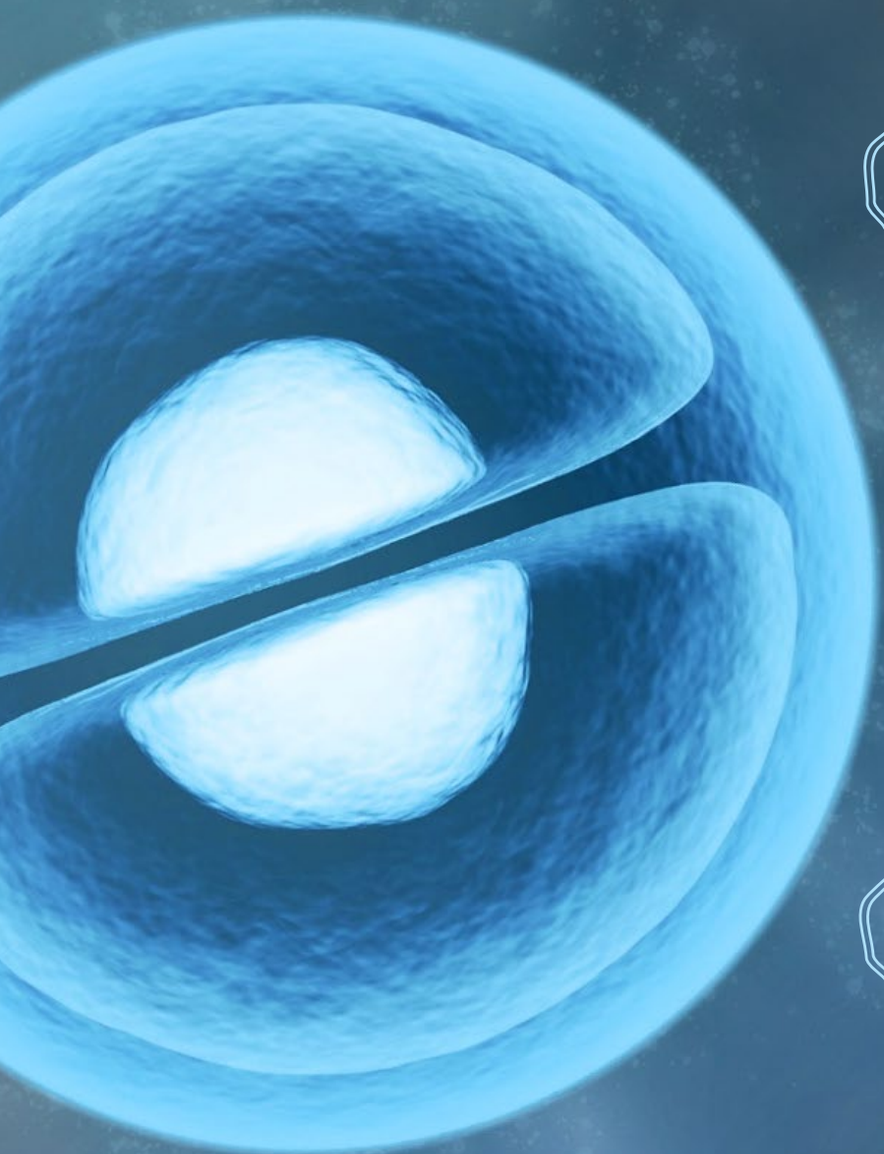
CELLSERIES

Cell Culture & Bioprocessing | Stem Cell & Regenerative Medicine | Cell & Gene Therapy | Biobanking

Pre-Event Newsletter Sept 2018



NOVOTEL LONDON WEST

25 - 26 OCTOBER 2018 | LONDON, UK

OXFORD GLOBAL CONFERENCES

Contents

This is an Interactive Newsletter.
You can click on elements such as website links or the contents below.

Meet the Team

Hayley Watson
Portfolio and Client Engagement Director

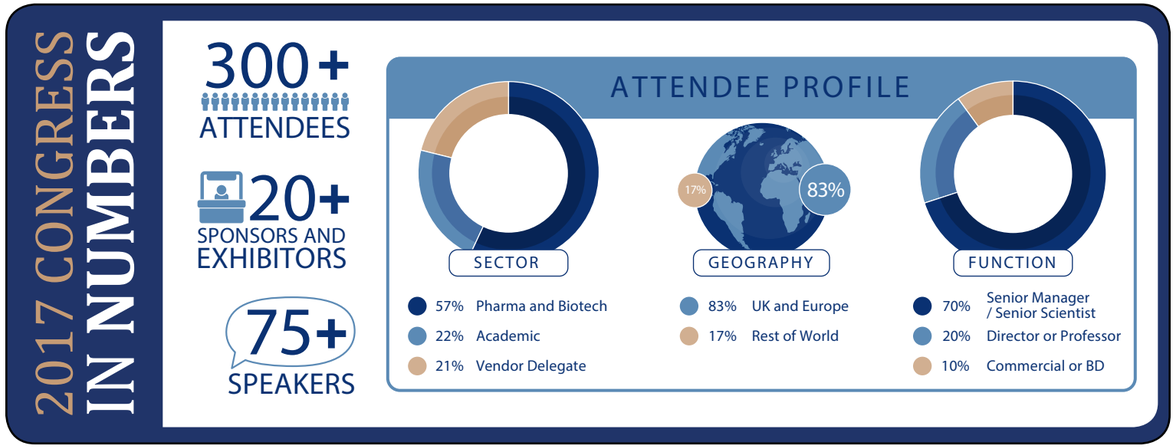
Lydia Millet
Head of Business Operations & HR

Jess Thomson
Senior Producer and Team Leader

Guillaume Alonso
Marketing & CRM Manager

Howard Clements
Project Manager

TEAM MEMBERS:
Account Managers - Henry Whitehouse, Jamie Morris
Junior Conference Producers - Ryan Leahy, Tom Cashman
Sponsorship Portfolio Manager - Tim Richters
Sponsorship Account Manager - Aaron Copestake



WELCOME TO OXFORD GLOBAL'S CELL SERIES PRE-EVENT NEWSLETTER!

