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ABSTRACT BOOK

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CELL & GENE THERAPY SUMMIT-2025

Session: Advancements in Cell and Stem Cell-based Therapies

Considerations for Allogeneic Dopaminergic Cell Products for Parkinson's Disease

Howard J Federoff

Chief Medical Officer and Co-founder, Kenai Therapeutics, TX

Abstract:

Parkinson's disease (PD) is a chronic, progressive neurodegenerative disorder affecting over 10 million people worldwide. It is characterized by the degeneration of dopaminergic (DA) neurons in the substantia nigra, leading to debilitating motor symptoms such as tremor, rigidity, bradykinesia, and postural instability. Current treatments, including levodopa and dopamine agonists, offer temporary symptomatic relief but fail to halt disease progression. Kenai is bringing forward a cryopreserved, allogeneic iPSC-derived dopaminergic neuronal stem cell product formulated for MRI-guided delivery to the putamen for the treatment of moderate to moderate-severe Parkinson's disease. This therapeutic modality is particularly attractive in Parkinson's disease, where dopaminergic neuronal loss is largely confined to a small, well-defined structure. Upon transplantation, the cells mature and integrate with the host circuitry, reinnervate their targets, and restore dopaminergic tone critical for motor function. In principle, this one-time intervention could permanently reestablish physiological dopamine signaling in the striatum, reverting the disease to an earlier state. Importantly, the reconstituted circuitry is expected to provide continuous, regulated dopamine release, offering the potential for long-term relief of motor symptoms without troublesome dyskinesias. Cell replacement therapy holds considerable promise as a disease-modifying approach for Parkinson's disease, driven by its potential to address the fundamental pathophysiological deficits. In this Keynote, a rationale and approach to prosecuting this therapeutic modality will be presented and placed in context with regard to other approaches.

Biography:

Howard J Federoff, MD, PhD is the scientific co-founder and Chief Medical Officer (CMO) of Kenai Therapeutics, Inc. Previously, he was co-founder, director and CMO of Ryne Bio. Howard is former CEO, President and director of Brooklyn ImmunoTherapeutics (Eterna, Nasdaq). He was recently a distinguished professor of neurology at the University of California, Irvine, the former CEO of UCI Health, vice chancellor for Health Affairs and dean of the UCI School of Medicine. Prior to UCI Health, he was EVP of Health Sciences and executive dean at Georgetown University. He has published more than 300 peer-reviewed and invited articles. He co-founded MedGenesis Therapeutix, Brain Neurotherapy Bio, Kaleibe Therapeutics, Ireneo Health, Ryne Bio and Kenai Therapeutics all advancing understanding and/or therapeutics for neurologic diseases. He was CEO of the regenerative medicine company, Aspen Neuroscience, Inc, in San Diego where he led funding of an A round. Howard chaired the NIH Recombinant DNA Advisory Committee, the NHLBI Gene Therapy Resource Program and the Board of the Association of the Academic Health Centers. He serves as an advisor/director for several companies. He is an elected Fellow of the AAAS and the NAI. He received his MD, MS and PhD from the Albert Einstein College of Medicine in New York. He completed his residency and clinical and research fellowships at Massachusetts General Hospital and Harvard Medical School.

A novel proteomic assay for monitoring cell transplantation

Eric Schuur

Chief Executive Officer and Founder, HepaTx Corporation, CA

Abstract:

Liver disease is the 12th leading cause of death globally. Orthotopic transplantation is the only curative treatment available for patients once the disease has become advanced. Hepatocyte transplantation has been demonstrated to be feasible and effective in rodent models of liver disease and is being developed for human therapy. Technologies to monitor hepatocyte transplantation in humans are invasive, nonspecific, and low resolution. To address this, we have developed a proteomics-based blood test that can identify and quantify transplanted hepatocytes by identifying amino acid substitutions in proteins secreted into the blood stream by donor hepatocytes. Bioinformatic methods were used to identify 89 candidate genes for mass spectrometry detection. Filtering for parameters favourable for mass spectrometry yielded 14 candidate alleles. Spike-in experiments confirmed the ability to detect proteins from these alleles at expected concentrations in plasma. Targeted assay development confirmed consistent detection of all alleles. Analysis of plasma samples from 11 donors revealed that no two donors had the same phenotype, confirming the ability to distinguish between individuals with this assay. The proof of concept will be extended by analysis of plasma samples from patients who have recently undergone liver transplant.

Biography:

Dr. Eric Schuur is a seasoned life science executive with over 25 years of experience driving innovation within early-stage companies. Trained at UCLA and Scripps Research Institute, he has a proven track record of building and scaling successful biotech ventures. His expertise spans regenerative medicine, gene therapy, diagnostics, and oncology. Dr. Schuur's leadership has been instrumental in bringing groundbreaking therapies and diagnostic tools to market, including a pivotal role in developing one of the first oncolytic viruses and leading a clinical team to FDA approval for an asthma treatment. He is currently focused on revolutionizing liver disease treatment at Hepatx. Beyond his entrepreneurial pursuits, Dr. Schuur is actively involved in mentoring and shaping the future of life sciences through his roles in academic and industry advisory boards.

Emerging novel technologies to enable *in vivo* cell engineering as an alternative to traditional cell therapies

Guobao Chen

AbbVie, MA, USA

Abstract:

Cell therapies including stem cell therapies and engineered cell therapies are widely accepted nowadays, especially the autologous CAR T cell therapies with multiple FDA approval in the past decade. However, the ex vivo engineered cell therapies, including autologous and allogenic CAR T cell therapies face multiple challenges in manufacturing, logistics and patient accessibilities. With the emerging novel technologies on in vivo delivery systems, now in vivo cell engineering is no longer a science fiction, and is happening in real life. This provides an alternative solution for patients who are not able to receive proper treatment due to the hurdles of ex vivo cell therapies. The field is rapidly evolving and a few in vivo CAR T cell therapies are already in the clinic. Although the clinical efficacy is yet to be determined, it is shining light from the end of the tunnel for patients, who are desperately waiting for curative therapies.

Biography:

Guobao Chen is a Principal Research Scientist from AbbVie Cambridge Research Centre. He is the group leader of 5 Senior Scientists who are working on novel delivery modalities to achieve in vivo cell engineering to bring cures to autoimmune disease patients.

Pioneering Spinal Cord Injury Treatment: NurExone's Innovative Exosome Based siRNA Therapy with FDA Endorsement and Expanding Pipeline for Neuronal Regeneration.

