UCC Future Pharmaceuticals

Research Showcase 2025

December 5th 2025

Showcase Booklet

(containing all posters)

UCC Future Pharmaceuticals
Research Showcase 2025

UCC
Coláiste na hOllscoile Corcaigh
University College Cork, Ireland

UCCFUTURES
Pharmaceuticals
Securing **Our Future** through Research Excellence.

Programme and Oral Presentations

9:00 - 9:25 Registration

9:25 - 9:40 Welcome addresses

Vice President for Research and Innovation (Prof. John Cryan)

Head of the College of Science, Engineering and Food Science (Prof. Sarah Culloty)

Director of UCC Future Pharmaceuticals (Prof. Anita Maguire)

9:40 - 10:10 Plenary guest speaker: Ireland's Pharma Future: Innovation, Disruption, and Opportunity; Phillip Gammell, ISPE Ireland President

10:10 - 10:25 Inés Có Rives: Induction of influenza-specific immunity in pigs using dissolvable microneedle patches to deliver an adenovirus-based vaccine

10:25 - 10:40 Fiona Kinsella: Using Flow and Mechanochemical Technology in the Synthesis of α-Sulfenyl-β-Chloroenones

10:40 - 11:30 Poster session 1

11:30 - 12:00 Plenary guest speaker: Formulation Challenges and Enabling Approaches for Poorly Water-Soluble Drugs; Anne-Marie Healy, Trinity College Dublin

12:00 - 12:15 Ilaria Neri Smarter and Greener: Transforming Chromatographic Method Development Through Prediction

12:15 - 12:30 Fatima Ballout: AI-Driven Supervisory Control and Digital Twin Framework for Smarter Bioreactor Systems

12:30 - 13:30 Poster session 2

13:30 - 13:45 Khaled ElKassas: Silica Powders as Novel Excipients for Biopharmaceutical Stability: Drying and Storage

13:45 - 14:00 John O'Sullivan: How Digitalisation of Product Platforms Leads to Organisational Change: Towards a Conceptual Framework for Product Platforms in Manufacturing Automation

14:00 - 14:15 Doireann Ní Chonaill: Taste and Smell Changes and Quality of Life among Ambulatory Cancer Patients Receiving Systemic Treatment.

14:15 - 14:30 Sean Walsh: Artificial Intelligence and Machine Learning Data Trends of Agarose Hydrogel Properties

14:30 - 14:45 Poster session 3

14:45 - 15:00 Awards and closing

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Welcoming addresses

Prof. Jorge Oliveira
Head of School of Engineering and Architecture (host)

Prof. John Cryan
Vice President for Research and Innovation

Prof. Sarah Culloty
Head of College of Science, Engineering and Food Science

Prof. Anita Maguire
Director of Future Pharmaceuticals
Head of School of Chemistry

Audience (71 registered participants)

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Oral Presentations

Phillip Gammell (*President of the Irish Affiliate of the International Society for Pharmaceutical Engineering)*

Prof. Anne-Marie Healy (*Trinity College, Dublin)*

Speakers (*Left to right: Jorge Oliveira, Doireann Ní Chonaill, Sean Walsh, Inés Có Rives, Ilaria Neri, Fatima Ballout, Fiona Kinsella, John O'Sullivan, Khaled ElKassas, Anne-Marie Healy, Anita Maguire)*

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Awards

Top prize for an oral presentation: Khaled ElKassas

Left to right: Saba Loftus (Head of Development, College of SEFS);
Prof. Anita Maguire (Director of Future Pharmaceuticals);
Aileen Kelly-O'Sullivan (Qualcomm);
Khaled ElKassas (Awardee, School of Pharmacy);
Jorge Oliveira (Host)

Runner-up for an oral presentation:Doireann Ní Chonaill

Left to right: Saba Loftus (Head of Development, College of SEFS);
Prof. Anita Maguire (Director of Future Pharmaceuticals);
Aileen Kelly-O'Sullivan (Qualcomm);
Doireann Ní Chonaill (Awardee, School of Food and Nutritional Sciences);
Jorge Oliveira (Host)

Top prize for a poster: Rachel Lapeyre

Left to right: Saba Loftus (Head of Development, College of SEFS);
Prof. Anita Maguire (Director of Future Pharmaceuticals);
Aileen Kelly-O'Sullivan (Qualcomm);
Rachel Lapeyre (Awardee, School of Biochemistry and Cell Biology);
Jorge Oliveira (Host)

Qualcomm

Awards supported by Qualcomm Inc.

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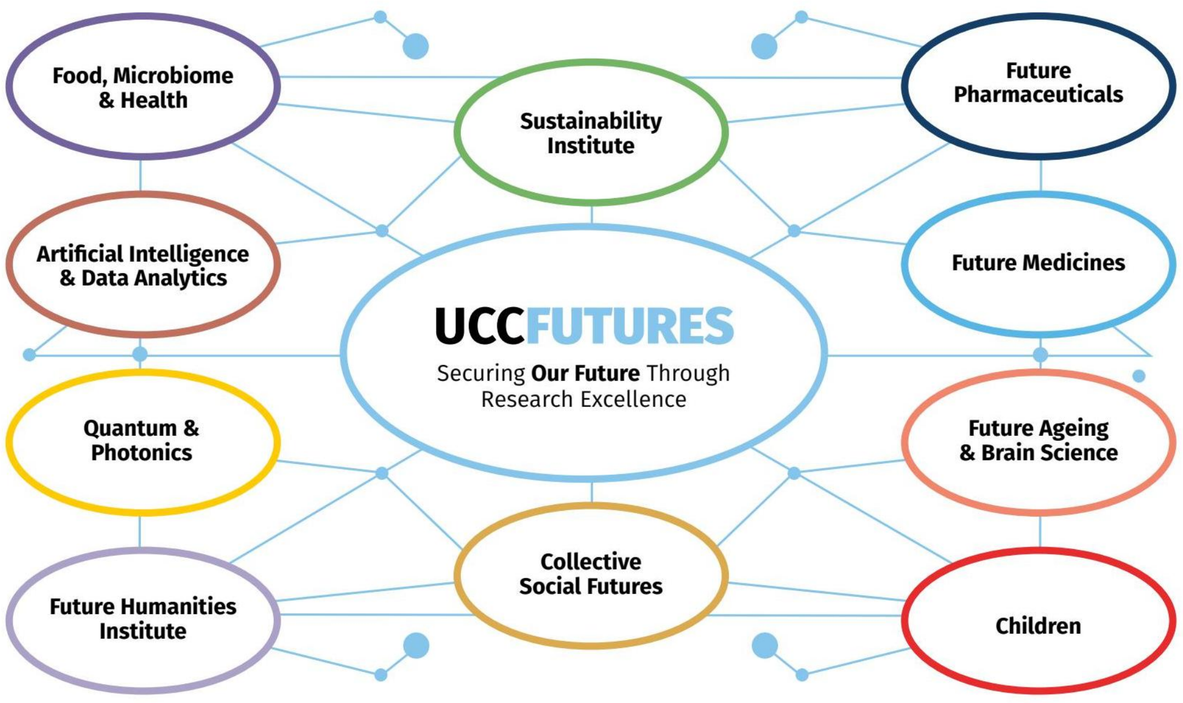
Posters

1	George Merrin	The coding potential of long non-coding RNAs in breast cancer
2	Inés Có Rives	Induction of influenza-specific immunity in pigs using dissolvable microneedle patches to deliver an adenovirus-based vaccine
3	Stephen O'Shea	Distinguishing insulin and insulin-like growth factor 1 receptors: Implications for drug design and selectivity
4	Rebecca O'Keeffe	Asymmetric C-H Insertions with Novel α-Diazosulfonates
5	Victoria McTigue Fennell	Decarboxylative carbon-carbon bond forming reactions using photochemistry in continuous flow
6	Ben O'Donoghue	Time-Resolved IR Spectroscopy for Evaluation of Phosphine Coligand Effects on the Ultrafast Behaviour of Mn(I) Precatalysts
7	Devansh Shah	Development of a Non-Porous Protein-A Silica Column for Rapid Quantification of Monoclonal Antibodies
8	Fiona Kinsella	Using Flow and Mechanochemical Technology in the Synthesis of α-Sulfenyl-β-Chloroenones
9	Geoffrey Stosse	Enantioselective Hayashi-Miyaura-type reactions on N–H containing compounds
10	Gian Reber	Accessing P-stereogenic molecules via stereoselective elimination
11	Ilaria Neri	Smarter and Greener: Transforming Chromatographic Method Development Through Prediction
12	Dr Eimear Courtney	31P NMR as a Fast Tool for Chiral Recognition of Phosphorus Compounds
13	Barry Lynch	Solubility of Gefitinib in Organic Solvents: Experimental and Theoretical Investigation of Stable and Metastable Forms
14	Chengbin Tang	Quality by design to approach spay freeze drying technology to food and pharmaceutical applications
15	Fatima Ballout	AI-Driven Supervisory Control and Digital Twin Framework for Smarter Bioreactor Systems
16	Muhamad Nabeel Haider	Sustainable Biogas Upgrading: Coupling carbon capture and valorisation of algal biomass for the pharma/biopharma sector
17	Sashank Bharatham Vijayaraghavan	Template-Assisted Crystallisation of Antisense Oligonucleotides: A Solubility-Guided Approach for Sustainable Purification
18	Yiran Wang	A Sheet-Based Contact-Aided Compliant Force-Limiting Mechanism for microneedle Patches
19	Ayse Kont	Quality by Design Approach to Medical Device Polymer Bead Process Optimisation
20	Khaled ElKassas	Silica Powders as Novel Excipients for Biopharmaceutical Stability: Drying and Storage
21	Mohamed Elkhashab	Probing the Stability of Drugs Formulated as Glassy Microneedles Structures Post Sterilisation
22	John O'Sullivan	How Digitalisation of Product Platforms Leads to Organisational Change: Towards a Conceptual Framework for Product Platforms in Manufacturing Automation
23	Doireann Ní Chonaill	Taste and Smell Changes and Quality of Life among Ambulatory Cancer Patients Receiving Systemic Treatment.
24	Sean Walsh	Artificial Intelligence and Machine Learning Data Trends of Agarose Hydrogel Properties
25	Bastian Bues	Dysregulation of neurofilaments in ATXN2-ALS motor neurons causes endo-lysosomal trafficking defects
26	Rachel Lapeyre	Developing an adenoviral vector-based vaccine against Staphylococcus aureus skin infections
27	Imane Allaoui	Impact of the vaccine delivery technology on the B cell repertoire in pigs.
28	Darragh Crowe	Computational design of Metal Organic Frameworks (MOFs) as nanocarriers for anti-cancer drug delivery
29	Jack Daly	Cut to the chase: Structure–Activity Insights into Antifungal Acylthiourea Complexes
30	Rebecca Galway	Dye-Loaded Aptamers as a Theranostic Platform for Breast Cancer Diagnosis and Therapy
31	Robyn O'Sullivan	From Simulation to Separation: Predicting Enantioselectivity in Chiral MOF Materials
32	Tara McInerney	Enter the Dragon: Next Generation Anti-cancer Therapy by Photo-oxidative Damage Targeted at Membrane-less Organelles of Human SMAUG1 Protein.
33	Alison Walsh	Synthesis and evaluation of novel pyridocarbazoles as inhibitors of Anaplastic Lymphoma Kinase (ALK)and cell cancer growth
34	Amy Twomey	Computational Design of Metal-Organic Frameworks for Pharmaceutical Solvent Recovery
35	Meadhbh Coomey	Sustainable Methods in Organophosphorus Chemistry
36	Ruth O'Connell	Synthesis of aromatic resolving analogues as potential anti-inflammatories
37	Fucheng Leng	metal assissted peptide crystallization
38	Diarmuid Carey	Characterisation of Solid-State Insulin: Exploring the Solid-State Physical Properties of Two Sources of Insulin
39	Katie O'Riordan	Characterization of Thermosensitive Hydrogel's as Biologic Drug Delivery Matrices
40	Rithwik Pradeep	Comparative Analysis of Common Potency Assays for Assessing Human TNF-alpha Neutralising Antibodies
41	Soaad Ahmed	Investigation into the Stability of Biopharmaceutical Therapeutics During Freeze-Thaw Processes.
42	Lyndsey Moore	Developing a thermostabilised malaria vaccine in microarray patches
43	Nerea Hernández Egido	Engineering circular RNAs for selective protein expression in dysfunctional endothelial cells.
44	Oscar Dunne	Development of novel, aryl-linked antiviral phosphonates
45	Stephen Sweetnam	Synthesis of a library of antimicrobial IMPDH inhibitors
46	Niamh McDermott	Therapeutic targeting of IGF-1R in thyroid eye disease
47	Meaghan Richardson	Engineering synthetic circular miRNA sponges as a novel therapeutic strategy for inflammatory disease
48	Emma Leen	Evaluating the effects of neurotrophic factors BMP5 and BMP7 on neuronal survival and growth in an in vitro model of cellular senescence

UCC Future Pharmaceuticals Research Showcase 2025

UCC is a vibrant community of diverse and independent thought leaders with a shared ambition to be a connected University with excellent research at its heart.

UCC Futures is an ambitious new programme of research prioritisation coupled with an innovative academic recruitment strategy across ten indicative areas of strategic importance that will build a foundation for economic, societal and cultural resilience and prosperity. Check us out at www.ucc.ie/en/futures/



Modern medicines are increasingly based on complex pharmaceuticals and advanced therapeutics. These new emerging treatments and therapies increase the complexity of component materials and processes. **UCC Futures - Future Pharmaceuticals** is advancing knowledge which underpins discovery, development and manufacturing, from small molecules to biopharmaceuticals.
Transcending traditional discipline boundaries is critical to ensure effective and advanced collaboration, development and production of new medicines at scale that ensure availability, affordability, efficacy and safety through a patient-centric approach.

For more information about **UCC Futures - Future Pharmaceuticals** check our website www.ucc.ie/en/futures/futurepharmaceuticals

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1

The coding potential of long non-coding RNAs in breast cancer

School of Biochemistry & Cell Biology, University College Cork

George Merrin[1]; Oza Zaheed[2], Kellie Dean[1]

[1]School of Biochemistry and Cell Biology

[2]EIRNA Bio, Bioinnovation Hub, HSB330, College Rd, Cork, Ireland

What I am doing

We are studying a group of RNAs called long non-coding RNAs (lncRNAs) that were once thought to be unable to make proteins. We want to see if some of these RNAs produce very small proteins, called microproteins, in breast cancer cells, and if these tiny proteins have roles in how cancer develops.

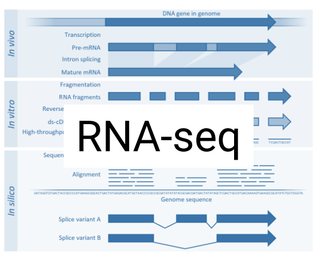
Why I am doing it

Although lncRNA expression is known to change in many cancers, we do not yet understand what many of these lncRNAs do. If some of them are used to make microproteins that affect tumour growth or spread, this could reveal new ways to detect, understand, or treat breast cancer.

How I am doing it

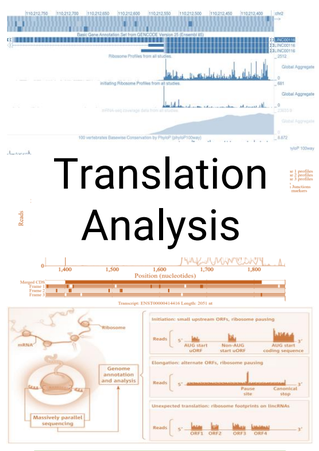
We compare RNA sequencing and ribosome profiling data from cancer cells and patients to find lncRNAs that might make microproteins. We then test these candidates in the lab to see if they are made into proteins, where they go in the cell, and which other proteins they interact with.

In silico analysis



Cell lines n = 43
Patient Samples n = 1224

Result → 400 differentially expressed lncRNAs when compared to normal samples



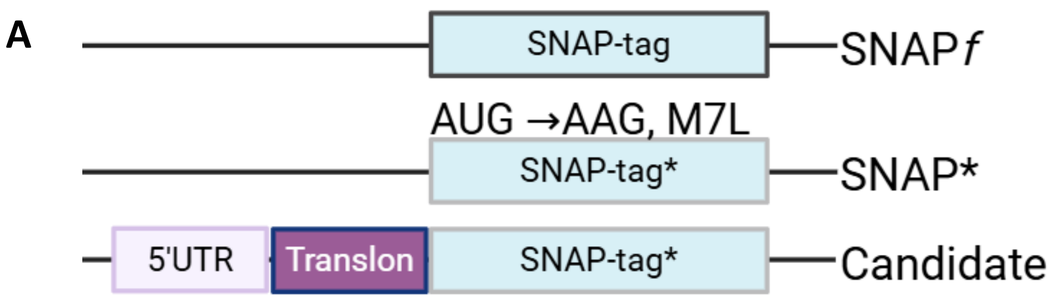
lncRNA with evidence of translons n = 64

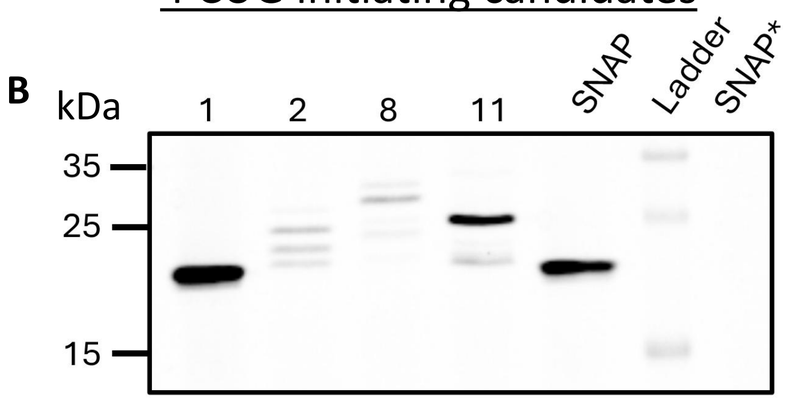
- **Translation potential**
- **Sequence information**
- **Proteomic evidence**
- **RNA localisation**

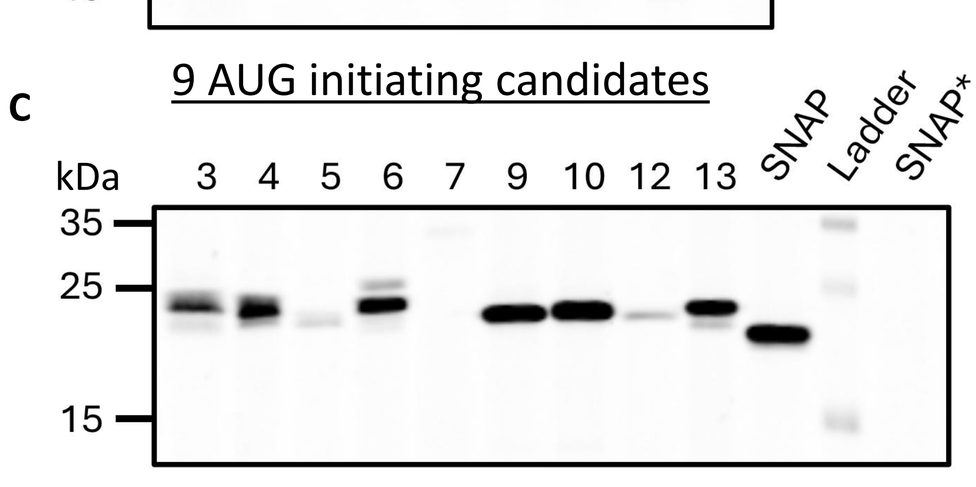
13 candidates selected

- 13 candidates were selected for *in vitro* experimentation after *In silico* analysis.
- All were C-terminally tagged with SNAP-tag for expression analysis.
- Candidates 1 and 7 were N-terminally tagged with 3xMYC tag for pulldowns and immunocytochemistry.

Experimental evidence







SNAP-tag expression of candidates

A. Schematic of SNAP-tag constructs.
B. SDS-PAGE gel showing translation of the 4 CUG initiating candidates. The presence of multiple bands indicates that translation is likely initiating at alternative start sites than predicted.
C. SDS-PAGE gel showing the translation of the 9 AUG initiating candidates. The candidates range in size from 9 to 117 amino acids.

What I hope to achieve in the end

We hope to prove that some lncRNAs can make functional microproteins and find out what these proteins do in breast cancer using cell lines as models of the disease. This will help uncover new layers of cancer biology and highlight possible new targets for drugs or diagnostics.

What is the potential impact in the Pharma area

This research will uncover entirely new targets for drug development and cancer detection. By discovering microproteins that are made from breast cancer-associated lncRNAs, these novel tiny proteins could have big impact for the pharma industry in the design of more precise and effective cancer treatments.

Contact us

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2

Induction of influenza-specific immunity in pigs using dissolvable microneedle patches to deliver an adenovirus-based vaccine

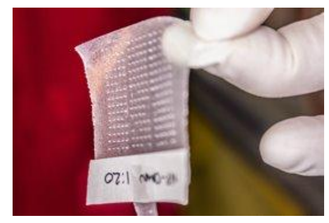
Inés Có-Rives, Katherine Acevedo, Imane Allaoui Kayan Tam, Emery G Dora, Grace Copithorne, Edgar Garcia Manzanilla, Kelly A S da Costa, Nigel J Temperton, Sean N Tucker, Ann Ying-An Chen, Anne C Moore,
School of Biochemistry and Cell Biology

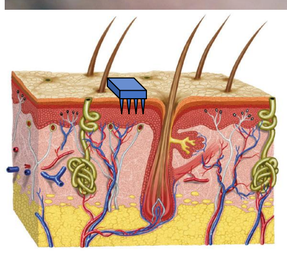
What I am doing and why

Global vaccine access is suboptimal due to:

Cold chain constraints

Need to train healthcare workers





DMN patches (top) and graphical representation of DMN patch on skin (bottom).

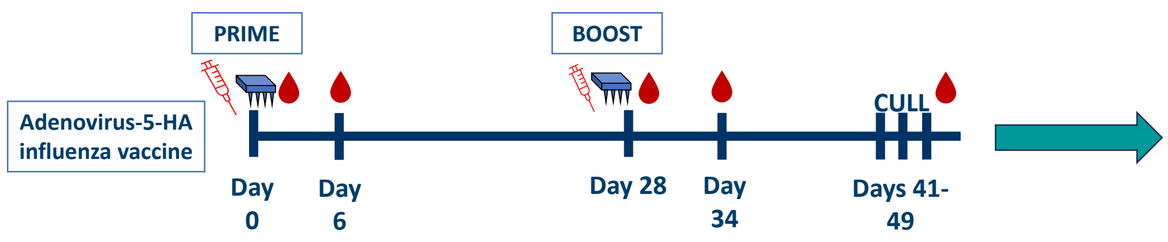
New injection-free, thermostable vaccine forms are urgently needed to address these issues. We are developing an **easy-to-administer microneedle (DMN) skin patch** that has previously demonstrated high levels of vaccine immunogenicity in mice (1, 2, 3).

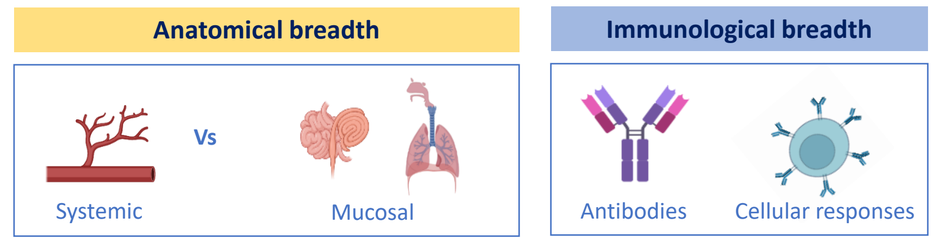
We aim to determine how this technology translates to pigs, which represent a **more relevant animal model**, compared to mice (4). We want to address the following questions:

1. Can DMN patch-based delivery of an adenovirus-based influenza vaccine induce antibody and cellular responses in pigs?
2. Does the patch skew the antibody response in favour of the antigen and away from the adenovirus vector, as observed in mice?
3. Does the delivery technology, injection (IM) or skin patch, impact on the vaccine-induced breadth of the immune response, in pigs?

How am I doing it?

To evaluate how the **magnitude and quality of the immune response** is affected by the change in **vaccine delivery technology** we are looking in depth at the antibody and cellular responses in pigs, compared to intramuscular injection.

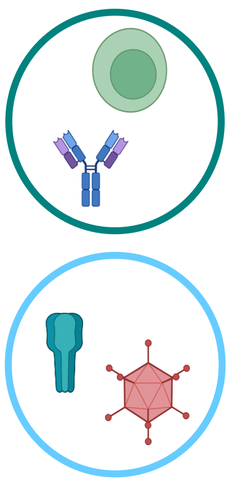




What I hope to achieve and some preliminary findings

We want to determine if a broader response is elicited in pigs when vaccinated with skin patches and to **understand how the cellular and antibody responses** in the mucosa correlate to those observed in easy to collect samples.

RESULTS TO DATE

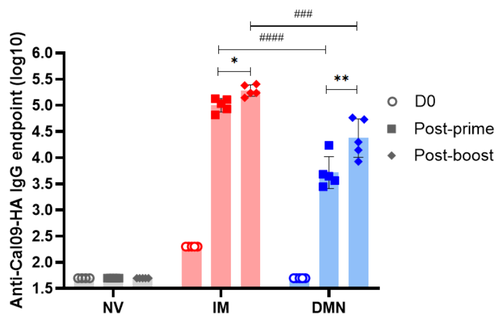


We have demonstrated, **for the first time**, that an adenovirus-based vaccine induces antibodies (*top figur*e) and T cells (*lower figure*), when delivered by DMN patches **successfully deliver** adenovirus, a **recombinant live virus vector vaccine**, to pigs. Patch-based vaccine delivery to skin:

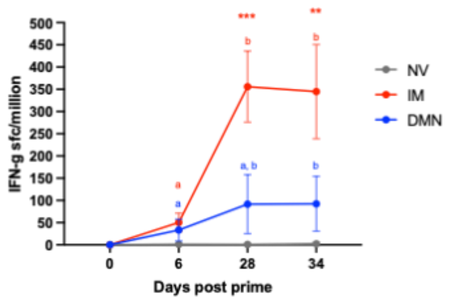
- Drives the antibody **response towards the antigen** and away from the vector *(not shown).*
  - ➢ *This permits repeated use of a recombinant virus vector*.
- Induces humoral response with the **same anatomical breadth as intramuscular** injection.
  - ➢ *DMN patches are not a technology to induce broader mucosal responses.*

DMN patches offer many advantages for addressing vaccine accessibility issues. Further studies are required to determine if the responses are protective.

Serum HA-specific IgG

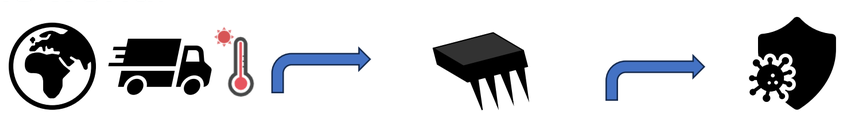


Blood HA-specific T cells



Potential impact

Our findings provide new insight and understanding on how the form and route of immunization impacts on immunogenicity. This knowledge will inform further development of alternative thermostable and easy-to-use delivery technologies that can **help improve vaccine accessibility around the world**.



1. Flynn O, Dillane K, Lanza JS, Marshall JM, Jin J, Silk SE, Draper SJ, Moore AC. Vaccines (Basel). 2021 Mar 22;9(3):299. doi: 10.3390/vaccines9030299.
2. Vrdoljak A, Allen EA, Ferrara F, Temperton NJ, Crean AM, Moore AC. J Control Release. 2016 Mar 10;225:192-204. doi: 10.1016/j.jconrel.2016.01.019.
3. Lanza JS, Vucen S, Flynn O, Donadei A, Cojean S, Loiseau PM, Fernandes APSM, Frézard F, Moore AC. Int J Pharm. 2020 Aug 30;586:119390. doi: 10.1016/j.ijpharm.2020.119390.
4. Có-Rives I, Chen AY, Moore AC. 2023 Feb 16;11(2):450. doi: 10.3390/vaccines11020450.

Taighde Éireann Research Ireland

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3

Distinguishing insulin and insulin-like growth factor 1 receptors: Implications for drug design and selectivity

Stephen O'Shea, Ángela Sánchez Rodríguez, Rosemary O'Connor
School of Biochemistry and Cell Biology

What I am doing

We study how the biological actions of two evolutionarily related hormones - insulin and insulin-like growth factor 1 (IGF-1) - are mediated through their respective cell surface receptors, insulin receptor (InsR) and IGF-1 receptor (IGF-1R). Despite sharing a common evolutionary origin and a high level of structural similarity, these cell surface receptors fulfil different physiological functions - with InsR broadly regulating metabolism in response to insulin, and IGF-1R primarily regulating growth and development in response to IGF-1.

Why I am doing it

Given their important functions, InsR/IGF-1R are strongly implicated in diseases of ageing, such as diabetes and cancer, making them highly sought after drug targets. While InsR has been a successful drug target for 100+ years, IGF-1R - long recognised for its pro-oncogenic role in cancer development - is known for being notoriously challenging to target, necessitating a better understanding of IGF-1R (and how it differs from InsR). After failure of many IGF-1R drug development programs, an anti-IGF-1R monoclonal antibody was recently repurposed to treat thyroid eye disease, reviving interest in anti-IGF-1R biologics and small molecules.

How I am doing it

We are studying/comparing the structures of InsR and IGF-1R in detail to understand how dissimilarities contribute to their unique biological functions and druggability. To accomplish this, we mutate/swap parts of these receptors, creating receptor "chimeras" that offer insight into the structural variation underpinning these differences.

What I hope to achieve in the end

We hope to identify unique parts of IGF-1R that may enable more effective/precise targeting. Due to the high degree of similarity between IGF-1R and InsR, many small molecule drugs are unable to distinguish between them (meaning many IGF-1R inhibiting drugs also target/inhibit InsR, causing off-target effects like hyperglycaemia at higher dosages). As such, our work may contribute to improving small molecule targeting strategies, in particular.

What is the potential impact in the Pharma area

With renewed interest in IGF-1R targeting, pharmaceutical companies must work to design trials that address past failures/limitations in this space - including identification of predictive biomarkers, combination therapies to address acquired therapeutic resistance and mitigation of off-target effects due to InsR co-targeting. Ultimately, our work may impact future identification/development/re-examination of small molecule drugs that target IGF-1R as they regain traction.

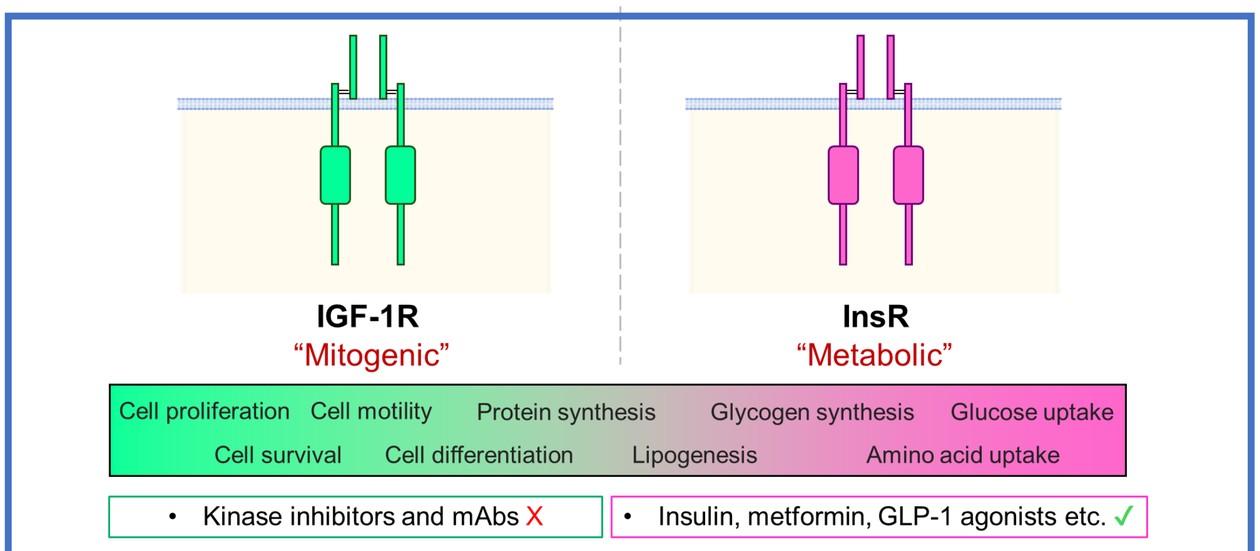

Fig 1: *Despite sharing a common evolutionary origin, InsR and IGF-1R fulfil different functions in physiology. Insulin action has been successfully targeted using recombinant insulin or indirectly using drugs like metformin and more recently GLP-1 agonists. Conversely, IGF-1R, a much sought after drug target in oncology, has proven a more challenging target.*

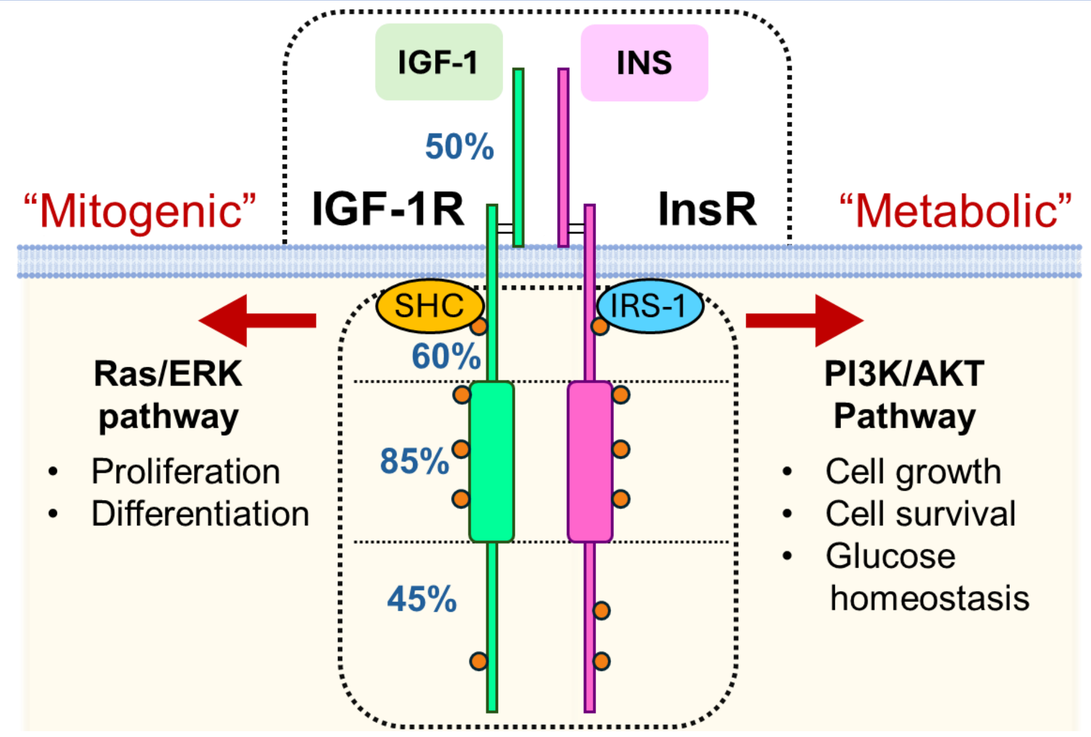

Fig 2: *InsR/IGF-1R become activated by binding of their respective ligands, insulin and IGF-1, and signal through overlapping cellular machineries to achieve their distinct biological effects. Due to their common ancestry, these receptors have retained structural similarities. The catalytic region responsible for transducing the biological effects of insulin/IGF-1 remains the most similar (85%). This highly homologous region is also the most viable/pursued target for small molecule targeting, making precise targeting of IGF-1R alone (and not InsR) challenging.*

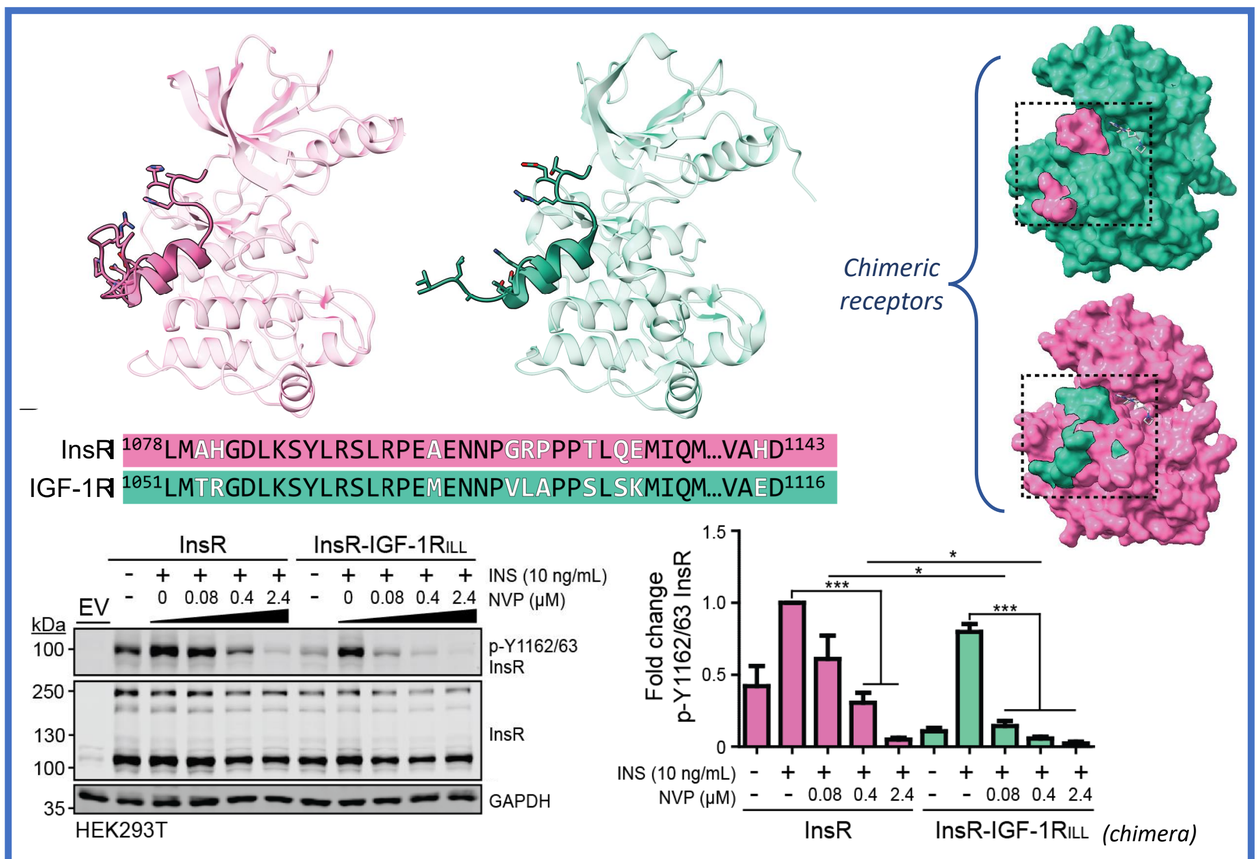

Fig 3: *The catalytic regions still display structural idiosyncrasies, some of which lie next to the site of small molecule targeting (outlined, with protein sequence alignment showing the amino acid residues that differ between InsR and IGF-1R). To study whether these dissimilar residues contribute to drug selectivity, we created chimeric receptors in which we swapped these residues around and tested whether this altered potency of a candidate IGF-1R inhibitor, NVP-AEW541 (Novartis), that shows apparent selectivity for IGF-1R over InsR (for unknown/explored reasons). Replacing the residues in InsR with the corresponding residues in IGF-1R sensitises the InsR to small molecule inhibition by NVP-AEW541 in cells, suggesting that more precise targeting is achievable and implicating the above residues in a mechanism for drug selectivity.*

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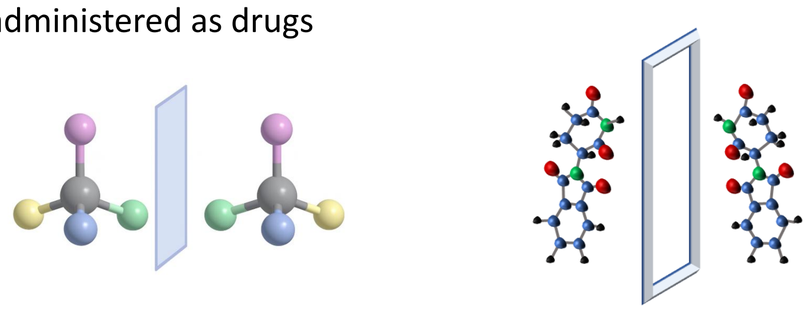
4

Asymmetric C–H Insertions with Novel α-Diazosulfonates

Rebecca O'Keeffe[a,b], Amy Shiely[a,b], Stuart G. Collins[a,b,d] and Anita R. Maguire [a,b,c,d]
[a]School of Chemistry, University College Cork; [b]Analytical and Biological Chemistry Research Facility, University College Cork;
[c]School of Pharmacy, University College Cork; [d]SSPC.
Email: 118347226@umail.ucc.ie, stuart.collins@ucc.ie, a.maguire@ucc.ie

Introduction to Asymmetric Synthesis

- Organic molecules used as medicines can exist in left and right-handed forms (enantiomers) which frequently display vastly different activities when administered as drugs



Enantiomers – Mirror image molecules

- As a result, the FDA require new drugs to be prepared and evaluated as single enantiomers (asymmetric synthesis)

Nobel Prizes in Chemistry awarded to researchers in the field

2001

William S. Knowles *Ryoji Noyori* *K. Barry Sharpless*

One half to Knowles and Noyori
"for their work on chirally catalysed hydrogenation reactions"
One half to Sharpless
"for his work on chirally catalysed oxidation reactions"

2021

Benjamin List *David W.C. MacMillan*

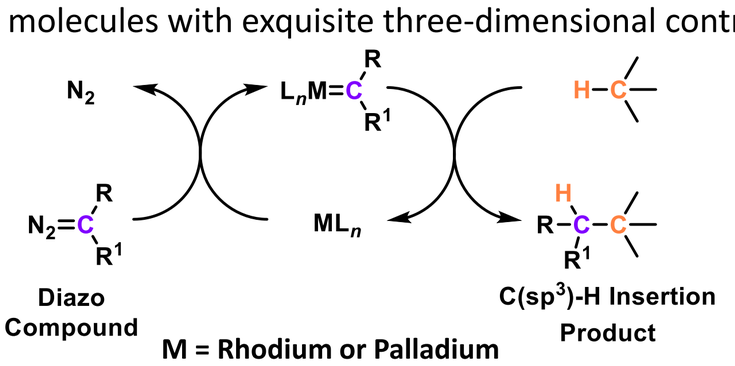
Jointly awarded to List and MacMillan
"for the development of asymmetric organocatalysis"

Asymmetric Catalysis with Transition Metals

Asymmetric synthesis commonly uses transition metal catalysts with chiral ligands that create a defined chiral environment at the metal centre

The C –H Insertion Reaction

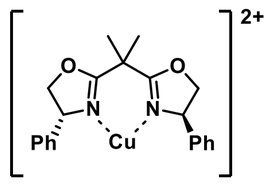
Transition metal catalysed C–H insertion reactions enable the formation of new C–C bonds, offering an efficient route to construct complex molecules with exquisite three-dimensional control[1-7]



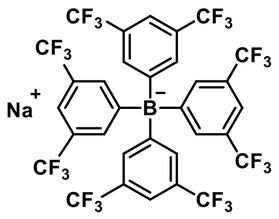
The Copper-bis(oxazoline)-NaBARF System

The Maguire group has published a series of papers over the past decade describing highly enantioselective intramolecular C-H insertion reactions in α-diazo-α-sulfonyl esters and ketones using copper bis(oxazoline) catalysts based on commercially available ligands[3-6]

Copper bis(oxazoline) catalyst



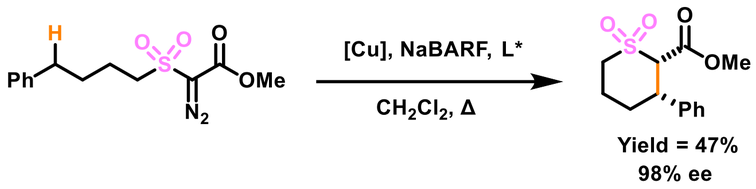
NaBARF



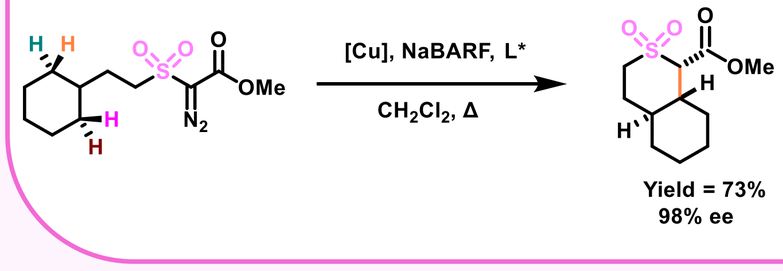
Key Findings

Previous Work in the Maguire Group[3-6]

C–H Insertion- sulfone series



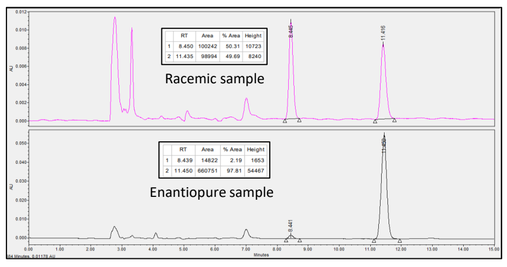
Desymmetrisation- sulfone series



Catalytic system is effective in achieving high levels of enantiocontrol across both series

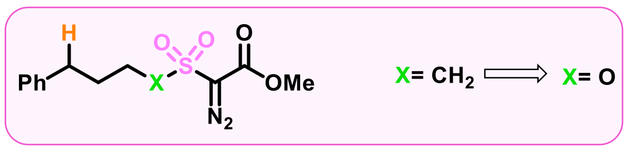
Enantioselectivity and diastereoselectivity are slightly reduced in sultone series

Enantioenriched products are accessible in high yields via desymmetrisation

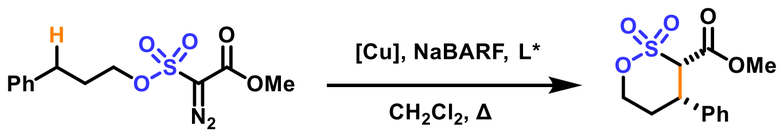


Chiral HPLC performed at 25 °C with IPA:hexane as mobile phase (15:85) at 1.0 mL min^{-1} with Phenomenex Lux® 3µm Amylose-1.

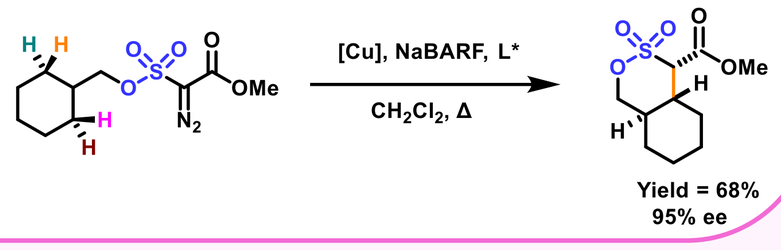
This Project



C–H Insertion- sulfonate series

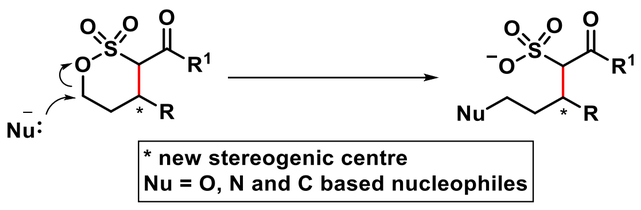


Desymmetrisation- sulfonate series



Project Impact

Synthetic Applications



Potential for ring opening reactions substantially broadens the application of the copper mediated C–H insertion in synthesis

Green Chemistry Focus

The pharmaceutical industry aims to reduce waste, improve energy efficiency, and use renewable resources

The principles of green chemistry state that catalytic reagents are superior to stoichiometric reagents

Copper:

Several advantages over traditional metals like rhodium

Earth abundant
26th most abundant element in Earth's crust (50-100 ppm)
Rhodium is 80th (0.001 ppm)

Cost effective
$0.0112 per gram
Rhodium is $267 per gram (20th Oct. 2025)

Essential element
Control of residual trace levels in API's is much less challenging

Acknowledgements

Taighde Éireann Research Ireland

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5

Decarboxylative carbon-carbon bond forming reactions using photochemistry in continuous flow

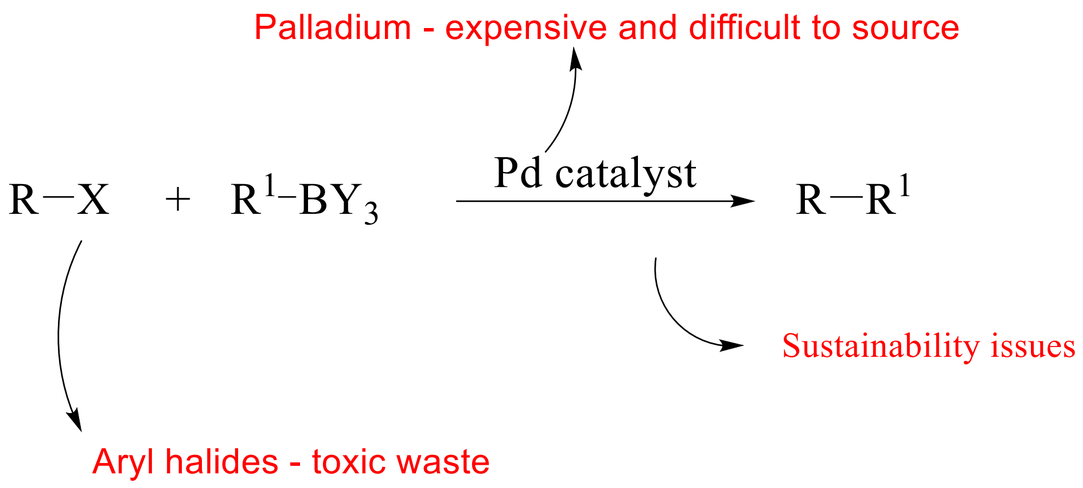
Victoria McTigue Fennell[a,b], Stuart G. Collins[a,b], Anita R. Maguire[a,b,c]

[a]School of Chemistry, University College Cork; [b]Analytical and Biological Chemistry Research Facility, University College Cork; [c]School of Pharmacy, University College Cork

Most widely used carbon-carbon bond formation

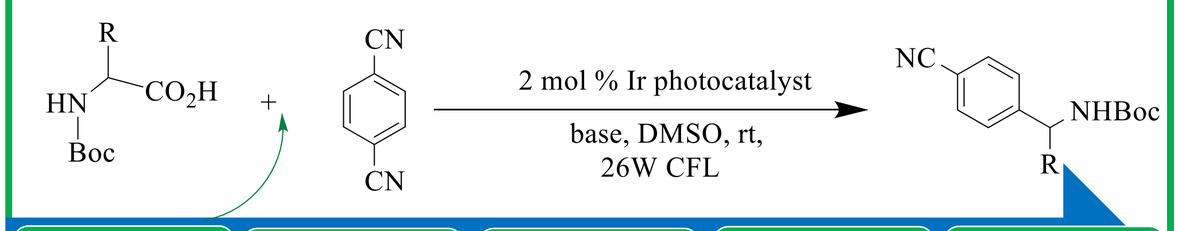
The Suzuki Miyaura coupling is the **#5** most widely used reaction in drug discovery and **#2** in manufacturing.[1,2,3]

Suzuki-Miyura, 1979



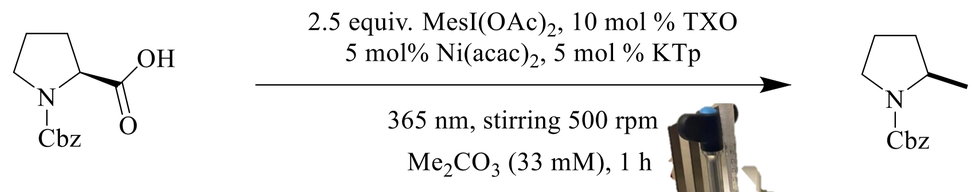
Decarboxylative carbon-carbon bond formation

MacMillan, 2014

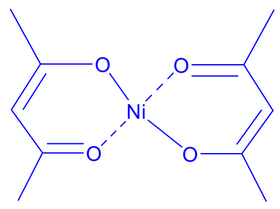


Iridium → Iridium and Nickel → Earth abundant metals → Nickel and organic photoredox catalysis → Organic photoredox catalysis

MacMillan, 2022



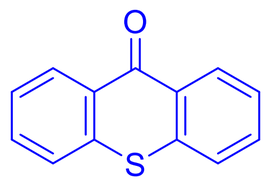
Combined nickel and organic photoredox catalysis



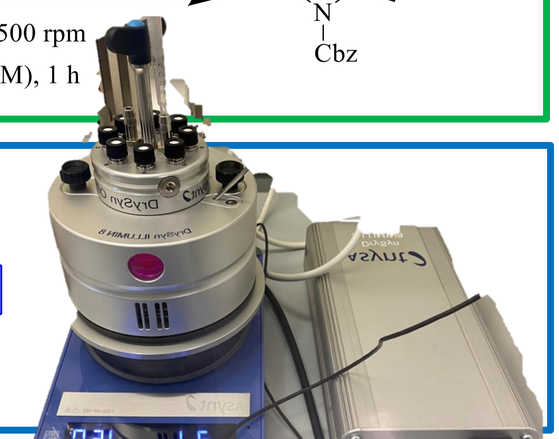
Ni(acac)$_2$

More abundant and cheaper metal relative to Palladium

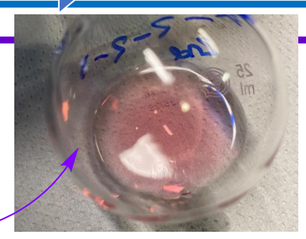
Common benzophenone organic photoredox catalyst



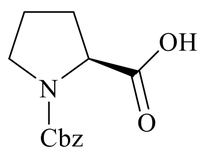
Thioxanthone



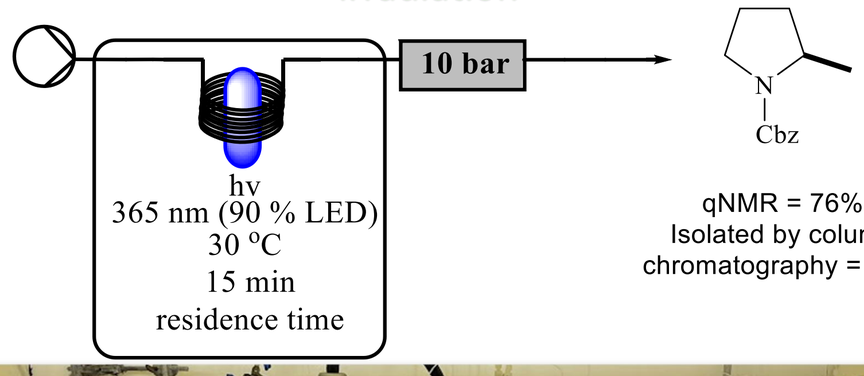
Transfer of reaction to continuous flow chemistry



Solution post irradiation

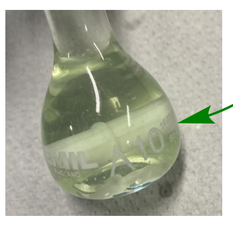


+ 2.5 equiv. $MesI(OAc)_2$, 6.7 mol % TXO
5 mol% $Ni(acac)_2$, 5 mol % KTp



qNMR = 76%
Isolated by column chromatography = 51%

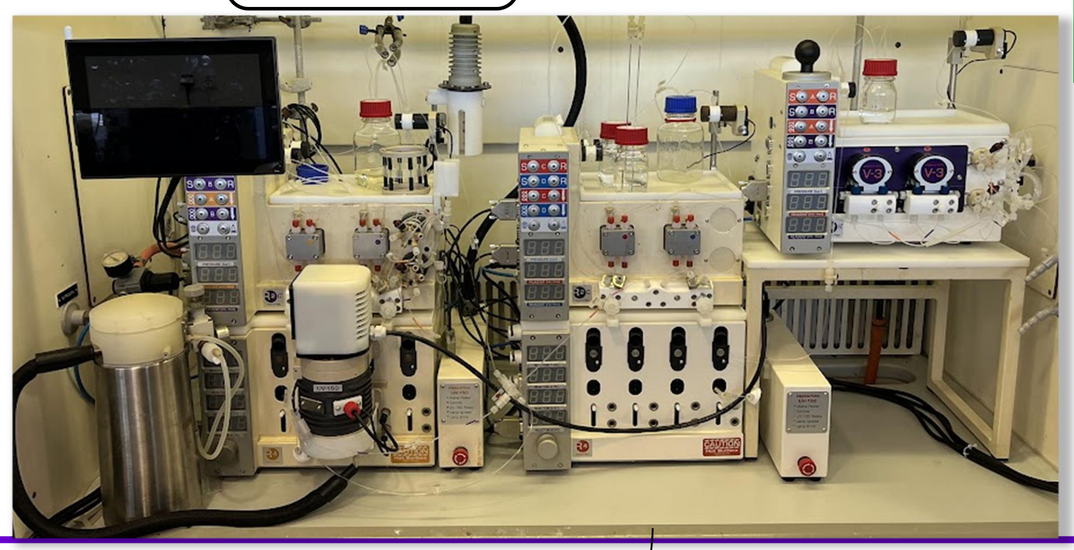
0.67 mL/min flow rate
Me_2CO_3
0.035 moles/L



Solution prior to irradiation

Continuous flow

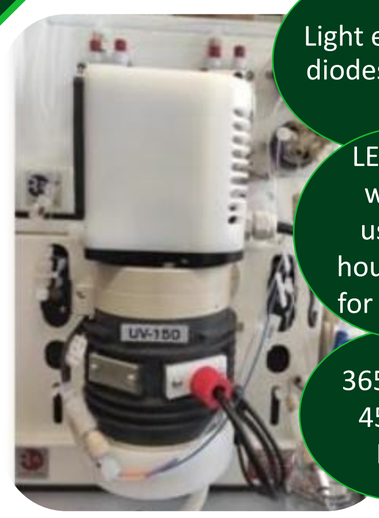
- More sustainable
- Improved safety
- Enhanced scalability



Difficult for light to fully penetrate solution in batch

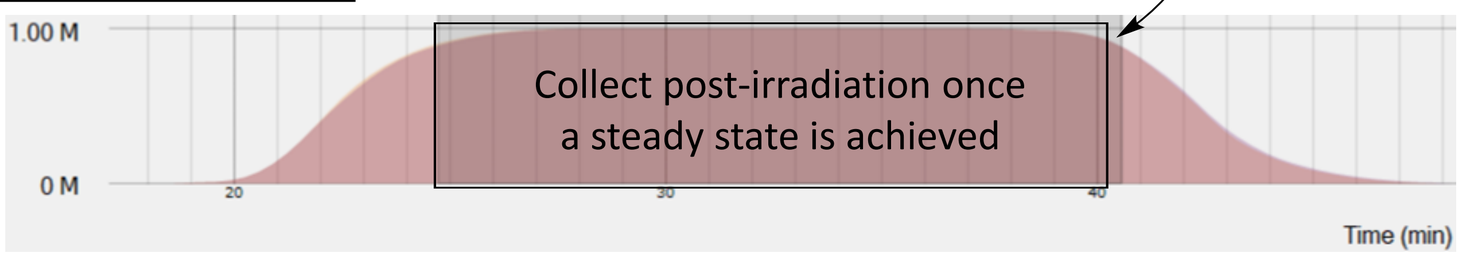
Determine homogeneity of solution in batch

Transfer to flow and scale-up



- Light emitting diodes (LEDs)
- LEDs are widely used in households for lighting
- 365 nm or 450 nm LEDs

Steady state collection



The Maguire-Collins research team, UCC

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MSD

SSPC

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6

Time-Resolved IR Spectroscopy for Evaluation of Phosphine Coligand Effects on the Ultrafast Behaviour of Mn(I) Precatalysts

Benjamin R. O'Donoghue [a,b], Ian J. S. Fairlamb [b], Jason M. Lynam [b], Gerard P. McGlacken [a]
[a]*Analytical and Biological Chemistry Research Facility, School of Chemistry, University College Cork, Cork, Ireland*
[b]*Department of Chemistry, University of York, Heslington, York, YO10 5DD, UK*

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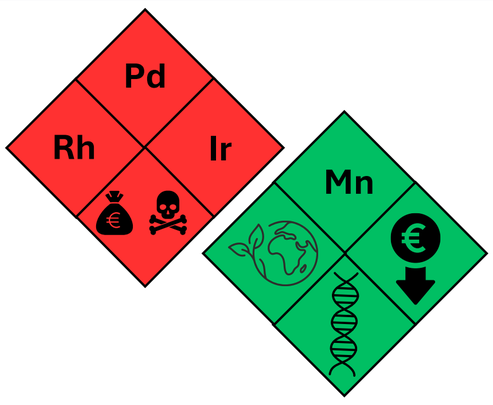
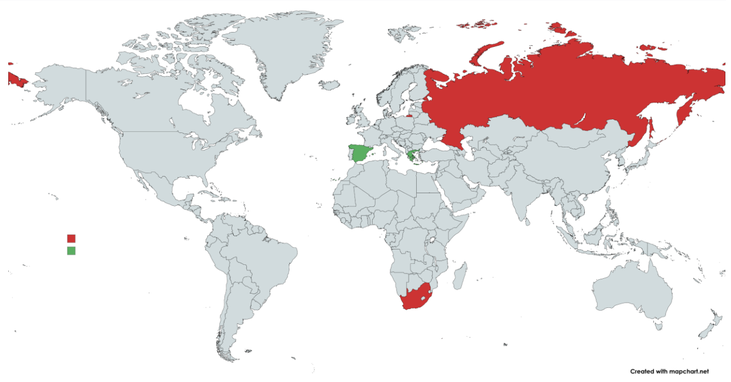
Introduction



Metal-catalysed reactions used in the pharmaceutical industry are vastly dominated by the use of precious group metals (PGMs) such as palladium and rhodium. These metals are expensive to purchase, are toxic, and many are subject to geopolitically sensitive supply routes.

