



# SSPC RESEARCH THEME FACT SHEETS

---



## MOLECULE 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](mailto:a.maguire@ucc.ie)  
Prof. Pat Guiry, [p.guiry@ucd.ie](mailto:p.guiry@ucd.ie)

[www.sspc.ie](http://www.sspc.ie)

HOST INSTITUTION



PARTNER INSTITUTIONS





## MOLECULE 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.

### 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](http://www.sspc.ie)

HOST INSTITUTION



PARTNER INSTITUTIONS



## MOLECULE 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 & 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. Donal O'Gorman**  
Funded Investigator/  
Joint Deputy Principal  
Investigator. National  
Institute for Cellular  
Biotechnology, Dublin  
City University



**Dr Andrew Kellett**  
Funded Investigator,  
Dublin City University



**Prof. Kevin Kavanagh**  
Funded Investigator  
Maynooth University



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

### Key Scientific Expertise

- > Microbial systems/antibiotic resistance
- > Diabetes models, glucose uptake, muscle, biological oxidation
- > Biological chemistry, design and in vitro evaluation 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](mailto:Martin.clynes@dcu.ie)  
Donal O'Gorman, [Donal.ogorman@dcu.ie](mailto:Donal.ogorman@dcu.ie)  
Finbarr O'Sullivan, [Finbarr.osullivan@dcu.ie](mailto:Finbarr.osullivan@dcu.ie)

Andrew Kellett, [Andrew.Kellett@dcu.ie](mailto:Andrew.Kellett@dcu.ie)  
Kevin Kavanagh, [Kevin.Kavanagh@mu.ie](mailto:Kevin.Kavanagh@mu.ie)

HOST INSTITUTION



PARTNER INSTITUTIONS

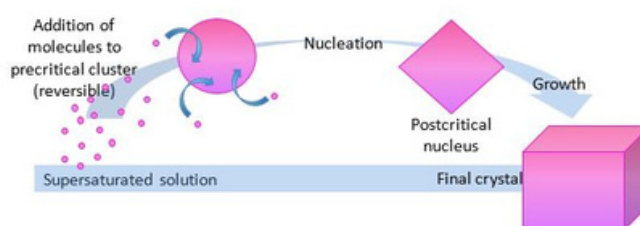
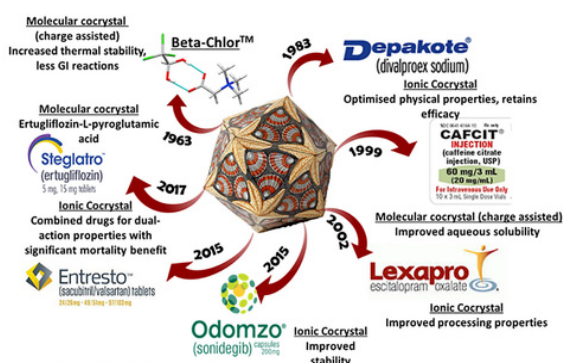




## MATERIALS RESEARCH THEME FACT SHEET

**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 cocrystals

### 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 cofomers such as the excipients used in drug formulations.
- The effect of conformer(s) on biological efficacy is unstudied and therefore unknown.

### 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.

### 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 cofomer(s).
- To determine the effect of cofomer(s) in biological efficacy.
- To enable predictive modelling of cocrystal structure and properties.

### 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.

### 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

### Summary of Research Goals

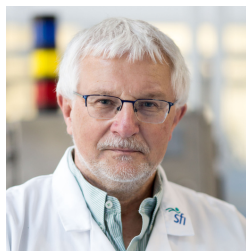
- To improve the understanding of nucleation and crystal growth rates for model based design of industrial processes.
- To develop predictive models for the influence of hydrodynamics and solid state mechanics on secondary nucleation
- To enable systematic approaches for additive and solvent choice to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

### 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.



## Dr 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 cofomers upon biological activity in a more efficient manner.