With Oxford Global's 2018 Cell Series taking place in October in London, I am delighted to bring you news of key features & exciting additions for this years congress.

The 2017 congress proved incredibly popular, bringing together over 300 attendees in London to discuss collaborative solutions, challenges and the latest developments within the Cell Culture, Bioprocessing, Cell & Gene Therapy and Stem Cell field. The feedback concerning the high-level talks and seniority & diversity of the attendees was overwhelmingly positive.

Building on the exciting talks and extensive networking opportunities from 2017, this year's congress will feature the addition of the Biobanking programme, offering attendees the opportunity to benefit from four co-located programmes, each with an impressive line-up of industry leading speakers and examining hot topics areas within Cell Culture, Bioprocessing, Cell & Gene Therapy, Stem Cell and Biobanking.

For 2018, there will be even further opportunity to learn from and knowledge with your peers through the addition of panel discussions and dedicated roundtable discussions across all four programmes fuelling an interactive and lively environment.

If that wasn't enough, this year will also see the addition of the Cell Series Dinner, taking place after the first day of the congress and offering attendees a chance to relax and unwind with a complimentary dinner and a glass of wine (or two) on us!

Welcoming over 350 attendees, the 2018 co-located programmes will feature 100+ presentations on key topics including;

Cell Culture & Bioprocessing: Shaping the cell culture and bioprocessing field, such as 3D Cell Culture applications, technologies and innovations, cost effective processing methods, high yield cell lines and novel large scale production tools and technologies.

Cell & Gene Therapy: case studies on commercialising CAR T Cell Therapy, successful cell and gene therapy development and effective technologies for bioprocessing and manufacturing.

Stem Cell: Addresses key challenges in stem cell bioprocessing, development, and clinical trials, as well as the current advances in cell based therapies for regenerative medicine, iPSC characterisation, technologies in stem cell drug discovery and development

Biobanking: Explore key insights into biosample management, standards and quality management, as well as future advances in mobile bio-banking and digital sample management. Discover collaborative solutions to managing biospecimens and their role in biomarker translational development through dedicated sessions on biomarker-driven clinical trials and precision medicine.

Read on for a range of interesting interviews and insights with some of our industry-leading speakers and participating sponsors, and I look forward to welcoming you to the 2018 Congress!

- Hayley Watson, Portfolio Director

CELL SERIES

4 EVENTS IN 1

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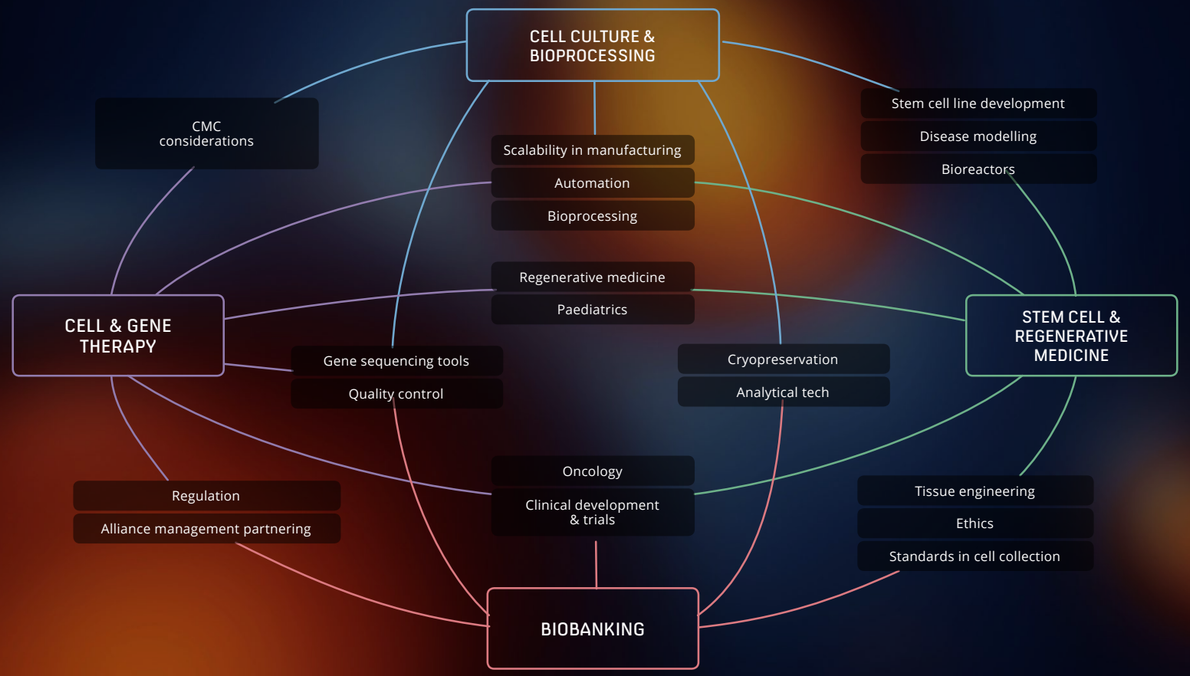

WHO IS ATTENDING?

For the full attendee list please contact
marketing@oxfordglobal.co.uk

- **400+ senior level delegates** representing global pharmaceutical organisations, leading biotech companies and internationally renowned academic institutions.
- **Directors, VPs, CEOs and Heads** working in bioprocessing, cell line engineering, CAR T-Cell therapy, manufacturing, gene therapy development, stem cell technologies, regenerative medicine and biobanking.

