BEST PRACTICE EBOOK

Boosting the Efficacy of Safe, Scalable, & Precise Vaccines

Innovations in mRNA Technology, RNA Therapeutics, and Cancer Immunotherapy for 2024

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Introduction

Advancements in vaccine development, such as mRNA technology, personalized vaccines, and nanoparticle delivery, are transforming the biopharmaceutical industry. The speed, precision, and scalability of vaccine production have all been improved in this boom, as well as the expansion of their potential to address diverse diseases from pandemics to cancer.

Although vaccines are currently experiencing a surge in innovation, experimentation, and therapeutic effectiveness, challenges for vaccine and immunotherapeutic developers remain persistent. In the age of immunotherapy, the mission for the developers of these drugs will be to **enhance vaccine and therapeutic effectiveness while overcoming limitations related to safety, scalability, and precision targeting.**

We gathered together industry leaders for a half-day digital event, not only to showcase the power of vaccines and immunotherapies, but to discuss efforts to overcome their challenges. All presentations tackle the difficulties of innovating either in the design, production, or delivery of vaccines and therapies to improve outcomes in combating infectious diseases and cancers.

This eBook will see best practice solutions practiced by experts to tackle these difficulties.

First, we'll look at vaccine development and manufacturing optimisation:

- Mats Lundgren, **Abera Bioscience**, confronts the fact that current polysaccharide-based pneumococcal vaccines are serotype-specific and prone to serotype replacement, limiting their effectiveness. There is also a need for a scalable, cost-effective mucosal vaccine for airborne disease transmission.
- Brian Schanen at **Sanofi** demonstrates the development of mRNA vaccines which face challenges such as improving potency, tolerability, thermostability, and reactogenicity. These must be addressed to expand beyond respiratory diseases and ensure clinical success.
- Mabrouka Maamra presents the **University of Sheffield**'s rapid and large-scale production of high-quality, low-cost mRNA vaccines which are needed for pandemic preparedness, with an emphasis on integrating digital tools and optimizing manufacturing processes.
- Mike Pipis outlines how **SGS** is ensuring consistent quality and regulatory compliance in vaccine production, from raw materials to final product testing, crucial for the safe and timely delivery of vaccines.

Second, we'll see innovations within RNA and nucleic acid therapeutic design:

- Tobias von der Haar of the **University of Kent** tackles designing RNA sequences, dealing with the complexity of the vast number of possible sequences and balancing factors like ribosome decoding speed and RNA structure, which impact protein expression and manufacturability.
- Tokihiro Tanaka from **NOF Corporation** shows that the toxicity of ionizable lipids limits the clinical use of nucleic acid therapeutics. Therefore, designing biodegradable, safe, and effective lipid nanoparticles (LNPs) is essential for improving delivery and therapeutic efficacy.

Finally, presentations will tackle the field of cancer immunotherapy and neoantigen targeting:

- Ola Nilson presents **NEOGAP**'s mission to develop cancer treatments that target tumour-specific neoantigens with personalized T-cell therapies while minimizing the risk of severe side effects and maximizing tumour-killing efficiency.
- Eric Halioua from **PDC*Line Pharma** highlights best practice solutions for developing off-the-shelf, antigen-presenting cell-based cancer vaccines that are scalable and effective for targeting solid tumors with high immune specificity.
- Samantha Paston of **Scancell** unravels advanced unresectable melanoma, which requires a vaccine that induces strong, tumour-specific T-cell responses while being effective as a non-personalized treatment in combination with immunotherapy.

We hope you find this eBook informative in finding the best practices for overcoming these challenges.

Tom Cohen
Senior Digital Content Editor, Oxford Global

Contents

Key Speakers Include

BRIAN SCHANEN,
Global Head,
Sanofi

ERIC HALIOUA,
Chief Executive Officer,
PDC* Line Pharma

MABROUKA MAAMRA,
Project Manager,
University of Sheffield

MATS LUNDGREN,
Chief Scientific Officer,
Abera Bioscience

MIKE PIPIS,
Regional Business Manager,**SGS Vitrology**

OLA NILSSON,
Head, **NEOGAP Therapeutics**

SAMANTHA PASTON,
Head, **Scancell**

TOBIAS VON DER HAAR,
Professor,
University of Kent

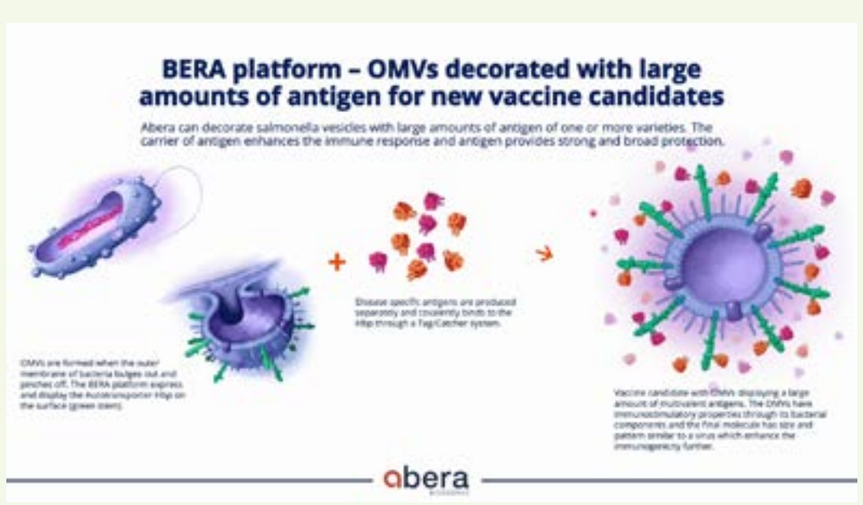
TOKIHIRO TANAKA,
Research Scientist,
NOF Corporation

Part 1: Vaccine Development and Manufacturing

OMV Vaccine Platform for Mucosal Immunisation

Mats Lundgren, the Chief Scientific Officer of Abera Bioscience, presented an overview of the company's work on developing new vaccine candidates using their proprietary BERA platform. Abera is a science-centric spin-out company that is now advancing to the clinical stage.

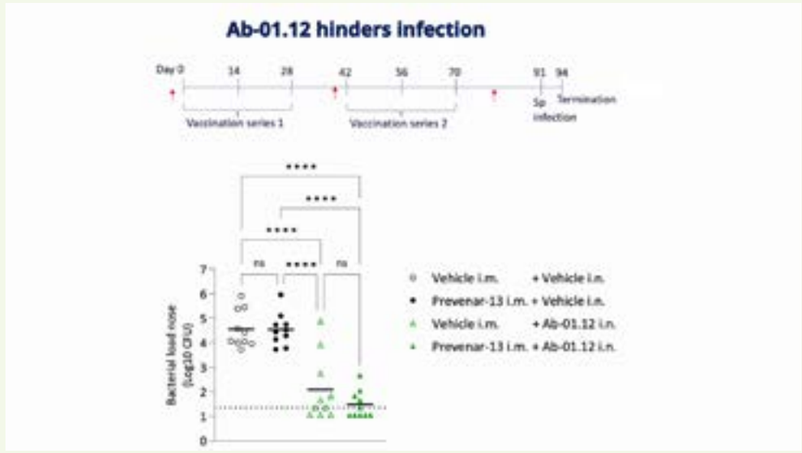
The lead candidate is a pneumococcal vaccine that is ready to enter phase one clinical trials. In addition, Abera is working on vaccine projects for COVID-19, influenza, chlamydia, and tuberculosis, all leveraging their BERA platform. This platform utilizes outer membrane vesicles (OMVs) derived from a proprietary salmonella strain. These OMVs have a protein structure on their surface that can covalently bind to antigens, creating a virus-like bacterial particle that is highly immunogenic.



Lundgren highlighted several key advantages of the BERA platform. It is a cost-efficient and scalable production process that does not require additional adjuvants, with a favorable safety profile. The OMVs can be compatible with both mucosal and parenteral delivery, with a focus on mucosal vaccination for pandemic preparedness. The high density of covalently bound antigens on the OMVs triggers a strong immune response, including both innate and adaptive immunity.

Mucosal vaccination is a key area of focus for Abera. Lundgren explained that inducing local immunity at the site of pathogen entry can help prevent transmission of airborne diseases. Mucosal vaccines also offer benefits like needle-free administration, stability at elevated temperatures, and the ability to mimic natural immune responses.

For the pneumococcal vaccine candidate, Lundgren addressed the limitations of existing polysaccharide-based vaccines, which are serotype-specific and subject to serotype replacement. Abera's universal vaccine targets conserved pneumococcal antigens, aiming for broad coverage and reduced risk of antibiotic resistance. Preclinical data in mice demonstrated strong systemic and mucosal immune responses, including IgG, IgA, and Th17 responses.