Lior Shaltiel

NurExone Biologic, Israel

Abstract:

NurExone is pioneering an exosome-based therapy for spinal cord injury (SCI) that leverages exosomes from bone marrow mesenchymal stem cells to deliver proprietary siRNA targeting the inhibitory protein PTEN, crucial for mTOR signaling. Our preclinical studies demonstrated significant improvements in motor, sensory, and structural recovery in rat models of SCI, utilizing both intranasal and intrathecal delivery methods. The therapy showed strong homing capacity to injury sites and successful optimization of large-scale production processes. With positive preclinical outcomes and FDA support, NurExone is set to expand its pipeline to address additional indications as we move towards clinical trials.

Biography:

Dr Shaltiel is an entrepreneur and an award-winning scientist with extensive multidisciplinary international experience, specializing in chemical engineering, molecular biology, electrophysiology, pharmacology and drug delivery systems. Lior has years of experience in accelerating Israeli start-ups. Lior has worked in several nano-drug delivery companies such as LipoCure and Ayana Pharma. Before joining NurExone, Lior was a VP and Partner at a boutique Chinese investment bank operating in Israel mapping the investment landscape and opportunities in the Israeli pharmaceutical industry. Lior is the initiator and head of the BioMed-MBA program at the Hebrew University.

In vitro assays to study neuroprotection and axon regeneration in human neurons differentiated from Neurogenin-2 engineered induced pluripotent stem cells.

Emani Maheswara Reddy*, Gaia Ruggeri, Soojin Kim, Archana Chavan, Flora Hinz,

Department of Biochemistry and Cellular Pharmacology, Genentech.

Abstract:

Drug discovery in neurodegenerative diseases is one of the most challenging therapeutic areas due to the lack of suitable models. Developing efficient and physiologically relevant *in vitro* neuroprotection and axon regeneration models enables us to understand neurodegeneration better and develop suitable therapeutic treatment strategies. Neuroprotection focuses on maintaining the health of surviving neurons after injury, while regeneration seeks to repair or replace damaged neurons and synapses. Relevant *in vitro* experimental models of neuronal damage are necessary to evaluate any treatment's effectiveness. The discovery of induced pluripotent stem cells (iPSCs) has revolutionized the modeling of human diseases, significantly boosting the confidence of *in vitro* neurological disease models. We have developed in vitro assays using some common insults to model and study neuroprotection/ axon regeneration, including chemical toxicity and mechanical damage in Neurogenin-2 engineered iPSC-derived human neurons (iNeurons). Integrating Artificial Intelligence (AI) methods to measure axon degeneration/regeneration showed robust neuroprotection and regeneration *in vitro*. These models could help us to find better therapeutic candidates for neurodegenerative diseases.

Biography:

Maheswara Reddy Emani (Mahesh) earned his PhD in biotechnology from the National Center for Cell Sciences (NCCS) at the University of Pune, India, where his research focused on the role of cancer stem cells in brain tumors. This deeply inspired him to explore the fundamental biology of stem cells. Consequently, in 2010, he joined Professor Riitta Lehesmaa's laboratory at Turku Biosciences in Turku, Finland, as a postdoctoral fellow. During his tenure there, he engaged in significant research projects that culminated in the identification and characterization of the novel pluripotency gene L1TD1, as well as its function in human embryonic stem cells and induced pluripotent stem cells (iPSCs). Subsequently, he joined Orion Pharma in Finland to leverage this technology in drug discovery, particularly utilizing iPS-directed differentiated target cells for drug discovery.

In 2017, he transitioned to the United States to join the Broad Institute of MIT and Harvard as a staff scientist. At the Broad Institute, his research concentrated on employing advanced stem cell technology and patient-derived kidney organoids to uncover the molecular mechanisms underlying epithelial cell injury and repair, with the goal of developing novel therapies for rare kidney diseases.

In 2020, Mahesh joined Genentech (a member of Roche) as a principal scientist and group leader, where he now leads his team on use of iPSC derived target cells and organoids (Brain, Retinal and Kidney) for in vitro pharmacology. These tools proved invaluable for identifying promising lead molecules and conducting mechanistic and toxicological studies. He is thrilled to be part of an environment committed to conducting science at the highest level and transforming these scientific discoveries into therapeutic solutions that can significantly benefit patients.

Session: Advancing Cell-based Immunotherapies: CAR-T, TCR-T and Beyond

Strategies to advance CAR T cell therapy development

Maryland Franklin, Ph.D.

Labcorp, MI, USA

Abstract:

Recent technological developments have led to advancements in precision medicine and sequencing, especially next-generation platforms that have been key enablers.

Over time, platforms that have higher capacity and throughput, and more importantly increased sensitivity, have resulted in more information being made available for researchers from which to gain a better understanding of biology as well as disease states. This explosion of information led to more options and improved approaches to developing targeted therapies to address both rare and complex disorders. Within oncology, chimeric antigen receptor (CAR) T-cell therapies have changed the landscape of blood cancer treatment options with seven autologous CAR T-cell therapies approved by the US FDA. Despite the tremendous advancements, numerous challenges remain, and the industry continues to work through solutions. One critical headwind is how to improve and expand manufacturing capabilities. To this end, this presentation will discuss preclinical use of a closed-system cell incubator instrument to grow human tumor cell lines and CAR T-cells under modified oxygen and pressure conditions. We will share data on transcriptomic analysis of long-term acclimated tumor cell lines and *in vitro* and *in vivo* data of research grade CD19-CAR T-cells under modified growth conditions. In the clinical setting, despite advances in hematologic malignancies, CAR T-cell treatment failure is among the top challenges in managing refractory diseases. The identification and use of specific biomarkers to help choose the right therapeutic approach for a patient, as well as to monitor for response or adverse events have led to important contributors in the advancement of new and developing oncology cancer therapies, including adoptive cell therapies. Biomarker approaches and strategies for CAR T-cell therapies will be discussed, including the utilization of a non-invasive methodology to measure overall copy number alterations (CNA) in cell-free DNA. Patients treated with CAR T-cell therapies who had serial evaluation of their CNA and concordance with tumor burden, CAR gene expression and image analysis will be addressed. Developing solutions to the key barriers of adoptive cell therapy growth is a critical step in further scalability and accessibility of these transformative medicines.

Biography:

Maryland Frankin is Vice President and Enterprise Head of Cell and Gene Therapy at Labcorp, leading strategy and development. She joined Labcorp in 2019 through an acquisition, having led a preclinical oncology CRO team driving scientific and business success. Prior to this, with 12 years in biopharma, she helped advance.

