David H. Hilko, Katherine T. Andrews, Sally-Ann Poulsen

Institute for Biomedicine and Glycomics, Griffith University, Nathan, QLD, Australia

Abstract

Analogues of the endogenous nucleoside thymidine are widely used as metabolic chemical probes to investigate DNA replication and dissect features of the cell cycle or other cellular processes. Plasmodium, the parasite that causes malaria, lacks the enzyme thymidine kinase needed for the incorporation of current thymidine-based chemical probes into its DNA. To address these limitations, we designed, synthesised and validated next-generation chemical probes based on the 5-vinyl-2'-deoxyuridine monophosphate (VdU-P1) scaffold in Plasmodium. The VdU-based probes enable the detection of labelled parasites via a catalyst-free inverse-electron-demand Diels-Alder (IEDDA) click-reaction with a fluorescent tetrazine dye and was compatible in live-cell DNA labelling and imaging, reported by us recently.¹ To provide malaria researchers with new and better tools to study the cell cycle and growth of Plasmodium, we designed VdU-based probes that enter the thymidine metabolism pathway further downstream than VdU-P1, skipping other kinases that are potential metabolic roadblocks. The synthesis of nucleoside di- and triphosphate probes using known methods is challenging due to very low product yields, complex mixtures of reaction byproducts, and the highly polar nature of the desired compounds, making purification difficult and laborious.² To address the limitations of current methods we have developed a novel solid-phase synthesis. Yields are high and the synthetic approach is compatible with sensitive functional groups, leading to clean reactions and uncomplicated purification (Figure 1). I will describe this new synthesis approach and the application of mono-, di- and triphosphates of VdU to study DNA synthesis in wild type *P. falciparum* parasites.

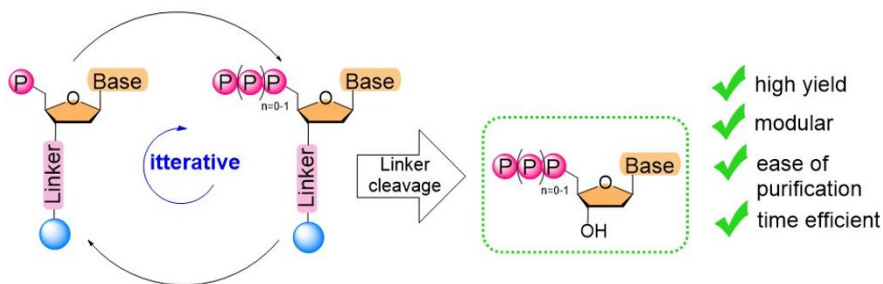


Fig. 1: New solid-phase synthesis method for nucleoside di- and triphosphate chemical probes.

- [1] Braun, A.-S. C.; Fisher, G. M.; Hilko, D. H.; Macdonald, J. R.; Thomas, S.; Andrews, K. T.; Poulsen, S.-A. Vinyl-DNA Detect Probes to Assess DNA Proliferation in Plasmodium Parasites using Inverse-Electron-Demand Diels-Alder Click Reactions. ACS Chem. Biol. 2025.
- [2] Roy, B.; Depaix, A.; Périgaud, C.; Peyrottes, S. Recent Trends in Nucleotide Synthesis. Chem. Rev. 2016, 116 (14), 7854.

Biography

Anne-Sophie completed her Bachelor's and Master's degree in Chemistry at the University of Freiburg, Germany, with a major in organic chemistry. Anne-Sophie is currently a third-year PhD candidate at Griffith University working in the field of Chemical Biology. Anne-Sophie's research focuses on developing novel synthetic chemistry methods for the synthesis of modified nucleoside analogues and using these compounds to visualise DNA proliferation in *Plasmodium* parasites.



Development of hY1R Specific Peptide-Drug Conjugates for the Treatment of Metastatic Breast Cancer

Luke Darveniza^{a,b,d}, Brett Paterson^c, Annette Beck-Sickinger^b, Kellie Tuck^a