Abera is now preparing to advance the pneumococcal vaccine into clinical trials, with plans for a phase one study at the Radboud University Medical Center. They also have a pandemic preparedness project, supported by a grant from the UK Vaccine Network, to rapidly produce vaccine candidates in response to emerging disease outbreaks.

In addition to the pneumococcal program, Lundgren provided updates on Abera's work on COVID-19, chlamydia, and tuberculosis vaccine candidates. These projects leverage the versatility of the BERA platform and collaborations with various partners and research institutions.

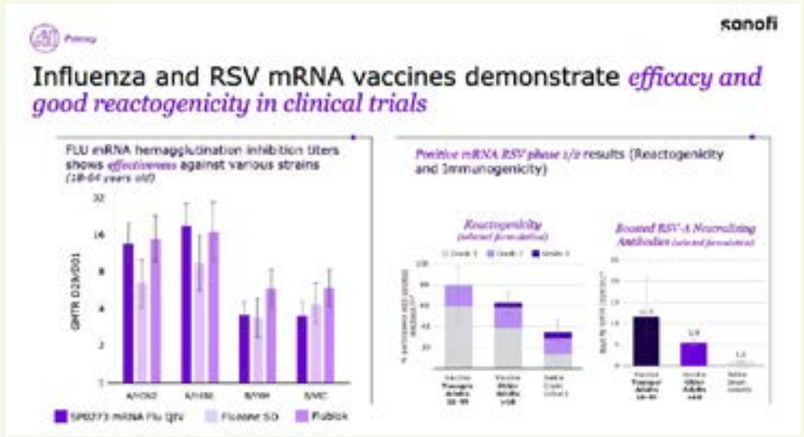
Concluding the presentation, Lundgren acknowledged the contributions of the Abera team, as well as the critical support from funders and collaborators that have enabled the company's progress. The summary highlights Abera's science-driven approach and the potential of their BERA platform to address unmet needs in infectious disease prevention.

Taking The Right Steps In Vaccine Preclinical Development To Achieve Clinical Success

Brian Schanen, the Head of Biomarker Research at Sanofi's mRNA Center of Excellence, provided an overview of how Sanofi is leveraging translational research approaches to accelerate their mRNA vaccine development.

Sanofi is a large pharmaceutical company with a significant global footprint, operating in 90 countries with over 91,000 employees and 59 manufacturing sites. The company has a strong history in respiratory infections like influenza and RSV, and their efforts on high-dose flu vaccines have demonstrated significant reductions in comorbidities. Sanofi's mRNA Center of Excellence was established just a few years ago and has experienced rapid growth, now with over 500 employees across research sites in France and the US.

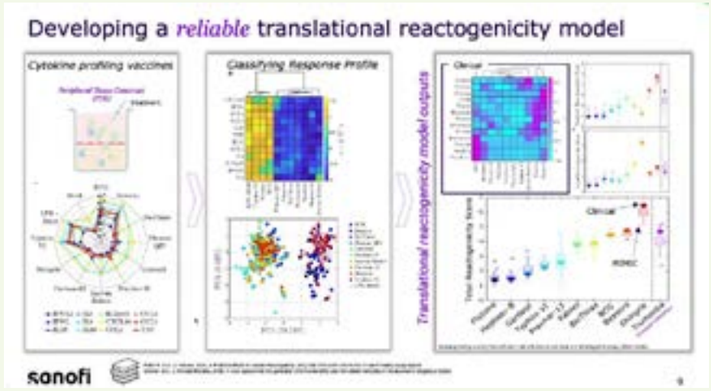
Schanen shared publicly disclosed data showing efficacy and good reactogenicity (side effects) for Sanofi's mRNA vaccines targeting influenza and RSV in clinical trials. However, he acknowledged that mRNA technology comes with challenges around potency, tolerability, and thermostability, as well as the need to expand beyond respiratory targets.



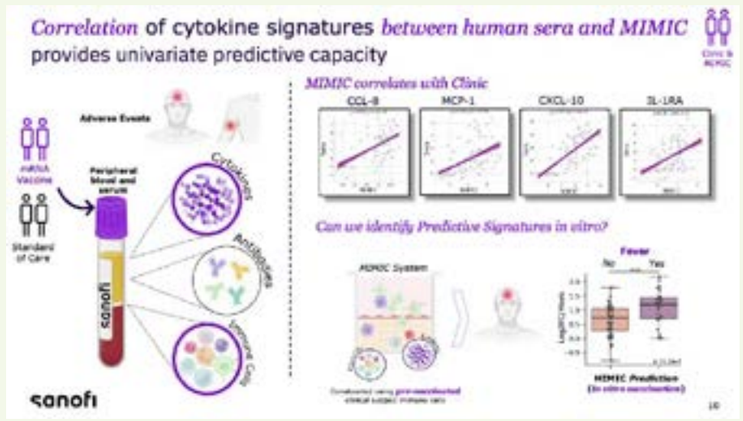
To address these challenges, Sanofi is taking a translational approach, leveraging computational and scientific knowledge to bridge gaps between design attributes and clinical performance. The key focus areas are improving reactogenicity, enhancing immunogenicity, and bettering thermostability, through various mRNA platform technologies.

Schanen emphasized the importance of improving reactogenicity and how Sanofi has developed an innovative in vitro model called MIMIC (Modular IMmune In vitro Construct). This fully autologous system uses human PBMCs from diverse donors to capture population-level differences in pre-immunity and response. MIMIC allows for the assessment of dendritic cell cytokine profiles and transcriptomic changes as readouts of reactogenicity.

Sanofi has validated the MIMIC as a reliable translational model, showing good correlation between in vitro cytokine responses and clinical outcomes. They have further applied MIMIC to mRNA vaccines, using pre-vaccination clinical samples to build associations between in vitro cytokine profiles and the probability of eliciting adverse events like fever.



By pairing the MIMIC system with in silico modelling, Sanofi can now predict the reactogenicity of mRNA vaccine candidates and rank them accordingly, allowing them to quickly deprioritize high-risk candidates. Additionally, MIMIC is being used to understand the mechanistic drivers of reactogenicity, such as the impact of lipid nanoparticle (LNP) composition on interferon signalling and IL-1 related cytokines.

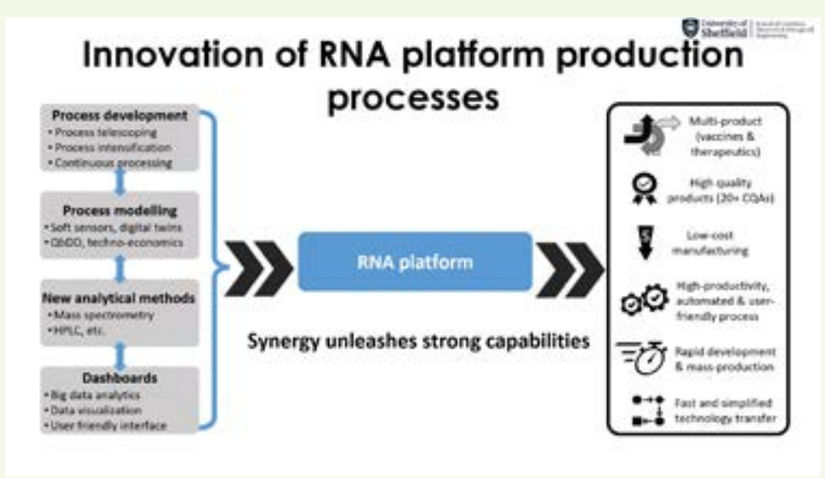


Looking ahead, Sanofi is focused on leveraging state-of-the-art immunology, improving antigen design, and integrating data using AI and machine learning to push the boundaries of mRNA vaccine development. The company is also exploring other vaccine technologies beyond mRNA to address a wide range of pathogens, including bacterial targets.