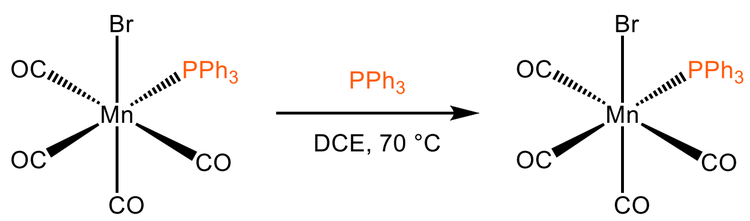
Manganese is an earth abundant metal (EAM), is cheaper, and is more tolerated biologically, while the EU has manganese reserves. Therefore, it has arisen in the last number of years as a viable alternative to PGMs.

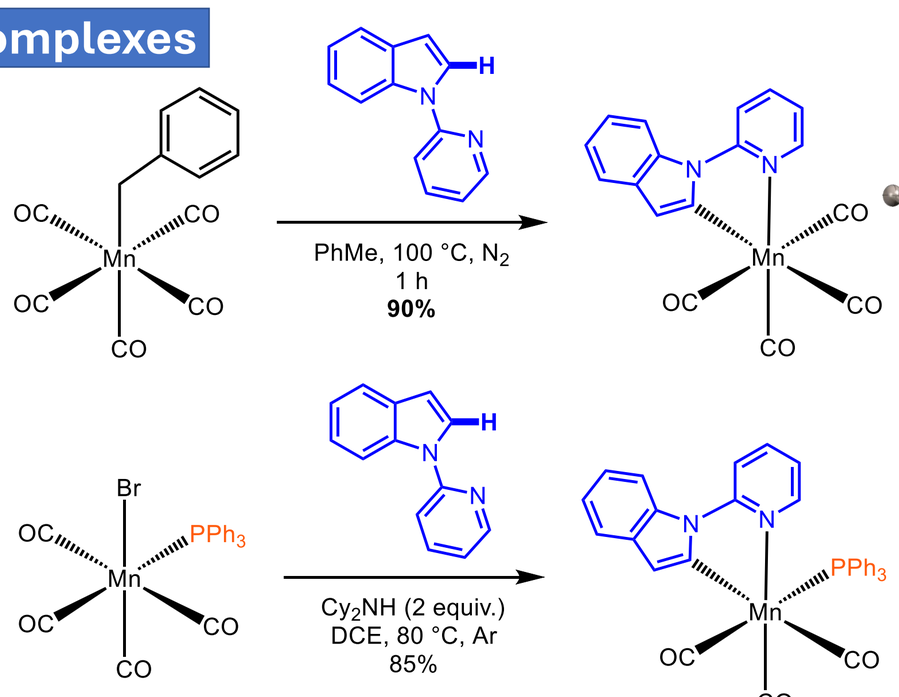
Understanding Mn catalysts and how ligands can affect their behaviour and activity in reactions is an essential step in moving to more sustainable metal catalysis.

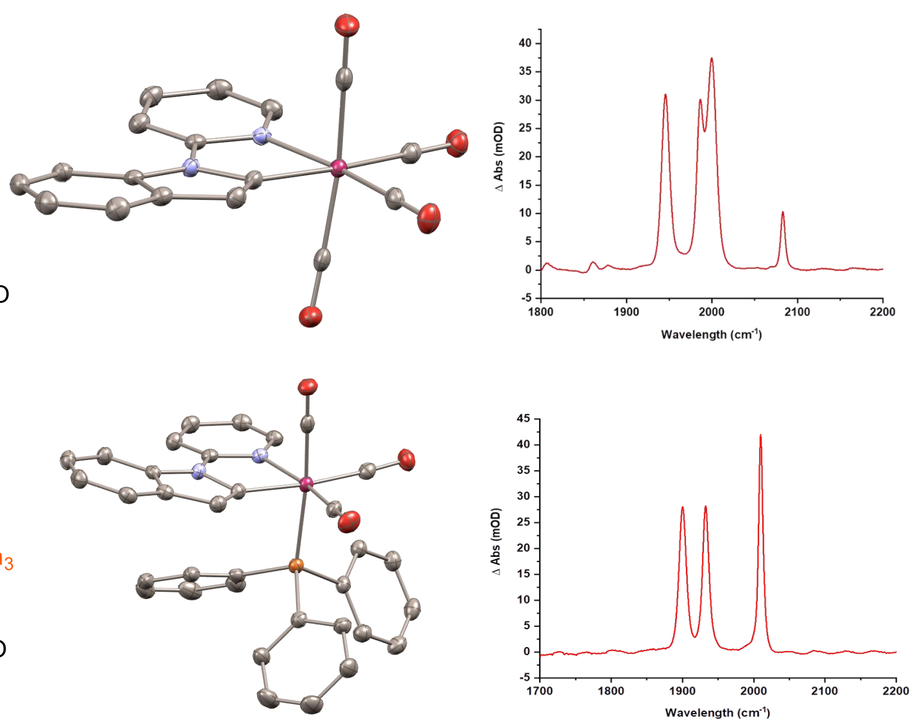


Preparation of Mn(I) Complexes

- High-yielding preparations from readily available materials
- Simple synthetic procedures
- Facile isolation and purification, special storage not needed
- Amenable to scaling up
- Structures confirmed by X-ray crystallography and infrared spectroscopy

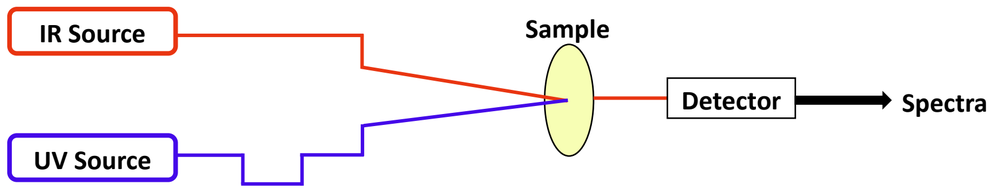


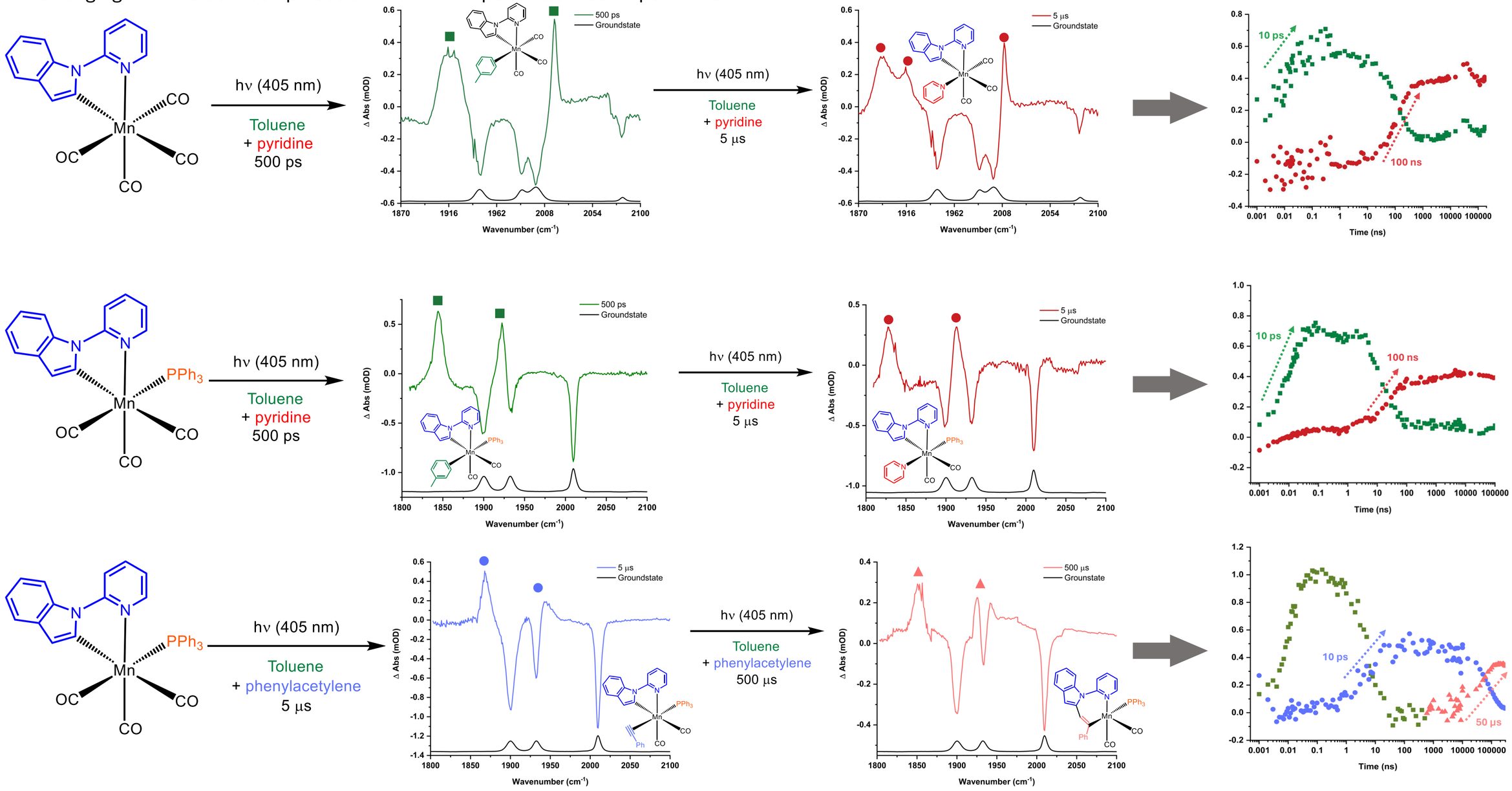




Time-resolved IR Spectroscopy (TR^{M}PS)

- CO groups are excellent reporters of changes in metal complexes
- Irradiation of these Mn(I) complexes with a UV-vis laser pulse induces loss of a CO group
- A subsequent pulse from an IR laser interrogates the resulting speciation and dynamics
- Changing the time between pulses allows for timepoints between 1 ps – 1 ms





Key Takeaways

- The ultrafast behaviour and key bond-forming processes of Mn(I) complexes are unaffected by the inclusion of a phosphine ligand
- Simple preparation, isolation, and storage would allow for ease of use in pharmaceutical industry
- The nature of the phosphine can be explored to potentially enhance performance and drive towards a step-change in the use of sustainable metals in API synthesis

References

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U. Schneider and S. Thomas, Eds., *Catalysis with Earth-abundant Elements*, The Royal Society of Chemistry, 2020.
Inorg. Chem. 2025, 64, 33, 16768–16780

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7

Development of a Non-Porous Protein-A Silica Column for Rapid Quantification of Monoclonal Antibodies

Devansh Shah[1,2], Eric Moore[1], John Hanrahan[2]
[1]School of Chemistry, University College Cork
[2]Glantreo Limited

What I am doing?

- Developing a High-Performance Protein-A affinity chromatography column using non-porous silica particles and evaluating its performance for monoclonal antibody (mAb) analysis.
- Combination of materials science, bioprocess analytics, and chromatography method development for rapid and accurate quantification of monoclonal antibodies (mAbs).

Why I am doing it?

- Protein-A HPAC (High Performance Affinity Chromatography) enables fast, precise, and reproducible mAb titer quantification.
- Reliable HPAC requires a mechanically and chemically robust affinity resin.
- Non-porous silica provides this robustness, with low fouling and minimal non-specific adsorption.

How I am doing it?

- Functionalising non-porous silica with a Protein-A ligand using controlled surface chemistry.
- Packing these materials into HPLC columns using optimised packing protocols.
- Assessing chromatographic performance with IgG standards and real mAb feedstock.
- Studying linearity, precision, temperature effects, and system suitability to match analytical-quality expectations

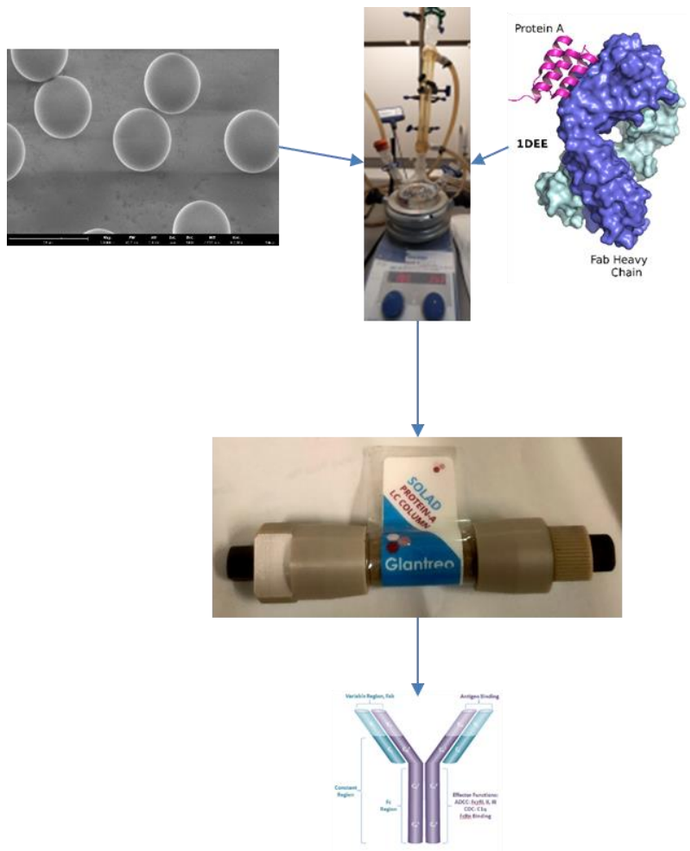

Fig.1: Development workflow

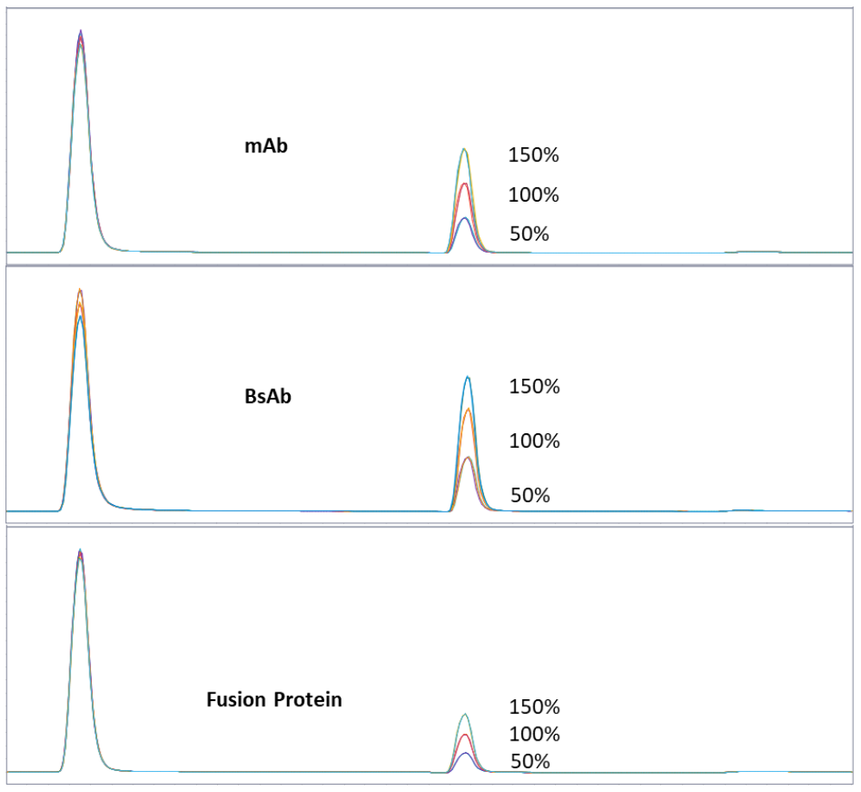

Fig.2: Accuracy test

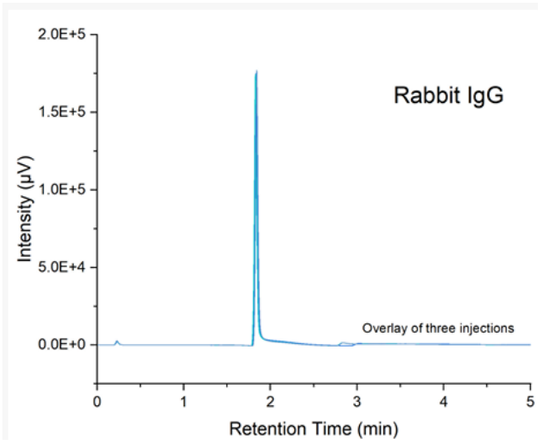

Fig.3: HPAC Analysis of Rabbit IgG standard

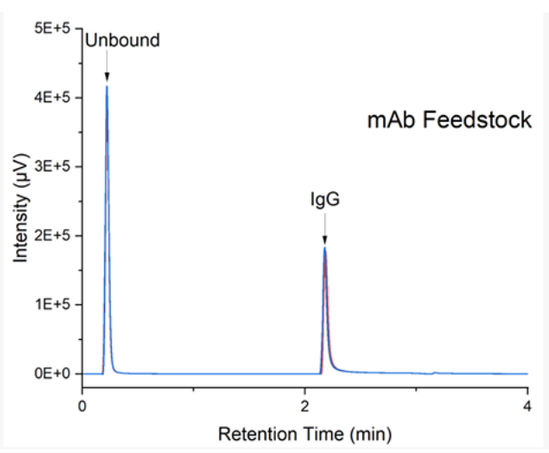

Fig.4: HPAC Analysis of mAb Feedstock sample

What I hope to achieve in the end?

- A fast, sharp, and reliable Protein-A column for accurate mAb quantification.
- Consistent performance suitable for routine analytical and QC workflows for mAb titer analysis.
- A platform technology that can be adapted to other affinity ligands (e.g., Protein-G, Protein-L).
- Demonstration that non-porous silica is a viable next-generation platform for HPAC.

What is the potential impact in the Pharma area?

- Speeds up mAb development with rapid and reproducible titer quantification.
- Offers a cost-effective, high-performance alternative to polymeric resins, based on durable non-porous silica technology manufactured in Ireland.
- Supports scalable, high-throughput QC testing for biologics and biosimilars.

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Glantreo

UCC Coláiste na hOllscoile Corcaigh University College Cork, Ireland

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8

Using Flow and Mechanochemical Technology in the Synthesis of α-Sulfenyl-β-Chloroenones

Fiona Kinsella[a,b], Stuart G. Collins[a,b] and Anita R. Maguire[a,b,c]
[a.]School of Chemistry, University College Cork, Cork, Ireland [b.]Analytical and Biological Chemistry Research Facility, University College Cork, Cork, Ireland [c.]School of Pharmacy, University College Cork, Cork, Ireland.

WHAT

In this work we synthesized and characterized a range of α-sulfenyl-β-chloroenones using batch, flow and mechanochemical conditions. This reaction proceeds via a complex chlorination cascade, with reaction intermediates that can be isolated and monitored.[1] The mechanochemical route is the first time these molecules have been synthesised in a solvent free process. The flow route is significantly faster than the batch process and has improved the safety and scalability of the process.

WHY

Recently, there has been growing interest in integrating modern technologies into synthetic organic chemistry to address challenges in reproducibility, sustainability, and scalability.[2] Most pharmaceutical API synthesis is carried out in batch reactors, however incorporating the use of new technologies, such as flow chemistry and mechanochemistry, has the potential to open new avenues for reactivity discovery and chemical innovation.[2] Incorporation of these technologies, or the development of a hybrid approach, can offer significant improvements, such as enhancing safety and reducing waste.[2]

HOW

Mechanochemistry is a sustainable and robust alternative to traditional solvent-based synthesis. This approach enables chemical reactions to be conducted in the absence of solvent.[2] Mechanical energy such as grinding, milling, or shearing, drives the reactions to completion. Successful completion of reaction cascade as complex as ours, is not trivial. Flow chemistry refers to conducting chemical reactions by pumping the reagents through tubes where they can mix and react. The reaction conditions, such as flow rate, temperature, pressure, and residence time are carefully controlled.

IMPACT

The impact of this in the pharmaceutical industry would be enhancing operator safety within synthetic chemistry. There is potential for major time saving in production of APIs and the capability to reduce solvent waste in production.

NCS Chlorination Cascade

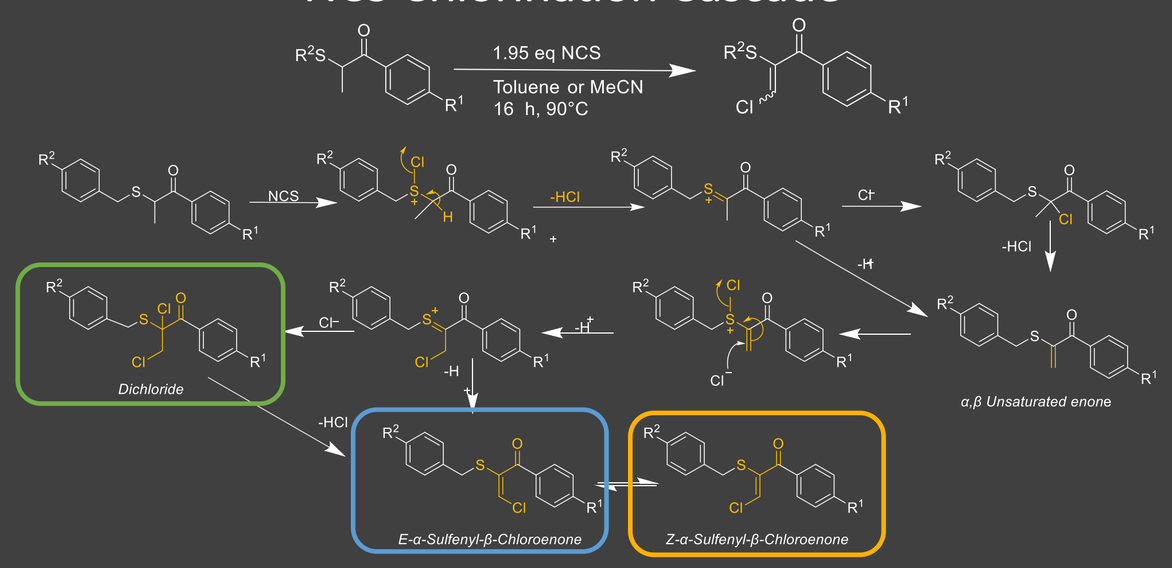
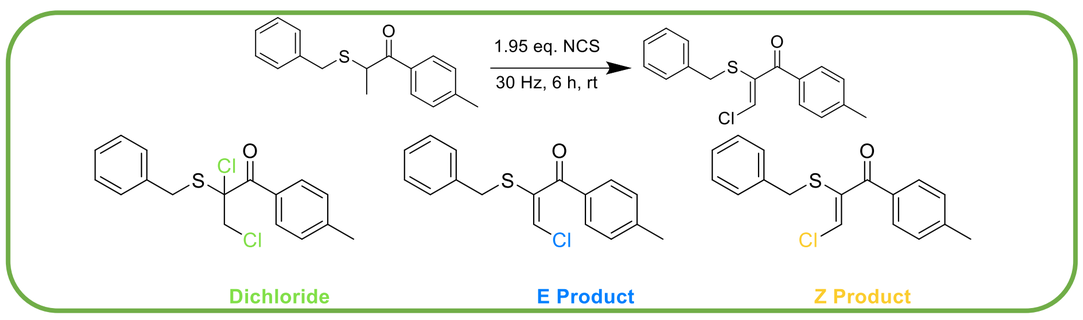


Figure 1. Key intermediates formed in chlorination cascade.

Mechanochemistry

A mechanochemical reaction is one in which mechanical energy such as grinding, milling, or shearing initiates the chemical reaction.[3] Inspired by a seminar from Prof Duncan Browne, a world leader in mechanochemistry, it was decided to explore if formation of the α-sulfenyl-β-chloroenones would be possible using this technology with efficient progress through the chlorination cascade. Results have demonstrated successful transformation to the α-sulfenyl-β-chloroenone on milling with NCS in a solvent free process.



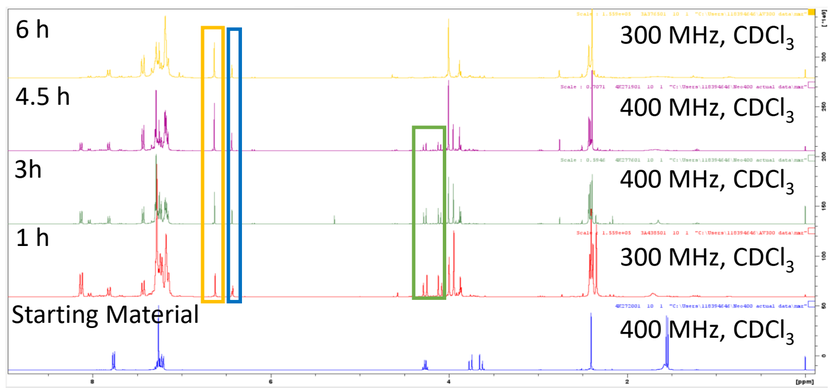


Figure 2.[1]H NMR spectra depicting the Z (orange), E (blue) and dichloride (green) β proton signals over time.

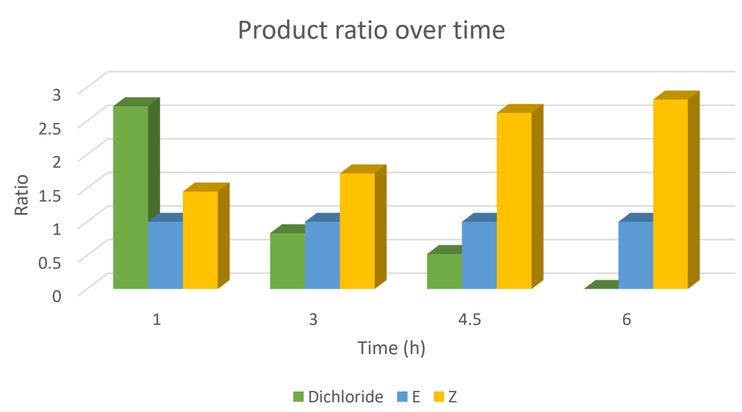
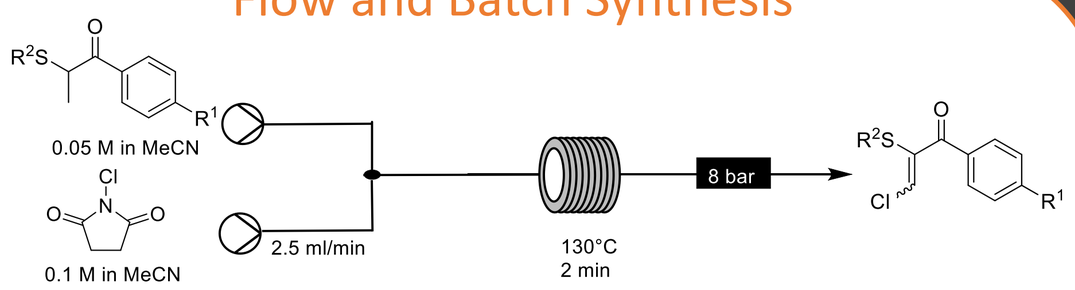


Figure 3. Ratio of product formation over time.

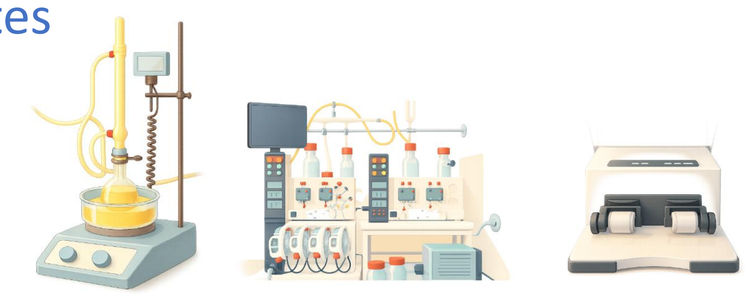
Flow and Batch Synthesis



α-Sulfenyl-β-Chloroenone	R^1	R^2	Flow MeCN Z:E	Batch Toluene Z:E	Batch MeCN Z:E
1	Me	Ph	1: 2.3	2.3 : 1	1 : 1.7
2	Me	Bn	1 : 2.7	2 : 1	1 : 2.2
3	OMe	Bn	1 : 2.4	2.4 : 1	1 : 2.1
4	H	Ph	1 : 2.4	1.6 : 1	1.8 : 1
5	Cl	p-$FC_6H_5CH_2$	1 : 3.3	2.6 : 1	1 : 4
6	F	Bn	1 : 3.2	1.4 : 1	-
7	H	Bn	1 : 3.1	3 : 1	-

Table 1.Comparison of flow and batch synthesis of α-sulfenyl-β-chloroenones.

Comparison of Synthetic Routes



	Batch		Flow	Mechanochemical
Time	16 h		2 min residence time	6 h
Temperature (°C)	90		130	25
Solvent	Toluene	MeCN	MeCN	N/A
E:Z	1 : 2.2	3.5 : 1	2.7 : 1	1 : 2.8
Isolated yield	81%	89%	86%	93 %
Scalability	Limited to 2 g		Yes	Limited to mill volume

Table 2. Comparison of the synthetic approaches.

References

1. A. M. Kearney, L. Murphy, C. C. Murphy, K. S. Eccles, S. E. Lawrence, S. G. Collins and A. R.Maguire , *Tetrahedron*, **2021**, 88, 132091.
2. S. Bonciolini, A. Pulcinella and T. Noël, *J. Am. Chem. Soc*, **2025**, 147, 28523–28545.
3. J.L Howard, Q. Cao, D.L Browne, *Chem. Sci.,* **2018** ,9 , 3080-3094.

Acknowledgements

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- Dr Simon Lawrence
- Dr. Mark Reihill

Taighde Éireann Research Ireland
Pfizer

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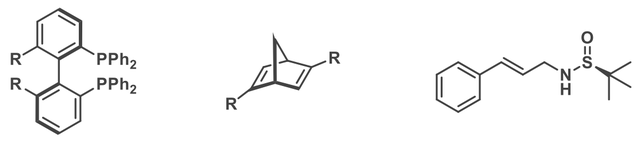
9

Enantioselective 1,4-addition on N–H containing compounds

Geoffrey Stosse, Mark Power, Katrina Mackey, Ching Ching Lam, Kendall N. Houk, Gerard P. McGlacken*
School of Chemistry

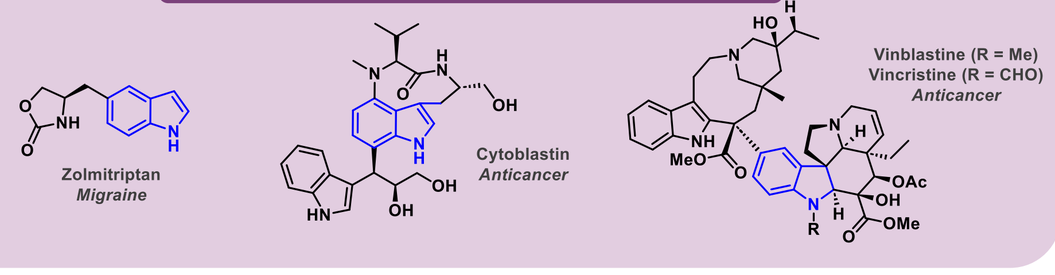
1. Introduction: Enantioselective Hayashi-Miyaura

Ligand =



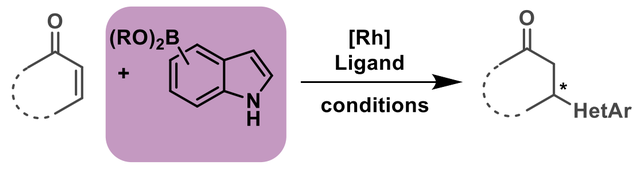
- The Hayashi-Miyaura reaction is a **C–C bond forming** reaction involving the β-position of α,β-unsaturated carbonyls[1]
- It boosts numerous advantages including:[2]
  - Utilises **mild reaction temperatures**
  - **No anhydrous** solvent (water is required)
  - Typically **high yielding** and **enantioselective**

Indole containing pharmaceticals



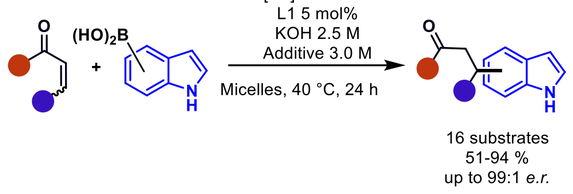
Current Limitations

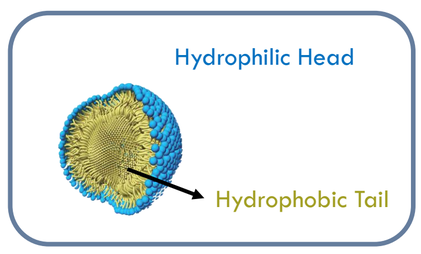
- ***Heteroaromatic* compounds** remain a challenge for asymmetric 1,4-addition reactions.[3] Especially indoles due to the challenges listed below:
  - **Unprotected N–H bonds:** these compounds are known catalyst poisons[4]
  - **Undesirable side reaction:** Protodeborylation
  - **Regioselective control** (vs. 1,2-addition)



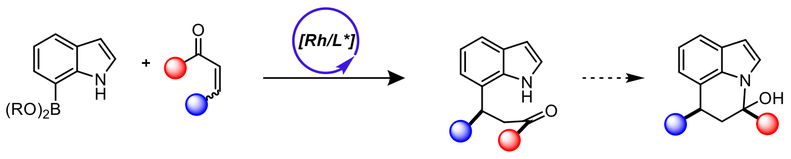
Aim: Can we develop a synthetic protocol using **Unprotected Indoles**?

2. Reaction Optimisation





- **An Highly efficient Hayashi-Miyaura Type Reaction** was developed using a wide range of **cyclic enones** and **indolyl-boronic acids.**
  - **All positions** of the indole backbone were accessed in **moderate to high yields, with excellent enantioselectivity**
  - Reaction carried out in **aqueous media** (micelles)



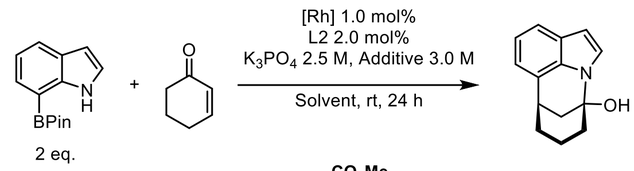
Unexpected reaction between **7-indolyl boronic acid** and **cyclohexenone** led to a **tandem reaction** generating a **new hemiaminal with two chiral centres with the exact same enantioselectivity**

Switching **boronic acid (€350/g)** to its **Bpin equivalent (€22/g)** leads to a **10x cost reduction:**[5]

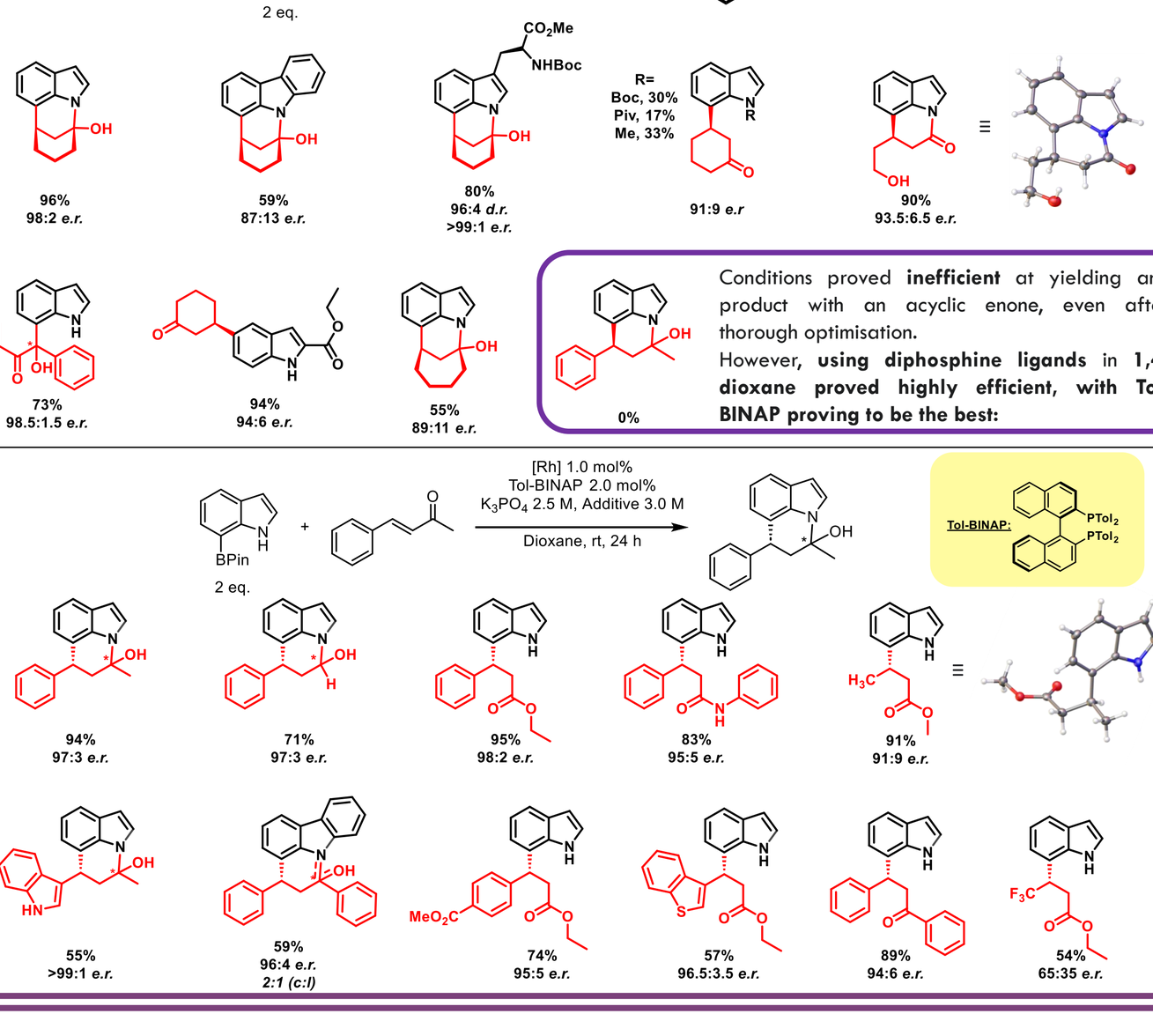
Entry	Cat. (mol%)	Ligand	Base (aq)	Temp. (°C)	Yield[a] (%)	e.r.[b]
1	2.5	L1	KOH	40	64	96:4
2	1.25	L1	KOH	25	80	97:3
3	1.0	L2	K_3PO_4	25	99	98:2

[a] Yield was determined by 1H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard
[b] Enantiomeric ratio was determined by chiral HPLC

3. Scope

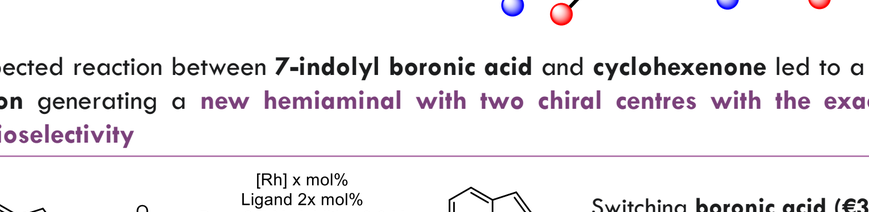


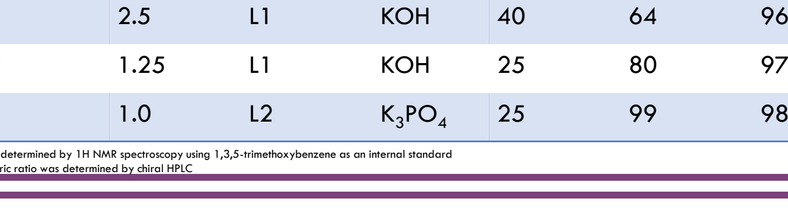
Reactions were performed at 0.3 mmol scale using optimised conditions. All yields are isolated. Stereochemistry is tentatively assigned after obtaining crystal structures and correspond [α] values.



4. Application to other N–H compounds

- Primary anilines more prone to side-reactions.[6]
- Minor changes allowed for successfully application of our methodology to anilines

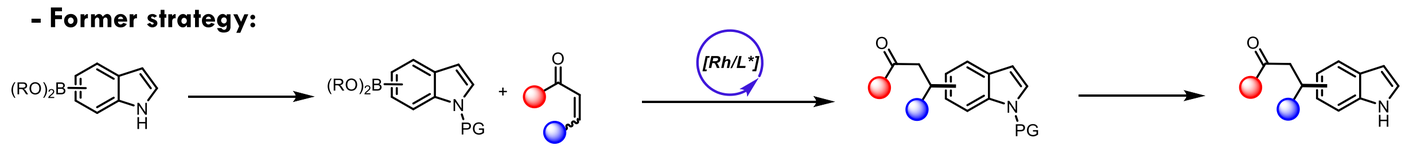




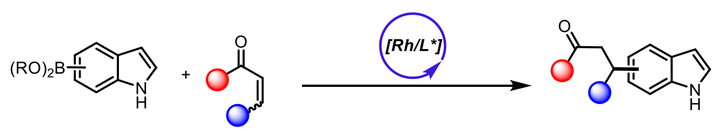
[a] HPLC conditions still being developed

5. Potential impact

- Former strategy:



- My work:



- ✓ 1 step
- ✓ Lower cost
- ✓ Lower environmental impact

6. Conclusion

To conclude, **we have developed a protocol for the asymmetric 1,4-conjugate additions to the phenyl backbone of indole, and aniline in excellent *e.r.* and high yields without the need of a protecting group.** This methodology is performed at mild temperature, in aqueous media and can easily be scaled up.

9. References

1. Clayden's Organic Chemistry, Chapter 22 Oxford University Press, Oxford, **2012**
2. *Tetrahedron Asymmetry*, **2016**, *27*, 513 - 588
3. *ACS Catal.* **2022**, *12*, 2434 - 2440
4. *Chemical Engineering Journal*, **2006**, *125*, 9-14
5. *Doug Discovery*. https://dougdiscovery.com/ (accessed 2025-08)
6. *Organometallics*, **2024**, *43*, 85–93

10. Acknowledgments

- Research Ireland
- UCC for the use of their facilities
- All staff, Post Doctoral researchers and other PhD students for their constant support

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10

Accessing P-stereogenic molecules via stereoselective elimination

Gian Reber, David Jones
School of Chemistry

What I am doing

My research project is about developing a new way of incorporating phosphorus atoms into medicinally-relevant molecules. My approach advances upon the state-of-the-art as it allows us to control the 3D configuration (stereochemistry) of the phosphorus atom with a high degree of precision. We have achieved this through the development of a new bio-derived reagent, based on the amino acid L-cysteine.

Why I am doing it

The stereochemistry of a drug molecule is highly significant as failure to control stereochemistry can result in a potential therapy becoming a deadly toxin. While there is significant recent interest in organophosphorus molecules with defined stereochemistry, the current state-of-the-art is severely limited in terms of how the compounds are made, as well as the potential scope of products that are possible to make. There is clearly an urgent need for new developments in this space. I am interested in not just meeting our current needs but also developing a robust method that will allow us to project forward to future demands in this space.

How I am doing it

We have taken a bio-inspired approach to achieving stereoselective synthesis by using a bespoke, novel reagent derived from the amino acid L-cysteine. By using our reagent, in combination with readily accessible bases, we can achieve traceless access to stereodefined organophosphorus compounds through a process we call stereoselective elimination. The use of L-cysteine as a feedstock for our process means that there is inherently a high degree of sustainability and scalability.

What I hope to achieve in the end

Using our approach, we hope to be able to make virtually any organophosphorus compound with excellent control of stereochemistry. We will show this through taking the products of our stereoselective elimination protocol and converting them to a wide range of functional molecules with potential relevance to medicinal chemistry and fine chemical production. We will also, in time, use enabling technologies such as continuous flow and photochemistry to make our processes more sustainable and suitable for production at scale.

What is the potential impact in the Pharma area

Fundamentally, we anticipate that this new method will become part of the standard toolkit of drug design as it is robust, easy to achieve and offers access to a wide range of high value molecules. Not only will it provide a convenient synthetic entryway to compounds of current interest, it will also serve as a useful strategy to make novel compounds of the future. This will allow for the development of new medicines, biological probes and functional materials.

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11

Smarter and Greener: Transforming Chromatographic Method Development Through Prediction

Ilaria Neri[1], Moriarty Merisa[2], Lucy Morgan[3], Adrian Davis[3], Melissa Hanna-Brown[1]

[1] School of Chemistry, University College Cork, Cork, Ireland
[2]Analytical R&D, Pharmaceutical Science Small Molecule, WR&D, Sandwich, U.K.
[3]Analytical R&D, Pharmaceutical Science Small Molecule, WR&D, Ringaskiddy, Ireland

What? I am doing

We are developing predictive tools that use experimental data and machine learning to forecast how compounds behave during chromatographic analyses. By combining chemistry knowledge with data science, we aim to build reliable models that can guide method development across different chromatographic systems, suggesting also more environmentally friendly conditions.

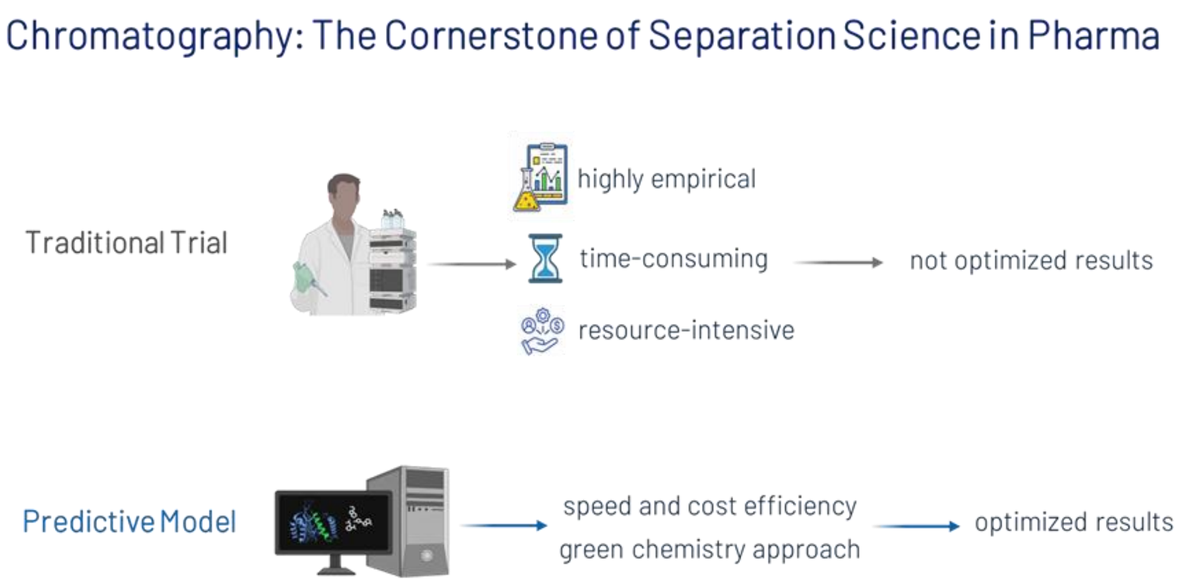

Figure 1. Graphic representation of motivation behind the study design.

