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MARCH 20-21, 2025

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EMIT Imaging is the pioneer in Cryo-Fluorescence Tomography (CFT), offering our state-of-the-art preclinical imaging system, Xerra™ and comprehensive CFT fee-for-service research to global scientific community. CFT is an ex vivo, volumetric tissue imaging technique that provides enhanced monitoring of the biodistribution of fluorescently labeled molecules or the expression of fluorescent reporter proteins with high resolution and high sensitivity. Anatomical and molecular images are co-registered, enabling unparalleled localization insights for drugs, delivery vehicles, proteins, and other biochemical processes in whole animals and tissues. EMIT Imaging is headquartered and conducts research services out of its Natick, MA office. Engineering and manufacturing are based out of the Owings Mills, MD production facility.

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Medicilon is a leading CRO company that provides comprehensive drug R&D services on a global scale. From drug discovery, pharmaceutical research to preclinical research, Medicilon has supported more than 2000 client R&D programs worldwide resulting in 520 IND filings. With proven scientific excellence and FDA-aligned methodologies, we help biotech and pharmaceutical innovators fast-track their path from discovery to IND success.

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BioAgilytix is the trusted partner for global bioanalytical services throughout every phase of the drug development process. We provide custom, fit-for-purpose, and comprehensive bioanalytical support for your program needs. With over a decade of gene and cell therapy experience, we have worked with over a hundred partners to build the right bioanalytical package based on the current regulatory expectations.

We provide the complete package of pharmacokinetic (PK), immunogenicity, biomarker, and CMC bioanalytical testing services in a GxP environment. Our labs provide immunoassay, cell-based assay, molecular biology, and LC/MS assay development, validation, and sample testing, eliminating the need for multiple providers, ensuring efficient data delivery for your therapeutic study.

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Boston BioProducts is a leading provider of biological buffers, media, and solutions for the life sciences. With nearly 30 years of experience in buffer and reagent manufacturing, our dedicated team of formulation scientists and in-house manufacturing capabilities support multiple applications including molecular biology, assay development, and bioprocessing.

FRONTAGE

Frontage Laboratories, Inc., is a global Contract Research Organization (CRO) which provides integrated, science-driven, product development services from drug discovery to late phase clinical process to enable biopharmaceutical companies to achieve their development goals. Comprehensive services include drug metabolism and pharmacokinetics, analytical testing

and formulation development, preclinical and clinical trial material manufacturing, bioanalysis, preclinical safety and toxicology assessment and early phase clinical studies. Frontage has enabled many biotechnology companies and leading pharmaceutical companies of varying sizes to advance a myriad of new molecules through development and to successfully file global regulatory submissions.

KCAS BIO

KCAS Bio is a top-tier contract research organization (CRO) that has 40 years of experience with both large pharma and biotech sponsors, providing comprehensive bioanalytical drug development services from early discovery through registration.

We have supported more than 300+ FDA approved drugs on the market, developed 5,000+ proprietary and non-proprietary assays to date, and undergone 18 FDA audits with no major findings.

Our presence in multiple locations throughout the US and Europe - and with a strategic alliance in Australia - allows us to serve sponsors globally with bioanalytical, biomarker, immunogenicity, cellular and molecular assay services along with clinical kitting and sample management.

With the expertise, capacity and flexibility sponsors require, we can fulfill our purpose, which is: to help accelerate the discovery and development of life-changing drugs smoothly, safely and sustainably.

LONZA

Lonza's Cell & Gene offering spans across development and manufacturing services, products, solutions, testing and automation platforms as well as tools and technologies to enable our customers to develop, de-risk and industrialize their therapies from basic research to commercialization. United by our vision to bring any therapy to life, we support our customers with a combination of technological insight, world-class manufacturing, scientific expertise, process excellence and innovation. Our work enables our customers to develop and commercialize their therapeutic discoveries, allowing their patients to benefit from life-saving and life-enhancing treatments.

MISSION BIO

Mission Bio is a life sciences company that accelerates discoveries and cures for a wide range of diseases by equipping researchers with the tools they need to better measure, characterize, and predict our resistance and response to new therapies. Mission Bio's multi-omics approach improves time-to-market for new therapeutics, including innovative cell and gene therapies that provide new pathways to health. The company's Tapestri Platform is being utilized by customers at leading research centers, pharmaceutical, and diagnostics companies worldwide. A Tapestri assay recently entered GMP qualification and validation, indicating that single-cell analysis is on its way to routine use in clinical trials to support the next wave of life-saving CGT treatments.

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TOXPLUS MONITORING

TOXPLUS Monitoring, established January 2020, is a dedicated, client-focused company that provides nonclinical operations support services including study monitoring, study management, vendor audits and regulatory writing support. We serve pharmaceutical and biotech companies in early to late-stage drug development. Services include:

- Study monitoring for non-GLP and GLP nonclinical studies: Our Study Monitors are located within driving distance to most CROs. They ensure that a study is conducted in compliance with an approved protocol, protocol amendments and regulatory guidelines. They provide oversite of procedures being performed, proper data collection and documentation of study results.
- Data audit for non-GLP and GLP studies: Our Data Auditors review all study notebooks to ensure data has been collected according to protocol and any deviations resolved.
- Vendor audit/qualification: Our Auditors will ensure that a CRO has the capability to conduct a study and is qualified to do so from both a technical and quality compliance standpoint.
- Study management of nonclinical studies: Our Study Managers will ensure your nonclinical program is executed according to its planned strategy. They will interact with Study Directors to address questions and keep the client up to date on all study events and outcomes. This is ideal for start-up to mid size companies without resources to support nonclinical study oversight.
- Regulatory writing support: Our regulatory writers support the writing of INTERACT and pre-IND meeting regulatory documents, IND and NDA Module 2.0 including tabulated summaries, summaries for other regulatory agencies, IBs, and Data QCing.

QIAGEN

QIAGEN pushes the boundaries of innovation to improve our understanding of DNA, RNA and proteins – the building blocks of life. We enable our customers to unlock valuable insights from any biological sample – be it blood, a throat swab or many other materials. Our products serve a wide range of applications, including cell and gene therapy. In this space, customers can find solutions for precise determination of plasmid quality, viral titer, vector copy number and robust contaminant testing. Our reputation is based on confidence in decisions, clarity of results and pride in the insights our customers achieve. More than 35 Nobel Prize winners among more than 500,000 customers worldwide are proof of that success. Together, we are making improvements in life possible. Discover more at http://www.qiagen.com.

