SSPC

EXECUTIVE PACK

TABLE OF CONTENT

One Introduction

Two SSPC themes

Three Bio-capabilities

Four How to Engage with us

Introduction

SSPC, the Science Foundation Ireland Research Centre for Pharmaceuticals is a world-leading hub for pharmaceutical research and development. As we continue to push forward, this year we reflect on the remarkable trajectory that has built 15 years of success and impact, which was made possible by the tireless efforts of all our researchers and support teams across Ireland, our industry partners and co-creators of our science, and our international network of academic collaborators.

Now in its second phase of funding as a centre, under the directorship of Prof. Damien Thompson, SSPC is the largest producer of PhD graduates for the biopharma sector in Ireland. SSPC has 49 industry partners, currently working across 54 projects, addressing current and future challenges for the sector with 41% of all collaborative industry research through global sites and 40% of SSPC industry members engage through their global sites and Irish sites.

Ireland is one of the leading countries in the world when it comes to pharmaceuticals. With a high number of PhD-level professionals, Ireland has been able to develop innovative products and services that have helped the country become an industry leader. The value proposition of pharmaceuticals in Ireland is strong, with exports and imports increasing every year. Statistics show that over €3 billion was exported from Ireland in 2019, making it one of the top exporters in Europe.

SSPC supports the sector, helping drive innovation and growth within the industry, helping to create jobs and boost economic prosperity across the country.

SSPC Bio Capabilities

Gene & Cell Therapy

- Proteomic profiling
- Cell models
- Gene and Protein expression patterns
- Engineering Nanotherapeutics for macromolecule delivery, including peptides, proteins and nucleic acids such as siRNA

Protein Engineering

- Crystallisation
- Characterisation (aggregation, structure, binding, activity, stability)
- Structure-function elucidation
- Rational computational design
- Site directed mutagenesis
- Sequence alignment

Drug Hybrid Conjugates

- Chemical ligation methods for accessing therapeutic proteins and protein conjugates
- Protein Glycosylation and PEGylation
- Protein oligomerisation
- Labelling of biomolecules

Protein Production

- Bacterial and mammalian fermentation
- Optimisation of bioprocess
- Purification Characterisation(aggregation, structure, binding, activity, stability)
- Formulation
- Lyophilisation

Modelling

- Molecular simulations
- Computational Fluid Dynamics for bioreactors, tubing and pumps
- Mathematical first -principles modelling

A selection of our biopharmaceutical project topics:

- Bacterial and Mammalian Cell Fermentation and Analysis
- Calixarene-controlled Protein Crystallization
- The stability of proteins and their chemically modified derivatives
- New expression systems for the production of immunomodulatory enzymes as therapeutics
- Real-time control of mAb glycosylation
- Optimisation of Transport and Hybrid Processes in (Bio)pharmaceutical Manufacturing
- Multiscale modelling of membrane separation operations, development of a multipurpose digital twin for pharmaceutically relevant membrane separation operations (nanofiltration/ultrafiltration)
- Accelerated Microfluidic Chemical Ligation for Synthesis of Peptide and Protein Therapeutics
- Enzyme Activated Peptides (EAPs): Application of EAPs as disease specific biological probes and targeted drug delivery vectors
- Peptide Synthesis
- Utilise Proteomic techniques to assess mode of action of antimicrobial agents
- Development of targeted ‘click chemistry’ strategies for the characterisation of drug uptake and localisation in cellular environments
- Bacterial and Fungal antibiotic resistance; mechanism discovery and screening systems
- In vitro mimetic scaffolds of intestinal, blood brain barrier, skin and cardiovascular mimetic system
- In vitro Cell Culture Models and Toxicity Testing
- Advanced therapies, including gene and cell-based products
- Excipient variability in a Biopharmaceutical Manufacturing
- Atomistic scale modelling to design coatings compatible with ALD for modulation of porosity in target polymers
- CFD Modelling and Scale Up
- Modelling self-assembly of peptides for next-generation pharmaceuticals
- Mathematical modelling of physicochemical processes

MOLECULES I RESEARCH THEME FACT SHEET

Overall Objective of the Molecule I Theme

To develop new methodologies for the asymmetric synthesis of existing APIs and future drug candidates with particular focus on the discovery and application of enzymes, small molecule organocatalysts and organometallic complexes for industrially-relevant, synthetic transformations.

Key Scientific Expertise: The team consists of internationally recognised researchers with expertise in the following areas of critical interest to the pharmaceutical industry in Ireland: biocatalysis (enzymology, genomics and metagenomics, synthetic biology, flow reactors); organocatalysis (thiourea-based catalysts, synthetic methodology development, anion abstraction, flow chemistry); transition metal catalysis (chiral ligands, mechanisms in asymmetric catalysis, C-H activation) and green/flow approaches to synthetic organic chemistry (total synthesis of natural products), all underpinned by predictive modelling/computational chemistry and applications in asymmetric synthesis/API synthesis.

Platform Projects

1. **Biocatalytic Approaches to Asymmetric Synthesis**
2. **Organocatalytic Approaches to Asymmetric Synthesis**
3. **Transition Metal-Catalysed Approaches to Asymmetric Synthesis**
4. **Green and Flow Chemistry for Synthesis**

RESEARCH THEME LEADERS

Prof. Anita Maguire

Vice President of Research & Innovation; Director ABCRF and Professor of Pharmaceutical Chemistry at University College Cork. B.Sc. and a Ph.D. in Organic chemistry. Inaugural Chair of the National Forum on Research Integrity, she was Chair of the Irish Research Council for Science, Engineering and Technology, and is actively engaged in R & I strategic policy development. Prof. Maguire demonstrates excellent leadership within the field of chemistry as a member of the Advisory Science Council and the Irish Research Council as well as serving on the Governance Committees of six of the 12 SFI Research Centres in Ireland.

Prof. Pat Guiry

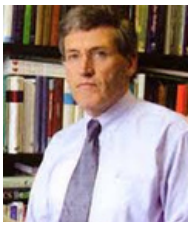
Director of the Centre of Synthesis and Chemical Biology and Full Professor of Synthetic Organic Chemistry at University College Dublin. B.Sc. and Ph.D. in Organic Chemistry. Elected as a Member of the Royal Irish Academy in 2013, awarded the Boyle Higgins Gold Medal in 2014, and in August 2015 became the first Irish academic to be elected President of the International Scientific Committee of the European Symposium of Organic Chemistry (ESOC).

