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Meeting Abstracts

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Proceedings of the 3rd Global Conference on Cell & Gene Therapy Summit (CGT – 2026)

Session I: Foundations & Translational Advances in Cell and Gene Therapy

The Development of Induced Pluripotent Stem Cell-derived Dopaminergic Progenitors for Parkinson's Disease

Howard J Federoff*

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Abstract

Kenai therapeutics is prosecuting a Ph1b/2a trial in idiopathic Parkinson's disease (PD) with an induced pluripotent stem cell-derived drug asset. The asset is an off-the-shelf, cryopreserved drug product that constitute dopaminergic progenitor cells. Kenai delivers these into the putamen of PD patients with an interest in safety and tolerability. In addition, clinical outcome measures and neuroimaging are readout that are also gathered. In this presentation the background on Kenai's drug product, preclinical data and trial design will be discussed.

Genomic Integration of Severe Acute Respiratory Syndrome Coronavirus-2 Sequences in Virus Infected and Viral RNA Transfected Human Cells

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Massachusetts Institute of Technology, USA

Abstract

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) sequences can be reverse-transcribed and integrated into the genomes of virus-infected cells by a LINE1-mediated retrotransposition mechanism. Whole genome sequencing methods revealed the footprints of LINE1 mediated retrotransposition (target site duplication, presence of a LINE1 endonuclease recognition consensus sequence and presence of a polyadenylation sequence at the integration site) indicating integration by the well-defined "target-site primed reverse transcription" mechanism. We have recently confirmed these results [1], and indirect evidence also indicates that retrotransposition of viral sequences occurs in tissues of virus infected patients because virus infection is toxic to the infected cells [2]. We were not able to isolate cells with retrotransposed nucleocapsid (NC) RNA copies. We have established an RNA-based reporter system to study LINE1-mediated retrotransposition. The RNA reporter system enables direct assaying retrotransposition of RNA introduced into cells and avoids the need to define parameters of RNA production and processing from transfected DNA plasmid used in the classic DNA plasmid reporter assay. We compared retrotransposition of human LINE1 (L1PA1), SARS-CoV-2 NC, green fluorescent protein and human globin RNA. We found that in-cis retrotransposition of LINE1 RNA was 10 to 100-fold more frequent than in-trans retrotransposition of the other RNA species, consistent with previous results. The reporter assay showed that SARS-CoV-2 NC subgenomic RNA was retrotransposed by LINE1, validating our previous results in virus-infected cells. The 3' untranslated region sequence of SARS-CoV-2 enhanced in-trans retrotransposition of all tested RNA species, suggesting that sequence context of the RNA influences the efficiency of LINE1-mediated retrotransposition [1]. The RNA-based reporter was sensitive and robust as it readily identified not only in-cis but also in-trans retrotranspositions which were not detected by the DNA-based reporter assay. Thus, the RNA reporter assay provides a useful and sensitive tool for studying LINE1-dependent trans-mobilization of any RNA.

References

1. Zhang L, Richards A, Barrassa MI, Hughes SH, Young RA, et al. 2021. Reverse-transcribed SARS-CoV-2 RNA can integrate into the genome of cultured human cells and can be expressed in patient-derived tissues. *Proc Nat Acad Sci USA*

118(21): e2105968118. https://doi.org/10.1073/pnas.2105968118

2. Zhang L, Punam B, Flamier A, Barrasa MI, Friesen M, et al. 2023. LINE-mediated reverse transcription and genomic integration of SARS-CoV-2 mRNA detected in virus-infected but not in viral mRNA-transfected cells. *Viruses* 15(3): 629. https://doi.org/10.3390/v15030629

Building the Bridge: Academic Good Manufacturing Practice Strategies for Translational Cell and Gene Therapy

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Abstract

Cell and gene therapies (CGTs) are advancing rapidly, creating new demands for good academic manufacturing practice (GMP) facilities to operate as translational engines that bridge discovery, compliance, and scalable clinical manufacturing. Unlike large industrial sites, academic centers must manage diverse product portfolios, constrained resources, and accelerated timelines while maintaining quality and regulatory rigor. This presentation will share strategies for developing resilient GMP frameworks that support investigational new drug-enabling CGTs in academic environments. A core element of success is risk-based quality management aligned with Foundation for the Accreditation of Cellular Therapy, College of American Pathologists, US Food and Drug Administration, and International Council for Harmonisation standards. Practical examples include bridging validations for rapid sterility methods, and risk-based decision tools that streamline operations while sustaining compliance. Equally important is workforce and culture development. Cross-functional teams spanning quality analyst, quality check, production, and regulatory must be empowered through structured training and shared values to deliver consistent, inspection-ready outcomes. Finally, I will discuss scalability and future directions: academic GMP sites are uniquely positioned as innovation hubs that de-risk early pipelines, accelerate first-in-human studies, and partner with industry and regulators to expand access.

Session II: Analytical Strategies, Vectors, Delivery & Precision Targeting

Milestone Momentum in Viral Vector Development: A Strategic and Flexible Approach to Driving Client Program Success

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Abstract

As the field of cell and gene therapy rapidly evolves, developers face complex challenges at every stage of their journey. Contract development and manufacturing organizations (CDMOs) are essential partners, providing the technical expertise and resources necessary to navigate these hurdles effectively. As a proven CDMO partner, MilliporeSigma, with over three decades of experience in viral vector development and manufacturing, offers the scalability and reliability required to advance complex programs with confidence. This presentation explores how we leverage our established production platforms, regulatory know-how, and operational flexibility to accelerate timelines and enable our clients to achieve their next milestone, ranging from earliest proof-of-concept to market access, and anywhere in between. Through case studies, we will highlight our adeno-associated virus and lentivirus production platforms, showcasing successful client projects that demonstrate our capability to navigate the complexities of cell and gene therapy development. Join us as we empower your journey towards groundbreaking therapies with the strategic support that drives success to every milestone.

De-risking Gene Therapy Programs Through Robust Particle Characterization

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Abstract

Evaluating particles during in-use clinical simulation provides critical insight into risks that may not be captured by standard release testing but directly impact patient safety and program success. Utilizing a broad suite of methodologies to enable rapid identification of particle origin, supports effective root-cause investigations, and reduces regulatory and program risk. Early phase-appropriate particle characterization builds product understanding, supports comparability, and establishes a scalable analytical foundation for late-stage development and regulatory submissions.

Integrated Bioanalytical Strategies for Complex Adeno-associated Virus Therapeutics

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Abstract

The development of adeno-associated virus-based (AAV) gene therapies for complex therapeutic indications require sophisticated bioanalytical frameworks to evaluate delivery, persistence, and efficacy. As pipelines evolve to include complex payloads, such as novel transcriptional regulators and AAV-driven siRNA, traditional single-analyte assays often fall short. Our objective was to develop a "fit-for-purpose" bioanalytical suite that utilizes multiplexed digital polymerase chain reaction (PCR) for the absolute quantification of vector genomes and genome integrity across multiple capsids, while concurrently measuring complex transgene expression as well as downstream target engagement in discrete target tissues. This framework addresses the critical industry need for matrix-tolerant assays in heterogeneous tissues, leveraging dPCR as the technology of choice due to its superior sensitivity, specificity, and high tolerance to PCR inhibition compared to traditional qPCR. Throughout the preclinical advancement of tissue-specific therapeutic platforms as well as downstream target engagement, it is vital to understand drug distribution across discrete physiological compartments and associated biofluids while monitoring for off-target accumulation in non-targeted organs. To maximize data yield from limited animal tissues, we implemented an optimized DNA/RNA/siRNA co-isolation process and multiplexed assays to obtain multiple readouts, including distinct transgene expressions and reference genes, from a single sample. Furthermore, we evaluated stem-loop, two-tailed, and splintR-ligation PCR methods for mature siRNA measurement to ensure accurate quantification without template interference. This integrated strategy establishes a reliable correlation between cellular kinetics, biodistribution and the resulting transgene or protein effect, providing the rigorous data necessary to inform dose selection and capsid engineering in next-generation gene therapy pipelines

Revealing Hidden Heterogeneity Using SPARTA®'s Single Particle Analytics for Compositional Assays and Beyond

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Abstract

Nano formulations have proven to be a versatile and translatable modality for future medicines, however, there are remaining challenges hindering the translation of future nanomedicines. Specifically, the difficulty in controlling self-assembly mechanisms and reagent concentrations on the nanoscale leads to population heterogeneity in loading, surface functionalization and chemical composition. These complex, multi-component systems therefore require detailed analytical methods, including single particle level detail. Therefore, Single Particle Automated Raman Trapping Analysis (SPARTA®) has been developed as a label-free, non-destructive technique to measure the detailed chemical profile of a nanoparticle population with single particle-level detail. This technique can be applied for detailed characterization of a range of nanocarriers including lipid nanoparticles (LNPs), exosomes, liposomes, polymer nanoparticles and viral vectors, to assess their heterogeneity, functionalisation degree, loading and preparation quality including aggregation and contamination. SPARTA®, commercialized by SPARTA Biodiscovery is available through the flagship automated gen 2 instrumentation system (AGIS-I) benchtop analyzer. The AGIS-I has already been adopted by academia and industry, accelerating development pipelines, improving product/formulation characterisation, and supporting robust decision-making. We will look at case-study examples assessing label-free compositional profiling of a range of different formulations such as LNPs and extracellular vesicles, including looking at heterogeneity of targeting moieties presented on nanoparticle surfaces, drug loading studies and contamination screening (Figure 1).

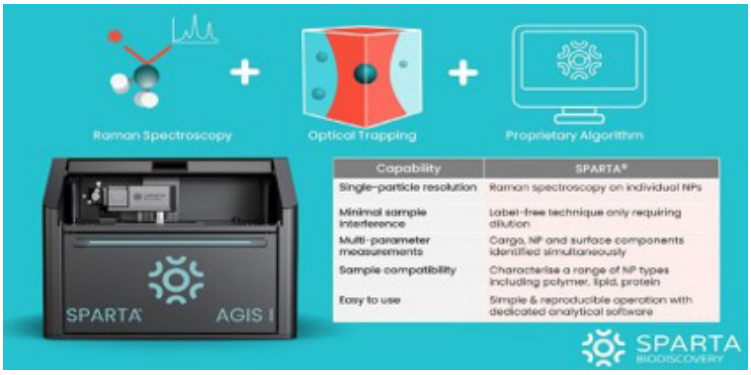

Figure 1: SPARTA biodiscovery is available through the flagship AGIS-I benchtop analyzer.

Clinical Development of Adeno-associated Virus-based Gene Therapy – Pre-existing Immunogenicity and the Impact on Science, Regulatory, and Patients

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Abstract

Immunogenicity testing has emerged as a critical factor in patient enrollment for gene therapy clinical trials. The field has witnessed a dramatic surge in gene therapy programs advancing to the clinic, driven by a remarkable wave of innovative therapeutic approaches. At the same time, regulatory expectations for the assays used to screen and select (or exclude) patients, have evolved substantially. This presentation will provide an overview of the underlying biology, the progression of regulatory guidance, and the real-world impact of these changes on patients.

Accelerating Gene Therapy Development with an U.S. Food and Drug Administration/Center for Biologics Evaluation and Research Advanced Manufacturing Technology-designated Nanoneedle Analytics Platform

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Abstract

The rapid expansion of the gene therapy landscape has fundamentally shifted the treatment paradigm for genetic disorders, moving the industry toward industrialized, platform-based modalities. However, as these genetic medicines advance from ultra-rare, to rare and more common diseases, the inherent molecular heterogeneity of delivery vectors, particularly recombinant adeno-associated virus (rAAV) products, presents a severe bottleneck. Maintaining stringent process control and ensuring product quality requires a complex matrix of legacy analytical methodologies. The persistent gap between early-stage physical analytics and true clinical potency drives operational complexity, constrains manufacturing scalability, and increases chemistry, manufacturing, and controls (CMC) uncertainty. To address these challenges, the U.S. Food and Drug Administration (FDA)/Center for Biologics Evaluation and Research (CBER) Advanced Manufacturing Technology (AMT) designation was established to accelerate the integration of innovations that substantially improve manufacturing efficiency and product consistency. Adopting an AMT-designated platform provides a strategic regulatory pathway, mitigating CMC risks through prioritized FDA engagement and expedited investigational new drug/biologics license applications reviews. Here, we present an integrated, multi-analyte AAV analytics platform utilizing nanoneedle technology that has secured the FDA/CBER AMT designation for its capacity to enhance product quality and reduce development timelines. This technology enables the harmonized characterization of capsid attributes and viral genome integrity within a single, unified assay framework. By merging precise full-length transgene quantification with total capsid measurements, the platform provides viral vector quantifications and accurate genome integrity analysis (true empty/full/partial ratios), bridging the gap between physical titers and potency. This minimizes analytical variability, reduces process development costs, and provides high-fidelity data insights from upstream process development to release testing. Ultimately, integrating this AMT-designated technology early in development empowers manufacturers to strengthen product quality, minimize analytical variability, and significantly accelerate the timeline for bringing next-generation gene therapies to patients.