AAPS

Founded in 1986, the American Association of Pharmaceutical Scientists (AAPS) is a professional, scientific organization of approximately 7,000 individual members and over 10,000 actively participating stakeholders employed in academia, industry, government, and other pharmaceutical science related research institutes worldwide.

Our mission: To advance the capacity of pharmaceutical scientists to develop products and therapies that improve global health

Our vision: Advancing the pharmaceutical sciences to drive prevention and cures.

Our five core values: Learning, Innovation, Service, Inclusiveness and Integrity.

AAPS is incorporated as a not-for-profit organization under the U. S. Internal Revenue Service Code, §501(c)3 in the District of Columbia.

PBSS

Pharmaceutical & BioScience Society, International (PBSS) is a non-profit professional organization of scientists and other professionals in the life science sector, working in diverse organizations such as the biotechnology and pharmaceutical industries, instrumentation and scientific product suppliers, academia, government laboratories and contract research organizations. PBSS has 5000+ members and is active through five member organizations in San Francisco Bay Area, San Diego Area, Boston, Vancouver and Korea, some of the largest life science clusters in the World.

BOSTON SOCIETY
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ORGANIZERS' WELCOME

Welcome to the 2025 Gene & Cell Therapy Conference.
Our organizers have gathered an excellent group of speakers for the second annual Gene & Cell Therapy Conference. The program is arranged to incorporate extensive audience participation and discussion. We encourage attendees to take full advantage of the opportunity to engage in discussion in order to receive the maximum benefit from the Gene & Cell Therapy Conference experience. Thank you for your participation.

ORGANIZING COMMITTEE

Nanda Balasubramanian, Bristol-Myers Squibb
Nagendra Chemuturi, Eli Lilly
Lei Ci, Moderna Therapeutics
Ivy Dong, Intellia Therapeutics
Anshul Gupta, Editas Medicine
Vibha Jawa, Bristol-Myers Squibb
Steven Louie, Medicilon USA Corp
Dale Miles, Genentech
Hardik Mody, Genentech
Stephanie Pasas-Farmer, Ariadne Software

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2025 AGENDA

THURSDAY, MARCH 20

7:30 - 8:30 AM **Registration & Breakfast**

8:30 - 8:40 AM **Conference Opening**
Vibha Jawa, BMS

8:40 - 9:20 AM **PLENARY:** ***Nonclinical Safety Assessment of Chimeric Antigen Receptor T Cell (CAR T) Therapies***
Kyle Kolaja, BMS

SESSION I: Current State of Cell Therapies
Moderator: Steven Louie, Medicilon

9:20 - 9:25 AM **Session Introduction**

9:25 - 9:50 AM ***Journey of India's First CAR-T Cell Therapy and Its Global Impact***
Alka Dwivedi, NIH

9:50 - 10:15 AM ***Overcoming Host Rejection in Allogeneic Adoptive Cell Therapy: Engineering Strategies for Persistence and Efficacy***
Johannes Stanta, Celerion

10:15 - 10:40 AM ***Cryo-Fluorescence Tomography: Transformative 3D Imaging to Monitor Gene and Cell Therapies***
Matt Silva, EMIT Imaging

10:40 - 11:00 AM Break

SESSION II: Emerging Cell Therapies
Moderator: Nagendra Chemuturi, Eli Lilly

11:00 - 11:05 AM **Session Introduction**

11:05 - 11:30 AM ***AI-Driven Approaches to Enhancing CAR Design***
Simon Bornschein, Coding Bio

11:30 - 11:55 AM ***Translational Development of the GbGm Vector for Sickle Cell Disease: Assessing Safety and Efficacy from Preclinical Models to Human***
Mohammad Shadid, Korro Bio

11:55 - 12:10 PM ***CMC Aspects of ASO Manufacturing***
Qingcong Lin, Medicilon

12:10 - 1:25 PM Lunch

SESSION III: Bioanalytical Assays
Moderators: Nanda Balasubramanian, BMS & Vibha Jawa, BMS

1:25 - 1:30 PM	**Session Introduction**
1:30 - 1:55 PM	***Advanced Bioanalytical Strategies to Determine PK and Biodistribution of Cell and Gene Therapy Products*** Salvatore Iovino, Editas Medicine
1:55 - 2:20 PM	***Harmonizing NAb Sample Testing and Reporting: Key Insights from the White Paper*** Jason DelCarpini, Moderna
2:20 - 2:45 PM	***Bioanalytical Strategies for Cell Therapies: Current Considerations*** David Williams, BioAgilytix
2:45 - 3:05 PM	**Panel Discussion**
3:05 - 3:25 PM	Break

SESSION IV: Clinical/Quantitative Pharmacology of Cell Therapies
Moderator: Dale Miles, Genentech & Yizhe Chen, BMS

3:25 - 3:30 PM	**Session Introduction**
3:30 - 3:55 PM	***Making Drugs from T cells: Mathematical Model-informed Design and Deployment of Next Generation T Cell Therapies*** Daniel Kirouac, Metrum Research Group
3:55 - 4:20 PM	***Clinical Pharmacology Considerations in the Development of Allogeneic Cell Therapies - Opportunities & Challenges*** Hardik Mody, Genentech

SESSION V: CMC
Moderator: Nanda Balasubramanian, BMS & Lei Ci, Moderna

4:20 - 4:25 PM	**Session Introduction**
4:25 - 4:50 PM	***CMC Development for Cell and Gene Therapies for the Treatment of β-hemoglobinopathies*** Tamara Monesmith, Editas Medicine
4:50 - 5:10 PM	**Panel Discussion** Andy Lin, Genentech and Tamara Monesmith, Editas
5:10 - 6:10 PM	**Reception**

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FRIDAY, MARCH 21

8:00 - 9:00 AM **Registration & Breakfast**

9:00 - 9:05 AM **Speaker Introduction**
Vibha Jawa, BMS

9:05 - 9:45 AM **PLENARY:** ***From Innovation to Translation to Patients: The Future of Genetically Engineered T-Cells for Human Therapeutics***
Bruce Levine, University of Pennsylvania