These companies and many more:

UCL, Merck, Biogen, Kite, Catapult Cell and Gene Therapy, UCB, Bayer, Boehringer Ingelheim, GlaxoSmithKline, The University of Edinburgh, Sanofi

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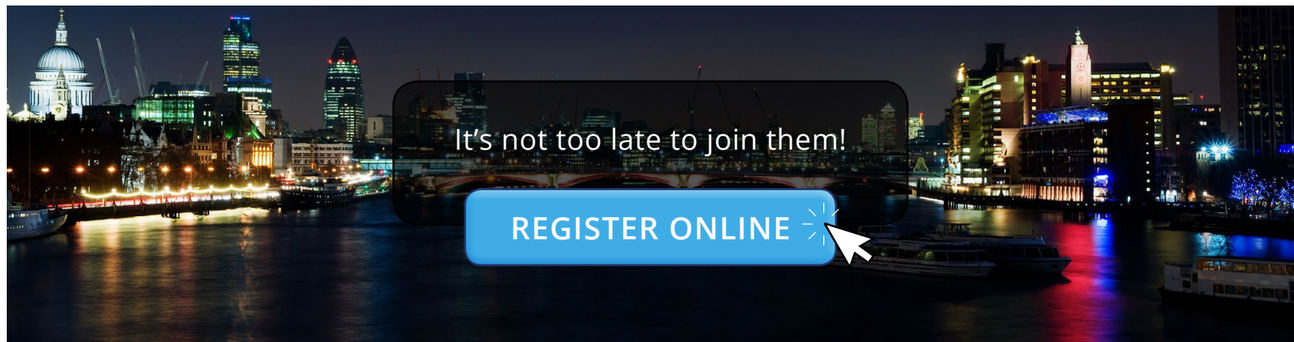


CELL ENGINEERING: PROVIDING AGILITY IN NAVIGATING THE PATH TO THE CLINIC

JESSICA CARMEN

Jessica Carmen, PhD
Director of Strategic Marketing for Cellular Therapy
MaxCyte, Inc.

Dr Carmen is the Director of Strategic Marketing for Cellular Therapy at MaxCyte, Inc. MaxCyte is driving the next generation of cell-based medicines with its best in-class cell modification technology which is used in the discovery, development, and manufacture of small molecule, biologic, and cell-based medicines. She is responsible for the growth of partnerships with key opinion leaders and developers of ex vivo-modified cellular therapies.

May we live in interesting times: 2017 and 2018 have been historic years with the approval of the first CAR-T therapy and an explosion of immunotherapeutic clinical trials. More than ever, time-to-market is a critical factor for companies' success in this fiercely competitive landscape.

A therapeutic developer's ability to foresee and skillfully navigate challenges while mitigating risk is key to rapidly bringing their therapy to market. Incorporating technologies early in the process that allow the agility to circumnavigate challenges and to integrate late-breaking scientific discoveries can play a significant role in the therapeutic efficacy of the product as well as time to market. This strategy only works if the technologies provide a foundation of high performance and clinical suitability.

Whether it's overcoming manufacturing challenges, toxicity limitations or attaining improved efficacy, MaxCyte's non-viral technology for cell engineering has proven to enable companies to develop novel, highly efficacious therapies that rapidly progress to the clinic. It provides the ability to safely and reproducibly modify primary cells with high efficiency, low cytotoxicity, and at the scale required to treat patients. MaxCyte currently has over 50 partnered clinical programs and is being used within 15+ clinical trials. Several real-world case studies are presented below:

Overcoming Viral Vector Toxicity: Rapidly Advancing an HIV Gene Editing Therapy to Clinical Trial

HIV infection is currently managed by lifelong antiretroviral therapy (ART), a modality that is associated with chronic toxicity, challenging patient compliance, and comes at a significant financial burden over a patient's lifetime. Numerous clinical and preclinical studies have demonstrated that blocking or mutating CCR5, an R5-tropic HIV-1 coreceptor, can render cells resistant to HIV-1 infection. CCR5 gene editing of hematopoietic stem cells (HSCs) has the potential to produce multiple lineages of HIV-1-resistant immune cells throughout a patient's lifespan offering hope of a single dose therapeutic alternative to ART.

ZFN-mediated disruption of CCR5 in adult CD34+ cells was developed using viral vectors and showed promise in a clinical setting. Unfortunately, cytotoxicity of the adenoviral vector prevented its use in the intended clinical trial.

The therapeutic developer turned to MaxCyte's non-viral, regulatory-compliant cell engineering technology in an effort to rapidly return the therapy to the clinic. Upon migration from viral transduction to transient ZFN expression via MaxCyte mRNA electroporation, bi-allelic gene disruption rates of 73% and HSC viability of >90% were reached at manufacturing-scale without impacting lineage potential or exhibiting tumorigenicity in *in vivo* studies.[1]

The high frequency gene editing efficiency, manufacturability, reproducibility, and general safety demonstrated in the preclinical IND-enabling studies using the MaxCyte GT® rapidly enabled the developers to initiate a clinical trial in HIV-1 patients to assess its feasibility and safety (Clinical Trial #: NCT02500849).

Next-Generation NK CAR Therapies: Bolstering Efficacy & Streamlining Manufacturing

NK cells represent a promising avenue for cell therapy as they: *i).* rapidly kill tumors in an antigen-independent fashion; *ii).* represent an allogeneic source of cells for improved safety and ease of manufacturing; and *iii).* have proven clinically safe upon transfer of unmodified autologous or allogeneic cells with modest anti-tumor efficacy. Researchers have looked to NK cell engineering to improve anti-tumor efficacy.

MaxCyte's high-performance NK cell engineering and clinical feasibility have allowed researchers to harness the power of this unique cell type and rapidly advance a next-generation, NK cell-based anti-CD19 CAR therapy to the clinic.

Researchers observed 82% efficiency and high NK cell viability following large-scale electroporation with mRNA encoding an anti-CD19 CAR using the MaxCyte GT®.[2] These engineered NK cells exhibited augmented cytotoxicity in an *in vivo* model of acute lymphoblastic leukemia. Importantly, the non-viral nature of the technology reduced patient-specific manufacturing time by a week, as well as eliminated the need for GMP bioproduction and safety testing of viruses, ultimately speeding the path to clinic (NCT01914479).

Viral & Non-viral Engineering Approaches Are Not Mutually Exclusive

MaxCyte offers a non-viral approach for cell engineering positioned to rapidly bring efficacious cell and gene therapies to the market. Viral and non-viral engineering, however, are not mutually exclusive. In fact, there are a growing number of products being evaluated in clinical trials which employ both viral and non-viral methods of cellular engineering. Most commonly these include the stable integration of CAR or TCR molecules via lentiviral transduction as well as the transient transfection of mRNA-based CRISPR/Cas9 systems for fine tuning of the cellular response in the tumor environment. Together, viral and non-viral delivery methods are enabling therapeutic developers to realize more complex levels of cellular engineering in order to achieve the appropriate, robust response in patients that is needed to address unmet medical needs.