Vivo Cell: An Accessible Delivery System with Proven Efficacy for *In Vivo* Engineering of T-cells

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Abstract

Cell and gene therapies hold great promise for treating complex diseases. For example, engineered chimeric antigen receptor (CAR) T-cell therapies have achieved clinical success in treating hematologic malignancies, and have the potential to treat solid tumor malignancies and autoimmune diseases. Despite this success and promise, widespread adoption and access to these life-changing therapies remains limited by scalability of manufacturing. Furthermore, current CAR T-cell therapies have shown limited efficacy against solid tumors. To overcome these challenges, Syenex developed Vivo-T, a safe, efficient, and broadly accessible T-cell-specific lentiviral vector system capable of delivering CAR expression constructs directly to T-cells within the patient. In collaboration with The Jackson Laboratory, we characterized Vivo-T delivery and efficacy using an anti-CD19 CAR and a B-cell lymphoma target in both humanized peripheral blood mononuclear cells (PBMC) and humanized CD34+ cell mouse models. We further characterized the safety profile of Vivo-T by evaluating performance across multiple vector doses and assessing transduction of both on-target and off-target cell populations. In collaboration with a third-party cell and gene therapy developer, we evaluated Vivo-T delivery and efficacy across vector doses using a custom CAR construct in a solid tumor model in humanized PBMC mice. In both B-cell lymphoma mouse models, Vivo-T consistently demonstrated high T-cell transduction, rapid and robust CAR-T expression and expansion, and potent anti-tumor activity against Raji cells. Compared to ex vivo engineered CAR T-cells, Vivo-T produced more CAR T-cells and comparable tumor control. Vivo-T vector dose correlated with CAR T-cell generation and tumor clearance, with significant antitumor activity detected even at low doses. We also identified Vivo-T vector designs with strong specificity for delivery to T-cells and minimal evidence of off-target delivery. In the solid tumor mouse model, we also observed dose-dependent T-cell transduction and expansion as well as tumor clearance across vector doses. Together, these results indicate that Vivo-T, a system readily compatible with current therapeutic genes of interest for *ex vivo* CAR-T, is an efficient and safe *in vivo* T-cell engineering system with potential for treating both liquid and solid tumors. Vivo-T is a broadly accessible, *in vivo* gene delivery system that offers solution to the limitations of current T-cell

therapy manufacturing. By simplifying manufacturing, reducing costs, and enabling targeted cell-delivery, VivoCell™ products will broaden the reach and improves outcomes of next generation genetic medicines.

Transforming Medicine from Within

Casey Perkins*

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Abstract

Neurodegenerative diseases such as Parkinson's and Alzheimer's remain among the most intractable challenges in modern medicine, constrained by the dual barriers of the blood-brain barrier (BBB) and the endosomal compartment, which together trap the majority of therapeutics before they reach their intended targets. Mercury bio is an intracellular immunotherapeutic biotech advancing a new class of therapeutics designed to overcome these limitations. Our patented MB-TIP™ technology uses yeast extracellular vesicles (yEVs)as a delivery vehicle that crosses the BBB, penetrates neuronal membranes, achieves endosomal escape, and releases cargo directly into the cytoplasm. Our lead program targets Parkinson's disease through delivery of anti-α-synuclein nanobodies to neurons of the substantia nigra. *In vivo* studies demonstrate significant reductions in pathogenic α-synuclein aggregates following peripheral administration, with supporting evidence from western blot validation, mitochondrial function assays, and biodistribution studies. The same approach is being extended to Alzheimer's disease as a follow-on indication. Beyond nanobodies, MB-TIP™ accommodates diverse cargo including mRNA, small molecules, and clustered regularly interspaced short palindromic repeats machinery, supporting three therapeutic strategies: NPAD™, TBC™, and NANOTAC™. This presentation will review the scientific rationale, *in vivo* evidence to date, and translational roadmap for advancing MB-TIP™ toward investigational new drug-enabling studies, alongside broader implications for intracellular delivery across central nervous system and beyond. Collectively, this body of work reframes what is achievable in neurodegenerative disease by transforming medicine from within the cell itself.

Session III: Precision Cell Therapy & Next-generation Engineering Approaches

Functional Characterization of Immune Cell Therapy Starting Materials to De-risk Manufacturing and Clinical Trials

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Abstract

Human peripheral blood mononuclear cells (PBMCs) isolated by apheresis are used for a variety of downstream applications, such as feeder cells and starting material for the manufacture of cell immunotherapy products, including chimeric antigen receptor-T, natural killer (NK), tumor-infiltrating lymphocyte and T-cell receptor-based approaches. While significant clinical progress has been made, variability in clinical responses are an issue. Multiple factors lead to this and including variability in the potency and consistency of the cell therapy itself. A key driver of the variability in the starting materials such as PBMC attributes, whether from healthy allogeneic donors or autologous patients. Studies have shown the diversity of immune function attributes that correlate with clinical outcomes such as effector function, metabolic fitness, memory potential and expansion potential vary significantly across donors and patients and impact final product potency and effectiveness in the clinic. Excellos has developed an analytical platform (Escore), which evaluates these attributes on various cell types, including T, NK and PBMC cell populations and has shown significant variability in these immune related factors in healthy young donors. The Escore allows assessment of the donor/patient starting material to assure higher quality starting material for final product manufacturing or to screen autologous patients for suitability of their immune cells for production of an effective therapy. Doing so has multiple benefits, including assurance of manufacturing success, increased potency, lower cost of goods sold and improved safety margins by the potential use of lower cell doses of the better-quality final product in patients.

The Mygotic Process: The Next Advancement in Autologous Totipotent Stem Cells from Somatic Cells

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Mygogenesis LLC, USA

Abstract

There are three models for cell therapies and regenerative medicine. These include embryonic stem cells (ESC), induced pluripotent stem cells (IPSC) and now mygotic process cells. All these have a pluripotent nature. ESC are the golden standard with the ability to differentiate into all cell and tissue types. However, they are not autologous, and are not used in view of ethical, legal and political issues and research defunding. IPSC's were developed. However, they are produced with viral vectors, mRNA, plasmids or other unnatural methods to deliver transcription factors to attempt production of pluripotent cells. This allows changes to the underlying DNA and chromosomal structure and introduces genetic changes and persistent over expression of embryonic genes. In view of this, there has been difficulty in developing reliable, autologous, robust, safe therapeutic cells and tissues for regenerative medicine. which makes them wholly unsuitable for human therapeutic applications. The Mygotic Process™ is revolutionizing the production of autologous pluripotent stem cells from somatic cells. This process involves the natural transformation of somatic cells to totipotent then to pluripotent stem cells, which are naïve autologous embryonic stem cells, devoid of any epigenetic changes. These are laboratory produced zygotic clones that we term Mygotes™, primed to become any cell type. Our proprietary process utilizes novel physical principles to remove epigenetic factors from the DNA of somatic cells returning them to a pluripotent state. No viral, mRNA, or other vectors are used. There are no changes to the DNA. This powerful, novel platform addresses the limitations of iPSCs, which currently exist for cellular therapies, gene therapies, and regenerative medicine. These cells can be sourced from a patient rapidly and efficiently to prepare autologous stem cells that can deliver therapies back to a patient without fear of cell rejection, changes in the DNA, or oncogenic changes.

Proto Natural Killer Cells from Pluripotent Stem Cells for Treatment of Metastatic Cancers

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Abstract

Natural killer (NK) cells eliminate circulating tumor cells to suppress cancer metastasis, which is responsible for as much as 90% of cancer-associated mortality. However, the biggest challenges facing NK cells as therapeutics are; (1) efficient supply chain: sustainable cell sources for production, (2) reasonable cost: affordable by most patients, and (3) scalable manufacture: industrial scale of healthy and efficacious cells for patients. HebeCell has developed a robust proprietary 3-dimensional (3D) ProtoNK platform with superior scalability and consistency compared to existing approaches for industrial scale manufacturing of pluripotent stem-NK cells: game changing, cost-effective, and off-the-shelf ProtoNK products for all patients around the world. In addition to expressing common NK activating and inhibitory receptors, about 80% of our ProtoNK cells are $CD8a^+$, which are substantially more potent than current other sources of NK cells. Good laboratory practice toxicology and tumorigenicity studies showed no association with any preterminal mortality, clinical observations, mass growth (tumor), body and organ weight changes, macroscopic or microscopic findings. Investigational new drug enabling animal studies demonstrated that our ProtoNK cells are particularly effective in treating metastatic cancers: significantly inhibited/prevented Ewing sarcoma lung and liver metastasis, paving the way for metastatic cancer treatment. First IIT clinical study for patients with metastatic Ewing sarcoma will start enrollments early 2026. In summary, our proprietary 3D ProtoNK platform allows scalable and reproducible production of ProtoNK cells, which will be affordable and available for ordinary patients and can be rapidly deployed worldwide.

Cell Therapy and Antigen-defined Precision Targeting in B-cell-mediated Autoimmune Disease

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Sanofi, USA

Abstract

B-cell-mediated autoimmune diseases are sustained by autoreactive B-cell clones that produce pathogenic autoantibodies and amplify inflammatory cascades. Therapeutic strategies targeting B-cells have reshaped disease management; however, most currently approved or investigational approaches rely on broad lineage depletion rather than selective elimination of pathogenic clones. Emerging cell therapies seek to move beyond lineage-wide depletion toward antigen-and B-cell receptor (BCR)-defined precision targeting. Pan-B-cell depletion strategies targeting surface markers such as CD20, CD19, or CD22 reduce circulating B-cell populations through antibody-mediated mechanisms. These therapies have demonstrated clinical benefit and are supported by established manufacturing and regulatory frameworks. Nevertheless, depletion is not clone-restricted, and protective humoral immunity is affected alongside autoreactive compartments. Furthermore, antibody-mediated cytotoxicity depends on endogenous effector mechanisms and does not selectively eliminate antigen-defined pathogenic B-cell subsets. Cell therapy represents a mechanistically distinct modality in which engineered lymphocytes mediate direct cytotoxicity independent of Fc or complement engagement. While CD19 chimeric antigen receptor-T therapy has been associated with drug-free remission, profound B-cell depletion, and naïve B-cell reconstitution in refractory systemic lupus erythematosus, the target landscape is expanding to address additional pathogenic compartments, including B-cell maturation antigen (plasma cell-enriched biology) and investigational B-cell lineage targets such as CD20 or CD22. Across platforms, potential advantages include antigen-driven expansion and persistence, serial cytotoxic engagement, and reduced dependence on endogenous effector variability, balanced against risks such as cytokine release, lymphodepletion requirements, and manufacturing complexity. To move beyond lineage markers, next-generation cell therapies incorporate BCR specificity. Chimeric autoantibody receptor T (CAAR-T) platforms display disease-defining autoantigens, such as desmoglein 3 (Dsg3) in pemphigus vulgaris, enabling selective elimination of autoreactive B-cells based on antigen recognition. In parallel, BCR-pattern-restricted strategies, including targeting IGHV4-34-expressing B-cells enriched in systemic lupus erythematosus, exploit stereotyped autoreactive binding signatures to confine depletion to disease-relevant subsets. These approaches enhance biological precision while preserving non-pathogenic B-cell populations. Extending this antigen- and BCR-defined targeting paradigm beyond engineered cell therapies, we recently developed a Dsg3-Fc fusion molecule designed to selectively engage Dsg3-autoreactive B-cell receptors and harness endogenous effector mechanisms for targeted elimination. *In vitro* and *in vivo* studies demonstrated selective depletion of Dsg3-specific B-cells, reduction of pathogenic autoantibodies, and attenuation of disease without lineage-wide B-cell loss. In conclusion, therapeutic evolution in B-cell-mediated autoimmunity reflects a transition from pan-B cell depletion toward antigen- and BCR-defined precision targeting. Integrating advances in cell therapy with antigen-engineered biologics may enable selective immune editing while preserving protective humoral immunity.