SESSION VI: Lessons Learned from Approved Cell Therapies
Moderator: Nagendra Chemuturi, Eli Lilly

9:45 - 9:50 AM **Session Introduction**

9:50 - 10:15 AM ***Role of Clinical Pharmacology in Efficient Development of CAR-T Cell Therapy: From FIH Starting Dose Selection to RP2D and Beyond***
Indrajeet Singh, J&J

10:15 - 10:40 AM ***Comprehensive Bioanalytical Cellular Kinetics Strategy for Adoptive T Cell Therapies***
Sebastian Guelman, Genentech

10:40 - 11:00 AM Break

SESSION VII: Regulatory Perspectives
Moderator: Steven Louie, Medicilon

11:00 - 11:05 AM **Session Introduction**

11:05 - 11:30 AM ***Navigating the Regulatory Landscape of Cell Therapies: Nonclinical Considerations***
Helen-Marie Dunmore, Certara

11:30 - 11:55 AM ***Regulatory Expectations and Safety Concerns with CART and Next Generation CART Programs***
Gabriela Hernandez-Hoyos, BMS

11:55 - 12:00 PM Closing Remarks

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ABSTRACTS

PLENARY

Nonclinical Safety Assessment of Chimeric Antigen Receptor T Cell (CAR T) Therapies

Kyle Kolaja, BMS

Chimeric Antigen Receptor T cell (CAR T) therapy represents a groundbreaking advancement in the treatment of patients afflicted with cancer and more recently auto-immune diseases. This presentation will delve into the nonclinical safety aspects critical to evaluating the risk-benefit profile of CAR T products. Unlike traditional modalities, the human nature of the CART cell product renders many classic toxicological studies irrelevant. Approaches that are germane to understanding potential toxicity will be discussed, including binder selectivity and tissue expression of the target antigen. Additionally, assays such as cytokine-independent growth and insertion site analysis are critical to address theoretical concerns related to insertional oncogenesis and subsequent secondary tumorigenesis. Furthermore, as the field evolves to more complex genetic engineering programs, novel approaches are warranted in the development of safe and effective CAR-T therapies. This comprehensive overview aims to provide insights into the methodologies and considerations essential for advancing CAR-T therapy from bench to bedside.

SESSION I

Journey of India's First CAR-T Cell Therapy and its Global Impact

Alka Dwivedi, NIH

Chimeric Antigen Receptor (CAR) T-cell therapy targeting CD19 has demonstrated significant success in treating relapsed and refractory (r/r) leukemia and lymphoma. However, the high cost of CAR T-cells – typically exceeding $400,000 – limits their availability to the small numbers of countries, health care systems, and individuals who can afford them. To address this critical issue in India, we developed our own novel humanized CD19 CAR vector. Preclinical testing demonstrated high efficacy both in vitro and in vivo in humanized mice. These data paved the way for a phase I/II clinical trial in patients with relapsed/refractory B-cell malignancies. The striking complete response rate of ≥60–70%, together with a low toxicity profile, led to the regulatory approval of our humanized CD19 CAR T-cell therapy (Actaly-cel, NexCAR19) from the Central Drugs Standard Control Organization (CDSCO) in 2023, marking a major milestone in India's biotechnology and healthcare sectors. NexCAR19 has the potential to expand global access to CAR T-cell therapy, particularly in low- and middle-income countries, by offering a cost-effective alternative to Western CAR T-cell products. Additionally, it fosters self-reliance in advanced cancer treatment, reducing dependence on imported therapies. Beyond its current applications, NexCAR19 is leading the development of next generation CAR T-cell therapies, driving advancement in the field of cellular immunotherapy.

Overcoming Host Rejection in Allogeneic Adoptive Cell Therapy: Engineering Strategies for Persistence and Efficacy

Johannes Stanta, Celerion

Allogeneic adoptive cell therapy (ACT) holds immense potential for off-the-shelf immunotherapy, offering scalable and immediately available treatments for cancer and other diseases. However, host immune rejection remains a major barrier, limiting the persistence and efficacy of infused cells. This talk will explore the mechanisms driving host-versus-graft rejection, including T-cell and NK-cell-mediated cytotoxicity, cytokine-driven inflammation, and alloimmune memory formation. I will then highlight key engineering strategies to overcome these challenges, including TCR knockout to prevent graft-versus-host disease (GvHD), MHC class I modulation

to evade host T and NK cell responses, and the use of alloimmune defense receptors (ADR) to selectively eliminate alloreactive immune cells. Additionally, I will discuss emerging cell sources such as virus-specific T cells (CAR-VSTs) and iPSC-derived CAR T cells, which offer improved persistence and reduced immunogenicity. Finally, I will review preclinical and clinical developments, addressing the challenges of balancing immune evasion with sustained anti-tumor function. By integrating genetic engineering and novel immune-evasive strategies, we can advance allogeneic cell therapies toward broader clinical application, paving the way for more durable and effective immunotherapies.

Cryo-Fluorescence Tomography: Transformative 3D Imaging to Monitor Gene and Cell Therapies
Matt Silva, EMIT Imaging

New vectors are being developed to enhance efficacy, including biodistribution and transduction, while reducing off-target effects. Visualizing vector biodistribution and gene transduction in preclinical models is essential but challenging with standard imaging modalities.

Cryo-Fluorescence Tomography (CFT) is a transformative 3D imaging technology providing high resolution and sensitivity fluorescence and anatomical imaging of whole animals or tissues. CFT has multiplexing capabilities, seamlessly integrates into existing workflows, and guides downstream analysis by providing sub-organ localization of drug products, proteins, and biomarkers.

SESSION II

AI-Driven Approaches to Enhancing CAR Design
Simon Bornschein, Coding Bio

Designing novel chimeric antigen receptors (CARs) is a complex challenge that requires a detailed understanding of molecular architecture and its impact on therapeutic outcomes. Coding Bio combines high-throughput data generation with advanced large language models and cutting-edge deep learning techniques to systematically identify key design parameters that optimize clinical efficacy and safety in next-generation cell therapies.