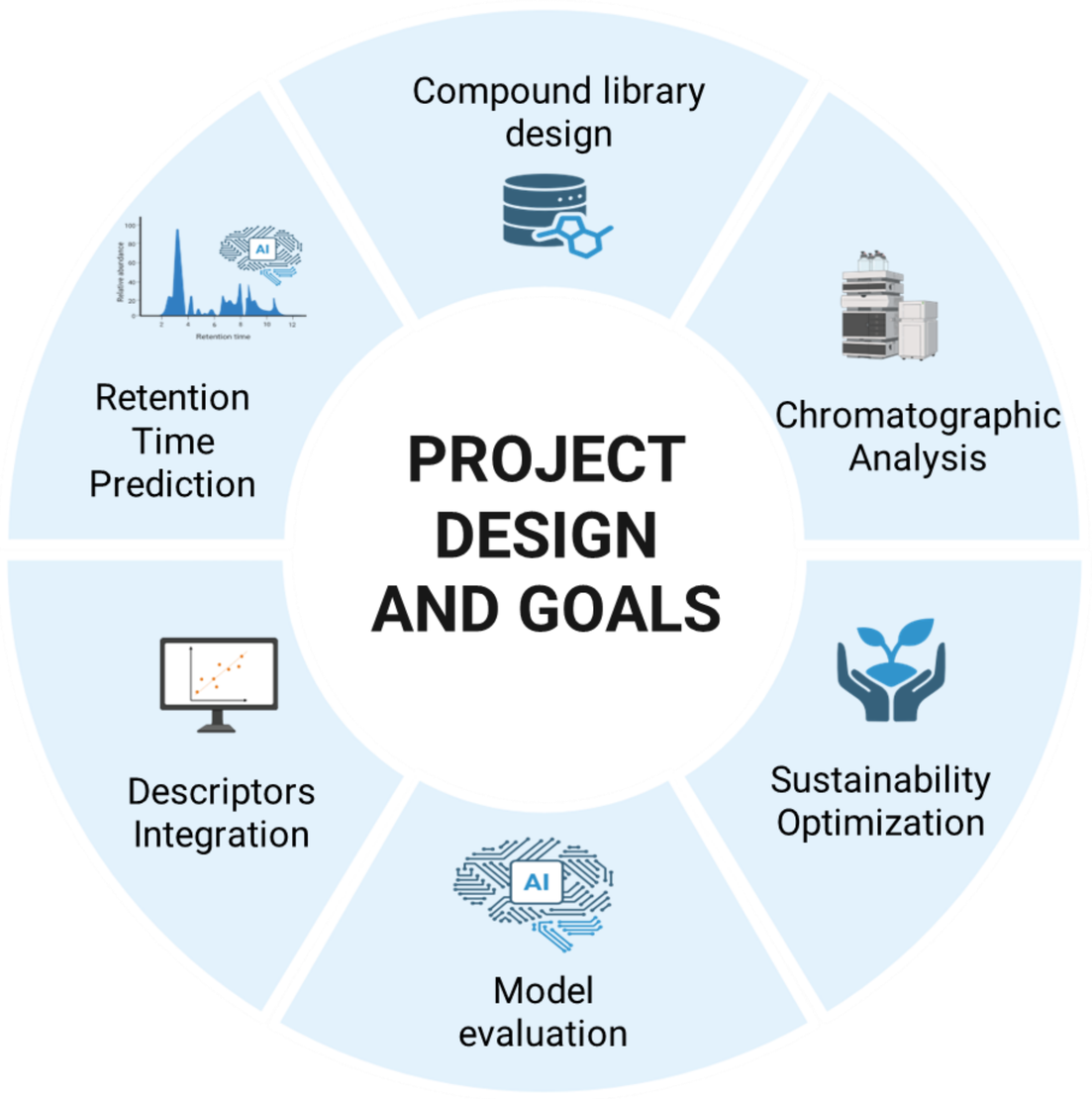

Figure 2. Graphic representation of project design and aims.

Why? I am doing it

Chromatographic method development is often slow, trial-and-error based, and resource-heavy. Data-driven predictions reduce the number of experiments needed, directly supporting sustainability goals. If the model can also recommend greener conditions, the environmental benefits become even greater, helping analytical and pharmaceutical laboratories minimizing environmental impact.

How? I am doing it

We're building a diverse, well-curated dataset of compounds tested under a range of chromatographic conditions, spanning both liquid chromatography (LC) and the more environmentally friendly supercritical fluid chromatography (SFC). Using this data, we train machine learning models that integrate molecular properties— including newly developed and more diverse molecular descriptors—along with operating parameters to predict retention times and help identify optimal, greener separation methods.

What I hope to achieve in the end

We aim to create reliable, broadly applicable models that accurately predict chromatographic outcomes across different chromatographic conditions. This will help scientists reduce experimental effort, shorten development timelines, and move toward more efficient and environmentally friendly analytical workflows.

What is the potential impact in the Pharma area

In the future, smart lab automation could seamlessly select the most suitable chromatographic conditions, perform comprehensive screening, and autonomously optimize all key parameters, accelerating the entire chromatographic method-development process. This vision enables more sustainable, data-driven decision-making across the pharmaceutical and biopharma industries.

Pfizer This research has received funding from Pfizer. A warmly acknowledgment to Prof. Melissa Hanna-Brown, for her mentorship throughout my research.

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12

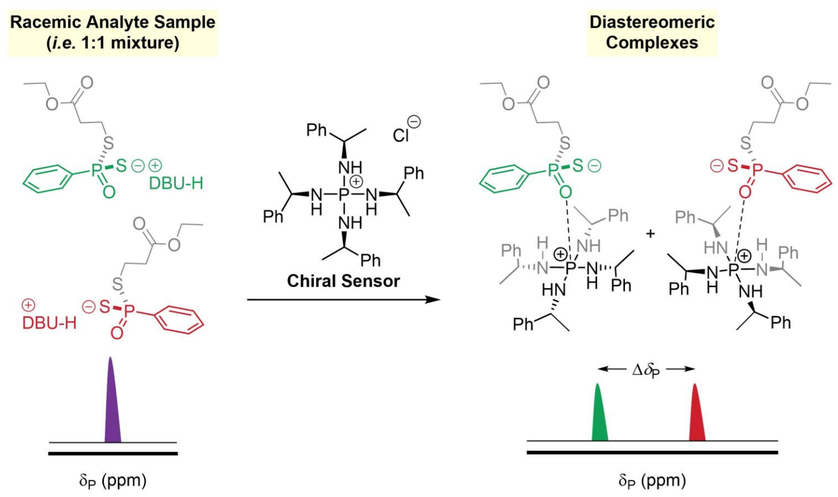
^{31}P NMR as a Fast Tool for Chiral Recognition of Phosphorus Compounds

Eimear Courtney[a,b], Emma Sheridan[a], Caoimhe Donovan[c], Smital Patil[a], Denis Lynch[a,b], Lorraine Bateman[a,b,c], David J. Jones[a,b*]

[a]School of Chemistry, [b]Analytical and Biological Chemistry Research Facility, [c]School of Pharmacy, University College Cork

What I am doing?

We are developing a rapid analytical method using ^{31}P NMR spectroscopy to determine the enantiopurity of chiral organophosphorus compounds without the need for time-consuming chromatographic techniques.

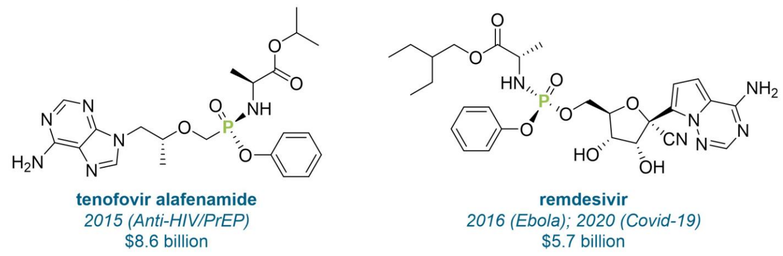


Scheme 1. *Enantiodiscrimination of racemic phosphonodithioate salts using ^{31}P NMR qNMR via the formation of diastereomeric complexes*

Why I am doing it?

The enantioselective recognition of chiral compounds is a vital and expanding area of chemical research, especially in pharmaceutical and agrochemical contexts, where different enantiomers can exhibit drastically different biological effects. Chiral organophosphorus compounds are key in drug development and catalysis.

Figure 1. *Examples of important chiral organophosphorus compounds*



Yet traditional methods for assessing enantiopurity, such as chiral HPLC or GC, require time-consuming method development, extensive purification, and generates waste, limiting high-throughput screening. A faster, more sustainable alternative is needed.

How I am doing it?

NMR spectroscopy offers a rapid, non-destructive alternative for enantiopurity analysis; however, enantiomers are indistinguishable in achiral environments. Introducing a chiral additive results in diastereomeric complexes with distinct chemical shifts ($\Delta\delta$), enabling enantiopurity measurement. Our method uses a chiral phosphorus-based sensor to reversibly form non-covalent complexes with chiral organophosphorus analytes, resulting in unique ^{31}P shifts without covalent derivatisation or complex preparation.

Development of Spectroscopic Method

Optimal spectroscopic method (OSM) established as ^{31}P qNMR in $CDCl_3$, 121 MHz, 300 K, no spin, 30-second delay (D1) and 32 scans (ns) as per literature precedent.

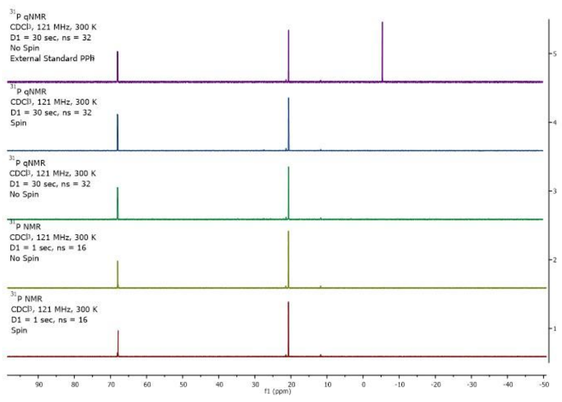
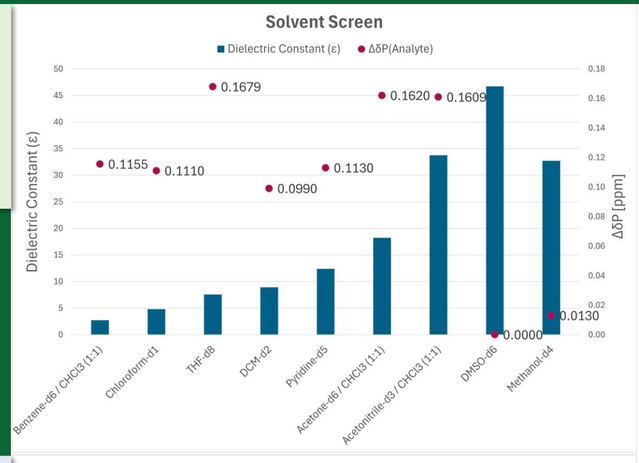
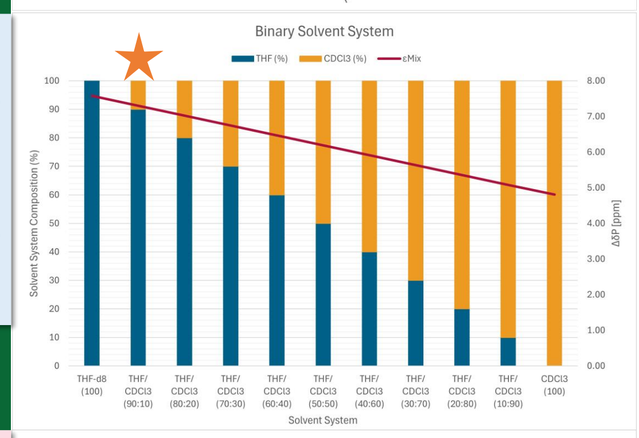


Figure 2. *Calibration of ^{31}P NMR spectroscopic parameters*

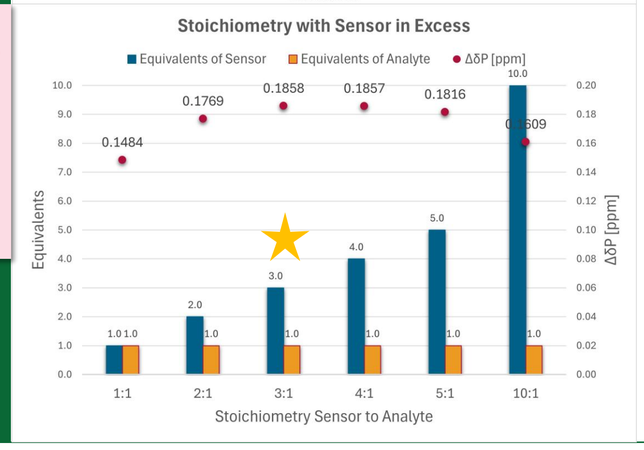
Solvent



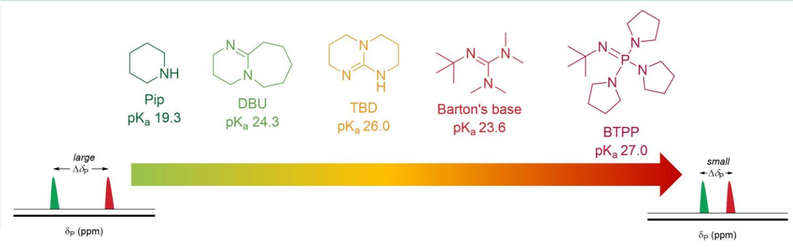
Binary Solvent System



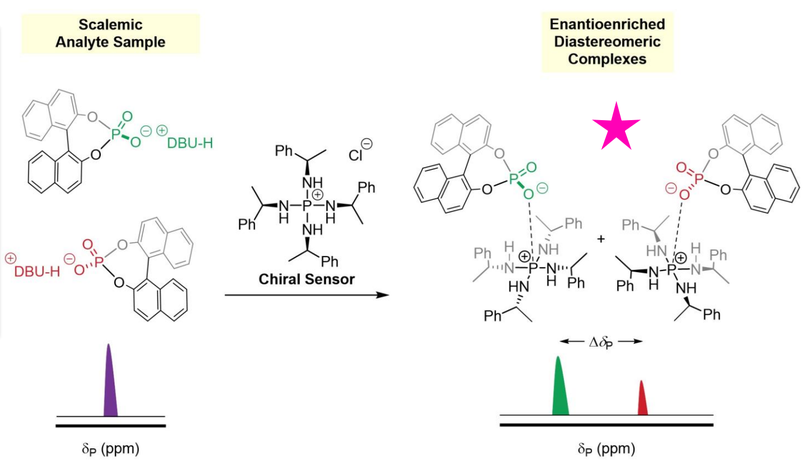
Stoichiometry



Anion Effect

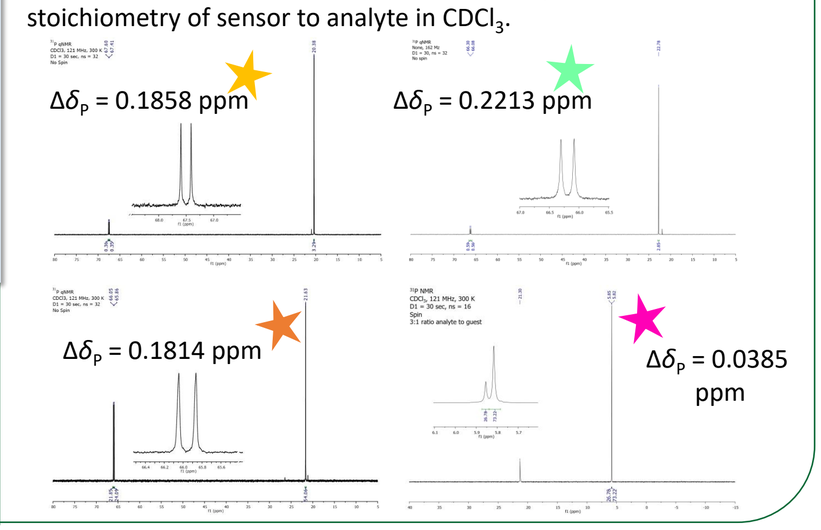


Scalemic Example



Key Results

The optimal method thus far: 0.0343 M sample concentration, 3:1 stoichiometry of sensor to analyte in $CDCl_3$.



What I hope to achieve in the end?

Our goal is to deliver a simple, generalisable platform for rapid enantiopurity analysis that reduces time, cost, complexity and environmental impact compared to traditional chromatographic methods, supporting efficient screening in synthetic and pharmaceutical workflows. Through thorough study of this method, in time we aim to create a 'Hitchhiker's Guide to ^{31}P Enantiodiscrimination' that can be applied to virtually any chiral organophosphorus compound.

What is the potential impact in the Pharma area?

This method could accelerate drug development by enabling high-throughput stereochemical analysis of chiral organophosphorus compounds (*e.g.,* anti-virals, phosphorothioate oligos and immune therapies), improving decision-making, and reducing development timelines. It offers a non-destructive alternative to chiral chromatography, enhancing efficiency and sustainability. Future work aimed at transferring our technology to benchtop NMR opens up accessibility to SMEs and other resource limited settings.

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13

Solubility of Gefitinib in Organic Solvents: Experimental and Theoretical Investigation of Stable and Metastable Forms

Barry Lynch, Jerry Heng, Eric Moore, Vivek Verma
School of Engineering and Architecture, School of Chemistry

INTRODUCTION

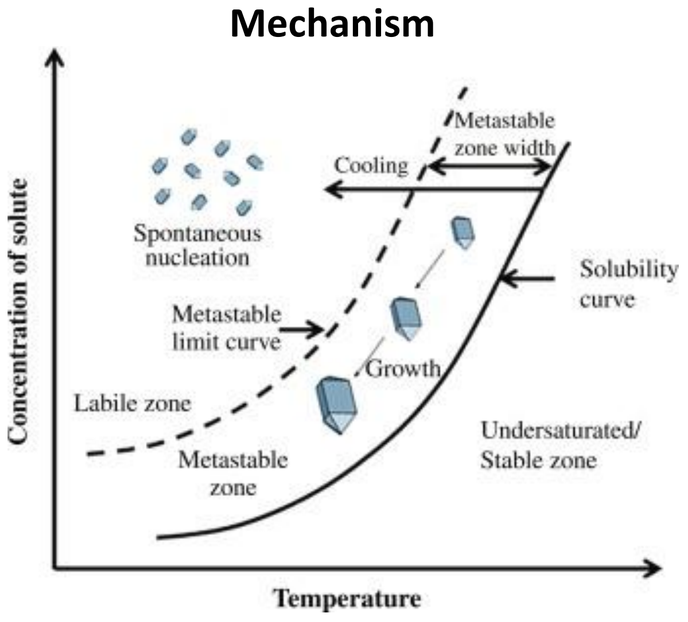
What is Crystallisation?

- A separation & purification technique during the phase transformation of a solute from a dissolved solution to an ordered solid crystal.

Why is it Important?

- > 90% of active pharmaceutical ingredients (API's) are crystallised.
- API's can adopt different forms (polymorphs).
- Metastable (unstable) drug forms generally enhance solubility Vs traditionally marketed 'stable' forms.

Mechanism



Research Focus:

- Gefitinib – small molecule API

1. Thermodynamic properties of stable form I.
2. Solubility in organic solvents (283.15 to 313.15 K).
3. Best fit semi-empirical models

Future Objectives:

- Crystallise metastable (form II) from marketed stable (form I).
- Apply 'Research Focus' steps 1-3 to form II
- Develop a solubility phase diagrams & crystallisation regimes.

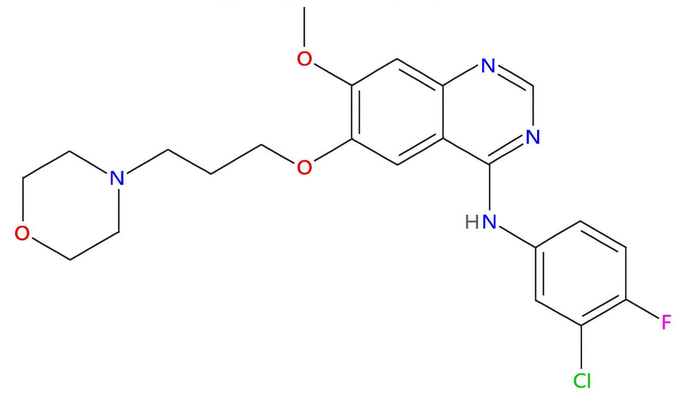
MATERIALS AND METHODS

Solvents used:

- Acetonitrile
- Ethyl Acetate
- Toluene
- 2-MeTHF

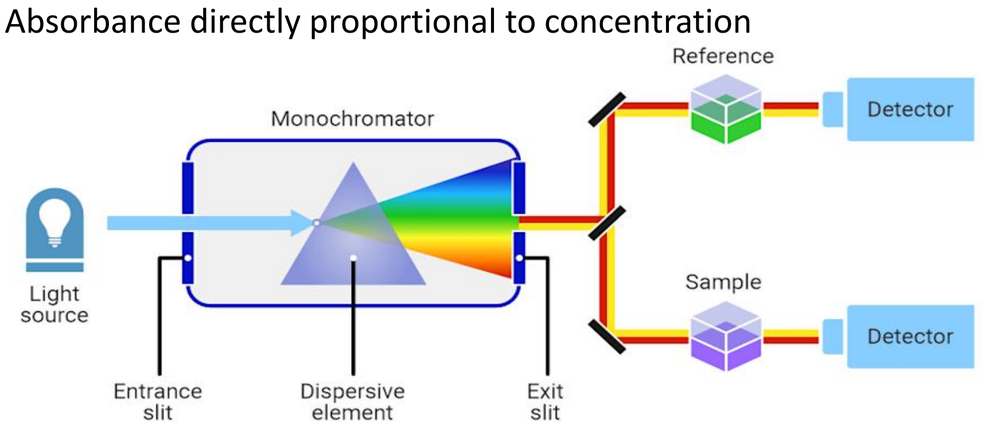
Gefitinib

$C_{22}\ H_{24}\ ClFN_4O_3$



Solubility:

- UV Spectroscopy
- Beer Lamberts Law principle:
  - Absorbance directly proportional to concentration



Modelling: Semi-empirical

- Thermodynamic solubility
- Models studied for best-fitting:
  1. Van't Hoff
  2. Apelblat
  3. **Yaws**
  4. λh
  5. Wilson
  6. NRTL

Google colab
Python coding
Data analysis

RESULTS

Thermodynamic analysis

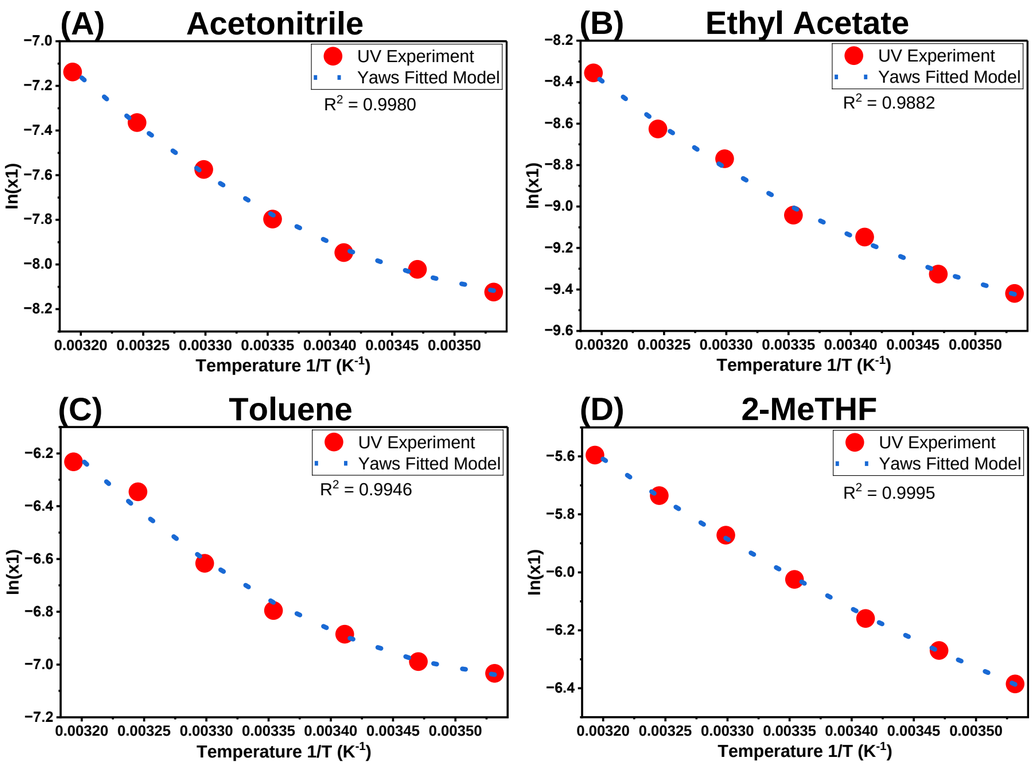


Figure 1. Temperature-dependent solubility of gefitinib from Fig. (A) to (D), in 4 selected organic solvents from 283.15 to 313.15 Kelvin, plotted as K^{-1} Vs ln(x1).

Solid state analysis

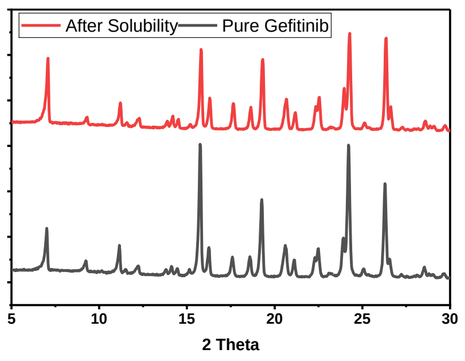


Figure 2. PXRD patterns

Pre/post solubility experiments in acetonitrile at 283.15 K confirms solid drug form remains unchanged

Crystal morphology analysis

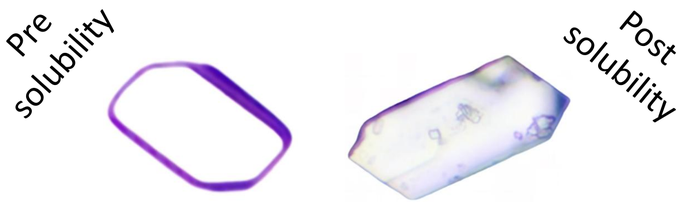


Figure 3. Gefitinib crystal habit.

Crystal habit unchanged post solubility

Data analysis

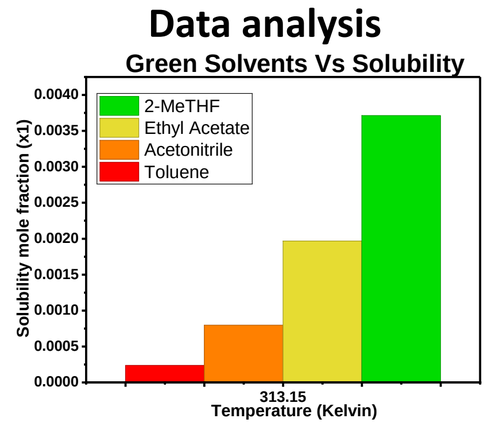


Figure 4. Green Analysis

Comparison of solvents at 313.15 K confirms greener solvents in this study display higher solubility with gefitinib

Polarity

Solvent polarity (low to high)
Toluene < 2-MeTHF < Ethyl Acetate < Acetonitrile confirms that the solubility scale of gefitinib in these solvents does not correlate to polarity

Best fit model = Yaws Equation

R^2 - Coefficient of Determination (highest)

$$\ln x_1 = A + B/T + C \ln T \qquad \text{Equation (1.0)}$$

Where:

x_1 = Gefitinib mole fraction solubility.
T = Temperature in Kelvin (K)
A, B and C are solubility correlated fitting parameters

CONCLUSION

- Gefitinib solubility presents strong temperature dependence in order: Toluene>Acetonitrile> Ethyl Acetate > 2-MeTHF (greenest).
- Solubility results and solvent polarity scales do not correlate.
- Morphology unchanged post solubility
- Yaws equation provided best semi- empirical fit (highest R^2)

REFERENCES

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- M. Ranjbar et al., Multidisciplinary Digital Publishing Institute, 18, (2025) 314.
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14

Quality by design to approach spay freeze drying technology to food and pharmaceutical applications

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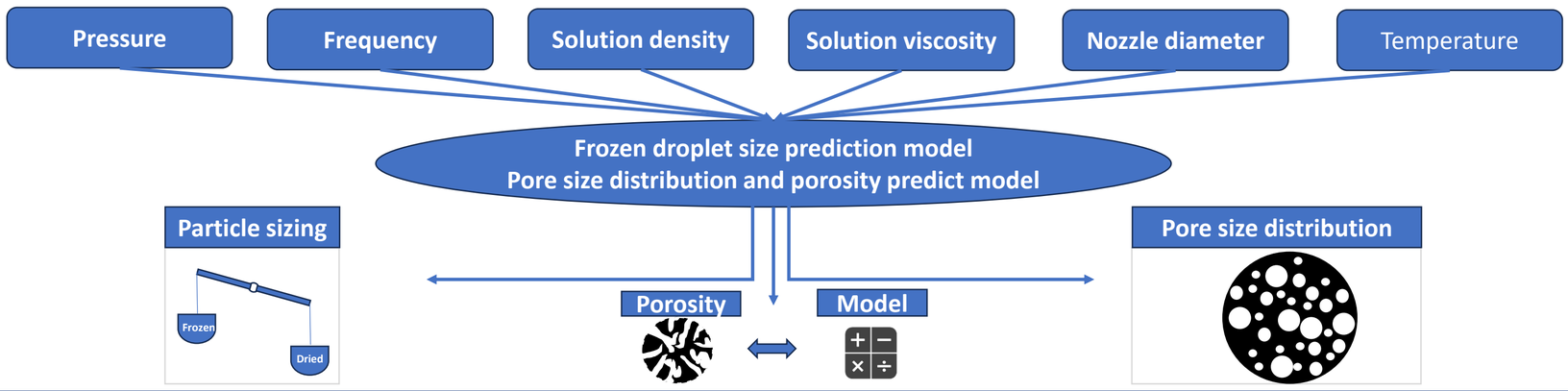
c School of Food & Nutritional Sciences, University College Cork, Cork, Ireland

d Teagasc Food Research Centre, Moorepark, Co. Cork, Ireland

What I am doing

A modelling approaches to predict spray freeze dried particle size distribution and particle porosity

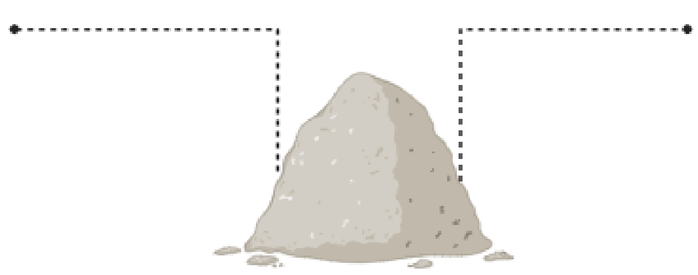


Why I am doing it

Particle size and porosity are two of the most important parameters in drug development.

Particle size

- Drug delivery
- Processing
- Dosage flexibility



Particle porosity

- Drug loading capacity
- Determine dissolution
- Aerosolization behavior

Figure 1 Powder of spray freeze dried particles
Image is generated by BioRender

How I am doing it

- A lab-scale experimental spray freeze drying process was established as figure 2
- A mathematical model was developed and validated by sucrose solution in prediction of frozen droplet size
- A second mathematical model was developed to predict particle porosity and being validated.

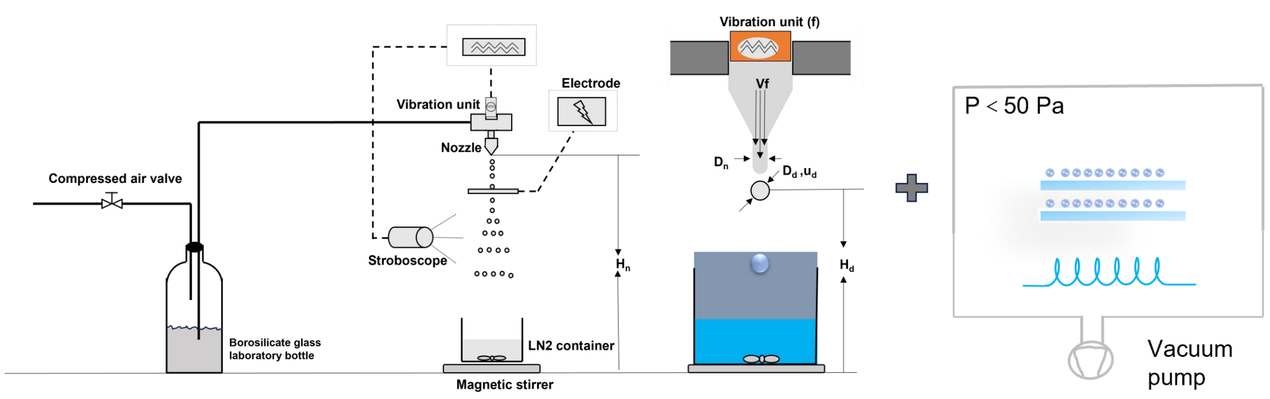


Figure 2 Spray freeze to the vapour over LN2 (SFV/L) + Conventional freeze drying

Frozen droplet size prediction model

$$\frac{P_1}{\rho g} + h_1 - h_2 = \frac{v_f^2}{2g}\left(1 - \frac{D_n^4}{D_1^4} + \frac{D_n^2}{2D_1^2} + \frac{7D_n^2}{5D_p^2}\right) + \frac{32\mu L D_n^2}{\rho g D_p^4} v_f$$

Pore size distribution and porosity prediction model

$$J(T) = K(T)e^{\left(-\frac{\Delta G^*}{K_B T}\right)} = n_w \frac{k_B T}{h} A e^{\left(-\frac{16\pi\sigma^3 T_m^2 f}{3k_B T (n_{ice} l_f)^2 \Delta T^2}\right)}$$

$$G_{ice} = \frac{\beta D_1 L_{s1}}{aRT_m T}\Delta T$$

What I hope to achieve in the end

The validated models can be applied to a more complex industrial-relevant formulation to check its utility.

Validated Particles size prediction model

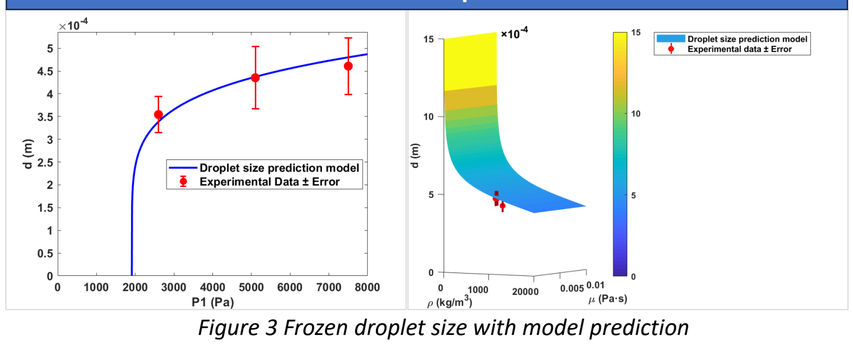


Figure 3 Frozen droplet size with model prediction

Validated Pore size distribution and porosity prediction model

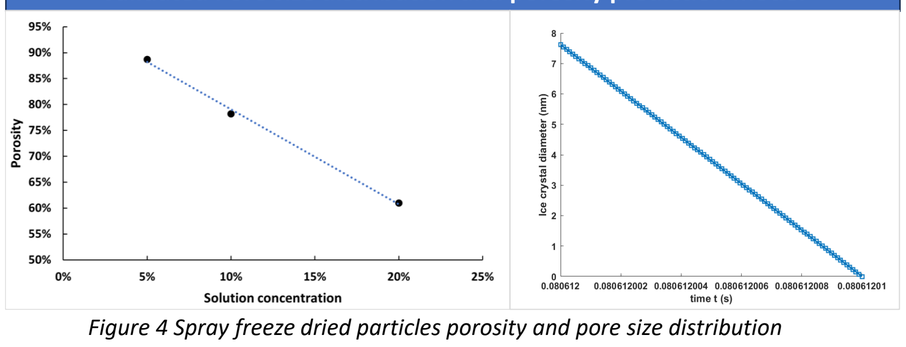


Figure 4 Spray freeze dried particles porosity and pore size distribution

Figure 5 Formulations development
Image is generated by BioRender

What is the potential impact in the Pharma area

Validated model can be a guidance for production of SFD particles with desired characteristics.

Acknowledgement

The financial supports from China Scholarship Council and Taighde Éireann – Research Irelandare acknowledged gratefully.

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AI-Driven Supervisory Control and Digital Twin Framework for Smarter Bioreactor Systems

15

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School of Engineering and Architecture, School of Microbiology
SUSFERM / CENTRE FOR SUSTAINABLE FERMENTATION

INTRODUCTION

- Bioprocesses are becoming more complex
- Daily Changes
- Cells Behave unpredictably
- Hard to maintain stable DO, substrate, biomass
- Need better prediction and adaptive control

What Is a Digital Twin?

- Virtual replica of the bioreactor (built using equations)
- High-fidelity mechanistic models
- Can run safe simulations (without risking a real batch failure)
- Powerful tool for optimization and control design(extreme oxygen limitation , sudden disturbance)

Limitations of Traditional Control

A simple feedback controller — What's PID Controller ?

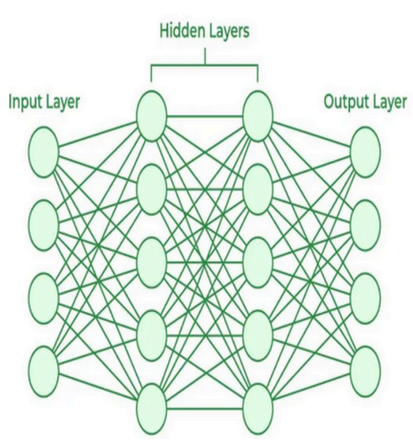
- Keeps a process variable at a set point
- Very common in industrial control
- Adjusts the actuator based on the error
- Easy to implement and low-cost
- But limited in complex biological processes

$$u(t) = K_p\left(e(t) + \frac{1}{T_i}\int_0^t e(\tau)d\tau + T_d\frac{d}{dt}e(t)\right)$$

- PID is **process-agnostic**
- Wide range of biological time scales
- Non-linear behavior (exponential growth, oxygen limits)
- Leads to process variability & instability

How ML & AI Improve Control

- Learns hidden biological patterns
- Predicts future behavior
- Enables proactive adjustments
- Acts as a **managing layer**



What My Project will develop ?

- Hybrid model: mechanistic + machine learning
- Predict how the system behaves
- Detect changes early
- Step toward a smart autonomous bioreactor

Phase 1: Building the Digital Twin

- Model cell growth & substrate uptake
- Model oxygen transfer
- Include sensors & controller
- Stress-test under many scenarios (e.g. low oxygen ,different feeding rate)

Pioreactor : small-Scale Bioreactor Platform

- Small, affordable bioreactor for research and teaching
- Built on **Raspberry Pi** for automation and control
- Real-time optical density (OD) monitoring
- Online platform to monitor & control experiments
- Scalable - run multiple units as a cluster

Phase 2: Validation with Real Data

- test with **Pioreactor**
- Compare predictions with real measurements
- Adjust parameters to improve accuracy
- Validate Digital Twin behavior

Expected Outcomes

- Intelligent and predictive control
- More stable cultures
- Improved reproducibility
- Easier scalability to larger reactors

Pharmaceutical Impact

- Supports Industry 4.0/5.0
- Reduces process variability
- Lowers production cost
- Open-source → accessible to industry + academia

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Sustainable Biogas Upgrading: Coupling carbon capture and valorisation of algal biomass for the pharma/biopharma sector

Muhamad Nabeel Haider, Archishman Bose, Linda O'Higgins, David M. Wall, Jerry D. Murphy
School of Engineering and Architecture

What I am doing

I am currently a 3rd year PhD student in the research project CABBBIE (Developing Cascading Biomethane Biochemicals and Biofertiliser Systems for a Circular Bioeconomy in Ireland) project funded by SEAI and DAFM. My research is entitled "Optimisation of microalgae biorefinery for photosynthetic biogas upgrading". The research involves bioprospecting and characterising indigenous microalgae for photosynthetic biogas upgrading, analysis of metabolic pathways and optimising their use for high-value applications such as in food and biopharmaceutical industries.

Why I am doing it

This work aims to utilise Ireland's local bioresources to enable a circular bioeconomy and meet Ireland's sustainability targets. It employs indigenous microalgae to develop a sustainable biorefinery capable of producing high-value metabolites which in turn could reduce dependence on imported high-value compounds such as bioactive compounds for pharma/biopharma applications.

How I am doing it

First step involved site selection for isolating algae based on pH, nutrient composition, and temperature, followed by purification by streak plate method and micro pipetting, with microscopic analysis to confirm purity. Genetic identification was done using 16S, 18S, and 23S rRNA primers. Optimisation strategies include manipulating nutrient profile, and adaptive laboratory evolution to boost the activity of algae at genetic level. Standard lab protocols are used for analysis of enzyme activity and metabolites (lipids, carbohydrates, proteins, and pigments). The prospects involved the whole genome sequencing and metabolomics of the algae.

What I hope to achieve in the end

The goal of the study is to determine the feasibility of locally isolated microalgae for photosynthetic biogas upgrading in Ireland and the valorisation of algal biomass for production of high-value metabolite for food and (bio)pharmaceutical applications. The specific objectives include

- Effective biogas upgrading
- Maximisation of microalgae growth and
- Maximisation of high-value metabolite content including protein (such as phycocyanin) and other bioactive compounds (such as chlorophyll a, chlorophyll b, and carotenoids).

What is the potential impact in the Pharma area

- This study will pioneer the application of native algal strains for carbon capture and utilisation via photosynthetic biogas upgrading.
- The extraction of bioactive compounds having antioxidant, antibacterial, and anti-inflammatory properties and polyunsaturated fatty acids, proteins and phycobiliproteins can lead towards sustainable biopharmaceutical products with their established therapeutic roles against obesity, diabetes, liver fibrosis, and cardiovascular diseases.
- Integration of this technology with the high-value metabolites will improve the supply chains of critical high-value metabolites for the local pharma industry.

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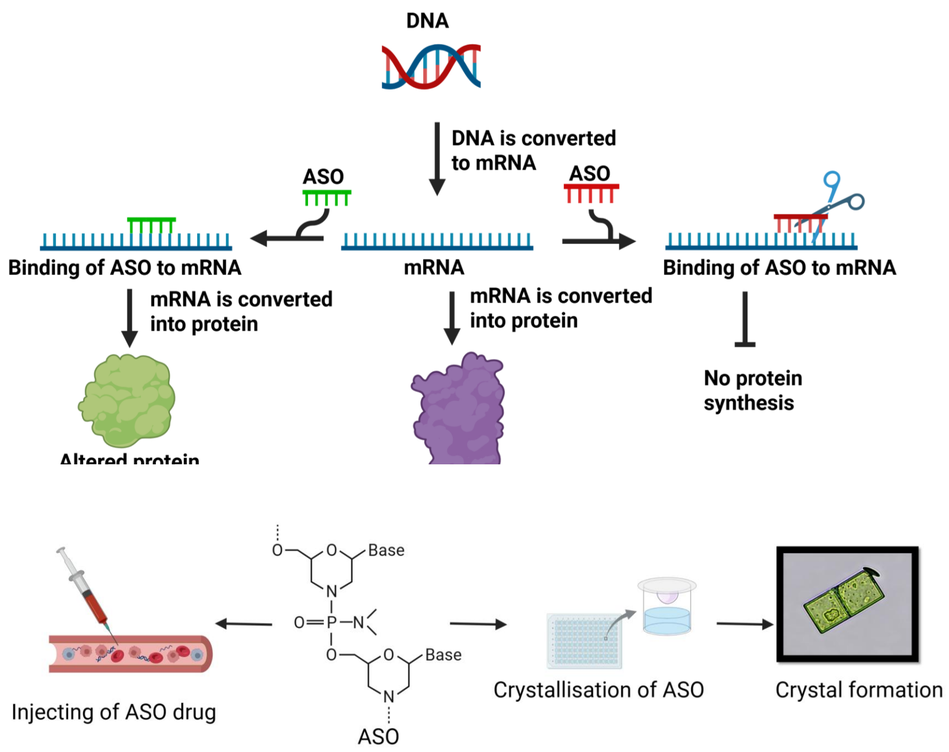
Template-Assisted Crystallisation of Antisense Oligonucleotides: A Solubility-Guided Approach for Sustainable Purification

Sashank Bharatham Vijayaraghavan[1], Anita R. Maguire[2], Vivek Verma[1]
[1] Department of Process and Chemical Engineering, [2] School of Chemistry and School of Pharmacy, UCC,
Email: 122109658@umail.ucc.ie
School of Engineering and Architecture

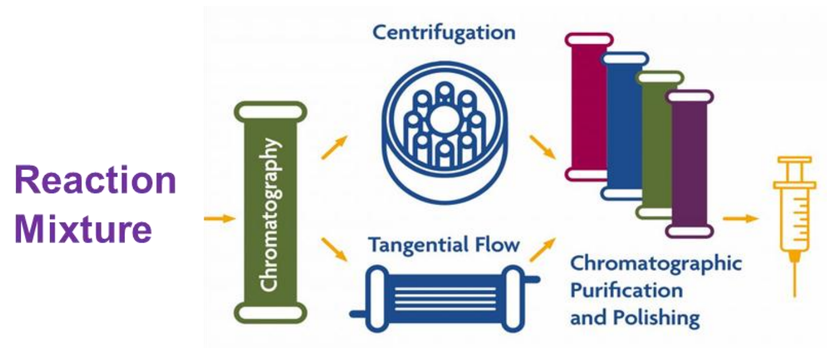
What I am doing

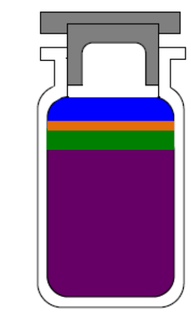
- Antisense oligonucleotides (ASOs) are short, synthetic strands of DNA or RNA that bind specifically to RNA in cells to block the production of proteins or correct genetic mutations.
- Design a protocol for template-assisted crystallisation to purify ASO drugs more sustainable, and cost-effective.



Why I am doing it

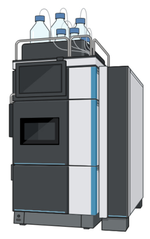
- Current antisense oligonucleotides manufacturing face multi- step purification bottlenecks, as they heavily rely on expensive and unsustainable chromatography which leads to high cost, and limiting scalability.





Cost Breakdown:
Upstream (10%)
Process (5%)
Others (5%)
Downstream (80%)

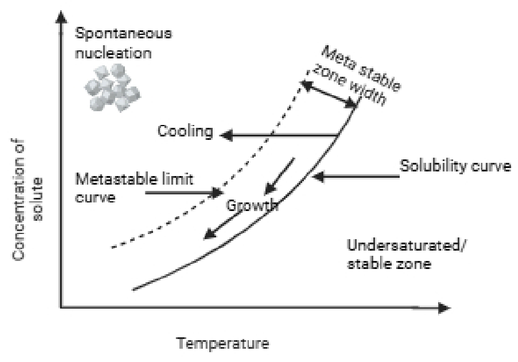
- Single main unit operation, recyclable solvents
- Lower material and energy consumption
- Scalable, batch or continuous, lower cost per kg



- Multiple unit operations, high solvent and resin use
- High operating and capital costs
- Energy- and waste-intensive, limited scalability

How I am doing it

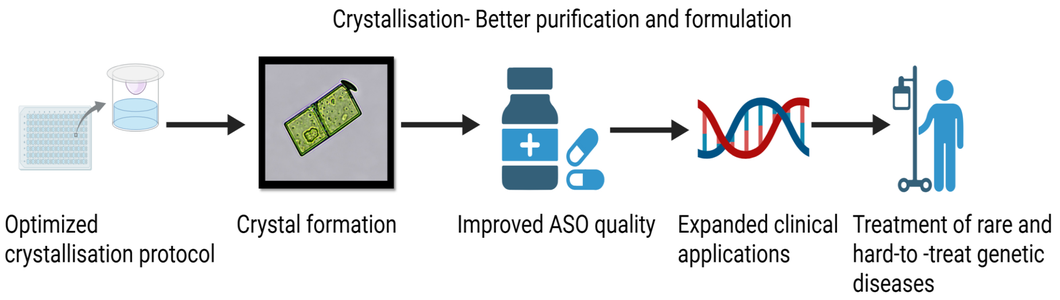
- I aim to construct detailed and robust solubility phase diagrams for mono-, di-, and trinucleotides, the fundamental building blocks of ASOs, across varied solvents.
- These diagrams guide the selection of optimal crystallisation conditions.
- In future, I plan to apply a templated crystallisation approach to direct nucleation and control crystal growth.



Sitting drop crystallisation

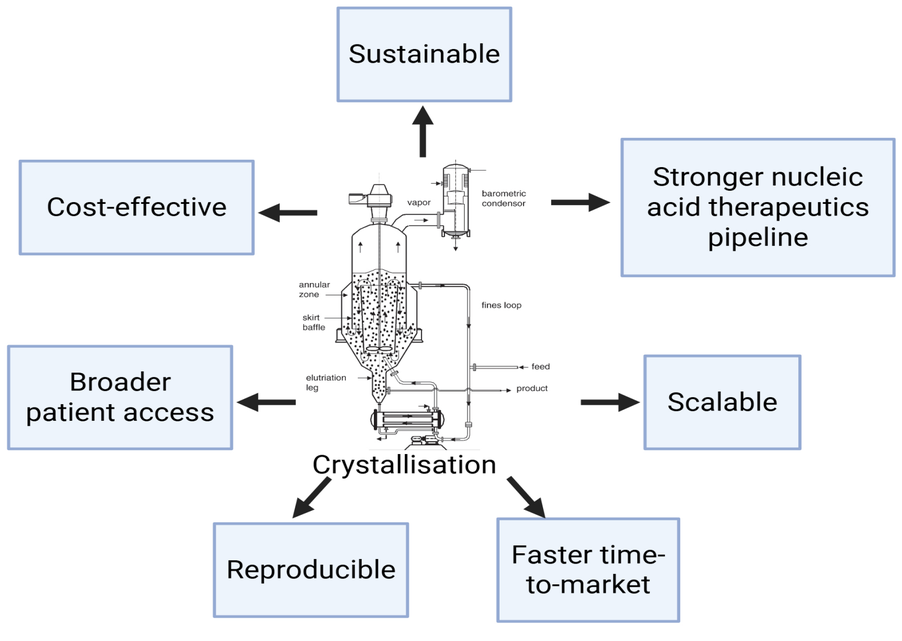
What I hope to achieve in the end

- I aim to establish robust, reproducible purification strategies for ASOs by controlling crystallisation parameters to optimize crystal quality attributes such as size, morphology, polymorphic form, solubility, and chemical stability.
- Achieving consistent, high-quality crystals will enhance formulation, bioavailability, and delivery, enabling scalable manufacturing.



What is the potential impact in the Pharma area

- Optimized crystallization and formulation strategies will improve manufacturing scalability, reproducibility, and cost-efficiency, reducing reliance on multi-step chromatographic purification.
- This can accelerate time-to-market, broaden patient access, support pipeline diversification, and strengthen the knowledge base for rational design of nucleic acid therapeutics.



Acknowledgements

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18

A Sheet-Based Contact-Aided Compliant Force-Limiting Mechanism for Microneedle Patches

Yiran Wang, Guangbo Hao
School of Engineering and Architecture

What I am doing

We developed a force-limiting microneedle applicator that ensures complete insertion by limiting the maximum input force. The proposed design offers sensor-free operation, compactness, portability, low cost, and reusability.

Why I am doing it

Currently, most microneedles are administered via thumb pressure. While convenient, this method cannot limit the maximum applied force. Excessive force may cause microneedle fracture, thereby reducing the drug delivery efficiency. More severely, it could lead to the microneedles contacting nerves and causing pain. Therefore, the design of a microneedle applicator capable of limiting the maximum input force is of paramount importance.

How I am doing it

The applicator achieves the function of limiting the maximum input force through a compliant force-limiting mechanism, which consists of two parts: a compliant sheet and a contact rod. When the contact rod contacts the flexible sheet, it induces deformation of the sheet. The deformation generates a reaction force acting on the contact rod, which is the injection force for microneedle. The injection force increases continuously as the contact rod keeps contacting the sheet over the moving process. When the contact rod detaches from the sheet the maximum allowable injection force is reached, and then the force decreases instantly to zero.

What I hope to achieve in the end

Based on the proposed design, a European patent has been filed and has successfully entered the second phase. We anticipate a successful grant of the patent, followed by the commercialization of the designed force-limiting applicator. The ultimate goal is to translate this design into a tangible product that provides a practical solution for microneedle injection.

What is the potential impact in the Pharma area

The proposed invention can be used for microneedle applicators (or similar medical applications), which can ensure that the microneedles are completely injected into the skin for drug delivery without causing pain to patients, via autonomously regulating the maximal reaction/injection force (therefore injection displacement) to avoid touching skin nerves. The device is compact and can be operated by two fingers by pushing the end-effector towards to the targeted object such as finger skin.

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Quality by Design Approach to Medical Device Polymer Bead Process Optimisation

19

Ayse Kont[1], Gareth Bell[2], Abina Crean[1]
[1]School of Pharmacy, University College Cork, Ireland
[2]Boston Scientific Cork

What?

A **collaborative project** with Boston Scientific Cork on **identifying critical quality attributes** of a **hydrogel bead** synthesis of a product in BSC's portfolio.

Boston Scientific — School of Pharmacy, University College Cork

1

CHEMISTRY PATHWAY:

PVA → PVA-macromer → Hydrogel beads → Purification & Sizing → Iodinated hydrogel beads

Why I am doing it

This investigation aims

- to benefit the existing products in understanding its features
- possible **expansion of its applications**
- **understanding of chemical processes used in combinational medical devices, a converging field of pharma and medical device industries**.

This advanced collaboration outside of the scope of traditional medical device research fostered a dynamic and interactive learning environment for both parties.

2

CHALLENGE:

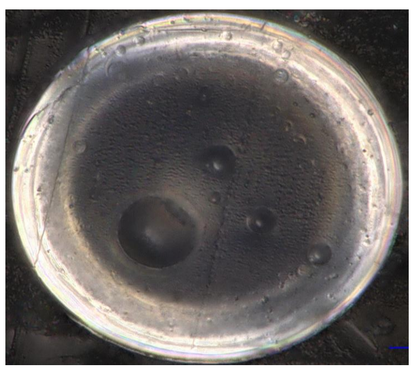
M0 and M1 beads exhibit **subtle differences** during iodine coupling despite being **synthesized** in the **same** reaction.

How I am doing it

Through detailed (1) **analytical analysis**, we uncovered potential reasons for variability in the process during bead synthesis.

→ ***Presence of pores*** on and in beads leading to the possible variation seen in iodine coupling.