15 FUNDED INVESTIGATORS

Prof. Alan Dobson
University College Cork

Dr Eoghan McGarrigle
University College Dublin

Prof. Edmund Magner
University of Limerick



Prof. Fergal O'Gara
University College Cork

Dr Marina Rubini
University College Dublin

Prof. Stephen Connon
Trinity College Dublin

Dr Gerard McGlacken
University College Cork

Prof. Declan Gilheany
University College Dublin

Prof. Paul Murphy
National University of Ireland, Galway

Dr Stuart Collins
University College Cork

Dr Andrew Phillips
University College Dublin

Dr Jerry Reen
University College Cork

Dr Peter Byrne
University College Cork

Dr Paul Evans
University College Dublin

Dr Marcus Baumann
University College Dublin

INDUSTRIAL SIGNIFICANCE

> Selecting the optimal synthetic route for API Manufacture;
> Making pharma greener; continuous manufacturing;
> Advanced manufacturing, asymmetrically synthesising complex molecules with more chiral centres.

CONTACT INFORMATION

Prof. Anita Maguire, a.maguire@ucc.ie
Prof. Pat Guiry, p.guiry@ucd.ie

www.sspc.ie

MOLECULES II RESEARCH THEME FACT SHEET

The Molecule II Theme Objectives

To develop molecules and methods for automated and in flow generation of targeted drug hybrids: drug - antibody, -peptide, -oligonucleotide and - glycoside conjugates; tailored control release formulations; sensing, assessment and imaging methods for screening drug delivery. Formulation of novel hybrid drugs opens up novel and unforeseen challenges that will be investigated and mastered.

Key Scientific Expertise

The team consists of leading international researchers, with proven expertise, including: synthetic chemistry; flow chemistry; chemical biology; bio-conjugations; hybrid inorganic and organic materials, biological-profiling; bio-inorganic; carbohydrate and automated peptide synthesis; photochemistry; molecular sensors and screening; structural analysis; physico- chemical characterization/analysis; protein expression, purification and modification; proteomics; metal-based drug conjugates, therapeutics and theranostics; imaging agents DNA targeting drugs; fluorescence and cellular/body imaging; material (nano-) chemistry, enzymatic drug activation and release.

Overview

Small-molecules incorporating biological substrates such as peptides and glycoconjugates have been recognised as highly versatile structures that can function as both biological probes and targeted delivery vectors depending on the design strategy employed. In these systems, the 'bio-component' unit modulates hydrophilicity and protein/enzyme/substrate binding properties as well as helping overcoming small molecule drug toxicity, yet maintaining high potency. This endows a number of additional beneficial properties, such as enhanced aqueous solubility, stronger ligand/substrate binding and enabling focused targeting (such as within tumour cell) and cellular uptake, all of which can result in improved pharmacokinetics for such derivatives. Importantly, many enzymes, such as glycosidase enzymes, either extra- or intracellular, can also be used to activate such conjugates through, for example, hydrolysis reactions, a mechanism that can be employed to enable better targeted delivery of a therapeutic payload or an imaging agent in vivo (such as by incorporation into soft-materials, supramolecular polymers, or coordination networks, or the combination of these). The combination of therapeutic and imaging component within a single structure is also highly attractive and ever more recognised as a major way forward to designing intelligent and targeted pharmaceuticals (theranostic).

Outcomes include smaller drug doses, which consequently can be favourable to improved scale up production methods being engineered such as production applicable flow conditions. One way of achieving this is the use of micro-reactors, where chemical reactions occur in continuous flow in channels that are only millimetres in diameter, rather than in large mixing vessels of conventional process technology. Because of the channels size, heat transfer is highly efficient resulting in more precise temperature control and hazardous reactions can be handled more safely than with traditional batch procedures, as large volumes of hazardous reagents are not mixed. These distinct advantages are of importance to antibody conjugation and peptide chemistries in which unwanted by-products formed because of imperfect reaction control leads to impurity formation. Impurity separation from antibody conjugates and peptides are the most challenging and costly to perform at production scale and remain a major obstacle to their efficient production. Delivery systems for drug-antibody and peptides remain an unmet challenge.

RESEARCH THEME LEADERS

Prof. Donal O'Shea

Professor, Head of Department, Pharmaceutical and Medicinal Chemistry, Royal College of Surgeons in Ireland, Dublin. Leads a research theme in lies in the advancement of new strategies for the synthesis and functional assessment of structurally complex molecules. The research having it's foundations in medicinal organic chemistry and chemical biology with strong collaborative links with biological imaging and medicine

Prof. Thorri Gunnlaugsson

Professor of Chemistry at Trinity Biomedical Sciences Institute, Dublin and member of the Royal Irish Academy (MRAI). Thorri's research interests are in the areas of supramolecular, bio- and medicinal chemistry, with emphasis on the recognition and targeting of biologically important analytes, and photophysical studies for applications in nano- and materials science.

