Medicines Manufacturing Innovation Foundry Event

Wednesday 17th January 2024 **New Modalities** Agenda

	DETAILS
09:30	*Arrival and registration with refreshments.*
10:00	Opening remarks: Introduction and outline of the day from Barrie Cassey, Technology Director – Medicines manufacturing at CPI. Foreword from Nabeel Umar, PwC.
10:30	Session 1 begins: **Nucleic Acids** • Beatrice Melinek (UCL) – DNA manufacture • Jiahao Huang, PhD (Nuclera) – eProtein benchtop synthesis • David Hodgson (U. Durham) – Nucleotide synthesis
11:30	*Break and opportunity to meet Session 1 innovators*
12:00	Session 2 begins: **Peptides & CPI** • Sara ten Have (Origin Peptides) • Daryl Williams (Imperial College) • Heather Walton (CPI) - New Modalities at CPI
13:00	*Lunch and opportunity to meet Session 2 innovators*
14:00	Session 3 begins: **Technology** • Karen Trickett (Keltic Pharma) • Piers Gaffney (Exactmer) • Glen Kemp (Biotoolomics)
15:00	*Break and opportunity to meet Session 3 innovators*
15:30	Review of the day with concluding thoughts from Barrie Cassey, CPI
16:00	*Networking session*
16:30	Event close

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Beatrice Melinek, University College London
A cell-free approach to enabling localised DNA manufacture.

We are working with a novel enzymatic/cell-free protocol (patent pending) for the manufacture of DNA from a template. The technology is a platform, which should allow streamlining of DNA production, reduced costs and time lines, minimise facilities and expertise required and reduce risks associated with antibiotic resistant sequences, recombination etc.

As "Newcleic", we aim to develop and commercialise a stand-alone, single-dose, automated device for DNA amplification based on a cell-free (enzymatic) technique. Imagine a coffee pod machine that produces DNA – with similar size and ease of use. A similar capsule-based approach will allow the user to pick their own flavour without any significant change in the production protocol they follow. In the future we hope to build up to a system with the flexibility of 3D printing. We envision that such a device will be used by researchers, therapeutic developers and in clinical settings to speed up the design-build-test cycle for nucleic acid based therapies and as a practical solution to the challenge of treating rare and ultra-rare diseases and to enable personalised therapies.

authors: Dr Beatrice Melinek and Professor Daniel Bracewell
Find out more

David Hodgson, Durham University
Scalable Preparation of Nucleoside Phosphates.

Nucleoside phosphates are the building blocks for the enzymatic synthesis of DNA and RNA, including modified mRNAs and associated cap structures. We are streamlining, upscaling and improving the robustness of existing routes towards nucleoside phosphates and also developing entirely new synthetic approaches. We use physicochemical approaches (e.g. kinetics, solubility control) and technology (e.g. flow chemistry) to improve the chemical steps.

We are also improving the throughput of purification through the use of new, off-the-shelf chromatography media. Here, a flavour of our work will be presented in the context of a ~1 g scale synthesis of a nucleoside diphosphate through simplified batch and flow methods. The chemical steps are scalable through flow technology and robust through the development of NMR-based analytical methods to ensure consistent concentrations of reagent and substrate.

Co-authors: Carlotta Pagli, Ian R. Baxendale.
Find out more

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Jiahao Huang, Nuclera
eProtein Discovery enables rapid protein access at your benchtop

Nuclera has launched the eProtein Discovery. It is the first and only benchtop system that within 24 hours in and end-to-end fashion discovers the best sequences and conditions to express, purify, scale, and manufacture custom protein reagents for drug discovery and synthetic biology applications. eProtein Discovery shrinks the laboratory (and thus carbon) footprint and dramatically reduces time-to-protein as a game-changing life science tool innovation that compresses and consolidates a key discovery workflow.

Find out more

Sara ten Have, Origin Peptides
Origin Peptides are a start-up biotech in Scotland based around a new method of making peptides.

Currently the method used for peptide manufacture is lengthy, has poor yields and uses a host of hazardous chemicals. It has a Product Manufacturing Intensity of 6000->20,000 (kgs of material needed to make 1Kg of peptide), and this results in 10s of millions of KGs of hazardous waste produced every year. Peptides are highly important medicines such as Insulin, and more recently Ozempic, as well as many others which treat HIV and hormonal pathologies. Our innovation eliminates all of the hazardous chemicals (aside from one which we recycle), and reduces the cost and time taken to produce peptides. This means peptide medicines could be more available, in cost and supply, and a greater variety will be viable to manufacture, all while benefitting the planet.