Multi-lineage Cellular Infusion Immunotherapy for Cancer

Richard C. Koya*

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Abstract

Engineered T-cells with T cell receptor (TCR) have demonstrated efficacy as cancer therapy, however their anti-tumor effect is often short-lived. We developed a new platform based on tumor-associated antigen specific TCR-T cells that target relevant antigens as a cellular immunotherapy. Our technology consists of major histocompatibility complex II (MHC)-TCR engineered human hematopoietic stem/progenitor cells (hHSC) which leads to durable *in vivo* supply of fully active T cells with anti-tumor activity and simultaneously providing sustained help to co-injected MHC I-TCR transduced (mature) effector T-cells. We will present results that confirm that the approach induces long-lasting tumor rejection in pre-clinical models. This will be the first time that a combined approach of MHC II- TCR transduced hHSC with MHC I-TCR transduced peripheral blood mononuclear cells leads to a synergistic and efficient in vivo control of tumor burden with high potential to benefit cancer patients.

Flowfect® Technology Enables Scalable Non-viral Transfection for Cell Therapy Development

John Zhao*

Process Development, Cell and Gene Therapy, USA

Abstract

Non-viral genetic modification of primary human T-cells remains a major challenge in developing advanced cell therapies, particularly for applications requiring delivery of DNA for clustered regularly interspaced short palindromic repeats (CRISPR) ribonucleoprotein (RNP) knock-in or for transposon/transposase integration systems. Achieving high efficiency and viability depends on balancing biological and process complexities while dealing with technological restrictions. Kytopen's Flowfect® technology integrates continuous fluid flow with precise control of electric fields to deliver a wide range of single or multiplexed payloads composed of mRNA, DNA, and/or RNPs, while preserving cell functionality. Leveraging the Flowfect Discover™ 96-well platform, we employed a machine learning driven approach to systematically optimize buffer formulations and electro-mechanical parameters. This led to the development of the Flowfect® Omni buffer, which significantly enhanced DNA delivery efficiency, increasing expression from 30% to 73% (Figure 1). Critically, optimized formulations and parameters translated directly to the Flowfect Tx® platform at ≥1 mL volumes, capable of processing billions of cells within minutes. Together, these findings demonstrate that combining algorithm-driven buffer optimization with scalable Flowfect® technology enables efficient, non-viral delivery of complex payloads, including RNP knock-in and transposon gene integration, across discovery to manufacturing scales. This system accelerates development timelines and supports rapid translation of next-generation, non-viral cell therapies to the clinic.

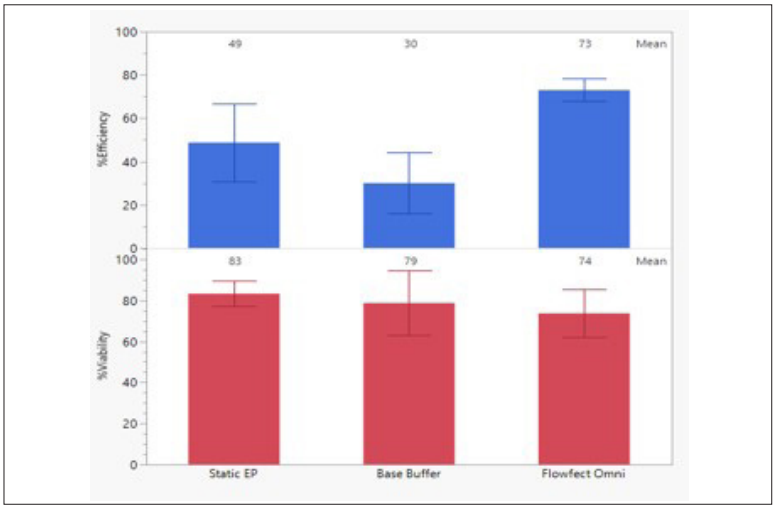

Figure 1: Machine learning algorithm driven buffer formulation development improved transfection of 4.8 kb plasmid DNA over base formulation. Data is aggregated from multiple isolated T cell donors. Error bars indicate ± 1 standard deviation.

Session IV: Cell Therapy Manufacturing, Artificial Intelligence & Process Innovation

AI-driven Decision Making in Genomic Medicine Development and Manufacturing

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Abstract

Genomic medicines – spanning cell, gene, and nucleic acid therapies (Cell and Gene Therapy (CGT)), have the unprecedented potential to treat and cure genetic disorders, cancer, and many other devastating diseases. However, the future of CGT is seriously hampered by very real and practical challenges in process development and manufacturing. Today, next-gen technologies are producing a multiplicity of data that could be transformed into actionable knowledge for production with the help of artificial intelligence (AI). BioCurie's mechanistic AI (mAI)-driven software enables CGT developers and manufacturers to improve speed, quality, cost of CGT production, thereby increasing patient access. Developed by Richard Braatz, thought leader in AI and advanced modeling for biomanufacturing, the mAI BioCurie Platform™ empowers lab scientists to conduct millions of experiments *in silico* to quickly predict and optimize manufacturing conditions for each therapy. The goal is to transform CGT process development and manufacturing from an inefficient, labor-intensive, and unpredictable state to a data-driven, intelligent, and robust state that enables faster delivery of lifesaving therapies that are safe, effective, and affordable.

C-Stem™: A Breakthrough Manufacturing Technology Addressing Scale, Quality, Safety, and Efficacy to Provide Cell Therapy for All

François Gianelli*

TreeFrog Therapeutics, France

Abstract

This presentation will explore innovative manufacturing modalities for cell therapies, addressing how emerging technologies are reshaping production processes. Scalable manufacturing of pluripotent stem cell (PSC)-based therapies remains a major bottleneck to commercial translation. Although differentiation processes are transitioning from two-dimensional (2D) to 3D systems to enable scale-up, conventional approaches relying on free-floating aggregates exhibit non-linear behavior across scales. Variations in bioreactor hydrodynamics, including mixing and shear forces, lead to inconsistent outcomes and limit the transferability of processes optimized at small scale to large-scale production. Here, we present C-stem™, a next-generation encapsulation-based manufacturing platform developed by TreeFrog Therapeutics, designed to overcome these limitations. This proprietary high-throughput cell encapsulation technology enables the expansion and differentiation of human PSCs within biomimetic 3D microenvironments in standard stirred-tank bioreactors. The capsules create a protective and tunable niche that buffers cells from scale-dependent physical perturbations, allowing precise control over proliferation and differentiation. Using this platform, we demonstrate linear scalability of PSC expansion (>300×/week) and differentiation across bioreactor volumes, establishing a bioreactor-agnostic process. Encapsulated PSCs reproducibly recapitulate key features of early human epiblast development including rosette organization and epithelial polarization. By modulating extracellular matrix composition within the capsules, we demonstrate that proper apico-basal polarization is critically dependent on matrix-derived cues rather than intrinsic cellular programming. In addition, the encapsulated microenvironment mitigates selective pressures that can drive genomic instability, thereby supporting the maintenance of genomic integrity during expansion and differentiation. Together, these results establish C-Stem™ as a robust and scalable platform for industrial manufacturing of PSC-derived cell therapies, enabling predictable scale-up while preserving developmental fidelity and cell quality.

Challenges in Scale-up, Characterization, and Comparability of Advanced Therapies (Case Study of Late Phase Asset Moving to Approval)

Phillip Ramsey*

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Abstract

Development of cell and gene therapies comes with a number of chemistry, manufacturing, and controls (CMC) opportunities and challenges and involves navigating a range of complexities that differ significantly from traditional biologics. This presentation will explore these opportunities and challenges and the necessity of adopting a progressive, incremental approach including phase-appropriate strategies to streamline from the traditional process to progress these therapies. We will discuss potential solutions for adapting these strategies to align with evolving regulatory guidance. A case study will be presented for a late-stage program with an accelerated approval pathway for an adeno-associated virus based product. The process validation and comparability strategy will be presented along with an alternate product presentation that provides improved cost of goods (Figure 1 and figure 2).

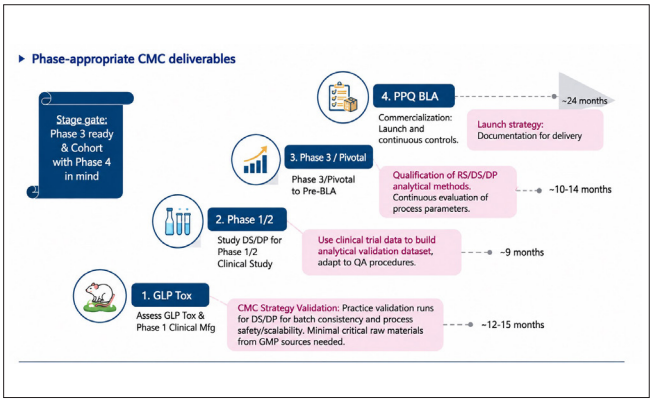

Figure 1: Phase appropriate CMC deliverables.

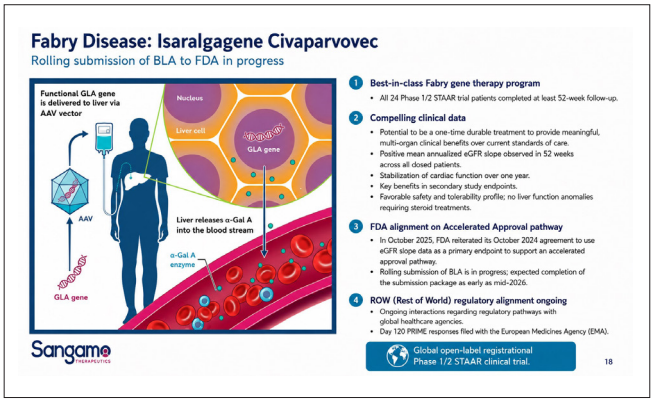

Figure 2: Fabry disease: isaralgagene civaparvovec.

Predictive Virtual Signalling Models: A Development-driven Framework for Rational Cell Therapy Design and Accelerated Clinical Translation

Samantha Dale Strasser*

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Abstract

Background: Pluripotent stem cell (PSC) therapies represent a transformative frontier in regenerative medicine. However, the translation of PSCs into clinical products is frequently hindered by an inability to comprehensively predict and control how cells respond to external signals during differentiation. Current efforts to develop protocols for target therapeutic cell types often require years of empirical, trial-and-error optimization of growth factor cocktails and timing. A predictive framework for signalling-driven state transitions would shift this paradigm to systematic engineering and open the doors to transformative therapies for patients.

Methods: We utilize a proprietary capsule-based, split-and-pool experimental platform to perform massively multiplexed, sequential perturbations of PSCs. By leveraging the paradigm of developmental biology and stem cell's innate ability to adopt all physiological cell states, we generated rich, pan-context signalling data to train a general model of cell signalling. Cellular responses were profiled using RNA sequencing to train machine learning models that map initial cell states and applied signals to predicted future states, forming a virtual cell-signalling model.

Results: We executed a massive-scale, fully tracked combinatorial perturbation experiment that successfully recapitulated complex human developmental pathways across all embryonic germ layers. Modeling demonstrates that this data is able to predict signalling behaviour across a range of cell contexts. This enables the model to screen countless candidate protocols *in silico*, predicting which sequence of signals will yield the highest purity of a therapeutic cell type. These findings demonstrate that PSC fate decisions are inherently learnable and can be generalized across diverse developmental trajectories.

Implications: This work establishes a scalable framework for building a foundation model of virtual cell signalling to guide cell therapy discovery and development. By approaching protocol optimization like an engineering discipline, predicting *in silico* before bench testing, protocol discovery time can be reduced from years to months. By replacing empirical trial-and-error with predictive modeling, this framework provides a foundation for rational therapy design, ensuring that the promise of regenerative medicine is fulfilled with urgency for patients.