INDUSTRIAL SIGNIFICANCE

· Methods for production of antibody, peptide and glycosylated drugs for targeted delivery.
· Functionalization of drug hybrids with luminescent probes, which have been in fully or part clinically investigated, and the application of biomolecules for achieving targeted drug payload release.
· Application of drug hybrids for therapeutic delivery by monitoring luminescence responses, providing a more effective screening processes allowing a more efficient identification of optimal conjugates.
· Use sensing methods to refine conjugation chemistries and determine better selectivity and sensitivity in drug-hybrid structures and bi-conjugated probes.
· Develop novel targeted 'drug-hybrids' using radical supramolecular chemistries; involving high-throughput one pot and in-flow technologies.
· Combining the above within crystalline or soft-material to allow for effective drug release that is triggered by enzymatic or light activated release.
· Gain precise in flow control over the drug to antibody and peptide conjugation chemistries to ensure defined and reproducible end products.
· Illustrate the potential of applying sequential flow micro-reactor technology coupled with flow liquid-liquid extraction technology to industry relevant drug antibody conjugations and peptide chemistries.
· Developing targeted drug candidates (either as pro-drugs, drug-conjugates, etc.) that can be selectively delivered thought 'triggered' release remains a challenge that this team will address.
· The use of highly selective, reproducible and scalable synthesis using novel industry relevant technologies and their adaption for into bio-conjugates, antibodies, etc. which remains a challenge that the team has in depth expertise in.
· Developing highly luminescent and in vivo applicable long-wavelength sensory/probes/imaging agent systems for use in screening technologies remains a challenge that this team has strong track record in delivering on; the next generation 'hybrid drugs' will strongly benefit from such developments.
· The use of soft-material and coordination networks that can be employed in delivering novel and smart drug-hybrids, or be used to incorporate sensors in for monitoring drug release, etc.
· Formulation of novel hybrid drugs opens up novel and unforeseen challenges that the team will investigate and master, particularly through the use of soft- and coordination polymer based materials.
· Controlled release formulations for highly water soluble antibodies and peptides remains a stumbling block for their more widespread clinical use. The most commonly utilized approach being pegylation for antibody delivery; this limiting drawback will be addressed by this expert team.
· Developments of novel targeting systems as 'drug-hybrids', 'pre-probes' and bio-conjugates (including antibody drugs, short peptides and polysaccharides, etc.) that can be selectively activated and delivered (and monitored) are major current challenges.
· Screening of drug candidates using fast luminescent methods coupled with enzymatic activations (and observed delivery) has been a hot topic in drug/medicinal chemistry. The programme put together by this team will greatly accelerate the progress of delivering such 'smart/intelligent' drug/pharmaceuticals.
· The use of soft-materials such as supramolecular gels and coordination networks that can dynamically report on drug delivery status offers the transformative breakthrough for drug delivery systems.
· Reactions carried out in flow rather than batch processes give rise to a paradigm shift from current need to "scale-up" a chemical reaction for production to "scaling-out" to reach production capacity, i.e. once a flow reaction is optimised it can be run indefinitely giving a continuous stream of product.

8 Funded Investigators

Prof. Eoin Scanlan
Trinity College Dublin

Prof. Joanna McGouran
Trinity College Dublin

Prof. Wolfgang Schmitt
Trinity College Dublin

Prof. Marc Devocelle
Royal College of Surgeons Ireland

Dr Darren Griffith
Royal College of Surgeons Ireland

Dr Robert Elmes
Maynooth University

Prof. Susan Quinn
University College Dublin

Dr Marco Monopoli
Royal College of Surgeons Ireland

www.sspc.ie

MOLECULES III RESEARCH THEME FACT SHEET

Molecule III Theme

The rationale around building the Molecules III leadership team was our opinion that many of the pure chemistry aspects of SSPC would be enhanced, particularly in terms of attractiveness of us to industry, by having access to systems to evaluate interaction with living biological systems.

In particular, we provide a range of in vitro cell culture systems for assessing tissue-specific toxicity and efficacy of specific/drugs in diseases such as cancer and diabetes , biocompatibility and interaction with surfaces.

Cell culture systems are generally faster, more ethically acceptable, cheaper and more flexible than animal testing even though some of this may be necessary afterwards - the initial use of cell culture systems is likely to reduce the extent to which animal testing is needed, and the number of animals used.

The specific research projects encompass:

*** Cancer Biology and Pharmacology – focus on pancreatic cancer**
*** Toxicity and Tissue -Specific human cell culture systems –focus on Tissue Engineering of the eye**
***Drug Resistance in Cancer**
***Diabetes, obesity, exercise physiology,muscle metabolism,**
***Biological Oxidation Processes**
***Process Development (upstream – downstream interaction) for the Biopharma Industry**
***Advanced LC-MS-MS Proteomic analysis**
***Bioorthogonal Click chemistry to develop hybrid drugs and new gene editing reagents**

NICB/Dublin City University

National Institute for Cellular Biotechnology, Dublin City University, Ireland

Government-designated National Centre of Expertise in Basic and Applied Molecular Cell Biotechnology since 1987.

RESEARCH THEME LEADERS & 5 FUNDED INVESTIGATORS

Prof. Martin Clynes

Martin Clynes is Emeritus professor of Biotechnology at Dublin city University. He was founding Director of the National Cell and Tissue culture Centre (1987) and the National Institute for Cellular Biotechnology (2000). Dr Clynes has edited books on Animal Cell Culture methods and on Drug Resistance in cancer and has over 250 peer-reviewed papers on aspects of cell culture, cancer research, diabetes research and biopharmaceutical production of recombinant proteins. He has had extensive collaborations with industry. In 2014 he was joint recipient of the nature senior lifetime award for scientific mentorship. Some would say that his obsession with cells over a period of 45 years is unhealthy, but he maintains that they are just good friends.

Prof. Kevin Kavanagh
Funded Investigator
Maynooth University

Prof. Andrew Kellett
Funded Investigator,
Dublin City University

Dr Finbarr O'Sullivan
Funded Investigator/ Joint Deputy Principal Investigator. National Institute for Cellular Biotechnology, Dublin City University

Dr Paula Meleady
Funded Investigator/Principal Investigator at National Institute for Cellular Biotechnology, Dublin City University

Dr Kieran McGourty
Funded Investigator
University of Limerick

Key Scientific Expertise

> Microbial systems/antibiotic resistance
> Diabetes models, glucose uptake, muscle, biological oxidation
> Biological chemistry, design and in vitro e valuation of novel potential cancer chemotherapy drugs
> Differentiated human cell models for intestinal transport, skin, ocular surface, lung
> Cell culture models for cancer and drug resistance; cells used by Biopharma

INDUSTRIAL SIGNIFICANCE

The specific research questions being addressed by the Molecules III Team are in themselves of interest to industry, in particular to industry developing new therapeutic agents for cancer, diabetes, obesity and bacterial and fungal infections.

In addition, the expertise being developed in this strand could, we believe, enhance the offerings to industry from other, more purely chemical, strands by providing biological information on toxicity, efficacy, biocompatibility and interaction between cells and surfaces. Some knowledge on demonstrated biological effects can help to derisk a project from Industry's point of view.

The Molecules III leadership team also has wide experience of research collaboration with the biopharmaceutical industry, and therefore a good understanding of what this industry is looking for externally in research collaborations
Two of the Molecules III Leadership Team (KK and MC) have successfully set up spinout campus companies.