Find out more

Heather Walton, CPI
The Oligonucleotide Programme at CPI

A summary of the present projects underway at CPI and partners in the oligonucleotide space, and an examination of the remaining challenge areas which we see as targets for future work

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Daryl Williams, Oscar Mercado and Othman Almusaimi, Imperial College London

The slow developments in core drug delivery, manufacturing and purification technologies is hindering the growth of peptide therapeutics. Current synthesis pathways depend predominantly on the traditional Merrifield synthesis, often combined with solution-based coupling reactions, which overall has a poor environmental footprint with very limited greening of the process. Overall the oral delivery of peptides is still problematic- simple linear structures for example generally have poor enzymatic stability and poor oral absorption in the gut. New synthesis approaches for developing novel peptide structures with superior oral delivery or new therapeutic modes of operation are very few. So cyclic, bicyclic and peptide scaffolds for example are expensive or impossible to make. In addition, peptide industrial separation is usually accomplished with gradient elution reverse phase liquid chromatography (RPLC) , which uses significant amounts of organic solvents, usually acetonitrile (ACN). The process is often neither optimal nor very green.

This paper will introduce a new method for industrial peptide synthesis which allows therapeutic peptides to be synthesised entirely in the solid state- no hybrid synthesis. This approach can develop novel peptide structures not possible using traditional methods, including cyclic, bicyclic and peptide scaffolds, and examples will be shown of the peptides which can be produced. In addition a new SMART RPLC approach for peptide purification which can decrease peptide impurity levels and increase purity of primary peptide species by ~ 10-20% will be introduced. Imperial College is spinning out a new peptide technology company “ADVANCED PEPTIDE TECHNOLOGIES” to develop this family of new technologies.

Piers Gaffney, Exactmer

Exact Polyethers in Pharmaceuticals

Poly(ethylene glycols), PEGs, have been used as versatile biocompatible and hydrophilic modifiers and linkers for a range of pharmaceutical entities, e.g. drugs, lipids, proteins and oligonucleotides. If they were available in defined molecular weights, the derived APIs would have exact, as opposed to dispersed, physical and biological properties, much improving analysis and characterisation. Such precise properties will assist regulatory approval, minimise batch variation and may refine biological behaviour.

Exactmer is developing the scalable iterative synthesis of PEGs via stepwise chain extension with smaller defined PEG building blocks, currently up to 5 kDa, or 112 ethylene glycol units. As with other forms of iterative polymer synthesis, there are challenges in regard to achieving complete coupling, selective removal of temporary protecting groups, and release of the finished product. Additionally, for polyethers the harsh conditions of Williamson etherification present unique problems.

Learning from the experience of exact PEG synthesis, Exactmer has developed a novel range of side-chain functionalised polyether building blocks that can be assembled into defined sequence, multi-functional linkers. The resultant PEGabets are being tested as linkers for antibody drug conjugates (ADCs). These complex molecules present additional challenges over PEGs because the side-chains chemistries must remain orthogonal to the harsh steps used to construct them.

Find out more

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Glen Kemp, BioToolomics
Agarose Chromatography: New tricks for an old dog!

Biotoolomics develops and manufactures novel agarose based chromatography resins. Most 'off the shelf' resins were historically developed for protein purification. We believe the novel characteristics of next generation DNA/RNA/CGT products require new chromatography modalities specifically designed for these applications. Biotoolomics is developing a range of chromatography media to address rapid feedstock clean-up, increase yields and recoveries of active therapeutics. They will also improve process efficiency and enable the separation of ds/ssRNA or empty/full AAV capsids. These new media also have the potential to reduce process costs and decrease process environmental footprint. Because they are based on agarose bead technology they are GMP compliant, fully scalable and can be used with existing chromatography systems.

Find out more

Karen Trickett and Andrew Tobin, Keltic Pharma
Keltic Pharma - transforming drug discovery

Keltic Pharma works in drug discovery, targeting proteins implicated in malaria, severe asthma and Alzheimer's disease and are using their innovative PEP SMOL discovery platform to develop drugs against these target proteins.

Find out more