SSPC Research Ireland Centre for Pharmaceuticals

Biopharma Spotlight Part 2

Since the approval of the first monoclonal antibody Orthoclone OKT3 in 1986, our deepening understanding of these medicines combined with our ability to design and deliver them safely and efficaciously has positively impacts millions of lives worldwide. As our knowledge expands, so do the possibilities. New horizons for drug design, enhanced manufacturing techniques, and novel delivery methods are constantly emerging. Here at SSPC, our researchers are at the forefront of this revolution. Through our collective expertise and ability to drive multidisciplinary, collaborative research, we are making exciting discoveries that are shaping the future of medicine. This spotlight highlights just a few of the innovative projects where we're tackling challenges and driving innovation in the biopharmaceutical landscape.

The Stability of Proteins and their Chemically Modified Derivatives



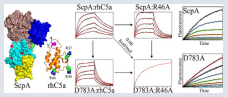
Associate Prof. Ioscani Jimenez del Val
Prof. Jennifer McManus
Dr Keith Fenlon (PhD)
University College Dublin

IgG1 molecules are the most widely used proteins in monoclonal antibody (mAb) therapy. Understanding how N-glycan composition and placement affect solution stability and inter-protein interactions informs future mAb formulation and glycan engineering. Protein PEGylation, a common strategy to enhance in vivo stability and half-life, was investigated for its impact on protein-protein interactions, solution behaviour, and viscosity – key factors in PEGylated biotherapeutic development. High-quality IgG1 material with intact Fc and Fab glycans was produced from CHO cells. Colloidal stability of native and glycoengineered IgG1 mAbs, as well as a model PEGylated biotherapeutic, was evaluated using liquid-liquid phase boundary measurements. Protein interactions were analysed by light scattering, and conformational stability by scanning fluorimetry. The effects of common excipients on mAb and PEGylated biotherapeutic stability were also assessed. This work advances understanding of how chemical modifications influence biotherapeutic stability and supports improved formulation strategies.

New Expression Systems for Biologics From Gram Positive Organisms – Recombine Production, Purification, and Characterisation of SpeB and ScpA


Prof. Jakki Cooney
Dr Todd Kagawa
University of Limerick

The research looked at developing a specific inhibitor for SpeB, a virulence factor produced by Streptococcus pyogenes implicated in tissue damage and destruction of host immune factors. The research has the potential to initiate the development of novel therapeutics for a wide range of diseases involving dysfunction of the immune system and sepsis. The PhD work contributed to a study on C5a peptidase from Streptococcus pyogenes (ScpA)which is a highly specific enzyme with potential therapeutic value. ScpA as a prototype for engineering therapeutic proteases that inactivate immunomodulatory proteins based on its high specificity for human complement C5a and C3a, along with the availability of methodologies for studying structure and now function of this enzyme.



Exosite binding modulates the specificity of the immunomodulatory enzyme ScpA, a C5a inactivating bacterial protease. Jain, M., Tecza, **M., Kagawa, T.F, Cooney, J.** *(2022) Computational and Structural Biotechnology Journal, 20, 4860-4869.*

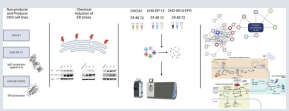
OptiViVax, Optimising a High Efficacy Vaccine for Plasmodium Vivax Malaria


Prof. Anne Moore
Dr Sonja Vucen
University College Cork

OPTIVIVAX

Plasmodium vivax is the most widespread human malaria-causing pathogen with 2.5 billion people living at risk in Africa, South America, Oceania, and Asia. OptiViVax, a newly created consortium across academia and industry, will build on exciting breakthroughs in malaria research to integrate state-of-the-art advances in parasite immunology, vaccine design, and innovative pre-clinical and clinical studies, to develop next-generation vaccines with increased efficacy against the P. vivax parasite. The OptiViVax consortium brings together academics, non-profits and industrial partners, with expertise in vaccine development, manufacturing, and clinical trials. Diversification of the portfolio of new antigens ready for clinical testing by reverse vaccinology will be enhanced, while also broadening their delivery by incorporating new platforms and adjuvants. These advancements will be achieved by leveraging sustainable and improved GMP bio-manufacturing know-how. In parallel, the efficacy of known leading antigens will be benchmarked for the first time using innovative design of clinical studies and CHMI models making these lead candidate vaccines ready for future field trials. Improved preclinical functional assays, using state-of-the-art transgenic parasite lines, will also allow for mechanisms of antibody-mediated protection to be deciphered. The availability of new functional assays and human challenge models will underpin the future framework for informed decision making by the clinical vaccine community, policy makers, funders and regulators. Two SSPC Funded Investigators Prof. Anne Moore and Dr Sonja Vucen are leading the development of thermostabilised forms of these new vaccines and defining pathways to GMP-based production in preparation for next-generation malaria vaccines.