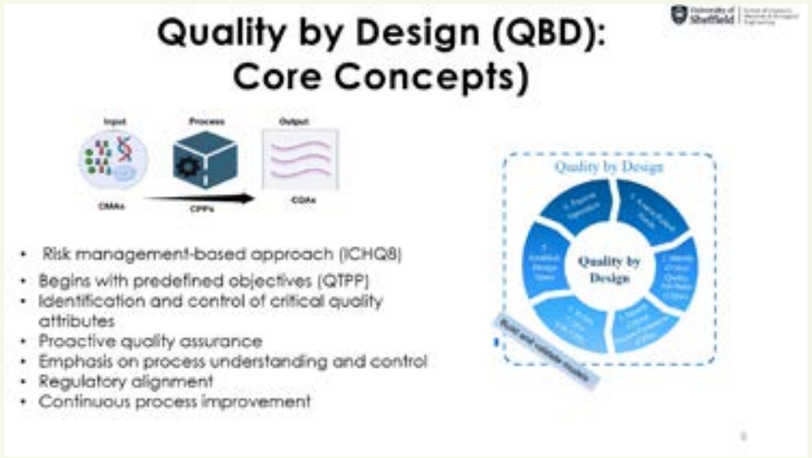
A Disease-Agnostic Digitalised Platform For Continuous Production Manufacturing Processes With Rapid, High-Volume Production Of High-Quality, Low-Cost mRNA Vaccines And Therapeutics

Mabrouka Maamra, Project Manager at the University of Sheffield, gave a talk focusing on the topic of quality by digital design for developing mRNA vaccines and therapeutic manufacturing processes. Maamra began by highlighting the significant impact of the COVID-19 pandemic, which led to over 7 million deaths and had a global economic cost in the billions to trillions of dollars. While mRNA vaccines have been a lifeline, providing rapid production and regulatory approval, Maamra emphasized the need for worldwide access to combat future pandemics.

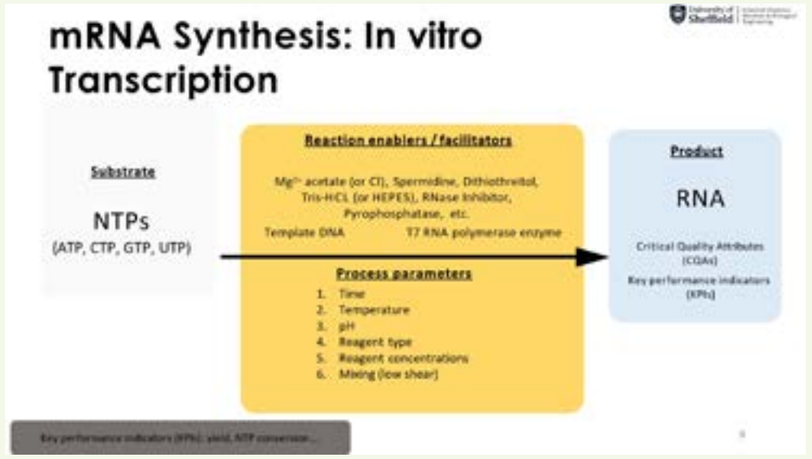
In December 2022, a team led by Dr. Zoltán Kis received a grant from the R3 program (RNA readiness response) by Wellcome Leap. The project aims to address the challenges of producing large volumes of RNA-based vaccines and therapeutics rapidly, at high quality, low cost, and in a disease-agnostic manner. The team consists of four PIs with expertise in process development, modelling, analytical methods, and dashboard development. By leveraging this synergy of expertise, the team aims to enhance the NI platform for multi-product production at high quality and low cost.



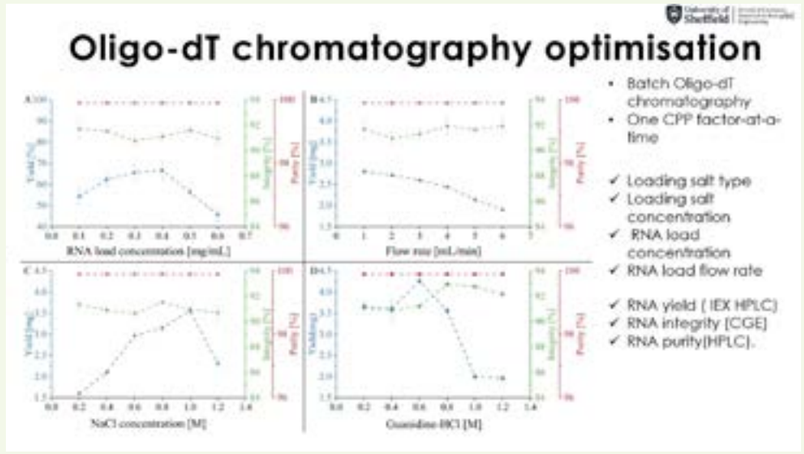
The presentation then delved into the quality by design (QBD) concept, which is based on a risk management approach. The QBD platform starts with predefined quality targets and identifies critical quality attributes (CQA). It emphasizes the importance of process understanding and control, relating critical process parameters (CPP) to CQA. This allows for continuous process improvement and the establishment of a design space aligned with regulatory requirements. The mapping of CQA and CPP is based on empirical data, prior knowledge, and uncertainty assessment.

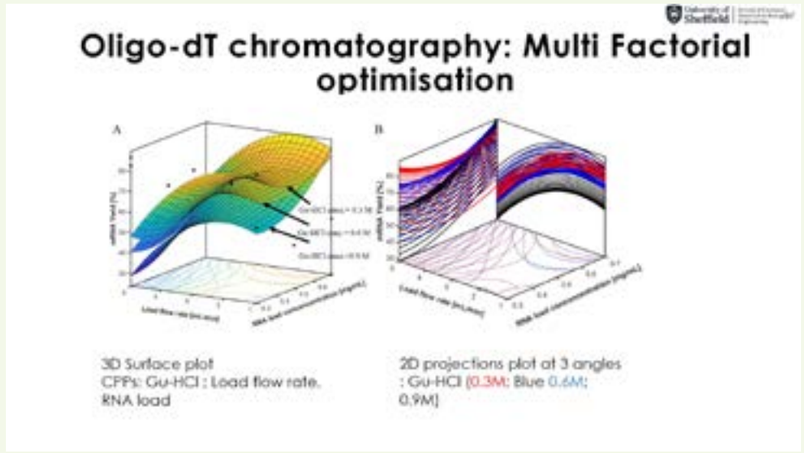


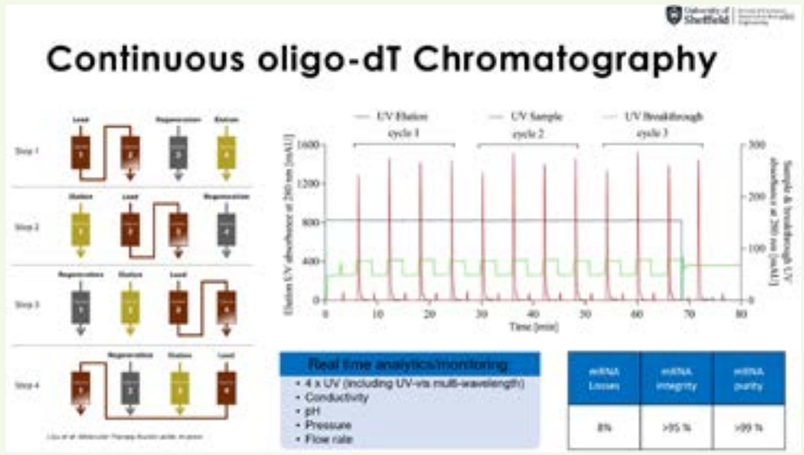
Maamra focused on the manufacturing processes for the mRNA drug substance, particularly the in vitro transcription (IVT) process. IVT involves a substrate (NTP) and reaction enablers like enzymes, templates, and RNase inhibitors, with process parameters like time, temperature, and pH. The goal is to achieve high yield and high NTP conversion while minimizing unused material and cost. The team has performed CQA-CPP mapping for IVT, established modelling conditions to maximize yield and minimize dsrNA, and gained insights into the IVT reaction kinetics.



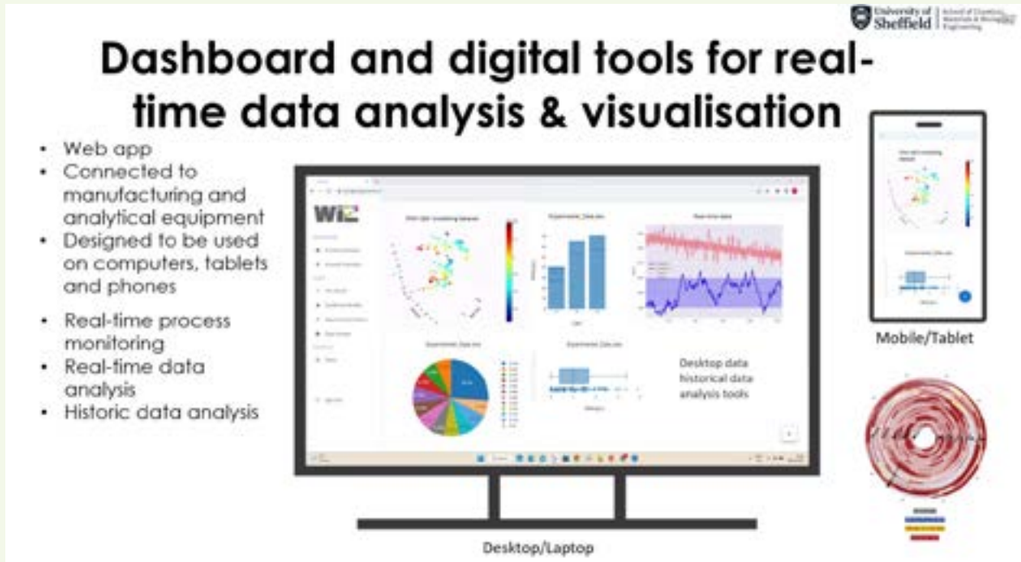
The presentation also covered the optimization of oligo-dT chromatography, a key purification step for mRNA. Experimental results showed high RNA purity (100%) and integrity (over 90%), with varying RNA yield based on different parameters. Multifactorial optimization and surface plots were used to determine optimal conditions for maximum yield and minimum loss. The team also implemented continuous oligo-dT chromatography for the first time for RNA, achieving significant improvements in productivity and cost reduction.