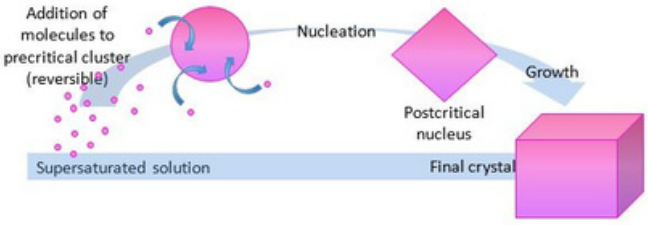
CONTACT INFORMATION

Martin Clynes, Martin.clynes@dcu.ie
Finbarr O'Sullivan, Finbarr.osullivan@dcu.ie
Kieran McGourty, Kieran.McGourty@ul.ie
Andrew Kellett, Andrew.Kellett@dcu.ie
Kevin Kavanagh, Kevin.Kavanagh@mu.ie
Paula Meleady, Paula.Meleady@dcu.ie

MATERIALS RESEARCH THEME FACT SHEET

Overall Objective of the Materials Theme: To advance our understanding of single-component crystalline materials (SCCMs) and multi component crystalline materials (MCCMs) in order to enable improved orally delivered drug products. The Materials Theme combines crystal engineering and the engineering of crystals approaches in a synergistic fashion to design processes that will produce crystalline materials with specific properties and functions.

Key Scientific Expertise: Crystal engineering; structural crystallography; database mining; solid-state characterisation; solid - liquid thermodynamics; cocrystal design and discovery; crystal structures; polymorphism; metallodrugs; modelling of crystallisation processes; phase diagrams; crystallization thermodynamics & nucleation and growth kinetics.



Crystal Engineering: To study the design, properties and pharmaceutical applications of corystals

Scientific Challenges

- Some classes of molecular cocrystals have established design principles but others, e.g. ionic cocrystals (ICCs) and chiral cocrystals (CCCs), are understudied.
- The properties of cocrystals cannot yet be predicted because modelling is not yet reliable enough to be predictive.
- It is unknown if cocrystals will persist in the presence of competing coformers such as the excipients used in drug formulations.
- The effect of conformer(s) on biological efficacy is unstudied and therefore unknown.

Summary of Research Goals

- To develop crystal engineering design principles for understudied supramolecular synthons.
- To investigate correlations between solubility and pharmacokinetics.
- To investigate the robustness of cocrystals in the presence of competing coformer(s).
- To determine the effect of coformer(s) in biological efficacy.
- To enable predictive modelling of cocrystal structure and properties.

Scientific Impact

- Predictive modelling that is reliable will be generally useful and has the potential to gain insight into;
  - ✓ Structure-property relationships in molecular solids with respect to physical stability, solubility and bioavailability.
  - ✓ The nature and hierarchy of noncovalent interactions, especially weak interactions that remain poorly understood.
  - ✓ Iterative improvement to modelling methods through the creation of synergy between experiment and theory.

Technological Impact

- Better medicines - Cocrystals can offer improved performance:
  - ✓ biological efficacy
  - ✓ physicochemical properties
  - ✓ safety margins
- Cheaper medicines - Less risk and time to develop a drug product:
  - ✓ 2018 FDA Guidance on pharmaceutical cocrystals + 505(b)(2) pathway enable new drug products from existing drug molecules (less risk).
  - ✓ Predictive modelling and/or new design principles will reduce the experiments needed to develop drug products (less time).

Engineering of crystals: Fundamental nucleation and growth during pharmaceutical crystallisation

Scientific Challenges

- The science and process engineering underpinning the crystallisation of complex organic molecules with conformational flexibility and a multitude of functional groups is poorly understood
- There is insufficient molecular level understanding of the crystallisation process like
  - molecular clustering in solution
  - the actual nucleation of the crystalline phase
  - the crystal solution interface
  - and the growth process.

Summary of Research Goals

- To improved the understanding of nucleation and crystal growth rates for model based design of industrial processes.
- To develop predictive models for the influence of hydrodynamics and solid state mechanics on secondary nucleation
- To enable systematic approaches for additive and solvent choice to promote nucleation and to stabilize the size distribution
- To design methods for nanoparticle isolation.

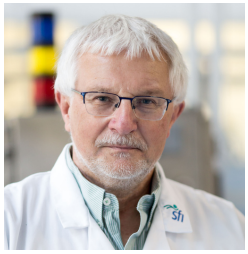
Scientific Impact

- Understanding and thus controlling crystal morphology and size distribution will allow for:
  - Systematic production of target crystal size distributions for complex organic molecules
  - Elucidation of the nature and impact of additive and impurity molecules on nucleation and particle growth processes
  - Iterative improvement to modelling methods through the creation of synergy between experiment and theory

Technological Impact

- Industrial crystallisation issues need process understanding to manage:
  - Process performance
  - Batch failure
  - Batch to batch discrepancies
  - Particle size distribution – wide or out of specifications
  - Unwanted polymorphism
  - Improved product stability

RESEARCH THEME LEADERS



Prof. Michael Zaworotko

SSPC Co-Director, Bernal Chair of Crystal Engineering at the University of Limerick and SFI Research Professor. Associate Editor for Crystal Growth & Design (ACS) and Founding director of SMMARTT(Smart Metal-Organic Materials Advanced Research and Technology Transfer) at Univ. S. Florida (USF) and Chair of Chemistry for 9 years at USF. Multiple publications/patents and features on the world list of Highly Cited Researchers.

Prof. Sarah Hudson

Lecturer in Pharmaceutical and Industrial Chemistry at University of Limerick. She is SSPC Materials Theme co-Leader and coordinator of an EU-ITN European Industrial Doctorate training programme on the development of long acting injectable crystalline suspensions, LongActNow.

INDUSTRIAL SIGNIFICANCE

A crystalline material is the active component (drug substance) of almost all orally delivered medicines. This is largely because crystallisation can afford high purity drug substances that are consistent and can be processed at large scale. New crystalline materials are able to offer IP protection for new chemical entities and existing molecules. When the crystalline form of a drug molecule has low solubility, is difficult to crystallise, incorporates impurities or exhibits poor stability then it will not be suitable for ultimate use in a drug product. Regulatory bodies require extensive screening and characterisation of the crystal forms of drug compounds. This theme will:

- Reduce time to market and develop advanced manufacturing strategies.
- Improve efficacy of drug products by developing predictive modelling tools for determining the structure and solubility of single and multi-component crystals to make screening for SCCMs and MCCMs faster and less costly.
- Develop predictive modelling tools for determining the compatibility of active drug substances with inactive polymeric and molecular excipients in order to de-risk formulation problems for active drug substances.
- Fundamental understand nucleation and crystal growth kinetics for the purpose of controlling the product crystal size distribution.
- Develop methods to enable rational selection of additives and methods for product isolation.
- Develop a high throughput microfluidic platform to assess the impact of active and inactive coformers upon biological activity in a more efficient manner.