→ ***Pores can be traced back to the bead synthesis processing step***



This insight brings us closer to identifying the **root cause with** (2) **Design of Experiment.**

→ Identification of **critical parameters** in bead synthesis to **control** pore

3

ACTION: Characterization of **hydrogel** beads

Chemical	Physical
Thermal analysis: TGA, DSC	Surface structure: Confocal microscopy
Stability testing: DVS	Size distribution: microscope, Mastersizer
Chemical structure: FT-IR, Raman	Internal structure: sectioning

What I hope to achieve in the end:

The comprehensive **review of both process and product** led to the implementation of **value improvement practices** at multiple stages of production. These enhancements not only streamline operations but also contribute to **long-term sustainability and cost-effectiveness.**

4

FUTURE IMPACT:

Deeper understanding and possible expansion of features/applications of hydrogel beads.

Understanding and prevention of occurrences in chemical processes in the Medical Device Space.

What is the potential impact in the Pharma area

Combinational medical devices are products of the converging field **of pharmaceutical and medical device industries** and require special attention in terms of quality. This requires adequate analytical techniques to guarantee quality.

→ seamless expansion of products in this converging field

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20

Silica Powders as Novel Excipients for Biopharmaceutical Stability: Drying and Storage

Khaled ElKassas, Abina Crean, Anne-Marie Healy
School of Pharmacy

Why

Protein biopharmaceuticals depend on a complex, structure to function. Interfacial interactions can result in protein destabilisation, which is more likely to occur in an aqueous milieu. Thus, stabilisation of proteins during manufacturing, transport, and storage, is achieved via drying processes, such as freeze-drying or spray-drying.

Spray drying is inherently stressful to proteins, with more complex ones being more sensitive to the thermal and mechanical stressors. Currently, spray drying of biologics is limited to smaller, more stable peptides lacking quaternary structure. To safeguard proteins during and after spray drying, sugars are typically used to form an amorphous matrix. However, the sugars can begin to crystallise under the effects of moisture during long-term storage, thus losing their protective properties. Silica has been shown to stabilise drug formulations by preventing crystallisation and protecting dried materials from the effects of moisture.

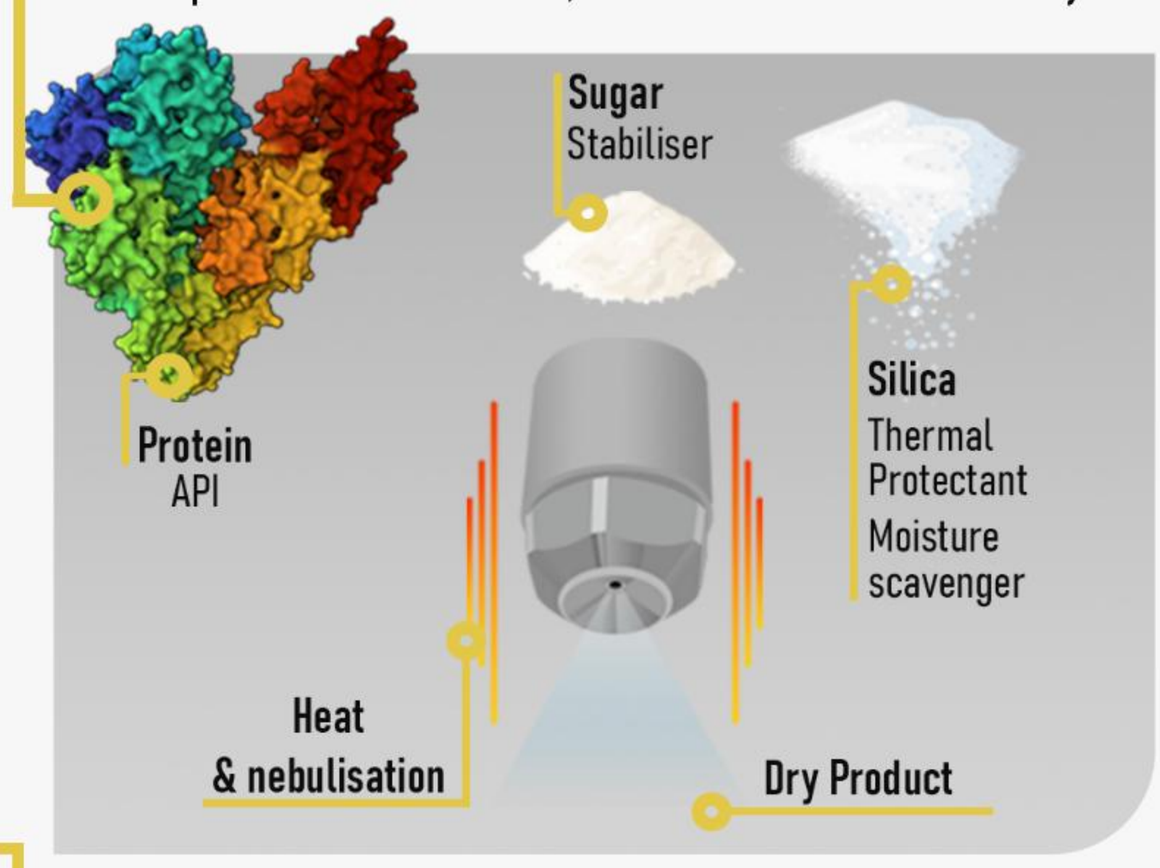
What

The goal was to obtain protein formulations that are stable during spray drying and long-term storage. By including silica powders in the pre-processed formulation, the protein could adsorb or become occluded within the silica's cavernous structure thus protecting the protein from thermal and mechanical stresses.

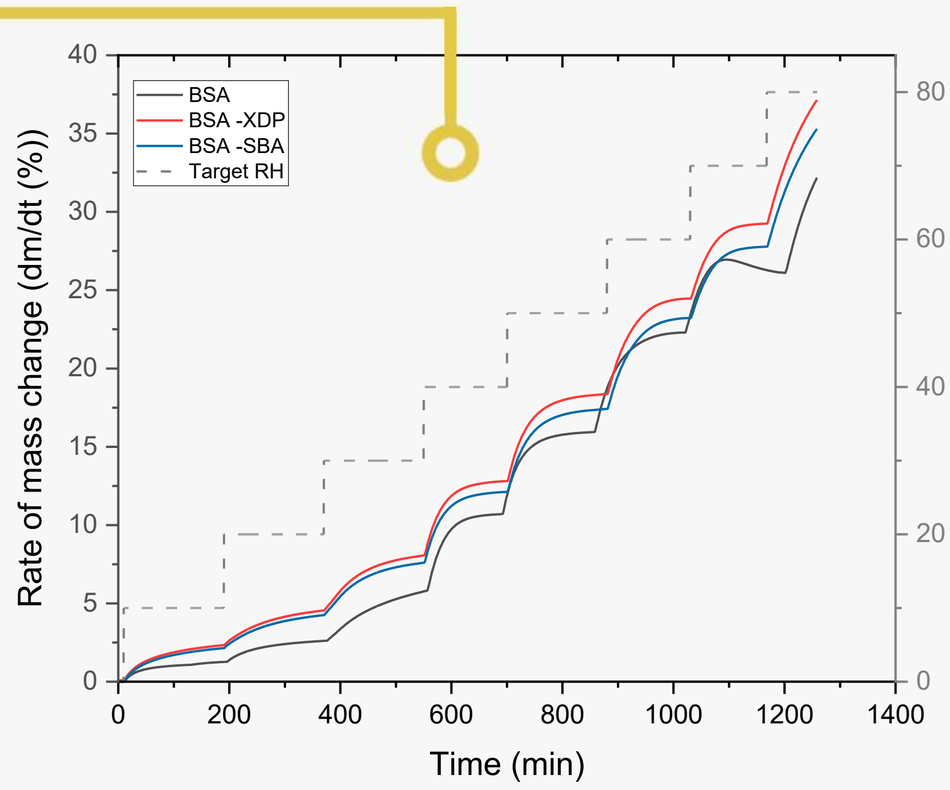
During long term storage the silica could act as a moisture scavenger, preventing excess moisture and humidity from destabilising the formulation.

How

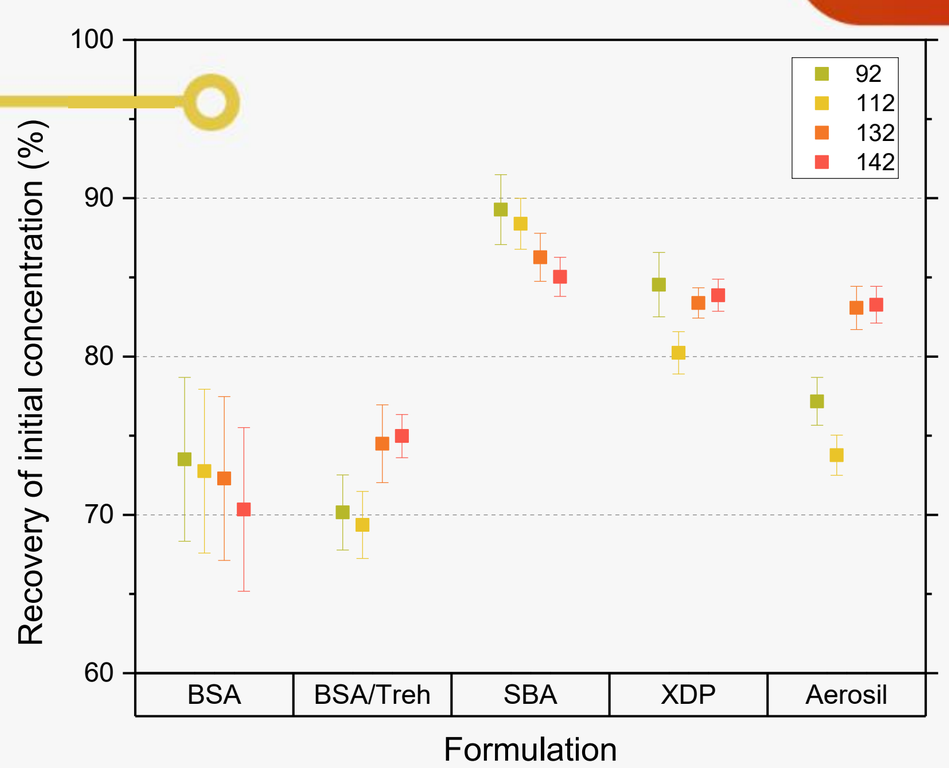
Proteins formulations containing trehalose and one of three different types of silica (SBA, XDP, Aerosil) with varying pore sizes were spray dried at 92, 112, 132, and 142 °C. Spray dried formulations were characterised by TGA (moisture content), DSC (glass transition temperature), dynamic vapour sorption (DVS) (water interactions) and SEM (morphology). Protein stability was analysed by circular dichroism (CD) for conformational stability, nanodrop-UV for concentration, and FTIR for chemical stability.



Results



DVS showed a mass gain event only for the non-silica formulation, a typical marker for crystallisation.



measured concentrations post-spray drying were higher for formulations containing silica.

Impact

The enhancements in processing and long-term stability for protein biopharmaceutical spray drying resulting from this research can facilitate novel formulation strategies such as those aimed at local delivery within the gastrointestinal tract.

Acknowledgement

This work was supported by the research grant from Taighde Éireann - Research Ireland, co-funded under the European Regional Development Fund (Grant number 12/RC/2275_P2).

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Probing the Stability of Drugs Formulated as Glassy Microneedles Structures Post Sterilisation

Mohamed Elkhashab, Ziad Sartwai, Denis Lynch, Sonja Vucen, Abina Crean
School of Pharmacy

What I am doing

We develop glassy microneedle patches, made entirely of drug without added polymers. These patches dissolve in the skin after application, allowing high drug loading and targeted delivery with minimal pain. We are investigating how gamma irradiation and ethylene oxide sterilisation affect the physical and chemical stability of microneedle patches containing five different drugs. Our goal is to ensure these microneedles can be effectively sterilised without compromising their chemical and physical structure or performance, meeting the sterility standards required for clinical use.

Why I am doing it

Microneedles penetrate the skin barrier and create microchannels that could allow microbes to enter, posing a potential infection risk. Sterilisation is therefore essential to ensure patient safety. Drug-only glass microneedles are sensitive to heat and chemicals, making sterilisation challenging. By identifying suitable sterilisation methods, we aim to ensure patient safety while preserving drug stability, enabling clinical translation of this technology.

How I am doing it

We sterilise microneedle patches and control drug samples using gamma irradiation or ethylene oxide. Sterility is confirmed according to European Pharmacopoeia standards. Physical stability is evaluated using visual inspection and microscopy to assess tip sharpness and structural integrity. Chemical stability is assessed using HPLC, LC-MS, DSC, and NMR to detect degradation, chemical modifications, or changes in thermal behaviour.

What I hope to achieve in the end

We aim to establish reliable sterilisation strategies that ensure complete microbial safety while maintaining the integrity and performance of drug-only microneedles. This would provide a clear, regulatory-compliant pathway for developing sterile microneedle products suitable for clinical use.

What is the potential impact in the Pharma area

These findings can help the pharmaceutical industry adopt microneedle technologies more efficiently by defining sterilisation methods that meet regulatory standards. This can reduce development time, support faster clinical translation, and enable new microneedle drug products that are both effective and safe.

UCC Coláiste na hOllscoile Corcaigh University College Cork, Ireland

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22

How Digitalisation of Product Platforms Leads to Organisational Change: Towards a Conceptual Framework for Product Platforms in Manufacturing Automation

John O'Sullivan, Brian O'Flaherty, Tom O'Kane
Cork University Business School

What I am doing

I aim to establish how the change in automation vendor offerings, from products to platforms, and from purchases to subscriptions (servitisation), is changing the automation vendor organisations.

Why I am doing it

I am curious as to how, by changing their market offerings, 1) the automation vendor companies change orgnisationally.

How I am doing it Part 1: The big picture, my PhD

I've written, presented and published a literature review on how IS is relevant to the manufacturing industry. I've developed a conceptual framework on how product platform digitalisation has resulted in organisational change in vendors. (This paper) My next step is to collect data by interviewing professionals in the vendor space, across two different companies and perform cross case comparison.

How I am doing it Part 2: This paper.

Definitions: Product Platform, Digitisation, Digitalisation, Digital Transformation, Industry and Manufacturing.

Search Strategy and Results: Figure 1.

Synthesis: Qualitative Data Analysis using Thematic Analysis.
- Phase 1: Familiarisation with the Data.
- Phase 2: Generation of Initial Codes.
- Phase 3: Searching for Themes. Figure 2 and Figure 3.
- Phase 4: Review of Themes. Figure 4.
- Phase 5: Definition and Naming of Themes.
- Phase 6: Production of the Report.

Propositions:
e.g. Digital Skills, Digital Infrastructure and ecosystems encourage and enable digitalisation.

What I hope to achieve in the end

I hope to prove or disprove that my conceptual framework is correct, and thus present a validated framework to automation vendors, which will, hopefully, inform them on future product offerings, and how to bring it to this particular market sector.

What is the potential impact in the Pharma area

In my experience, the pharmaceutical sector is a highly regulated environment, where technology (automation and data systems, not pharmacological) is integrated in a restricted, validated and controlled method. This can stifle innovation and restrict speedy delivery. Potentially, new methods of delivering automation technology to the factory floor will result in better patient outcomes.

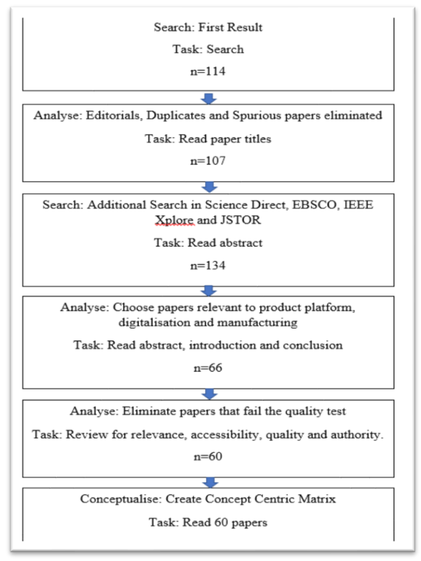

Fig.1
Process flow of search, filtration, screening, content analysis and conceptualisation.

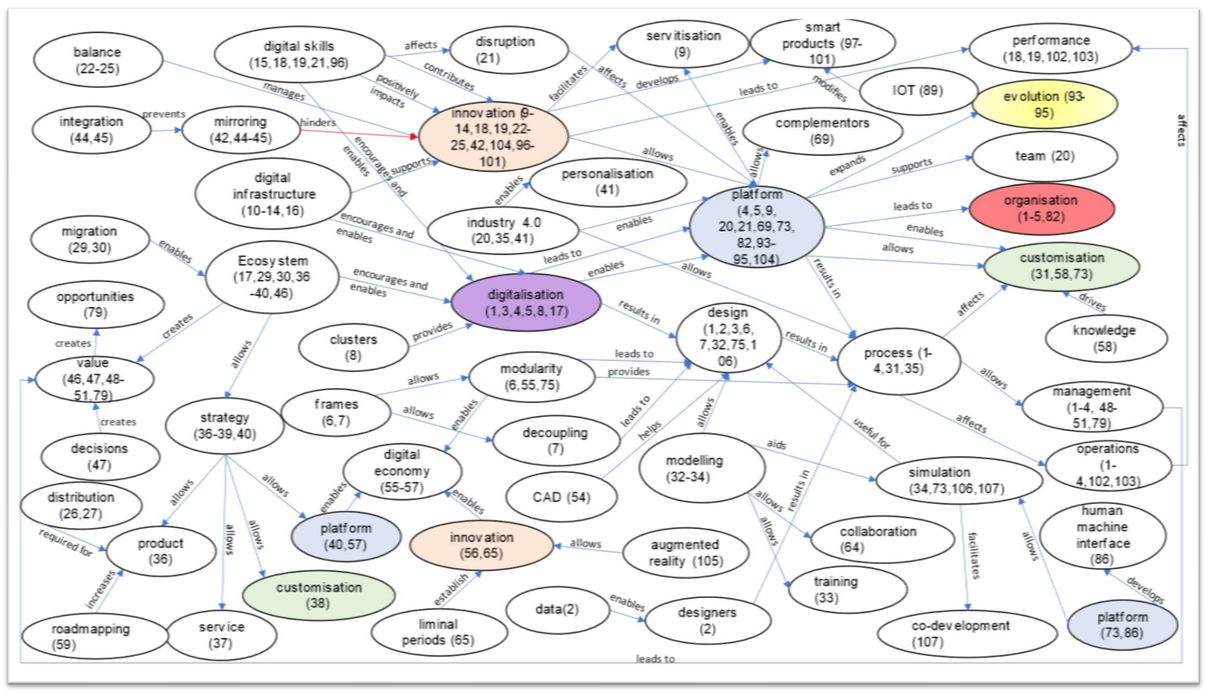

Fig.2 Initial Thematic Map.

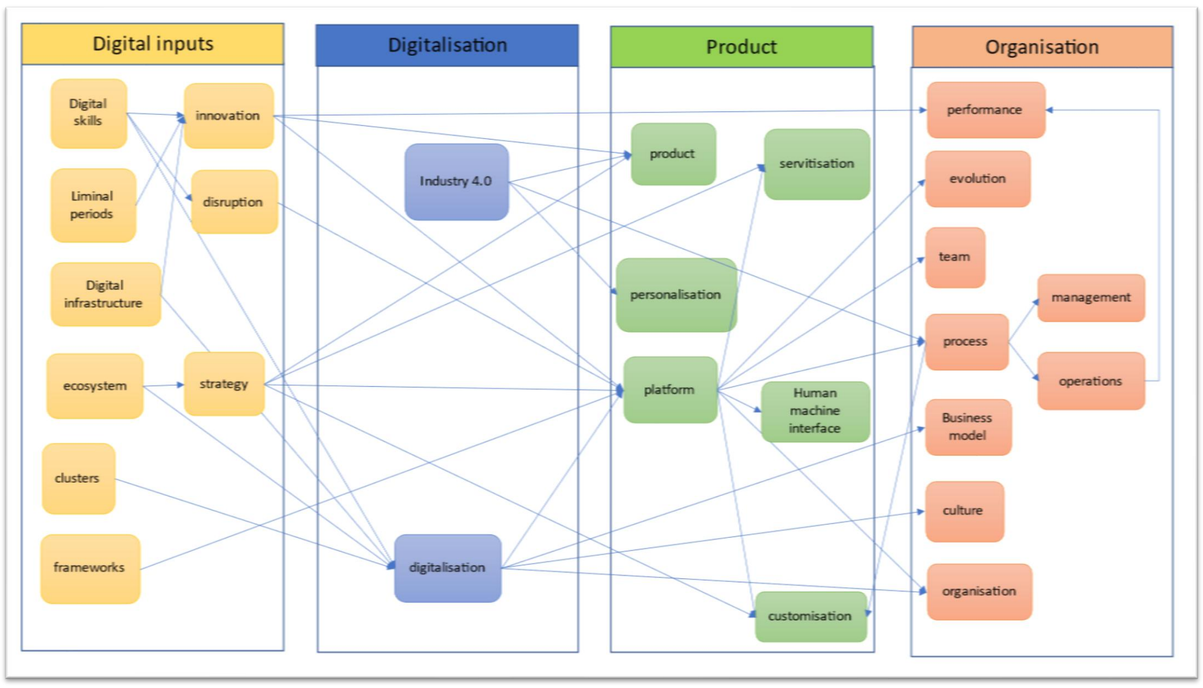

Fig.3 Developed Thematic Map.

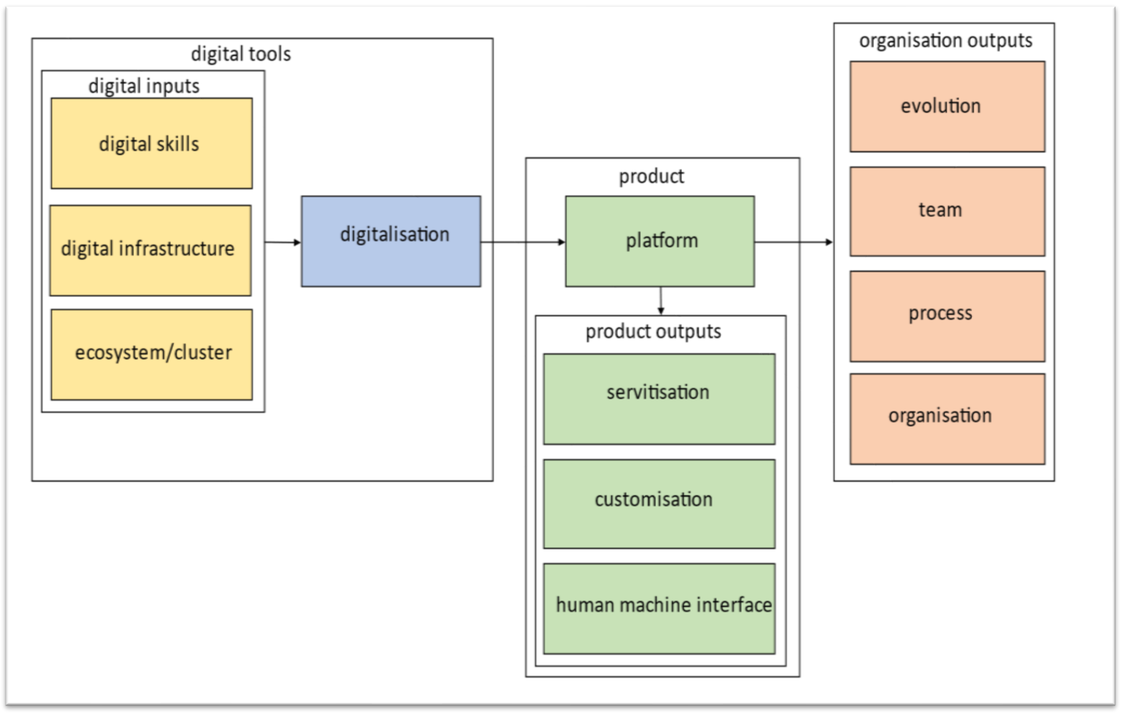

Fig.4 Conceptual Framework.

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Taste and Smell Changes and Quality of Life among Ambulatory Cancer Patients Receiving Systemic Treatment.

Doireann Ní Chonaill[1], Erin Stella Sullivan[1, 2], Derek G. Power [3, 4], Aoife M. Ryan[1, 3]

[1]School of Food & Nutritional Sciences, College of Science, Engineering and Food Science, University College Cork, Cork, Republic of Ireland; [2]Department of Nutritional Sciences, School of Life Course & Population Sciences, Faculty of Life Sciences & Medicine, King's College London, UK; [3]Cancer Research @UCC at University College Cork, Cork, Republic of Ireland; [4]Department of Medical Oncology, Mercy and Cork University Hospitals, Cork, Republic of Ireland.

Background

Taste and smell alterations (TSAs) are common side-effects of anti-cancer treatment and can negatively affect patients' food choices, food intake, nutritional status and quality of life (QoL).

Poor oral intake is a risk factor for cancer-related weight loss, particularly muscle wasting, which has been shown to predict tolerance to chemotherapy, quality of life and survival[1].

Evaluation of the prevalence of TSAs, as well as their predictive factors can help identify patients at increased nutritional risk and lead to better symptom management and QoL.

Aims

1. To assess the prevalence of taste and smell alterations among a cohort of Irish patients with cancer, who were receiving systemic anti-cancer treatment (i.e. IV chemotherapy, targeted therapy, immunotherapy etc.).

2. To identify any demographic, clinical or therapeutic factors that may be associated with TSAs.

Methods

n=1,015 patients who were undergoing chemotherapy at two University Teaching Hospitals in Cork were enrolled in the SARCONC study between 2012-2017. It investigated the nutritional status, QoL (EORTC-QLQ-30 validated questionnaire) and treatment outcomes of patients receiving systemic anti-cancer treatment[1,2].

This study is a secondary analysis of the patients recruited from 2015-2017, after which additional survey questions on TSAs were introduced following ethical approval.

Quantitative analyses were completed using SPSS v28 and included chi-squared tests, Independent Samples T-tests, and logistic regression models. Multivariate analyses compared those who did experience taste changes with those who did not. Significance was determined at $p<0.05$.

Results

TSA data was available for a total of 292 patients, all receiving systemic-anti-cancer treatment, of which 50.3% reported taste changes and 20.8% reported smell changes (see Fig 1).

Fig 1: Prevalence of Taste and Smell changes

Females experienced significantly more taste and smell changes than males (63.3% Vs 36.7%, p=0.007, 75% vs 25%, p<0.001, respectively).

Cancer sites with the highest frequency of TSAs were breast, lung and gastro-intestinal cancers (see Fig 2 across).

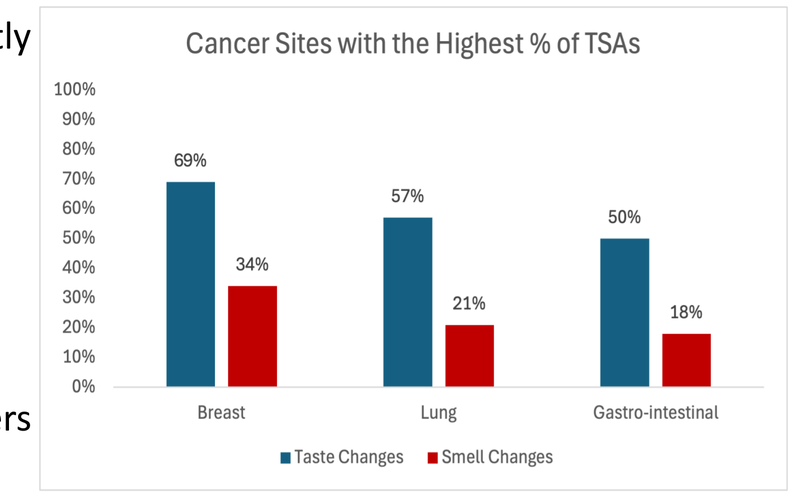

Fig 2: Cancer Sites with the highest frequency of TSAs

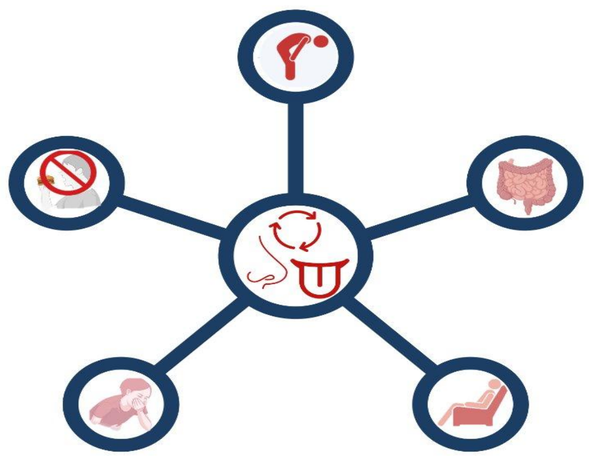

Fig 3: Other symptoms associated with TSAs

TSAs were significantly more likely to present within symptom clusters, including anorexia, constipation, nausea, dyspnoea and fatigue (see Fig 3).

'Metallic' (34.9%) and 'bland' (25.3%) were the most commonly described changes in food taste.

Patients receiving taxane-based chemotherapy were more likely than not to report taste changes (62% Vs 36%, p=0.009), while those receiving monotherapy with immunotherapy (excluding trastuzumab) were less likely to report taste changes (21% Vs 78%, p=0.001).

The majority of patients (63%) who experienced taste changes did not enjoy taking oral nutritional supplements, when it was prescribed to them.

On Multivariate analysis (controlling for age, sex and cancer type), lower global QoL score was independently associated with taste changes (OR: 0.979 [95%CI: 0.967-0.992], p=0.001) and the drug Paclitaxel (OR:2.376 [95%CI: 1.168-4.834], p=0.017). Lower global QoL score was also independently associated with smell changes (OR: 0.976 [95% CI: 0.962-0.991], p=0.002).

What is the potential impact in the Pharma area

This study revealed that TSAs are very common in patients receiving systemic anti-cancer treatment and are associated with specific demographic, clinical and treatment-related factors.

Taxane-based chemotherapy, and in particular Paclitaxel, are associated with TSAs, which impact on nutritional intake and compliance with oral nutritional supplements.

Taste and smell changes are independently associated with lower global quality of life scores and are more likely to present within symptom clusters.

Increasing awareness of TSAs in patients on chemotherapy allows for better symptom and nutritional management, in turn maximising oral intake and preserving nutritional status during treatment.

CRF-UCC HRB Clinical Research Facility University College Cork
CUH Ospidéal na hOllscoile Corcaigh Cork University Hospital
Mercy University Hospital Compassion Excellence Justice Respect Team Spirit
King's College London

References

1. Sullivan ES, Daly LE, Scannell C, Ní Bhuachalla ÉB, Cushen S, Power DG, et al. A large, multi-centre prospective study demonstrating high prevalence of malnutrition associated with reduced survival in ambulatory systemic anti-cancer therapy patients. Clinical Nutrition ESPEN. 2022 Dec 1;52:208–17.
2. Ní Bhuachalla ÉB, Daly LE, Power DG, Cushen SJ, MacEneaney P, Ryan AM. Computed tomography diagnosed cachexia and sarcopenia in 725 oncology patients: is nutritional screening capturing hidden malnutrition? Journal of Cachexia, Sarcopenia and Muscle. 2018;9(2):295–305.
3. Image created in: https://BioRender.com

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Artificial Intelligence and Machine Learning Data Trends of Agarose Hydrogel Properties

Sean Walsh[1,4], Simon Corrie[2], Lisbeth Grøndahl[3] and Imanda Jayawardena[4]

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[2] Chemical and Biological Engineering Department, ARC Centre of Excellence in Carbon Science and Innovation, Monash University, Clayton, VIC 3800, Australia.
[3] School of Chemistry and Molecular Biosciences, University of Queensland, Brisbane, QLD 4072, Australia.
[4] Tyndall National Institute, Lee Maltings Complex, Dyke Parade, Cork, Co. Cork T12 R5CP, Ireland.

What I am Developing

I am **developing an AI pipeline** that quickly and consistently **measures pore size and structure** in agarose hydrogels.

- **Replaces** slow and subjective **manual tracing**
- Uses both **semi-automated and fully-automated** methods
- **Converts** images into **binary pore maps** for **accurate analysis**

Why This Work Matters

Hydrogel performance depends on how easily drugs and cells **move through their pores**, but **current** measurement **methods are slow** and inconsistent.

- **Manual outlining** leads to **inconsistent results** across labs
- **Difficult to** reliably **predict drug diffusion** and cell behaviour
- Industry **needs faster and more standardised pore analysis**

My Approach

I **compare three methods** for analysing hydrogel images, with **pores highlighted in black**:

- **Manual tracing**
- **Semi-Automated Machine Learning (Ilastik)**
- **Fully-Automated Deep Learning (PoreD²)**

Each method is **tested against reference images** to **evaluate their performance**.

Manual Tracing (Outlining The Pores)

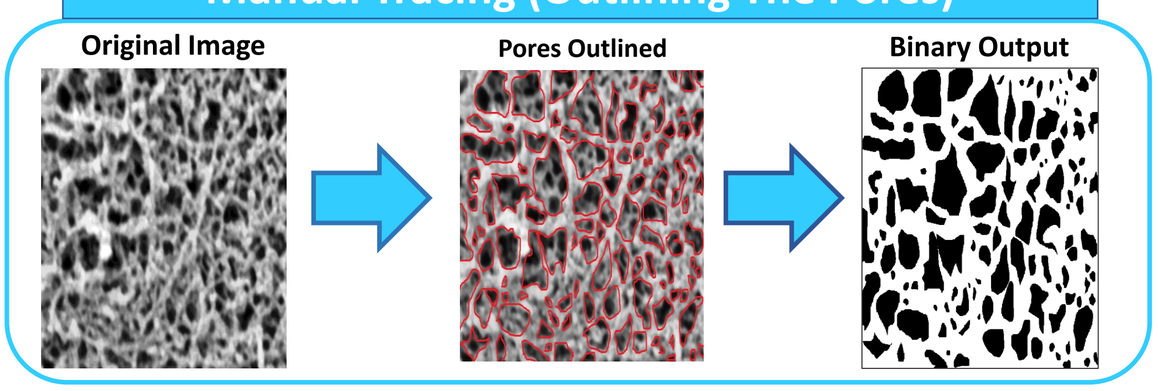

Figure 1: *Converting raw Cryo-SEM images into binary outputs, where pores are isolated as black regions for automated analysis.*

The Outcome

This project delivers an **AI pipeline** that:

- Produces **fast and fully objective pore measurements**
- **Works** consistently **across different imaging techniques**
- **Helps compare hydrogels** more effectively
- **Helps understand hydrogel behaviour** more clearly

Semi-Automated Machine Learning (Ilastik)

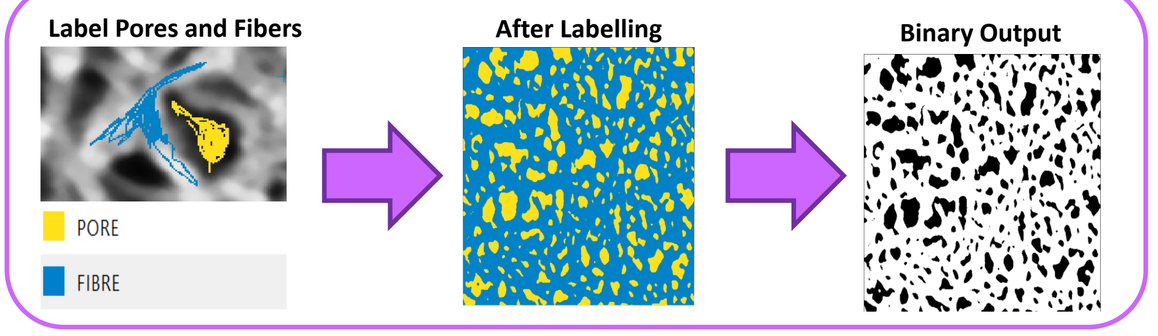

Figure 2: *Ilastik machine learning labels pores and fibers to produce binary and segmented hydrogel images for automated structural analysis.*

Value for the Pharma Industry

These **AI tools improve quality control and speed up** development of **hydrogel-based drug-delivery systems**.

- **Reduces variability** between labs
- **Improves prediction** of drug release
- **Supports design** of more reliable biomaterials
- **Cuts time and cost** in hydrogel characterisation

Fully-Automated Deep Learning (PoreD²)

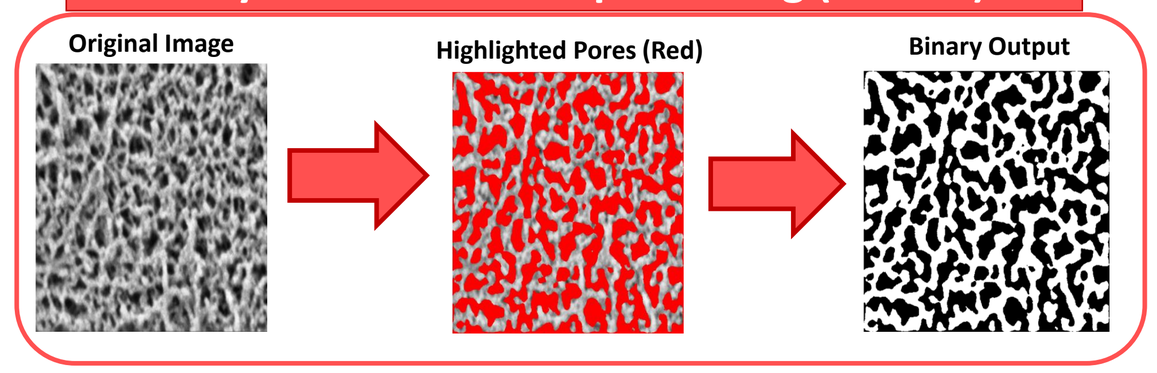

Figure 3: *Deep-learning (PoreD²) pipeline illustrating automated pore detection—from raw hydrogel imaging to highlighted pore regions and final binary segmentation.*

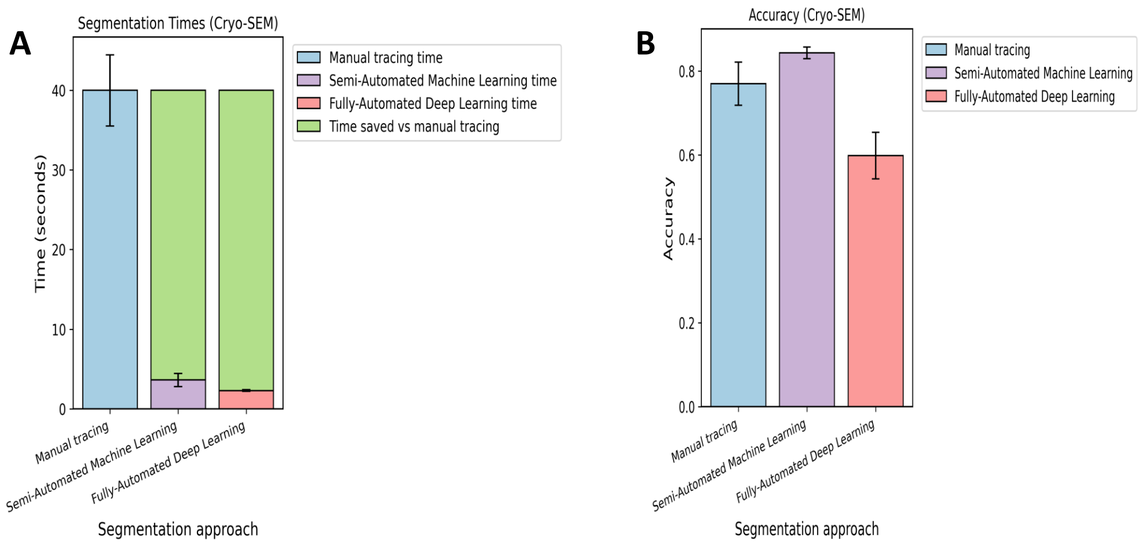

Figure 4: *Manual Tracing, Semi-Automated Machine Learning, and Fully-Automated Deep Learning methods differ in segmentation time and time saved (A) as well as the accuracy of each method (B).*

The Best Method?

Semi-Automated Machine Learning (Ilastik) provides the **best overall balance of speed, accuracy and reliability.**

- **Manual:** Slow and inconsistent
- **Fully-Automated Deep learning:** Fast but poor accuracy
- **Semi-Automated Machine Learning:** Best balance between accuracy and speed.

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Dysregulation of neurofilaments in ATXN2-ALS motor neurons causes endo-lysosomal trafficking defects

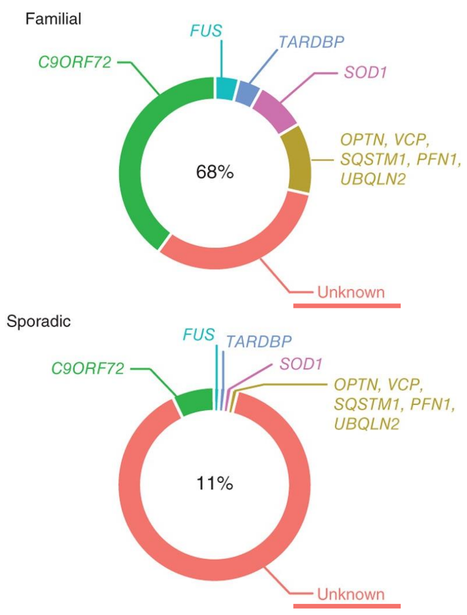
Bastian Bues, Vivian Dambeck, Katie O'Mahony, Mathias Bähr, Jeroen Pasterkamp, Katja Burk
School of Biochemistry and Cell Biology

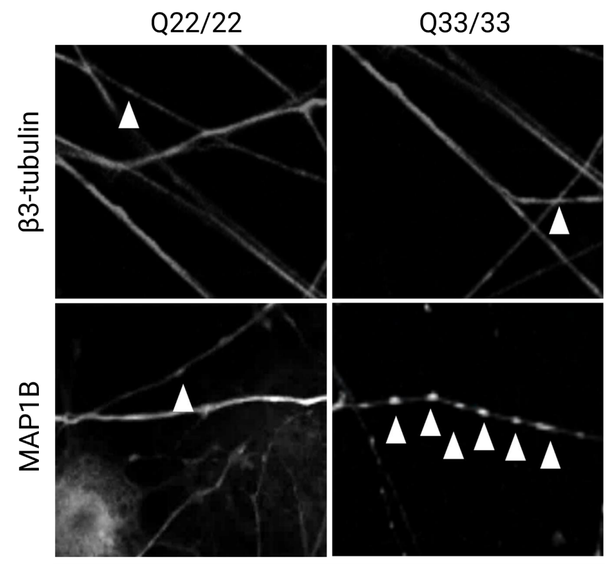
What I am doing

I am investigating how intermediate-length polyglutamine expansions in the Ataxin-2 (ATXN2) gene, a known ALS risk factor, affect neurofilament organization and stability in human iPSC-derived motor neurons. My work focuses on identifying how this genetic change alters neurofilament dynamics and associated cellular pathways such as endo-lysosomal trafficking.

Why I am doing it

Amyotrophic lateral sclerosis is a rapidly progressing fatal motor neuron disease. 95% of ALS cases are sporadic and only 11% of sporadic cases can be explained by the mutations found so far. This is why looking into genetic modifiers such as polyQ Atxn2 is important. Additionally, neurofilament abnormalities are a consistent but poorly understood hallmark of ALS. By uncovering the molecular mechanisms that cause neurofilament dysregulation in ATXN2-linked ALS, I aim to clarify how early cytoskeletal defects contribute to motor neuron degeneration and identify potential points for therapeutic intervention.

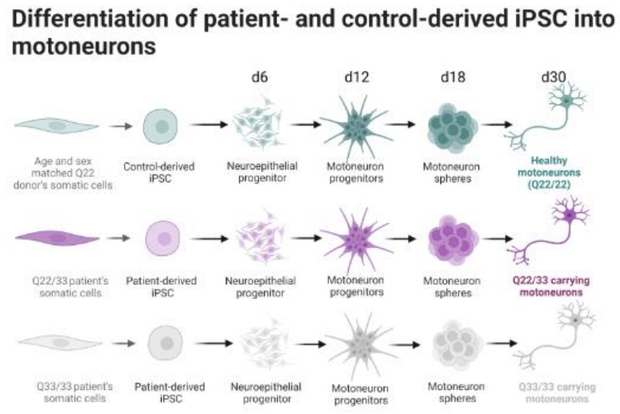


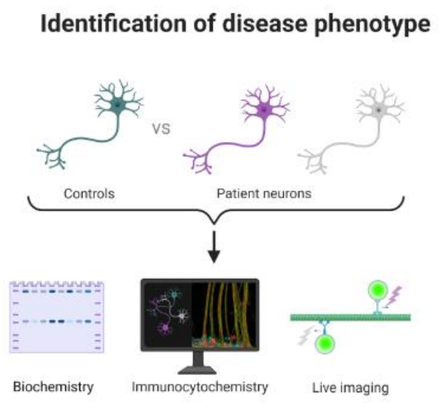


Visualisation of defects in the cytoskeleton.

How I am doing it

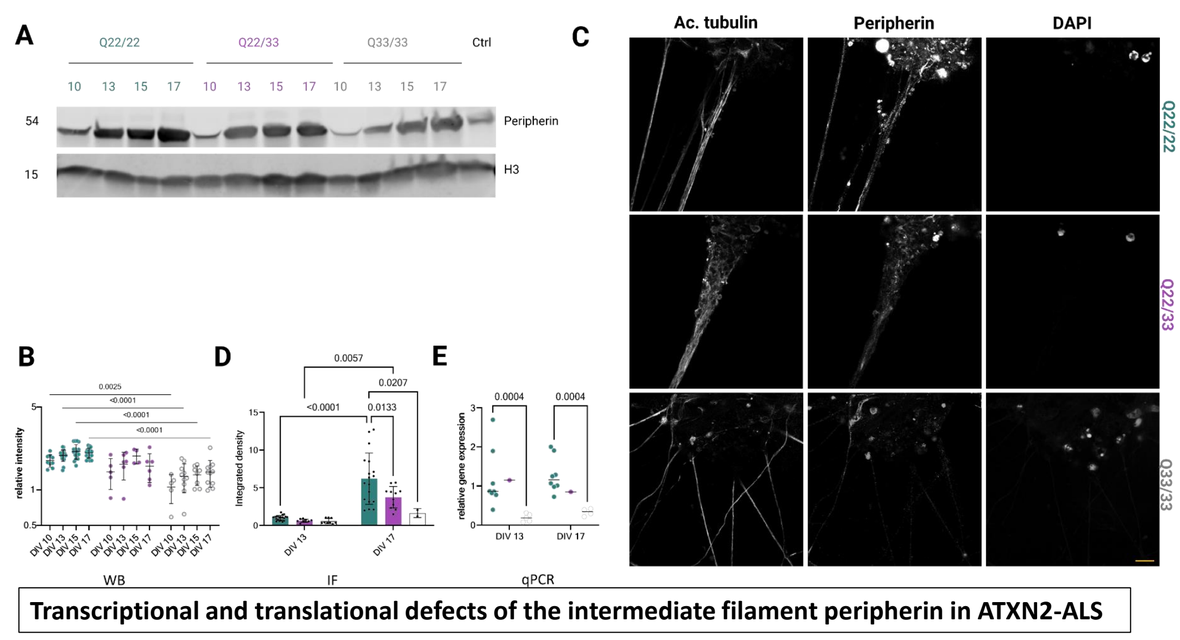
I use iPSC-derived motor neurons from ALS patients carrying ATXN2 intermediate-length expansions to model the disease in vitro. Using molecular, biochemical, and imaging approaches, I assess (neuro-)filament composition and solubility, and intracellular trafficking events. Next, I will test whether restoring peripherin expression can rescue these cellular defects.





What I hope to achieve in the end

I aim to define how ATXN2 regulates neurofilament homeostasis and identify mechanisms that initiate neurofilament pathology in ALS. Establishing this causal link may uncover novel molecular targets or pathways whose modulation could help maintain neuronal integrity and slow disease progression.
One of the most intriguing findings so far is the downregulation of a specific type of neuronal cytoskeletal protein called peripherin that so far has always been described to be upregulated in ALS and to exhibit intracellular aggregation. Many other phenotypes seem to be dependent on this loss.



Transcriptional and translational defects of the intermediate filament peripherin in ATXN2-ALS

What is the potential impact in the Pharma area

Preclinical animal model data have routinely failed to have translational potential. Further, the phenotypic heterogeneity between patients as well as the lack of disease biomarkers makes the search for therapeutic targets and therefore drug development more challenging. This work advances understanding of a shared ALS mechanism relevant across genetic backgrounds, highlighting ATXN2 and cystoskeletal components as potential therapeutic targets. These findings could guide drug discovery efforts toward restoring cytoskeletal integrity in motor neurons, contributing to mechanism-based strategies for ALS treatment.

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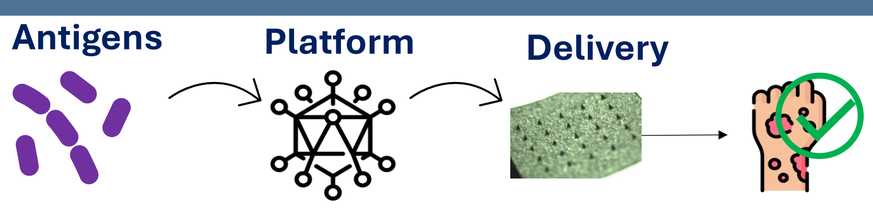
Developing an adenoviral vector-based vaccine against *Staphylococcus aureus* skin infections

Rachel Lapeyre, Anne Moore
School of Biochemistry and Cell Biology

What is my project?



My project consists of developing an **adenoviral vaccine** expressing ***Staphylococcus aureus*** *("SA")* antigens to protect against skin infection and disease.

Why use the adenovirus platform?

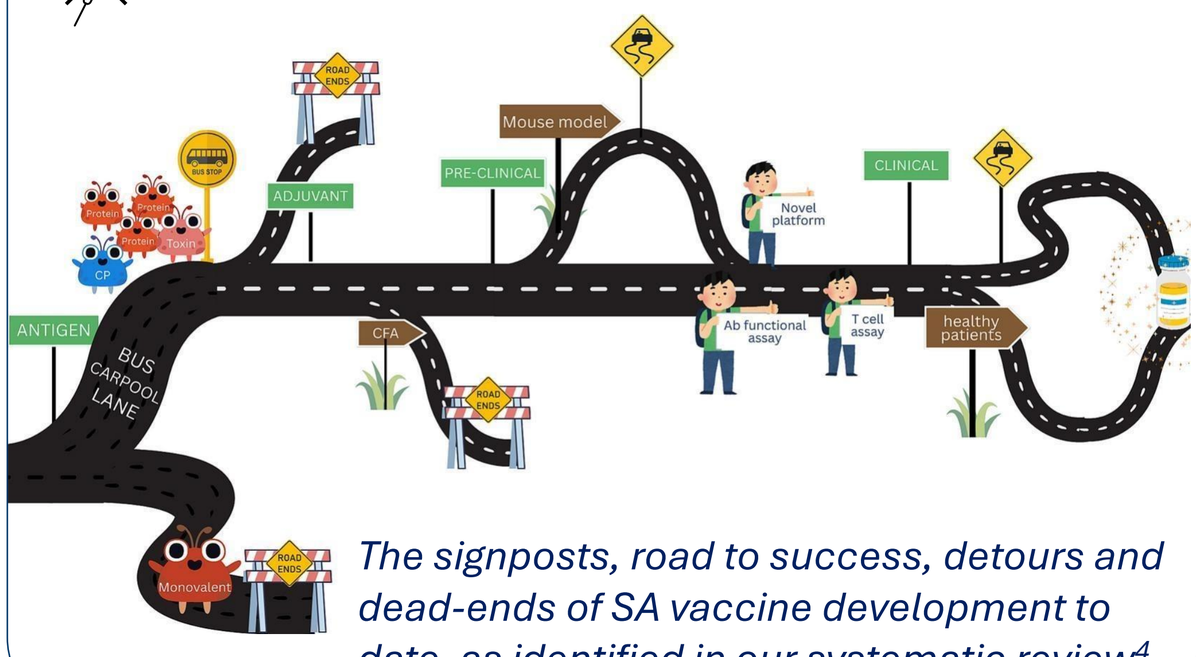
- **Licensed** vaccine platform (COVID-19, Ebola virus).
- Induces **antibody + T cell immunity**[1] → interesting for bacterial infection.
- Already being tested for other **bacteria** such as meningococcus or tuberculosis.

What is the goal of my project?

- Induce **protective immunity** against *S. aureus* using the **adenovirus platform**.
- Induce **protective skin-resident immunity** using **dissolvable microneedle patches** developed in the lab.

About *S. aureus* vaccine development

- **Leading cause** of bloodstream, lower respiratory tract and **skin and soft tissues infections**[2].
- **Methicillin resistant** *S. aureus (MRSA)* is a **major threat**[3].
- **No vaccines** licensed for humans.



The signposts, road to success, detours and dead-ends of SA vaccine development to date, as identified in our systematic review[4].

What do I do in the lab?

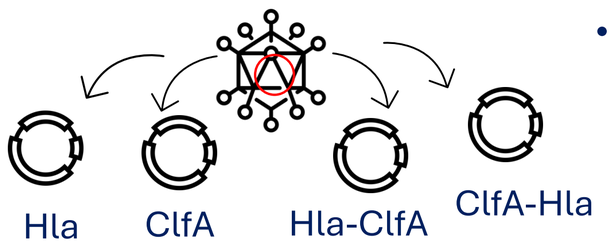
1. Identified 2 antigens

→ Alpha haemolysin **(Hla)**
→ Clumping Factor A **(ClfA)**

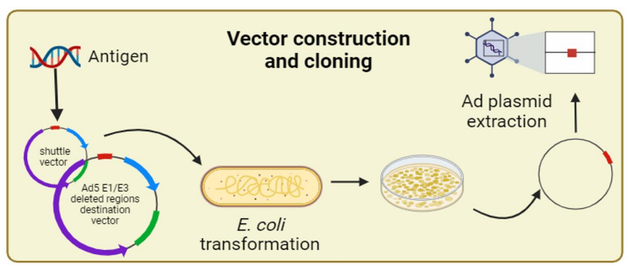
- Pore-forming **toxin**
- Vaccine-induced **antibodies** to protect against disease.

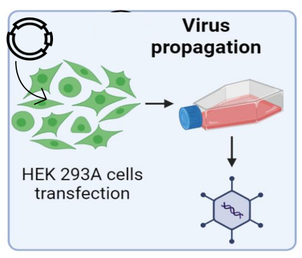
- **Surface** protein
- Vaccine-induced **T cells** to protect against bacterial load.