Publication Highlight

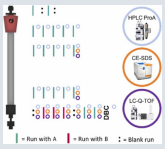


Label-free quantitative proteomics analysis of producer and non-producer Chinese Hamsters Ovary (CHO) cells under ER stress conditions. Ryan D, Sideri C, Efeoglu E, Henry M, **Meleady P.** *(2023) Current Research in Biotechnology, 10014.*

Multi-Product Resin Reuse for Biopharmaceutical Manufacturing


Prof. Sarah Hudson
Dr Stanislas Helle (PhD)
University of Limerick

The increasing need for early diagnosis of chronic diseases coupled with the ever-growing demand for monoclonal antibody based therapeutics has resulted in a global shortage of Protein A resin. Protein A resin is a critical material used almost universally in the purification of antibodies. There is no clear regulation on the practice of reusing protein A resins across multiple antibody processes. Without this flexibility, it is not possible to realise the full capacity and value of the resin, resulting in higher COGs and increased waste. This project used state of the art research instrumentation to explore the possibility and feasibility of reusing resins, making the production of antibody medicines, faster, cheaper and more sustainable.



Carryover analysis by liquid chromatography mass spectrometry in a multiproduct resin reuse context. Helle, S.| Santos da Silva, F.V.| McAvinue, J.| Coffey, L.| Arthur, A.| Cawley, J.| Brophy, M.| O'Neill, A.| Sheehy, M.| Kelly, R.M.| Ahern, T.| Osborne, M.D.| Horgan, C.P.| Foley, D.| Hayes, R.| Monaghan, D.| O'Brien, P.| Mahon, J.| **Hudson, S.** *(2024) Process Biochemistry, 156, 547-559.*

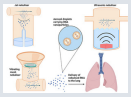
Meet the SSPC Researchers

Professor Abina Crean
Professor Anne Moore
Professor Andrew Kellett
Professor Lidia Tajber
Professor Brendan Griffin
Professor Damien Thompson
Professor Sarah Hudson
Professor Jakki Cooney
Associate Prof. Ioscani Jimenez del Val
Associate Prof. Emmet O'Reilly
Associate Prof. Steven Ferguson
Associate Prof. Constantina Papatriantafyllopoulou
Associate Prof. Jessica Whelan
Associate Prof. Luis Padrela
Associate Prof. Joanna McGouran
Associate Prof. Paula Meleady
Dr Marco Monopoli
Dr Sonja Vucen
Dr Katie Ryan

Interrogating the Processing and Formulation of Biologicals Using Novel Techniques to Ensure Safe and Efficacious Medicines

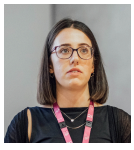

Dr Katie Ryan
Michael Neary (PhD)
University College Cork

The aim of this study is to support the advancement of novel processing techniques such as microfluidics and 3D printing as effective methods to produce efficacious RNA formulations and contribute towards the growth of the current repertoire of processing techniques which are used in the production of RNA-containing medicines. It Investigates the associated process parameters with each processing technique, their impact and optimisation for producing adequately stable and efficacious RNA formulations and examines the impact of formulation parameters on RNA delivery systems e.g., lipid vs polymer vs hybrid-based nanoparticles, PEGylation, etc to produce formulations with desirable critical quality attributes (CQAs).



Nebulised delivery of RNA formulations to the lungs: From aerosol to cytosol. Michael T. Neary| Lianne M. Mulder| Piotr S. Kowalski| Ronan MacLoughlin| **Abina M. Crean**| **Katie B. Ryan**. *(2024) Journal of Controlled Release, 366, 812-833.*

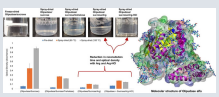
Next Generation Pharmaceutical Processing: A Systematic Approach to Formulating and Manufacturing both Pharmaceutical and Biopharmaceuticals with Enhanced Particle Properties for Alternative Delivery Applications

Assoc. Prof. Emmet O'Reilly
Dr Laura Foley (PhD)
University of Limerick

Biologic therapies are traditionally administered via intravenous (IV) injections or infusions, often limiting patient compliance and accessibility. This work explores the potential of pulmonary delivery as an alternative route for administering biologic therapeutics, aiming to overcome the challenges of systemic administration. The study focuses on optimizing spray drying processes for both large and small molecule therapeutics, with the goal of developing a robust process for delivering inhalable dry powder formulations suitable for local or systemic delivery via the lungs. This approach promises to offer improved therapeutic outcomes, reduced systemic side effects, and enhanced patient compliance through a non-invasive and convenient delivery route.

Further Publication highlights



On the role of excipients in biopharmaceuticals manufacture: Modelling-guided formulation identifies the protective effect of arginine hydrochloride excipient on spray-dried Olipudase alfa recombinant protein. Sharma, A.**| Cazade, P.| Khamar, D. |** Hayden, A.| **Thompson, D.|** Hughes, H. *(2024), International Journal of Pharmaceutics, 5 (662), 124466.*

Developing an in vitro lipolysis model for real-time analysis of drug concentrations during digestion of lipid-based formulations. Ejskjær, L.| O'Dwyer, P.J.| Ryan, C.D.| Holm, R.| Kuentz, M.| Box, K.J.**| Griffin, B.T.** *(2024) European Journal of Pharmaceutical Sciences, 194, 106681.*

Process control and design of drying technologies for biopharmaceuticals – A review. Brytan, W.| Amorim, R.| **Padrela, L.** *(2024) Powder Technology, 449, 120395.*