Translational Development of the GbGm Vector for Sickle Cell Disease: Assessing Safety and Efficacy from Preclinical Models to Human
Mohammad Shadid, Korro Bio

TSickle cell disease (SCD) is an autosomal recessive genetic disorder caused by a mutation in the β-globin chain genes leading to sickle hemoglobin production (hemoglobin S or HbS) instead of the normal adult hemoglobin, HbA. Expressing fetal hemoglobin (HbF) has been shown to correct the sickling of the blood cell. The GbGM inventors modified the γ-globin gene by substituting glycine at codon 16 with aspartic acid (G16D) in the Aγ-globin gene to generate GbGM LV. This change is expected to improve the activity of the Aγ-globin. In the present study, we describe the long-term safety of GbGM in wild-type mice after primary and secondary transplants. The safety of GbGM was assessed by monitoring the effects on body weight, hematological parameters, histopathology of selected organs, malignancy formation, and survival. We also assessed gene transfer and engraftment of human HSC in two immunocompromised mouse models: Persistent stable GbGM -transduced cell engraftment was comparable to that of untransduced cells with no detrimental effects on hematopoiesis up to 20-weeks post-transplant. These robust preclinical studies in mouse and human HSC allowed its translation into sickle cell patients.

SESSION III

Advanced Bioanalytical Strategies to Determine PK and Biodistribution of Cell and Gene Therapy Products
Salvatore Iovino, Editas Medicine

Cell and gene therapies (CGTs) represent a transformative shift in modern medicine, offering potential cures for genetic and acquired diseases. However, the bioanalytical and biomarker strategies for these complex modalities remain challenging due to the intricate biological mechanisms, heterogeneity of therapeutic products, and the evolving regulatory landscape. A key challenge is the development and validation of polymerase chain reaction (PCR)-based assays, which are critical for tracking vector biodistribution, transgene persistence, and genome integration. Despite their importance, there is a lack of standardized regulatory guidance, leading to variability in assay design, validation criteria, and data interpretation across clinical programs.

Recent clinical trials highlight these challenges. For instance, quantitative PCR (qPCR) is frequently used to assess vector shedding and persistence, yet inconsistencies in sensitivity thresholds complicated regulatory submissions. Similarly, CAR-T cell therapies for hematologic malignancies faced hurdles in safety and cellular kinetics, expansion and persistence due to variability in ddPCR assay performance across different laboratories. Furthermore, the application of biomarkers to monitor immune responses and safety, such as cytokine profiling in CGTs, remains in its infancy, further complicating efficacy and safety assessments.

This abstract will discuss emerging bioanalytical strategies, including PCR-based approaches, improved standardization efforts, and biomarker-driven methodologies to enhance CGT development. Addressing these challenges through collaborative regulatory frameworks and standardized assay validation practices will be critical to advancing the field and ensuring robust clinical and regulatory outcomes.

Bioanalytical Strategies for Cell Therapies: Current Considerations

Dave Williams, BioAgilytix

The emergence of cell and gene therapies has led to the increased utilization of specialized technology platforms in regulated bioanalysis. In this presentation, we will discuss considerations for the bioanalytical strategy of cell therapies with various platforms. We will evaluate the different technologies that are used in determining pharmacokinetics (PK) of cell therapies including qPCR/dPCR and flow cytometry, and strategies that can be used to understand immunogenicity of cell therapies with plate-based and cell-based assays. Moreover, common considerations when developing and validating these assays will be addressed with case studies as examples.

SESSION IV

Making Drugs from T Cells: Mathematical Model-Informed Design and Deployment of Next Generation T Cell Therapies

Daniel Kirouac, Metrum Research Group

Engineered T cells have emerged as highly effective treatments for hematological cancers. Hundreds of pre-clinical and clinical programs are underway in efforts to expand the efficacy, safety, and applications of this immuno-therapeutic modality. However, these 'living drugs' make unruly therapeutics, as the drug product proliferates, differentiates, traffics between tissues, and evolves through interactions with patient immune systems. Using publicly available clinical data from Chimeric Antigen Receptor (CAR) T cells, we demonstrate how mathematical models and machine learning workflows can be used to quantify the relationships between product characteristics, patient physiology, pharmacokinetics and clinical outcomes.

For next generation T cell therapies, the design space at play is vast and combinatorial: CAR/TCR designs, gene edits, synthetic biology-based regulatory switches, novel cell sources and expansion protocols. As scientists work to integrate these new technologies, they must also navigate an increasingly competitive and evolving therapeutic landscape. I will provide some examples and perspectives on how computational systems modelling can be employed to integrate data, inform decisions, and translate hypotheses into clinical strategy.

Clinical Pharmacology Considerations in the Development of Allogeneic Cell Therapies – Opportunities & Challenges
Hardik Mody, Genentech

Adoptive Cell Therapy is one of the most rapidly expanding branches of cancer immunotherapy due to unprecedented clinical successes and regulatory approvals of multiple autologous CD19 and BCMA-targeting Chimeric Antigen Receptor (CAR)-T cell therapies for the treatment of B-cell hematological malignancies. Despite the success, challenges continue to exist for autologous CAR-T therapies including relapse, safety concerns, long 'vein-to-vein' time, less flexibility for repeat dosing, high cost and manufacturing hurdles. To address the challenges associated with the autologous CAR-T therapies, 'off the shelf' allogeneic cell therapies are under investigation. Like autologous cell therapies, allogeneic therapies also present unique clinical pharmacology challenges due to their unique cellular kinetics profile, convoluted dose-exposure-response relationships that is impacted by various patient- and product-specific factors. In addition, shorter in vivo CAR-T persistence and graft-vs-host disease are challenges that are unique to allogeneic cell therapies. Here, Clinical Pharmacology approaches for allogeneic cell therapies will play a key role in optimizing dose selection, dosing frequency and regimen, optimizing lymphodepleting regimen, and identifying key patient- and product-specific characteristics impacting clinical outcomes. This presentation will cover the current development landscape of allogeneic cell therapies and unique considerations for its development. In addition, key clinical pharmacology learnings from early stage clinical programs including dose-exposure-response relationship, patient- and product-specific factors impacting PK/PD, repeat dose learnings, and impact of different lymphodepletion regimens will also be discussed.