Finally, Maamra discussed the development of digital tools and the implementation of quality by digital design (QbDD). This includes a web app for real-time visualization and analysis, as well as the use of soft sensors and digital twins to facilitate communication between physical processes and process controllers, providing predictive capabilities and fault detection.



The presentation concluded with the team's plans to build a compact RNA manufacturing process (RNA box) for rapid access to mRNA technology and high-quality vaccine production. The team is also working on innovations in mRNA IBT and downstream purification, as well as integrating more analytics and improving digitalization within the production process.

Explore Our Comprehensive Content

Advanced Antibody Engineering: AI, ML, and Computational Tools

Rapid Analytical Approach for Biologics Characterization Using Mass Photometry

Harnessing Bispecific T Cell Engagers and T Cell Primers in Cancer Treatment

Supporting Vaccine Manufacturers with QC GMP Testing

The presentation was given by Mike Pipis, the Regional Business Manager at SGS Glasgow. He introduced SGS and its global network, explaining that the company has over 25 labs in 11 countries, serving more than 5,000 customers. The Center of Excellence for biosafety is located in Glasgow, and it supports the entire lifecycle of biologics, from start to finish.

Pipis provided an overview of SGS's biopharmaceutical labs, which are located in the US, Belgium, and Glasgow. These labs specialize in QC and release testing for various biologic medicines, including biosimilars, monoclonal antibodies, and cell and gene therapies. The Glasgow site is a standalone lab focused on biosafety testing for global clients.

The presentation then delved into the different stages of the manufacturing process and the testing capabilities that SGS can provide. In the cell virus bank and starting material phase, SGS follows FDA and European Pharmacopeia guidelines, conducting tests for microbial contaminants, adventitious virus detection, specific virus detection, identity and genetic stability testing, and detection of retrovirus.

For the bulk harvest and drug substance stages, SGS performs similar testing for microbial contaminants, adventitious viruses, specific viruses, identity for control cells, and detection of retrovirus. Additionally, they offer genetic stability and integrity testing, as well as assays for residual impurities like host cell DNA and endotoxin. Replication-competent virus and vector concentration tests are also available.

In the drug product phase, SGS collaborates with its Brussels Wavre group to conduct release assays required for the European Union market. These include tests for bacterial endotoxin, osmolality, pH, and vector aggregate stability.

Pippis highlighted SGS Glasgow's excellent audit history, having been successfully audited by the FDA and MHRA. The mutual recognition of GMP certificates between these regulatory bodies simplifies the audit process.

The presentation also delved into the company's method validation practices, which adhere to USP, ICH Q2, and Q2R2 guidelines. The team at SGS Glasgow has a long history, dating back to the mid-1990s, when they pioneered the development of GMP biosafety testing technologies. This expertise was crucial during the COVID-19 pandemic, as SGS Glasgow played a central role in releasing over 4 billion doses of the COVID vaccine.

Pippis emphasized SGS's commitment to on-time delivery, with the company achieving over 97% on-time delivery across all departments this year. He attributed this success to the company's scientific expertise and the long-standing team, led by Dr. Archie Lovatt, a pioneer in real-time PCR and per technology for biologics.

In conclusion, the presentation highlighted SGS's capabilities, expertise, and customer-centric approach, inviting the audience to reach out and discuss potential solutions for their vaccine or biologic testing needs.

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Advanced Antibody Engineering: AI, ML, and Computational Tools

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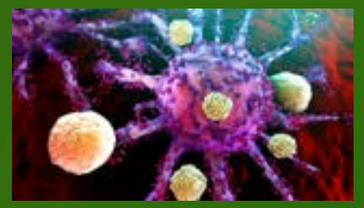


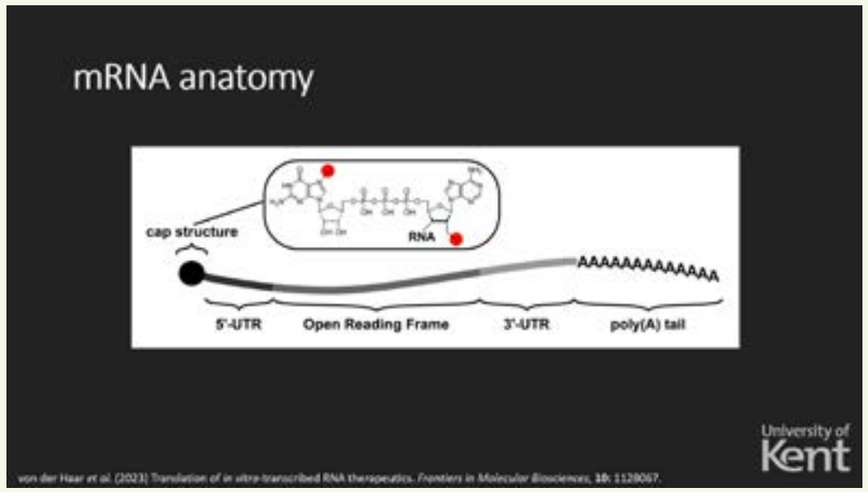
Part 2: RNA and Nucleic Acid Therapeutic Design

Sequence Design For Efficient & Manufacturable RNA Therapeutics

Tobias von der Haar, Professor of Systems Biology at the University of Kent, presented his work on designing efficient and manufacturable RNA therapeutics. He began by drawing a parallel between modern RNA therapeutics and Edward Jenner's pioneering smallpox vaccination, noting that the core concept remains the same - introducing something harmless to stimulate an immune response against a harmful pathogen. However, the complexity of what is being introduced into the human body has evolved significantly.

Von der Haar explained that with RNA therapeutics, there are two key steps: first, the RNA must be translated into a therapeutic protein, and then the protein must engage the immune system to generate the desired effect. Expertise in both RNA synthesis and protein therapeutic effects is required to get both parts right for an effective RNA therapeutic.

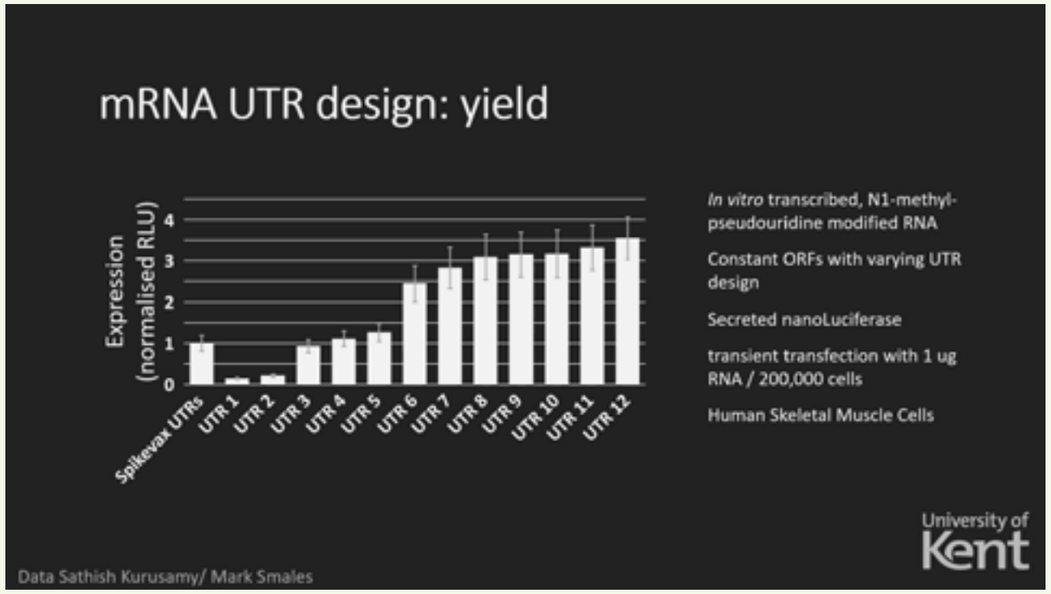
He provided an overview of the key components of a functional messenger RNA in eukaryotes, including the open reading frame, 5' and 3' untranslated regions, cap structure, and poly-A tail. The mechanistic process of protein synthesis from RNA was also described, highlighting the importance of translation initiation factors and the ribosome.