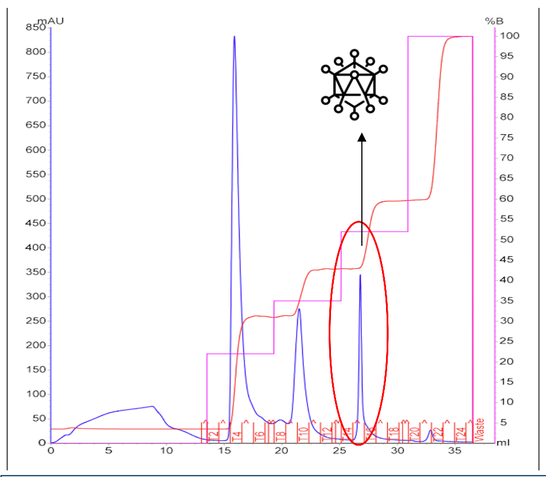
2. Created 4 AdV constructs



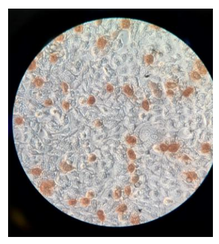
3. Implemented vaccine production process and quality control







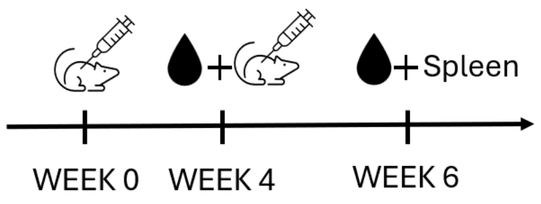
Anion-exchange chromatogram of monovalent Ad-ClfA vaccine

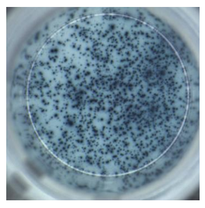


Hexon staining assay to quantify adenovirus infectious units.

80% recovery after purification

4. Pre-clinical trials with vaccine candidates





Preliminary results from preclinical trials:
The two monovalents vaccines **Ad_Hla and Ad_ClfA** induce a **T cell immune response** in mice.

ELISPOT well with mouse splenocytes stimulated with Hla antigen.

5. Next step: evaluation of efficacy of the vaccine

Looking at the big picture: what can this research bring to the Pharma industry?

Most vaccines developed against *Staphylococcus aureus* use **subunit** vaccines. This approach has **failed** to develop efficacious vaccines. If successful, our research will demonstrate the potential of using **adenovirus platforms** and **open the pharmaceutical field to new perspectives for the development of such anti-bacterial vaccines**. Vaccines offer a credible solution to tackling the global antimicrobial resistance (**AMR**) crisis and could potentially **save 5 million of lives annually**.

1 Elshina, E. et al. Vaccine 37, 502–509 (2019).
2 Ikuta, K. S. et al. The Lancet 400, 2221–2248 (2022).
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27

Impact of the vaccine delivery technology on the B cell repertoire in pigs.

Imane Allaoui, Inés Co Rives, Katherine Acevedo, Ann Chen, Anne C. Moore.
School of Biochemistry and Cell Biology

What am I doing?

Investigating the impact of delivering the same vaccine by **a dissolvable microneedle patch, oral tablet or by injection** on the **B cell repertoire** in pigs.

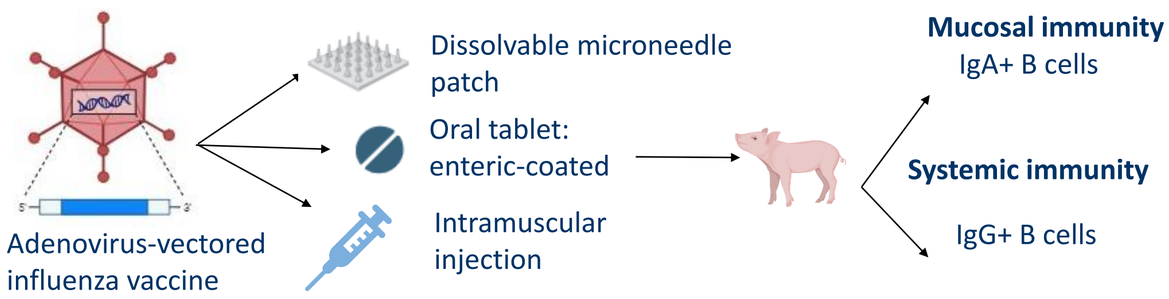

Figure 1: Representation of the influenza vaccine and the routes of immunization in this project**.** Made with Biorender..

The B cell Ig surface receptor is formed by recombination of VDJ gene segments.

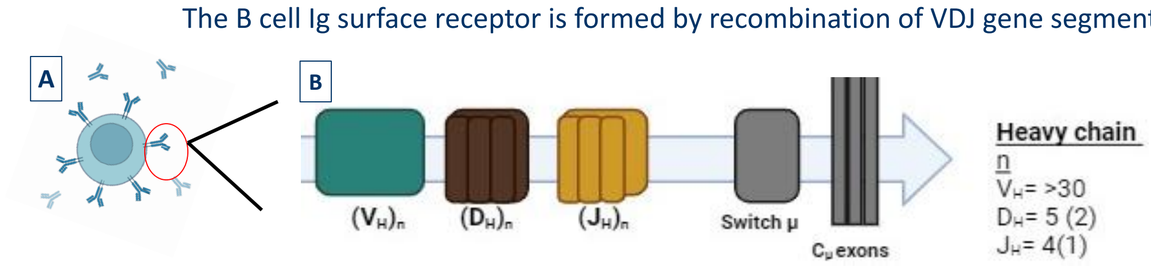

Figure 2: A. Representation of producing antibodies B cell and its Ig surface receptor. **B.** Pig Ig gene organisation, with V(D)J and constant domains (Adapted from Butler et Wertz, 2012).

The **B cell repertoire** refers to the host's unique and diverse collection of B cell clones, recognizing antigen through their Ig surface receptor. The receptors' sequences are highly unique and arise through random mutation during B cell development. The immune system contains then a large range of B cells, capable of recognising a diverse range of antigens. Upon vaccination or infection, specific clones of B cells recognizing the antigen are selected, based on their greater capacity of recognition.

- Studying changes provides insights on the breadth of the adaptive immune response after infection or vaccination.

Why am I doing it?

Figure 3: Representation of global vaccine accessibility issues, caused by the need of cold storage and injection-based method. Made with Biorender.

Global vaccine accessibility issues are caused by the need for cold chain storage and injection-based administration. **Dissolvable microneedle patches** and **oral tablets** aim to address these issues.

Aims:

- Determine how these **new technologies** impact **B cell vaccine-induced immunity** (VDJ gene usage, clonality).
- Provide knowledge to support further **clinical development** of vaccine technologies.
- Understand if **broader antigen-specific antibody response,** previously demonstrated with patch (Vrdoljak et al., 2016)**,** comes from the level of B cell clonality.

How am I doing it?

1. Wet lab-work

Pig blood sampling → RNA extraction & cDNA synthesis → B cell gene sequence prep and sequencing

2. Bioinformatics

Raw data processing and cleaning → Mapping data to the pig reference genome → B cell repertoire analysis

3. Data interpretation and preliminary findings

What are the changes in the B cell repertoire based on vaccine delivery ?

- **Gene usage**: Similar and consistent VDJ gene usage across vaccination groups
- **Antigen binding region diversity:** Slight variation in region size distribution across vaccine groups.
- Further analysis is ongoing .

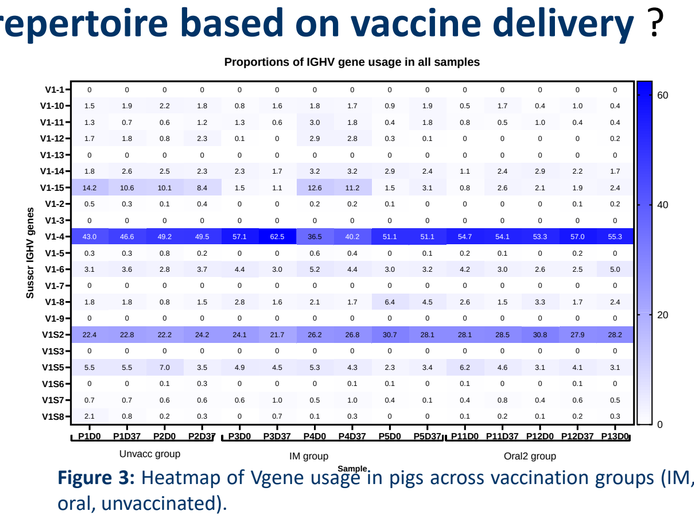

Figure 3: Heatmap of Vgene usage in pigs across vaccination groups (IM, oral, unvaccinated).

What do I hope to achieve in the end?

- To determine if and how **non-traditional vaccine delivery techniques -** patches and tablets - **influence vaccine-induced B cell responses**, compared to injection, in a large animal model.

What is the potential impact in the Pharma area?

A greater understanding of how **non-traditional vaccine platforms** work at the **B cell level could:**

- Underlie the tailoring of their use.
- Influence how the universality of current influenza vaccines could be improved.
- Contribute to the development of accessible, non-injectable vaccine delivery technologies.

References:
Butler, J. E., & Wertz, N. (2012). The porcine antibody repertoire: Variations on the textbook theme. *Frontiers in Immunology*, *3*. https://doi.org/10.3389/fimmu.2012.00153
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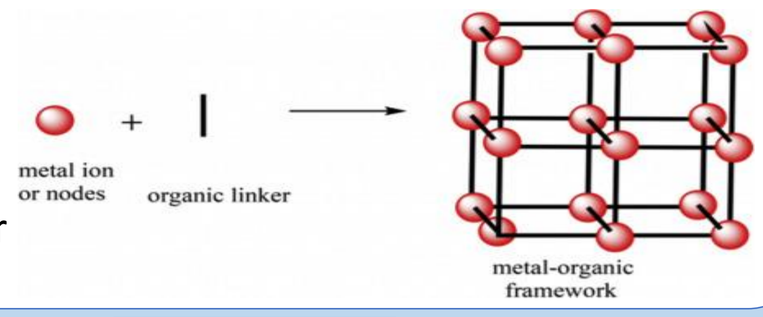
Computational Design of Metal-Organic Frameworks (MOFs) as Nanocarriers for Anti-cancer Drug Delivery

Darragh Crowe, Dr. Davide Tiana, Dr. Simon Lawrence
School of Chemistry

Background

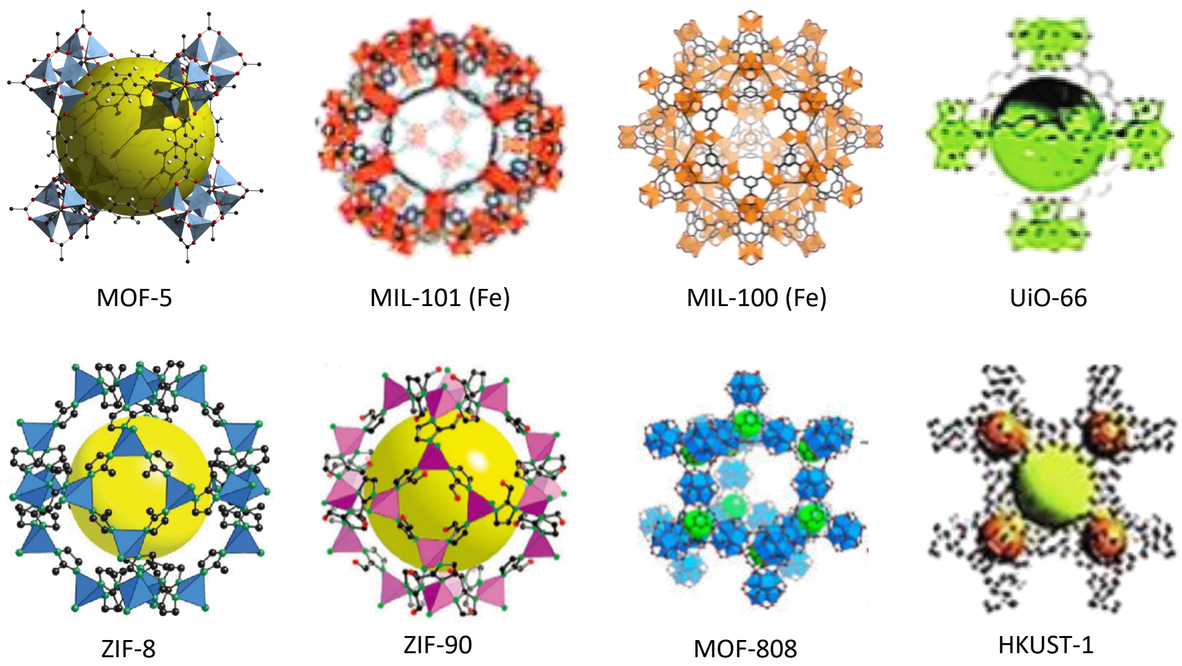
- **Metal-Organic Frameworks (MOFs)** are **crystalline, highly porous materials** consisting of metal ions or clusters coordinated to organic ligands.[1]
- **Tunable pore sizes, adsorbent surfaces** and high surface areas allow for various applications.[2]
- **Therapeutic agents**, such as doxorubicin, can be **incorporated into the MOF** by either encapsulation or surface attachment.



What?

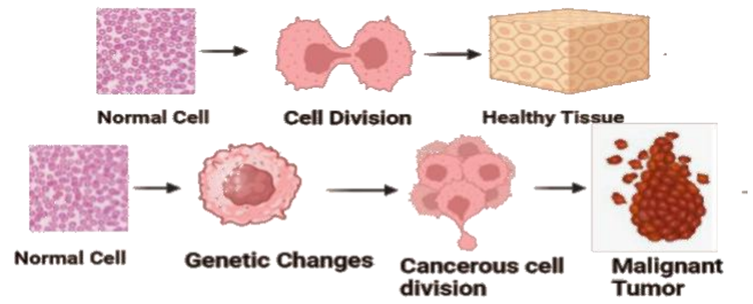
- Investigating the use of **MOFs as next-generation nanocarriers** for anti-cancer drug delivery.
- In this research, a range of **different MOF-drug combinations** will be studied.
- **Multi-drug delivery** using MOFs will be explored for potential **combination therapy** applications.

MOFs used for Drug Delivery

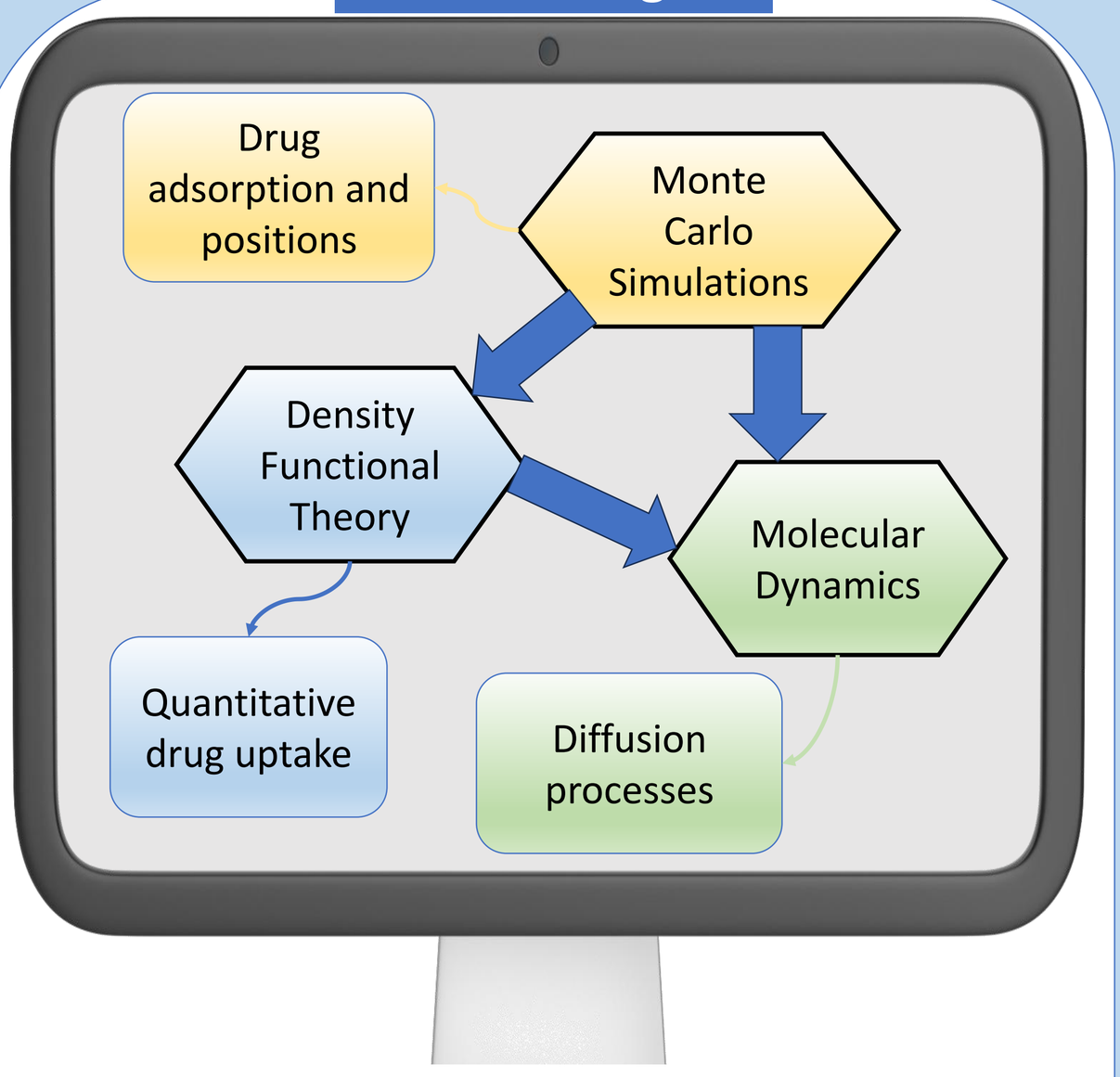


Why?

- **Cancer** results in **millions of deaths** annually.[3]
- **Existing treatments**, such as chemotherapy, **lack selectivity** and have significant **side effects**.
- This research focuses on **creating alternative treatment methods** that can improve efficiencies and reduce side effects.



Methodologies



- **Computational chemistry** will be employed to **model MOF-drug interactions.**
- Two simulations will **assess adsorption sites and loading efficiencies** within the MOF.
- The third simulation provides a description of the **drug diffusion and release mechanisms**.[4]

Goal and Impact

- **Construct an extensive**, computationally driven **database of MOFs** with strong potential **for drug delivery.**
- **Categorise shared characteristics and key design features** for improved drug delivery, such as pore size, ligand composition, defect percentage, etc.
- Simulation based research:

1. **Reduces** trial and error **experiments**
2. **Accelerates** the **R&D** process
3. **Lowers costs** for the company

- MOF-drug systems can offer **new production opportunities** to pharmaceutical companies.

Acknowledgements

Many thanks to Dr. Davide Tiana, Dr. Simon Lawrence, Mr. William Daly

ucc computational chemistry and programming group

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Cu-t to the chase: Structure–Activity Insights into Antifungal Acylthiourea Complexes

Jack Daly, William Daly, Conor Hill, Jerry Reen, Piero Macchi, Dave Otway, Davide Tiana
School of Chemistry

Why and What am I doing?

- Fungal infections are an increasing global health threat, driven by rising resistance to existing antifungal agents.[1]
- Metal-based therapeutics remain underexplored yet offer opportunities for new mechanisms of action. Copper(II) acyl thiourea complexes have shown promising antifungal properties, including a previously developed complex now under patent review.[2]
- This work supports global health priorities aligning with WHO and UN goals to develop novel antifungal solutions.[3]
- The ligands possess a high degree of tunability due to their varied functionalisation, are bioavailable and can be synthesised in a few steps.[4]

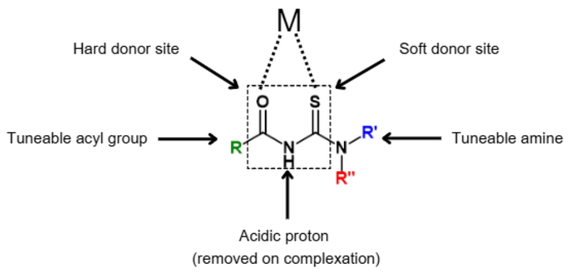
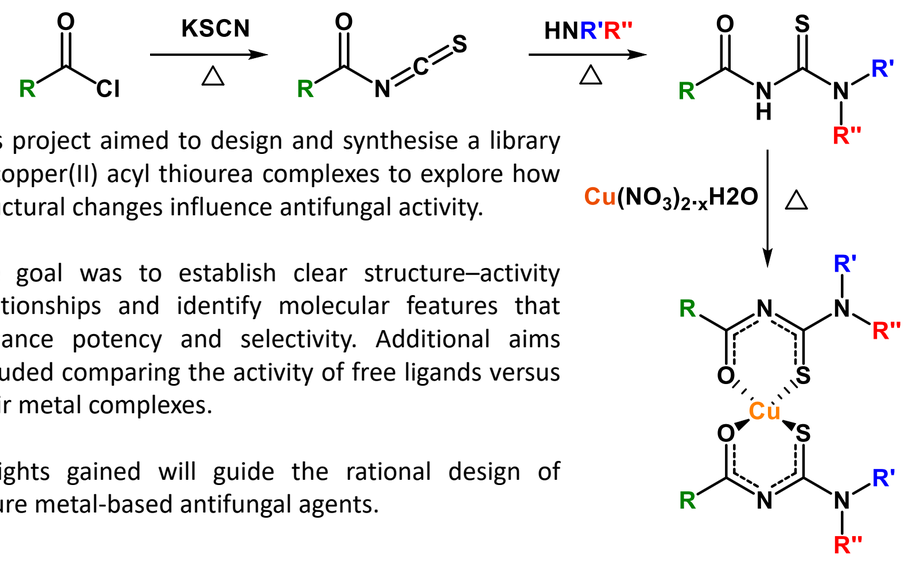


Figure 1 *General N,N-disubstituted-N'-acylthiourea ligand*

What do I hope to achieve in the end?



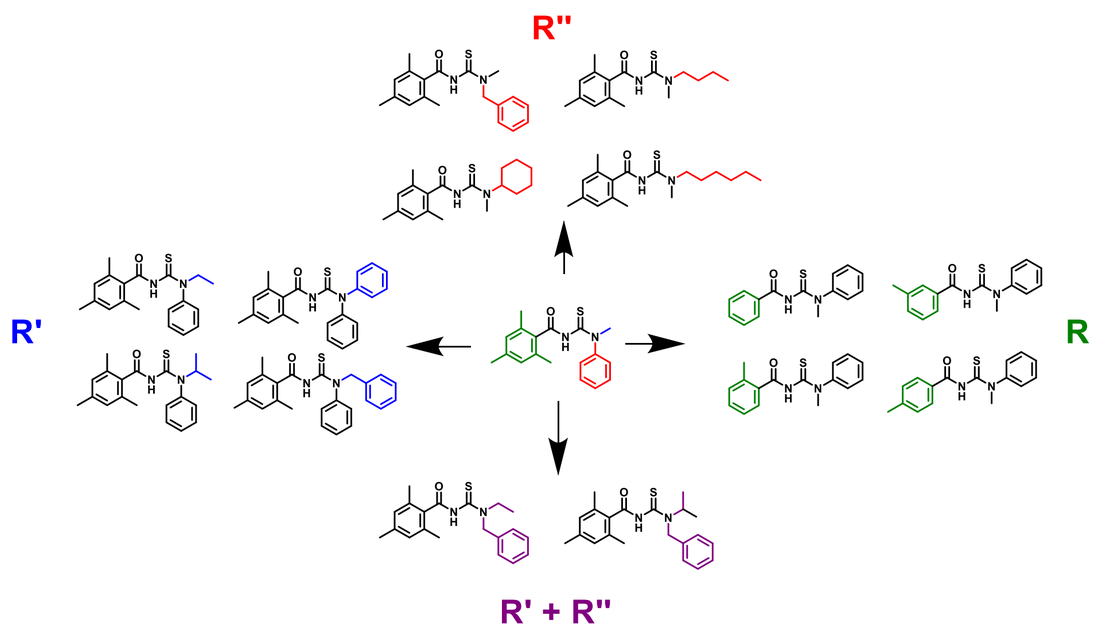
- This project aimed to design and synthesise a library of copper(II) acyl thiourea complexes to explore how structural changes influence antifungal activity.
- The goal was to establish clear structure–activity relationships and identify molecular features that enhance potency and selectivity. Additional aims included comparing the activity of free ligands versus their metal complexes.
- Insights gained will guide the rational design of future metal-based antifungal agents.

Scheme 1 *Schematic of the N,N-disubstituted-N'-acylthiourea ligand and complex*

How am I doing it?

Ligand	Complex	R	R'	R''
HL^1	A	Mes	Me	Ph
HL^2	B	Mes	Et	Ph
HL^3	C	Mes	iPr	Ph
HL^4	D	Mes	Ph	Ph
HL^5	E	Mes	Bn	Ph
HL^6	F	Mes	Me	Cy
HL^7	G	Mes	Me	Bu
HL^8	H	Mes	Me	Hex
HL^9	I	Mes	Me	Bn
HL^{10}	J	Mes	Et	Bn
HL^{11}	K	Mes	iPr	Bn
HL^{12}	L	Ph	Me	Ph
HL^{13}	M	o-Tol	Me	Ph
HL^{14}	N	m-Tol	Me	Ph
HL^{15}	O	p-Tol	Me	Ph

Table 1 *Functionalisation of ligands and complexes*



Scheme 2 *Substitution of ligands and complexes*

- A rational design strategy was employed by systematically varying ligand substituents(R, R', R'') to probe electronic, steric, and hydrophobic effects.
- Four structural groups were created to understand how single or combined substituent changes affect biological performance.
- The design was based on a previously successful copper(II) complex, used as the structural template.

Biological results

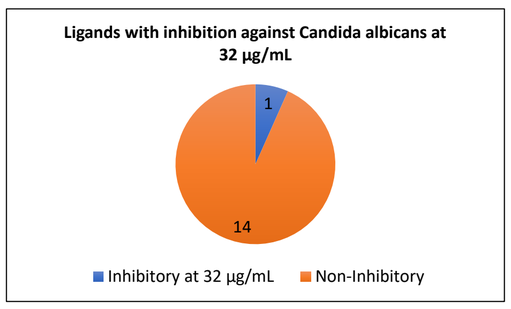
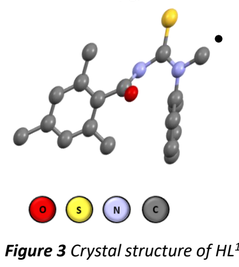


Figure 2 *Pie chart* Ligands with inhibition against Candida albicans at 32 µg/mL



- **1** out **15** organic ligands showed inhibition.

Figure 3 *Crystal structure of* HL^1

Ligand	32 µg/mL	16 µg/mL	8 µg/mL	4 µg/mL
HL^1				
HL^2				
HL^3				
HL^4				
HL^5				
HL^6				
HL^7				
HL^8				
HL^9				
HL^{10}				
HL^{11}				
HL^{12}				
HL^{13}				
HL^{14}	X			
HL^{15}				

Table 2 *Functionalisation of ligands and complexes*

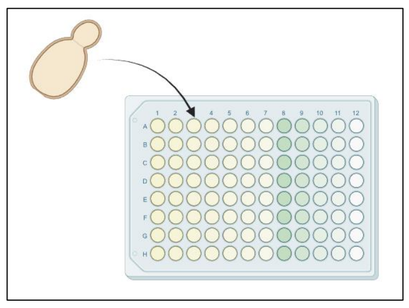


Figure 4 *MIC testing against Candida albicans in 96 well plate*

- MIC testing was performed on Candida albicans grown in YMB, and concentrations were tested from 32-4 µg/mL.

Complex	32 µg/mL	16 µg/mL	8 µg/mL	4 µg/mL
A	X	X		
B	X			
C				
D				
E				
F	X			
G	X			
H	X			
I				
J				
K				
L	X			
M	X			
N				
O	X			

Table 3 *Functionalisation of ligands and complexes*

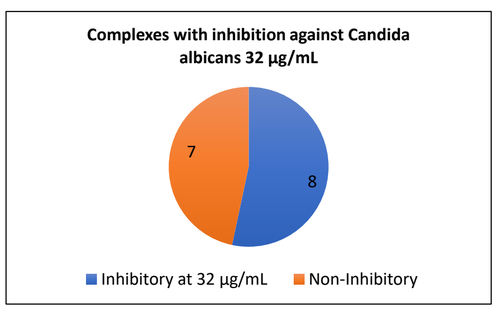
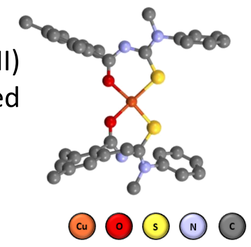


Figure 5 *Pie chart complexes* with inhibition against Candida albicans at 32 µg/mL



- **8** out **15** Cu(II) complexes showed inhibition.

Figure 6 *Crystal structure of complex A*

Structure Activity Relationship

- Activity retained for **phenyl**, ***o*** and ***p*** *methyl* substitution.
- ***Meta*** removed activity.
- Changing both **R' and R''** caused complete loss of activity, likely due to the **benzyl group**.

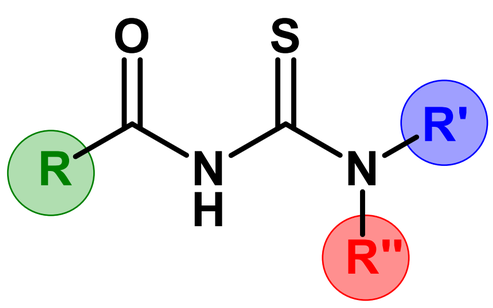


Figure 7 *Structure activity relation for complexes and ligand*

- **Longer chains** had no effect.
- **Branching**, **symmetric aromatics**, and **benzyl** all eliminated activity.
- **Chain length** or **aromaticity** made little difference.
- **Benzyl** removed activity.

What is the potential impact in the Pharma area?

- The creation of a library of copper(II) acyl thiourea complexes identifies compounds with significant antifungal activity, providing **new metal-based alternatives** to traditional organic drugs.
- The established SAR highlights key structural features that enhance activity, enabling **rational design of future compounds** to combat antifungal resistance. Currently working on mechanistic studies to further improve future compounds.
- These findings offer **potential for patentable, innovative therapeutics**, addressing the growing threat of antimicrobial resistance and expanding the chemical space for drug discovery.

Acknowledgements

- Many thanks to Mr William Daly*, Dr Davide Tiana*, Dr David Otway*: for guidance and support.
- Dr Jerry Reen and Mr Conor Hill for their assistance with biological testing.
- Dr Piero Macchi from the University of Milan : for crystallographic services.
- Royal Society of Chemistry : for bursary and grant support.

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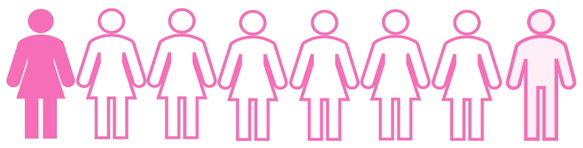
Dye-Loaded Aptamers as a Theranostic Platform for Breast Cancer Diagnosis and Therapy

R. Galway,[ab] E. Moore,[a] and C. S. Burke,[ab]
[a]School of Chemistry, University College Cork, Ireland;
[b]Analytical and Biological Chemistry Research Facility, University College Cork, Ireland.

Why and What am I doing?

- **Breast cancer** is a leading oncological concern in Ireland, where cancer is the most common cause of death.
- Early-stage diagnosis and timely treatment is crucial, however, the current drawback in ensuring accurate histopathology is the reliance on costly, unstable, cross-reacting antibodies that are difficult to produce reproducibly and to store.



In Ireland 1 in 7 women will be diagnosed with breast cancer in their lifetime.

Globally 2.3 million women were diagnosed in 2022 and 670,000 deaths were reported by the World Health Organisation.

Aptamers form non-canonical DNA → G-quadruplex

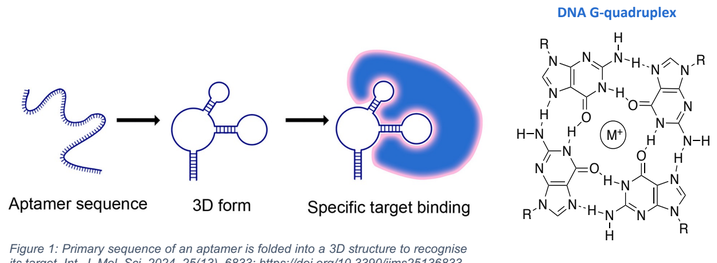
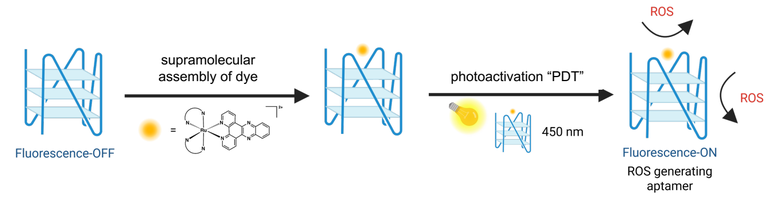


Figure 1: Primary sequence of an aptamer is folded into a 3D structure to recognise its target. Int. J. Mol. Sci. 2024, 25(13), 6833; https://doi.org/10.3390/ijms25136833.

- To overcome antibody-based problems, a newer generation of cancer treatments led by **targeted therapies** is being investigated using aptamers.
- **Aptamers** are synthetic, ssDNA that show selective binding for biomarkers, including receptors expressed at the surface of cancer cells.
- **DNA G-quadruplexes** contain G-G bonds instead of the classical G-C bonds. Certain breast cancer selective aptamers form G-quadruplexes.

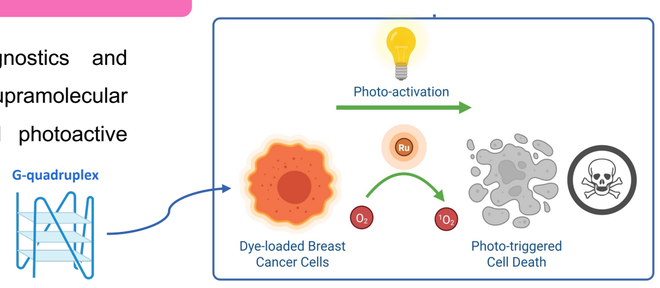
Targeted cancer therapies using photoactive metallodrugs for photodynamic therapy (PDT)

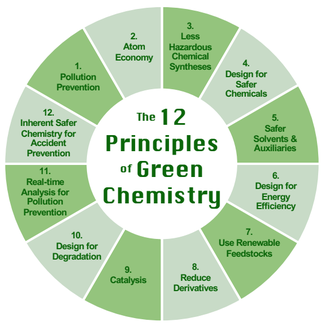
- Current efforts to exploit aptamers for biosensing is reliant on difficult covalent chemical modification at the surface with reporter labels.
- Hence, Ru(II) light-switch complexes will be loaded into aptamers via a supramolecular assembly using the **intercalation** ability of the dye for a **self-assembled** targeted drug delivery, (Ru-dppz binding constant; $K_b \approx 10^6\ M^{-1}$).
- Since Ru(II) complexes are great sensitisers of phototherapy, proof of diagnostic targeting of breast cancer biomarkers with a Ru-aptamer platform will provide new theranostics for targeted cancer cell phototherapy.



What do I hope to achieve in the end?

- **Overarching aim:** explore new diagnostics and therapies of breast cancer, including the supramolecular combination of targeting aptamers and photoactive metallodrugs.



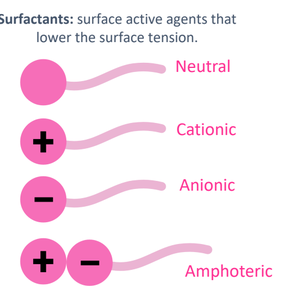


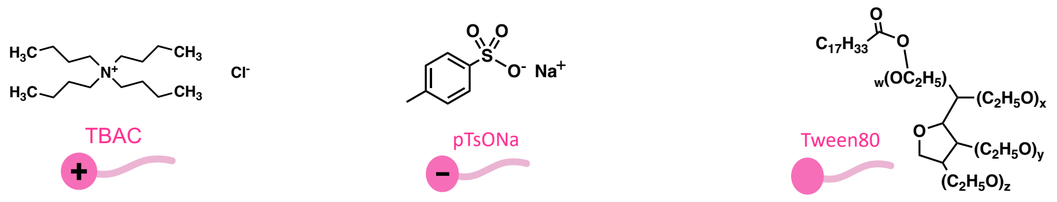
- At this development stage of the project, a green surfactant-mediated synthesis in water that has broad implications across diverse fields of Ru(II) polypyridyl chemistry, from bio-applications to solar fuels. Advantages to this approach are: low cost, increased reaction efficiency and the use of non-toxic solvents.

How am I doing it?

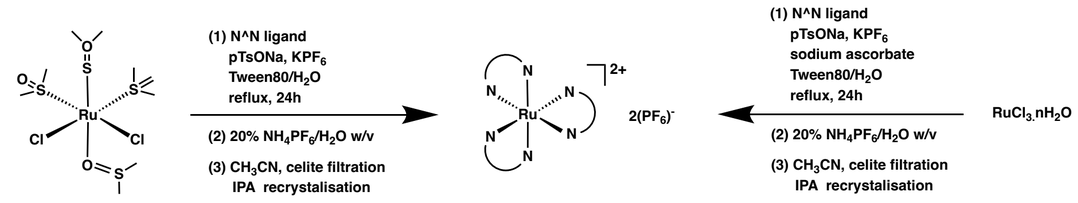
- Herein, greener approaches to syntheses of Ru(II) polypyridyl complexes are described.
- Protocols developed include the exploration of **surfactant mediated syntheses in water**, and use of auxiliary anionic agents, to provide the complexes from common precursors; $RuCl_3.nH_2O$ and $[Ru(DMSO)_4Cl_2]$.
- The next stage of this work is to use such Ru(II) polypyridyl complexes in combination with targeting aptamers as a photoactive platform for sensing and therapy of breast cancer.

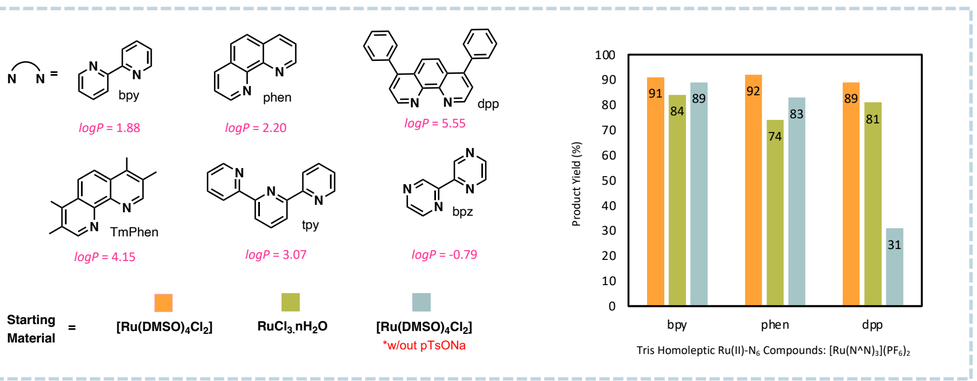
Surfactants: surface active agents that lower the surface tension.





Development of Surfactant-Mediated Syntheses





^{1}H NMR results demonstrate greener purification of Ru(II)-N_6 compounds for a broad range of *logP* values expanding drug loading capabilities

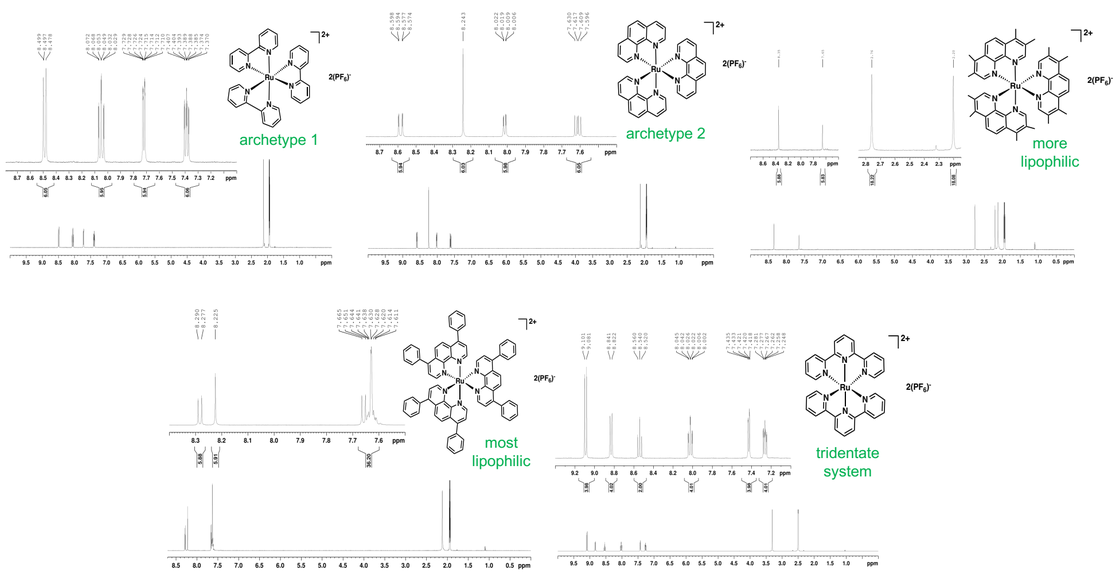
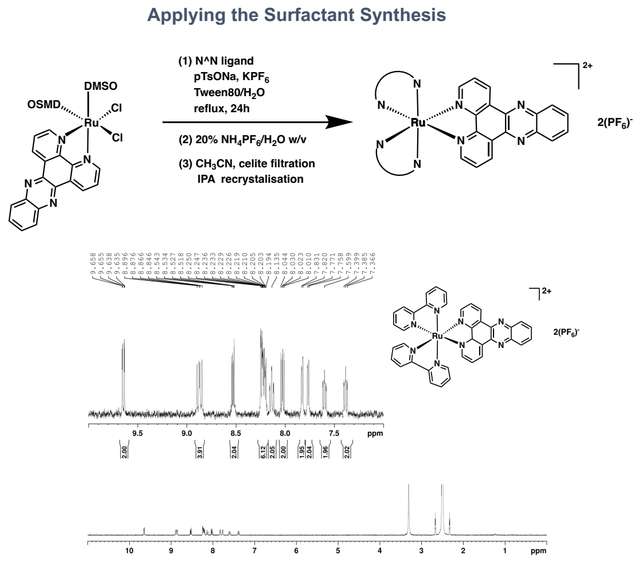


Figure 2: ^{1}H NMR (400 MHz, $[CD_3CN]$ or $[(CD_3)_2SO]$) spectrum of $[Ru(N^N)_3](PF_6)_2$ from $RuCl_3.nH_2O$.

- Overall, a **surfactant-mediated water-based synthesis** in preparation of a broad scope of Ru(II) polypyridyl compounds has been achieved that avoids the use of toxic solvents like DMF. Onerous purifications via classical flash column chromatography have been avoided, by recrystallising the product from IPA.
- Limitations: dichloride intermediate; $[Ru(N^N)_2Cl_2]$, forms as the major product for pyrazine systems (bpz).

Preliminary work: Molecular Light-Switches for DNA

Applying the Surfactant Synthesis



Molecular Design: Development on Light-Switch Compounds

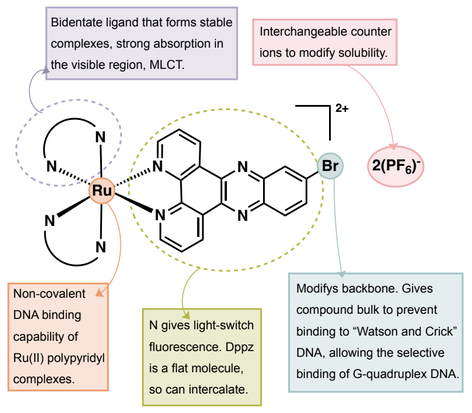
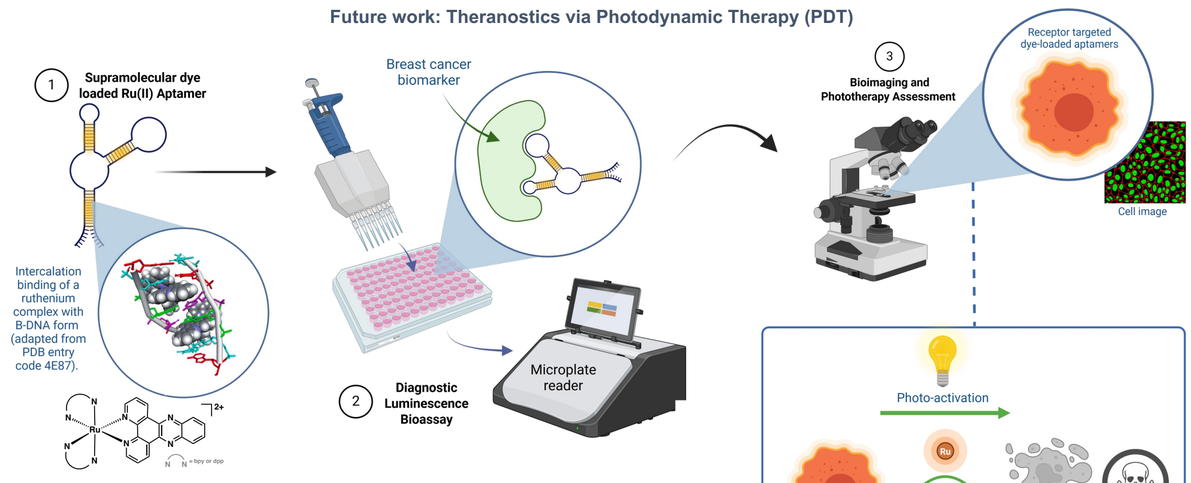


Figure 3: ^{1}H NMR (400 MHz, $[(CD_3)_2SO]$) spectrum of $[Ru(bpy)_2(dppz)](PF_6)_2$; first Ru-dppz light-switch target synthesised.

What is the potential impact in the Pharma area?

Future work: Theranostics via Photodynamic Therapy (PDT)



- Metallodrugs are well-established in oncological treatments; platinum chemistry is the cornerstone of many anti-cancer drugs and there are several Ru(II) drugs progressing through clinical trials such as TLD1433 as a PDT agent for bladder cancer.
- Similarly, aptamers have long been seen as reproducibly producible biomolecules that enable cancer targeting and treatment. If successful, this work will demonstrate new design rules to approach next generation metal-based PDT agents, including combination treatments with DNA aptamers.

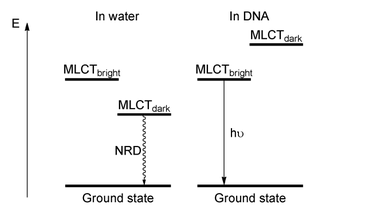


Figure 4: Energy diagram of excited states involved in the light-switch effect. Light-up probes are not luminescent in water but do emit brightly in DNA containing aqueous solutions. Molecules 2022, 27(5), 1541; https://doi.org/10.3390/molecules27051541.

Acknowledgements

- Many thanks to my supervisor Dr. Christopher Burke for all the advice and support.
- This publication has emanated from research conducted with the financial support of Taighde Éireann - Research Ireland under Grant number [GOIPG/2024/3447].

Taighde Éireann Research Ireland

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31

From Simulation to Separation: Predicting Enantioselectivity in Chiral MOF Materials

Robyn O'Sullivan, Melissa Hanna-Brown, Davide Tiana
School of Chemistry

What am I doing?

Molecular dynamics simulations reveal how chiral MOF-520 interacts with drug enantiomers, guiding the design of smarter stationary phase materials for cleaner, more precise separations and safer medicines.

How do we efficiently and accurately identify chiral stationary phase materials that can selectively separate enantiomeric drugs, without relying on slow, expensive, trial-and-error laboratory testing?

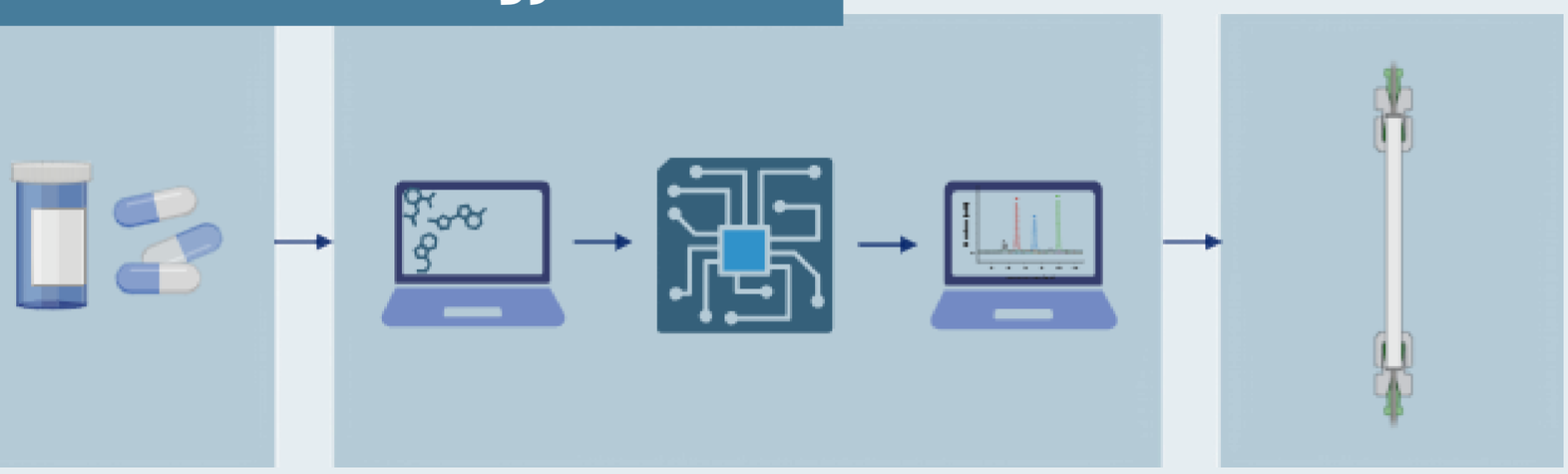
Why does this matter?

1. Enantiomeric separations of pharmaceutical are vital for regulatory approval of drugs.
2. Alternative stationary phases make way for the green revolution of chromatographic techniques.

Simulations show which molecules stick

Computational models allow us to predict how these chiral materials will recognise and separate enantiomers before making them.

Methodology



What is Molecular Dynamics?

Molecular dynamics is a computational chemistry technique that iteratively solves the equations of motion to simulate the behaviour and interactions of atoms and molecules over time at the nanoscale.

Acknowledgements:/References/

I would like to thank my supervisors Dr. Davide Tiana and Prof. Melissa Hanna-Brown for their guidance and support.

Hess, B., Kutzner, C., van der Spoel, D., & Lindahl, E. (2008). GROMACS 4: Algorithms for Highly Efficient, Load-Balanced, and Scalable Molecular Simulation. *Journal of Chemical Theory and Computation*, 4(3), 435–447.

Potential Pharmaceutical Impact

<u>Faster and Greener Method Development:</u>
Computational predictions reduce the need for time consuming and resource intensive lab experiments.

<u>Advanced Material Design:</u>
Insights at the molecular level guide the creation of smarter, more selective chiral stationary phases for HPLC.

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Enter the Dragon: Next Generation Anti-cancer Therapy by Photo-oxidative Damage Targeted at Membrane-less Organelles of Human SMAUG1 Protein

Tara McInerney,[ab] James Stack,[ac] Colin Hill,[c] Kellie Dean,[b] Christopher Burke [a]

[a] School of Chemistry, [b] School of Biochemistry and Cell Biology, [c] School of Microbiology. *Email: 120383871@umail.ucc.ie*

What I am doing

- **Membrane-less organelles (MLOs)** are transient biomolecular condensates that dynamically form and dissolve through **liquid–liquid phase separation** (LLPS), playing key roles in cellular regulation.
- **Human SMAUG1 protein** forms its own type of MLO called SMAUG1 bodies that compartmentalise enzyme-encoding mRNA to govern mitochondrial function.
- In this work, **metal complexes** capable of stimulating biological oxidative damage through light activation will be targeted to SMAUG1 bodies for **anti-cancer photodynamic therapy** at membrane-less organelles.

Why SMAUG1 bodies are a promising therapeutic target

Cancer Types
Dysregulation of SMAUG1 linked to specific cancer types

Drug Resistance
Dysregulation of SMAUG1 linked to chemotherapy drug resistance

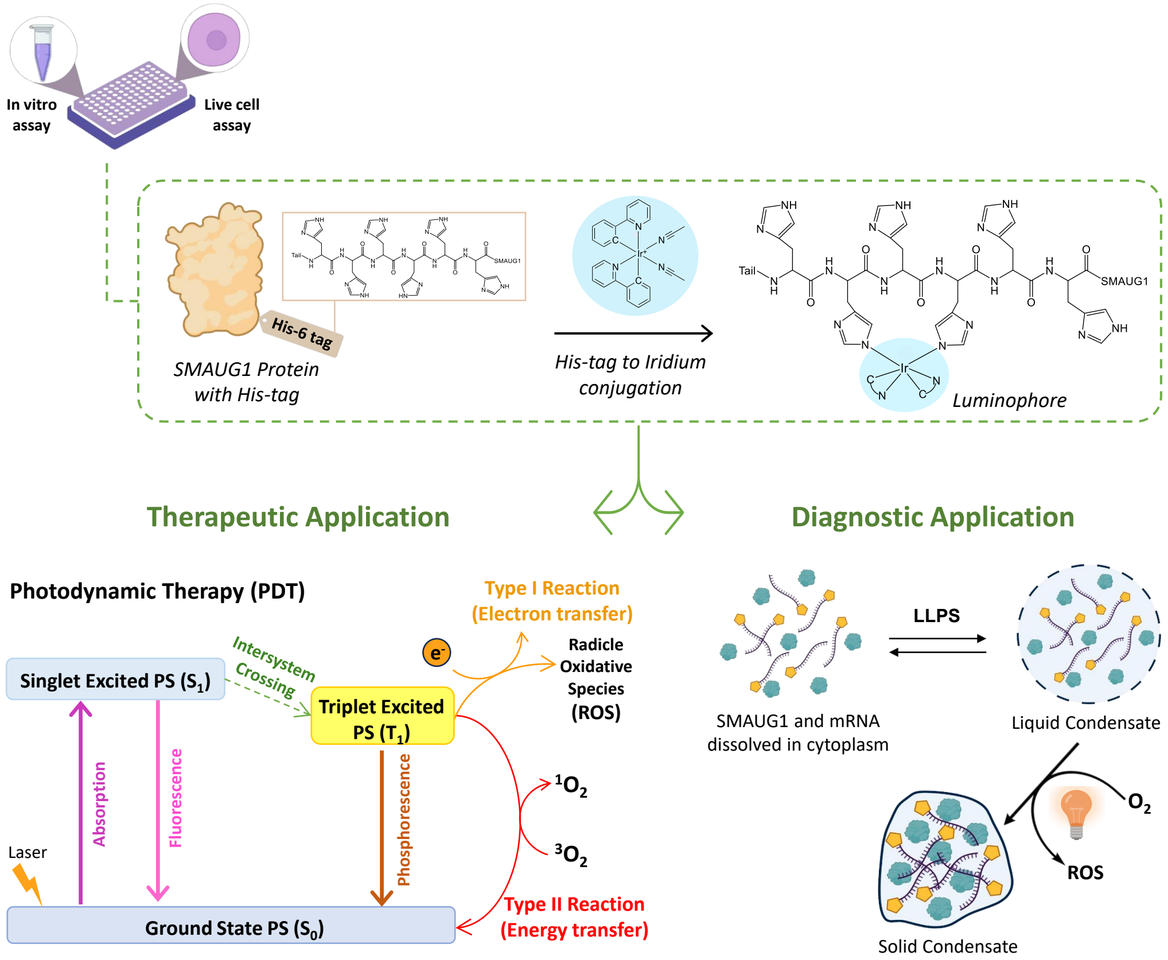
Attenuated Malignancy
Dysregulation of SMAUG1 linked to attenuated malignancy progression

Poorly Understood Dynamics
The dynamics of MLO's remain poorly understood

Opportunity to Advance
Advance the field by elucidating mechanistic roles of SMAUG1 bodies

How I am doing it

We aim to **exploit transition metal chemistry** for both diagnostic and therapeutic applications by developing **bioconjugate strategies** to label SMAUG1 with luminescent complexes.