> *"For companies contemplating whether it's the right time to add non-viral approaches to their pipeline products, I would say that it's a smart idea. We've seen the first wave of virus-based products come to market, but I think there will be a transition to non-viral approaches within 5–10 years."*
> - Jessica Carmen

Alternatively, viral vector production typically requires transfection of a virus-producing cell line. Many contract manufacturing organizations (CMOs) are booking 18 months out or longer for viral vector bioproduction. MaxCyte's electroporation-based technology enables in-house, clinical-scale transfection of virus-producing cell lines for high-titer, GMP-compliant manufacturing of viral vectors. This provides an alternative manufacturing method to companies who are dedicated to using viruses and may be struggling to secure a manufacturing slot ■

Jessica's will be expanding on this topic in her presentation '*Enhancing Efficacy Of T- And NK-Cell Therapeutics With Non-Viral Cell Engineering*', on Day One of our 4th Annual Cell & Gene Therapy Congress

References

1. Preclinical development and qualification of ZFN-mediated CCR5 disruption in human hematopoietic stem/progenitor cells. (2016) *Mol Ther — Methods & Clinical Development*, 3, 16067.

2. Clinical scale zinc finger nuclease-mediated gene editing of PD-1 in tumor infiltrating lymphocytes for the treatment of metastatic melanoma. (2015) *Mol Ther* 23(8): 1380-1390.

AN INTERVIEW WITH **STEFAN PRZYBORSKI**

Stefan Przyborski, Professor of Cell Technology, Durham University; Chief Scientific Officer, ReproCELL Europe

Professor Przyborski holds an academic position as Professor in Cell Technology at Durham University. He has over 25 years experience in cell biology with specific interests in cell culture technology, neuroscience and stem cell research. In recent years he has developed a multi-disciplinary approach through collaborative projects with physical scientists to develop novel ways of solving biological problems. He has formed alliances with pharmaceutical and biotech companies, has published over 100 scientific papers and has filed several patents. He is also the founder and Chief Scientific Officer of Reinnervate (now part of ReproCELL Europe), a biotechnology company founded in 2002 as a spinout from Durham University UK

Which area of research do you think has most benefitted from 3D cell culture?

The concept of 3D cell culture is not new and has been around for over a century. What has changed more recently is the ease of access to new innovative technologies on the market that enable researchers to more readily practice 3D cell culture [...] There is no single solution and researchers must select the technology most appropriate for their needs to address the scientific questions that are interested in. In answer to this question, 3D culture has had impact in multiple areas in basic academic research, drug screening, and safety assessment. Certainly 3D culture has developed in the area of oncology and maintenance of 3D spheroid micro-tissues; it has also benefitted drug toxicology studies and the production of liver spherioids; the formation of tissue constructs such as skin equivalents for assessment of chemicals; and there are many other examples. New areas are also emerging such as personalized medicine and the maintenance of tissues ex vivo within a 3D format.

What do you see as the greatest hurdle to 3D cell culture? What can be done to address this?

Many researchers are 'comfortable' with the current practice of conventional 2D cell culture, which is routine, easy to perform, and relatively inexpensive. Also many in vitro and biochemical assays have been developed around the 2D cell culture platform [...] 3D culture is more challenging, often more expensive, and requires change of current practice. This can often be perceived as a hurdle to adoption of new technology, even though the benefits of 3D are clear [...] Many pioneering researchers have now tested 3D culture methods for their purposes and have published the benefits. Slowly others begin to follow and we are now seeing more researchers benefitting from using 3D culture technologies. The greatest endorsement of such technologies is their adoption and use by others, through publications and presentations of new data and findings.

How close to in vivo do you think it is possible to get with 3D culture?

I see the concept of 3D culture to improve the structure and function of cells and enable the formation of tissue-like structure in vitro. To reproduce the conditions in vivo requires many other factors such as oxygen control, perfusion, growth factors, cytokines, hormones, mechanical stiffness, etc. the list goes on. Today we are applying technology to improve current practice, to make incremental advances over existing models, to enable greater insight into biological processes. As technology advances, we will further improve our cell culture models, edging closer to in vivo conditions, but we must always remember that it is a model we are studying in the lab and not real tissue. There will always be limitations and it is important to recognize these and take them into account.

How is 3D culture currently being used in drug discovery? Do you think that 3D cell culture could lead towards more personalized methods of treatment in the near future?

3D culture does already have a place in drug discovery. As time passes more companies will adopt the technology. There remain issues concerning high throughput analysis and application of current assay/imaging techniques. Again more technology development is required to overcome these issues. Slowly adoption is happening as companies realize the benefit of data generated from cells growing in 3D versus 2D [...] We are already seeing the concept of growing cells in 3D and tissue fragments ex vivo for testing various drug combinations prior to determining the most appropriate drug dose/combination. This will have a big impact on personalized medicine

Where do you see 3D cell culture leading us in the next few years?

These advances will continue to enable biomedical researchers to recreate the structure and function of human tissues in the lab for research, screening and safety assessment. This technology combined with human stem cell science will open new opportunities for tissue engineering in the lab where renewable sources of human cells can be generated to create robust and reproducible 3D models of human tissues ■

Stefan Przyborski will be presenting on Day Two of the 7th Annual Cell Culture & Bioprocessing Congress with his talk *'Development And Application Of Bioengineered Models Of Human Tissues In Vitro'*

A MICROFLUIDIC PLATFORM FOR PERSONALISED ONCOLOGY
MICHELE ZAGNONI

Dr Michele Zagnoni,
Senior Lecturer, Electronic and Electrical Engineering,
University of Strathclyde, Glasgow

Dr Michele Zagnoni leads a multidisciplinary research group focussed on the development of microfluidic technologies for healthcare applications, including fundamental biological research, drug screening, personalized medicine therapy, organ-on-a-chip and synthetic biology (www.zagnonilab.com). Recently, he became the Chief Scientific Officer of ScreenIn3D (www.screenin3d.com)

Microfluidic technologies facilitate personalised oncology by enabling patient-derived tissue to be tested prior to treatment using biopsy-derived spheroid cancer models

High-attrition rates during development of new cancer therapies persist despite several $BN investments are made per compound for discovery and validation of new anticancer molecules. Failure to translate promising preclinical drug candidates into clinical success exposes the limitations of our current drug discovery approaches, due in part to the lack of robust preclinical ex vivo models. Within this context, microfluidic and lab-on-a-chip technologies facilitate handling of small volumes of fluid containing chemicals and cell material and, therefore, have emerged as potentially highly relevant tools in cancer research.