SESSION V

CMC Development for Cell and Gene Therapies for the Treatment of β-Hemoglobinopathies
Tamara Monesmith, Editas

Renizgamglogene autogedtemcel (reni-cel) is an investigational autologous, CRISPR-gene edited CD34+ hematopoietic stem and progenitor cell (HPSC) therapy for the treatment of sickle cell disease (SCD) and transfusion-dependent β-thalassemia (TDT). It consists of autologous CD34+ cells edited at the HBG1 and HBG2 promoters by an engineered AsCas12a gene-editing nuclease. Multiple naturally occurring mutations in the HBG1 and HBG2 promoter region are associated with a benign condition termed hereditary persistence of fetal hemoglobin (HPFH), where fetal hemoglobin (HbF) levels remain elevated throughout adulthood without affecting other hematological parameters. Elevation of HbF has been shown to ameliorate disease for individuals with β-hemoglobinopathies. The edits in reni-cel mimic these naturally occurring variants of HPFH in the HBG1 and HBG2 promoters that reactivate γ-globin expression and increase HbF production. Reni-cel is intravenously infused into myeloablated patients where it is expected to engraft in the bone marrow, self-renew, and differentiate into all hematopoietic lineages including erythroid progenitors that harbor an array of insertions and deletions (indels) in HBG1 and HBG2 promoters. Reni-cel has demonstrated a favorable safety and efficacy profile in clinical trials. This presentation provides an overview on the approach to develop manufacturing processes and analytical methods as well as administration procedures for reni-cel to enable successful clinical translation. Consistency in product quality attributes in reni-cel lots manufactured for SCD and TDT patients is demonstrated. Moving forward, to decrease the patient burden and simplify the manufacturing journey, an in vivo gene editing medicine delivered to target cells is in development using the same clinically validated editing strategy as reni-cel.

PLENARY

From Innovation to Translation to Patients: The Future of Genetically Engineered T-Cells for Human Therapeutics
Bruce Levine, University of Pennsylvania

Since the 1990's, we have conducted clinical trials of gene modified T cells. Chimeric antigen receptor (CAR) T cells targeting CD19 on B cells leukemias and lymphomas which have induced durable complete responses in patients who are relapsed or refractory to all other available treatments. New designs for genetically modified T cells include switches and potency enhancements that will be required for targeting solid tumors. Determining the critical quality attributes, dose, potency, and anticipating pharmacokinetics of a living, dividing drug presents unique challenges. Improving patient access to advanced cell and gene therapies entails not only on scientific progress in targeting, gene modification and cellular manipulation, but also on meeting automation, engineering, clinical site onboarding, and health policy challenges.

SESSION VI

Comprehensive Bioanalytical Cellular Kinetics Strategy for Adoptive T Cell Therapies
Sebastian Guelman, Genentech

Adoptive T cell therapy is a relatively new therapeutic modality and as such, there is no clear consensus in industry on the design of cellular kinetics (CK) strategies. During this presentation, a detailed bioanalytical CK strategy developed for an autologous TCR-T cell program for solid tumors will be discussed. This comprehensive clinical CK strategy combines two ddPCR assays and a flow cytometry method to enable a clear analysis of the expansion, persistence and immunophenotype of the engineered T cells in circulation. The challenges and solutions in the development of these assays, as well as critical reagent selection and qualification/validation data to support a first-in-human study will be examined. This integrated CK approach can be applied to future autologous and allogeneic therapies.

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SPEAKER BIOGRAPHIES

SIMON BORNSCHEIN, PHD, Coding Bio
Dr. Bornschein, PhD in Immuno-Oncology, specializes in cell therapy and CAR therapy development. He has contributed to advancing anti-cancer CAR therapies at Celyad and worked on engineering immunosuppressive cells for autoimmune disease prevention at Quell Therapeutics. As CEO & Co-Founder of Coding Bio, he applies biological insights and machine learning to improve therapeutic discovery and development.

JASON DELCARPINI, Moderna
With over 20 years in the pharmaceutical and biotech industries, Jason DelCarpini is a leader in bioanalytical science, specializing in pharmacokinetics, pharmacodynamics, and immunogenicity for innovative therapies, including mRNA-LNP, protein, gene, and cell-based treatments. As Director of Bioanalytics at Moderna, he develops and oversees clinical and preclinical bioanalytical strategies, ensuring regulatory compliance and advancing GLP/GCLP-regulated processes.

Jason has played key roles in founding and managing bioanalytical laboratories, with a focus on continuous improvement, adopting new technologies, and implementing digital workflows to enhance efficiency and compliance. An active contributor to the bioanalytical community, he regularly participates in industry seminars, publications, and working groups to advance knowledge and standards across the field.

HELEN-MARIE DUNMORE, Certara
Helen-Marie Dunmore is Senior Director in Toxicology who has significant experience consulting on the nonclinical regulatory requirements of advanced therapy medicinal products (cell and gene therapies) and a wide range of large and small molecules. Prior to being a consultant at Certara and Charles River Laboratories, she served as a Senior Nonclinical Reviewer at the Medicines & Healthcare product Regulatory Agency in the UK and as a NonClinical Expert to the European Medicines Agency, reviewing nonclinical submission packages in support of clinical trial applications or marketing applications across therapy areas and drug modalities. Helen-Marie has experience presenting nonclinical findings and making recommendations to UK and EMA Advisory Committees (e.g., CHM and CHMP) and providing scientific and regulatory advice (on behalf of the MHRA and/or EMA). She was involved in writing regulatory guidance and representing the agencies on working groups or industry global consortia eg. BioSafe and the Association of British Pharmaceutical Industry. Helen-Marie has a Master's degree in Applied Toxicology from the University of Surrey in the UK and is a board registered toxicologist.

ALKA DWIVEDI, PHD, NIH
Dr. Alka Dwivedi has pioneered the development of a novel CAR T-cell-based therapy in India, with the potential to greatly expand global access to this innovative cancer treatment. She had been instrumental in bringing forward NexCAR19, the world's most affordable CAR T-cell drug and is a co-founder of ImmunoACT, an Indian company commited to making affordable cell therapy treatments for cancer accessible worldwide. Her groundbreaking work earned her recognition on the *TIME100 Health List* of the most influential people in 2024.

Dr. Dwivedi is currently a postdoctoral research fellow at the National Cancer Institute in Bethesda, Maryland. She earned her doctoral degree from the Indian Institute of Technology in Bombay, India in 2021 in Biosciences and Bioengineering.