### Funded Investigators:



**Dr Simon Lawrence**  
University College Cork



**Dr Andrea Erxleben**  
National University of Ireland, Galway



**Dr Constantina Papatriantafyllopoulou**  
National University of Ireland, Galway



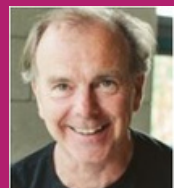
**Dr Humphrey Moynihan**  
University College Cork



**Prof. Kevin Ryan**  
University of Limerick



**Dr Luis Padrela**  
University of Limerick



**Prof. Mark Davies**  
University of Limerick



**Assoc. Prof. Pat Frawley** University of Limerick

[www.sspc.ie](http://www.sspc.ie)

### CONTACT INFORMATION

Michael Zaworotko, [michael.zaworotko@ul.ie](mailto:michael.zaworotko@ul.ie) - Sarah Hudson, [sarah.hudson@ul.ie](mailto:sarah.hudson@ul.ie)



PARTNER INSTITUTIONS



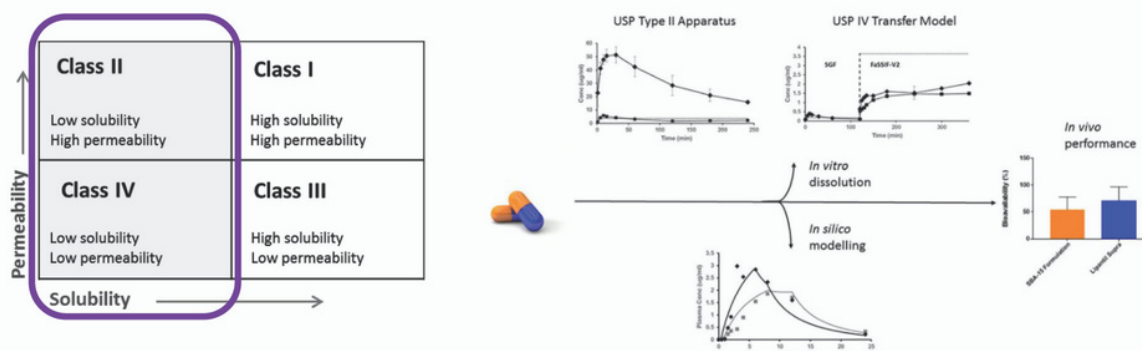
## MEDICINE RESEARCH THEME FACT SHEET

**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.

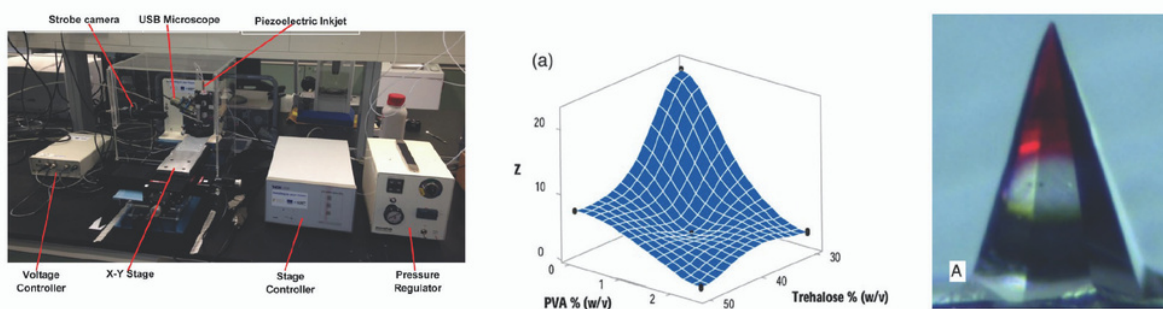
**Key Scientific Expertise:** Preformulation and formulation of solid dosage forms; amorphous materials; microneedles; solid state characterization; pharmaceutical processing; dissolution studies; dissolution modelling; in vivo animal (pig) model; in vitro-in vivo correlations.

### Platform Projects

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

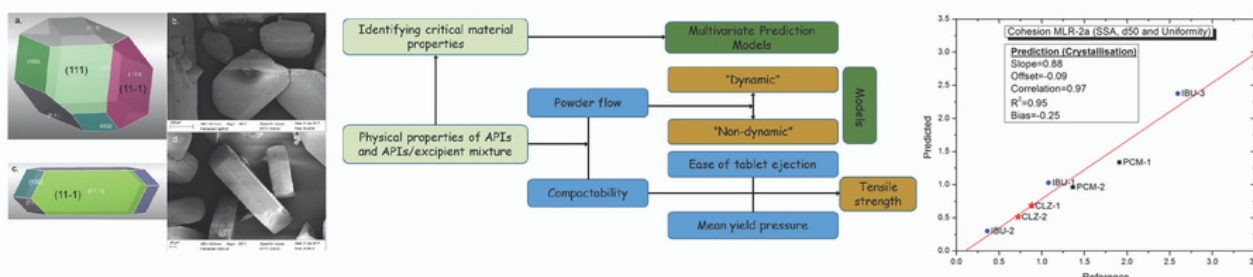


#### 2. Flexible manufacturing platforms & formulation approaches for personalised & age-appropriate medicines



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](mailto:healyam@tcd.ie) 01-8961444