High-Fidelity, Precise Gene Editing with Cas-CLOVER Technology for Allogeneic CAR-T Cell Therapy

Meena Narayanan

Poseida Therapeutics, CA, USA

Abstract:

Among the three main generations of development in gene-editing technology, CRISPR/Cas9 is a highly effective gene-editing tool that is widely used by the scientific community. However, there are still concerns regarding off-target gene editing in therapeutic applications. Hence, Poseida developed a novel and precise site-specific gene editing technology named 'Cas-CLOVER' technology that is mediated through the Cas-CLOVER Site-Specific Nuclease (SSN). Cas-CLOVER is a dimeric, fusion SSN that consists of deactivated Cas9 (dCas9) and the nuclease domain of Clo51 (CLOVER) that is guided by a left and right sgRNA. This fusion nuclease system cuts DNA only when one monomer interacts with another, both independently guided to target DNA, and forms a dimer: thus, providing high fidelity (*1*).

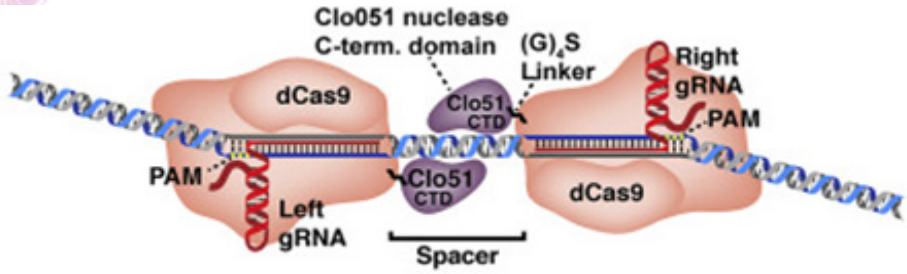

Fig 1: Graphical illustration of generation of Cas-CLOVER (*B.Madison et al Mol Ther Nucleic Acids Sep 2022 - 1*).

The goal of this study is to measure and test the functionality of Cas-Clover mRNA. Therefore, we developed an *in vitro* Luciferase-cleavage assay using human hepatocarcinoma cell line (HepG2) that constitutively expresses Luciferase due to the stable genomic integration of a firefly luciferase expression construct. The selected cell line, HepG2 cells are plated in a 96-well plate and transfected with a range of concentrations of Cas-CLOVER and luciferase specific L+R sgRNA using lipofectamine transfection reagent. The left and the right sgRNAs targeting the luciferase gene is designed with a short protospacer adjacent motif (PAM) on either side for directing cleavage. After 48 hours of transfection, cell luminescence is measured using the Bright-Glo Luciferase assay system. In early development, when Cas-CLOVER and the L+R sgRNA was successfully introduced into the HepG2 cells constitutively expressing firefly luciferase, a significant reduction in the level of luciferase expression (Relative Luciferase Unit; RLU) was achieved. This cell-based functionality assay quantifies the reduction in Relative Luminescence Units (RLU) due to the disruption of luciferase gene *in vitro* and reduction in luciferase expression caused by Cas-CLOVER editing. Further development of this assay will provide the ability to quantitatively measure different levels of Cas-CLOVER activity, critical for assessing the stability of Cas-CLOVER mRNA.

In conclusion, this cell-based functionality assay provides a read-out of the efficiency of Cas-CLOVER technology, a tool that delivers efficiently edited TCR KO CAR-T cells in Poseida's off-the-shelf allogeneic CAR-T drug product candidates.

Madison B, Patil D,Richter M,Li X, Tong M, Cranert S,Wang X, Martin R, Xi H, Tan Y, Weiss L,Marquez K, Coronella J, Shedlock D, Ostertag E. Cas-CLOVER is a novel high-fidelity nuclease for safe and robust generation of Tscm-enriched allogeneic CAR-T cells. PMID:36189080; PMCID: PMC9481872; DOI: 10.1016/j.omtn.2022.06.003

Biography:

Meena Narayanan is a Project Lead Scientist with over a decade of academic research experience and three years in the biotech industry, specializing in CMC and Process Analytics for Cell and Gene Therapy. Her expertise spans analytical method development, validation, process optimization, late-stage development, tech transfer, and cross-functional collaboration across QC, manufacturing, and supply chain teams.

From Bench to Batch Release: Building a Reporter Gene Based Potency Assay for TCR-T Cell Therapy

Boning Zhang*, Khaled Ying, Dong Xu, Justin McCue

TScan Therapeutics, MA, USA

Abstract :

Potency is a key Critical Quality Attribute (CQA) for cell therapy products, serving as a direct indicator of their biological activity and anticipated clinical performance. In the context of TCR-T cell therapies, potency assessment must reflect the therapy's complex mechanism of action, which encompasses antigen-specific recognition, cytokine secretion, and targeted cytotoxicity. At TScan Therapeutics, we are developing a diverse pipeline of TCR-T products against seven tumor-associated antigens across hematologic and solid tumor indications, leveraging our proprietary TargetScan discovery platform. To support consistent product quality and enable regulatory-compliant lot release, we have developed a robust, scalable, and high-throughput potency assay designed for seamless technology transfer. Central to this effort is the creation of stable target cell lines in which a luciferase reporter gene has been precisely inserted into the AAVS1 genomic safe harbor via CRISPR/Cas9 genome editing. When co-cultured with TCR-T effector cells, the system enables quantification of antigen-specific killing based on luminescence output, with EC_{50} values calculated from dose-response curves across varying effector-to-target (E:T) ratios. To enhance assay performance, we implemented rigorous process controls and optimized parameters such as incubation duration, cell seeding density, and post-assay media handling, significantly improving signal-to-background ratios and reproducibility. Intra-plate variability was tightly controlled, with coefficient of variation (CV) values consistently below 30%. As a critical reagent in the assay, the engineered target cell line is banked and thoroughly characterized to ensure consistent stability and performance across more than six passages over a one-month period. In parallel, a reference standard for the effector TCR-T cell product has been established, with the release assay applied to confirm potency and ongoing stability monitored over time. Relative potency (RP) can be used a reporting value using the reference standard effector as a benchmark. Importantly, the streamlined assay format can be fully adapted to automated execution using a liquid handling system, significantly enhancing intermediate precision and reducing operator variability in the workflow. This luminescence-based co-culture platform offers a versatile, efficient, and regulatory-ready approach to potency testing, and its straightforward format and high-throughput compatibility make it ideally suited for implementation in GMP environments. It stands as a critical link between early bench-side development and clinical-grade manufacturing, providing a fit-for-purpose release assay for TCR-T cell therapies.