Traditionally, drug discovery has relied upon 2D cell monolayer models, 3D clonogenic assays and small animal models, mostly utilizing cancer cell lines that do not recapitulate the complexity of in vivo tumours. It is now accepted that such preclinical models poorly predict clinical response. Therefore, development of more predictive, patient-specific models of human cancer are required for profiling novel anticancer drugs, as well as reconsider existing compounds in combinatorial studies. Additionally, technological advances in high-throughput and content phenotypic screening and 3D cell culture techniques provide new solutions for reshaping several key processes during drug discovery and development.

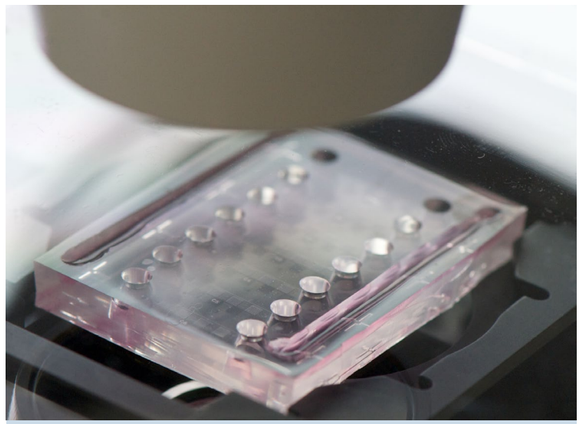


Figure 1.
Microfluidic platform for spheroid drug screening

The unique combination of microfluidic and lab-on-a-chip technologies with physiologically relevant tumour models, based on 3D spheroids derived from primary human tissue, enables drug testing to be personalised. The ability to micro size drug-cell interactions will allow pharmaceutical and biotech companies do 100-fold more testing for the same money spent, increase productivity and access multiple readouts, concurrently.

We have developed a microfluidic, large-throughput 3D ex-vivo system which provides a robust, customisable and cost-effective screening platform (Figure 1). The novel characteristics of this platform enable rapid decision making to prioritize the most promising drug candidates, as well as biomarkers and drug combination strategies for preclinical drug discovery and development. An advantage of the platform is the ability of cells to form a spheroid without the presence of exogenously added scaffolds.

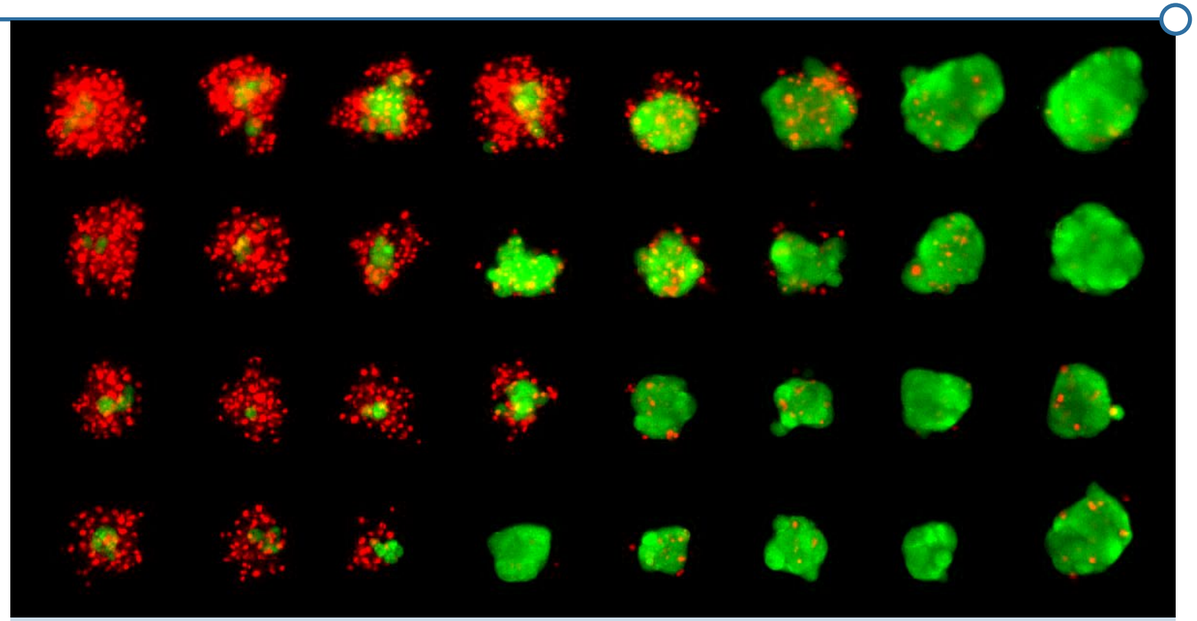


Figure 2.
Image of cancer spheroid responses (live/dead) exposed to a microfluidic concentration gradient of a compound

Thus, spheroids are formed using the endogenously produced extracellular matrices. This, together with the precise control of convective and diffusive mass transport, enables formation of human tissue derived spheroids in less than 3 days. Moreover, the system enables long-term culture as well as fractionated chemo- and targeted-therapy to study drug efficacy, as well as acquired drug resistance.