SEBASTIAN GUELMAN, PHD, Genentech
Sebastian Guelman is a Senior Principal Scientist in the BioAnalytical Sciences Department at Genentech. He currently leads the development of bioanalytical strategies to support a number of cancer immunotherapy programs in Genentech's pipeline, including advanced modalities such as T-cell bispecific antibodies, T cell therapy and Individualized Neoantigen-specific Immunotherapy. Prior to joining Genentech, Sebastian worked at Iconic Therapeutics, developing pre-clinical pharmacokinetic, immunogenicity and biomarker assays to support oncology programs. Prior to that role, Sebastian worked in the development of immunoassays for clinical diagnostics using different platforms. Sebastian received his PhD degree in Biochemistry and Molecular Biology from the Pennsylvania State University and was a post-doctoral fellow in the Department of Pathology at Genentech.

SALVATORE IOVINO, PHD, Editas Medicine
Dr. Salvatore Iovino is a biopharmaceutical leader with a proven track record in driving drug discovery and development programs from early-stage research to Ph.1-3 clinical trials (NTLA2001 ATTR, MAGNITUDE; and Sana SC291/SC261 GLEAM, VIVID). After obtaining his PhD, he completed a postdoctoral fellowship at Joslin Diabetes Center, Harvard Medical School, publishing his research on cardiometabolic disease in top peer-reviewed journals (including Cell, Cell Metabolism, PNAS).

With 15 years' experience in bioanalytical, biomarker and translational sciences, Dr. Iovino managed teams at leading biotech and pharmaceutical companies such as Merck, Sana Biotechnology, Editas Medicine, Intellia and Carbon Biosciences.

In his current role at Editas Medicine, Dr. Iovino is leading regulated and non-regulated bioanalytical and biomarker sciences efforts in support of PK/PD, DMPK and ADME studies for LNP-mediated delivery of CRISPR/Cas genetic medicines. He has a relevant background in multiple modalities including cell and gene therapies, iPSC/stem cells, and small/large molecules to advance drug development programs for a variety of genetic, cardiovascular and cancer diseases.

DANIEL KIROUAC, PHD, Metrum Research Group
Dr. Kirouac heads the Quantitative Systems Pharmacology department at Metrum Research Group, a global leader in biomedical modeling and simulation. He previously held scientific positions in large pharma, mid-size biotech, start-ups and consulting. He has been developing mathematical models of biological systems for over 20 years, co-authoring 28 scientific publications on dynamical systems modeling, bioinformatics, machine learning, drug development and cell therapy. An engineer at heart, Dr. Kirouac did post-doctoral training at MIT and Harvard Medical School, holds a PhD in Biomedical Engineering from the University of Toronto, and Bachelors degrees in both Chemical Engineering and Genetics.

KYLE KOLAJA, PHD, DABT, FELLOW, ATS, BMS
Kyle Kolaja is currently Scientific Vice President at BMS (heritage Celgene). In this role, he leads the Investigative Toxicology (Summit, NJ), the Cell Therapy Safety (Seattle, WA) the Development and Reproductive Toxicology, Genetic & Occupational Toxicology, and Immunotoxicology Groups (New Brunswick, NJ) and is responsible for the preclinical safety and regulatory submissions for the entire BMS cell therapy portfolio.

Previously, Dr Kolaja was Vice President, Business Development and Cell Therapy at Cellular Dynamics, where he sought and established clinical and preclinical applications of pluripotent stem cells and their derived tissues. Prior to joining CDI, he was Global Head of Predictive Toxicology Screens and Investigative Toxicology at Roche, where he oversaw laboratories in US and Europe that conducted all safety screening assays, provided toxicology

support to projects, and applied stem cell derived tissues to safety. Prior to joining Roche, he was Vice President of Chemogenomics and Toxicology at Iconix Pharmaceuticals and prior to that, was a project toxicologist and site head of investigative toxicology at Searle/Pharmacia. Dr Kolaja is a Fellow of the Academy of Toxicological Sciences (and past President) and a Diplomate of the American Boards of Toxicology and served on the Board of Directors for both organizations. He has served as President of the SOT's Specialty Sections for Drug Discovery Toxicology and Stem Cells and Toxicology. He has served as Associate Editor/Editorial Board for a number of journals including Toxicological Sciences. Dr. Kolaja has over 80 peer-reviewed publications and reviews, received his BS from Michigan State University and his Ph.D. in Toxicology from Indiana University (mentor James Klaunig) and conducted his post-doctoral research at the University of Kansas (mentor Curt Klaassen).

BRUCE LEVINE, PHD, University of Pennsylvania

Dr. Bruce Levine, Barbara and Edward Netter Professor in Cancer Gene Therapy, is the Founding Director of the Clinical Cell and Vaccine Production Facility (CVPF) in the Department of Pathology and Laboratory Medicine and the Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania. He received a B.A. (Biology) from Penn and a Ph.D. in Immunology and Infectious Diseases from Johns Hopkins. First-in-human adoptive immunotherapy trials include the first use of a lentiviral vector, the first infusions of gene edited cells, and the first use of lentivirally-modified cells to treat cancer. Dr. Levine is co-inventor of the first FDA approved gene therapy (Kymriah), chimeric antigen receptor T cells for leukemia and lymphoma, licensed to Novartis. Dr. Levine is co-inventor on 32 issued US patents and co-author of >200 manuscripts and book chapters with a Google Scholar citation h-index of 110. He is a Co-Founder of Tmunity Therapeutics, and of Capstan Therapeutics both spinouts of the University of Pennsylvania. Dr. Levine is a recipient of the William Osler Patient Oriented Research Award, the Wallace H. Coulter Award for Healthcare Innovation, the National Marrow Donor Program/Be The Match ONE Forum 2020 Dennis Confer Innovate Award, the American Society for Gene and Cell Therapy Jerry Mendell Award for Translational Science, and serves as Immediate Past-President of the International Society for Cell and Gene Therapy. He has written for Scientific American and Wired and has been interviewed by the NY Times, Wall Street Journal, Washington Post, NPR, Time Magazine, National Geographic, Bloomberg, Forbes, BBC, and other international media outlets.