^a School of Chemistry, Monash University, VIC, Australia

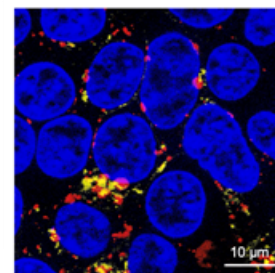
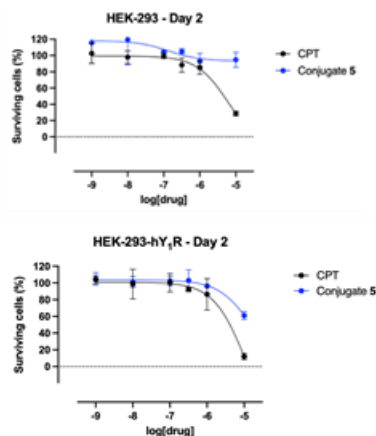
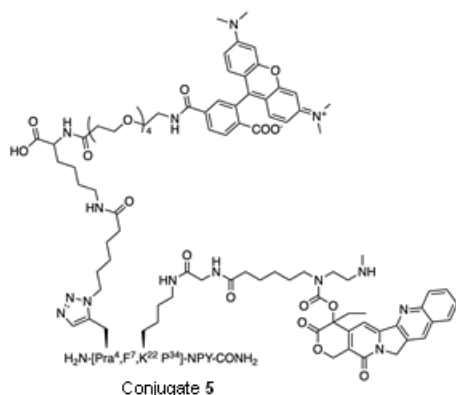
^b Institute of Biochemistry, Leipzig University, Saxony, Germany

^c Centre of Advanced Imaging, University of Queensland, QLD, Australia

^d Molecular Imaging and Therapy Research Unit, SAHMRI, SA, Australia

Abstract

Breast cancer accounts for over 15% of cancer mortalities in women, and late-stage metastatic breast cancer is currently considered incurable. Peptide-drug conjugates (PDCs) have emerged as a promising way of targeting specific disease sites in the body, and the neuropeptide Y analogue [F⁷, P³⁴] NPY has been found to selectively target the human Y1 receptor which is overexpressed in 100% of breast cancer metastases. Camptothecin is a small molecule drug that can be used as a payload for inducing cancer-cell apoptosis but is hampered by unfavourable drug properties and damaging off-target effects. It was hypothesised that binding the active site of camptothecin to a PDC via a self-immolative linker would increase drug solubility and decrease off target effects. This presentation will describe the design, synthesis and in-vitro testing of a lead candidate PDC, which displayed selective binding, rapid internalisation and pronounced cell death in hY1R-expressing breast cancer cells. Variants of this lead will also be discussed that were bound to diagnostic and therapeutic radionuclides, showing versatility of the PDC beyond pure chemotherapeutic applications.



Biography

Dr. Luke Darveniza was the first doctoral candidate to complete a joint PhD between Monash University and Leipzig University (Germany), focused on developing peptide-drug conjugates for the treatment of metastatic breast cancer. He currently works as a post-doctoral fellow in the Molecular Imaging and Therapy Research Unit of SAHMRI, specialising in the development of novel radiopharmaceuticals for the detection and treatment of disease.



Developing new chemical tools to understand the biology of fatty acid binding protein 4

Imesha Hettige, Jason Pun, Kieren McDowell, Menachem Gunzburg, Naureen Akhtar, Indu Chandrashekar, Gautham Balaji, Luke Adams, Bishwa Subedi, Olga Ilyichova, Chris Porter, Bonan Liu, Michelle Halls, Bradley Doak, Ben Capuano and Martin Scanlon

Monash Institute of Pharmaceutical Sciences, Monash University, Parkville 3052, Australia

Abstract

Fatty acid-binding proteins (FABPs) are a family of small, soluble proteins involved in diverse physiological processes, including lipid transport and cellular signalling. FABPs have been implicated in diseases associated with disrupted lipid metabolism. Among them, FABP4 is highly expressed in adipocytes and macrophages. Genetic studies have shown that loss of FABP4 function can ameliorate metabolic and inflammatory conditions such as diabetes and atherosclerosis, highlighting FABP4 as a potential therapeutic target. Despite this, the molecular mechanisms through which FABP4 contributes to these disease pathways are still not well understood. Existing high-affinity FABP4 ligands often suffer from poor physicochemical properties, including excessive lipophilicity, limited aqueous solubility and non-specific binding, restricting their utility as chemical probes.

This research focuses on the development of selective, high-affinity FABP4 ligands with improved drug-like properties using an integrated fragment- and structure-based drug discovery approach. Fragment screening identified promising chemical starting points, which were subsequently optimised through iterative compound design and synthesis, incorporating microscale parallel chemistry. Binding kinetics were assessed using off-rate screening by surface plasmon resonance (SPR), enabling rapid prioritisation of promising compounds for further investigation. Prioritised compounds were resynthesised and further characterised using complementary biophysical and structural techniques, including SPR, isothermal titration calorimetry, NMR spectroscopy and X-ray crystallography, to validate binding and guide optimisation. This approach led to the identification of several ligands with improved binding affinity, including submicromolar binders. Selected ligands were also evaluated in cellular assays as an initial assessment of their activity in a cellular context. Overall, this work has generated diverse FABP4 ligand series, including compounds with improved binding affinity and selectivity, and provides a foundation for the continued development of chemical tools to investigate FABP4 biology.