Biography:

Boning Zhang is an experienced scientist specializing in analytical development and cell therapy assay design, with a strong background in TCR-T and allogeneic CAR T cell platforms. Currently at TScan Therapeutics, she leads the development and qualification of potency assays for T cell therapies, leveraging Design of Experiments (DoE), risk assessments, and automated workflows. As a subject-matter expert, she has successfully transferred complex flow cytometry-based assays to QC and CDMO settings and manage a high-performing team supporting cross-functional analytical needs. Previously at Intellia Therapeutics, Boning contributed to the pre-IND development of an allogeneic CAR T program, optimized CRISPR-based engineering processes, and played a key role in assay development, patent filings, and multi-team collaborations. Her expertise spans immunophenotyping using flow cytometry, cell-based assay optimization, and cross-functional communication, backed by experience in regulatory-driven environments.

Rejuvenating Innate Immune Competence to Enable CAR-T and Immunotherapies to Eliminate Solid Tumors

Alex Blyth

Lift Biosciences, United Kingdom

Abstract:

Lift has raised over $21 million and is a global leader in neutrophil immunotherapies. We're preparing to enter clinical trials aimed at treating solid tumors, particularly those no longer responsive to checkpoint inhibitors (CPIs). Our approach leverages Immunomodulatory Alpha Neutrophils (IMANs) to replace dysfunctional neutrophils in cancer patients, helping to overcome treatment resistance.

Recent *Cell* publications highlight the vital role of neutrophils in fighting tumors. Lift's IMANs are unique in that they target cancer cells without relying on antigens, offering a solution for cancers that evade other treatments. These IMANs have a long-lasting effect, persist for up to four weeks, and can transform cold tumors into hot ones, enhancing the immune response.

With scalable production and a competitive cost structure, Lift is positioned to capture a $43 billion market opportunity. Our global patents, dating back to 2016, further solidify our leadership in the neutrophil cell therapy space.

Biography:

Alex Blyth founded LIfT BioSciences in 2016 after the loss of his mother to pancreatic cancer, driven by a determination to transform cancer treatment. He envisioned a novel immune-cell therapy, building on the incomplete work of renowned immunologists Professor Zheng Cui and the late Dr. Lloyd J. Old, a pioneer in tumor immunology. A serial entrepreneur, inventor, economist, and biologist, Alex brings over 20 years of experience in disruptive healthcare innovation. He has played a pivotal role in the development and commercialization of multiple first-in-class biopharma drugs, including T-Vec, the first oncolytic vaccine; Erbitux, the first cancer treatment guided by genetic testing; and Abraxane, one of the few drugs approved for pancreatic cancer in the past decade. Alex's leadership at LIfT BioSciences focuses on advancing cutting-edge therapies to combat solid tumors and revolutionize patient outcomes in oncology.

Considerations for Donor Starting Material Characterization

R. Tressler, *T. Cabreros, *J. Huang

Excellos, CA, USA

Abstract:

Allogeneic cell immunotherapies for the treatment of various diseases using healthy donors have increased, with numerous clinical trials currently ongoing. It is well known that there is significant variability in the quality of the immune cells derived from healthy donors, but little has been done to address this issue, with most characterization efforts focussing on yield, safety and viability, but not on the required functions for effective disease control. This has led to the need for better funtional characterization of the donor starting material to assure the manufacturing of consistent high quality therapeutic products. We have developed a multiparametric analysis platform, called the Escore, that evaluates key functional characteristics of donor immune cells relevant to clinical benefit responses. These properties include effector potential, metabolic fitness, proliferation potential and memory potential where appropriate. We have carried out Escore analyses on over 100 healthy donors, evaluating their PBMCs or T cell populations. The data indicate significant variations in functional immune attributes for all donors tested, including those younger in age (<35 years old). This demonstrates the need to reduce the risk of suboptimal manufacturing of cell immunotherapies if there are no functional screening criteria employed for selection higher quality allogeneic donor starting material for various adaptive immunotherapeutics.

Biography:

Executive and senior researcher with over 20 years of industry experience in preclinical pharmacology, leading discovery and development programs across oncology, stem cell therapeutics, cardiovascular, immunology, and age-related diseases. Co-founder of Telomax Pharma, focused on telomerase modulation for age-related conditions, and formerly Vice President of R&D at Cellerant Therapeutics, where he advanced oncology programs from discovery to IND and led stem cell therapies through Phase I/II trials. As Executive Director and Head of Research at Geron Corporation, he oversaw a 30-member preclinical division spanning Discovery, Pharmacology, Bioanalytical/PD, Toxicology, and ADME. He has also held senior roles at Matrix Pharmaceuticals and Chiron. A published expert and peer reviewer, he has co-authored over 30 scientific publications and book chapters, and is an inventor on multiple patents. Recognized for building multidisciplinary R&D platforms and translating innovative science into clinical programs.

Elucidating Genomic Mechanisms in Human Tissues to Inform Appropriate Therapeutics for Age-related Macular Degeneration

Meg DeAngelis

University at Buffalo, NY, USA

Biography:

Dr. Margaret DeAngelis is a systems-biology researcher who investigates molecular mechanisms of blinding eye diseases such as AMD, glaucoma, and diabetic retinopathy, as well as their links to Alzheimer's and cardiovascular disease. Funded by NIH, industry, and private foundations, she leads a translational lab that created the first standardized human-donor eye bank for genomic and biochemical studies, publishing 100+ papers. A mentor and educator across neuroscience and genetics, Dr. DeAngelis sits on journal editorial boards and steering committees for major international eye-genetics consortia.

Restoring Sight: Modifier Gene Therapies from Mechanistic Insight to Therapeutic Reality

Haider, Neena * Corresponding author

Harvard Medical School, Shifa Precision, MA, USA

Abstract:

Our studies demonstrated that many genes function in concert for normal development and function of the retina. Genetic mutations in any one of the genes in these networks lead to retinal degeneration. Our mutation agnostic gene therapy is able to reset these changes and attenuate retinal disease.

Retinitis pigmentosa (RP) are a large group of genetically heterogeneous disorders that result in severe vision loss with degeneration of the peripheral retina. Over 150 unique gene mutations in over 100 genes have been associated with RP, with high variability in disease onset, severity, and progression. Stargardt disease, in contrast, is mainly due to mutations in the *Abca4* gene and is a juvenile form of degeneration of the central retinal region, the macula. These diseases occur as a result of the mutational load on the biological systems which include the primary mutation as well as other factors such as genetic modifiers and epigenetic factors. Our studies revealed that nuclear hormone receptors such as *Nr2e3* and RORA regulate several key biological networks that are essential for normal retinal development and function. These NHRs play a critical role in maintaining homeostasis in the retina and regulate gene networks including phototransduction, survival, apoptosis, immunity, oxidative stress, ER stress, neuroprotection and metabolism. Our studies have shown that both *Nr2e3* and *RORA* are power modifier gene therapies that can reset homeostatic state and thereby ameliorating disease.