Manufacturing CD1a Chimeric Antigen Receptor-T Cells for T-acute Lymphoblastic Leukemia: Overcoming Tumor Cell Contamination from Apheresis to Good Manufacturing Practice Release

Víctor Manuel Díaz Cortés*

OneChain Immunotherapeutics, Spain

Abstract

T-cell acute lymphoblastic leukemia (T-ALL) is an indication of very high unmet medical need, affecting both adults and children. It poses distinctive challenges for chimeric antigen receptor (CAR)-T cell manufacturing due to the shared lineage between malignant blasts and therapeutic T cells. CD1a has emerged as a highly selective target for cortical T-ALL, supported by extensive preclinical studies, intellectual property protection (WO2020165350), and translational research culminating in an ongoing first-in-human clinical trial (NCT05679895). While CD1a-directed CAR-T cells demonstrate potent and selective anti-leukemic activity, their clinical manufacturing requires disease-specific process adaptations beyond conventional CAR-T production workflows. A major manufacturing challenge arises from the frequent, albeit variable, presence of circulating leukemic blasts in leukapheresis material obtained from T-ALL patients. This creates a critical risk of inadvertent CAR transduction of malignant cells, which could compromise product safety and efficacy. To mitigate this risk, the CD1a CAR-T manufacturing process incorporates a dedicated blast depletion step prior to CAR transduction, together with a final detection step, introducing additional operational complexity and quality control requirements compared with standard autologous CAR-T processes. In this presentation, we will describe how insights from preclinical development informed the design of a clinically compliant and automated manufacturing strategy addressing the specific constraints of T-ALL. Particular emphasis will be placed on the implementation of blast depletion methods compatible with good manufacturing practice production, including process robustness and integration into the overall manufacturing workflow. The speaker will discuss the analytical and quality control framework established to ensure quantitative depletion of leukemic blasts prior to transduction, as well as sensitive in-process and release assays designed to detect and exclude the presence of transduced tumor cells in the final CAR-T product. In addition, the development of potency assays tailored to the biological mechanism of action of CD1a CAR-T cells will be discussed. These assays are designed to reflect target-specific cytotoxic activity and functional CAR expression, supporting product comparability and batch release in a complex autologous setting. The presentation will also address ongoing efforts to introduce automation into key manufacturing steps to improve process consistency, reduce operator-dependent variability, and facilitate future scalability. Finally, preliminary manufacturing experience and early clinical data from the ongoing clinical trial will be presented, illustrating how disease-tailored manufacturing strategies and rigorous quality control approaches can enable the safe clinical translation of CAR-T therapies for T-cell malignancies (Figure 1).

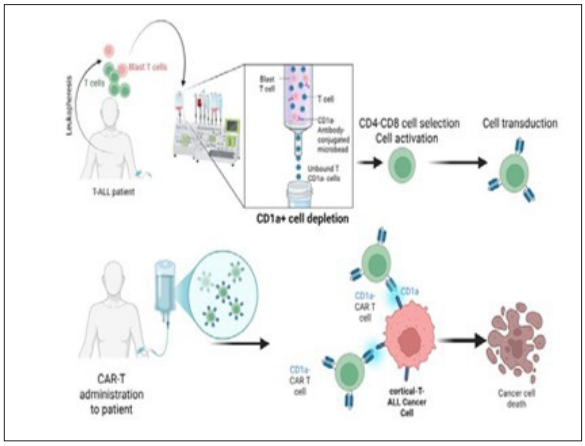

Figure 1: Manufacturing CD1a CAR-T cells for T-ALL.

Continuous Adaptive Multiparameter in Action: Artificial Intelligence-enabled Continuous Adaptive Control for Decentralized Chimeric Antigen Receptor-T Manufacturing

Ohad Karnieli*

ADVA Biotechnology, Israel

Abstract

Artificial intelligence (AI)-enabled continuous adaptive control for decentralized chimeric antigen receptor (CAR)-T manufacturing next-generation cell therapy manufacturing demands systems that can continuously sense, interpret, and respond to the dynamic biology of living products. The Adva X3™ platform, powered by continuous adaptive multiparameter (CAMP) control, represents a major leap toward this future. In this talk, we present how X3 AI and CAMP together establish a decentralized, intelligent manufacturing architecture capable of delivering high-quality CAR-T products directly at the point of care. CAMP technology integrates dense sensor data, inline analytics, and real-time AI models to create a manufacturing environment that is not static, but alive to process variability. Instead of relying on fixed recipes, the system continuously evaluates multiple biological and process parameters, activation markers, metabolic state, growth trajectory, transduction performance, and more, and adapts controls accordingly. This allows the platform to maintain optimal culture conditions despite heterogeneous patient starting material and site-to-site variability, addressing core barriers that have historically limited decentralized manufacturing. We will share a detailed CAR-T case study demonstrating how CAMP's adaptive control loop stabilizes key quality-defining attributes and improves reproducibility. Real-time micro-adjustments to cytokine dosing, feeding schedules, and environmental parameters were driven by predictive X3 AI models that identified early divergence in expansion kinetics and lineage pathways. This resulted in more consistent cell potency, reduced operator burden, and a markedly lower risk of batch failure. From an operational perspective, CAMP shifts manufacturing from manual, labour-intensive oversight to an automated, intelligent system that scales with demand. By embedding continuous optimization directly into the manufacturing pod, the Adva X3 platform enables true next-generation, distributed manufacturing networks, where each site benefits from cumulative learning across the entire fleet while maintaining data segregation required for clinical and regulatory compliance. Looking forward, continuous adaptive multiparameter control is poised to become a foundational layer for all advanced cell therapies from CAR-T to engineered natural killer cells and beyond. By merging automation, AI, and deep biological monitoring, the Adva X3 ecosystem provides a blueprint for responsive, resilient manufacturing systems capable of supporting the global deployment of personalized cell therapies. This talk will highlight how CAMP turns next-generation manufacturing from aspiration into practice, enabling scalable, accessible, and consistently high-quality therapies for patients everywhere.

Constant, Reproducible Cell Conditions in a Decentralized Manufacturing Paradigm

Alicia Henn*

BioSpherix, LLC, USA

Abstract

Patients that need cell therapies the most are often too sick to travel to centralized treatment sites where facilities for cell-based therapeutic manufacturing exist. When considering a distributed manufacturing model of cell therapy manufacturing, enabling the therapy to be performed closer to the patient, the experiences of the cells in the process must be of paramount concern and the environment the cells are in is vital. When patient cells are taken out of an incubator, even in the cleanest cleanroom, they are at their most vulnerable, exposed to highly variable and non-physiologic conditions in room air. Utilizing a closed, modular system, it is possible to control conditions for cells and tissues constantly. Data shows that using the Xvivo System® to enclose human bone marrow mesenchymal stem cells (MSC) under constant temperature and physioxia for all culture and processing steps prevents HIF-1a modulation, reduces cell senescence, and helps maintain cell growth longer than traditional room air conditions. Here, we report taking that one step further to isolate human bone marrow MSC under constant physioxia to produce cell lines that have never encountered room air. Full-time closure of the production environment also enables dramatic reductions in microbial contamination risks by not only physically separating technicians and cultures but also controlling the relative humidity to levels at which microbes cannot reproduce. Data on cell processing conditions that are both Cytocentric® and anti-microbial can also be monitored remotely and integrated with artificial intelligence and digital twins for real-time process control. This closed and reproducible cell production environment can help enable safe distributed cell therapy production networks nearer the patients that need them.

Mitigating Fill/Finish-induced Stress in Cell Therapy Manufacturing: A Risk-focused Strategy

Ryan Murray*

Bayer, USA

Abstract

Cell therapy products, as living modalities, are uniquely sensitive to process-induced stress across manufacturing steps, with the fill/finish phase presenting concentrated risks to viability, potency, and lot consistency. Unlike traditional modalities, cells encounter multiple stressors during formulation and filling, including osmotic fluctuations that can trigger apoptosis and genetic modifications, and physical factors—shear forces, viscosity differences, and density gradients that promote clumping and aggregation. Subsequent cryopreservation or liquid nitrogen storage can exacerbate heterogeneity through cell settling and cryoprotectant chemical gradients, compromising product uniformity. To address these risks, we propose a fill/finish-focused framework that emphasizes in-process monitoring of settling and aggregation, mixing strategies tuned to minimize shear and maintain homogeneous suspensions, and improved handling practices to reduce variability at the point of fill. The approach centers on identifying and controlling critical process parameters such as osmolarity shifts during formulation, shear exposure during transfer, and residence time that can influence aggregation dynamics. We align these controls with regulatory expectations from agencies including U.S. Food and Drug Administration and European Medicines Agency, highlighting the importance of rigorous documentation and traceability to enhance patient safety. This work systematically consolidates current practices, emerging solutions, and practical modifications that monitor and minimize cell stress at fill/finish. By targeting the most stress-intensive steps with robust monitoring and process discipline, manufacturers can improve post-fill stability, maintain cell quality and uniformity, and strengthen compliance for clinical and commercial cell therapy operations.

From Code to Cure: Innovating the Future of Genomic Medicines

Emmanuelle Cameau*

Genomic Medicine, Cytiva, France

Abstract

This presentation highlights the rapid evolution of genomic medicines, focusing on advances in gene and cell therapies, manufacturing innovation, and strategic industry challenges. Genomic medicines now outpace antibody-based therapies in scale and diversity, with a surge in approvals for oligonucleotide, immune cell, and adeno-associated virus (AAV)-based gene therapies. Despite this progress, the field faces significant hurdles: regulatory scrutiny, high costs, and the need for improved delivery systems. Key innovations include the adoption of flexible, automated manufacturing platforms and the development of stable cell lines, such as Cytiva's ELEVECTA™, which enhance efficiency and product quality. Quality control measures, like DFFB knockout, have dramatically reduced host cell DNA impurities in AAV preparations, meeting U.S. Food and Drug Administration standards. Automation and modular approaches are reducing labour costs and process variability, making advanced therapies more scalable and accessible. The convergence of molecular biology and cell processing has enabled landmark achievements, including the first personalized clustered regularly interspaced short palindromic repeats (CRISPR) gene-editing therapy. Lipid nanoparticles (LNPs) are emerging as superior tools for gene editing and delivery, offering higher efficiency and reduced cell handling time compared to traditional methods. Collaborative initiatives, such as the Danaher-IGI Beacon for CRISPR Cures, demonstrate the potential of platform-driven innovation to address rare diseases. Looking forward, the field is moving toward integrated, modular workflows that combine mRNA, CRISPR, and LNP technologies. Standardization and platform approaches are expected to accelerate clinical development and expand patient access. Strategic advances in manufacturing, automation, and delivery are essential for making genomic therapies sustainable, effective, and widely available.

Session V: Viral Vector Manufacturing & Processing

Innovations in Viral Vector Manufacturing: Improving Quality, Scalability, and Purity from Plasmid Design through Good Manufacturing Practice Production

Tatiana Nanda*

SK pharmteco, USA

Abstract

SK pharmteco is a global viral vector contract development and manufacturing organization and a portfolio company of SK Inc., advancing gene therapy manufacturing through innovation designed to improve quality, scalability, and cost-efficiency. Across adeno-associated virus (AAV), adenoviral, and lentiviral platforms, early development decisions and downstream process design can have a profound impact on product quality, manufacturability, and program timelines. One example is Plasmid-IQTM, SK pharmteco's proprietary approach to plasmid design, which builds on internal work showing that origin-of-replication orientation can significantly influence proximal inverted terminal repeat integrity, with important implications for downstream AAV yield and overall quality. These findings underscore how thoughtful construct optimization at the outset can reduce downstream risk and save valuable development time. Additional gains can be achieved by converting adherent-based AAV and adenoviral processes to suspension platforms, enabling greater scale and lower cost of goods without compromising product quality or creating unnecessary comparability concerns. For lentiviral vectors, SK pharmteco's downstream processing innovations are opening new possibilities for both *ex vivo* and *in vivo* applications by improving purity, recovery, and process consistency. Together, these examples position SK pharmteco, not only as a world-class global good manufacturing practice viral vector manufacturer, but as an innovation partner helping gene therapy developers unlock more robust, scalable, and clinically relevant manufacturing solutions.