CONTACT INFORMATION

chael.zaworotko@ul.ie - Sarah Hudson, sarah.hudson@ul.ie

10 Funded Investigators:

Dr Simon Lawrence
University College Cork

Dr Humphrey Moynihan
University College Cork

Dr Andrea Erxleben
University of Galway

Prof. Peter Crowley
University of Galway

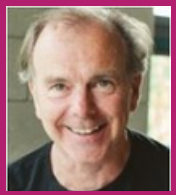
Dr Constantina Papatriantafyllopoulou
University of Galway

Prof. Kevin Ryan
University of Limerick

Dr Luis Padrela
University of Limerick

Dr Shalini Singh
University of Limerick

Prof. Pat Frawley
University of Limerick



Prof. Mark Davies
University of Limerick

www.sspc.ie

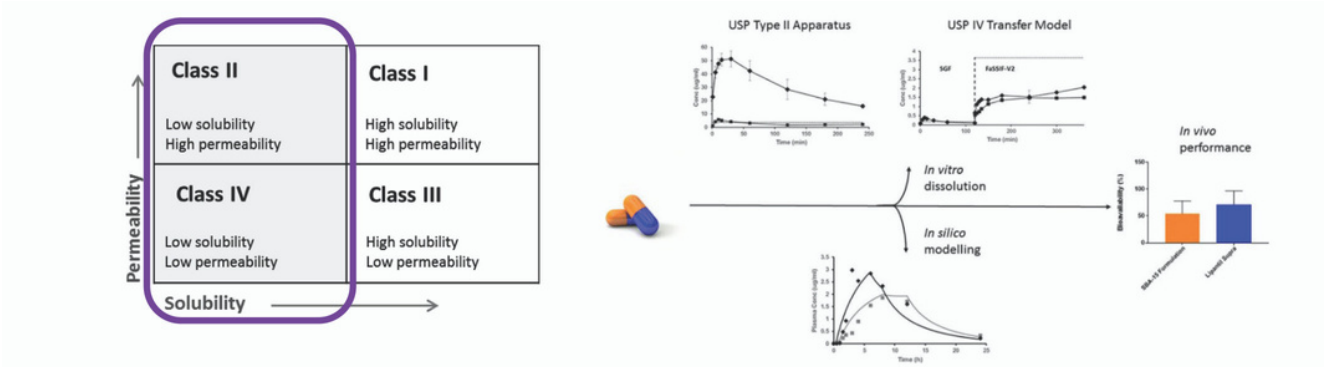
MEDICINE RESEARCH THEME FACT SHEET

Overall Objective of the Medicine Theme: To optimise the development, production and use of safe and effective medicines focusing on poorly soluble drugs, personalized and age appropriate medicines, and rational formulation approaches with predictive performance.

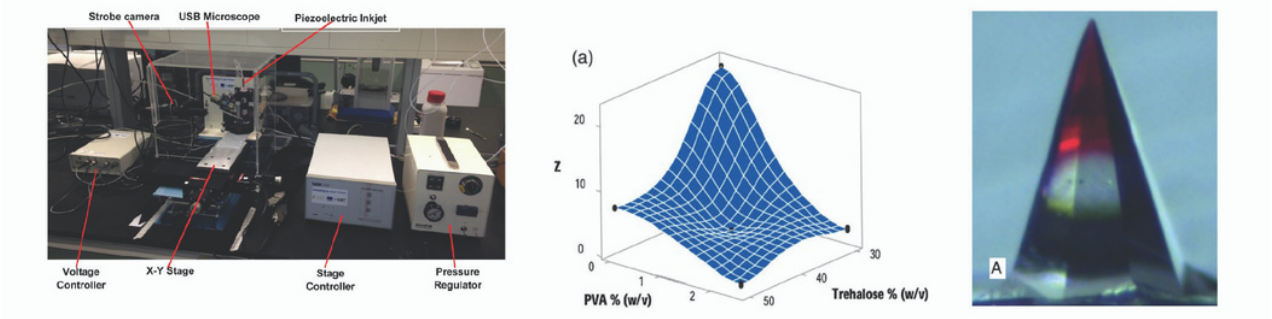
Key Scientific Expertise: Preformulation and formulation of solid dosage forms; amorphous materials; microneedles; solid state characterization; pharmaceutical processing; dissolution studies; dissolution modelling; in vivo animal (pig) model; in vitro-in vivo correlations.

Platform Projects

1. Optimisation & modelling of in vitro and in vivo performance of enabling formulations for poorly soluble drugs

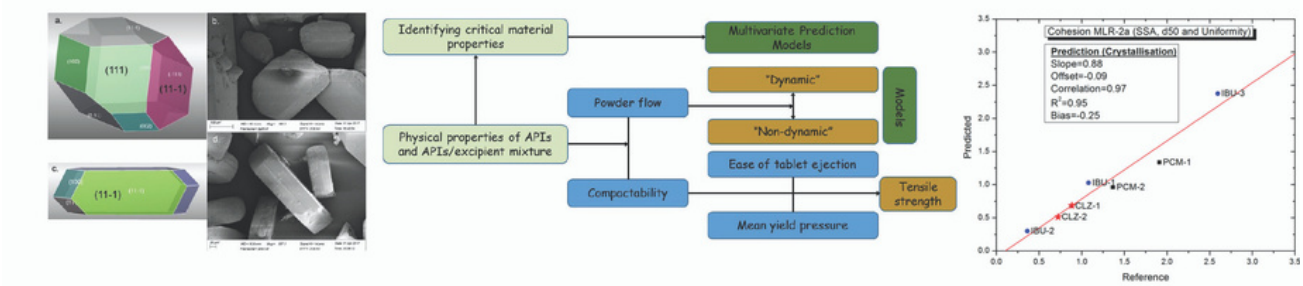


2. Flexible manufacturing platforms & formulation approaches for personalised & age-appropriate medicines



Allren, EA., et al. Dissolvable microneedle fabrication using piezoelectric dispensing technology. Int. J. Pharm., 500 (1-2) (2016) 1-10.

3. Advanced material characterisation for solid dosage forms with predictive formulation design



Worku, Z.. et al., Modelling and understanding powder flow properties and compactability of selected active pharmaceutical ingredients, excipients and physical mixtures from critical material properties. Int. J. Pharm., 531 (1) (2017) 191-204.