One of the main challenges in designing efficient RNA sequences, von der Haar explained, is the exponential growth in possible sequences as protein length increases. For example, there are 10632 possible RNA sequences that could encode the SARS-CoV-2 spike protein, making it impractical to test all possibilities.

Von der Haar then discussed how different codon choices can impact parameters like ribosome decoding speed, GC content, and RNA secondary structure. These interdependent factors must be carefully balanced in the sequence design process. He presented experimental data demonstrating the significant impact of sequence design on protein expression levels and manufacturability, such as avoiding early transcription termination motifs.

An interesting example was provided on the issue of ribosomal frame shifting, where ribosomes can slip and produce incorrect peptides. This was shown to be more prevalent in modified RNAs containing N1-methyl-pseudouridine, leading to unwanted immune responses against the frame shift peptides. Sequence design approaches to mitigate this effect were highlighted.



Finally, von der Haar discussed the challenges in connecting in vitro expression levels to in vivo efficacy, noting the often non-linear relationship. He emphasized the importance of understanding how peak expression, expression duration, and total expression amount correlate with therapeutic efficacy, rather than just optimizing for high expression.

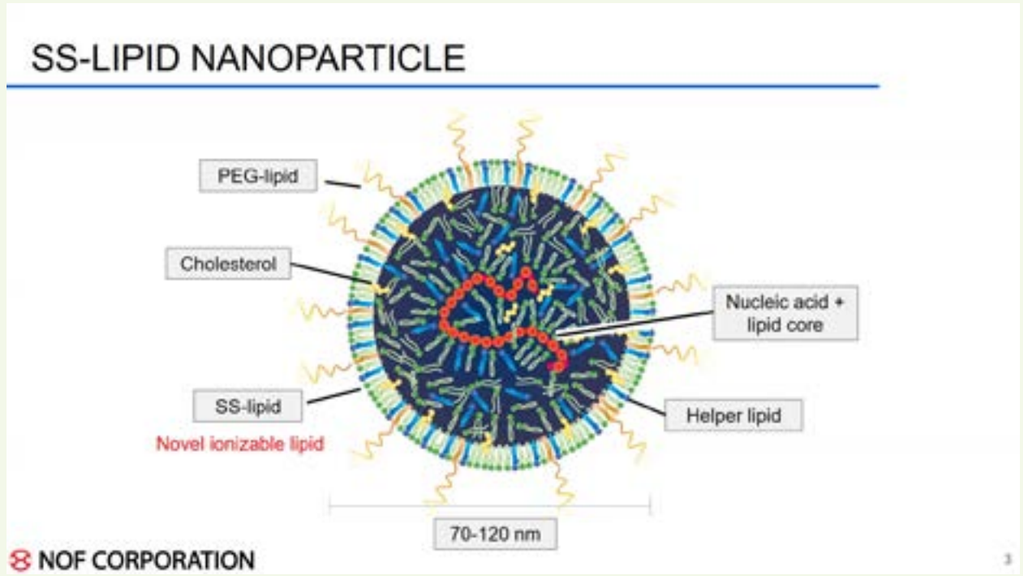
In conclusion, von der Haar's presentation underscored the significant progress made in controlling the various aspects of RNA therapeutics through sequence design, while also outlining the ongoing challenges and areas for further research and development.

Biodegradable Lipid Nanoparticles for Gene Therapy and Vaccines

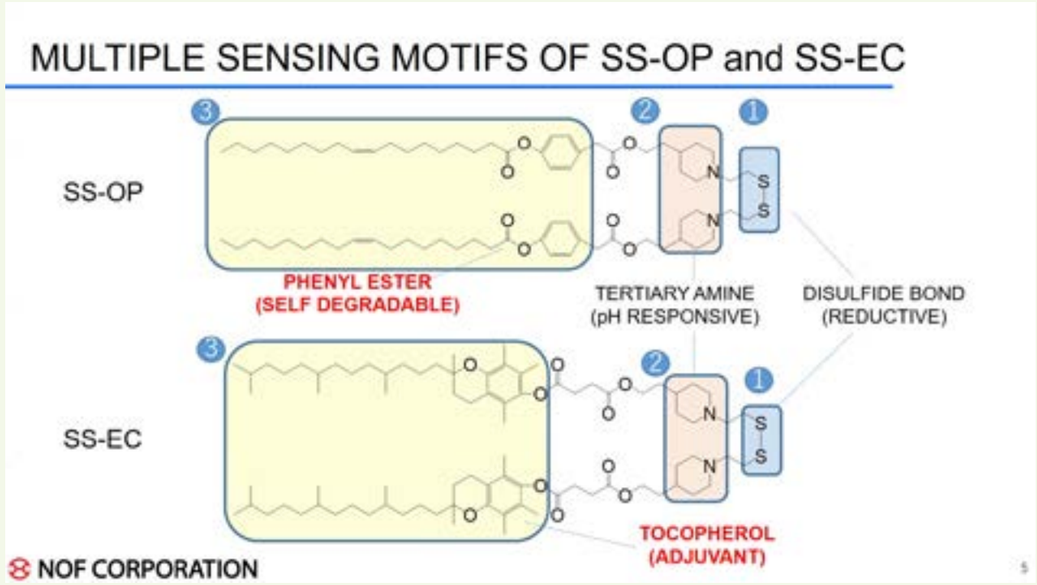
Tokihiro Tanaka, a Research Scientist from NOF Corporation is responsible for developing novel ionizable lipids and lipid nanoparticle (LNP) formulations. The focus of his presentation was on NOF's ionizable lipids called the "SS series" for gene therapy and vaccine applications.

Tanaka began by explaining the importance of nucleic acid therapeutics, which have a wide range of applications from vaccines to gene editing. However, the toxicity of ionizable lipids has limited their clinical use, so molecular design to minimize toxicity is a key issue. Biodegradability is important for reducing cytotoxicity and improving intracellular delivery of cargo.

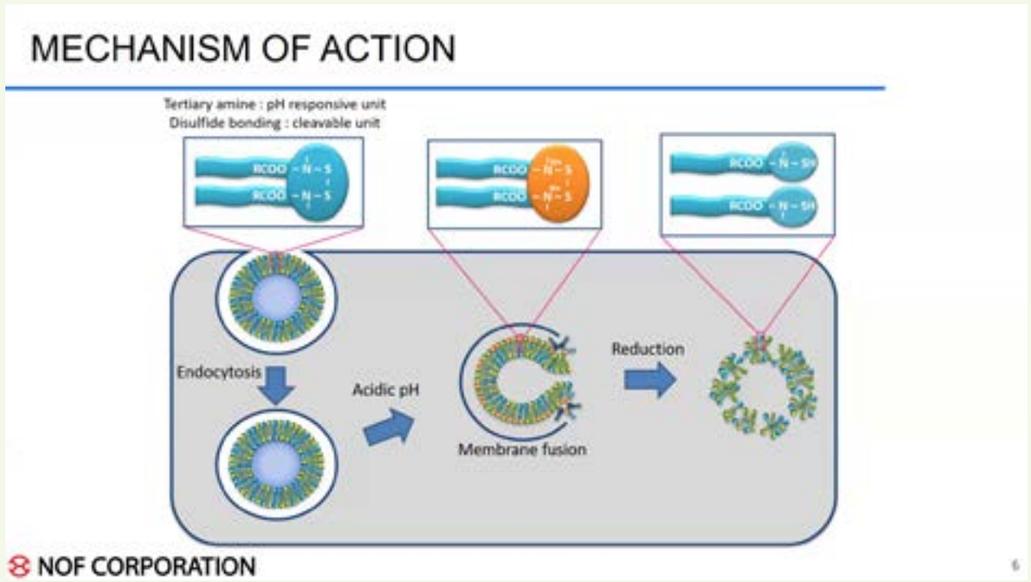
Tanaka then described the components of LNPs, which typically include an ionizable lipid, helper lipid, cholesterol, and PEG lipid. NOF has developed unique ionizable lipids called "SS lipids" that can be easily degraded under cytoplasmic conditions to enhance RNA and DNA delivery.