> *"Our microfluidic platform offers users the ability to reduce and replace animal models in cancer research and is targeted at improving anticancer drug treatment and accelerating development of new personalised medicine solutions using patient derived tissue."* - Michele Zagnoni

The platform has been validated by assessing spheroid formation and the efficacy of standard of care compounds against multiple cancer types including glioblastoma, prostate, ovarian, lung and pancreatic cancers. The platform, together with dedicated imaging software, provides multiparametric label-free and end-point measurements that include viability measurement (Figure 2), changes in spheroid size and shape, immunohistochemistry and assessment of the temporal evolution of spheroid response post drug treatment. Conveniently, the system also allows researchers to retrieve spheroids for proteomics and biomarker analysis post treatment. We are in the process of developing new models (aimed at immunotherapy testing and neuroscience).

Among other 3D ex vivo platforms available, our system provides a versatile tool well suited for cancer drug testing, particularly in the early development and profiling of a broad spectrum of molecules including small and targeted molecules, as well as facilitating development of personalised treatment. The technology has a variety of academic applications, as well as finding a commercial application with the provision of screening services via the University of Strathclyde spin out ScreenIn3D (www.screenin3d.com), commercialised through AMS Biotechnology (Europe) Ltd (AMSBIO) ■

Dr Michele Zagnoni will be presenting on Day Two of the 7th Annual Cell Culture & Bioprocessing Congress with his talk *'A Microfluidic HTS Platform For 3D Oncology'*

COMPUTATIONAL MODELLING AIMS TO PREDICT CELL CULTURE STRATEGIES FOR OPTIMISING GLYCOSYLATION

CLEO KONTORAVDI

Cleo Kontoravdi,
Senior Lecturer,
Imperial College London

Dr Cleo Kontoravdi leads an interdisciplinary group working in the area of Biological Systems Engineering. The group is well known for the development of predictive models for the analysis and optimisation of biological processes involving the culture of cells for the production of therapeutic proteins and other high-value compounds. A unique feature of her research is the integration of engineering principles with biology and biochemistry through mathematical modelling but firmly supported by targeted experiments.

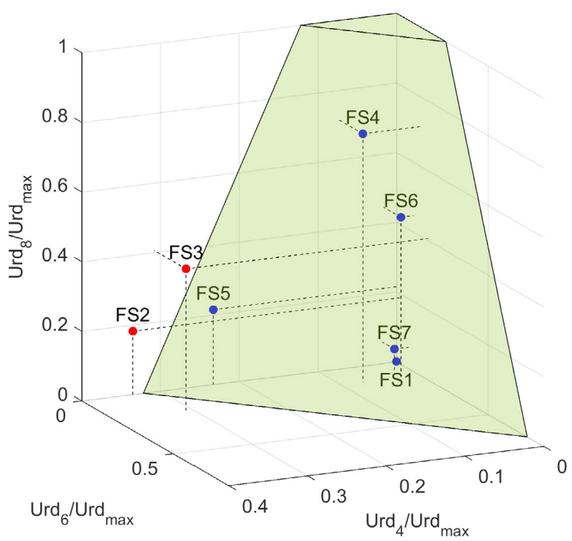
Glycosylation of therapeutic proteins can affect their efficacy and stability, so predicting culture strategies that optimise glycosylation could accelerate process development.

The Kontoravdi group from Imperial College London and the Klymenko group from the University of Surrey worked with MedImmune on building a modelling framework to design optimal cell culture conditions for desired antibody galactosylation.

What methods did we use?

We used a previously developed mathematical model that describes the impact of feeding galactose and uridine to cell culture processes on cell growth, antibody productivity and extent of galactosylation. We also applied a new computational method called constrained global sensitivity analysis.

We used these methods together to design cell culture experiments that we anticipated would give rise to higher-quality antibody without being detrimental on cell growth or antibody titre. We had a minimum threshold for both titre and galactosylation that we wanted our cultures to achieve.



Our method identified a subset of 556 out of the 8192 designs that should, according to the model, result in protein with the desired characteristics. We then tested 4 designs and a control experimentally, and compared the experimental results to the model predictions for each set of conditions (Figure 1). We also tested 2 designs that would fail to achieve the constrained targets, as proposed by the model.

What were our main findings?

That the model could successfully describe the culture conditions to achieve protein production with the desired characteristics! The model could predict the viable cell density of cell cultures over time, the concentration of monoclonal antibodies and the glycosylation pattern at the end of culture.

Moreover, the model proved capable of identifying the correct designs that could and that could not lead to the desired product. Hence, following the paradigm of Quality by Design (QbD) the mathematical model is considered capable of identifying the appropriate Design Space.

The proposed concept of use, could reduce the expenses and the time needed for research and development of new biopharmaceutical products or already existing therapeutics ■

Cleo Kontoravdi will be presenting on Day Two of the 7th Annual Cell Culture & Bioprocessing Congress with her talk *'Effect Of Culture Scale And Temperature On The Profi le And Clearance Of HCP Impurities In Antibody-Producing CHO Cell Processes'*

VISICORT - A CASE STUDY IN CELL THERAPY TRANSPORTS

PEADAR MAC GABHANN

Each transport of cell therapy products requires in-depth, case-by-case analysis & validation. This is very difficult to anticipate and plan in our rapidly changing world.

Corneal disease is a leading cause of blindness worldwide & affects all genders & age groups. There are >100,000 corneal transplants performed annually. Unfortunately, 20-30% of transplants fail within five years & 40-60% within ten years. VISICORT is an EU FP7 project researching ways to improve the success rate of Corneal Transplantation. Biostór Ireland, a lead partner in the consortium, was tasked with biospecimen management and transport. To date we have performed >195 VISICORT cold-chain transports from clinical trial sites in Germany, Denmark, France, UK and Ireland. In addition, we have created a Foundation biobank of >50,000 biospecimens for future research in eye diseases.

VISICORT is developing a cell therapy to activate the immune system in order to reduce the risk of acute rejection of corneal re-transplants. The clinical trial will establish the safety and tolerability of two IV infusions of allogeneic human bone marrow-derived mesenchymal stromal cells (BM-MSC) and evaluate the potential efficacy of pre-transplant intravenous infusions of allogenic-BM-MSC on high-risk corneal transplantation patients. Seven cell therapy transports are planned between the Centre for Cell Manufacturing Ireland (CCMI) in Galway and the clinical trial site in Charite Hospital, Berlin.