RESEARCH THEME LEADERS

Prof. Anne Marie Healy

Professor in Pharmaceutics and Pharmaceutical Technology in the School of Pharmacy and Pharmaceutical Sciences, Trinity College Dublin (TCD). B.Sc. in Pharmacy and a Ph.D. in Pharmaceutics. Elected Fellow of Trinity College in 2010. Over twenty five years' experience in pharmaceutics, pharmaceutical technology and drug delivery research. More than 90 peer reviewed publications. Has graduated 16 PhD students and mentored 22 postdoctoral researchers.

Prof. Abina Crean

Senior Lecturer in Pharmaceutics in the School of Pharmacy, University College Cork (UCC). B.Sc. (Pharm) and PhD in Pharmaceutics. Over twenty years' experience in formulation and pharmaceutical technology in a combination of commercial R&D, production and academic settings. More than 40 peer reviewed publications. Has graduated 10 PhD students and supervised 12 postdoctoral researchers.

INDUSTRIAL SIGNIFICANCE

In the context of advancing formulation approaches we have identified three significant current challenges that need to be addressed, namely:

Poorly soluble drugs: It is estimated that more than 60% of new drug molecules display poor aqueous solubility. There is an on-going need for enabling formulations for such therapeutic agents which have suboptimal bioavailability.

Personalised and age-appropriate medicines: Translation of personalised medicines to large patient groups requires the development of novel formulation approaches to deliver tailored dosage for individual patient needs. By harnessing new and emerging technologies we will seek to provide age-appropriate formulations for paediatric and geriatric populations, where demand for such approaches is growing.

Rational formulation approaches with predictive performance: The implementation of predictive modelling approaches to reduce drug product development times, control the impact of material variability on manufacture, reduce drug product variability and support real time drug release is a key challenge, and can only be addressed through an improved understanding of how material and processing characteristics impact product performance.

CONTACT INFORMATION

Prof. Anne Marie Healy healyam@tcd.ie 01-8961444
Prof. Abina Crean a.crean@ucc.ie 021-4901667

12 Funded Investigators

Dr Deirdre D'Arcy
Trinity College Dublin

Prof. Lidia Tajber
Trinity College Dublin

Dr Tim Persoons
Trinity College Dublin

Prof. Caitriona O'Driscoll
University College Cork

Dr Anne Moore
University College Cork

Prof. Brendan Griffin
University College Cork

Dr Katie Ryan
University College Cork

Dr Sonya Vucen
University College Cork

Dr Peter McLoughlin
SETU Waterford

Dr Joseph O'Mahony
SETU Waterford

Dr Niall O'Reilly
SETU Waterford

Prof. Elizabeth Topp
NIBRT/Purdue

www.sspc.ie

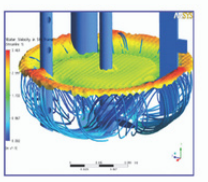
MANUFACTURING RESEARCH THEME FACT SHEET

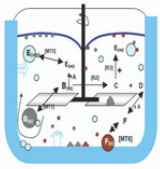
Overall Objective of the Manufacturing Theme: Enabling a disruptive change in the manufacture of drug substances and drug products, through the development and implementation of continuous manufacturing, flow chemistry and end-to-end manufacturing methodologies ("Pharmaceuticals 4.0").

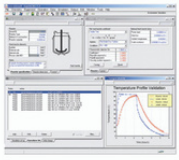
Key Scientific Expertise: Process Engineering, Bioprocess Engineering, Process Analytics, Continuous Processing, Polymer chemistry, Biochemistry, Customised technology; additive manufacturing

Platform Projects:
Hybrid Processing and Automated Process Design

- Next generation "substance" manufacturing methodologies – computational fluid dynamics - process modelling – enabling automation via digital control systems for design of flexible process modules

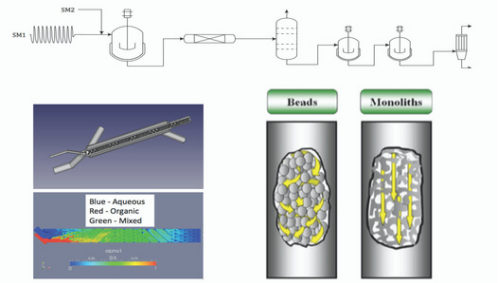

CFD


Modelling

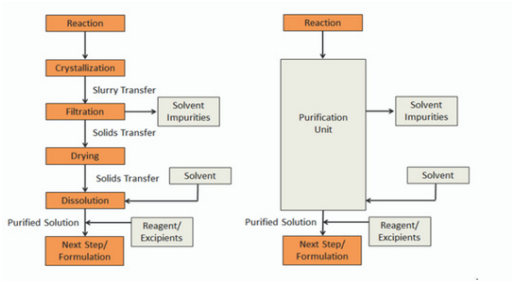

DCS


FPM

Continuous & Miniaturised Manufacturing

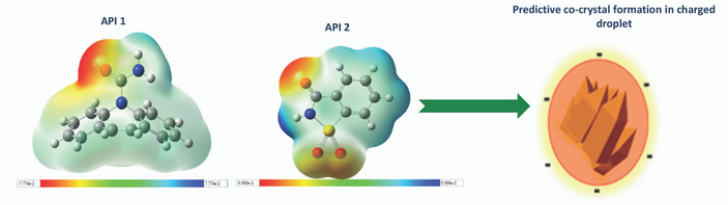


productivity ≈ 20 g/min
≈ 400 kg/L.day
Compared to batch
-< 1 kg/L.day
"Plant in a hood"



Advanced Manufacturing Techniques

- Electrospraying of Pharmaceutical Co-crystals



- Obtain predictable control of co-crystal polymorphism by optimisation of electro-spraying parameters such as charge density, electric potential, API/Co-former ratios and solvent surface tension.

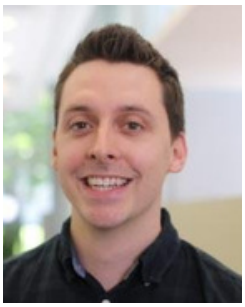
Additive Manufacturing/3D Printing

- Develop a prototyping platform whereby the properties of existing API/excipient combinations can be evaluated for 3D printing "personalized medicine" applications with alignment to Industry 4.0.
- In tandem with CFD and FEA modelling develop a data informed route map for inkjet and 3D printing pharmaceutical API/Co-formers.