Methods: Several mouse models including *rd1*$^{-/-}$, *Rho* $^{-/-}$, and *rd7* $^{-/-}$ and *Abca4*$^{-/-}$ were used in these studies. Retinas were evaluated pre- and post- treatment of AAV5.h*Nr2e3* (OCU400O) and AAV5.h*RORA* (OCU410) clinically by fundus examination, functionally by electroretinogram (ERG), and molecular evaluation by immunohistochemistry.

Results and Conclusions: Monogenic diseases such as RP have been studied for the loss of single genes. However, our studies reveals that there is significant downregulation in expression of key retina transcription factors in several models of RP. This shift in turn causes misregulation of key homeostasis gene networks as disease progresses in each model and this mutational load of the system likely contributes to disease. AAV5. hNr2e3 therapy attenuates retinal degeneration in each of these models and results in increased expression of key retinal transcription factors and a reset of retina homeostasis.

Biography:

Dr. Neena Haider, renowned geneticist and visionary scientist, is the founder of Shifa Precision and a faculty member at Harvard Medical School. A pioneer in gene therapy, Dr. Haider has brought multiple life-changing therapies to the clinic. Dr. Haider was a key contributor to the Human Genome Project and during her career has identified more than a dozen genes linked to various diseases, including blindness, kidney disorders, and autism. With a strong commitment to scientific leadership, Dr. Haider has served and serves in numerous leadership roles at institutions such as Harvard Medical School, National Institute of Health (NIH), the U.S. Congress, National Science Foundation (NSF) and NASA. Dr. Haider's groundbreaking research has been published in leading scientific journals, cited over 3000 times, and incorporated into global textbooks. Dr. Haider's lab at Harvard Medical School discovered novel types of gene therapies that have broad capabilities to treat multiple forms of blindness. She has a U.S. patent issued and her therapies were granted several orphan disease designations (ODD), Regenerative Medicine Advanced Therapy (RMAT) and expanded access status with the FDA that allows expeditious development and review of promising therapies, as well as European Medicines Agency (EMA) approval for clinical trials. Recognizing the need for personalized healthcare, Dr. Haider founded Shifa Precision, a science driven, AI-powered precision medicine diagnostic testing and analysis center which provides predictive health analysis to assist clinicians. Shifa Precision has a whole-health analysis platform that will significantly reduce the time and costs associated with the current state of reactive care, ultimately improving patient outcomes. The innovative approach empowers clinicians to proactively mitigate diseases through predictive and preventative measures.

Development of genome-modified NextGen AAV vectors

Arun Srivastava

University of Florida, FL, USA

Abstract:

A number of investigators, including us, have developed capsid-modified next generation (NextGen) of AAV vectors for high-efficiency transduction. However, beyond capsid-modifications, it is equally important to pursue genome-modifications to improve transgene expression from AAV vectors since it is the genome, more specifically the viral inverted terminal repeats (ITRs), beyond the promoters an enhancers, and not the capsid, that plays an important role in modulating the expression of the therapeutic transgene. We have developed three different ITR-modified (GenX, GenY, and GenZ) AAV vectors that mediate up to ~20-fold increased transgene expression in human cells in vitro and in mouse hepatocytes in vivo. Encapsidation of these ITR-modified genomes into capsid-modified NextGen capsids, resulting in optimized (OptX, OptY, and OptZ) AAV serotype vectors is likely to significantly improve the performance of these vectors at further lower doses, with improved safety as well as reduced vector production costs, for gene therapy of a wide variety of diseases in humans.

Biography:

Arun Srivastava is Professor in the Division of Cellular and Molecular Therapy in the Departments of Pediatrics and Molecular Genetics & Microbiology, and Powell Gene Therapy Center at the University of Florida College of Medicine in Gainesville, Florida. He obtained his PhD degree from the Indian Institute of Science in Bangalore, and completed his postdoctoral training at the Memorial Sloan-Kettering Cancer Center in New York. He worked as a research associate in the Late Dr. Kenneth I. Berns' laboratory at the University of Florida. He has worked with AAV and AAV vectors for over 44 years. For nearly two decades, he was on the faculty at Indiana University School of Medicine in Indianapolis, where he rose to the rank of Professor. He was recruited back to the University of Florida in 2004 as George H. Kitzman Professor of Genetics and Founding Chief of the Division of Cellular & Molecular Therapy. In the past over four decades, he has mentored 42 Postdoctoral Fellows and 10 Clinical Fellows. Four students have graduated with MS degrees, and 12 students have received their PhD degrees from his laboratory. He has received uninterrupted research funding from the National Institutes of Health (NIH) for 41 years. He has also been awarded 22 US Patents with 21 additional US patent applications that have been filed on his research on AAV and their potential use as vectors in human gene therapy. He currently serves on an NIH Study Section as well as on the Editorial Boards of 10 scientific journals. He has published 222 peer-reviewed research articles, book chapters, reviews, and miscellaneous articles, and 261 abstracts. He was the founding scientist of the very first AAV gene therapy company, Avigen, which was launched in 1992. He was a co-founder of a second AAV gene therapy company, Lacerta Therapeutics, which was launched in 2017. In 2023, he launched a third AAV gene therapy company, sAAVient Therapeutics, and a fourth AAV gene editing company, nAAVigen Therapeutics, in 2024. The current focus of his research is on gene therapy of genetic diseases such as hemophilia and muscular dystrophies; gene therapy of malignant disorders such as hepatoblastoma and hepatocellular carcinoma; and gene therapy and "nuclease-free" genome editing for β-thalassemia and sickle cell disease.

rAAV8 Encapsidated HMR-001 Mediates High Efficiency of Viral Transduction and Bleeding Normalization in HA Mice Mice

***Xiaomo Wu[1,2,3], Xiaorong He[1], Jinying Zhong[1], Junyong Wong[3]**

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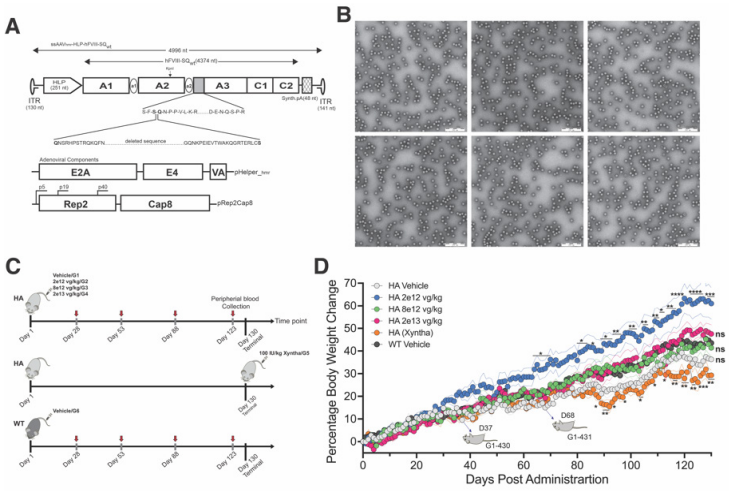
[3]Humvira Therapeutics, East Lake High-tech