ANDY LIN, PHD, Genentech

Andy is currently the VP of Individualized and Cell Therapies Development at Genentech/Roche responsible for a talented team of engineers and scientists developing a range of products including neoantigen based cancer vaccines, allogeneic CAR-T and regenerative medicine clinical products. He has held various roles at Genentech including leading teams from FIH studies to the launch of commercial products and post marketing changes. Prior to Genentech, Andy was at Cell Genesys and Chiron working in the areas of vaccines, therapeutic proteins and ATMPs. Andy received his Ph.D. in Chemical Engineering from Northwestern University and B.S. in Chemical Engineering from the University of California, Berkeley.

HARDIK MODY, PHD, Genentech

Dr. Hardik Mody is currently a Principal Scientist at Genentech within the Clinical Pharmacology department, with over 7 years of drug development experience. As a Clinical Pharmacology lead, he is guiding Clin Pharm strategies, supporting regulatory submissions, performing M&S analysis for novel modalities (such as cell therapy), biologics (such as T-cell engagers), small molecules within oncology and non-oncology therapeutic areas. He has previously worked in the Translational PK/PD group at Janssen, supporting early discovery, preclinical and early clinical development of therapeutic biologics in oncology and other therapeutic areas. He has also served as the PK/PD SME (Subject Matter Expert) for cell and gene therapies within his organization. He has authored >20 peer-reviewed scientific journal articles and several scientific abstracts in the field of PK/PD, oncology, and drug delivery

and has been an invited speaker at external scientific conferences. He has received MS and PhD from the Ohio State University in Pharmaceutical Sciences and Postdoctoral experience from the Center for Pharmacometrics & Systems Pharmacology, University of Florida.

TAMARA MONESMITH, Editas Medicine
Tamara T. Monesmith is the Senior Vice President of Technical Development at Editas Medicine. Since joining Editas Medicine in 2018, she has built teams and capabilities in Process Development, Analytical Development, and Manufacturing Sciences and Technology to support CRISPR-based gene editing medicines. With more than 25 years of experience in CMC strategies for therapeutics, she led Editas' Technical Development efforts to drive reni-cel to BLA. Prior to joining Editas, she held various roles with increasing responsibility at Argos Therapeutics, including development of their autologous dendritic cell immunotherapeutic platform process, clinical manufacturing for phase 2 and phase 3 trials in oncology and infectious diseases, and establishment of the strategy for supply chain and logistics to support a global phase 3 clinical trial in renal cell carcinoma. She holds a BS degree in Chemical Engineering from the University of Arizona and a MS degree in Biological Engineering from North Carolina State University.

MOHAMMAD SHADID, PHD, Korro Bio
Dr. Mohammad Shadid is an accomplished translational development leader, renowned for his expertise in guiding multiple drug modalities from early research to clinical trials. Currently serving as the Vice President of Translational Sciences at Korro Bio, Dr. Shadid oversees all IND-enabling activities, including PK/PD modeling, human dose projections, and GLP toxicology, as well as Phase 1 supporting activities such as determining starting human doses, clinical pharmacology, and biomarkers. Dr. Shadid has co-authored and facilitated a wide array of regulatory interactions both within the United States and internationally. His extensive experience spans various modalities, including cell therapy, AAV gene therapy, oligonucleotides, LNP-based therapies, small molecules, and antibody-drug conjugates. Prior to his role at Korro Bio, Dr. Shadid served as the Head of Preclinical Development at Aruvant, the center of excellence for cell and gene therapy at Roivant. He has also held increasing responsibilities in nonclinical development at Sarepta, Biogen, and Takeda.

MATT SILVA, PHD, EMIT Imaging
Matt Silva, PhD, is the CEO of EMIT Imaging, the leader in Cryo-Fluorescence Tomography (CFT) imaging. Previously, he served as CEO of Invicro, a global imaging CRO and led the strategic vision and mission to support the drug discovery and development community with diverse imaging services spanning preclinical and clinical applications. Prior to Invicro, he led imaging biomarker groups at Vertex, Amgen, Millennium and Takeda Pharmaceuticals. Matt holds a Ph.D. in Biomedical Engineering from Worcester Polytechnic Institute.

INDRAJEET (JEET) SINGH, PHD, Johnson and Johnson
Indrajeet (Jeet) Singh is a Senior Director, Group Leader Clinical Pharmacology, at Johnson and Johnson Innovative Medicine. He oversees the Multiple Myeloma portfolio and is responsible for developing and driving clinical pharmacology and pharmacometric strategies within the Heme Disease Area Stronghold. Jeet has over 15 years of experience in small and large molecule clinical development, with more than 10 of these in immuno-oncology (various modalities eg. Bi-specifics, Tri-specifics, CAR-T). Jeet worked in roles of increasing leadership in team and people's management in different pharmaceutical companies including Gilead Sciences, Janssen, Amgen and Abbvie.

He is proficient in applying quantitative pharmacology, and mechanistic PK/PD modeling & simulation (M&S), Quantitative Systems Pharmacology (QSP) based strategies to influence decisions throughout development from pre-clinical to late development. Jeet is actively involved in IQ consortium initiatives and is highly visible externally

at conferences and served as invited speaker at FDA sponsored workshops.

Jeet earned his PhD in Chemical and Biological Engineering from the University of Buffalo and his Bachelor of Technology in Chemical Engineering from the Indian Institute of Technology in India.

In his spare time, Jeet loves to travel with his family and spend time outdoors hiking and biking. Jeet has visited 4 of the 7 wonders of the world and he hopes to visit the remaining three.

JOHANNES STANTA, PHD, Celerion
Johannes Stanta, PhD, works at Celerion as Scientific Director being in charge of the global scientific leadership in the bioanalytical laboratories in Lincoln, NE and Zürich, Switzerland. In his role, Johannes strengthens Celerion's service offering with GLP and GCP compliant bioanalytical analysis to support the development of new drugs and therapies. He previously worked at Freeline Therapeutics where he had the overall bioanalytical responsibility of several gene therapy clinical trials, including the companion diagnostic analytical and clinical development. He previously worked in senior scientific leadership roles in bioanalysis and clinical laboratory at LabCorp and Hammersmith Medicines Research.

DAVE WILLIAMS, PHD, BioAgilytix
Dave Williams, Ph.D., is the Vice President of Operations and General Manager of BioAgilytix, Durham, NC. He has over 20 years of experience in bioanalytical science including immunoassays, flow cytometry, molecular assays, and other bioanalytical techniques. His expertise is in large molecule and advanced modality therapeutics. Dave received his Ph.D. in Toxicology from the University of Kansas Medical Center.