RESEARCH THEME LEADERS

Prof. Gavin Walker

Bernal Chair in Pharmaceutical Powder Engineering at the University of Limerick and SSPC Co-Director since June 2017. Prof. Walker is also a Co-PI within the SSPC MOMEnTUM Spokes project. He has been awarded €26,000,000 as Principal Investigator on 35 research projects on process engineering and advanced manufacturing from EU H2020, UK government, EPSRC, Irish Government, UK Charities and Industrial sources.



Prof. Steven Ferguson

Funded Investigator in both SSPC and I-form Research Centres. 4 Years Asst. Professor in the School of Chemical & Bioprocess Engineering, University College Dublin. Lead engineer: Global flow chemistry team at Biogen, led development of integrated continuous manufacturing prototype line for commercial drug. Developed/selected clinical drug form allowing 3 clinical candidates to transition from dug discovery to clinical development.

The manufacturing theme will be aligned to industry needs and follow a predictive design-led approach in the development of next generation pharmaceutical products and processes. It is widely recognised that within the next decade there will be a disruptive change in how we manufacture drug substance (DS) and drug product (DP) at End-to-End levels. This will align to an Industry 4.0 approach in manufacturing and ultimately to a “Pharmaceuticals 4.0” approach by 2025. To establish itself at the forefront of such developments, SSPC will expand its existing expertise in the development and implementation of Continuous Manufacturing (CM) techniques, Flow Chemistry and End-to-End manufacturing methodologies from DS to DP. Manufacturing (DS, DP and coupled DS-DP) in the future is likely to be ‘skid mounted’, agile and mobile. This requires manufacturing research to be truly multi-disciplinary, leading to innovation at the interfaces between chemistry, process engineering, data analytics and mathematical modelling. CM in particular offers low facility cost, flexible batch (supply chain flexibility), platform tech, better QA (not better quality), yield improvements, and decreased Technology Transfer effort. In terms of implementation of CM, regulatory input from MHRA and EMA indicate that there is no difference in inspecting CM vs Batch, although there is a need to demonstrate control. Batch inspection is already defined in ICH Q7, with PAT and RTR well established (QbD). Recent developments in regulatory aspects include, process flexibility, which is supported by ICH Q8/9/10 allowing different control strategies and to ICH Q12 harmonization. Also, SSPC-PharM5 will assist in enabling new strategies and promote innovation and continual improvement, strengthen QA and reliable supply of product, including proactive planning of supply chain adjustments. This will allow regulators (assessors and inspectors) to better understand firms’ Pharmaceutical Quality Systems for management of post-approval CMC changes.

Industry 4.0 will require manufacturing systems that have full feedback control and self-correcting processes. This requires Theme 4 to advance Process Modelling and PAT for model predictive control of pharmaceutical manufacturing. It is also predicted that as industry moves to increased localisation, with the requirement to perform manufacturing in countries to achieve regulatory approval, this will drive different manufacturing modes for efficiencies in small volume manufacture in developing countries. This requires Theme 4 to also focus on intensified manufacturing, modularisation and process control systems.

CONTACT INFORMATION

Gavin Walker, gavin.walker@ul.ie
Steven Ferguson, steven.ferguson@ucd.ie

9 Funded Investigators:

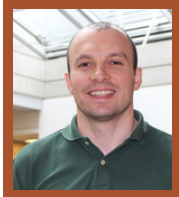
Prof. Vivek Ranade
University of Limerick

Prof. Elizabeth Topp
NIBRT/Purdue

Dr Jessica Whelan
University College Dublin

Dr Ioscani Jimenez del Val
University College Dublin

Dr Philip Donnellan
University College Dublin



Dr Luis Padrela
University of Limerick

Dr Jakki Cooney
University of Limerick

Dr Emmet O'Reilly
University of Limerick

Prof. Jennifer McManus
University College Dublin
Bristol University

www.sspc.ie

MODELLING RESEARCH THEME FACT SHEET

Overall Objective of the Modelling Theme:

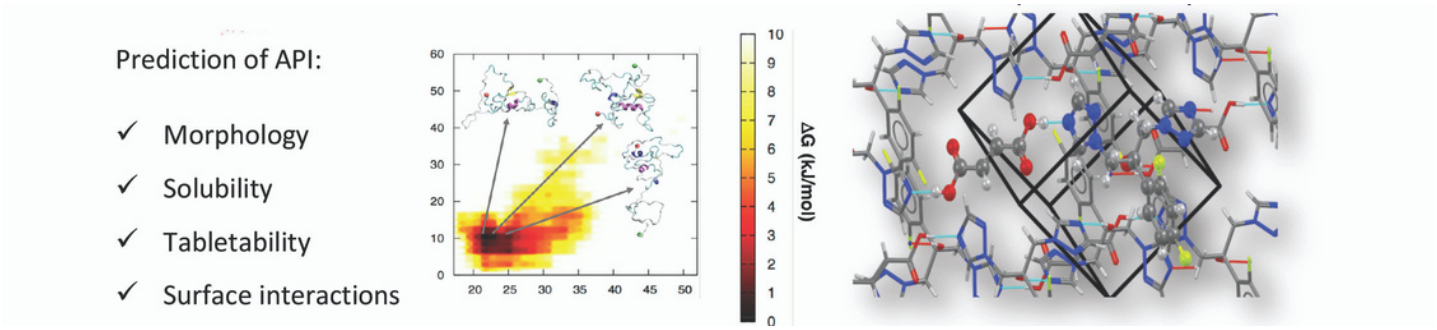
MODELLING will address the key challenges by developing new techniques to design and predict behaviour in silico in order to reduce trial-and-error experimentation.