Prof. Abina Crean [a.crean@ucc.ie](mailto:a.crean@ucc.ie) 021-4901667

### 10 Funded Investigators



**Dr Deirdre D'Arcy**  
Trinity College  
Dublin



**Assoc. Prof. Lidia Tajber**  
Trinity College Dublin



**Dr Tim Persoons**  
Trinity College Dublin



**Dr Brendan Griffin**  
University College  
Cork



**Prof. Caitriona O'Driscoll**  
University  
College Cork



**Dr Anne Moore**  
University  
College Cork



**Dr Katie Ryan**  
University  
College Cork



**Dr Peter McLoughlin**  
Waterford IT



**Dr Joseph O'Mahony**  
Waterford IT



**Dr Niall O'Reilly**  
Waterford IT



**Prof. Elizabeth Topp**  
NIBRT/Purdue



## MANUFACTURING RESEARCH THEME FACT SHEET

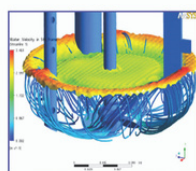
**Overall Objective of the Manufacturing Theme:** Enabling a disruptive change in the manufacture of drug substances and drug products, through the development and implementation of continuous manufacturing, flow chemistry and end-to-end manufacturing methodologies (“Pharmaceuticals 4.0”).

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

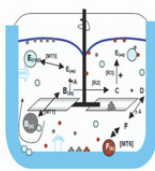
### Platform Projects:

#### 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

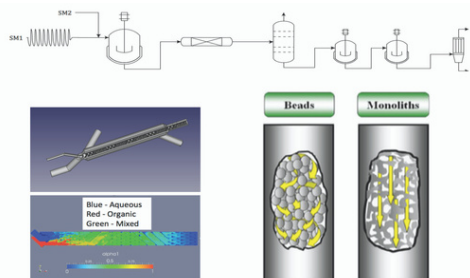


DCS

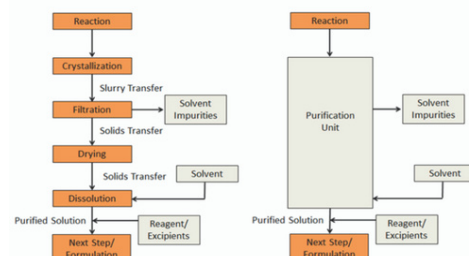


FPM

### Continuous & Miniaturised Manufacturing

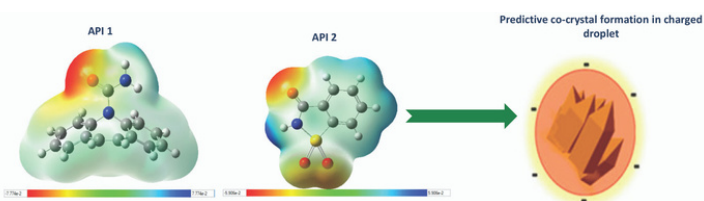


productivity  $\approx 20$  g/min  
 $\approx 400$  kg/L.day  
Compared to batch  
 $< 1$  kg/L.day  
"Plant in a hood"



### 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.



## Dr 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 drug discovery to clinical development.

### INDUSTRIAL SIGNIFICANCE

The manufacturing theme will be aligned to industry needs and follow a predictive designed 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](mailto:gavin.walker@ul.ie)  
Steven Ferguson, [steven.ferguson@ucd.ie](mailto:steven.ferguson@ucd.ie)

### Funded Investigators:



**Prof. Peter Crowley**  
National University Galway



**Dr Jessica Whelan**  
University College Dublin



**Dr Philip Donnellan**  
University College Dublin



**Dr Ioscani Jimenez del Val**  
University College Dublin



**Dr Luis Padrela**  
University of Limerick



**Dr Jakki Cooney**  
University of Limerick



**Dr Emmet O'Reilly**  
University of Limerick



**Prof. Vivek Ranade**  
University of Limerick



**Prof. Elizabeth Topp**  
NIBRT/Purdue

[www.sspc.ie](http://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.