Toward Profitable Low-cost Adeno-associated Virus Production: Engineered Human Embryonic Kidney Cells and Advanced Manufacturing Tools Combine to Enable High-productivity Producer Cells

Larry Forman*

CHO Plus, Inc., USA

Abstract

Current viral vector manufacturing methods are expensive, limiting gene therapy access and discouraging pharmaceutical and venture investment for developing new treatments. Furthermore, large numbers of doses required for treating common diseases cannot be manufactured at any cost using current methods. Our breakthrough technologies engineered high-productivity cells and non-leaky, inducible promotors—enable efficient, large-scale production of adeno-associated virus (AAV), overcoming current barriers of cost and limited supply. We are also implementing the use of landing pads to shorten the time required to create inducible, stable producer cells. AAV has emerged as a significant therapeutic modality in gene therapy. Challenges such as high cost, poor yield, and variable product quality persist in the viral vector manufacturing space, and we are addressing these problems using two approaches: our cell engineering technologies to increase and improve productivity, and tools such as non-leaky inducible promotors for creating producer cells. Our cell engineering platform for improved AAV production addresses critical challenges in gene therapy manufacturing and presents an innovative modality for improving cells for production of viral vector therapeutics. Our platform, which creates cells with improved AAV production and critical quality attributes, can significantly bolster the efficiency and cost-effectiveness of gene therapy manufacturing, and can accelerate current development timelines. We use a directed-evolution approach based on repeated cell fusions to shuffle the cell genome, and to amplify whole chromosomes of human embryonic kidney (HEK)-293 host cells. Engineered clones with enriched mitochondria phenotypes were isolated, then used as transient-transfection hosts, and for creating stable packaging cell lines. For creation of stable packaging and producer cell lines, we developed a novel, non-leaky inducible system that maximizes capabilities of the inherent viral production machinery. Engineered HEK-293 clones grown in suspension culture exhibited up to 20-fold productivity improvement via triple transient transfection for AAV1, AAV2, AAV5, and AAV9 serotypes with capsid titers as high as 1017 viral particles/L (vp/L) at least 10-fold higher than current industrial manufacturing processes. Screening for certain mitochondria phenotypes resulted in a 2-fold improvement in full-to-empty ratio—up to 55% full in crude supernatants. Finally, our engineered stable packaging cell lines achieved capsid titers of up to 1016 vp/L. We demonstrated a multi-modal cell-engineering platform that has significantly improved yield and manufacturability via transient transfection, and for stable packaging cell line methods. Taken together, our several related platform technologies presented here provide solutions for meeting current and future gene therapy manufacturing challenges.

Breaking the Bottleneck: Intensified Viral Vector and Oncolytic Virus Production via Integrated Tangential Flow Depth Filtration Perfusion

Rachel Legmann*

Gene Therapy, Repligen Corporation, USA

Abstract

Introduction: As the clinical pipeline for viral vectors and oncolytic viruses expands, the industry faces an urgent need for intensified manufacturing strategies capable of delivering high infectious doses at scale. Lentiviral vectors have become a cornerstone of the cell and gene therapy revolution, yet their inherent complexity and the shift toward treating larger patient populations have made manufacturing scalability a primary bottleneck for commercial viability. Traditional perfusion technologies often struggle with membrane fouling and viral retention at high cell densities, leading to compromised productivity and complex downstream processing that hinders the transition from benchtop to 2000 L scales.

Methodology: This study evaluates the implementation of tangential flow depth filtration (TFDF) as an integrated cell-retention and continuous-harvest solution. We conducted parallel evaluations across two distinct systems: the production of a fusogenic rVSV-NDV oncolytic virus using suspension BHK-21 cells in a 3 L bioreactor, and the production of lentiviral vectors (LV) using human embryonic kidney (HEK)-293 cells. To specifically address the challenge of LV scalability, the process was transitioned from a 2 L bioreactor to a 50 L manufacturing system to assess process robustness and consistency.

Results: The TFDF system enabled stable, high-cell-density cultivation with continuous clarified permeate collection for both modalities. For oncolytic virus production, the TFDF perfusion process achieved an 11-fold increase in infectious titer and a 460% improvement in space-time yield compared to optimized batch processes. Scaling the LV production to 50 L confirmed the platform's ability to maintain product yield, identity, and potency while minimizing product loss during continuous harvest, proving its readiness for clinical and commercial demands.

Conclusion: These results demonstrate that TFDF serves as a robust, single-use, and scalable platform that streamlines cell retention and clarification into a single unit operation. By reducing process complexity and manufacturing risk, this integrated approach provides a clear path for the robust scale-up of lentiviral and oncolytic virus production to meet the growing global demand for next-generation therapies.

From Bench to Batch: Streamlining Lentiviral Vector Production for Clinical and Commercial Applications

Vladimir Slepushkin*

MedTherapy Biotech, USA

Abstract

Lentiviral vectors (LVs) remain foundational to gene therapy and cell-based immunotherapies, particularly in the engineering of chimeric antigen receptor-T cells. Despite their clinical utility, conventional manufacturing strategies continue to face limitations in scalability, consistency, and cost-effectiveness. This review introduces a suite of innovative methodologies designed to advance LV production through upstream and downstream process enhancements. We compare two large-scale bioreactor platforms for LV manufacturing. The first utilizes suspension-adapted human embryonic kidney-293T cells cultured in chemically defined, serum-free media optimized for high-titer transient transfection, integrated with scalable perfusion-based bioreactor systems. The second employs fixed-bed bioreactors supporting adherent 293T cell growth in fetal bovine serum-containing media under perfusion conditions. Both upstream strategies are implemented alongside packaging and producer cell lines to support vector generation. Downstream, a streamlined purification workflow combining membrane-based chromatography and tangential flow filtration significantly enhances vector recovery and potency, while effectively reducing host cell protein and residual DNA contaminants. Collectively, these approaches yield higher functional titers and improved process reproducibility. Our findings establish a robust, good manufacturing practice-compliant framework for LV manufacturing, with direct implications for accelerating the clinical translation and commercial deployment of gene-modified cell therapies.

Physics-driven Optimization of Lentiviral Vector Downstream Processing Enables Scalable, High-recovery Manufacturing for Next-generation Cell and Gene Therapies

Brian Tomkowicz*

SK pharmteco, USA

Abstract

Lentiviral vectors (LVVs) are central to *ex vivo* and emerging *in vivo* cell and gene therapies, yet conventional downstream purification, particularly diffusion-limited resin-based anion exchange (AEX) chromatography—has constrained recovery, scalability, and robustness. We describe a physics-driven optimization of LVV downstream processing using convective membrane-based AEX capture. By shifting from diffusion-limited to convective mass transfer, we achieved improved vector recovery, impurity clearance, and processing speed. Load-challenge studies across a broad LVV concentration range demonstrate that performance is governed primarily by transport phenomena rather than membrane brand or supplier-specific attributes. The optimized platform delivers consistently high step recovery, multi-log host cell protein clearance, and reduced residual DNA from benchtop to 50 L scale. End-to-end downstream processing—from clarified harvest to drug substance—can be completed within a single working day, minimizing hold times and preserving vector integrity. This scalable, format-agnostic purification strategy aligns with evolving regulatory expectations as LVVs transition from *ex vivo* intermediates to systemically administered drug products. As a global contract development and manufacturing organization partner, SK pharmteco integrates cell line development, plasmid engineering, viral vector manufacturing, and analytical characterization into a unified platform to support flexible, high-performance LVV production across clinical and commercial programs.

Session VI: Delivering Cell and Gene Therapy: Access and Commercialization

Empowering Patients. Delivering Access

George Eastwood*

Emily Whitehead Foundation, USA

Abstract

Emily Whitehead was the first pediatric patient in the world to receive chimeric antigen receptor (CAR)-T cell therapy. More than a decade later that breakthrough has reached thousands, yet most patients who could benefit still cannot get to it, blocked by where they live, how their care is referred, and how these therapies are paid for. This keynote traces the path from a single cured child to a disease-agnostic movement and makes the case that the defining work of this era is no longer only inventing therapies but delivering them: building the connective tissue between patients, clinicians, payers, and manufacturers so that access keeps pace with the science. Drawing on the Foundation's CAR-T vision to action blueprint, George Eastwood will show what it takes to put the patient and family voice at the centre of how cell and gene therapies are delivered, paid for, and improved, and challenge the room to help build the table where that work actually gets done.

Scaling Precision Genetic Treatments for Rare and Orphan Diseases: The Dawn of a New Model for Access and Impact

Casey McPherson*

AlphaRose Therapeutics, USA

Abstract

Despite rapid innovation in genetic treatments, the majority of rare genetic diseases remain without approved treatment, even though the technology exists to treat many of them. While platforms have advanced significantly, translational bottlenecks in target validation, regulatory alignment, manufacturing, and clinical endpoint issues create difficult hurdles for approvals. AlphaRose Therapeutics is developing a scalable framework to advance precision genetic treatments, using antisense oligonucleotides (ASOs), for ultra-rare conditions through an engineered translational strategy. This approach combines rigorous genetic validation, early regulatory pathway mapping, and capital-efficient development sequencing to reduce downstream risk, cost, and clinical trial time. This presentation will outline a structured model for rare disease program advancement as it pertains to ASOs and ultra rare diseases, by building the technologies and processes around the patients. In parallel, the session will explore new business models of genetic therapies, and how they could transform how academics fund their research, biotech raises capital, investors make a return, and ultimately how more patients get treated faster. This framework offers practical insights for biotech founders, investors, investigators, and translational researchers working to expand access to genetic medicines in their institutions.

Bridging Innovation and Access: Ensuring Patients Benefit from Cell and Gene Therapy Breakthroughs

Clorinda Walley*

Good Days, USA

Abstract

As cell and gene therapies rapidly advance from breakthrough science to clinical reality, a critical question is emerging across the healthcare ecosystem. Who will be able to access these life-changing treatments, and under what conditions? While innovation is accelerating at an unprecedented pace, affordability and access remain among the most significant barriers to realizing the full potential of market adoption and impact on patient lives. This session will explore the evolving landscape of patient access in the era of high-cost, cutting-edge treatments, with a focus on the practical, real-world challenges facing patients, providers, and manufacturers. Drawing on more than 18 years of experience leading one of the nation's largest patient assistance organizations, this discussion is informed by direct engagement with more than 400,000 patients annually who rely on Good Days to access specialty care, including advanced cell and gene therapy treatments. The session will bring these challenges to life through real examples of families who have navigated complex barriers to access, sharing how Good Days helps patients obtain life-saving treatments. Attendees will gain insight into the financial, structural, and systemic barriers patients encounter when seeking cell and gene therapies, including coverage limitations, high out-of-pocket costs, and disparities in access. The session will also

examine emerging trends in how stakeholders are responding, including evolving reimbursement models, expanded patient assistance programs, and cross-sector partnerships. Importantly, this discussion will highlight the critical role patient assistance organizations play in bridging the gap between innovation and access. Attendees will leave with a clearer understanding of how access challenges shape patient outcomes and how patient assistance programs help ensure that scientific progress translates into real-world impact.

Taming Complexity in Cell Therapy Logistics

Tony Jagan*

Aurion Biotech, USA

Abstract

This presentation outlines a summary on how to build and scale a standardized cell therapy logistics model across the full end-to-end patient journey, with an emphasis on predictability, repeatability, and clear documentation. Presentation highlights the need for thoughtful planning when expanding across regions and products, supported by the right team structure, tools, and training. Ultimately, focusing on well-executed supply chain practices and smart use of technology are key to ensuring reliable operations and timely patient treatment.

Strategic Molecular Bioanalysis to Accelerate Cell and Gene Therapy Development

Agostinho Rocha*

Smithers - Pharmaceutical Development Services, USA

Abstract

Advancing cell and gene therapy programs efficiently requires more than innovative science, it depends on generating the right data at the right time. For biotech companies working under aggressive timelines, limited resources, and increasing regulatory expectations, strategic molecular bioanalysis is critical to keeping programs on track. When planned early, it can reduce risk, avoid delays, and accelerate progress from preclinical studies to clinical milestones. This presentation will explore how molecular bioanalytical strategies can be aligned with development stage, program goals, and product modality. Key applications include biodistribution, persistence, vector shedding, transgene expression, vector copy number, cellular kinetics, and biomarker endpoints. Practical considerations for selecting appropriate technologies, including polymerase chain reaction (qPCR) and ddPCR platforms, will be discussed, with emphasis on sensitivity, robustness, turnaround time, and scalability. The session will also address how assay strategies should evolve across the product lifecycle, from exploratory methods to qualified and fully validated assays supporting good laboratory practice toxicology studies, investigational new drug-enabling programs, and clinical sample analysis. Common pitfalls that slow development will be reviewed, including poor platform selection, assay transfer challenges, and delayed validation planning. Attendees will leave with a practical framework for using strategic molecular bioanalysis to accelerate timelines, support regulatory submissions, and achieve key development milestones (Figure 1).

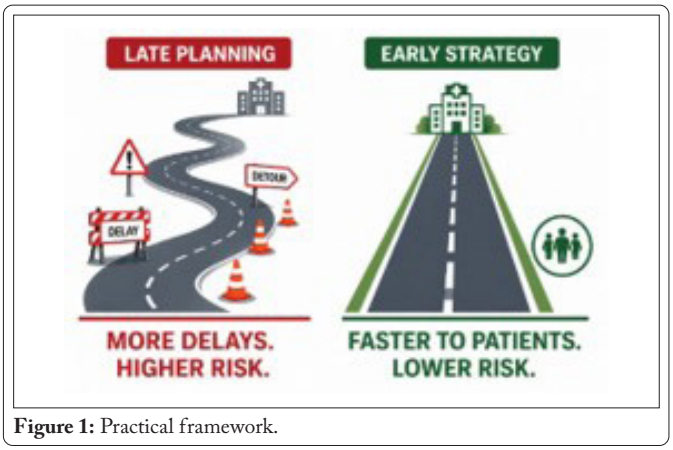

Figure 1: Practical framework.