Abstract:

Hemophilia A (HA), the most common X-linked inherited bleeding disorder caused by a deficiency of clotting factor VIII, has primarily been managed through replacement therapy (RT) using exogenous factor VIII or non-factor hemostatic agents. However, adeno-associated viral vectors enabling endogenous FVIII production have emerged as a promising therapeutic approach under clinical investigation to address various limitations of RT, including progressive joint disease, high rates of inhibitor development, and the significant burden of lifelong treatment. Although the development and recent approval of AAV-mediated gene therapy represent a landmark in HA therapeutics, limited durability and gradually diminishing FVIII activity have been observed, with fractional participants returning to regular treatments. These remaining challenges are now the primary focus of AAV vector innovation and bioengineering. The high-performance recombinant vector HMR-005, encapsidated with AAV8 and encoding the B domain-deleted FVIII (hFVIII-SQ version), was systematically evaluated in this preclinical investigation aimed at HA gene therapy. Intravenous administration of HMR-005 cross different dose range resulted in dose-dependent hFVIII antigen plasma levels in HA mice, and the correction of blood loss was achieved in the highest dose cohort. A high-resolution in situ RNAscope assay revealed active transcription activities and uniformly distributed viral transduction four months after AAV delivery. Significantly high concentrations of full-length vector genomes were determined by a high-order triple linkage ddPCR assay, with 3.74 [2.34-5.13, 95% CI], 21.55 [13.33-29.77, 95% CI], and 48.52 [42.02-55.01, 95% CI] copies per diploid genome for administration doses of 2×10^{12} vg/kg, 8×10^{12} vg/kg, and 2×10^{13} vg/kg, respectively, demonstrating substantially improved viral transduction and full-length FVIII-BDD viral genome preservation and persistence.



Keywords: Hemophilia A, Gene Therapy, Transduction efficiency, AAV Purity

Biography:

Dr. Xiaomo Wu is the lab head of Regenerative Medicine & Gene Therapy and former Deputy Director of the Dermatology Institute of Fuzhou. Wu received a B.A. in Medicine in 2002 from the University of Wuhan (Wuhan, China), followed by a M.S. in Genetics from the University of Fudan (Shanghai, China) in 2006. In 2008, Wu joined the group of Prof. Walter J. Gehring in the Biozentrum of the University of Basel (Basel, Switzerland) and received her PhD in Genetics in 2012. She conducted her postdoctoral research in Bettler's LAB, Biomedicine Department, the University of Basel, Switzerland. In 2018, Wu was recruited as the deputy director of a newly founded medical research centre in the Dermatology Hospital of Fuzhou (Fuzhou, China). In recent years, WU Lab has been dedicated to developing therapeutic interventions based on genetic modification and alteration for the treatments of inherited skin diseases as well as various blood and immunodeficiency disorders.

Cell and Gene Therapy Development for Hereditary Connective Tissue Diseases: Overcoming dominant negative phenotype

Erik Foehr

Kin Therapeutics and BioTether Sciences

Abstract:

Hereditary connective tissue diseases are a group of genetic disorders that affect the body's extracellular matrix proteins, such as collagen, elastin, and fibrillin. Vascular Ehlers-Danlos syndrome (vEDS), characterized by fragile blood vessels and life-threatening aortic dissection due to COL3A1 gene mutations, presents a critical need for innovative therapies. Other similar disorders, such as Marfan's Syndrome and Lowey-Dietz (Mutations in FBN1 and TGFbeta respectively) also cause aneurysms and aortic dissection. These syndromes are caused by autosomal dominant-negative mutations, that disrupt normal tissue function. Gene therapy aims to deliver functional COL3A1, FBN1, TGFbeta, and other relevant genes, restoring normal extracellular protein production and strengthening vascular integrity. Approaches include viral vector-mediated gene transfer. Homologous recombination initiated by donor template delivery replaces the mutated allele with the normal allele, thus overcoming the dominant-negative phenotype. Cell therapy, involving transplantation of genetically modified cells, could also initiate repair and replacement of damaged tissue. Here we describe development of cell and gene therapeutics for hereditary connective tissue diseases.

Biography:

I am a biopharmaceutical expert with over 20 years of research and development experience. I received my Ph.D. in Physiology and Biophysics at the University of California, Irvine and Post-Doctoral Fellowship at the Gladstone Institute of Virology and Immunology. I have worked in the biopharmaceutical industry for decades and continue to grow as a professional, teach, learn and lead. This body of work includes significant contributions to FDA-IND, MHRA, and EMA submissions. I have led teams at BioMarin Pharmaceuticals, Pacific BioLabs, AGY Therapeutics, and founded BioTether Sciences and Kin Therapeutics.

Synthetic DNA for Cell & Gene therapy, and vaccine applications

P. Thiaville*, E. Young, A. Dhir, A. Bouchareb, G. Tezcan, Z. Whiffen, A. Walker

4basebio, FL, USA

Abstract :

The manufacture of plasmid DNA is a major bottleneck in the production of cell & gene therapies and vaccines, relying on bacterial fermentation methods. Synthetic DNA, prepared by an entirely cell-free, enzymatic process, offers an innovative alternative, not only enhancing safety, but also providing greater flexibility of scale and faster turnaround times in GMP DNA manufacturing. In this talk, we will explore how 4basebio's synthetic DNA technology surpasses traditional plasmids in critical applications, including mRNA production, adeno-associated virus (AAV) vector development, and gene editing.

Biography:

Patrick Thiaville is a biotech innovator with a passion for advancing patient care and scientific discovery, backed by a proven track record in technical leadership, facility design and operations, and cross-functional collaboration. Recognized as an industry expert in the design and manufacturing of nucleic acid therapeutics, I combine deep technical expertise with dynamic communication and strategic insight. I hold dual PhDs in genetics and genomics, focused on the comparative and functional genomics of RNA modification, with a mission to annotate genes of unknown function and integrate that knowledge across public genome databases. My professional journey spans roles in quality assurance, analytical testing, drug design, and pharmaceutical manufacturing, evolving from hands-on analyst to executive leader. I've contributed to both early-stage startups—as an early hire building infrastructure from the ground up—and large multinational corporations, where I've driven strategic initiatives, innovation, and business growth.

mRNA Therapeutics for Cardiovascular Diseases

Ajit Magadum

Department of Cardiovascular Sciences, Lewis Katz School of Medicine at Temple University

Abstract:

Modified mRNA (modRNA) technology, lauded for its triumphs in COVID-19 vaccine development, is emerging as a promising strategy against cardiovascular diseases (CVD). With 19.1 million global deaths in 2020 and a prevalence of 620 million, CVD demands innovative solutions. Despite medical strides, the lack of a cure intensifies public health concerns. My presentation spotlights our work on modRNA therapies fostering cardiac regeneration and combating cardiac fibrosis, hypertrophy, and cell death in CVD animal models. We also showcase our cell-specific modRNA expression platforms, contributing to evolving modRNA therapeutic landscapes for CVD.