Advantages of Transition Metal Complexes as Probes:

- Small size enables monitoring of MLO assembly.
- Efficient photosensitisers (PS) for Photodynamic therapy (PDT).
- Easy chemical modification allows for tunability of physical and photophysical properties.

Preliminary Results

Iridium solvate complexes, which fluoresce selectively upon direct binding to **di-histidine motifs**, have been selected as our first metal complex candidate.

1. Synthesis

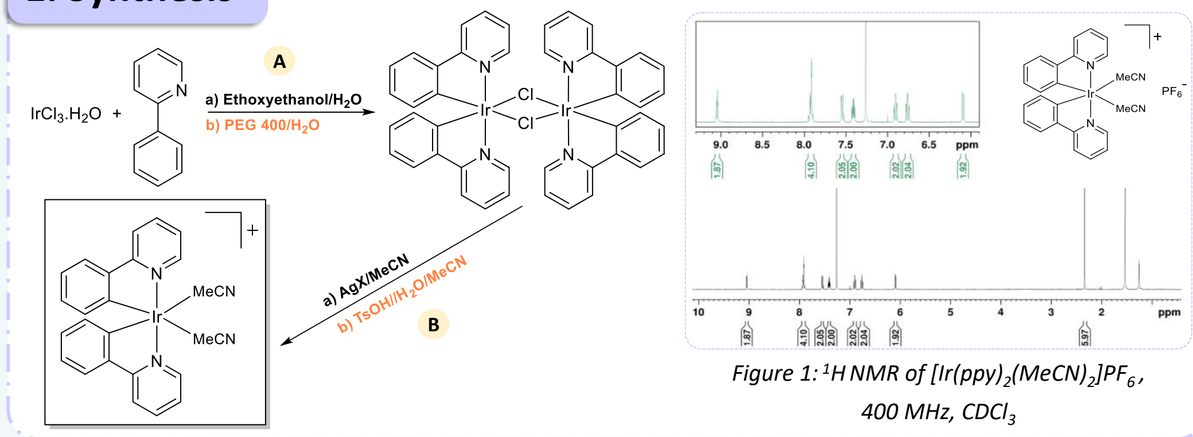


Figure 1: ^1H NMR of $[Ir(ppy)_2(MeCN)_2]PF_6$, 400 MHz, $CDCl_3$

KEY
- ❑ **Series** of Ir-solvate dyes has been successfully **synthesised**.
- ❑ **Greener** synthetic pathway **developed** by replacing (A) toxic ethoxyethanol with polyethylene glycol (PEG) and (B) silver salts with tosic acid.

2. Biological Testing

Light switch

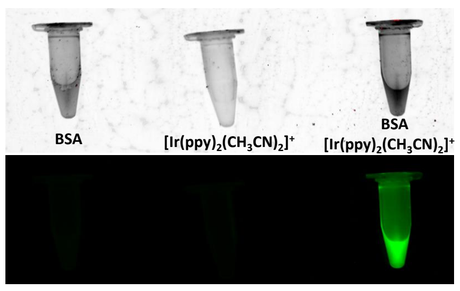


Figure 2: Switch-on fluorescent effect of Ir Solvate in histidine rich protein BSA

Selectivity

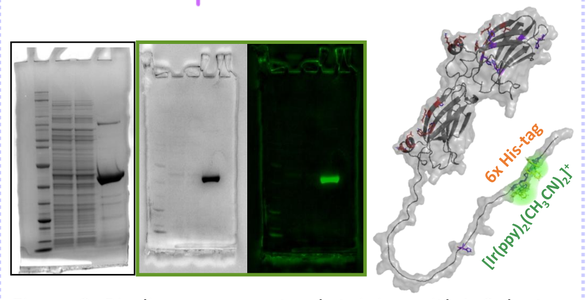


Figure 3: Binding assay post gel staining with Ir Solvate. Lane 1: E. Faecium cell lysate, Lane 2: Cell lysate + LysH1 CBD, Lane 3: LysH1 CBD control

KEY
- ❑ **Switch-on** of fluorescence in the presence of **histidine** demonstrated.
- ❑ **Selectivity** for histidine demonstrated through post-staining of gel with cell lysate containing CBD protein with a genetically engineered **His-tag**.

What I hope to achieve

Metal-based Drug Development

Develop a series of **photoactive metal-based drugs** to be applied to a **novel anti-cancer target** for both diagnostic and therapeutic purposes.

Phase Separation Toolkit

Provide a **toolkit** for biologists **to better understand** phase separation dynamics, using SMAUG1 as a **model protein.**

Potential Impact in the Pharma Area

- **Broaden scope** of **metal-based therapeutics** beyond established agents such as platinum compounds.
- Investigate **MLO's** as novel targets for **anticancer** intervention.
- Explore **metal** complexes as **PDT agents**.
- Explore the potential of metal complexes as **bioconjugate targeting agents**.

Acknowledgements: This work is supported by the Research Ireland under the Government of Ireland Postgraduate Scholarship (GOIPG/2025/6468) and Enterprise Partnership Scheme (EPSPG/2023/1807) with enterprise partner Novus Diagnostics.

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Synthesis and evaluation of novel pyridocarbazoles as inhibitors of Anaplastic Lymphoma Kinase (ALK) and cell cancer growth

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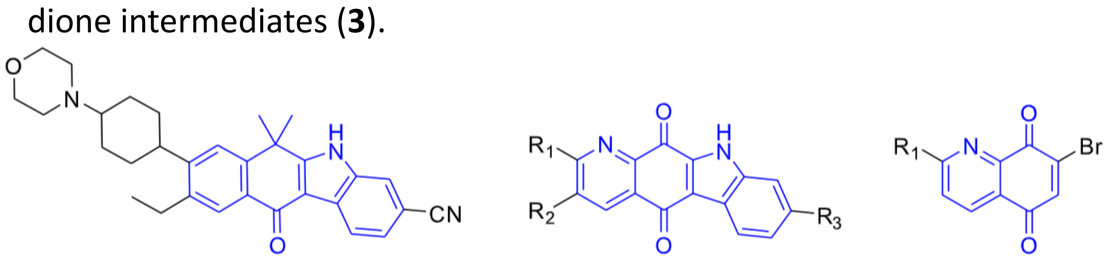
School of Chemistry and ABCRF, University College Cork, Western Road, Cork, Ireland, T12K8AF2
120317573@umail.ucc.ie

What I am doing

My project aims to design, synthesise and evaluate new selective molecules for the treatment of non-small cell lung cancer (NSCLC). Anaplastic Lymphoma Kinase (ALK) is a membrane tyrosine kinase receptor which is a target in approximately 5% of all NSCLC cases. NSCLC accounts for 80 – 85% of all lung cancer cases and is unfortunately responsible for a very poor prognosis.[1] Resistance to current treatments such as ALK inhibitors has been identified in recent years. Alectinib (**1**) is an example of one of these treatments whose structure is based on the pyridocarbazolequinone (PCQ) (**2**) framework.[2] This project outlines the synthesis of structural derivatives of PCQs derived from structurally similar quinoline-5,8-dione intermediates (**3**).



1 **2** **3**

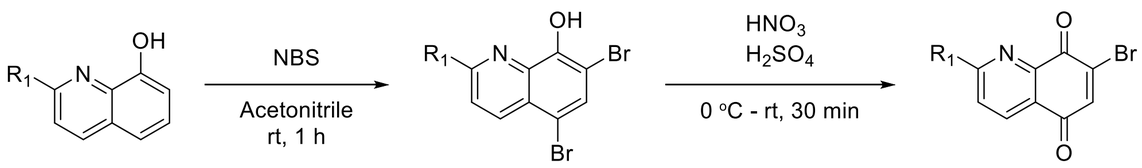
Figure 1

Why I am doing it

Urgent action is required to counter the growing problem of resistance to current treatments of ALK-positive NSCLC. Previous work within the McCarthy group has resulted in the development of PCQ derivatives with proven anticancer activity equipotent to alectinib. Building on this proven work, I aim to address the problem of multidrug resistant NSCLC through ALK inhibition.

How I am doing it: Synthesis of quinoline-5,8-diones

- My work has involved the synthesis of reactive intermediates known as quinoline-5,8-diones, a class of compounds with known anti-cancer properties.
- I have synthesised quinoline-5,8-diones in high yields from cheap and readily available quinolinol starting materials using bromination and oxidation reactions.



4a: R_1 = H
4b: R_1 = Me

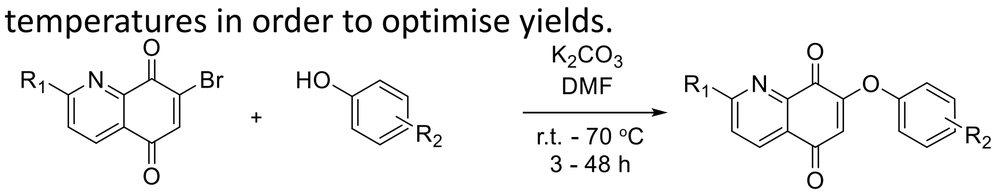
5a: R_1 = H, 81%
5b: R_1 = Me, 85%

3a: R_1 = H, 78%
3b: R_1 = Me, 71%

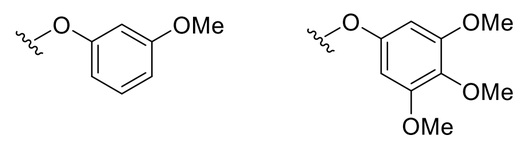
Scheme 1

How I am doing it: Substitution of quinoline-5,8-diones

- A range of functional groups can then be added to the quinoline-5,8-dione intermediates at specific positions on the structure.
- Phenol groups were substituted using varying reaction times and temperatures in order to optimise yields.



R_2 =

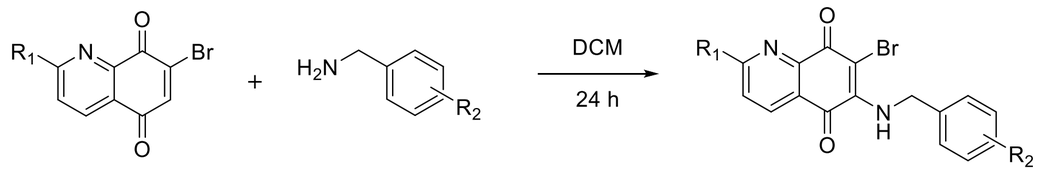


4a: R_1 = H, 1%
4b: R_1 = Me, 18%

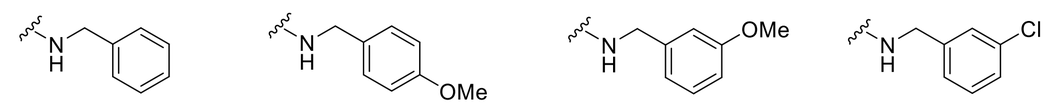
5a: R_1 = H, 3%
5b: R_1 = Me, 11%

Scheme 2

- The addition of a range of benzylamines proceeded successfully under ambient conditions



R_2 =



6a: R_1 = H, 39%
6b: R_1 = Me, 76%

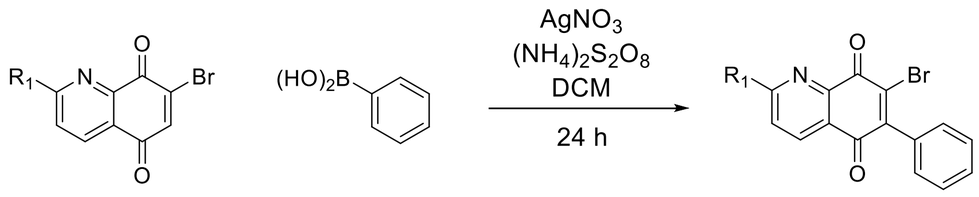
7a: R_1 = H, 71%
7b: R_1 = Me, 25%

8: R_1 = H, 21%

9: R_1 = H, 28%

Scheme 3

- Silver nitrate was utilised as a metal catalyst in the oxidative coupling of phenylboronic acid to the quinoline-5,8-dione structure



Scheme 4

10a: R1 = H, 9%
10b: R1 = Me, 69%

Future work and potential impact

- The ultimate goal of this project is to inhibit ALK and therefore reduce the growth of NSCLC cells. Future work will include ring closing reactions of the above compounds to synthesise the final PCQ framework which will be furnished at the C(2), C(3) and C(8) positions using a versatile range of functional groups.
- The final result will be a panel of compounds tailored to inhibit ALK activity which will undergo biological testing using the NCI 60 cell line panel.
- The need for new NSCLC treatments for patients cannot be understated. The synthesis and evaluation of novel PCQs will provide potential drug leads and a more detailed understanding of ALK and multidrug resistance to the pharmaceutical industry.

References

1. Soda, M.; Takada, S.; Takeuchi, K.; Choi, Y. L.; Enomoto, M.; Ueno, T.; Haruta, H.; Hamada, T.; Yamashita, Y.; Ishikawa, Y.; Sugiyama, Y.; Mano, H. *Proc Natl Acad Sci U S A.* **2008**, *105* (50). www.pnas.orgcgidoi10.1073pnas.0805381105.
2. Rolfo, C.; Passiglia, F.; Castiglia, M.; Raez, L.E.; Germonpre, P.; Gil-Bazo, I.; Zwaenepoel, K.; De Wilde, A.; Bronte, G.; Russo, A.; Van Meerbeeck, J.P.; Van Schil, P.; Pauwels. *Transl. Lung Cancer Res.* **2014**, *3* (4), 250-261.

Acknowledgements

Thank you to Dr Florence McCarthy for his guidance. Thank you to Research Ireland for the research funding.

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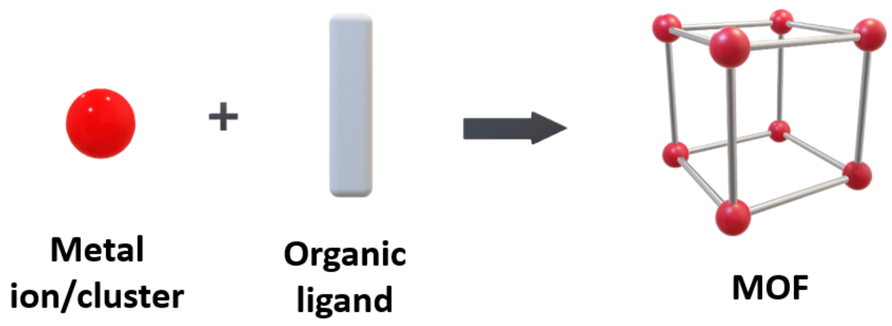
Computational Design of Metal-Organic Frameworks for Pharmaceutical Solvent Recovery

Amy Twomey, Davide Tiana
School of Chemistry

Overview

- This work focuses on the design of zirconium-based MOFs optimised for solvent recycling in pharmaceutical manufacturing
- MOFs are crystalline materials made from metal ions or clusters linked by organic molecules
- Self-assemble into repeating, porous, grid-like structures
- Widely used in catalysis, drug delivery, water treatment and gas storage/separation



I Chemical and Thermal stability
II Tuneable Porosity
III High Surface Area
IV Flexibility
V Uniform Pore Structure

Background

- Conventional solvent recovery methods like distillation and membrane filtration are energy-intensive and struggle with complex solvent mixtures or overlapping boiling points
- MOFs offer precise control over pore chemistry and size, allowing selective adsorption of target solvents

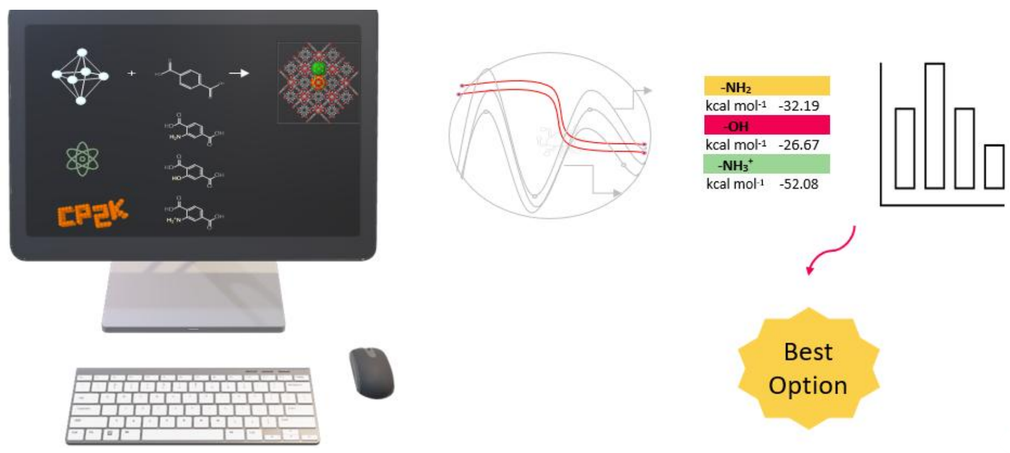
Research Aim

To design MOF structures with the optimal balance of adsorption energy and selectivity for use in sustainable solvent recycling systems

- The computational insights from this work will guide the synthesis of high-performance materials that enable low-energy solvent recovery in pharmaceutical processes

Computational Approach

- Density functional theory calculations (DFT) in CP2K are used to model solvent adsorption on functionalised UiO-66 frameworks
- By tuning MOF functional groups, we can compare calculated adsorption energies for key pharmaceutical solvents to identify the most selective and efficient structures for recovery
- Solvents such as butanol, ethanol and acetonitrile are modelled to evaluate how polarity, hydrogen bonding, and molecular size influence adsorption in functionalised UiO-66



Potential Impact

- Integrating MOF-based solvent recycling in pharmaceutical manufacturing can:
  - ☑ Reduce energy consumption
  - ☑ Improve solvent purity
  - ☑ Enhance compliance with regulatory standards
- Enables continuous manufacturing with reduced environmental impact, boosting sustainability and efficiency in pharmaceutical production

Acknowledgments

Taighde Éireann Research Ireland
ICHEC Irish Centre for High-end Computing
UCC computational chemistry and programming group

References

1. O. Yaghi, G. Li, and H. Li, *Nature,* 1995, **378**, 703-706.
2. J. Hutter, M. Iannuzzi, F. Schiffmann and J. Vandevondele, *Wiley Interdiscip Rev Comput Mol Sci*, 2014, **4**, 15-25.
3. Y. Bai, Y. Dou, L. H. Xie, W. Rutledge, J. R. Li and H. C. Zhou *Chem. Soc. Rev.*, 2016, **45**, 2327-2367.

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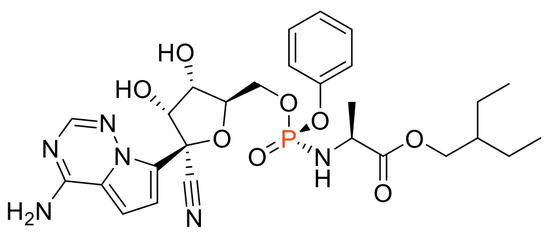
Sustainable Methods in Organophosphorus Chemistry

Meadhbh Coomey,[a] Dr Eimear Courtney,[a] Aoibhe O'Donnell,[a] Dr Tim O'Sullivan,[a,b] and Dr David J. Jones [a]

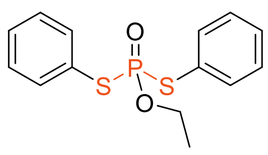
[a]*School of Chemistry & Analytical and Biological Chemistry Research Facility, University College Cork, T12 YN60, Ireland.*
[b] *School of Pharmacy, University College Cork, T12 YN60, Ireland.*

Introduction

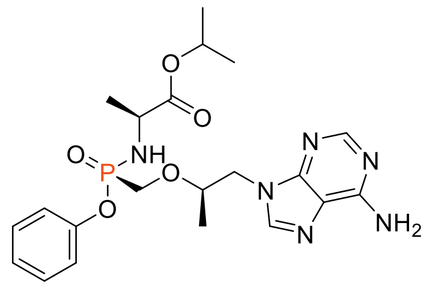
- Phosphorus is present in many life-saving medicines, including anti-cancer and anti-HIV drugs, and new methods for incorporating phosphorus into drugs are urgently required.[1,2]
- The development of new and sustainable methodologies for their preparation is likely to be highly impactful — particularly in the context of the global phosphorus supply chain.



Remdesivir: antiviral

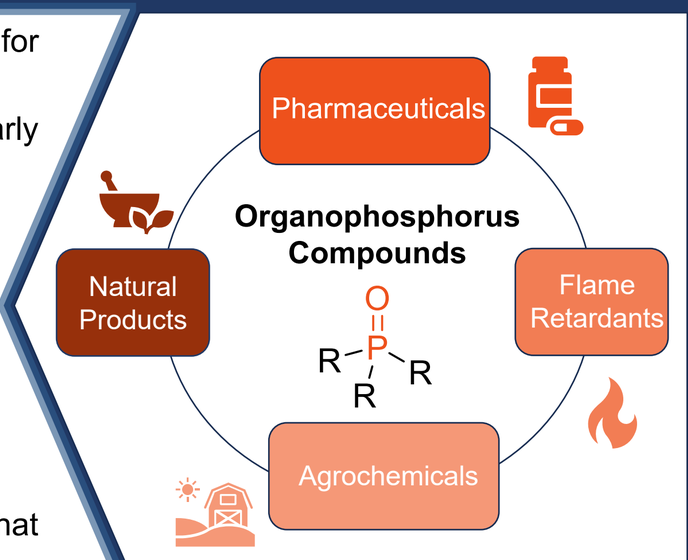


Edifenphos: fungicide



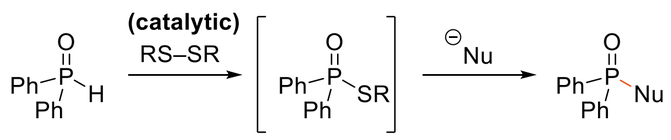
Tenofovir alafenamide: antiviral

- Compounds with phosphorus–sulfur bonds are increasingly commonplace in gene therapy medicines which means that new chemistry will also potentially have an impact on this exciting, developing field of drug discovery.



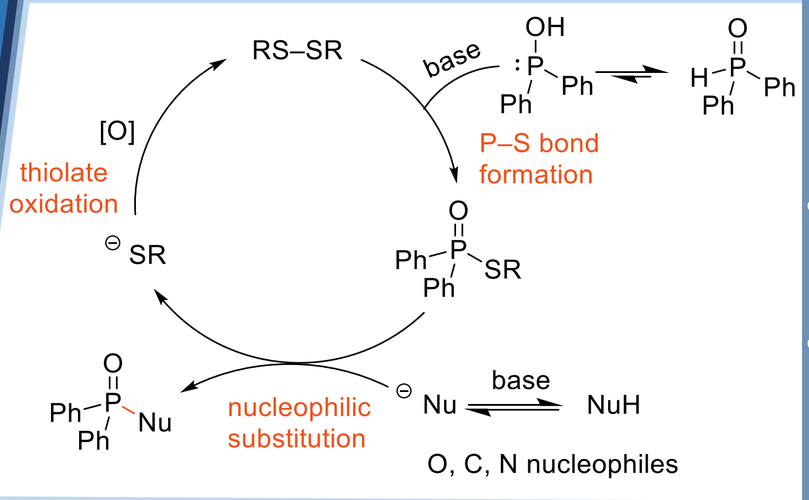
Project Overview

This project focuses on developing a new way to sustainably incorporate phosphorus atoms into high value materials using an organosulfur reagent as a catalyst.



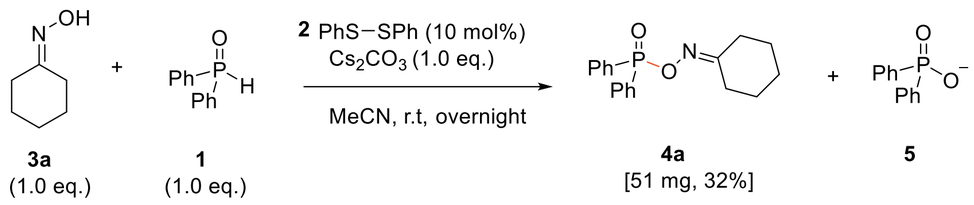
- Reacting diphenylphosphine oxide, a secondary phosphine oxide, with a catalytic amount of diphenyl disulfide forms a phosphinothioate *in situ*.
- This electrophilic phosphinothioate then undergoes nucleophilic substitution with a nucleophile, displacing a thiolate anion.
- Oxygen in ambient air oxidises the thiolate back to the disulfide, which then goes on to activate another molecule of secondary phosphine oxide, turning over the catalytic cycle.

Catalytic Cycle



Results

1. Proof of concept

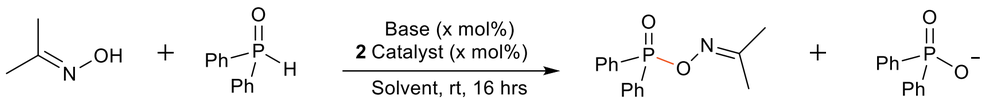


3a (1.0 eq.) + **1** (1.0 eq.) → **4a** [51 mg, 32%] + **5**

2 PhS−SPh (10 mol%), Cs_2CO_3 (1.0 eq.), MeCN, r.t, overnight

- The feasibility of the catalytic process was demonstrated when the phosphinoylimine product **4a** was isolated in 32% yield.
- The yield exceeding the catalytic loading confirms that catalysis is occurring. Diphenylphosphinate **5** is the hydrolysis product of the reaction.

2. Optimisation of catalytic cycle



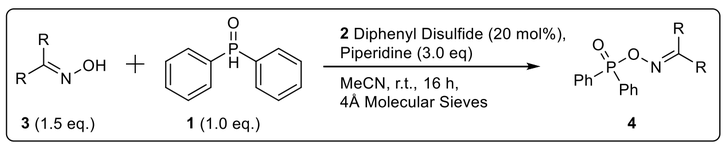
3b + **1** → **4b** + **5**

Base (x mol%), **2** Catalyst (x mol%), Solvent, rt, 16 hrs

Screen	Entry	Solvent	Base	Base (mol%)	Catalyst **2**	Catalyst (mol%)	Yield[a] **4** (%)	Yield[a] **5** (%)	Unreacted[a] **1** (%)
Base and catalytic loading	1	MeCN	Cs_2CO_3	200	diphenyl disulfide	10	41	27	18
	2	MeCN	Cs_2CO_3	100	diphenyl disulfide	10	28	17	30
	3	MeCN	Cs_2CO_3	50	diphenyl disulfide	10	29	20	0
	4	MeCN	Cs_2CO_3	100	diphenyl disulfide	20	43	27	22
	5	MeCN	Cs_2CO_3	100	diphenyl disulfide	10	28	17	30
	6	MeCN	Cs_2CO_3	100	diphenyl disulfide	5	21	39	17
	7	MeCN	Cs_2CO_3	100	diphenyl disulfide	2	6	36	41
	8	MeCN	Cs_2CO_3	50	diphenyl disulfide	20	42	26	20
Base	9	MeCN	DBU	100	diphenyl disulfide	10	19	27	25
	10	MeCN	TBD	100	diphenyl disulfide	10	7	50	0
	11	MeCN	Piperidine	100	diphenyl disulfide	10	28	10	36
	12[b]	MeCN	Piperidine	300	diphenyl disulfide	20	72[c]	22	0
	13	MeCN	Barton's base	100	diphenyl disulfide	10	20	33	0
	14	MeCN	K_3PO_4	100	diphenyl disulfide	10	36	18	26
Solvent	15	DCM	Cs_2CO_3	100	diphenyl disulfide	20	16	22	30
	16	DCE	Cs_2CO_3	100	diphenyl disulfide	20	23	20	30
	17	EtOAc	Cs_2CO_3	100	diphenyl disulfide	20	33	31	24
	18	THF	Cs_2CO_3	100	diphenyl disulfide	20	10	22	0
	19	Toluene	Cs_2CO_3	100	diphenyl disulfide	20	8	26	43
Catalyst	20	MeCN	Cs_2CO_3	100	dimethyl disulfide	20	49	37	0
	21	MeCN	Cs_2CO_3	100	4-nitrophenyl disulfide	20	24	55	0
	22	MeCN	Cs_2CO_3	100	*p*-tolyl disulfide	20	25	27	2
	23	MeCN	Cs_2CO_3	100	4-chlorophenyl disulfide	20	26	34	1
	24	MeCN	Cs_2CO_3	100	bis(4-methoxyphenyl) disulfide	20	46	35	0
	25	MeCN	Cs_2CO_3	100	2,2'-dipyridyle disulfide	20	21	46	0

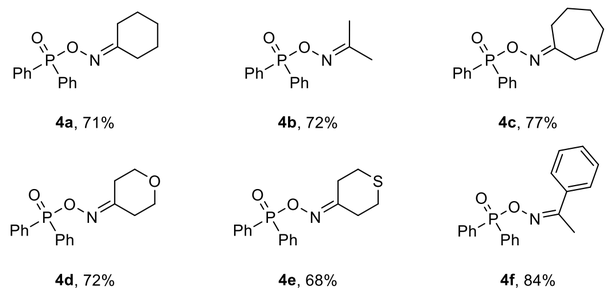
[a] Yields were calculated using triphenylphosphine oxide as an internal standard in ^{31}P NMR.
[b] 1.5 equivalents of **1** were used. All glassware was flame dried prior to reaction. Reaction was run with 4Å molecular sieves, and a drying tube was used.
[c] Isolated yield *via* flash chromatography.

3. Substrate Scope investigation



3 (1.5 eq.) + **1** (1.0 eq.) → **4**

2 Diphenyl Disulfide (20 mol%), Piperidine (3.0 eq), MeCN, r.t., 16 h, 4Å Molecular Sieves



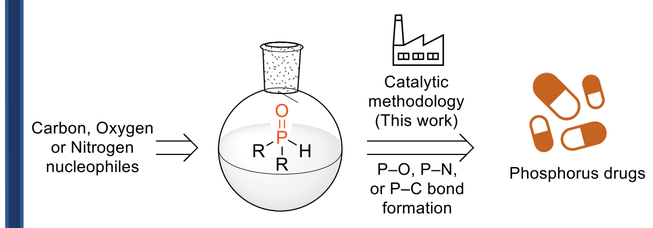
4a, 71% | **4b**, 72% | **4c**, 77%

4d, 72% | **4e**, 68% | **4f**, 84%

All substrate scope experiments were carried out on 2 mmol scale.

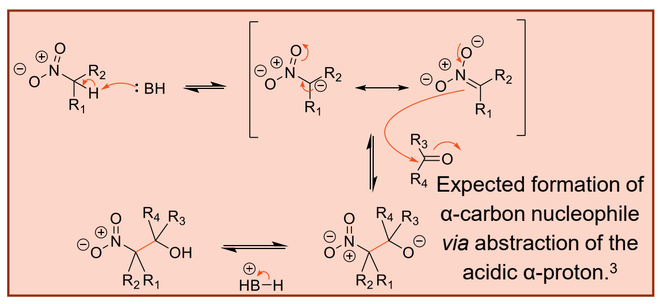
4. Applications to Pharma

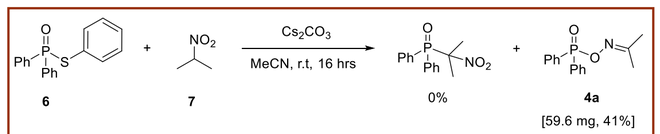
- This methodology will add to the knowledge base for synthesis of P–O, P–C, and P–N bonds.
- It will allow for new types of medicinally relevant organophosphorus compounds to be prepared for the first time, thus expanding the chemical space available for drug discovery in the pharmaceutical industry.



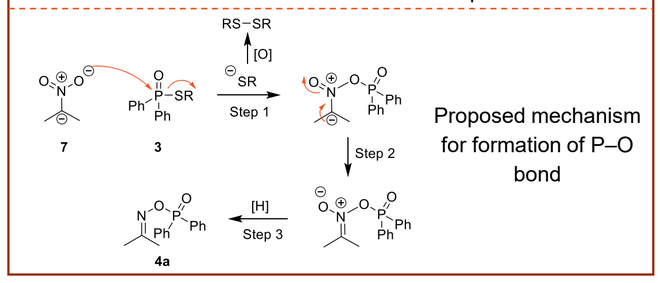
5. Unexpected results

1. Surprise Reaction: 2-Nitropropane





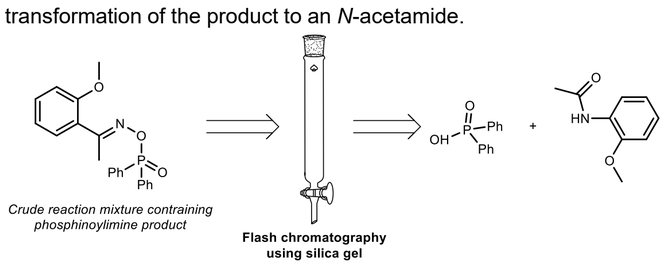
Result: P–O bond instead formed instead of expected P–C bond



Proposed mechanism for formation of P–O bond

2. Aza-Baeyer-Villiger rearrangement on silica column

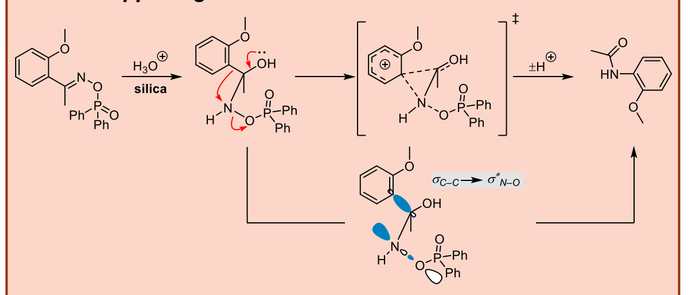
Purification of the 2'-methoxyacetophenone oxime product *via* flash chromatography on silica gel resulted in an Aza-Baeyer-Villiger transformation of the product to an *N*-acetamide.



Crude reaction mixture contraining phosphinoylimine product

Flash chromatography using silica gel

What is happening on the column?



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Acknowledgements

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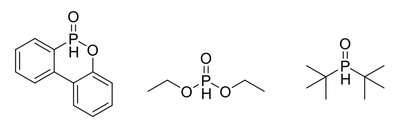
IRISH RESEARCH COUNCIL An Chomhairle um Thaighde in Eirinn

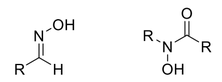
Conclusion

- We established and optimised an efficient catalytic platform for P–O bond formation *via* disulfide organocatalysis.
- We expanded the scope of the methodology to several oxime nucleophiles, and will further expand the scope of the nucleophiles and secondary *H*-phosphonates in future work.

Future Scope



Secondary *H*-phosphonates



Oximes

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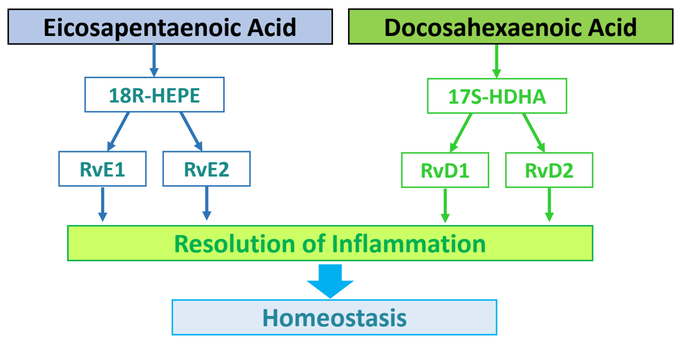
Synthesis of aromatic resolvin analogues as potential anti-inflammatories

Ruth O'Connell, Gangireddy Sujeevan Reddy, Timothy P. O'Sullivan
School of Pharmacy, School of Chemistry, & ABCRF

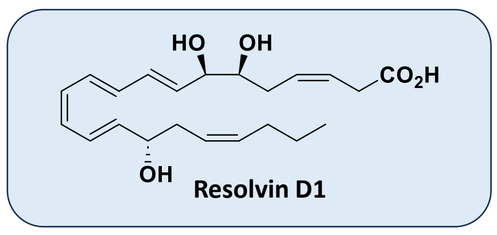
What is the project?

Our goal is to ***synthesise new anti-inflammatory compounds*** based on ***resolvins:*** molecules which are present in the human body at a site of inflammation. Resolvins ***restore tissue homeostasis*** once an inflammatory stimulus has been removed.[1] Resolvin analogues should have strong anti-inflammatory action with few side effects.



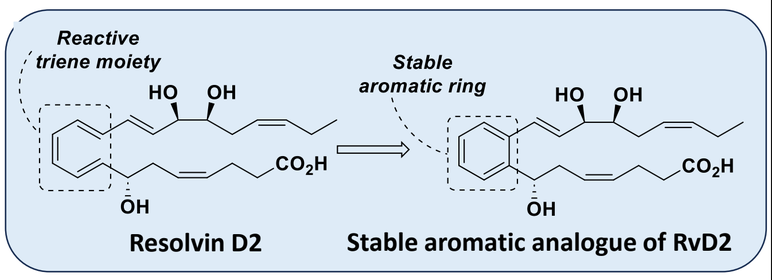
Why resolvins?

Resolvins are extremely potent and have anti-inflammatory action ***at nanogram concentrations***.[2] ***Resolvin D2*** resolves inflammation by reducing neutrophil recruitment and cytokine production.[3] The hope is that compounds based on ***Resolvin D2*** will be equally ***active at low concentrations with limited side effects.*** Analogues of other resolvins have already been shown to have the same effects as the molecules on which they are based, e.g. Resolvin D1 analogues.[4]



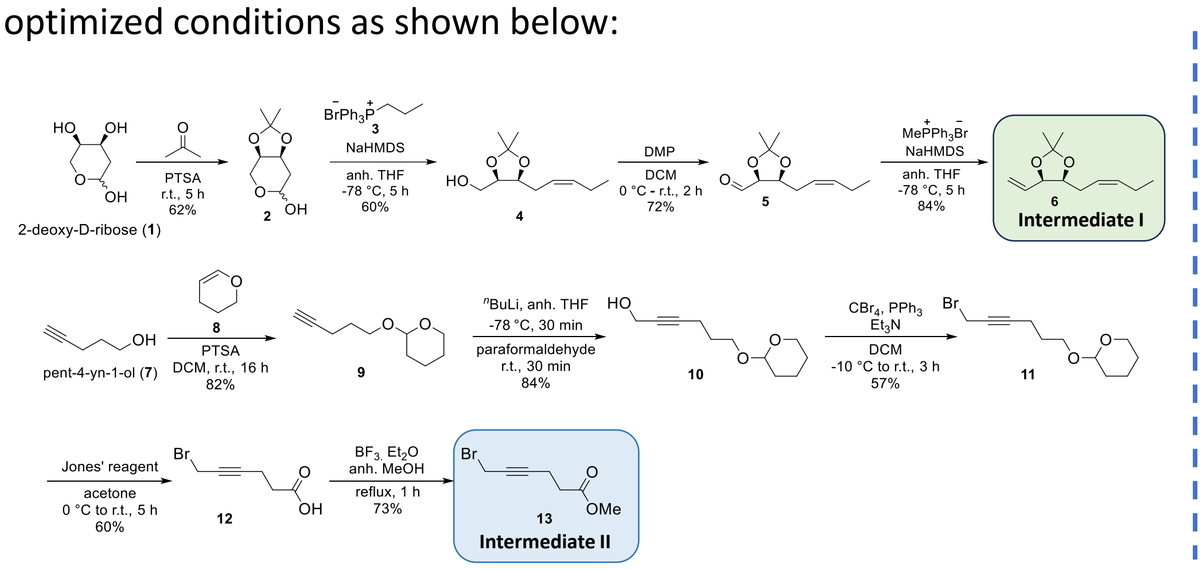
Problems with resolvins?

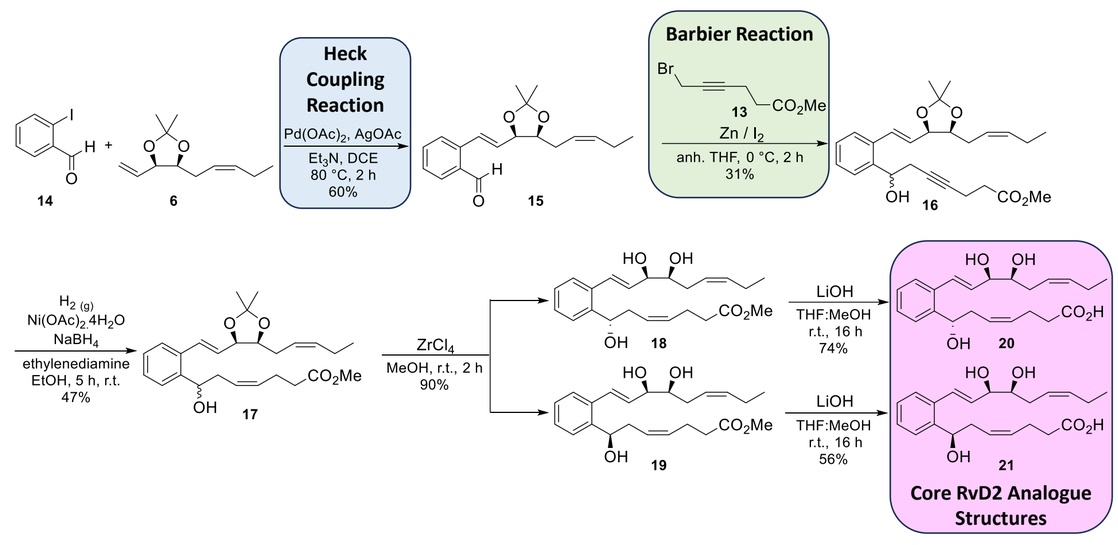
Natural resolvins are ***rapidly degraded by enzymes***,[5] so our resolvin D2 analogues will include ***key structural changes*** to resist metabolic deactivation and ***extend anti-inflammatory activity***. The ***conjugated triene system*** in resolvin D2 is susceptible to autoxidation. Replacing the triene system with a ***more stable benzene ring*** makes it ***resistant to this enzymatic degradation*** while retaining the key Δ10-Z geometry.[6]



The Chemistry: What are the key steps?

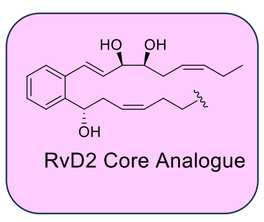
The ***convergent synthesis*** of our core Resolvin D2 analogue involves ***two key intermediates coupled to a benzene ring*** via ***Heck coupling***[7] and a zinc-mediated ***Barbier reaction***[8]. These two intermediates were identified using ***retrosynthetic analysis.*** We have carried out this synthesis and optimized conditions as shown below:

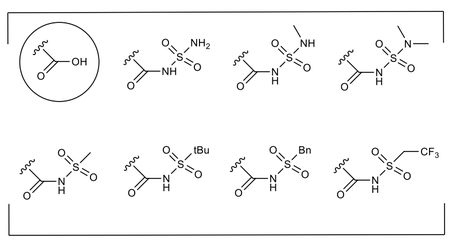




Where is the project headed?

The next aim is to develop a ***library of novel compounds*** with ***varied logP and pKa values***. They will be sent for biological testing to identify any promising anti-inflammatory activity. The library will be generated via ***coupling of sulfonamide groups to the core RvD2 structure*** with EDC and DMAP.





Why is this project relevant?

Chronic inflammation is an underlying cause of several serious diseases like Alzheimer's, Rheumatoid Arthritis and IBD.[9] These diseases have ***profound impact*** on patients, healthcare systems, and wider society.

Current anti-inflammatory drugs (***NSAIDs***) are responsible for a ***significant portion*** of all ***adverse drug reactions***. These drugs primarily inhibit ***COX enzymes*** to stop promotion of inflammation. However, because COX enzymes are also found in the gut, kidneys and heart, their inhibition leads to ***severe side effects*** including renal damage, G.I. bleeding and even myocardial infarction.[10]

Conclusion: What do we hope to achieve?

Ultimately the hope is that a new class of compounds would ***provide better relief*** to patients with ***fewer side effects***, thereby improving quality of life and contributing to pharmaceutical research. These compounds will help to ***resolve inflammation rather than prevent it***, which should result in less side effects compared to drugs currently on the market.

Acknowledgments

- Dr. T. P. O'Sullivan,
- Dr. G.S. Reddy.
- E. Collins, M. O'Driscoll, O. Dunne, S. Sweetnam

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Metal assisted peptide crystallization

Fucheng Leng
School of Engineering and Architecture, School of Chemistry

What I am doing

I am investigating and comparing the crystallization behavior of carnosine and its zinc and copper complexes. This study aims to reveal how metal coordination affects the crystallization of peptide molecules and to determine whether introducing biocompatible metals can enhance crystal formation, quality, and reproducibility.

Why I am doing it

The rapid growth of peptide therapeutics like semaglutide has exposed a major bottleneck in peptide production: expensive, time-consuming, and wasteful chromatography. Peptide crystallization offers a greener, cheaper alternative, but is rarely successful due to unpredictable crystallization behavior. MAPcryst addresses this gap by systematically using metal–peptide chemistry to enable consistent and efficient crystallization.

How I am doing it

This work will measure and compare important crystallization properties (including metastable zone, induction time..) of carnosine,zinc-carnosine and copper-carnosine, analyze their difference with the assisstance of computational modelling method.

What I hope to achieve in the end

This work seeks to clarify how metal coordination influences peptide crystallization and to identify the optimal metal–peptide combination for promoting stable, high-quality crystals. The results will provide mechanistic understanding and design principles that can guide the broader application of metal-assisted crystallization in peptide purification.

What is the potential impact in the Pharma area

By revealing how metal ions promote or modify peptide crystallization, this study will expand the scientific understanding of peptide solid forms and metal–peptide interactions. The insights gained can guide the development of greener, chromatography-free purification routes for peptide drugs. Industrially, this could lower production costs and solvent waste, while socially it may improve access to affordable, sustainable peptide-based medicines.

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Characterisation of Solid-State Insulin: Exploring the Solid-State Physical Properties of Two Sources of Insulin

Diarmuid Carey[a,b], Lorraine Bateman[b,c], Joseph O'Shea[a,b], Abina Crean[a,b]

[a] SSPC, Taighde Éireann – Research Ireland Centre for Pharmaceuticals

[b] School of Pharmacy, University College Cork, Cork, T12K8AF, Ireland

[c] Analytical and Biological Chemistry Research Facility, School of Chemistry, University College Cork, Cork, T12YN60, Ireland

What I am doing

I am conducting an in-depth physical characterisation of two sources of insulin with varying morphologies (supplied by Novo Nordisk and Merck). Temperature and moisture are two pivotal factors impacting peptide stability. Therefore, I am comparing the physical properties of Novo Nordisk and Merck insulin both before and after storing samples in a controlled environment in terms of temperature and relative humidity (40°C/75% relative humidity) for four weeks.

Why I am doing it

The numbers of peptide and protein therapeutics are continually increasing. However, most biopharmaceutical drugs are delivered parenterally to patients. I wish to contribute research to the field of oral peptide delivery. The two main challenges preventing adequate bioavailability of peptides delivered orally are low membrane permeability and instability. Research in the field to date has focused almost entirely on the identification and development of various excipients to overcome the membrane permeability aspect. However, much less research has been conducted on the stability of peptides in the solid-state.

The aim of the work presented is to investigate how the solid-state characteristics of a peptide impact its physical stability upon exposure to environmental temperature and humidity. For this study, insulin is selected as a model peptide.

How I am doing it

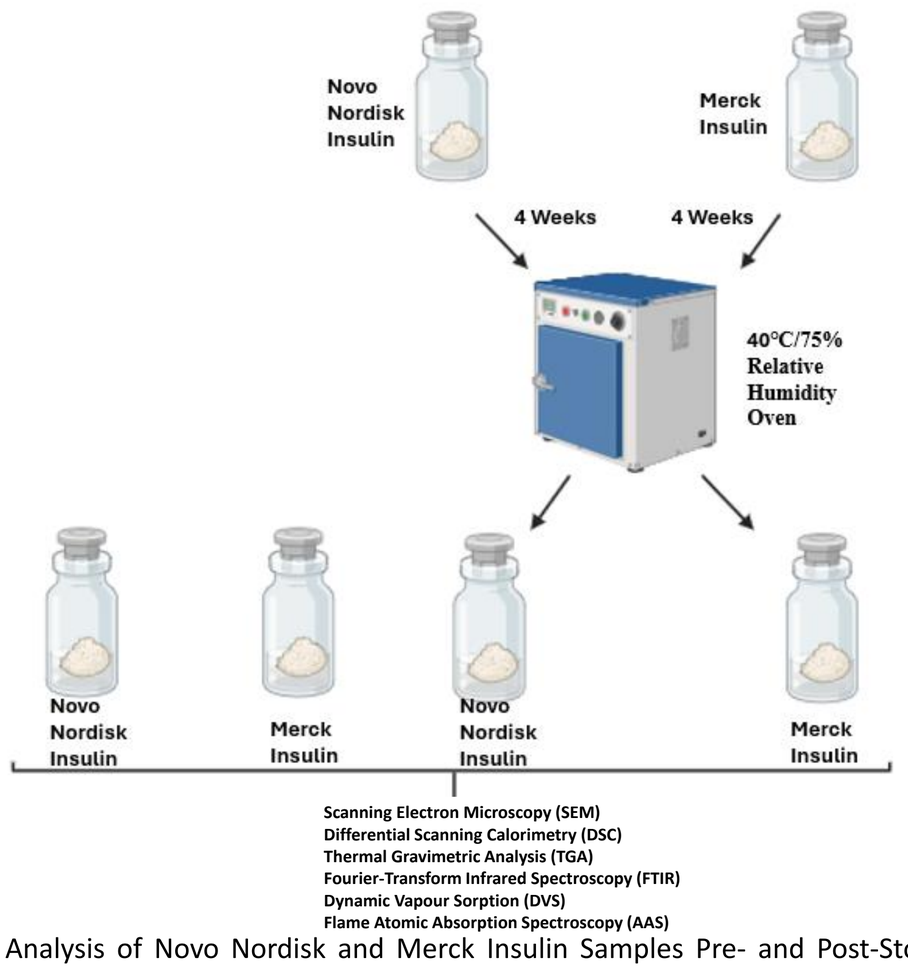

Figure 1: Analysis of Novo Nordisk and Merck Insulin Samples Pre- and Post-Storage at 40°C/75% Relative Humidity for Four-Weeks

How is it looking

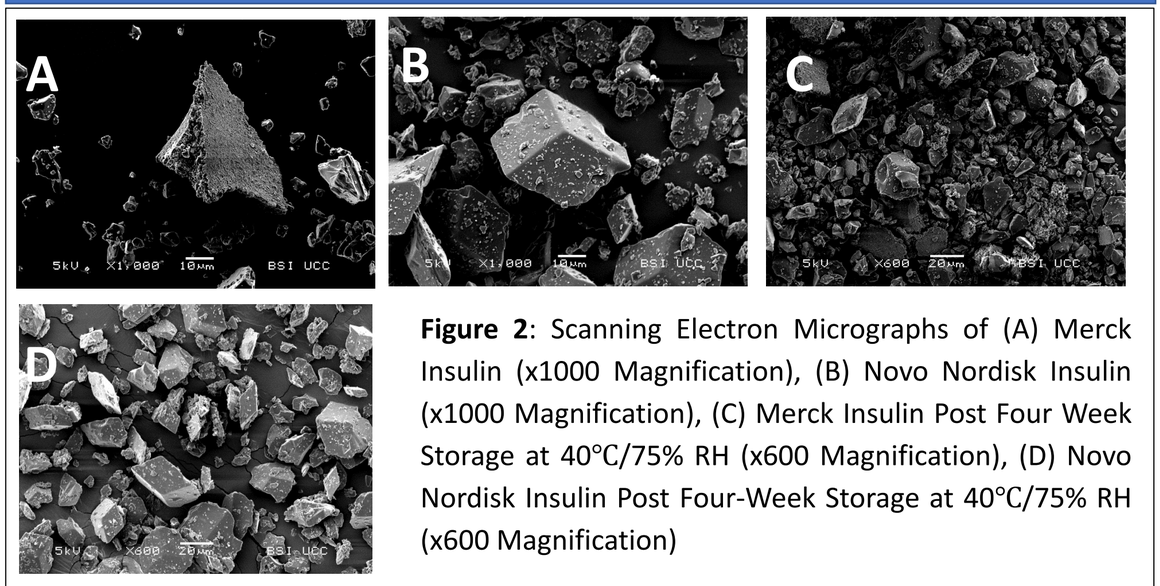

Figure 2: Scanning Electron Micrographs of (A) Merck Insulin (x1000 Magnification), (B) Novo Nordisk Insulin (x1000 Magnification), (C) Merck Insulin Post Four Week Storage at 40°C/75% RH (x600 Magnification), (D) Novo Nordisk Insulin Post Four-Week Storage at 40°C/75% RH (x600 Magnification)

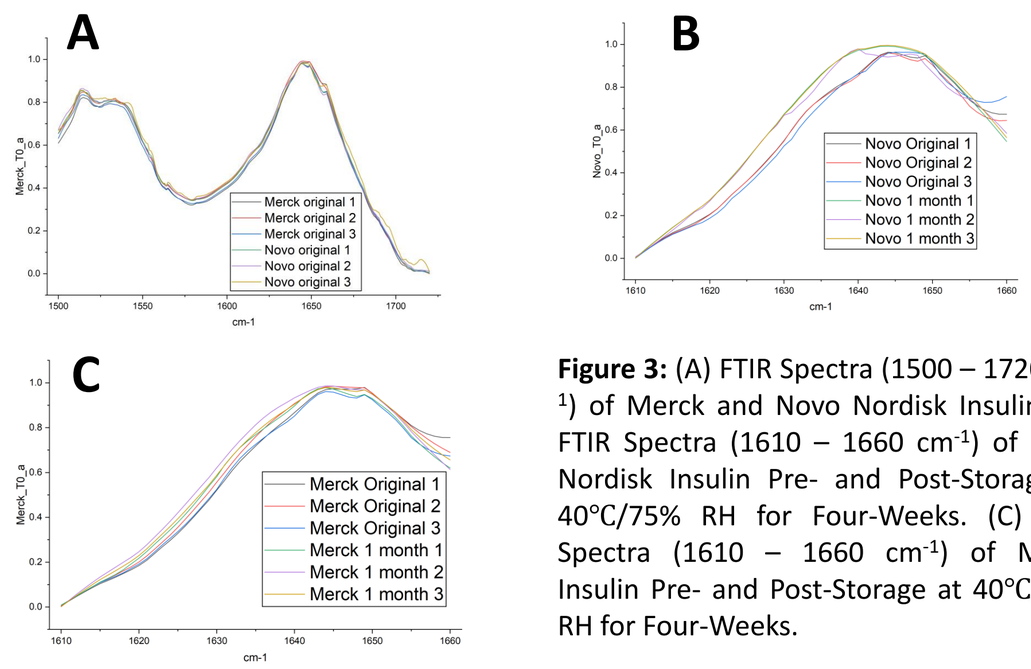

Figure 3: (A) FTIR Spectra (1500 – 1720 cm^{-1}) of Merck and Novo Nordisk Insulin. (B) FTIR Spectra (1610 – 1660 cm^{-1}) of Novo Nordisk Insulin Pre- and Post-Storage at 40°C/75% RH for Four-Weeks. (C) FTIR Spectra (1610 – 1660 cm^{-1}) of Merck Insulin Pre- and Post-Storage at 40°C/75% RH for Four-Weeks.