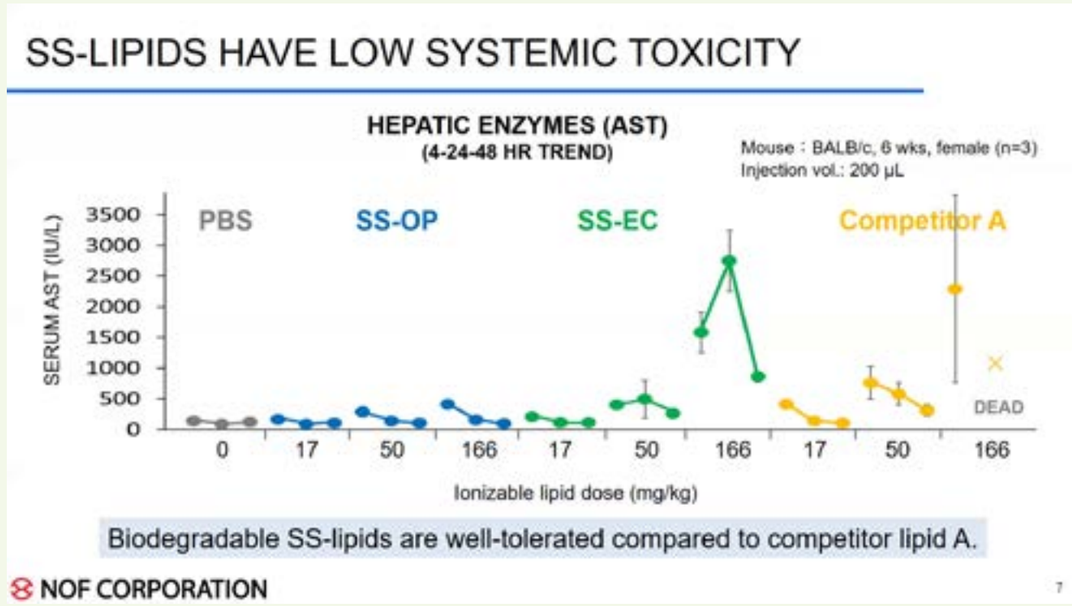
The two main SS lipids discussed were SS-OP and SS-EC. These have three key features: 1) a disulfide bond that can be cleaved in the reductive cytoplasmic environment, 2) a tertiary amine head group with a pKa around 6.5 to facilitate membrane fusion, and 3) a phenyl ester linker that is more biodegradable than typical ester linkers.



Tanaka explained the mechanism of action, where the neutral LNPs become positively charged in the acidic endosomal environment, enabling membrane fusion and cytoplasmic release of the cargo. The disulfide bonds are then rapidly cleaved by glutathione, leading to rapid excretion of the degraded lipids.



Safety studies in mice showed that SS-OP had lower toxicity compared to a competitor lipid. Application data was then presented for hepatic delivery, splenic delivery, and RNA vaccine formulations. SS-OP demonstrated higher mRNA expression and gene editing efficiency compared to competitors. For RNA vaccines, SS-OP induced higher humoral immunity, while the SS-EC formulation enhanced cytotoxic T cell responses, suggesting potential for cancer immunotherapy.



Finally, Tanaka discussed the development of LNPs containing a novel SS lipid for long-term stability, showing that these formulations maintained gene expression activity for up to 1 year at 4°C for freeze-dried LNPs and 1 month at -20°C for freeze-thaw LNPs.

In summary, the SS series of biodegradable ionizable lipids developed by NOF show promising results for enhancing the delivery and efficacy of nucleic acid therapeutics while improving safety and stability profiles.

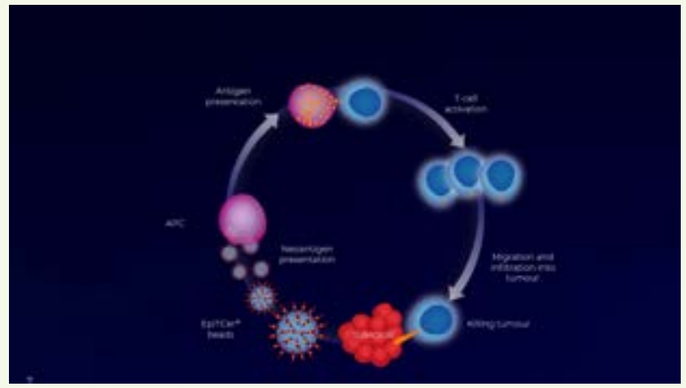
Part 3: Cancer Immunotherapy & Neoantigen Testing

pTTL – A Novel, Neoantigen-Targeting T Cell Therapy From Tumour-Draining Lymph Nodes

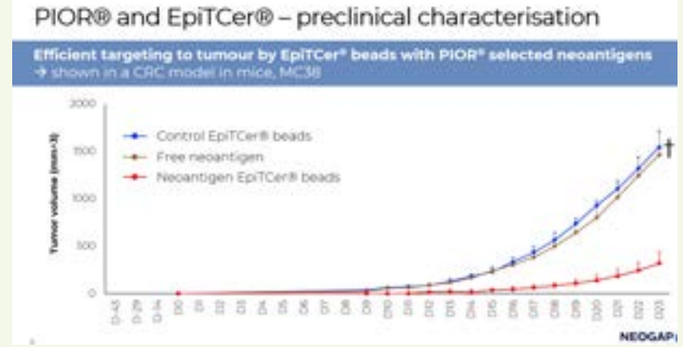
Ola Nilsson, the Head of Neoantigen Production and Development at NEOGAP Therapeutics, presented on the company's novel neoantigen targeting T cell therapy called PTTL. He began by showing a captivating video demonstrating how T cells can attack and kill tumour cells, highlighting the potential of T cell-based therapies for cancer treatment. Nilsson noted that the recent FDA approval of Iovance's tumour-infiltrating lymphocyte (TIL) therapy for malignant melanoma has opened the door for other cell therapies to reach the market.

Nilsson explained that cancer is caused by DNA mutations that lead to the formation of neoantigens - new peptides or proteins not found elsewhere in the body. These neoantigen-derived peptides are presented on the surface of tumour cells, allowing T cells to recognize and attack them. NEOGAP's innovative technology uses machine learning to train and activate tumour-specific T cells, creating a truly personalized cell therapy with a low risk of serious side effects, unlike genetically modified CAR-T cells.

The pTTL production process starts by sequencing the DNA and RNA from a patient's tumour and normal blood samples. NEOGAP's proprietary software, PIOR, analyses the sequencing data to predict the best neoantigen candidates. These neoantigens are then manufactured and attached to microscopic magnetic beads called 'EpiTCer beads'. The EpiTCer beads are fed to cells derived from the patient's lymph nodes, leading to the expansion of tumour-specific T cells. After two weeks, the EpiTCer beads are removed, and the patient's own cells are infused back.



Nilsson highlighted several advantages of the EpiTCer technology. Unlike synthetic peptides, the EpiTCer beads are selected to be the optimal size to utilize the natural antigen uptake mechanism of antigen-presenting cells (APCs), making the antigen presentation less HLA-sensitive. Studies in mice showed that neoantigen-coupled EpiTCer beads delayed tumour development and enhanced CD8+ T cell infiltration compared to control treatments.



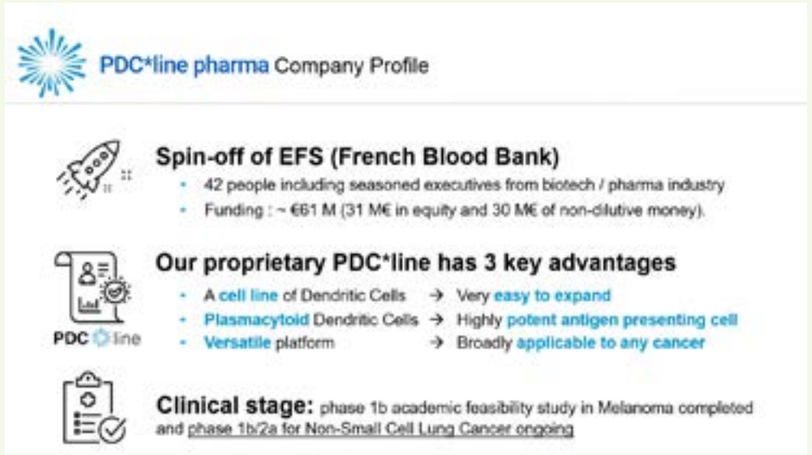
The first clinical trial of pTTL is currently recruiting 12-16 patients with advanced, metastatic colorectal cancer. The dose escalation study will assess safety and monitor for potential efficacy signals, such as tumour shrinkage. Samples will be analysed to detect and characterize the PTTL-derived T cells.

Nilsson also presented data on the characteristics of the expanded T cells, including their specific activation towards the personalized EpiTCers and the predominance of central and effector memory T cells, indicating their functionality. The T cell clonality analysis showed that the production process selectively expands specific T cell clones, suggesting specificity towards the included neoantigens.