As with all EU-funded projects, estimated budget requirements were submitted with the project proposal in 2012. Six years later the reality is very different as are the transport costs. One major issue that has significantly impacted road transport of human cell products for human application is the current European Refugee Crisis which started in 2015 when increasing numbers of people began arriving in the European Union (EU), from across the Mediterranean Sea and overland through Southeast Europe. To stem illegal immigration routine X-Ray of trucks was introduced at ports.

An LN2 Cryoshipper can be efficiently transported from Biostór Ireland in Rosslare to the Charite Hospital in Berlin, Germany across the UK land bridge in 3 days, well within the 12-day validated window and at a relatively low cost of €400. However, since the advent of the Refugee Crisis, all trucks travelling between the UK port of Dover and the French port of Calais are now subject to X-ray. As you can appreciate, it is nearly impossible to coordinate a transport of cells between the UK and French customs from the island of Ireland, add to that the likeliness that the driver is not fluent in either language and may not understand the special requirements of the cargo s/he is transporting. So, in the future, road transport of human cells for human applications from Ireland to EU countries can no longer be considered. The alternative, air shipment is highly efficient with next day delivery. However, it includes more third-party handling and is 4-5 times more expensive. To avoid X-ray transport scans, Biostór was required to become a "Known Consigner" with the Irish Aviation Authority (IAA) – a detailed systematic process involving: police vetting, extensive training and training validation in airline security, followed by a comprehensive, on-site audit of security procedures with associated costs that were not included in the VISICORT budget.

Peadar Mac Gabhann,
Managing Director,
Biostór Ireland

Peadar Mac Gabhann graduated from the National University of Ireland, Dublin with a M.Sc. in Industrial Microbiology. He carried out post graduate research at the Netherlands Cancer Institute (NKI) Amsterdam, Biogen at ETH Zurich and the Faculty of Medicine at Kyoto University Japan. He joined Schering Plough Corporation as a key member of staff in the start-up of the first, world-wide Biopharma facility in Cork to produce Interferon in 1983. As Director/board member of Schering Plough Japan, he led the company's research and Asian business development. Peadar has >30 years' experience in the international pharmaceutical industry. In the past 10 years, he co-founded and directed two Life Science start-ups and participated in several international EU FP7 projects: He is a regular presenter at international events & presented a position paper on "Biobanks - Key Resources for Advancement of Biotechnology & Human Health" to the expert group of the EU Parliament on the Future of Medicine.

Currently he consults with Jacobs Engineering on the design/construction of major Biopharma facilities throughout Europe, he lectures in Pharmaceutical Business at Griffith College Dublin as well as running a certified Tissue Establishment in Wexford, Biostór Ireland.

What's next to impact cell transports from Ireland? With the BREXIT March 2019 deadline looming one wonders what customs issues will impact the ports between Ireland, the UK, and the EU to further complicate the transportation of products in our fledgling Cell Therapy logistics business. It is estimated that borders will require 10 times more customs staff than they currently have in order to process the endless paperwork needed to enter the EU from a Third Country: an export declaration, an ATA Carnet from customs officers, invoices for products they are hauling, insurance certificates and a transport permit for each EU country they will drive through etc. etc.

For a glimpse of what border trade between a Third Country and the EU could look like post-Brexit see Turkey's northern border with Bulgaria, one of the busiest crossings in Europe and a good example of how bad things can become. On a good day, a 5km line of trucks crawls along the highway towards the border. On a normal day, there is a 7-8km line of trucks. The record is 18km and it can take up to 30 hours to get through. For the highly-regulated life science industry BREXIT has the potential to become catastrophic resulting in added administrative requirements, uncertainty over duties, extra databases, additional security checks, listings and rules of origin procedures, And it doesn't appear that any country has started to put the infrastructure and the trained personnel in place to deal with this pending bureaucratic nightmare which is only 6 months away ■

This project has received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement no. 602470.

Peadar Mac Gabhann will be presenting at the Cell Series with his talk *'VISICORT – A Case Study In Management Of A Multi-Centre Clinical Study In Corneal Transplantation'*

IN-HOUSE RAPID MYCOPLASMA TEST QUALIFICATION PROVIDES A COST-EFFECTIVE, QUICK TURNAROUND SOLUTION FOR CELL THERAPY PRODUCT RELEASE TESTING

BRANDY SARGENT

The strategy of qualifying a commercially available, in-house, rapid mycoplasma test enables cost-effective and timely in-process and final release testing solution

Brandy Sargent,
Editor in-chief,
The Cell Culture Dish and
The Downstream Column

Brandy Sargent is the Editor in-chief and frequent author of *The Cell Culture Dish* and *The Downstream Column*, She has worked in the biotechnology industry for over eighteen years, first in corporate communications and public relations, then in technical sales and marketing, and most recently as a writer and publisher. She strives to introduce topics that are interesting, thought provoking, and possible starting points for discussion by the biomanufacturing community. She has been fascinated by the different applications of biotechnology since she first started working in the industry and continues to be fascinated as her experience and exposure has grown. Brandy shares her enthusiasm by authoring scientific articles and she enjoys watching the industry evolve and thrive.

Cell therapy products have unique manufacturing requirements that necessitate the development of new processes and technologies to support manufacturing. Like other biologics, most cell therapies require microbial testing including, mycoplasma, sterility, and endotoxin analysis prior to final product release. Since the cells are the final product, they cannot be put through a sterile filtration step or undergo a harsh sterilization step. Both of these options would harm cells and thus negatively impact the product itself. As a result, in-process and final product microbial testing is a critical part of meeting the stringent regulatory requirements for cell therapy products. Traditional testing methods for mycoplasma, sterility and endotoxin can take several weeks to over a month, which doesn't fit the needs of the quick turnaround time for cell therapies. This is why rapid microbial methods, including rapid mycoplasma tests, provide an important solution to a significant challenge in cell therapy manufacturing.

In a recently published paper titled, "Strategy for an Abbreviated In-House Qualification of a Commercially Available Rapid Microbiology Method (RMM) for Canadian Regulatory Approval" (*Cytotherapy* December 2017), authors present a timely and cost effective solution to the challenge for in-process and final product release mycoplasma testing of their investigational cell therapy product, an autologous mesenchymal stromal cell therapy product under review for treatment of patients with knee osteoarthritis.