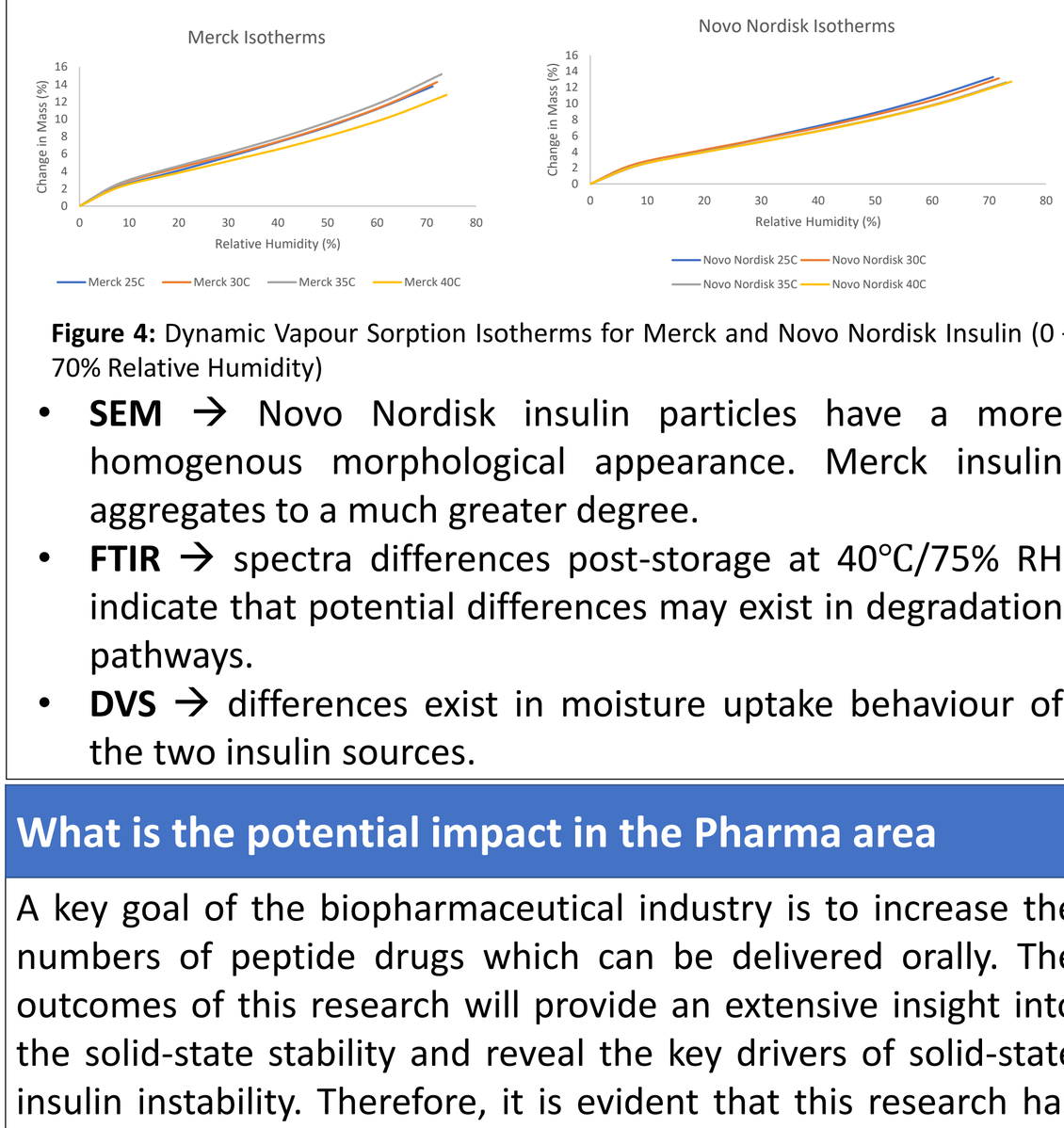

Figure 4: Dynamic Vapour Sorption Isotherms for Merck and Novo Nordisk Insulin (0 – 70% Relative Humidity)

- **SEM** → Novo Nordisk insulin particles have a more homogenous morphological appearance. Merck insulin aggregates to a much greater degree.
- **FTIR** → spectra differences post-storage at 40°C/75% RH indicate that potential differences may exist in degradation pathways.
- **DVS** → differences exist in moisture uptake behaviour of the two insulin sources.

What is the potential impact in the Pharma area

A key goal of the biopharmaceutical industry is to increase the numbers of peptide drugs which can be delivered orally. The outcomes of this research will provide an extensive insight into the solid-state stability and reveal the key drivers of solid-state insulin instability. Therefore, it is evident that this research has the potential to inform the pharmaceutical sphere of excipient choice in oral insulin tablets to mitigate instability. The potential impact of this research is highly exciting in terms of advancing the field of oral peptide deliver, peptide-coated medical devices and microneedle peptide drug delivery.

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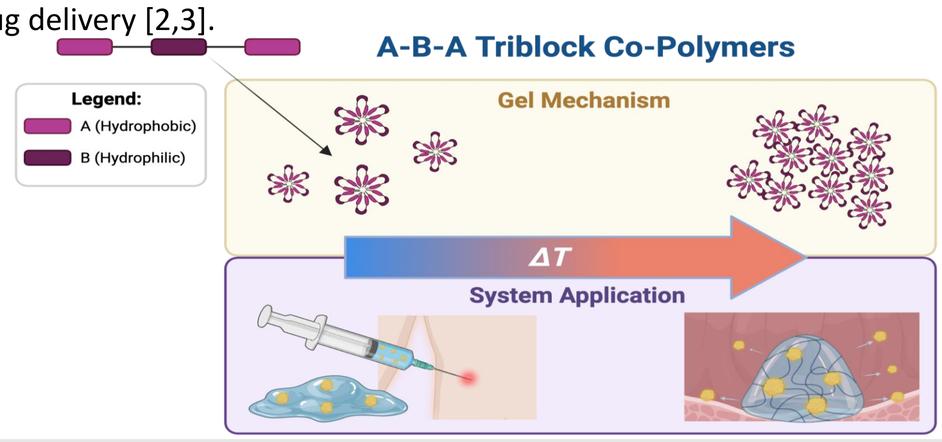
Characterization of Thermosensitive Hydrogel's as Biologic Drug Delivery Matrices

Katie O'Riordan[1], Abina Crean[1], Katie Ryan[1], Philip Dorgan[2]

1. SSPC, Taighde Éireann – Research Ireland Centre for Pharmaceuticals, School of Pharmacy, University College Cork, Ireland, katie.10oriordan@gmail.com
2. Boston Scientific, Model Farm Rd, Cork, Ireland

Introduction

Localized delivery of biologic therapeutics has the potential to enhance biologic efficacy while reducing systemic toxicity, a challenge which often constrains pharmaceutical development [1]. Achieving such targeted delivery requires the identification of carrier matrices capable of stabilizing biologics and enabling sustained release. PEG Based Thermosensitive ABA triblock co-polymers which undergo sol-gel transition at physiological temperatures represent a promising class of biodegradable hydrogels for in-situ drug delivery [2,3].

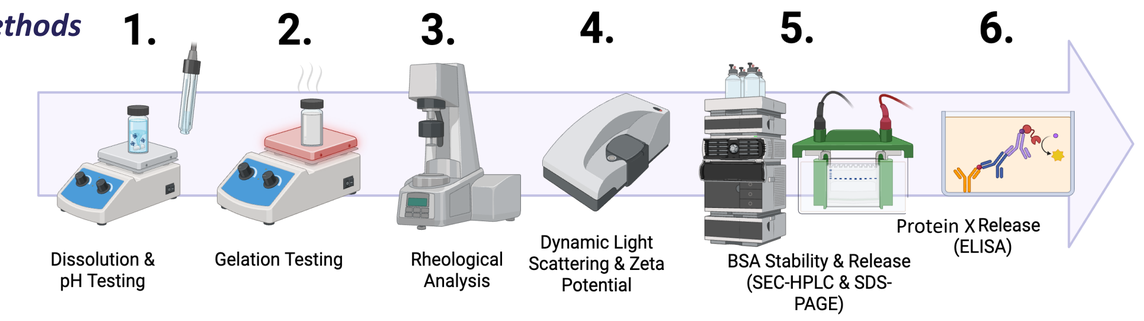


Materials & Methods

Materials

ABA triblock copolymers analyzed supplied by Ashland Specialties Ireland.

Methods



Objective

To evaluate PLCL–PEG–PLCL as an in-situ biologic drug delivery matrix by assessing its solubility, pH, gelation behaviour, protein stability, and release kinetics, and comparing its performance to the benchmark polymer PLGA–PEG–PLGA.

Results

Physicochemical Analysis

Solubility & Gelation Testing

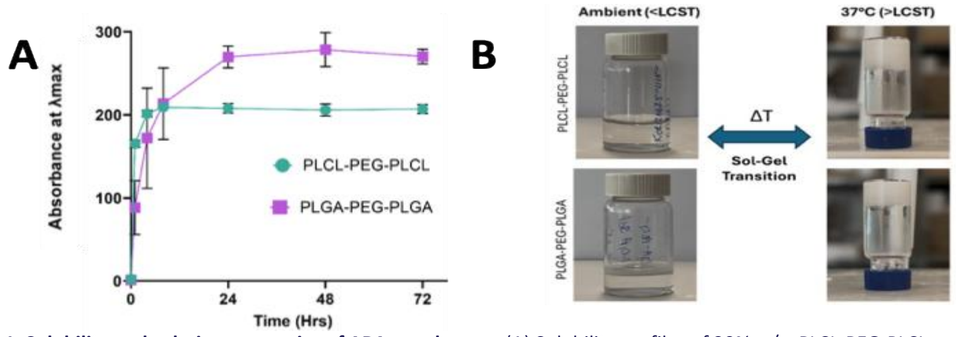


Figure 1. Solubility and gelation properties of ABA copolymers. (A) Solubility profiles of 30% w/w PLCL-PEG-PLCL and PLGA-PEG-PLGA in D.I water over time, assessed by UV-Vis spectroscopy (n=3, s=3; λ max 210 nm and 209 nm, respectively). (B) Thermoresponsive gelation behaviour of both polymers at 30% w/w.

Table 1. Effect of diluent on PLCL-PEG-PLCL solutions pH (30%w/w)

Diluent	pH
D.I water	2.7
Carbonate buffer (pH 10.2, 0.1M)	7.4

Buffer Effect on Gelation

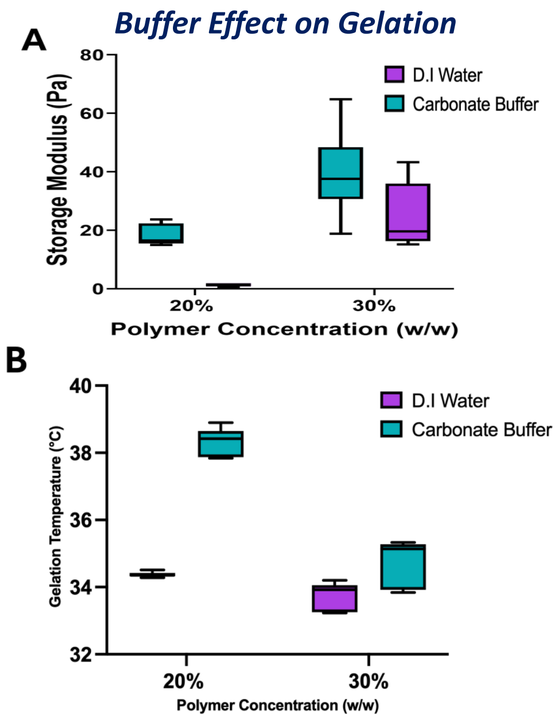


Figure 2. Buffer effects on PLCL-PEG-PLCL gelation kinetics. Storage modulus (G') at 37 °C and gelation temperature were measured for 20% and 30% w/w solutions (n=9; 3 samples measured in triplicate). (A) G' profiles at 37 °C.(B) Corresponding gelation temperatures for both concentrations.

Buffer Effect on Size & Zeta Potential

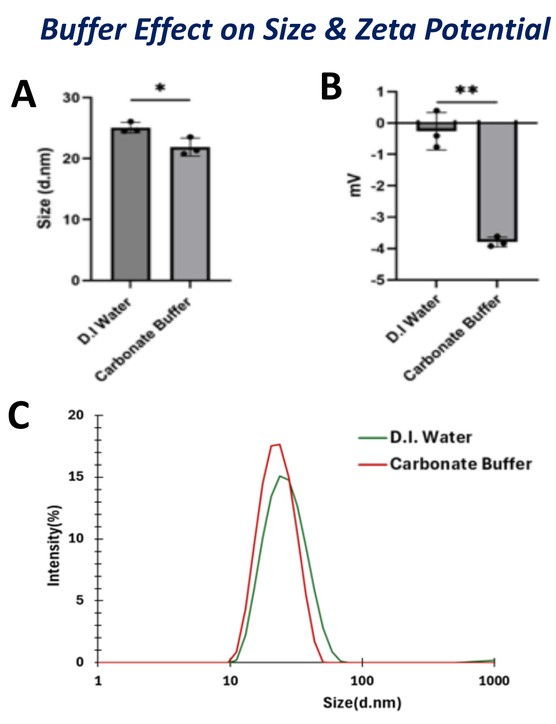


Figure 3. Effect of buffer systems on PLCL-PEG-PLCL size and charge. Hydrodynamic size (A) and zeta potential (B) were measured for formulations in different buffers (n=3). Statistical significance: *p < 0.0332, **p < 0.0021. (C) Representative DLS profile for 10% w/w PLCL-PEG-PLCL.

Protein X Release from Thermosensitive Hydrogels

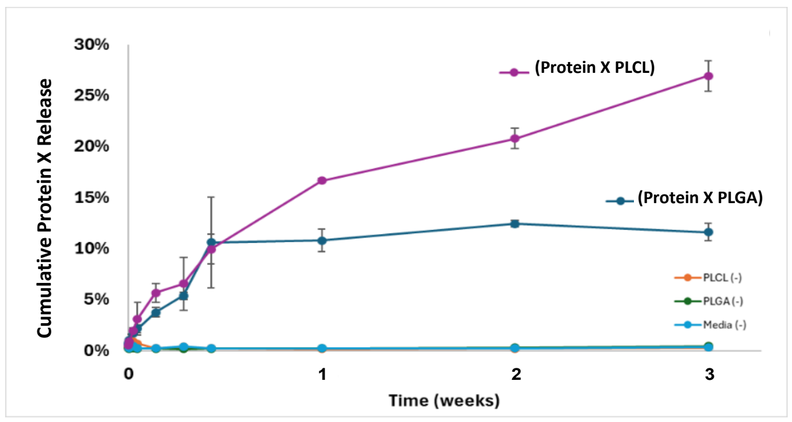


Figure 6. Cumulative Protein X release from thermoresponsive hydrogels. Release profiles are shown for PLCL-PEG-PLCL and PLGA-PEG-PLGA systems (n=3). Negative controls (blank hydrogels and release media; N=1) overlap and may not easily distinguishable.

BSA Loaded PLCL-PEG-PLCL Analysis

Gel Assessment

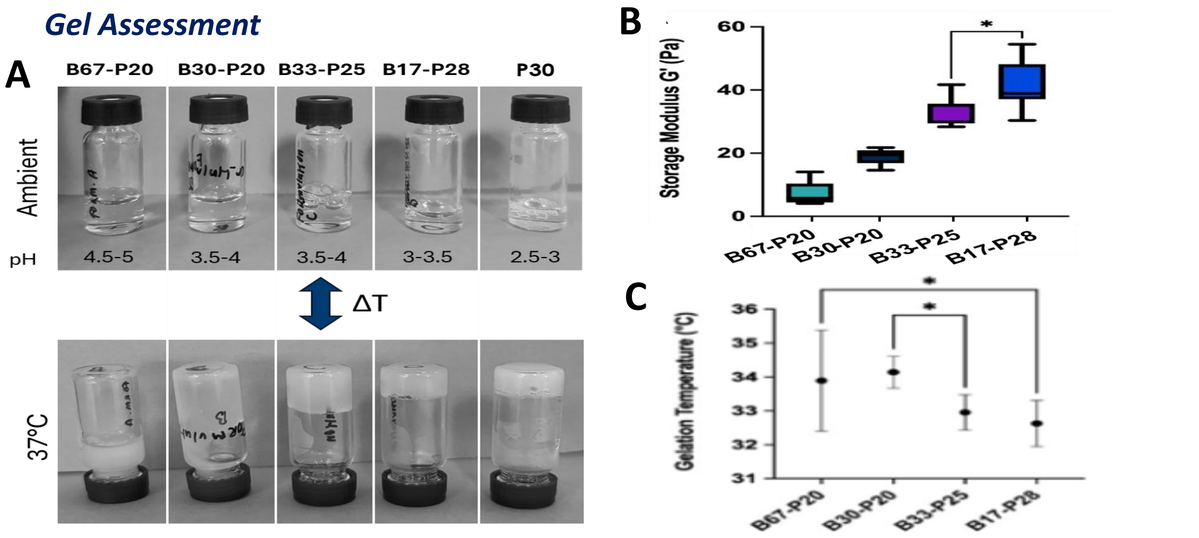


Figure 4. Gelation behaviour of BSA–PLCL-PEG-PLCL formulations. (A) Four formulations with varying BSA (mg/mL) and PLCL-PEG-PLCL (% w/w) concentrations (notation: B = BSA concentration (mg/mL) , P = polymer concentration (%w/w)); inversion test after heating to 37 °C for 30 min, compared with polymer-only control. (B) Storage modulus (G') of BSA–polymer formulations at 37 °C. (C) Sol–gel transition temperatures. Statistical significance: *p < 0.0332.

Protein Stability Assessment

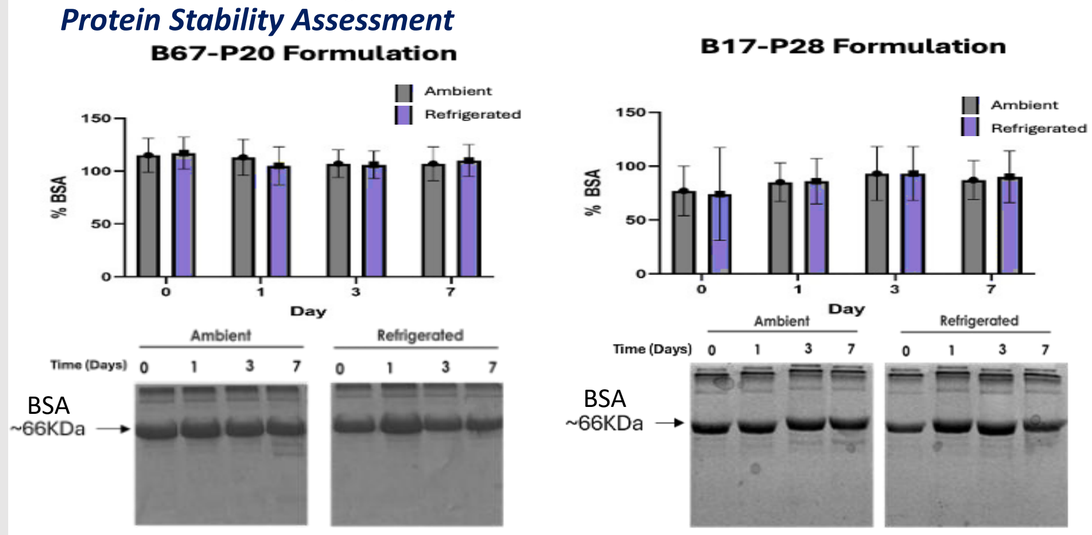


Figure 5. Stability analysis of BSA formulations. **Top (SEC-HPLC Analysis):** Stability of high-BSA/low-polymer (B67-P20) and low-BSA/high-polymer (B17-P28) formulations (n=3, s=3). Refrigerated samples (grey) ambient samples as black squares (purple). **Bottom (SDS-PAGE):** BSA and hydrogel formulation stability for B67-P20 and B17-P28 under both storage conditions. (n=1)

Conclusion & Impact

Conclusion

- PLCL-PEG-PLCL solubility and gelation temperature aligned with desired attributes for an in-situ drug delivery system.
- System pH could be altered to within desired range (pH 4-8) using a buffer system, without affecting gelation at high polymer concentrations (30%w/w)
- UV-Vis & SEC-HPLC methodology developed to characterise polymer solubility and protein stability in solution
- PLCL-PEG-PLCL hydrogel encapsulation appeared to have a negligible impact on BSA stability
- PLCL-PEG-PLCL demonstrated sustained release of Protein X over 3 weeks

Impact Statement

The project has provided a knowledge base as to the capabilities of PLCL-PEG-PLCL as a biologic therapeutic delivery matrix, as well as the current limitations of the polymer system. It has also allowed for establishment of a workflow for characterization of ABA triblock co-polymers.

HOST INSTITUTION: UCC University College Cork, Ireland Coláiste na hOllscoile Corcaigh

SUPPORTED BY: SSPC, Ashland always solving, Boston Scientific

FUNDED BY: Taighde Éireann Research Ireland, Boston Scientific

1. Minnar, C.M., Lui, G., Gulley, J.L., Schlom, J. and Gameiro, S.R., 2023. Preclinical and clinical studies of a tumor targeting IL-12 immunocytokine. *Frontiers in Oncology*, 13.
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Comparative Analysis of Common Potency Assays for Assessing Human TNF-alpha Neutralising Antibodies

Rithwik Pradeep, Alexander Zhdanov, Evin Allen
School of Pharmacy

What I am doing

I am evaluating monoclonal antibodies that neutralize TNF-α, a key inflammatory cytokine. Using hybridoma-produced antibodies, I am comparing two potency assays—L929 cytotoxicity and HEK293 Blue NF-κB reporter—to assess their sensitivity, reproducibility, and biological relevance. The study examines how these assays complement each other in accurately reflecting antibody function.

Why I am doing it

TNF-α antibodies are vital biologics for autoimmune diseases, but assessing their potency reliably remains challenging. I aim to understand how assay choice and antibody production influence activity measurements. By comparing two established assays, I hope to support more consistent, meaningful, and reproducible potency testing for therapeutic antibody development.

How I am doing it

Hybridoma cells produce anti-TNF-α antibodies, which are purified and tested in two assays. The L929 cytotoxicity assay measures protection from TNF-α-induced cell death, while the HEK293 Blue assay detects early NF-κB signaling. Both showed comparable IC_{50} values and neutralization at 30:1–60:1 ratios, confirming their complementary strengths.

What I hope to achieve in the end

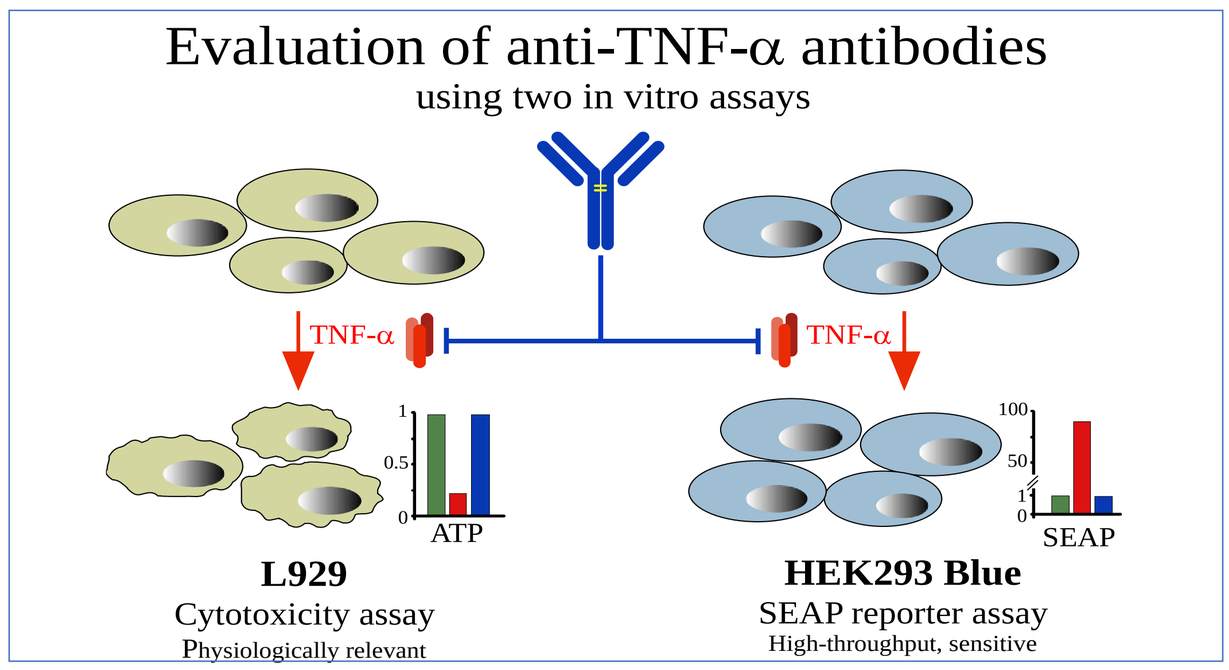
I aim to define how both assays can be strategically applied for antibody potency evaluation. The HEK293 Blue assay offers fast, reproducible screening, while L929 provides physiological insight. Demonstrating their complementarity supports a dual-assay strategy for more reliable and biologically relevant antibody characterization.

What is the potential impact in the Pharma area

This study supports using both assay types for robust antibody potency assessment. The HEK293 Blue assay enables rapid, high-throughput screening, while the L929 model captures later biological effects. Together, they strengthen analytical reliability, improve biopharma testing accuracy, and enhance therapeutic antibody development efficiency.

Highlights

- Two potency assays are optimised for thorough analysis of TNF-neutralising mAb
- HEK293 Blue reporter and L929 cytotoxicity assays show similar IC_{50} values
- High sensitivity and speed make the reporter assay ideal for high-throughput use
- L929 assay captures late TNF-α effects and offers stronger physiological relevance
- Dual potency assay method enables robust functional assessment of therapeutic mAbs



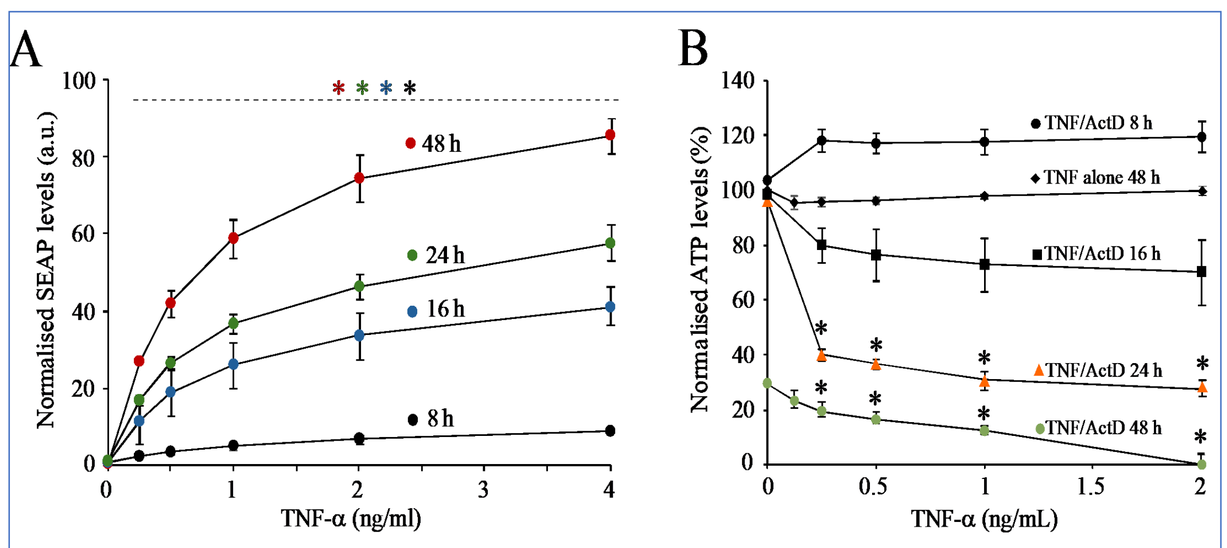


Figure 1. Characterisation of the time- and concentration-dependent effects of hTNF-α on HEK293 Blue and L929 reporter cells.

A. Production of SEAP by HEK293 Blue cells in response to TNF. ***B***. Total ATP-based viability test of L929 cell treated with TNF (with and without ActD). Asterisks show significant difference from non-treated cells; N=3.

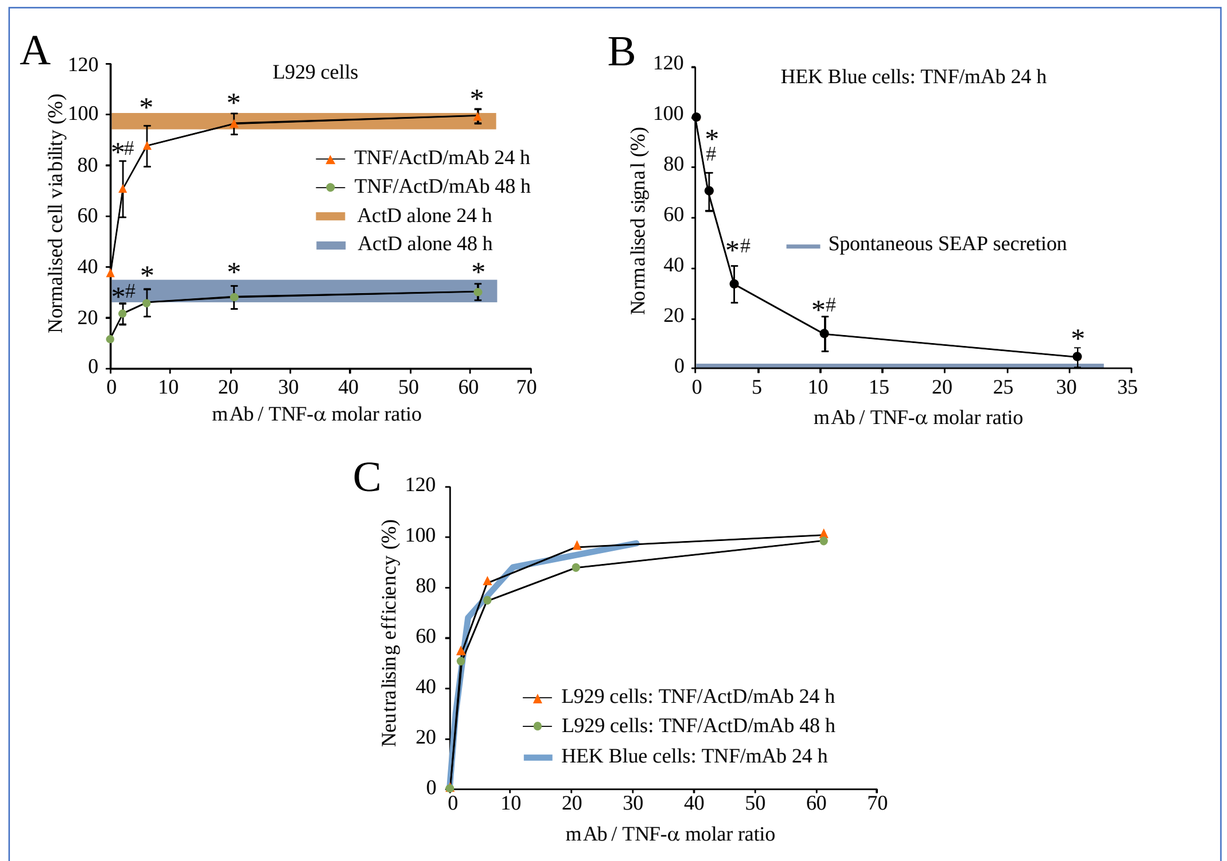


Figure 2. **Analysis of the TNF-α neutralising capacity of 357-101-4 monoclonal antibody**.

A. Inhibition of the TNF-α cytotoxic effects on L929 cells. ***B***. Inhibition of SEAP secretion by HEK293 Blue cells. ***C***. Neutralising efficiency (NE) of the antibody calculated according to the equation: $NE = |S_{TNF} - S_{TNF/mAbsX}| / |S_{TNF} - S_{Mock}|$, where S is assay signal, i.e., cell viability or SEAP secretion, when cells are treated with TNF alone (S_{TNF}), TNF in the presence of antibodies at ***X*** concentration ($S_{TNF/mAbsX}$), or mock (S_{Mock}). In (A-C), a molar ratio between the assembled antibody and monomeric TNF are used to demonstrate antibody efficiency. Asterisks show significant difference from samples treated with TNF without neutralising mAbs; hashtags – from samples not treated with TNF. N = 3.

R. Pradeep, A. Zhdanov, E. Allen (2025). Comparative Analysis of Common Potency Assays for Assessing Human TNF-alpha Neutralising Antibodies. *Analytical Biochemistry*, 116011

Acknowledgments

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Freeze-thaw Behavior of Biopharmaceutical Excipient Solutions

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School of Pharmacy

01 Introduction

Freezing and thawing processes can cause protein structural instability due to interfacial and cryo-concentration stress[1].

Therefore, it is critical to design formulations that optimize therapeutic biologic formulation stability during freeze-thaw processes[2].

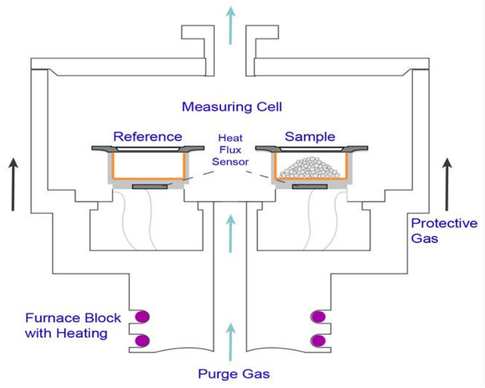
Understanding the thermal properties of excipients used in biologic formulations can inform the design of biologic formulations stabilized for freeze-thaw processes.

02 Objective

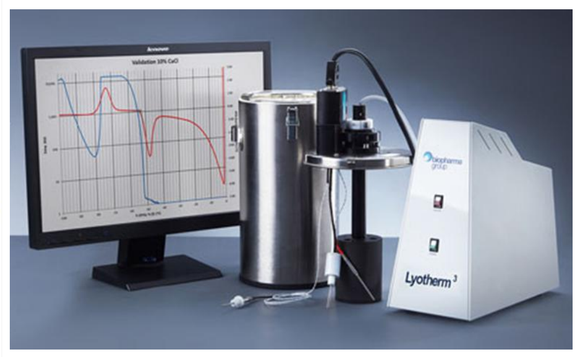
Investigate the thermal behavior of solutions of commonly used excipients in the biologic formulations during freezing and thawing.

Determine the ability of differential scanning calorimetry, impedance analysis and differential thermal analysis to characterize excipient solution thermal behavior.

03 Methodology



Differential scanning calorimetry (DSC)



Lyotherm 3®
Impedance analysis
Differential thermal analysis (DTA)

04 Results

- DSC analysis determined ice nucleation temperature, glass transition temperature of amorphous water (Tg_w), maximally freeze-concentrated excipient glass transition (Tg'), onset of melting and enthalpy of fusion.
- Using enthalpy of fusion, the percentage of water as ice was calculated for each sample.

Figure 1. DSC thermogram of Trehalose 10% (a) Cooling Stage (b) Heating Stage

Figure 2. The percentage of water as ice calculated for excipient solutions studied. Y error bars indicate standard deviation (n=3).

- The glass transition of amorphous water (Tg_w) was determined close to –136 °C, and this event was found across all the solutions tested indicating the presence of amorphous water.

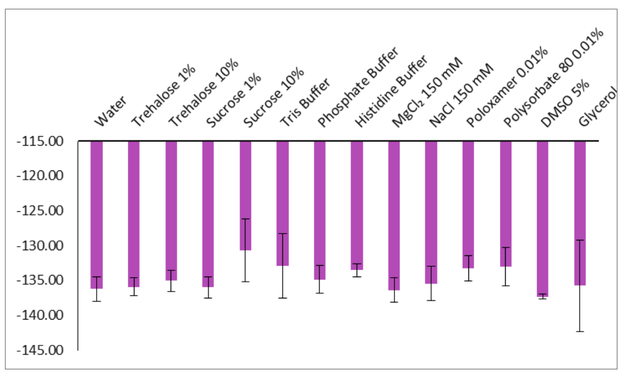


Figure 3. Glass transition temperatures of amorphous water measured in excipient solutions. Results shown are average values ± standard deviation, n=3.

- Sucrose and trehalose solutions investigated are known to have a glass transition (Tg') from the glassy state to the rubbery state upon increasing temperature, which is shown during the heating stage in DSC analysis.
- Tg' temperatures were also determined for histidine buffer and glycerol solutions.

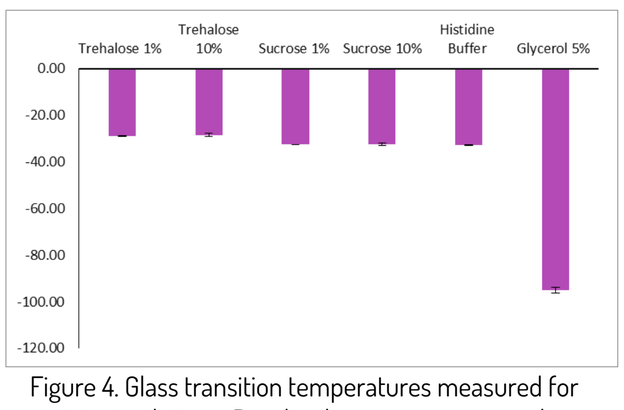


Figure 4. Glass transition temperatures measured for excipient solutions. Results shown are average values ± standard deviation, n=3.

- In all the samples, a decrease in impedance was noted during heating indicating increase in mobility of the molecules in the solution.
- The three methods of analysis cross-validate each other, thermal events seen by DSC/DTA can be linked to functional structural changes detected by impedance.

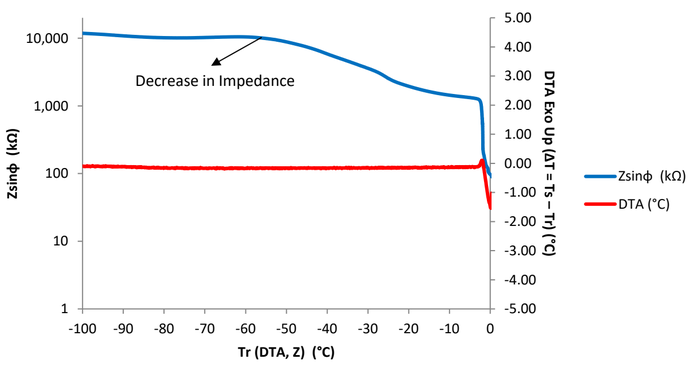


Figure 5. Representative impedance and DTA plots for deionized water sample.

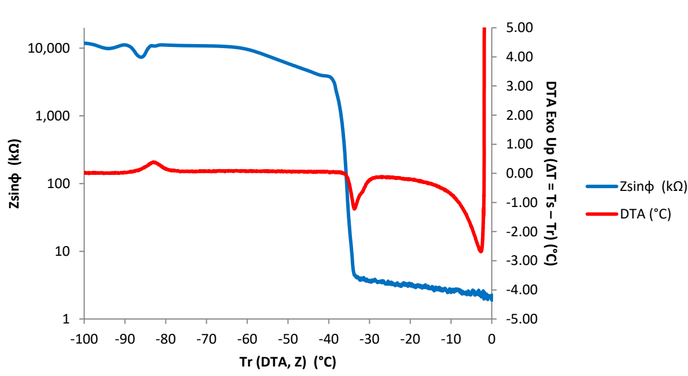


Figure 6. Representative impedance and DTA plots for 150mM $MgCl_2$ sample showing an exothermic crystallization event (around -85°C) not previously reported and eutectic event at -40°C.

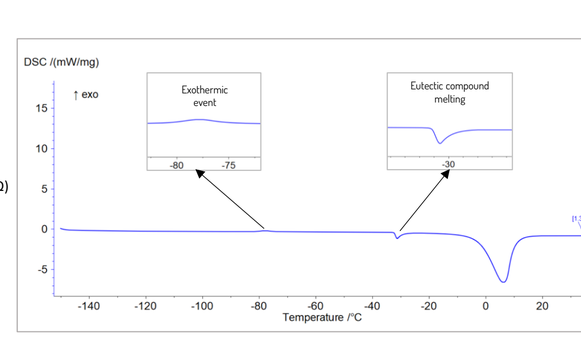


Figure 7. Representative DSC thermogram for 150mM $MgCl_2$ showing an exothermic crystallization event between and eutectic melt event around -40°C

05 Conclusion

- The study provides insights into the thermal characters behind the cryo behavior of selected excipients and highlights potentially undesirable properties of others, such as crystallization, softening, or eutectic formation.
- Together, these insights enable more reliable identification of critical formulation temperatures and deepen our understanding of the freeze-thaw behavior of individual excipients.
- This information will be essential in the next stages of the work, where more complex excipient combinations and formulations containing adenoviral vector serotype 5 will be investigated.

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Developing a Thermostabilised Malaria Vaccine in Microarray Patches

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Background

We are developing an injection-free, easy-to-administer, *Plasmodium vivax* malaria vaccine microarray patch (MAP) for skin-based immunisation. Despite progress in licensing *P. falciparum* vaccines, none exist for *P. vivax,* which is the most widespread human malaria. Licensed *P. falciparum* vaccines contain saponin-based emulsion adjuvants and are in the liquid form for injection. The key challenge is to develop a process and identify formulations to dry this emulsion-based vaccine into a patch without degrading it. Previous research identified lyophilisation and spray-drying processes to dry similar adjuvant types; however, these are not relevant for producing MAPs. We are therefore developing new formulations and processes for a next-generation vaccine MAP to increase thermostability and ease-of-administration, thus improving vaccine accessibility and effectiveness.

How I am doing it?

Developing and analysing MAP formulations

- Identify MAP formulations that maintain the emulsion physical properties when dry.
  - Analyse emulsion properties before and after drying using dynamic light scattering (DLS).

Fabricating MAPs

- Produce MAPs.
  - Use formulations identified in development phase as maintaining emulsion properties.

Assessing MAP performance

- Determine leading vaccine MAPs stability when packaged and stored under room temperature conditions:
  - Assess MAP mechanical stability via texture analyser and skin penetration assays.
  - Assess adjuvant and antigen stability via DLS profile and ELISA.
- Determine leading vaccine MAPs immunogenicity in mice.

Project Outputs

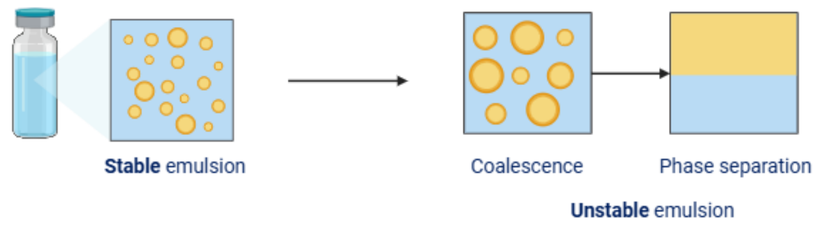
- Developed knowledge base for drying emulsion-based vaccines into thermostable MAPs
- Final key output: dossier to support GMP technology transfer of an immunogenic P. *vivax* vaccine MAP.

Anticipated impact for Pharma

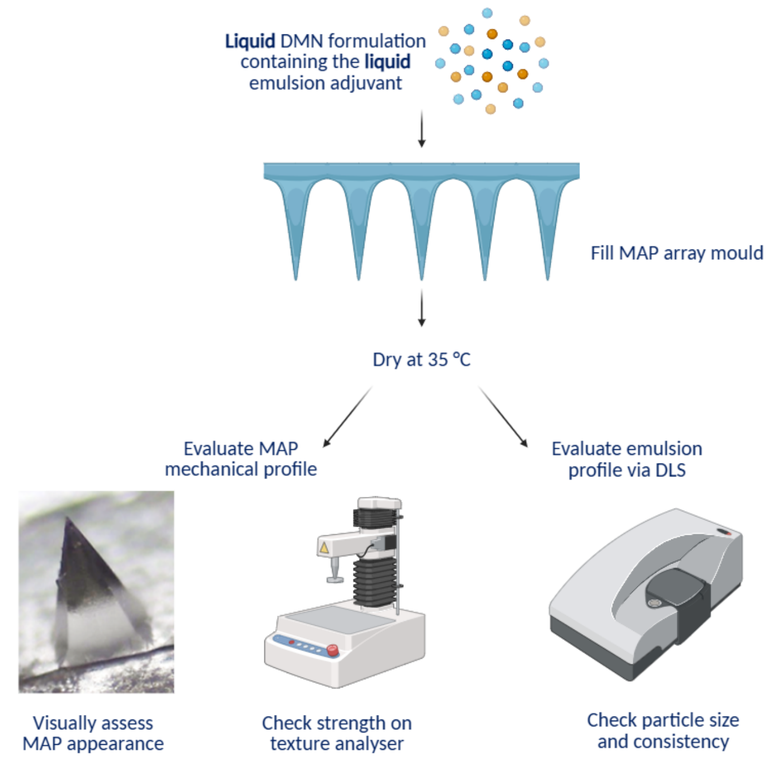
- ✓ GMP-transfer-ready formulations and processes to dry oil-in-water emulsions into solid dosage forms.
- ✓ New knowledge will impact on efforts to stabilise other lipid-based drugs and vaccines in solid forms.
- ✓ Long-term positive impact on immunisation campaigns by developing a stabilised, easy-to-administer, efficacious vaccine system.

Overview of production and evaluation process

Currently, the licensed oil-in-water emulsion-containing *P. falciparum* vaccines are in the liquid form and the emulsion remains stable due to interactions between the droplets in the oil phase and the water phase.



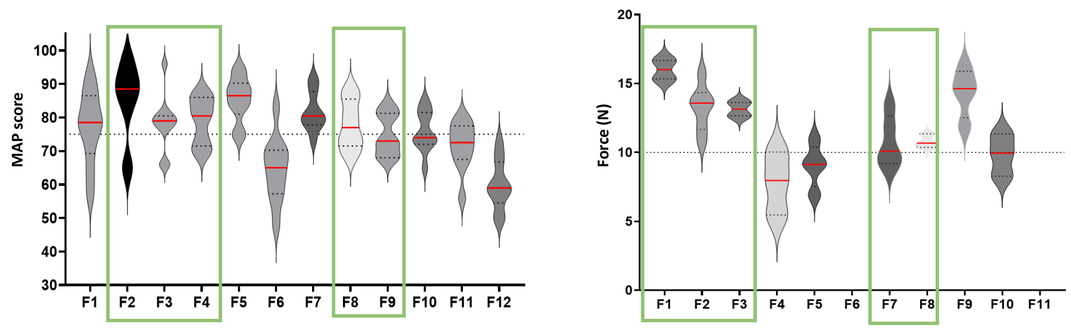
As we dry our MAPs, the water phase is removed. Therefore, we need a formulation which maintains the size of the droplets in the oil phase when dried but also produces a MAP which can pierce the skin.



Screen using Design of Experiments (DoE)

We need to balance all of the components of our MAP formulation to produce the optimal formulation.

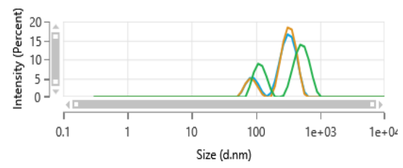
✓ **Some formulations produce visually acceptable MAPs** ✓ **Some MAPs are strong enough to pierce the skin**



Ultimately, we want to achieve a formulation that is mechanically strong and compatible with the emulsion:

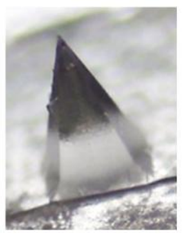
Bad MAP formulation:

- x **Swollen shaft**
- x **Poorly defined geometry**
- x **Blunted tip**

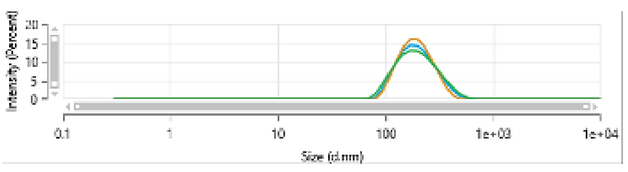


- x **Emulsion particle size too large (360.9 nm)**
- x **Emulsion particle population inconsistent (PDI = 0.44)**

Good MAP formulation:



- ✓ **Smooth, tapered shaft**
- ✓ **Correct 8-sided geometry**
- ✓ **Sharp tip**



- ✓ **Emulsion particle correct size (181.0 nm)**
- ✓ **Emulsion particle population consistent (PDI = 0.15)**

nibrt National Institute for Bioprocessing Research and Training

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Engineering circular RNAs for selective protein expression in dysfunctional endothelial cells for the treatment of sepsis

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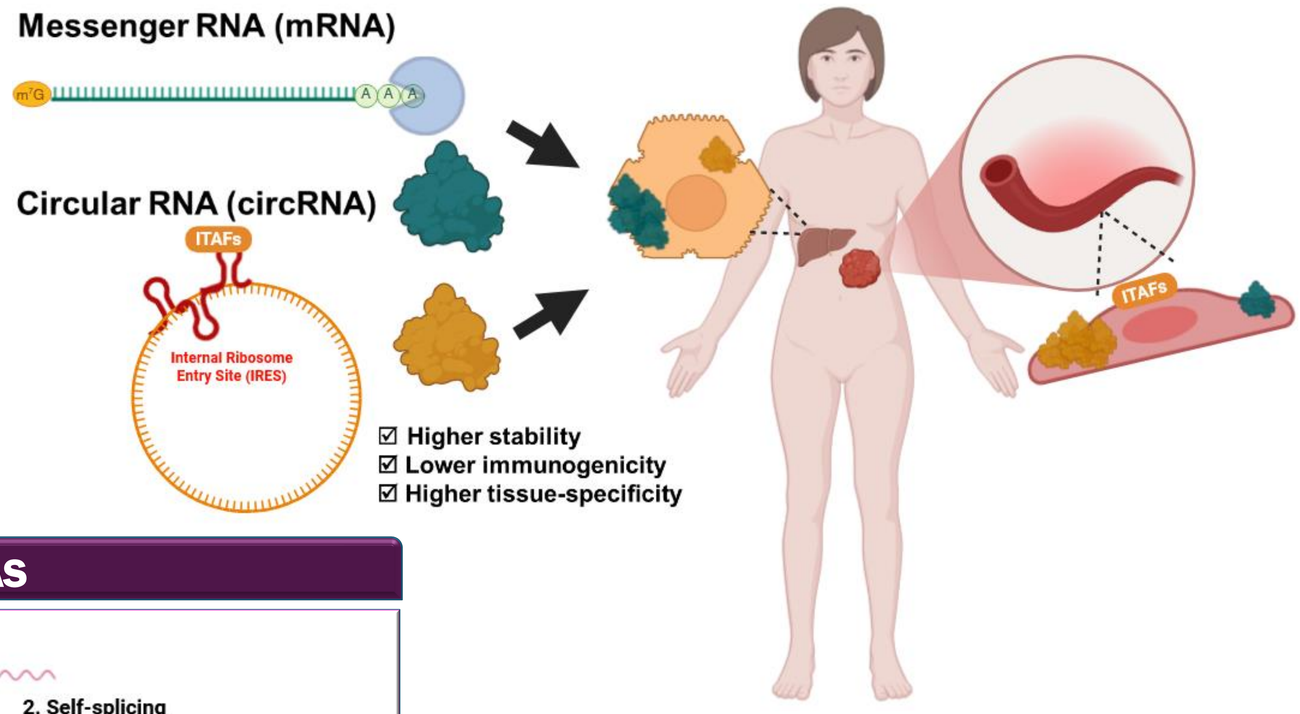
Introduction

The success of the messenger RNA (**mRNA**)-**based vaccines** against COVID-19 proved the **clinical potential** of **RNA technology** for **protein production in vivo.** However, under **stress** experienced during disease, **protein expression** from mRNA is **impaired.** Circular RNA (**circRNA**) is a new class of single-stranded RNA with a closed-loop structure that improves its **stability** due to the lack of free ends necessary for degradation by exonucleases. Moreover, it does **not** require **nucleoside modifications** for diminished immunogenicity (1). In contrast to mRNA, circRNA allows unique Internal Ribosome Entry Site (**IRES**)-**mediated translation** that often **relies on** the assistance of factors known as IRES Trans-Acting Factors (**ITAFs**) which vary in their expression depending on the cell type and cell state (2, 3, 4).



Preparation of protein coding circRNAs

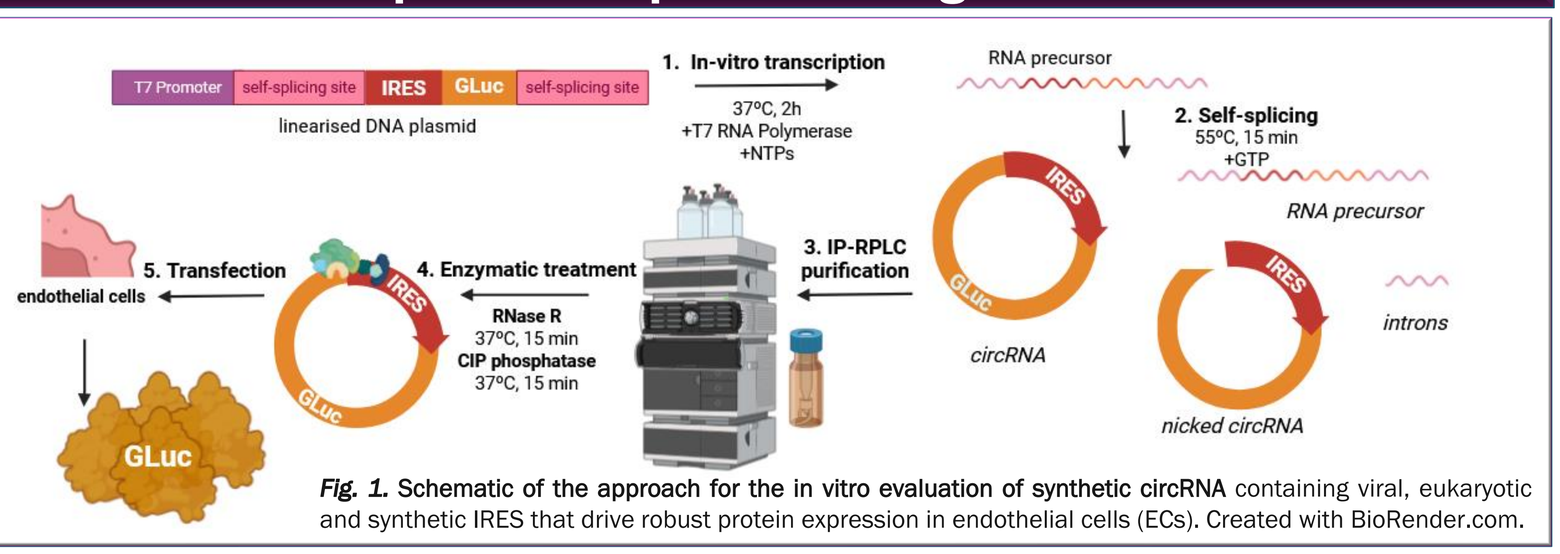


Fig. 1. **Schematic of the approach for the in vitro evaluation of synthetic circRNA** containing viral, eukaryotic and synthetic IRES that drive robust protein expression in endothelial cells (ECs). Created with BioRender.com.