New Class Of Antigen-Specific Cancer Active Immunotherapies Based On An Off-The-Shelf Antigen Presenting Cell Line (PDC*line)

PDC*Line Pharma is a clinical-stage company developing a new class of conserved vaccines based on a unique cell line derived from a leukaemia patient. The company was spun off from the French blood bank and has a team of 42 people, having raised €61 million in funding so far.

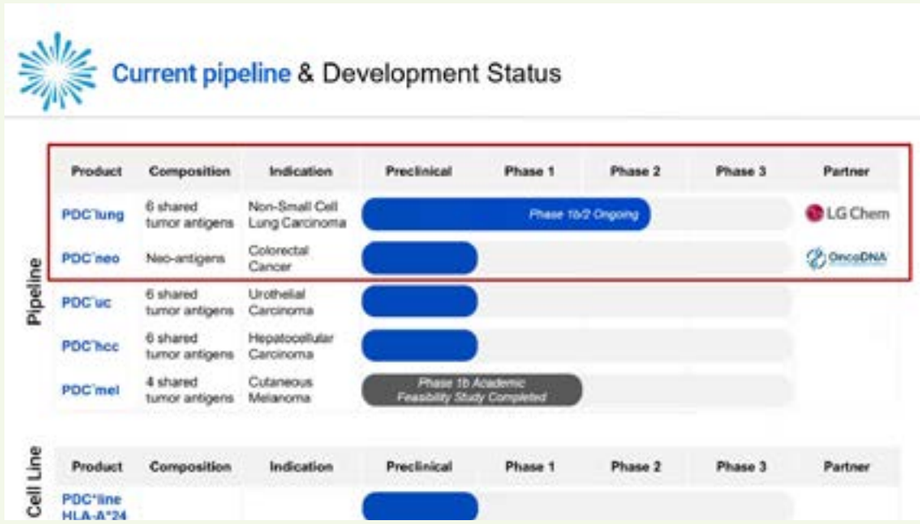
The technology is based on a plasmacytoid dendritic cell line that was isolated from a patient with plasmacytoid dendritic leukaemia. This cell line has several advantageous properties - it is easy to expand, can grow in suspension without synthetic media, and has the capacity to prime and expand cytotoxic CD80 cells. Importantly, the cell line is homozygous for HLA-A*201, allowing the use of HLA-A*201 restricted peptides.

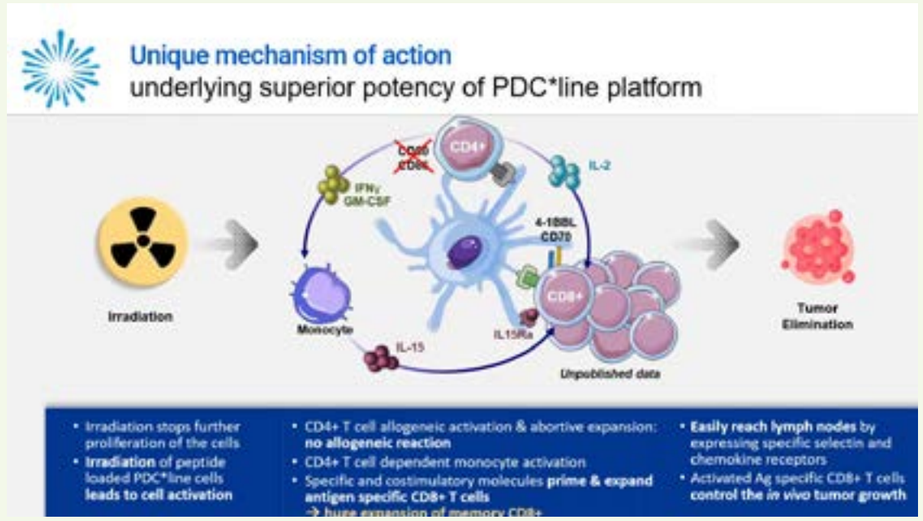


The manufacturing process involves developing primary, master, and working cell banks to ensure batch-to-batch consistency. The cells are grown in suspension in synthetic medium and then loaded with specific tumour antigen peptides. This process has already produced 15 batches of the PDC*lung cancer vaccine with over 90% release.

The company's pipeline includes two lead assets - a non-small cell lung cancer vaccine combining six shared tumour antigens, and a personalized vaccine for colorectal cancer patients based on their tumour mutations. The company has also signed a licensing deal with LG Chem for exclusive rights in South Korea.

The cell line's unique properties stem from over 20 years of research by the scientific founder. It does not get rejected because it expresses HLA Class II molecules and activates CD4+ T cells without proliferating. Its potency comes from the involvement of CD4+ T, antigen-presenting cells, and the production of IL-15, which leads to robust expansion of tumour-specific CD8+ T cells.





In vitro studies have demonstrated the cell line's ability to prime and expand CD8+ T cells against various tumour antigens. The ongoing clinical trial in non-small cell lung cancer is targeting patients with high PDL-1 expression, comparing the vaccine alone and in combination with pembrolizumab.

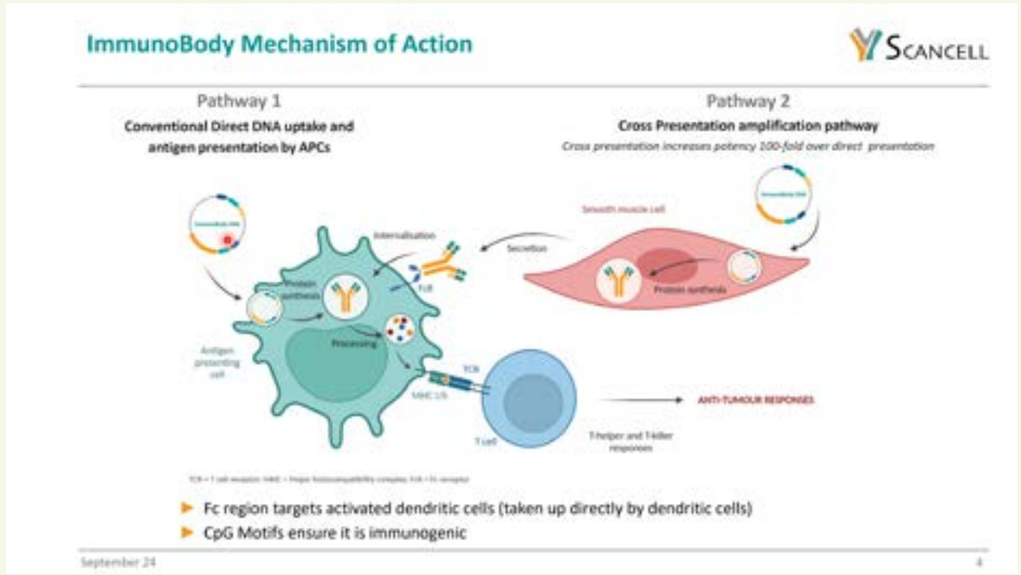
Immunomonitoring results show significant expansion of tumour-specific CD8+ T cells, with the highest responses in the high dose vaccine plus pembrolizumab cohort. The clinical results so far are promising, with a 66.6% overall response rate and 10.9 month median progression-free survival, compared to 39% and 7.1 months for pembrolizumab alone.

The company plans to launch a randomized phase 2b trial for the non-small cell lung cancer vaccine in combination with a checkpoint inhibitor, as well as a trial for the personalized colorectal cancer vaccine. To finance these trials, PDC Line Pharma aims to raise €70-90 million.

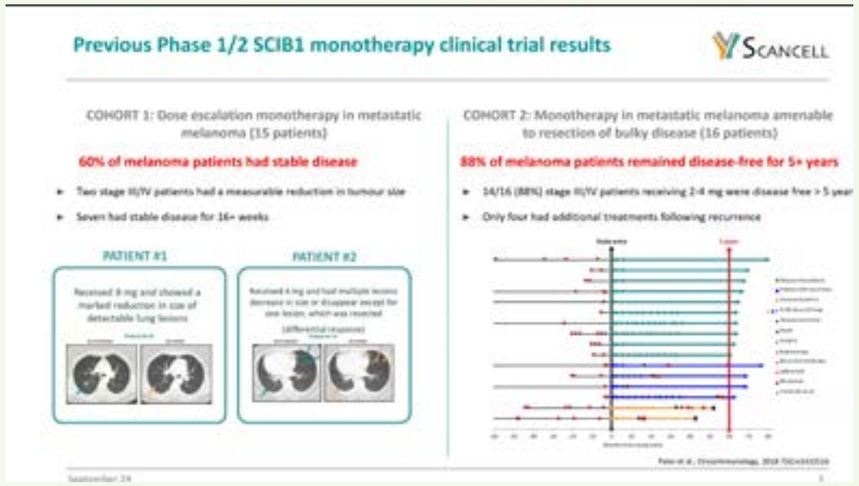
Phase 2 Clinical Trial, A DNA Cancer Vaccine, SCIB1, In Patients With Advanced Unresectable Melanoma Receiving Nivolumab and Ipilimumab

Samantha Paston, the Head of Translational Research at Scan Cell, presented an overview of their DNA cancer vaccine called SCIB1, which is currently in phase two clinical trials for patients with advanced unresectable melanoma. The vaccine is designed to induce tumour-specific, high-affinity T-cell responses in cancer patients.