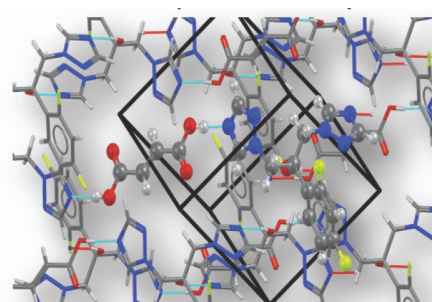
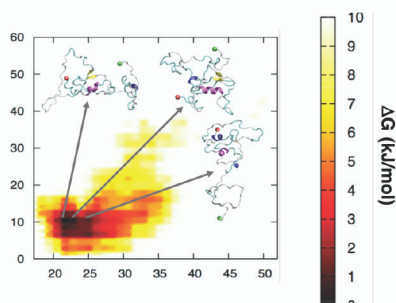
Modelling in the fields of fluid mechanics, turbulence, multi-phase flow and transport phenomena; simulations: computational fluid dynamics, lattice Boltzmann simulations.

### Demonstrating expansion of the State of the Art:

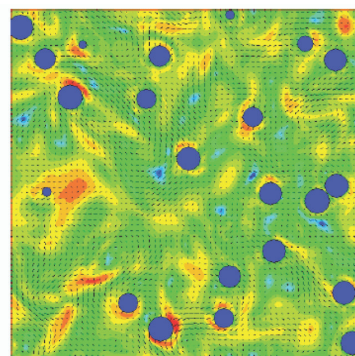
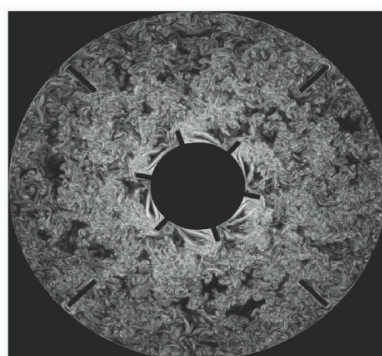
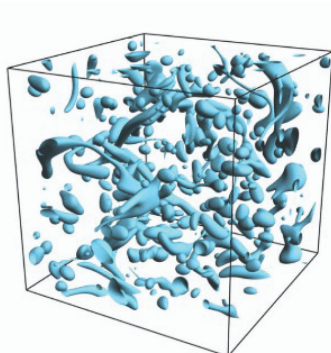
- Framework to understand and predict multi-component solid forms from first principles
- Deciphering nanoscale design rules of macromolecular self-assembly
- Mathematical modelling of physicochemical processes
- Multi-Scale Simulations of Flow and Crystallisation in Industrial Crystallisers

Prediction of API:

- ✓ Morphology
- ✓ Solubility
- ✓ Tableability
- ✓ Surface interactions



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).



HOST INSTITUTION



PARTNER INSTITUTIONS





# 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

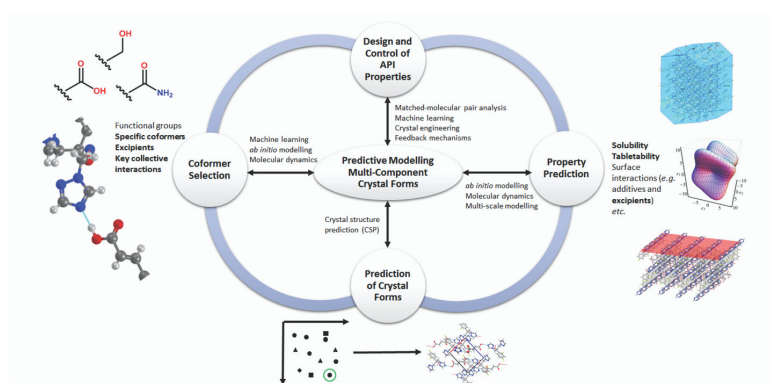
Damien Thompson leads the predictive materials modelling group at Bernal Institute UL, designing novel architectures based on directed self-assembly of nanoscale building blocks (molecules, nanoparticles, and proteins), in collaboration with leading experimental and industry partners.

### INDUSTRIAL SIGNIFICANCE

Modelling provides the central unifying pillar of Pharm5. 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](mailto:harry.vandenakker@ul.ie)  
Damien Thompson, [damien.thompson@ul.ie](mailto:damien.thompson@ul.ie)

## 6 Funded Investigators

Eleven postgraduate students and four postdoctoral research fellows will provide state of the art predictive designs, ranging from quantum mechanical models of drug molecule tableability to massively parallel simulations of nucleation in industrial crystallisers, to guide and accelerate experiments and technology transfer.



### Dr Davide Tiana

University  
College Cork



### Prof. Stephen O'Brien

University of  
Limerick



### Dr Sarah Mitchell

University of  
Limerick



### Prof. Norma Bargary

University of  
Limerick



### Assoc. Prof. Patrick Frawley

University of  
Limerick



### Prof. Michael Vynnyky

University of  
Limerick

[www.sspc.ie](http://www.sspc.ie)