Session VII: Regulatory, Quality & Development Strategies in Cell and Gene Therapies

Regulatory Perspectives - Preparing for Investigational New Drug Submissions

Brian Furmanski*

Kriya Therapeutics, USA

Abstract

The regulatory landscape for cell and gene therapies (CGT) continues to evolve rapidly, presenting both unprecedented opportunities and complex challenges for sponsors preparing investigational new drug (IND) applications. U.S. Food and Drug Administration (FDA) commitment to advancing CGT is evident through dedicated review divisions, specialized guidance documents, and programs like regenerative medicine advanced therapy and initial targeted engagement for regulatory advice (INTERACT). The agency has issued critical guidance on chemistry, manufacturing, and controls, long-term follow-up, and more recently, considerations for neurodegenerative diseases and ophthalmologic conditions. Understanding how to leverage these frameworks while addressing FDA's heightened focus on manufacturing consistency, biodistribution data, and dose justification is essential for efficient regulatory pathways. CGT sponsors face unique hurdles including limited preclinical-to-clinical translation models, particularly for adeno-associated virus (AAV) vectors, complex dose extrapolation from animal studies, evolving potency assay requirements, and the need for robust early characterization of product-related impurities. Manufacturing scalability and comparability protocols present ongoing challenges, especially for early-stage companies. Additionally, demonstrating appropriate patient selection criteria and safety monitoring plans requires careful consideration of the risk-benefit profile for these novel modalities. Early and substantive engagement with FDA through pre-IND meetings and INTERACT programs can significantly de-risk development. Model-informed drug development approaches are increasingly valuable for dose selection and justification. Leveraging available platforms (AAV serotypes, manufacturing processes) while demonstrating product-specific understanding can accelerate timelines. Artificial intelligence (AI) and machine learning tools are transforming IND preparation. However, sponsors must understand FDA's evolving expectations around algorithm validation, transparency, and appropriate use of AI. Success in CGT IND submissions requires balancing scientific innovation with regulatory pragmatism. Understanding FDA's perspective, investing in robust preclinical packages, engaging early with regulators, and thoughtfully integrating emerging technologies positions sponsors for efficient clinical entry and ultimately, patient access to transformative therapies.

From Discovery to Durable Value: Why Advanced Therapies Need Integrated Planning for Development, Investment, Evidence Generation, and Access

Mark Leney*

Uniphar, USA

Abstract

Early scientific optimism surrounding gene therapy gave way to the now well-known major setbacks exposing the difficulty of translating promise into routine use. While the last decade has been marked by renewed enthusiasm and significant, perhaps unfocused, investment, today's advanced therapy assets are subject to a far more selective investment landscape, coupled with a still complex development environment. Together frame a new scepticism. Compelling science is no longer sufficient to drive a project forward for most sponsors. Even a regulatory approval does not guarantee durable value. Sponsors operating in this landscape must connect development strategy with the practical realities of access, medical execution, logistics, and commercialization, including reimbursement, to achieve long-term success and truly reach patients and reward investors. Given that even some of the most experienced developers have failed to make a success of therapies that looked good in the clinic, no sensible investor is putting money into advanced therapies that lack a credible plan to achieve the milestones at each of these steps. In this presentation we will share our perspective on current challenges and what it takes to overcome them, informed by Uniphar's unparalleled real-world experience in assisting sponsors with development and delivery of advanced therapies, now covering over a dozen advanced therapy programs, with more than 500 patients treated, in more than 40 countries.

Extending Quality Systems Assessment Beyond Traditional Pathways

Jeff Wren*

Biotherapies, Association for the Advancement of Blood & Biotherapies, USA

Abstract

Biotherapies facilities involved in laboratory processing, storage, and/or manufacturing services increasingly operate outside traditional accreditation frameworks, yet many still seek credible, third-party assessment of their quality management systems beyond the requirements of regulators and other competent authorities. This presentation explores how established quality system frameworks, namely the Association for the Advancement of Blood & Biotherapies (AABB) quality system essentials—can be adapted to address this emerging need. These essentials provide a structured approach to system-level controls, including error prevention, traceability, staff competency, and deviation management. Drawing on AABB's experience developing quality standards for blood banking and cellular therapies, this session will examine the rationale for systems-focused certification as a complement to manufacturer specifications and requirements from regulators. Key considerations include distinguishing quality systems assessment from product or regulatory evaluation and defining appropriate program boundaries. The presentation will address practical challenges in program design, including how to position a quality-focused offering that supports patient safety. Attendees will leave with a framework for evaluating when systems-focused certification may be appropriate, key questions to consider during program design, and strategies for communicating scope to diverse stakeholders. This session is relevant for quality professionals and healthcare organizations considering how to extend quality assessment services to emerging segments of the biotherapies and laboratory services landscape.

Advancing Viral Adventitious Agent Testing for the Safety of Cell and Gene Therapy Products: Replacing Conventional Assays with Next-generation Sequencing

Jonathan Rodriguez*

Cedars-Sinai Biomanufacturing Center, USA

Abstract

Operationalizing viral safety testing in cell and gene therapy (CGT) manufacturing presents practical challenges when relying on legacy *in vitro* and *in vivo* assays, including long turnaround times, large sample volume requirements which has a direct impact on the manufacturing scale and consequently the cost of goods (COGs), and significant facility and staffing burden. With the recent ICH Q5A(R2) revision endorsing next-generation sequencing (NGS) for adventitious agent testing, there is a clear opportunity to adopt workflows that are better aligned with modern CGT manufacturing needs. This presentation aims at describing the integration of an NGS-based viral safety platform into a good manufacturing practice quality control (QC) environment and evaluates its operational impact relative to traditional assays. The implementation of this NGS-based adventitious agent testing strategy was performed in partnership with PathoQuest using their validated metagenomic sequencing and bioinformatics platform. The sequencing workflow required substantially less sample volume, reducing pressure on upstream teams to increase manufacturing scale solely to meet testing demands. This directly improved material utilization and lowered COGs. The reduction in batch size requirements also enabled earlier, more frequent, and more strategically placed testing points throughout the process. Turnaround time improved from months to weeks due to streamlined library preparation and automated analysis pipelines. Removing *in vivo* studies eliminated animal facility coordination, quarantine delays, and test failures commonly observed during these types of studies. NGS also reduced investigation workload by providing precise sequence-based identification, mitigating false positives common to cell line–based assays. From a QC perspective, NGS represents a more efficient, scalable, and resource-conserving alternative to legacy adventitious agent testing. Its adoption modernizes viral safety operations, supports ethical testing principles, and strengthens overall CGT manufacturing agility (Figure 1).

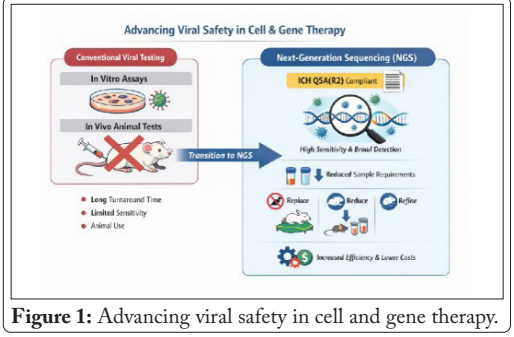

Figure 1: Advancing viral safety in cell and gene therapy.

Protecting Your Inventions: Strategies for Successful Patent Protection of Gene and Cell Therapy Products

Allison Gilder*

Foley Hoag LLP, USA

Abstract

Scientific research in cell and gene therapies is rapidly evolving, leading to exciting therapeutics with the potential to address some of the world's most significant and widespread diseases and disorders. Protecting the intellectual property of companies at the forefront of this evolution is paramount for successful commercialization of such therapies. Unfortunately, patent law and eligibility is not as dynamic and fast-moving as the development of cell and gene therapy therapeutics, leading to obstacles and uncertain pitfalls when filing for intellectual property protection. In this presentation (or panel), I will discuss the recent court decisions regarding patents protecting gene and cell therapies, as well as legal guidance and strategy when obtaining patent protection in front of the U.S. Patent and Trademark Office (PTO). Specifically, courts and the PTO have been scrambling to assess patent eligibility of gene and cell therapy patents, and I will address how companies can design experimental workflows and strategically file patent applications that will overcome common obstacles under these eligibility statues to successfully protect their assets. I will also present my analysis of current trends case law regarding antibodies and eligibility statues, and use this analysis to anticipate future eligibility case law regarding gene and cell therapies. Finally, I will demonstrate how this anticipation of future case law should be used as a backbone for patents filed today to ensure valid protection of intellectual property.

A Bioinformatic Workflow using Long-read Sequencing Technologies to Characterize Recombinant Adeno-associated Viruses (AAVs)

Alexandra Bridgeland*

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Abstract

Adeno-associated viruses (AAVs) have become a prominent platform for gene therapy due to their safety and efficacy in delivering therapeutic genes. The manufacturing process for AAVs is complex, typically involving the transfection of multiple plasmids into producer cell lines to generate viral particles. Each plasmid plays a critical role in producing AAV particles that encapsulate the gene of interest, flanked by inverted terminal repeat (ITR) regions. Comprehensive characterization methodologies for recombinant AAV drug products are essential to ensure their safety and effectiveness. Long-read next generation sequencing (NGS) has emerged as a robust biotesting tool to characterize the contents of the encapsidated AAV particles. While short-read NGS techniques, such as those offered by the Illumina platform, are commonly used for identity and variant detection purposes, they present certain challenges in molecular characterization. For example, polymerase chain reaction (PCR)-based library preparation methods can introduce biases, fragment size information is lost, and the ITRs are difficult to capture with short-read sequencing. In contrast, long-read sequencing, such as Oxford nanopore technologies, enables the direct sequencing of longer DNA fragments, allowing for the resolution of complex genomic regions and providing a complete view of the AAV genome. Long-read methods also eliminate the need for PCR amplification, reducing biases and enabling the accurate assessment of full-length sequences, including the challenging ITR regions. This presentation highlights an automated bioinformatic analysis workflow used to characterize AAVs (Figure 1). We present data from a real AAV manufacturing run, emphasizing the comprehensive characterization of recombinant AAVs achieved through long-read sequencing techniques. Our findings demonstrate that long-read Oxford nanopore sequencing effectively captures the entire AAV genome, including the challenging ITR regions, thereby providing a detailed view of the viral vector. This advancement allows for precise length assessments of client-submitted sequences, including yield analysis based on length. Furthermore, we can quantify the percentage of full-length reads that encompass the gene of interest, enhancing our understanding of the therapeutic payload. In addition to these insights, we will present data on the ability to characterize AAV manufacturing plasmids and assess for any mistakenly encapsidated plasmids or other sequences through a capsid content assessment. Collectively, these methodologies provide a robust framework for understanding the AAV sequence landscape and improving the quality of AAV-based therapies.

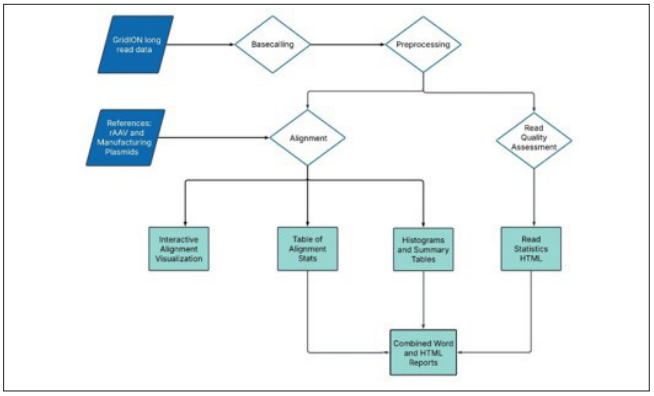

Figure 1: AAV characterization bioinformatic analysis workflow.