Biography:

Ajit Magadum is an Assistant Professor in the Department of Cardiovascular Sciences & ACDC at the Lewis Katz School of Medicine, Temple University in Philadelphia, USA. He earned his Ph.D. from the Max Planck Institute for Heart and Lung Research in Germany in 2014, focusing on the molecular and cellular aspects of cardiovascular diseases (CVD) and repair mechanisms.

During his postdoctoral tenure at Mount Sinai in New York, he made significant advancements in developing mRNA delivery systems tailored for the cardiovascular system, utilizing various carriers to ensure robust and sustained mRNA expression within cardiac tissues. In 2016, he developed the first-of-its-kind cell-specific mRNA delivery platform known as SMRTs (Specific Modified mRNA Translation System). This innovation allowed for precise targeting of mRNA expression in either cardiomyocytes or non-cardiomyocytes within the heart, paving the way for cell-specific mRNA therapeutics for CVD. He joined Temple University in 2020 as an Associate Scientist. His groundbreaking research has identified a series of novel genes (five targets) delivered as mRNA to the heart, promoting cardiomyocyte proliferation, cardiac regeneration, angiogenesis, and inhibition of cardiac hypertrophy, oxidative stress and fibrosis. He has published over 25 research papers n peer-reviewed journals and has successfully filed three patents, which have been licensed to leading biotechnology companies. In recognition of his contributions, He received the Outstanding Research Innovation Award from Mount Sinai Hospital in 2017 for his work on mRNA therapeutics for CVD. In 2022, he was honored with the ISHR-NAS Young Investigator Award (runner-up) and the Melvin L. Marcus Early Career Investigator Award from the American Heart Association (AHA, finalist) in 2022.

Currently, his research focuses on identifying novel targets and leveraging mRNA and cell-specific mRNA as innovative therapeutic modalities to target CVD.

Nuclear microRNA gene therapy: Use of AI-assisted discovery platform for transcriptional regulation

Mikko Turunen

RNatives Inc., Finland

Abstract:

The most studied and well-described mode of action of miRNAs is their binding to the 3′ UTRs of target messenger RNAs, thereby downregulating gene expression through post-transcriptional gene silencing (PTGS). However, recent research, including our own, has demonstrated that small non-coding RNAs (ncRNAs) can also bind directly to the promoter regions of genes, either activating or repressing their transcription. This process depends on the specific loci targeted within the gene promoter, which can lead to either silencing or activation of gene transcription. The mechanism involves the recruitment of protein complexes to the promoter regions, resulting in modifications of the epigenetic status, such as histone modifications, at the chromatin level.

Utilizing this mechanism for therapy presents several advantages. Firstly, targeting non-coding RNA at the gene promoter rather than mRNA in the cytoplasm requires much less miRNA to reach the target within the cell. When miRNAs target mRNAs that are continuously produced, new miRNA must be constantly delivered to counteract the newly produced RNAs. Conversely, targeting transcription via the epigenetic mechanism requires fewer miRNA copies per cell and fewer administrations, as the effect is longer-lasting. Additionally, targeting the cell's own gene yields a more natural cellular response, as all potential splice forms of the mRNA are regulated by the same promoter-targeting miRNA.

Our lead asset, poised for clinical trials, targets the upregulation of VEGFA for the treatment of peripheral artery disease. Independently conducted in vivo trials have demonstrated the therapeutic efficacy of our RNA medicine, providing a strong foundation for its further development. Leveraging our Platform Technology Co-Development model, powered by AI-assisted cutting-edge in-house software, we are pioneering the search for regulatory small RNAs across a broad spectrum of diseases, from oncology to neuroinflammatory conditions.

Biography:

Mikko Turunen, PhD, Adjunct Professor of Molecular Medicine at the University of Eastern Finland, has +27 years of experience in the development of gene therapies. Throughout his career, his research focus has been non-coding RNAs, cardiovascular disease, and gene delivery to animals. He was the first to show transcriptional gene activation by small RNAs in vivo (2009).

Modifier gene therapy platform for the treatment of ocular diseases

Arun Kumar Upadhyay

Ocugen,, PA, USA

Abstract:

Inherited or multifactorial ocular diseases resulting from genetic mutations or dysregulated molecular pathways can lead to gradual vision loss and ultimately result in blindness. Traditional gene therapy approaches, which target single genes, are often impractical for these diseases due to their heterogeneous nature. To this end, the modifier gene therapy approach is unique as it utilizes a transgene that can correct or rescue the detrimental effects caused by the dysregulation or mutations in the unrelated gene(s). A novel class of nuclear hormone receptors (NHRs) are modifier genes that provide a gene-agnostic mechanism of action and regulate multiple functions in the retina. One such NHR is nuclear receptor subfamily 2 group E member 3 (NR2E3), which regulates multiple transcriptional networks that can modulate retinal cell homeostasis. OCU400 (AAV5-NR2E3), targets broad Retinitis Pigmentosa (RP) and Leber congenital amaurosis (LCA) patients covering mutations in more than 125 genes and over 125,000 individuals in the USA. Preclinical studies in RP mouse models indicated that subretinal delivery of NR2E3 rescued the retinal degeneration phenotype by resetting the molecular pathways and restored retinal morphology and function. A phase 1/2 clinical trial of OCU400 showed that it is safe and well-tolerated across mutations and dose levels, with improvements in visual acuity and functional vision, supporting a gene-agnostic mechanism. Our second candidate in the platform, OCU410, targets Retinoic Acid Receptor-Related Orphan Receptor Alpha (RORA,) the NHR implicated in regulating multiple pathways associated with the pathophysiology of dry age-related macular degeneration (dAMD). Currently approved treatments for dAMD target only a single pathway contributing to the disease pathogenesis, requiring frequent intravitreal injections. In contrast, RORA has the potential to regulate pathways related to complement activation, inflammation, oxidation and lipid metabolism which contribute to AMD pathophysiology. Our third candidate, OCU410-ST has the potential to treat Stargardt disease (STGD), a rare genetic disorder involving >1,200 gene variants in the *ABCA4* gene, with vision loss starting in childhood. Preclinical studies in STGD model *Abca4*$^{-/-}$ mice demonstrated that OCU410-ST rescued retinal degeneration and improved retinal morphology and function. Additionally, the treatment showed no overt evidence of toxicity or abnormal structure changes in the retinas of treated *Abca4*$^{-/-}$ mice or in the untreated contralateral eyes. The data demonstrate that OCU410-ST has the potential to be a therapeutic to effectively treat retinal degeneration due to *ABCA4* gene mutations.