Biography

Imesha Hettige obtained a BSc (Honours) in Chemistry at the University of Sri Jayewardenepura and a Graduateship in Chemistry at the Institute of Chemistry Ceylon, Sri Lanka. In 2022, she commenced her PhD in Medicinal Chemistry at the Monash Institute of Pharmaceutical Sciences (MIPS), Monash University, under the supervision of Prof. Martin Scanlon, A/Prof. Ben Capuano and Dr Indu Chandrashekar. Her research focuses on developing new chemical tools to investigate the biology of fatty acid-binding protein 4 (FABP4), integrating fragment- and structure-based drug design, medicinal chemistry and biophysical approaches. Her work has been recognised through several poster presentation awards, including a Best Poster Prize at the 2025 EFMC International Symposium on Advances in Synthetic and Medicinal Chemistry in Porto, Portugal, which featured over 440 poster presentations, and Best Poster Presentation at Fragment-Based Drug Discovery Down Under 2024.



Selective Antiplatelet Action Through Targeted Covalent Inhibition of Pyk2 at a Paralog-Specific Cysteine

Kayla Williams

University of Sydney

Abstract

Platelet-driven thrombosis underlies major cardiovascular disorders including ischemic stroke and myocardial infarction.¹ Although antiplatelet agents are widely used to prevent thrombus formation, their clinical utility is often limited by an increased risk of bleeding. The non-receptor tyrosine kinase Pyk2 (FAK2) has emerged as an attractive therapeutic target because genetic and pharmacological studies suggest that inhibition of Pyk2 suppresses thrombosis while largely preserving physiological haemostasis.^{2,3} However, the development of selective Pyk2 inhibitors has been hindered by the high degree of homology shared with its paralogue, FAK1.⁴

Here, we report the structure-guided development of the first covalent Pyk2 inhibitor that exploits a unique cysteine residue (Cys545) located adjacent to the ATP-binding pocket and absent in FAK1. Starting from the reversible inhibitor PF-4594755, we incorporated electrophilic warheads and rationally designed linker architectures to enable selective covalent engagement of Cys545. Screening of a focused library identified compound 2-1 as a potent lead, with intracellular target engagement confirmed using washout-based NanoBRET assays. Mutation of Cys545 abolished irreversible inhibition, validating the proposed covalent mechanism. Chemoproteomic profiling using an alkyne-tagged analogue further demonstrated excellent target selectivity across the cellular proteome.

Functionally, compound 2-1 produced sustained inhibition of platelet activation, strongly suppressing thromboxane-dependent aggregation while having only modest effects on ADP- and thrombin-mediated responses. The compound reduced thrombus formation under physiologically relevant arterial and venous flow conditions and significantly enhanced recombinant tissue plasminogen activator-mediated thrombolysis in a murine thrombosis model without increasing bleeding. These findings establish Cys545 as a tractable paralog-selective cysteine for covalent kinase inhibitor design and highlight targeted covalent inhibition of Pyk2 as a promising strategy for the development of next-generation antithrombotic therapies with improved safety profiles.

[1] M. Koupoukova, et al, "Thrombosis and Platelets: An Update", *Eur. Heart J.* 2017, 38, 785-791.

[2] I. Canobbio, et al, "Impaired Thrombin-Induced Platelet Activation and Thrombus Formation in Mice Lacking the Ca²⁺-Dependent Tyrosine Kinase Pyk2", *Blood* 2013, 121, 648-657.

[3] G. F. Guidetti, et al, "Focal Adhesion Kinases in Platelet Function and Thrombosis", *Arterioscler. Thromb. Vasc. Biol.* 2019, 39, 857-868.

[4] C. A. Lipinski, et al, "Differential Role of Proline-Rich Tyrosine Kinase 2 and Focal Adhesion Kinase in Determining Glioblastoma Migration and Proliferation", *Mol. Cancer Res.* 2003, 1, 323-332.

Biography

Dr Kayla Williams, is an Associate Lecturer in the School of Pharmacy at the University of Sydney. She completed her PhD in Chemistry under the supervision of Dr Xuyu Liu, where her research focused on precision medicine approaches for the modulation of a variety of target proteins. Her research lies at the interface of medicinal chemistry and chemical biology, with particular interests in the design of selective small-molecule modulators, covalent inhibitors, and targeted protein degradation strategies, including PROTACs. Her work aims to develop innovative therapeutic approaches to better understand and selectively manipulate disease-relevant proteins. In addition to her research, Kayla teaches medicinal chemistry and pharmaceutical sciences at the University of Sydney.