The authors worked with Health Canada to create an abbreviated qualification plan for use of Roche CustomBiotech's MycoTOOL PCR Mycoplasma Detection Kit for in-process and final product release mycoplasma contamination testing. According to the European Pharmacopoeia (EP), chapter 2.6.7, it is stated, "…Where commercial kits are used for part or all of the analytical procedure, documented validation points already covered by the kit manufacturer can replace validation by the user. Nevertheless, the performance of the kit with respect to its intended use has to be demonstrated by the user…". By incorporating the supplier's kit validation information, based on the validation requirements of the EP 2.6.7 in the subchapter "Validation of Nucleic Acid Amplification Techniques (NAT) for the Detection of Mycoplasmas: Guidelines," authors were able to significantly reduce the amount of effort for their product specific validation that needed to be done in order to implement the kit. Authors only had to show that the kit worked as intended in their cell culture medium and matrix and with their lab and staff in their facility. This combined with a mycoplasma-free history at their facility created an abbreviated qualification plan approved by Health Canada. Results showed using the MycoTOOL PCR Mycoplasma Detection Kit provided them with data that met Health Canada requirements and provided a more cost-effective testing solution that met their quicker turnaround timelines.

According to the study, they were able to reduce their cost 3-fold and reduce testing turnaround time from over 12 days to as little as 48 hours when compared with outsourcing PCR based testing to a GMP lab. The paper provides full details of both the qualification methods used and the results of the study.

I was fortunate to be able to interview Dr. Sowmya Viswanathan, corresponding and senior author on the study about her work. She provided great insight into the motivating factors for changing their testing processes, the benefits they saw, leveraging these gains for future products.

Dr. Viswanathan said that the primary driver and ultimate benefit was the reduced cost. They were able to complete mycoplasma testing for a third of the cost of outsourcing, even taking into consideration labor and other facility costs.

While the cost savings were certainly compelling, there were other important benefits to moving to in-house testing. Turnaround time, which dropped from a couple weeks to as little as 48 hours, now permitted close to real time in-process information. In addition the ability to test closer to release strengthened the safety profile. They were also not at the mercy of another lab or shipping delays to get the results they needed and this put them in control of timing for sampling and results.

Dr. Sowmya Viswanathan, corresponding and senior author - *Strategy for an Abbreviated In-House Qualification of a Commercially Available Rapid Microbiology Method (RMM) for Canadian Regulatory Approval*

This article was first published in *Cell Culture Dish*, a blog designed to provide a community for scientists and others involved in biotechnology to share expertise and best practices as well as discuss topics of interest to the community. The blog covers areas important to the application, development and regulatory approval of cell culture processes and products. This includes biomanufacturing, vaccines, cell culture media and equipment, regenerative medicine, cord blood stem cells, cellular therapy, cell-based assays, diagnostic antibodies, life science research and related applications of cell culture.

Follow the link below to read the entire article and full interview with Dr. Viswanathan:

In-house Rapid Mycoplasma Test Qualification Provides a Cost-effective, Quick Turnaround Solution for Cell Therapy Product Release Testing

cellculturedish.com/2018/04/in-house-rapid-mycoplasma-test-qualification-provides-cost-effective-quick-turnaround-solution-for-cell-therapy-product-release-testing/

When asked about future implementation of this strategy, Dr. Viswanathan said that this qualification was done for a product in clinical Phase I/II, but felt that the same approach would be applied for commercial manufacturing with similar benefits of cost savings and reduced turnaround time. For new products, they will have to at least do matrix interference testing, but this would be true for any of the testing methods. Dr. Viswanathan also sees this as an important strategy to be used for both sterility and endotoxin testing. She sits on the Standard Council of Canada's Mirror Committee for International Organization for Standardization (ISO TC276) on Analytical Methods and Bioprocessing, and is on the steering and working committee of an international Standards Coordinating Body (SCB) that conducted a workshop in April to look at how rapid microbial methods can be expanded and standardized industry wide ■

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FORTHCOMING EVENTS

OXFORD GLOBAL CONFERENCES

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12th Annual Proteins & Antibodies Congress
24 - 25 April 2019 | London, UK

6th Annual Peptides Congress
24 - 25 April 2019 | London, UK

6th Annual Biosimilars & Biobetters Congress
24 - 25 April 2019 | London, UK

Co-located Events

Biomanufacturing Congress
September 2019 | London, UK

Biomarkers Series

UK

14th Annual Biomarkers Congress
21 - 22 February 2019 | Manchester, UK

US

4th Annual Biomarkers & Precision Medicine USA Congress
October 2019 | San Diego, USA

Cell Series

UK

7th Annual Cell Culture & Bioprocessing Congress
25 - 26 October 2018 | London, UK

5th Annual Stem Cell & Regenerative Medicine Congress
25 - 26 October 2018 | London, UK

4th Annual Cell & Gene Therapy Congress
25 - 26 October 2018 | London, UK

Co-located Events

Biobanking Congress
25 - 26 October 2018 | London, UK

US

Cell Culture & Bioprocessing Congress USA
14 - 15 May 2019 | Boston, USA

Co-located Events

Cell & Gene Therapy Congress USA
14 - 15 May 2019 | Boston, USA

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US

2nd Annual Formulation & Drug Delivery USA Congress
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2nd Annual Inhalation & Respiratory Drug Delivery USA Congress
18 - 19 March 2019 | San Diego, USA

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08 - 09 November 2018 | London, UK

Synthetic Biology Congress
08 - 09 November 2018 | London, UK

Co-located Events

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4th Annual Next Generation Sequencing & Clinical Diagnostics USA Congress
23 - 24 October 2018 | Boston, USA

4th Annual Single Cell Analysis USA Congress
23 - 24 October 2018 | Boston, USA

Co-located Events

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2nd Annual Synthetic Biology USA Congress
14 - 15 May 2019 | Boston, USA

Co-located Events

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2nd Annual Industrial Synthetic Biology Congress
October 2019 | Munich, Germany

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