Key Scientific Expertise:

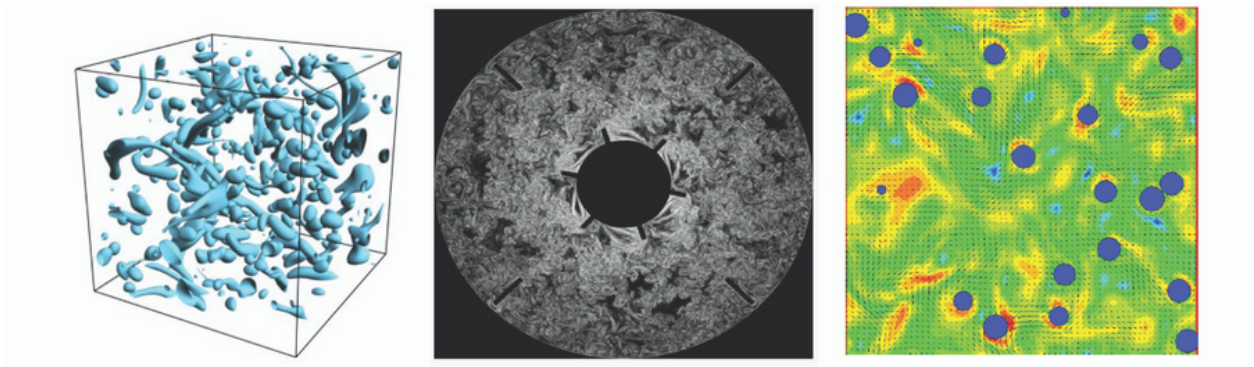
Atomic-scale modelling; computer-aided design of experiments; molecule-molecule, molecule-solvent and molecule-surface interactions; complex APIs; molecular formulation.
Modelling in the fields of fluid mechanics, turbulence, multi-phase flow and transport phenomena; simulations: computational fluid dynamics, lattice Boltzmann simulations.

Demonstrating expansion of the State of the Art:

- Framework to understand and predict multi-component solid forms from first principles
- Deciphering nanoscale design rules of macromolecular self-assembly
- Mathematical modelling of physicochemical processes
- Multi-Scale Simulations of Flow and Crystallisation in Industrial Crystallisers



Computational Fluid Dynamics techniques provide a better understanding of the dynamics of both the local phenomena and processes (by means of completely resolving them, in DNSs) and the overall flow and mixing behaviour of process equipment (by using advanced models).



RESEARCH THEME LEADERS

Prof. Harry Van den Akker

Harry Van den Akker, Bernal Professor of Fluid Mechanics at the University of Limerick, has published 130 peer reviewed journal papers and is a renowned expert in (computational) fluid mechanics and multiphase mixing, preferentially using lattice Boltzmann techniques

Prof. Damien Thompson

Damien Thompson leads the predictive materials modelling group at Bernal Institute UL, designing novel architectures based on directed self-assembly of nanoscale building blocks (molecules, nanoparticles, and proteins), in collaboration with leading experimental and industry partners.

Prof. Norma Bargary

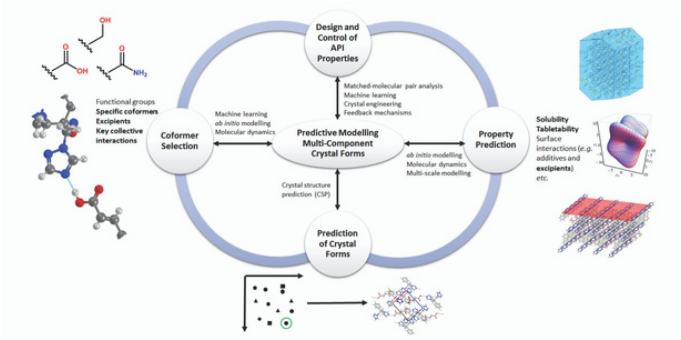
Norma Bargary is Chair of Data Science and Statistical Learning in the Dept of Mathematics and Statistics at the University of Limerick. She is Principal Investigator with multiple Centres and the the UL Vice-Director of the SFI Centre for Research Training in Foundations of Data Science

INDUSTRIAL SIGNIFICANCE

Modelling provides the central unifying pillar of SSPC's research programme. By rationally designing from the molecular to materials to macro scale we will dramatically reduce the number of experiments that must be performed to discover and design new molecules, crystals, co-crystals and nanoparticle-enabled deliveries, and to engineer and optimise formulation and processing conditions to deliver new pharma and biopharma solutions.

Example project: framework for understanding and predicting multi-component solid forms from first principles

• Employ first-principles modelling to quantify solid-state interactions driving stability of crystals & improve rapid informatics-based approaches to predict likely multi-component solid forms & their properties



- **The platform will push beyond current state of the art by developing new transformative physical models that are sufficiently fast, accurate, and intuitive for broad uptake in drug product manufacture**

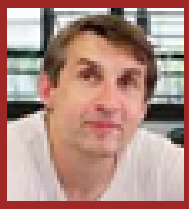
CONTACT INFORMATION

Harry Van den Akker, harry.vandenakker@ul.ie
Damien Thompson, damien.thompson@ul.ie
Norma Bargary, norma.bargary@ul.ie

9 Funded Investigators

Dr Davide Tiana
University College Cork

Prof. Patrick Frawley
University of Limerick



Prof. Michael Vynnyky
University of Limerick

Dr Sarah Guerin
University of Limerick

Dr Kevin Moroney
University of Limerick

Dr Doireann O'Kiely
University of Limerick

Dr Orest Shardt
University of Limerick

Matthias Vandichel
University of Limerick

Prof. Stephen O'Brien
University of Limerick

www.sspc.ie

How to engage with SSPC

Since its inception, SSPC has successfully collaborated with over 47 industry partners, composed of indigenous and foreign operations, whose size range from small to multi-national. Collectively, this demonstrates a strong track-record in delivering applied research that enables industry to solve challenges leading to the development of better medicines. Our industry partners benefit from the depth and breadth of expertise available within SSPC and through our collaborations augment their R&D capabilities and increase opportunity for technology transfer and commercialisation.

Industry membership

SSPC supports an industry membership model providing many benefits to members including access to training, ability to host a PhD student placement, gateway to a talent pipeline and the opportunity to network and collaborate with both the Centre's academic and industry community. In 2022 the Centre expanded its member base to include 7 new industry members and currently comprises over 46 partners.

Working with us

Industry projects can be supported in a number of ways in SSPC.

1. Companies have the option to initiate fully funded industry specific research projects and own all project IP thanks to a flexible Irish IP protocol that facilitates industry led project collaborations with Irish research performing organisations.
2. Companies can also avail of SSPC Co-Funding (max. 50%), providing organisations with the opportunity to licence back any IP arising.

Working in partnership with SSPC your organisation can:

- solve key industrial challenges
- develop R&D capabilities
- attract new talent
- co-author publications
- upskill staff
- Network with industry peers in a world leading international community of practice

For more information on how we can work with you please contact our Business Development Manager, Jamie.Guidera@ul.ie

Industry Engagement Manager, Aisling.Arthur@ul.ie

Research Programme Manager, Targeted Projects, Kristy.Sirr@ul.ie