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POSTER ABSTRACTS

Single-cell Multi-omics Analysis Reveals Differential Lineage-specific Vector Copy Number Distribution in CAR-T Cell Products

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2. Children's Hospital Colorado, 13123 East 16th Ave, Aurora, CO 80045;
3. National Institute of Standards and Technology. Gaithersburg, MD

PURPOSE:
Chimeric antigen receptor T-Cell (CAR-T) immuno-therapies have been transformative solutions to treat cancer patients. As most CAR-T therapies rely on the introduction of CAR into host cells using lentiviral vectors followed by re-introducing the modifi ed T-cell back into patients, the quality of CAR-T is extensively regulated. Key safety and effi cacy attributes such as transduction effi ciency and transgene copy number, or viral vector copy number (VCN), needs to be accurately measured. Yet conventional methods for measuring gene transfer lack the resolution and representation to truly refl ect sample composition and either report a population average (bulk) or involve laborious and time-consuming clonal outgrowth.

METHODS:
Mission Bio has developed an end-to-end solution from panel design to data analysis for single-cell targeted DNA sequencing to interrogate transgenes. We applied this single-cell protein + DNA multi-omic VCN workfl ow to analyze a bi-cistronic CD19 and CD22 CAR-T product.

RESULTS:
Our VCN analysis confi rmed the distribution of VCN in the product closely adhered to the expected Poisson distribution throughout the expansion, suggesting a low risk of biased functional clonal expansion favoring cells with high VCN. Additionally, we quantitatively measured surface protein expression for lineage assignment.

CONCLUSIONS:
This revealed differential transduction percentages and VCN distribution patterns across cell lineages (e.g., CD4+ and CD8+ T cells), providing insights into factors potentially infl uencing treatment outcomes.

Development of a Multiplex RT-qPCR Assay for Highly Similar mRNA Sequences

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PURPOSE:
The rapid evolution of gene and cell therapy has underscored the need for robust bioanalytical techniques to accurately quantify and characterize complex mRNA therapeutics. Among these, reverse transcription quantitative polymerase chain reaction (RT-qPCR) remains a gold standard due to its sensitivity and specificity. However, its application to similar mRNA molecules—particularly those encapsulated in lipid nanoparticles (LNPs)—poses challenges in amplification efficiency, reproducibility, and quantification.

METHODS:
We developed and optimized an RT-qPCR assay for quantifying higher similar mRNA in cynomolgus monkey serum. Key aspects of the method include primer-probe design refinement, enhanced RNA extraction strategies, and mitigation of matrix effects to improve assay performance.

RESULTS:
This presentation will highlight RT-qPCR method development strategies to improve assay robustness, accuracy, and reproducibility for highly similar mRNA analysis. We will discuss specificity enhancements, and multiplexing strategies to streamline RT-qPCR workflows. Additionally, we will explore the application of multiplexing and bridging strategies to refine bioanalytical RT-qPCR method development and validation for mRNA therapeutic analysis.

CONCLUSIONS:
By implementing unique primer-probe strategy, we aim to develop robust bioanalytical RT-qPCR method for measurement of LNP-encapsulated mRNA in cynomolgus monkey. Our findings might have significant implications for regulatory compliance, assay standardization across laboratories, and the broader success of gene and cell therapy programs.

Leveraging complex liver microphysiological system to characterize delivery vehicles and evaluation of pharmacology and safety of candidate gene therapy products

PURPOSE:
As cell and gene therapies (GT) become more prevalent for selectively targeting previously untreatable or rare diseases, there is a growing need for efficient and predictive preclinical models to validate drug candidates. The current state of the art models are lacking in complexity, human relevance, and translatability to the clinic because of the industry's reliance on traditional 2D cultures and animal models. Traditional cultures lack the complexity of the organ including the ability to model inflammation and fibrosis. Whereas animal models lack human relevance leading to development of species-specific surrogate GT products. In this study, we have developed complex liver model with in vivo like cyto-architecture in the Javelin Liver Tissue Chip (LTC) for gene therapy applications. The LTC contains a high volume of media enabling multiple read outs for toxicity, including fibrosis and inflammation; flow and 3D cytoarchitecture for a more biomimetic design; recirculation for a more clinically relevant dosing scheme; and long-term (14+ days) culture for prolonged monitoring. Three studies are described: the first displaying the feasibility of a study on antisense oligonucleotide (ASO) drug, Mipomersen, on a hepatocyte and Kupffer cells on LTC, the second characterizing a four-cell type LTC increasing the complexity of the model, and the last showing comparable gene expression on LTC to native tissue of key genes related to lipid nanoparticle uptake.

METHODS:
Complex cultures were bioengineered on LTC containing exclusively primary human cells with varied complexity: monocultured hepatocytes, co-cultures of hepatocytes and Kupffer cells, or complex cultures of hepatocytes, Kupffer cells, stellate cells, and liver sinusoidal endothelial cells. The complex culture was maintained under dynamic environment at least for 2 weeks while maintaining metabolic and functional activity.

RESULTS:
LTC models developed in this work supported research and biomarkers for gene therapy utility. The study of ASO drug Mipomersen showed efficacy with an decrease in apolipoprotein B-100 (APO-B100) and toxicity with a drop in albumin over 3 days in culture. We also assessed the PD effects of a single dose over an extended period, highlighting the need for multiple doses to sustain drug efficacy. The four cell type LTC showed inducible inflammation and fibrosis in response to appropriate stimuli over 14 days culture, validating the ability to study these outcomes to novel drug stimuli. And preliminary transcriptomic analysis on LTC showed expression of key genes for lipid nanoparticle uptake, LDLR and ASGPR, and levels matched those found in freshly isolated tissue better than static or spheroid models.

CONCLUSIONS:
This work displays the utility and advantages of using Javelin LTC for gene therapy applications. The LTC is more biorelevant than other models at the transcriptomic level, supports more customizable and complex cultures, enables clinically relevant dosing schemes in its long term culture and recirculating flow system, and contains a high media volume for downstream analysis. Future work will begin studies on gene therapy applications utilizing lipid nanoparticles for mRNA delivery and diseased culture models.

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