Poster Presentations

Preparing Cell and Gene Therapy Labs for Commercial Readiness Through Automation

Stacey Erickson*

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Abstract

Cell and gene therapy (CGT) companies face a critical inflection point when transitioning from early-stage development to pivotal trials, where the speed and structure of commercial operations become urgent priorities. In this session, we'll explore how laboratory automation and informatics are enabling CGT organizations to make this leap successfully and compliantly. As therapies advance toward commercialization, labs must evolve quickly from highly manual, R&D-centric workflows to scalable, reproducible systems that support increased volume and time-sensitive demands. Designed for CGT professionals navigating this transition, the session will highlight how electronic laboratory notebooks, integrated laboratory information management system, and automation tools can streamline core processes, reduce manual intervention and accelerate turnaround times. We'll address how to adopt automation within existing frameworks and how to future-proof lab operations for full-scale commercial manufacturing. Key objectives include understanding the automation technologies most applicable to late-stage and commercial CGT programs, exploring how to reduce risk and increase efficiency during pivotal trial scale-up, identifying actionable strategies to bridge R&D and commercial systems without disrupting ongoing clinical work, and discussing practical examples of automation tools tailored to CGT workflows. Attendees will walk away with a roadmap for shifting from manual to automated lab processes and insight into how leading CGT companies are leveraging informatics to meet the demands of commercial readiness.

Building Scalable, Patient-centric Commercial Models in Cell and Gene Therapy

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Abstract

As life sciences companies grow, the complexity of commercializing products and managing patient engagement increases, especially in cell and gene therapy (CGT). In this session, we will explore key elements of a successful commercialization strategy for CGT, including the systems and platforms needed to support growth, the importance of mapping the patient journey, and the role of orchestration platforms in integrating clinical, manufacturing, and commercial workflows. Drawing from project work with leading CGT organizations, this session will provide actionable insights into how companies can build scalable, patient-centric commercial models that drive success. Key objectives include identifying the critical components of a CGT commercialization roadmap, from phase 3 planning through launch and scale-up, understanding how to align systems and platforms with growth strategies to support key functions like sales, patient scheduling, treatment site coordination, and risk evaluation and mitigation strategy compliance, learning how mapping the patient journey—including eligibility screening, apheresis, treatment delivery, and follow-up can inform strategic decisions and enhance outcomes, exploring the role of orchestration platforms in streamlining processes and improving cross-functional collaboration, especially across manufacturing,

regulatory, field services, and commercial teams, and analysing real-world examples to uncover best practices and lessons learned from CGT product launches. Attendees will walk away with insights into the systems and platforms essential for managing key functions like manufacturing, scheduling and patient onboarding. They'll learn best practices for mapping and leveraging the end-to-end CGT patient journey to inform commercialization decisions and understand how orchestration platforms can unify disparate processes and improve efficiency across the clinical-to-commercial continuum. Finally, attendees will gain a clear roadmap for integrating technology and processes to build patient-centric, growth-ready commercial models that account for CGT-specific regulatory, operational, and logistical challenges.

Achieving Commercialization Readiness in Cell and Gene Therapy

Stacey Erickson*

Clarkston Consulting, USA

Abstract

As life sciences companies transition from solely R&D to include commercial operations, strategic preparation is critical, and in cell and gene therapy (CGT), this transition is uniquely complex. In this session, we will provide actionable insights into the key aspects of commercial readiness for CGT companies, including infrastructure development, regulatory compliance, patient engagement strategies, and supply chain optimization. With challenges like autologous supply chains and long manufacturing lead times, CGT organizations must plan early and deliberately. Attendees will gain a roadmap to navigate the complexities of launching CGT products, supported by real-world examples of successful commercialization strategies in this space. Key objectives include understanding the essential components of commercialization readiness in CGT, exploring strategies for aligning regulatory, operational, and market considerations, like chain-of-identity and chain-of-custody, identifying the systems and processes necessary to support scalable growth, learning how to map the patient journey and integrate it into commercialization plans, and analysing case studies of successful CGT product launches. Attendees will walk away with a comprehensive framework for achieving commercialization readiness in the CGT landscape, insight into building the infrastructure to support market entry and growth, and strategies for aligning cross-functional teams. They'll also gain tools to enhance patient engagement and integrate patient needs into CGT commercialization strategy, along with best practices for navigating CGT-specific regulatory requirements such as risk evaluation and mitigation strategy programs and long-term safety monitoring, while mitigating risks across the product lifecycle.

A Robust, Scalable Solution for High-throughput Screening and T-cell Engineering Using the DTx™ Electroporation Platform

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Abstract

As demand for advanced therapies rises, the biopharma industry faces mounting pressure to accelerate innovation in high-risk, high-reward applications. Developers face numerous challenges, including high costs, extended timelines, and variable gene expression. To address these issues, the DTx™ electroporation platform was developed to enable rapid, scalable, and customizable electroporation of up to 96 samples in under 3 min, offering high-throughput efficiency, consistent results, and compatibility with diverse cell types. Optimized conditions on the DTx™ seamlessly scale to other MaxCyte electroporation systems, supporting transitions from small-scale screening to good manufacturing practice-compliant manufacturing. In this study, we evaluated the DTx™ in high-throughput screening workflows to optimize clustered regularly interspaced short palindromic repeats/Cas engineering. First, we screened guide RNAs for T-cell knockout using varying ribonucleoprotein concentrations. We then screened small and medium sized plasmid homology-directed repair donor templates to knock-in a CD19 chimeric antigen receptor to the TRAC locus. To account for donor-to-donor variability, we used our optimized workflow to assess three healthy T-cell donors and showcased scalability from the DTx™ to the GTx®. These results highlight the DTx™ electroporation platform as a powerful and versatile solution for high-throughput cell engineering, offering seamless scalability and robust, reproducible performance, to streamline the transition from discovery to clinical manufacturing.

A Comparison of Size Distribution Techniques for Characterizing and Quantifying Adeno-associated Virus Capsid Fill-states

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Abstract

Recombinant adeno-associated viruses (rAAVs) are widely used vectors in gene therapy, requiring precise analytical techniques to characterize capsid fill-states and ensure product quality. In this poster, we compare the results from three common biophysical methods used to evaluate AAV heterogeneity: sedimentation velocity analytical ultracentrifugation (SV-AUC), mass photometry (MP), and size exclusion chromatography with multiple angle lights scattering (SEC-MALS). The results highlight the strengths and inherent limitations of each analytical approach. SV-AUC enables high-resolution separation and accurate DNA quantification across capsid species, including low and high molecular weight impurities, albeit with greater sample and time demands. MP offers rapid, label-free quantification of intact capsid populations with minimal material consumption, though its ability to resolve minor impurities is limited. SEC-MALS, with fairly low material requirements and medium analysis time, provides orthogonal assessment of absolute molecular weight and aggregate content; however, information on capsid fill-state distributions is limited due to co-elution and reliance on compositional model assumptions. Our findings underscore the complementary nature of these tools in drug development workflows, with SV-AUC suited for in-depth characterization and regulatory support, MP suited for high-throughput screening, and SEC-MALS used for supporting comparability.

Cell and Gene Therapy Requirements for Investigational New Drug Filing

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Abstract

Cell and gene therapies (CGT) are revolutionizing the field of medicine with their ability to target underlying diseases at the genetic and cellular level. CGT products mediate an expression of transferred genetic materials or specifically alter the target genome of the cells. U.S. Food and Drug Administration required safety assessments for CGT include pre-clinical assessment, gene expression, vector safety, vector shedding, and biodistribution and persistence analysis. Pre-clinical assessments help evaluate the toxicity, safety, pharmacology, and dosing of the CGT in relevant animal models. Vector safety assesses the vector source used including the identity, purity, and stability which is done throughout the study. This is done for both the biodistribution and persistence studies as well as the vector shedding assessment of the target vector source. Vector shedding studies assess CGT targets that shed and exit the body without targeting the intended sample target matrices while biodistribution and persistence studies assess CGT targets and potential off-target effects, supporting that the genetic material does not persist in unintended sample target matrices, determination of the level of expression of target product in vector genome positive samples to determine the characterization of the activity and safety profiles following product administration, as well as assessing potential risk of potentially transferring recombinant genetic vector to other through contact with biofluids and waste. Additionally, there also can be screening for the potential for replication-competent viruses, replication-competent retroviruses, and human herpesvirus screening are among the recommended vector safety assessments. At Labcorp, we specialize in molecular bioanalysis assessing the biodistribution and persistence studies as well as vector shedding of a variety of different CGT's ranging from adeno-associated virus's, chimeric antigen receptor-T's, mRNA, small oligoes and other CGT therapies extracted from substrate sample matrix which are quantified utilizing a variety of polymerase chain reaction (PCR) based techniques including qPCR, dPCR, and ddPCR assessment.

Artificial Intelligence-driven Innovation in Advanced Therapy: CelMo and ChemplifyTM Transform T-cell Manufacturing

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Abstract

Introduction: The success of advanced therapy depends on the ability to manufacture high-quality therapeutic cells efficiently and consistently. In T cell-based therapies, clinical progress is increasingly limited not by target selection, but by challenges in producing functional T cells at scale. Conventional cytokine-driven culture systems are often slow, variable, expensive, and

prone to inducing senescence and exhaustion. To address this, we developed CelMo, a virtual cell platform that can predict and understand cell behaviour and automates the discovery of cell-modulating small molecules for biomanufacturing. By integrating computational modelling with biological data, CelMo designs and optimizes compounds that enhance cell function and viability across multiple cell types. Chemplify™, CelMo's first product, demonstrates this capability in T cell manufacturing.

Methodology: CelMo integrates multi-omics datasets, including genomics, transcriptomics, proteomics, and metabolomics, with advanced artificial intelligence (AI) models to identify druggable targets and design optimized small molecules *in silico*. Candidate compounds are refined for potency, safety, and manufacturability before synthesis and experimental validation. This approach accelerates the discovery of scalable solutions tailored to specific cellular needs. Chemplify™, identified through this platform, is added directly to T cell cultures at a recommended 1:10,000 dilution during the expansion phase and has been evaluated across multiple culture systems, cytokine regimens, and manufacturing formats.

Results: Chemplify™ consistently accelerated T cell expansion across healthy and poor peripheral blood mononuclear cells, tumor-infiltrating lymphocytes (TILs), gene-edited T cells, gamma-delta T cells, and chimeric antigen receptor-T (CAR-T) cells, achieving over 1,000-fold expansion within 11 days compared with approximately 200-fold under standard cytokine-only conditions. Treated cells showed improved viability, reduced senescence and exhaustion markers, enhanced memory phenotypes, and reduced cytokine dependency. In a leukaemia NSG mouse model, CAR-T cells manufactured with Chemplify™ showed 100% one-month survival vs about 50% in controls. In TIL studies, Chemplify™ improved expansion and viability, reduced exhaustion and senescence, and better-preserved potency after freeze-thaw. It also rescued poorly performing T cells and significantly improved their viability and expansion. No observable toxicity was detected in animal studies, even at concentrations higher than those used in culture.

Conclusion: Chemplify™ addresses key bottlenecks in T cell manufacturing by improving stability, reproducibility, scalability, and cost-effectiveness. Together, the CelMo-Chemplify™ system provides an end-to-end solution that links AI-driven small-molecule discovery with a plug-and-play culture additive compatible with existing workflows, enabling faster and higher-quality T cell production.

Evaluation of Media Supplement Candidates as Replacement for Serum in Feeder-free Natural Killer Cell Expansion

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Abstract

Effective natural killer (NK) cell therapy is dependent on robust cell culture methods, among others, for the activation and expansion of *ex vivo* NK cells. However, NK cells comprise a small percentage of peripheral blood mononuclear cells and clinical doses require large amounts of cells. Current expansion protocols rely on the use of feeder cells and serum (foetal bovine serum (FBS) or human serum) to obtain large numbers of NK cells but these raise safety and regulatory concerns. Current media formulations utilized in NK cell production have not been fine-tuned to enhance NK cell expansion, function, gene delivery efficiency, and overall therapeutic efficacy. To bridge this gap, we seek to identify biomolecules crucial for NK cell expansion with the aim to develop a serum-free, xeno-free, chemically defined culture media supplement or culture media formulation that can support feeder-free NK expansion. We demonstrated robust NK cell expansion and target cell killing in SK-OV-3-luc and K562-luc cell lines across multiple donors using our inhouse feeder-free NK cell expansion protocol. Out of the few commercial serum replacements (SRs) tested, we identified one SR that selectively expanded NK cells successfully although not to levels observed with FBS. Using the inhouse protocol (FBS supplemented) as the baseline, we collected samples from FBS and SR cultures across 5 timepoints, profiled the spent media using mass spectrometry, and performed bulk RNA sequencing on the cell pellets. Ongoing work to identify the common metabolites consumed and specific metabolites consumed by either FBS or SR will provide insights into the metabolic requirements of NK cell growth by understanding their roles in the metabolic pathways. Thereafter, we aim to validate these candidate biomolecules in SR cultures. These findings will be useful for the incorporation of chemically defined biomolecules in medium specific for expansion and potency of NK cells.