In silico validation of selected IRES and potential ITAFs

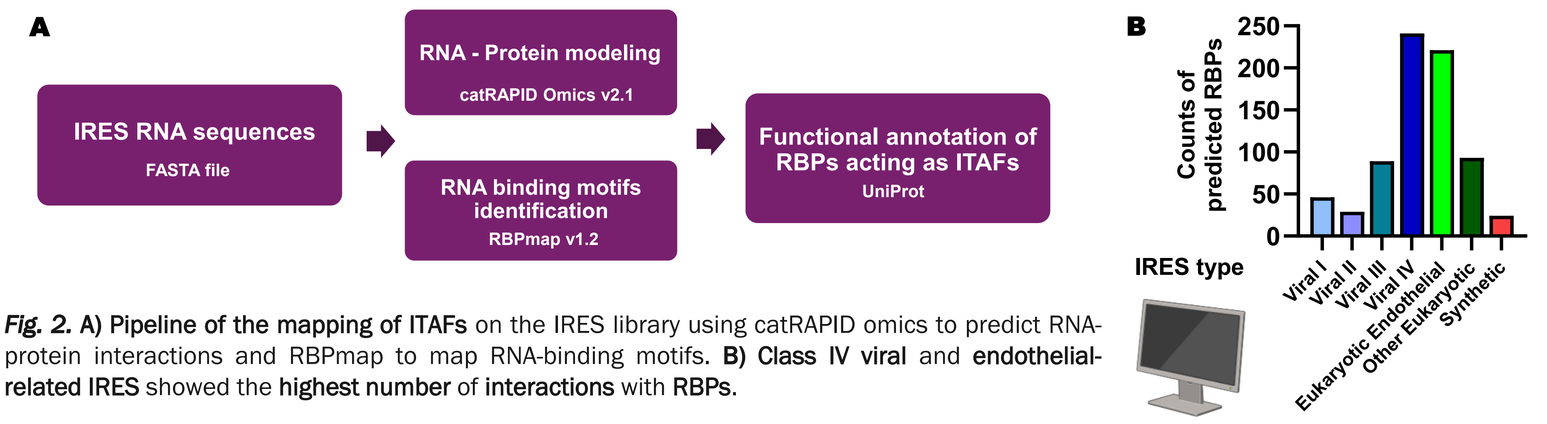


Fig. 2. **A) Pipeline of the mapping of ITAFs** on the IRES library using catRAPID omics to predict RNA-protein interactions and RBPmap to map RNA-binding motifs. **B) Class IV viral** and **endothelial-related IRES** showed the **highest number** of **interactions** with **RBPs.**

Evaluation of IRES in endothelial cells under resting conditions

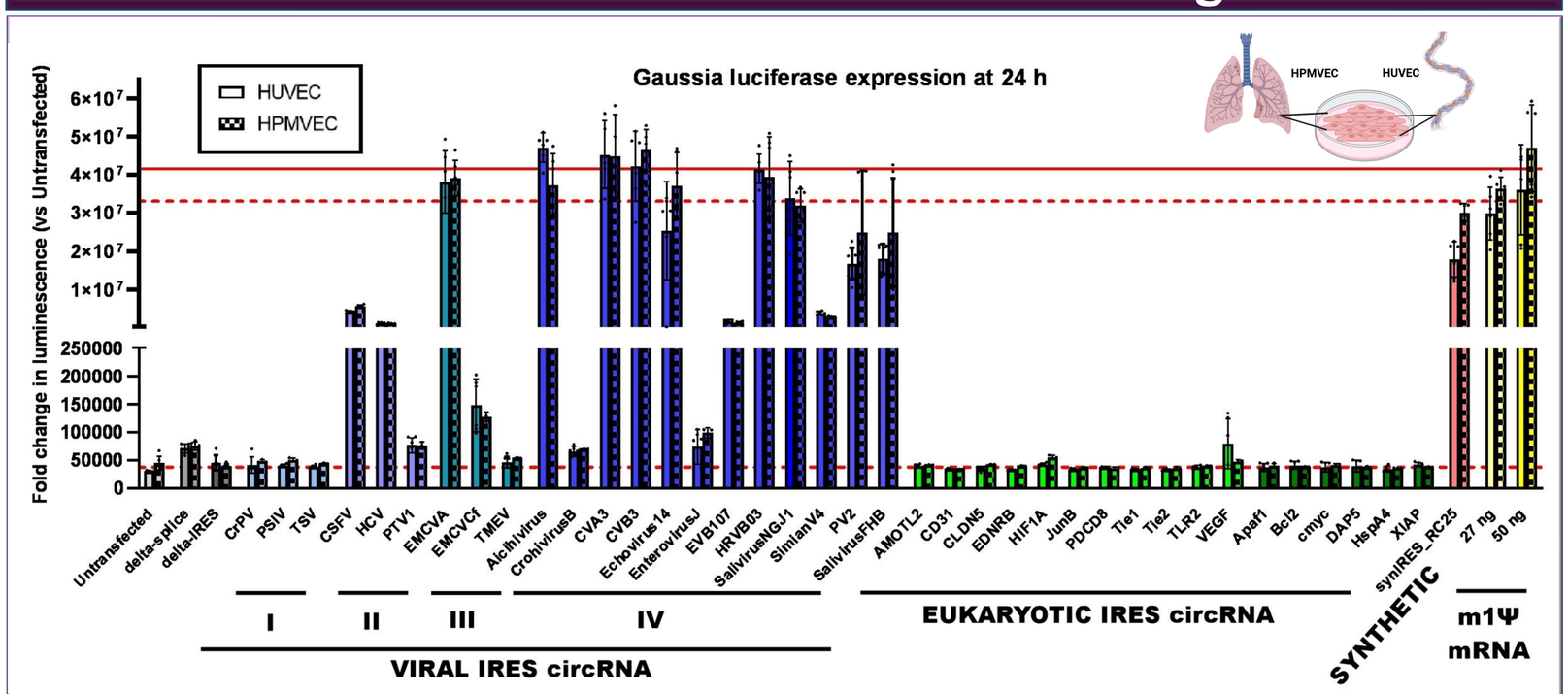


Fig. 3. **Class IV Viral IRESs drive robust protein translation in ECs.** Our results show that class IV viral IRES led to the highest GLuc activity at 24 hours after transfection in both ECs (HUVEC, HPMVEC) with a molar dose of circRNAs containing the indicated IRESs, equivalent to 50 ng of CVB3-containing circRNA. Protein expression levels were comparable to 50 ng dose of m1ψ-modified mRNA and higher than its equimolar dose (27 ng). This level of expression was followed by class III and class II viral IRES. GLuc activity was measured and normalised to cell viability.(Data are presented as mean ±SD for N=2 independent experiments).

Aim

With this study we hope to demonstrate that the **circularisation of coding RNA** is a promising alternative to **overcome the limitations** of **mRNA technology** regarding its duration, specificity of protein production and cost of modified nucleosides. **IRES engineering** could provide an avenue for tissue-specific expression by making **circRNA** the **preferred RNA** for the ribosome **in a cell under stress conditions** such as hypoxia and inflammation, relevant in high-medical-need diseases such as **sepsis** or **cancer.**

Pharma impact

This project will apply basic molecular biology knowledge regarding the mechanism of tissue/condition-specific circRNA translation into the field of personalised medicine. It will exploit the **potential of circRNA translation** to **expand** the toolbox of **therapeutic RNA** and to allow **long-lasting protein production at the site of disease.**

IRES evaluation under stress

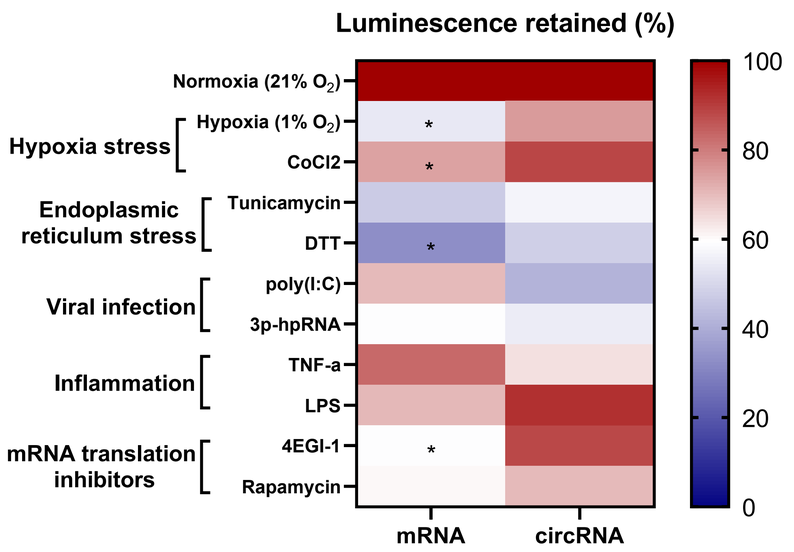


Fig. 4. **Heatmap showing the effect of different cellular stressors in mRNA and circRNA translation in HUVEC.** Hypoxic stress induced by 1% O_2 and $CoCl_2$ demonstrated the benefit of IRES-mediated circRNA translation in comparison to cap-dependent mRNA translation. DTT-induced endoplasmic reticulum stress and the use of the translation inhibitor 4EGI-1 showed significant differences between mRNA and circRNA translation. Other stressors displayed not statistically significant differences between mRNA and circRNA translation. Viability under all treatments is > 70%. (Data are expressed as % luminescence retained and presented as mean, *p<0.05, mRNA vs circRNA Tukey's multiple comparisons test).

Conclusions

- We designed a **library** of **viral**, **eukaryotic** and **synthetic IRES** and in silico predicted their **potential interaction** with **ITAFs.**
- We evaluated the IRES-containing circRNA library for robust protein expresion in ECs under resting conditions, concluding that **class IV viral IRES** led to the **highest translation of circRNAs** with **comparable** protein expression levels **to m1ψ-modified mRNA.**
- We observed **significant differences** in translation between **circRNA** and **m1ψ mRNA** under **hypoxia** in HUVEC. Other cellular stressors including DTT and 4EGI-1 showed significant differences between mRNA and circRNA translation.

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44

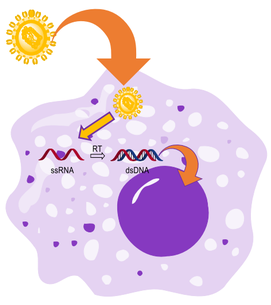
Development of Novel Aryl-Linked Antiviral Phosphonates

Oscar Dunne, Emily A. Collins, Timothy P. O'Sullivan
School of Pharmacy, School of Chemistry

Taighde Éireann Research Ireland

What is HIV and why we care.

- HIV is a retrovirus which can cause a chronic infection in humans and can progress to acquired immunodeficiency syndrome (AIDS). It attacks the host immune system by targeting $CD4^+$ Helper T cells. This leaves the host susceptible to infections that an immunocompetent person would normally fight off.
- As of 2024, there were 40.8 million patients living with the virus and it had claimed the lives of *ca*. 44.1 million people since the original epidemic.[1]

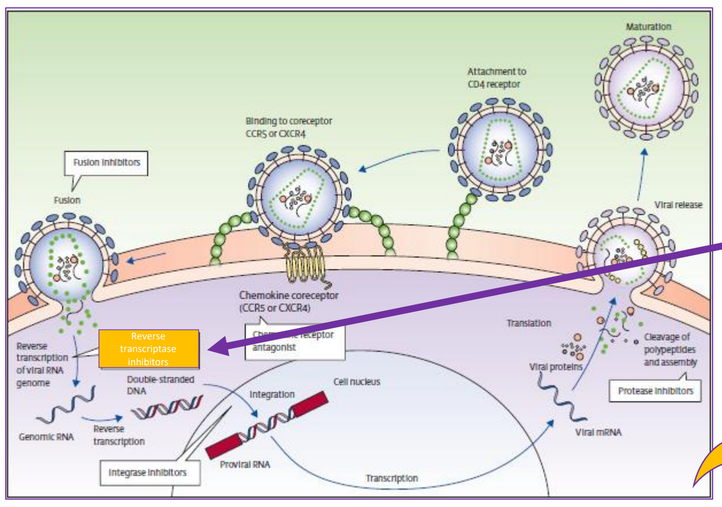


	People living with HIV	People acquiring HIV	People dying from HIV-related causes
Total	**40.8 million** [37.0–45.6 million]	**1.3 million** [1.0–1.7 million]	**630 000** [490 000–820 000]
Adults (15+ years)	**39.4 million** [35.7–44.0 million]	**1.2 million** [950 000–1.5 million]	**550 000** [430 000–720 000]
Women (15+ years)	21.0 million [19.0–23.5 million]	530 000 [410 000–710 000]	240 000 [180 000–320 000]
Men (15+ years)	18.5 million [16.5–20.7 million]	650 000 [530 000–830 000]	320 000 [240 000–410 000]
Children (<15 years)	**1.4 million** [1.1–1.8 million]	**120 000** [82 000–170 000]	**75 000** [53 000–110 000]

Adapted from WHO HIV statistics information sheet.[1]

How is it treated?

- As a retrovirus, HIV can rapidly mutate its genes and therefore develop resistance to antiviral drug treatments and vaccines. As part of its lifecycle, it integrates its own genome into the host cell genome making it extremely difficult to eradicate.
- Accordingly, the mainstay approach to managing HIV as a lifelong infection is the use of highly active antiretroviral therapy (HAART) which can offer HIV-positive patients a near-full life expectancy if taken correctly. HAART employs combinations of several antiviral drug classes which target the virus. Of particular interest are the nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), which is the focus of this work.[2]

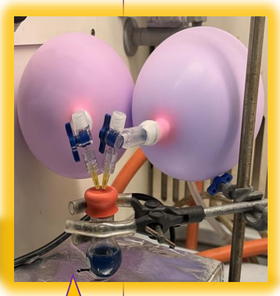


Adapted from Colledge *et al.*[3]

Truvada® contains the NRTIs tenofovir disoproxil fumarate and emtricitabine

SCAN ME [4]

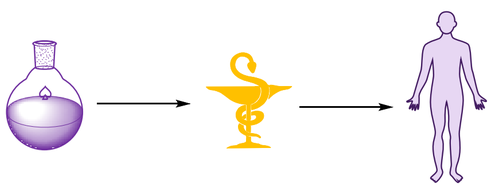
Scan to see how reverse transcriptase (RT) works and how it can be inhibited!



Setup for the Chan-Lam reaction

What is the potential impact of this research?

- This research could potentially generate new antiviral drugs with greater potency and selectivity than their predecessors. This would bolster the arsenal of potential medications that can be used in HAART and possibly reduce the risk of drug resistance that HIV can so often develop.[5]
- Additionally, by developing drugs with greater potency, lower doses are required for treatment and so the risk or severity of side effects are reduced.[6] Therefore, this could improve patient acceptability, medication adherence to prescribed HAART regimens and ultimately, patient quality of life.[7]

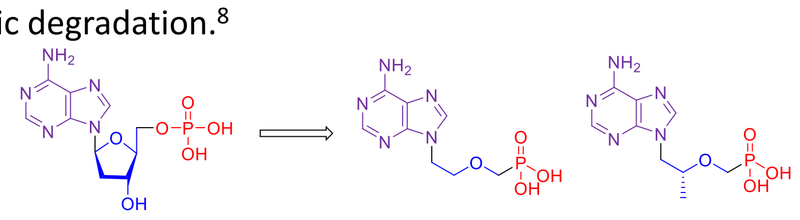


Acknowledgements

- Dr T. O'Sullivan
- E. Collins, M. O'Driscoll, R. O'Connell, S. Sweetnam, Dr G.S. Reddy, Dr D. Jones

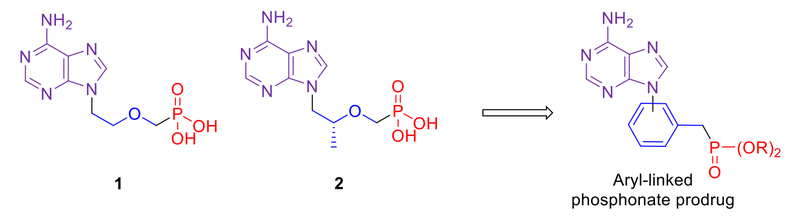
What is our strategy?

- Of the NRTIs which form the backbone of many HAART regimens, there exists a subclass called the acyclic nucleoside phosphonates (ANPs). Examples of ANPs include adefovir (**1**) and tenofovir (**2**). In these drugs, the deoxyribose moiety of a nucleotide such as deoxyadenosine monophosphate (**3**) has been replaced by an acyclic ether chain (blue) and the phosphate has been replaced by a phosphonate (red) to reduce enzymatic degradation.[8]



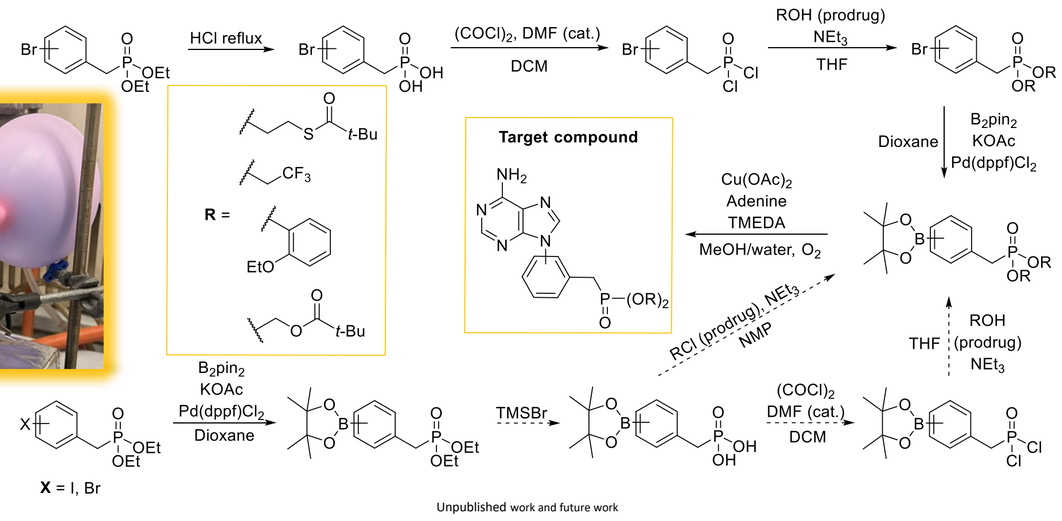
3 1 2

- Due to the extraordinary ability of HIV to mutate, resistance to antivirals is common. Given that an infected patient will require lifelong treatment with antivirals, there is constantly a need for the development of safer, more effective drugs.[5] We aim to develop novel, aryl-linked analogues of these ANP-type drugs whereby the acyclic ether chain has been replaced with an aryl linker moiety. Additionally, the poorly orally-bioavailable phosphonate groups will be masked with more lipophilic prodrug groups which are known to boost uptake and potency and can be cleaved to liberate the free phosphonate *in vivo*.[9]



How are we working to accomplish this strategy?

- By having an aryl moiety directly attached to the nucleobase, we can take advantage of the Chan-Lam reaction. The Chan-Lam reaction is a powerful and robust coupling method in synthetic chemistry which permits new C-N bond formation between an sp^2-hybridised carbon and nitrogenous nucleophile under mild conditions with excellent functional group tolerance.[10]



Unpublished work and future work

- Several potential antiviral compounds with distinct prodrug moieties ("R" groups) have been developed already using this strategy with the nucleobase attachment at the *para*- position of the aryl linker. One potential antiviral compound with the nucleobase attachment at the *meta*- position of the aryl linker has been prepared with more *para*- and *meta*- analogues on the way.

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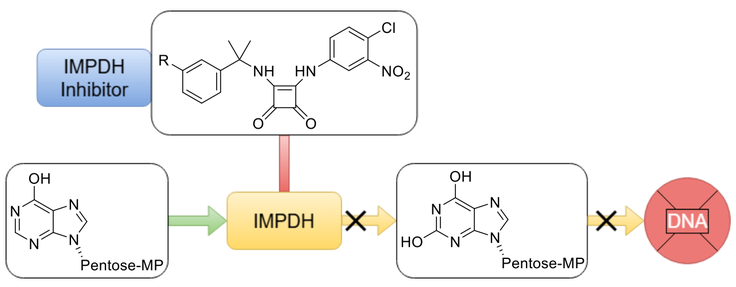
Synthesis of a library of antimicrobial IMPDH inhibitors

Stephen Sweetnam, Amit Upadhyay, Dr. Timothy P. O'Sullivan
School of Pharmacy, School of Chemistry, & ABCRF

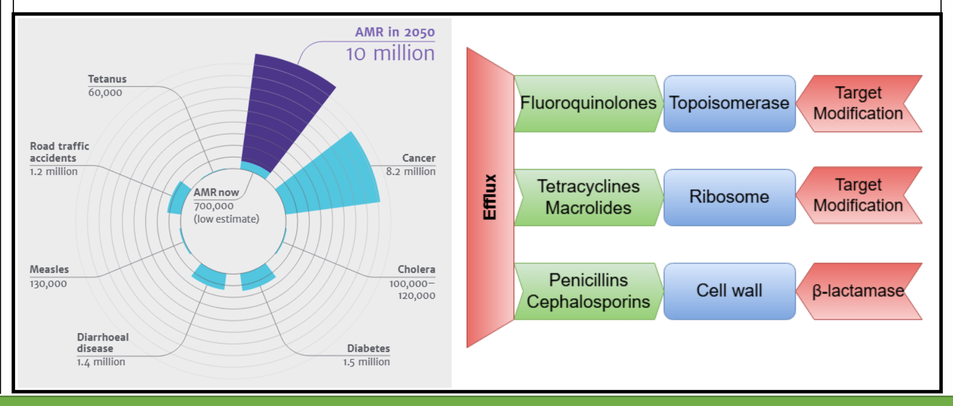
What is the project?

Our goal is to generate a library of squaramide based inhibitors of the **inosine monophosphate dehydrogenase enzyme (IMPDH)**. This enzyme is critical for DNA and RNA synthesis. IMPDH inhibitors prevent this enzyme from working, halting microbial growth. This **novel mechanism of antimicrobial action** could result in a new class of clinical antimicrobials that are desperately needed to combat the growing problem of antimicrobial resistance.



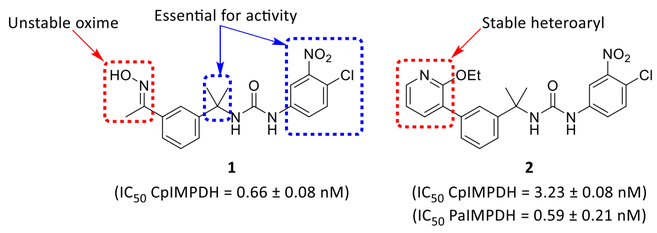
Why am I doing it?

Antimicrobial resistance (AMR) is a growing public health threat. Many antimicrobial medicines have the same mechanism of action, and overuse has driven the rise of AMR. **AMR is predicted to kill more people than cancer by 2050**[1]. A variety of pathogens have a common IMPDH structure. **IMPDH inhibition could work to treat otherwise resistant microbial infections**[2], as resistance genes have not been selected, and the pathogen is naïve and susceptible to the inhibitors effects.



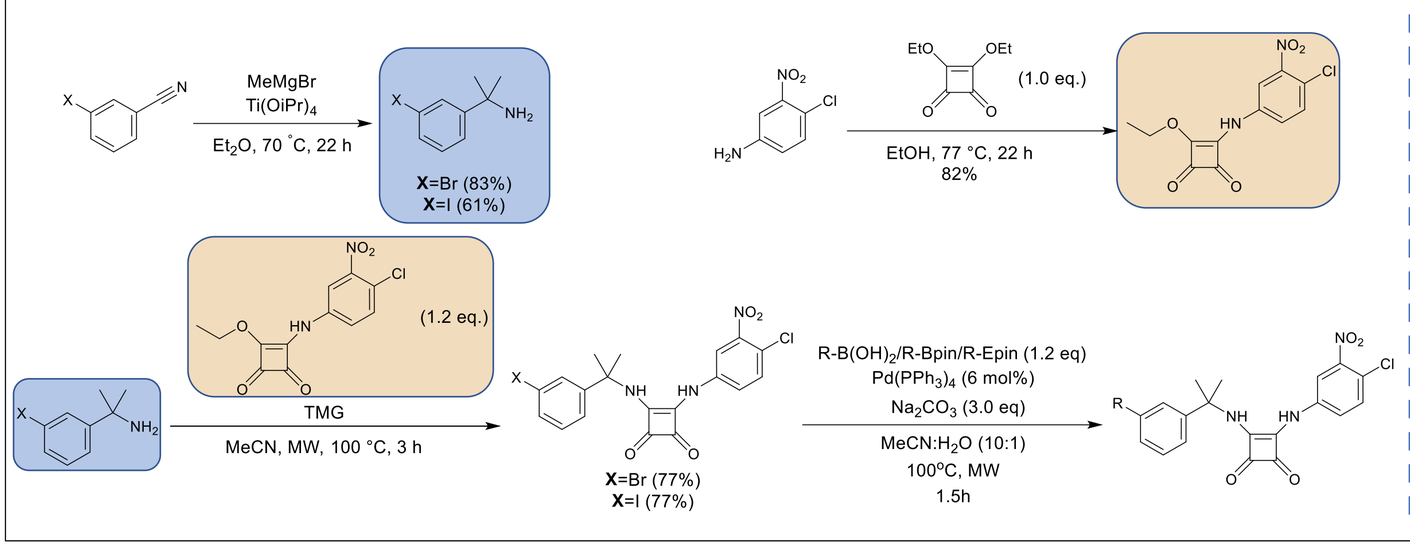
Existing IMPDH inhibitors

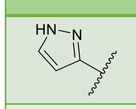
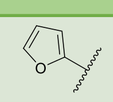
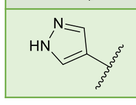
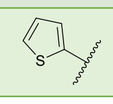
Gorla *et al*. discovered a **highly potent and selective inhibitor for *C. parvum* IMPDH** through high throughput screening[3]. Previous work in the O'Sullivan group replaced the **metabolically unstable oxime group** with a variety of **stable heteroaryl rings,** with some library members having **sub-nanomolar activity against *P. aeruginosa***[4-5]*,* a highly resistant pathogen associated with serious hospital acquired infections.

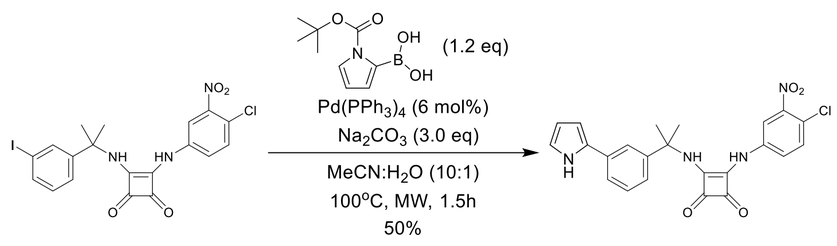


How am I doing it?

Our aim is to further optimise the inhibitor potency and stability by replacing the urea group with a squaramide. **Squaramides have greater hydrogen bonding capacity which may enhance IMPDH inhibitor binding and potency**[6]**.** The squaramide containing scaffold is prepared in 3 steps, followed by a diversification step using Suzuki-Miyaura coupling to generate a compound library.

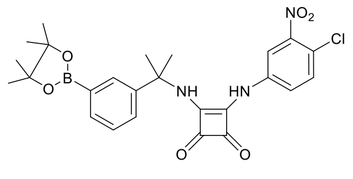


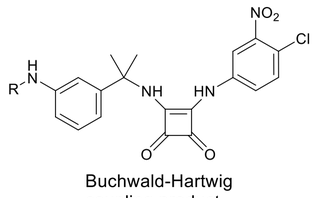
R	X	Boronate	Yield	R	X	Boronate	Yield
	Br I	B(pin) B(pin)	55% 75%		Br Br	$B(OH)_2$ B(Epin)	18% 20%
	Br I	B(pin) B(pin)	52% 63%		Br I	$B(OH)_2$ B(Epin)	0% 66%



Where is the project headed?

The next aim is to swap the Suzuki coupling partners by **synthesizing the Bpin ester** of the squaramide, accessing the huge coupling library of heteroaryl halides. We also will **generate a compound library using Buchwald-Hartwig coupling and a variety of amines**. These compound libraries will be sent to our partners for biological testing and the data used to further improve the inhibitors.


Bpin ester


Buchwald-Hartwig coupling product

What is the potential impact

This work will contribute to research into IMPDH inhibitors as a new class of antimicrobial drug. Microbial pathogens present a threat to public and personal health, with resistant infections being able to spread quickly with no effective treatment to halt the spread. **The COVID-19 pandemic demonstrated the colossal economic and social impact an infectious disease can have**. The mRNA vaccine technology used in that pandemic had been developed over many years beforehand[7], and this work in IMPDH inhibitors may serve a similar role in a future outbreak or pandemic.

Conclusion: What do we hope to achieve?

Thus far, we have:

- Synthesised **five novel squaramide-based inhibitors.**
- **Improved Suzuki–Miyaura coupling yields** by replacing aryl bromides with aryl iodides.
- Investigated **alternative boron coupling species.**

Future work will focus on:

- **Expanding** the current IMPDH inhibitor library.
- Generating additional compound libraries using **alternative coupling chemistries.**

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Acknowledgments

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- Amit Upadhyay,
- E. Collins, M. O'Driscoll, R. O'Connell, O. Dunne

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Therapeutic targeting of IGF-1R in thyroid eye disease

Niamh McDermott
School of Biochemistry and Cell Biology

What I am doing

We study the Insulin-like growth factor 1 receptor (IGF-1R), an essential receptor tyrosine kinase that promotes cell growth and survival and is overexpressed in many cancers. Despite these factors presenting IGF-1R as a candidate for therapeutic inhibition in cancer, it has been notoriously difficult to target. Our lab studies the biochemical pathways that regulate IGF-1R activity, and how we may interfere with these pathways to successfully target IGF-1R. Recent success with an anti-IGF-1R monoclonal antibody, teprotumumab, for treating thyroid eye disease (TED) supports the idea that IGF-1R can be successfully therapeutically targeted.

Why I am doing it

The IGF-1R is an ideal anti-cancer therapeutic target on paper. However, despite initial successes in in vitro studies and pre-clinical models, anti-cancer therapies targeting IGF-1R have largely failed in clinical trials. The success of teprotumumab in targeting IGF-1R in TED and reversing disease symptoms has shown that IGF-1R is amenable to therapeutic targeting in the context of this inflammatory disease. Therefore, enhanced understanding of IGF-1R status and its environment in TED may lead to the repurposing of previously developed orphan drugs for treatment of cancers which may have IGF-1R in a similar context to that observed in TED.

How I am doing it

We are studying IGF-1R activity and its inhibition in both inflammatory and non-inflammatory environments. Using these models, we are investigating the different biochemical pathways in which IGF-1R is involved, in inflammatory vs non-inflammatory conditions, enabling us to discern how IGF-1R is promoting inflammatory and survival signalling. By understanding IGF-1R activity in these environments, we may understand how IGF-1R can be successfully therapeutically targeted in this context. This understanding may then be applied to cancer patients, who may be responsive to anti-IGF-1R therapies depending on IGF-1R status in their condition.

What I hope to achieve in the end

We are hoping to gain an understanding as to how IGF-1R is successfully therapeutically targeted in an inflammatory context and use this to further understand why targeting IGF-1R in cancer has failed. While teprotumumab treats TED effectively, the mechanism by which it does is not well understood. If we can understand why targeting IGF-1R is successful in this context, we may then be able to search for sub-groups of cancer patients whose cancers may have IGF-1R in a similar context and therefore be responsive to anti-IGF-1R therapies. This may lead to the repurposing of previously developed anti-IGF-1R orphan drugs for compatible cancers.

What is the potential impact in the Pharma area

By studying how IGF-1R promotes disease progression, and by identifying the context in which IGF-1R can be therapeutically targeted, we may apply this knowledge to potentially treat other diseases that present with IGF-1R in this context. This may promote the re-purposing of previously developed drugs to treat these different diseases, thus expediting drug development for a lesser cost than developing brand new therapies. In addition to this, by understanding the pathways through which IGF-1R drives disease, we may identify other therapeutic targets, targeting of which may synergise with anti-IGF-1R therapies to better treat these diseases.

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Engineering Synthetic Circular Noncoding RNAs as A Novel Therapeutic Strategy For Sepsis

Meaghan Richardson[1,2,+], Nerea Hernandez Egido[1,2], Kellie Dean[3], Piotr S. Kowalski[1,2]

[1]School of Pharmacy, University College Cork (UCC), Cork, Ireland [2] APC Microbiome Ireland, UCC [3] School of Biochemistry and Cell Biology, UCC

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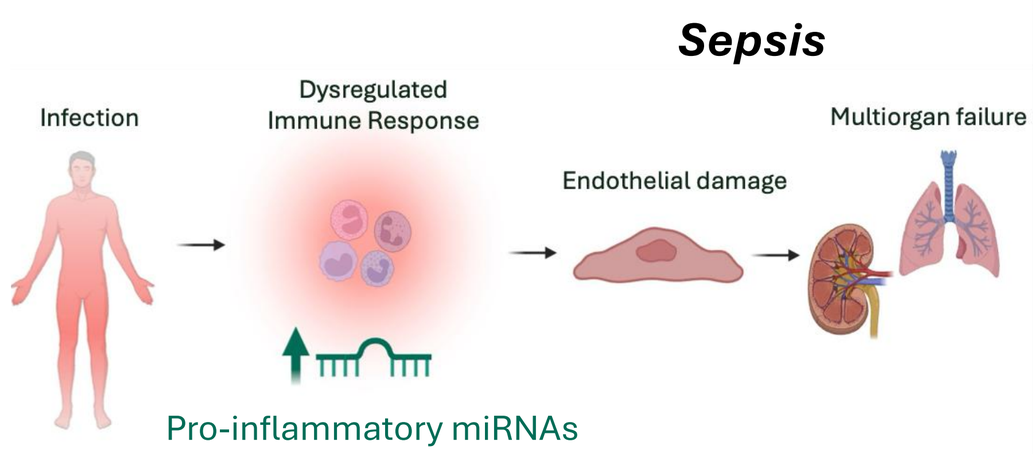
MOTIVATION

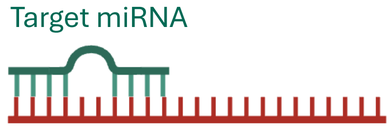
Sepsis is a life-threatening condition due to **dysregulated immune response to infection** leading to **endothelial damage and multiorgan failure**.
Despite advances in understanding the pathophysiology of sepsis, **numerous clinical trials have failed** to identify therapies that can treat sepsis by **intervening with the disease process,** leading to **unacceptably high mortality.**
The dysregulation of pro-inflammatory microRNAs (miRNAs) is of particular interest as miRNAs can bind to tens or even hundreds of genes, enabling them to regulate entire pathways. **Modulating miRNA levels represents an attractive therapeutic approach** in complex diseases such as sepsis in which entire networks of genes in affected cells are dysregulated.



APPROACH

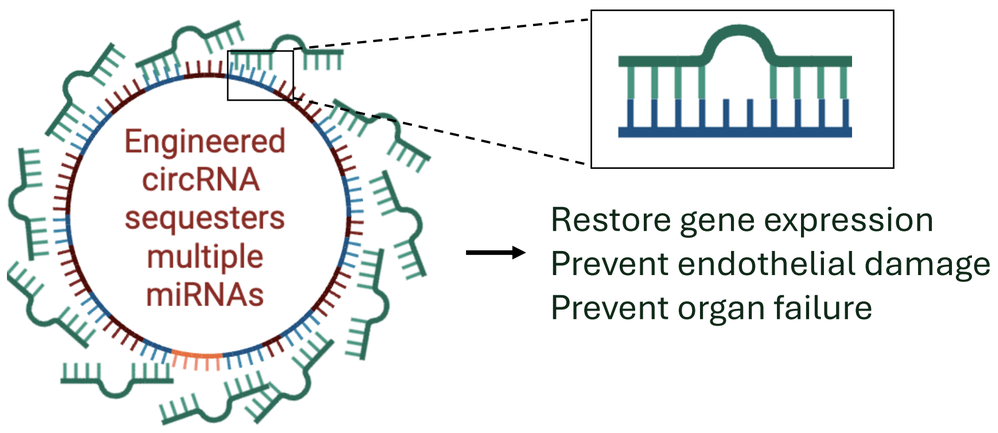
Circular RNAs (circRNAs) are a novel class of therapeutic RNA molecules with unique features that could the limitations of existing drugs and offer a novel approach for therapeutic intervention in sepsis.
I am developing noncoding circRNAs with **two key functions** as a novel therapeutic strategy for sepsis:

(1) circRNA miRNA sponges: sequester pro-inflammatory miRNAs implicated in sepsis-associated endothelial dysfunction.



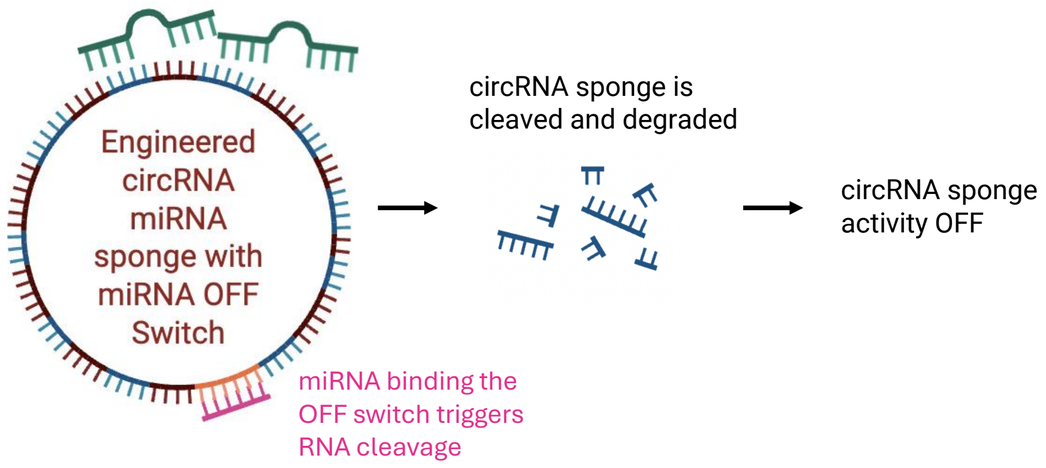
Multiple bulged binding sites for target miRNA are spaced throughout engineered circRNA

Proposed function in target cells:



(2) miRNA OFF switch: engineering tissue specificity by integrating a cell-specific miRNA binding site that results in cleavage of the circRNA in off-target cell types.

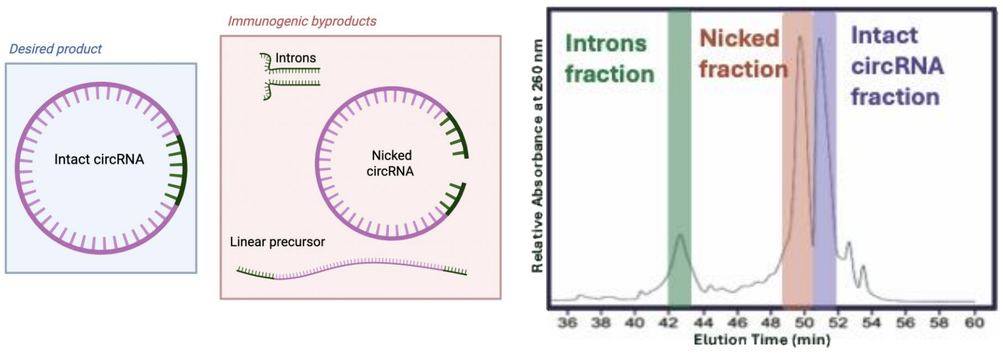
In off-target cells:



STRATEGY

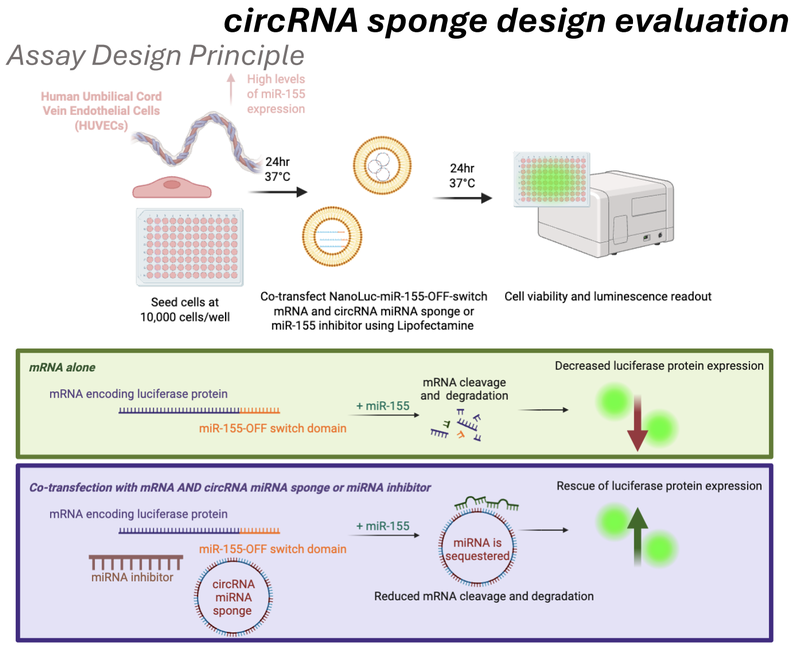
circRNA construct design, production, and purification

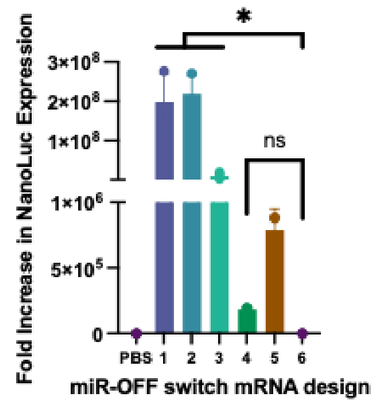
circRNA sponge constructs were generated incorporating 12 – 60 binding sites for miR-155 implementing two different design strategies.



Optimized ion-pairing reverse phase (IP-RP) HPLC method for circRNA purification eliminates immunogenic byproducts.

circRNA sponge design evaluation in endothelial cells





Evaluation of six initial miR-155-OFF switch designs in HUVECs. NanoLuc activity was measured and normalised to cell viability. Data are presented as mean ±SD for N=3, *p<0.05, Dunnett's multiple comparisons test.

AIM

This aim of this work is to demonstrate the potential of a therapeutic noncoding circRNA to **regulate multiple biological pathways and restore function in a dysregulated disease state.**

IMPACT

The technology developed in this project lays the foundation for a **modular platform** whereby circRNAs can be engineered to target any miRNA of interest and **exert tunable control of biological pathways with precision.**

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Evaluating the effects of neurotrophic factors BMP5 and BMP7 on neuronal survival and growth in an *in vitro* model of cellular senescence

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What I am doing

This work aims to explore the ability of neurotrophic factors BMP5 and BMP7 to restore senescent traits in aged neuronal models. Using different types of stressors, we aim to recreate different types of senescent impairments that cause cellular damage to study the potential of neurotrophic factors to restore them. Neurotrophic factors are known for their potential to restore neurite length, a key indicator of neuron's health, in different neurodegenerative cell models, and to protect against oxidative stress.

Why I am doing it

Cellular senescence is a state of stable terminal proliferation arrest to which cells transit as a result of different stressors such as overexpression of oncogenes, exposure to chemicals, mitochondrial dysfunction or pro-inflammatory factors. Senescence is a key factor in aging and in the development of age-related diseases. By alleviating senescence damage to cells, therapies that target senescent traits, that could potentially treat age-related diseases such as Parkinson's disease or Alzheimer's disease, can be developed.

How I am doing it

We developed an oxidative stress induced senescence cell model using SH-SY5Y human neuroblastoma cell line exposed to hydrogen peroxide (H_2O_2). We assessed the restorative effects of neurotrophic factor therapy, specifically BMP5 and BMP7, on neurite length (key indicator of neuron's health), expression of BAX (pro-apoptotic regulator that translocates to the mitochondria during apoptosis, triggering cell death) and oxygen consumption rate (OCR) in this senescence model.

What I hope to achieve in the end

We aim to determine whether neurotrophic factor therapy has the potential to restore cell damage induced by a pro-oxidant agent, specifically hydrogen peroxide. By achieving this, we hope to advance therapeutic strategies targeting oxidative stress-related neuronal damage and use this combination of oxidative stress induced senescence cell model plus neurotrophic factor therapy as a physiologically relevant *in vitro* model for neurodegenerative diseases such as Parkinson's disease.

What is the potential impact in the Pharma area

Targeting senescence damaging traits has a significant impact for the pharmaceutical industry, as it opens new lines for developing senomorphics (drugs that suppress the harmful effects of senescent cells without killing them). This can lead to new treatments for a wide range of age-related diseases, such as neurodegenerative diseases like Parkinson's or Alzheimer's, by targeting the root causes of cellular dysfunction. This could also have the potential to repurpose existing drugs, like certain anticancer therapies, for these new senotherapeutic applications.

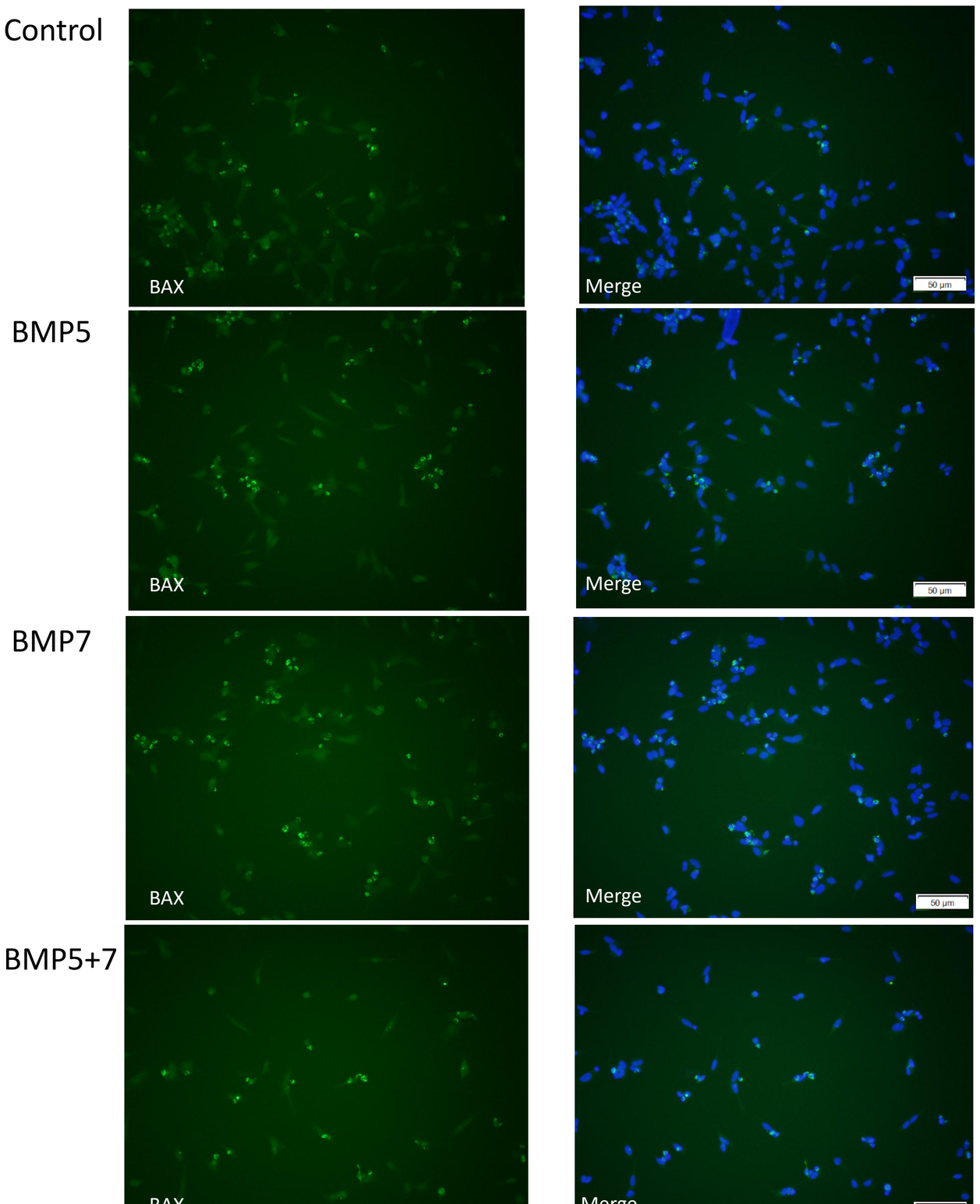

Figure 1. Immunocytochemistry stained for Bax

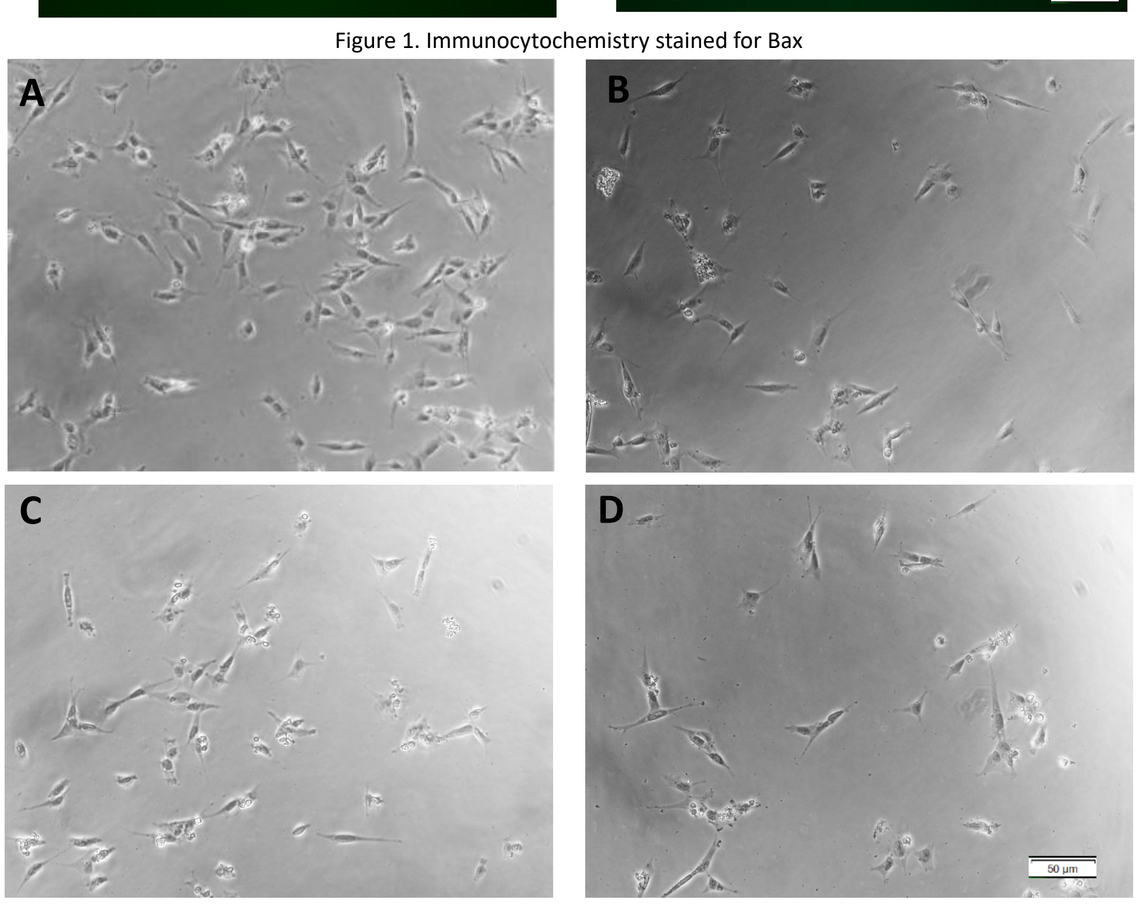

Figure 2. Representative of neurite length of Control (A), BMP5 (B), BMP7 (C), BMP5+7 (D)

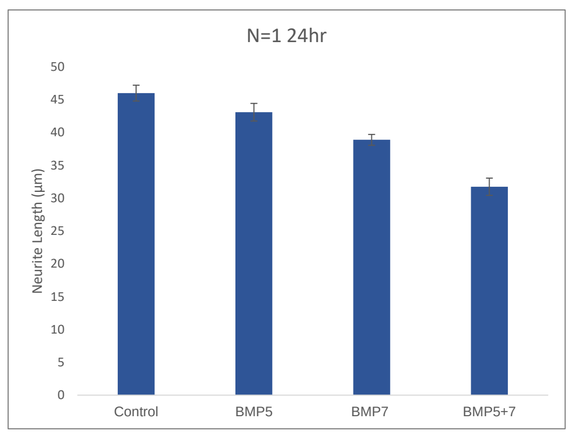

Figure 3. Neurite length in µm

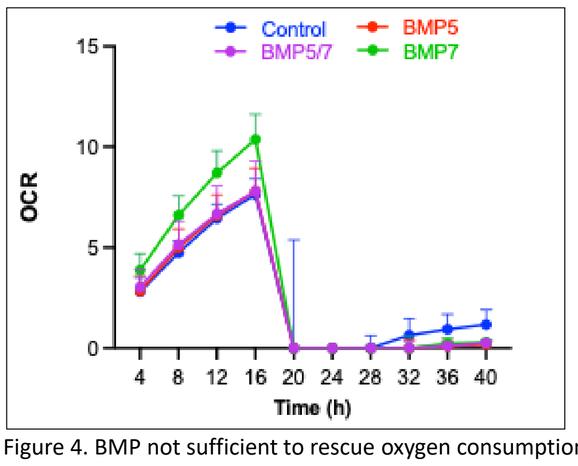

Figure 4. BMP not sufficient to rescue oxygen consumption rate