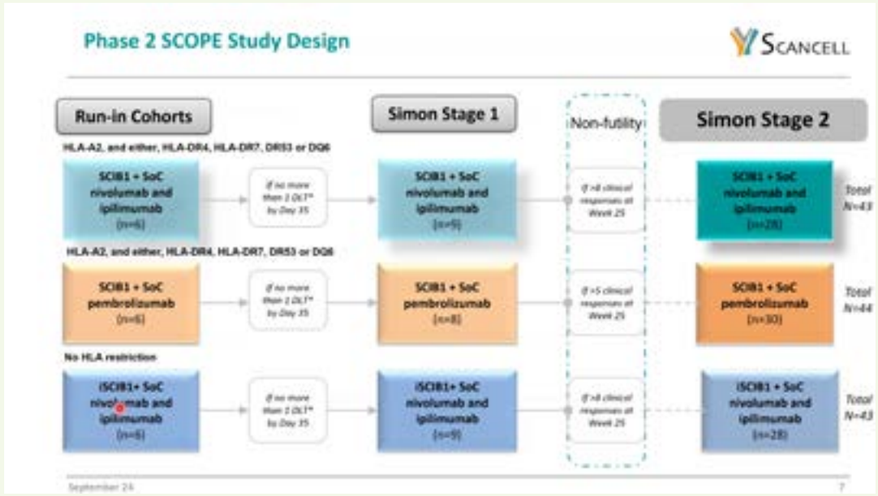
SCIB1 is a non-personalized vaccine that encodes an antibody with epitopes from the melanoma antigens gp100 and TRP=2 inserted into the CDR regions. The vaccine can be taken up by antigen-presenting cells through a conventional DNA uptake pathway, leading to protein synthesis and T-cell recognition. Alternatively, the DNA can be taken up by smooth muscle cells, resulting in antibody secretion and T-cell recognition via Fc receptors.



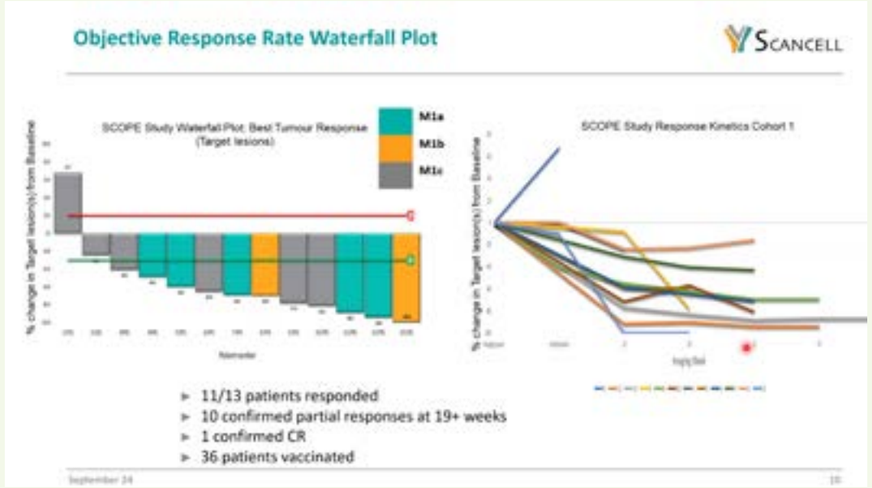
Paston presented data from previous phase one and two trials of SCIB1 in the monotherapy setting. In the first cohort, 60% of 15 metastatic melanoma patients had stable disease, with seven patients maintaining stable disease for 16 weeks or more. In the second cohort of 16 patients with resectable disease, 88% remained disease-free for five years or more. The trials also demonstrated that SCIB1 was able to generate T-cell responses to all four epitopes included in the vaccine, with 89% of patients showing a T-cell response.



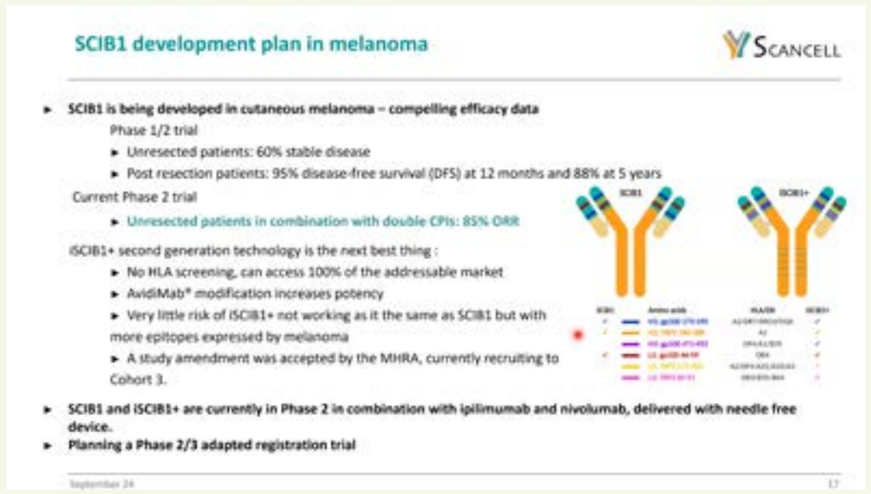
The current Phase II trial has three cohorts: SCIB1 with ipilimumab and nivolumab (Cohort 1), SCIB1 with pembrolizumab (Cohort 2), and a second-generation vaccine called iSCIB1+ with additional epitopes and no HLA restriction, given with ipilimumab and nivolumab (Cohort 3). Cohort 1 has shown an impressive 85% objective response rate in the first 13 patients, while Cohort 2 has seen slower tumour regression in the three patients enrolled so far.



Paston also presented data on the T-cell responses and functional assays performed on the Cohort 1 patients. The analysis identified specific TCRs responsible for the responses, including TCR1 which showed a 15% abundance and reactivity to the TRP2 peptide. Further functional assays confirmed the specificity of these TCRs.



Looking ahead, Scan Cell is planning a phase II/III adapted registration trial for SCIB1 and iSCIB1+ in the UK and US. Recruitment for Cohort 1 is expected to be completed by the end of 2022 or early 2023, while Cohort 3 with the second-generation vaccine has already started recruiting and is expected to finish by the first quarter of 2023.



Paston acknowledged the contributions of the Scan Cell team, translational research group, and clinical group, as well as the trial sites, doctors, nurses, and patients involved in the study. The presentation concluded with a round of applause, highlighting the promising progress and potential of the SCIB1 vaccine.

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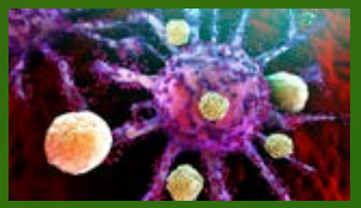

Report Summary

The challenges facing the development of vaccines and immunotherapies are complex, but companies are actively finding innovative solutions. Throughout this eBook, we've seen how advancements in mRNA technology, nanoparticle delivery, and cancer immunotherapy are paving the way for safer, more scalable, and more precise treatments. However, hurdles like ensuring scalability, addressing reactogenicity, and enhancing the precision of therapeutic targeting remain prominent.

To tackle these issues, companies are focusing on optimizing manufacturing processes, improving delivery mechanisms such as biodegradable lipid nanoparticles, and leveraging data-driven platforms to streamline production. For example, efforts to enhance mRNA vaccine efficacy, as demonstrated by Sanofi, are complemented by breakthroughs in cancer immunotherapy, where neoantigen-targeting technologies like those from NEOGAP Therapeutics are pushing the boundaries of personalized medicine.

Looking ahead, the future of vaccines and immunotherapies appears promising, with continued innovations that could revolutionize the fight against both infectious diseases and cancer. These developments will be further discussed at our upcoming event, NextGen Biomed 2025 from 12 - 14 March 2025, which will feature focused sessions on vaccines and immunotherapies, among other cutting-edge biomed topics. It will provide a platform for in-depth conversations on the latest breakthroughs and how the industry can continue to evolve.