Antioxidant-mediated Enhancement of Corneal Endothelial Cell Proliferation and Long-term Expansion Toward Donor-independent Regenerative Therapy

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Abstract

Background and Rationale: Corneal endothelial dysfunction is a leading cause of global blindness. Although keratoplasty can restore vision, its widespread application is limited by donor tissue shortages, immune rejection, surgical complexity, and the need for lifelong postoperative management. Cell-based therapies represent a promising donor-independent alternative; however, corneal endothelial cells (CECs) exhibit inherently low proliferative capacity due to G1-phase arrest and frequently undergo endothelial-to-mesenchymal transition (EndMT) during prolonged in vitro expansion. Oxidative stress is a major driver of these degenerative changes, implicating redox imbalance as a critical barrier to scalable corneal endothelial expansion. Therefore, antioxidant-based strategies may offer a targeted approach to preserve CEC phenotype, sustain proliferation, and enable long-term culture.

Objective: To investigate whether selected antioxidant classes—direct reactive oxygen species (ROS) scavengers, vitamin C and its stable derivatives, and thiol-based redox modulators—used individually or in combination, can enhance proliferation, maintain morphology and functional marker expression, and extend the expansion potential of bovine corneal endothelial cells (BCECs) up to passage 6 (P6).

Methods: BCECs were cultured with optimized concentrations of antioxidants representing three functional classes: fast-acting ROS scavengers, culture-stable antioxidant derivatives, and glutathione-enhancing thiol compounds. MTT-based cytotoxicity screening was performed to identify non-toxic candidates, following which three lead antioxidants were shortlisted. Cell proliferation was evaluated through Ki-67 expression, while cell-cycle progression was assessed using BrdU incorporation assays. Morphological stability was monitored microscopically throughout serial passaging up to P6. To assess synergistic effects, antioxidant combinations were evaluated for their ability to enhance proliferation and sustain cell-cycle activity at advanced passages.

Results: Cytotoxicity screening identified optimal, non-cytotoxic concentrations of three antioxidants suitable for long-term culture. Individually applied antioxidants preserved BCEC viability and characteristic hexagonal morphology up to P4, but proliferative activity declined beyond this stage, reflected by reduced Ki-67 expression. In contrast, combination-treated BCECs displayed significantly higher Ki-67 expression compared to untreated controls at later passages. Flow cytometric analysis confirmed a sustained increase in Ki-67 positive cells across all passages, with proliferative indices at P6 comparable to untreated low-passage P2 cultures. BrdU assays corroborated these findings, demonstrating increased s-phase entry at mid and late passages. Functional analyses showed that antioxidant-treated BCECs retained strong expression of ZO-1 and Na^+/K^+-ATPase at higher passages, indicating preserved tight junction integrity and pump function. Combination-treated cells maintained native hexagonal morphology with reduced EndMT-associated changes, whereas untreated cells underwent extensive mesenchymal transformation. A formulation combining a stable ROS scavenger with a thiol-based modulator yielded the most robust effects.

Conclusion: Targeted antioxidant combinations significantly extend BCEC proliferative capacity while preserving functional and morphological characteristics at advanced passages. This redox-based strategy addresses a key limitation in corneal endothelial cell expansion and supports the development of scalable, donor-independent corneal endothelial therapeutics (Figure 1).

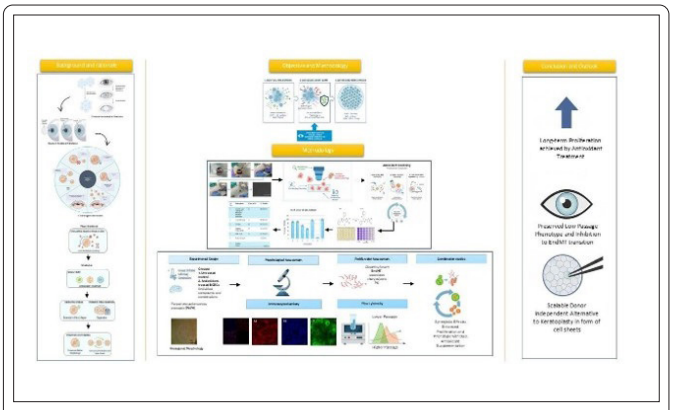

Figure 1: Antioxidant-mediated enhancement of corneal endothelial cell proliferation and long-term expansion toward donor-independent regenerative therapy.

Enhancement of Gene Delivery via Inhibition of the Nuclear Restriction Factors

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Abstract

Purpose: The viral vectors that are used for current gene therapies have significant drawbacks, including immunogenicity, oncogenic risks, and high cost. These issues have motivated a shift towards safer and more affordable non-viral gene delivery systems that use cationic lipids or polymers to deliver plasmid DNA. Unfortunately, some cell lines have defense mechanisms that inhibit the non-viral delivery and expression of plasmid DNA (e.g., human foreskin fibroblast-1 (HFF) and T cells). For example, most viruses express proteins that protect their genome in the cytosol, actively translocate their genes into the nucleus, and then inhibit host cell restriction factors that would sequester or silence foreign genes. In contrast, the delivery of bare plasmid DNA into the cytosol can trigger an innate immune response in the cytosol and epigenetic silencing in the nucleus. This work focuses on the latter problem, in which transgenes are repressed in the nucleus by a "restrictosome" complex that forms when the nuclear DNA sensor interferon-inducible-16 (IFI) oligomerizes onto foreign DNA and recruits additional proteins (PML, ATRX, etc.) that epigenetically silence the bound transgene by adding repressive histone modifications and DNA methylation marks.

Methods: Initial mRNA-sequencing experiments were conducted to identify restrictosome proteins that are actively expressed in two cell lines that are known to be resistant to non-viral transgene delivery –HFF-1 and Jurkat T cells. Transgene repressors were then inhibited by established small-molecule inhibitors (SMIs) or putative SMIs identified via *in silico* screening with MolSoft ICM. Alternatively, transgene repressors were also inhibited by electroporating cells with synthetic mRNA transcripts encoding inhibitory viral proteins (e.g., ICP0 inhibits IFI16) and then lipofecting the cells 48 h later with pEF-GFP (control = mCherry mRNA).

Results: While many of the screened SMIs failed to enhance transgene expression, treatment of HFF-1 cells with one of the drugs (SMI #1278) or an mRNA encoding the IE1 protein from human cytomegalovirus (hCMV) significantly increased transfection efficiency. For example, 100 nM of SMI #1278 significantly increased transfection efficiency to 23.5% ± 3.0 green fluorescent protein (GFP+) cells relative to the control cells that were only treated with dimethyl sulfoxide (DMSO) (12% GFP+ ± 1.9 cells). This concentration of the drug also significantly increased transgene expression per cell by 3-fold, from 10,500 ± 8545 for the DMSO controls to 34,650 ± 5939. Likewise, electroporation of 250,000/well HFF-1 cells with 1.6 pmol of IE1 mRNA significantly increased transgene expression 6-fold (mean fluorescence intensity (MFI) = 23318 ± 11858) relative to control cells electroporated with an mCherry transcript (MFI = 5481± 7296). Additionally, electroporation of the cells with the IE1 transcript significantly enhanced transfection efficiency to (60.97% ± 7.3 GFP+ cells) relative to electroporation of cells with the mCherry transcript resulted in transfection efficiency (10.4% ± 2.8 GFP+ cells).

Conclusion: These results show that restrictosome proteins are actively expressed in cells that are difficult to transfect with non-viral gene delivery methods. However, inhibiting them with SMIs or viral proteins can significantly enhance transgene expression (Figure 1).

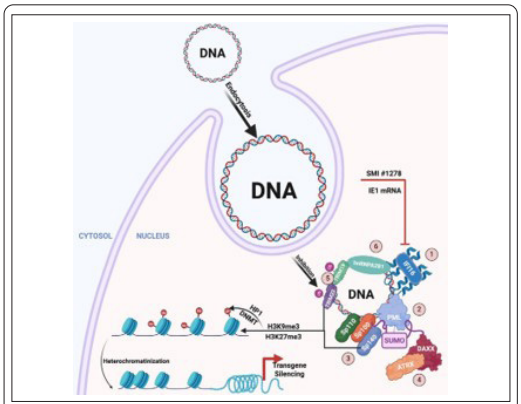

Figure 1: Antioxidant-mediated enhancement of corneal endothelial cell proliferation and long-term expansion toward donor-independent regenerative therapy.

High-throughput Amplification-free Clustered Regularly Interspaced Short Palindromic Repeats-kinetic Assay for Rapid Quantification of On/Off-target Edits, Genomic Titer, and Genome Integrity

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Abstract

Introduction: The development of cell and gene therapies is hindered by slow, labor-intensive quality control (QC) assays. Traditional methods like droplet digital polymerase chain reaction (ddPCR) and next-generation sequencing (NGS) introduce amplification bias, require complex primer design, and have lengthy turnaround times. There is a critical need for analytical platforms combining speed, sensitivity, and high-throughput scalability without amplification. Here we present new applications of the (quantification using initial clustered regularly interspaced short palindromic repeats (CRISPR) kinetic rates) (QUiCKR) platform: a novel amplification-free assay for adeno-associated virus (AAV) characterization and a stem cell genome integrity analysis. We also describe latest improvements in automation and sensitivity for detection directly from genomic DNA.

Methods: The QUiCKR assay leverages Cas12 enzymes to quantify DNA targets via fluorescence kinetics. We developed two novel applications: 1) An amplification-free AAV genomic titer assay that quantifies viral titer and structural variants (e.g., splice variants, truncated viral genomes, contaminants) in under 1 h and 2) A genome integrity assay for quantifying copy numbers of stem cell genomic variants via multiplexed PCR followed by QUiCKR readout. To increase throughput, we implemented a fully automated, hands-off workflow compatible with standard liquid handlers. This system was stress-tested in collaboration with a leading Boston-based editing company on editing dose response studies, processing 1,000 samples in one week. Three plate formats (23 to 96 samples/plate) were evaluated for flexibility. Finally, we developed proprietary molecular switches enabling direct detection from scarce DNA, removing the need for amplification.

Results: The AAV assay quantified genomic titer and structural variants with an R2 of 0.95 vs ddPCR (N = 16). It was automated with a biotech partner, achieving a 1h turnaround with 10 min hands-on time. In genome integrity applications, the assay flagged instabilities in 90% of positive samples with 0% false-positives (N = 15). The automated HT platform achieved R2 = 0.86 correlation with NGS editing efficiency data (N = 1000) and high reproducibility (%CV = 8%). Significantly, the assay's new limit of detection of approximately 10 femtomolar (fM) enables direct, amplification-free quantification of low-abundance targets, eliminating PCR amplification bias and streamlining gene editing quantification.

Conclusion: We demonstrated a fully automated CRISPR-kinetic platform capable of processing thousands of samples per week. By providing amplification-free quantification with fM sensitivity, this technology removes PCR bias and significant analytical bottlenecks, enabling rapid, high-fidelity QC for AAV and gene editing workflows.

Solutions for Simultaneous Single Cell Transcriptome Analysis and Immune Receptor Profiling

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Abstract

The adaptive immune system is composed of a diverse array of antigen binding T-cells and B-cells. The diversity in T-cell and B-cell receptor sequences are governed by the recombination and somatic hypermutation in the V variable (V), diversity (D), and joining (J) gene segments. Advancements in multi-omics approaches at single-cell resolution have led to adapting the cutting-edge GEXSCOPE® microwell-based technology to provide gene expression data combined with the T-cell or B-cell receptor sequences, including the sequence information on the complementarity determining region 3. The improved performance of our GEXSCOPE® single cell V(D)J kit enables detection of high pairing rate of immunoreceptors. For full length immunoreceptor single cell sequencing, Singleron offers the sCircle® single cell full length T-cell receptor or B-cell receptor sequencing library kit, which enables full length V(D)J region sequencing at a single cell level. Characterization of therapeutical antibodies or T cell therapies at a single cell level can now be conveniently performed on both human and mouse immunoreceptors. Singleron's immune profiling kits offer unique high-throughput single cell solutions for clonal analysis, antibody discovery, or developing chimeric antigen receptor-T therapies, which can be used without the necessity of specialized equipment.

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