Biography:

Arun Upadhyay, PhD, Chief Scientific Officer, and Head of Research & Development, drives Ocugen's innovation and product development. He leads science and operations, creating and implementing fit-for-purpose strategies that enable scientific and business solutions. He oversees the development of various product modalities, such as biologics, vaccines, cell and gene therapy, and regenerative medicine and is responsible for all product development activities including discovery, proof of concept, preclinical, bioanalyses, CMC, clinical, safety, medical support, and global regulatory submissions across entire R&D pipeline. Dr. Upadhyay received the American Association of Pharmaceutical Scientists' "Innovation in Nanotechnology Award" for developing novel ocular drug delivery systems. Dr. Upadhyay has authored more than 40 scientific publications and holds more than 15 patents.

Nuclease-free genome editing with AAV-B19 hybrid and chimeric vectors

Arun Srivastava

University of Florida, FL, USA

Abstract:

The use of CRISPR/Cas9 for genome editing in human hematopoietic stem cells in patients with β-thalassemia and sickle cell disease has shown clinical efficacy. More recently, the use of base editors, and prime editors has also shown promise in pre-clinical animal models. However, the long-term safety of CRISPR/Cas9, base editors, and prime editors remains to be determined. We have identified AAV6 as the most efficient vector in transducing primary human hematopoietic stem cells *in vitro* and in a mouse xenograft model *in vivo*. We have also documented erythroid lineage-restricted transgene expression from the human parvovirus B19 promoter. More recently, we have developed AAV6-B19 hybrid and AAV6-B19 chimeric vectors for their potential use in "nuclease-free" genome editing for b-thalassemia and sickle cell disease in humans.

Biography:

Arun Srivastava is Professor in the Division of Cellular and Molecular Therapy in the Departments of Pediatrics and Molecular Genetics & Microbiology, and Powell Gene Therapy Center at the University of Florida College of Medicine in Gainesville, Florida. He obtained his PhD degree from the Indian Institute of Science in Bangalore, and completed his postdoctoral training at the Memorial Sloan-Kettering Cancer Center in New York. He worked as a research associate in the Late Dr. Kenneth I. Berns' laboratory at the University of Florida. He has worked with AAV and AAV vectors for over 44 years. For nearly two decades, he was on the faculty at Indiana University School of Medicine in Indianapolis, where he rose to the rank of Professor. He was recruited back to the University of Florida in 2004 as George H. Kitzman Professor of Genetics and Founding Chief of the Division of Cellular & Molecular Therapy. In the past over four decades, he has mentored 42 Postdoctoral Fellows and 10 Clinical Fellows. Four students have graduated with MS degrees, and 12 students have received their PhD degrees from his laboratory. He has received uninterrupted research funding from the National Institutes of Health (NIH) for 41 years. He has also been awarded 22 US Patents with 21 additional US patent applications that have been filed on his research on AAV and their potential use as vectors in human gene therapy. He currently serves on an NIH Study Section as well as on the Editorial Boards of 10 scientific journals. He has published 222 peer-reviewed research articles, book chapters, reviews, and miscellaneous articles, and 261 abstracts. He was the founding scientist of the very first AAV gene therapy company, Avigen, which was launched in 1992. He was a co-founder of a second AAV gene therapy company, Lacerta Therapeutics, which was launched in 2017. In 2023, he launched a third AAV gene therapy company, sAAVient Therapeutics, and a fourth AAV gene editing company, nAAVigen Therapeutics, in 2024. The current focus of his research is on gene therapy of genetic diseases such as hemophilia and muscular dystrophies; gene therapy of malignant disorders such as hepatoblastoma and hepatocellular carcinoma; and gene therapy and "nuclease-free" genome editing for β-thalassemia and sickle cell disease.

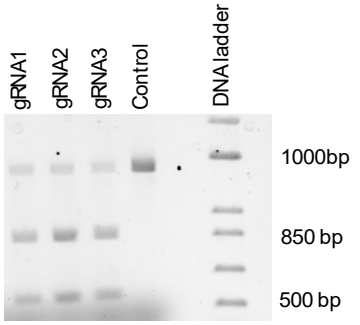
Morpholino based modification in sgRNA showed efficient CRISPR-Cas gene editing in HeLa and SH-SY-5Y cells

S. Ganguly*, M. J. Ciba, M. Caruthers

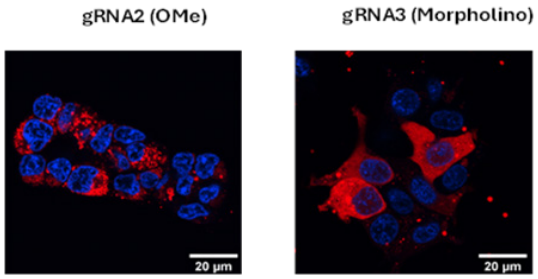
University of Colorado, Boulder, CO, USA

Abstract:

CCRISPR -Cas9 is a powerful gene editing tool that has been widely adopted in therapeutics targeting various genetic disorders. Although genome editing using the CRISPR-Cas system is highly efficient in human cell lines, extent of editing can show variability due to different reasons. Efficiency of the gRNAs to direct site-specific DNA cleavage and to co-deliver the RNP complexes into cells may contribute in this. We report a new Morpholino based modification in chemically synthesized chimeric single guide RNA (sgRNA) which was co-delivered into HeLa and SH-SY-5Y cells with Cas9 protein to study PTEN induced kinase 1 (PINK1) gene editing. The RNP based delivery showed efficient gene editing without toxicity to both the cell lines. Chemical modifications comprising 2'-O-Methyl and Morpholino were incorporated into sgRNA backbone, and a comparative study was performed to observe cellular uptake, gRNA localization and gene editing in cells against the no- modification sgRNA variant. Further studies are being carried out with primary cell lines, efficient gene editing in which is in general found more challenging than immortalized cell lines.



gRNA1: **Not-modified sgRNA**
gRNA2: **OMe modified sgRNA**
gRNA3: **Morpholino modified sgRNA**



Blue: DAPI/ Cell nuclei
Red: Cy3 labeled guide RNAs

A. B.

Figure A: Agarose gel data of biochemical in vitro DNA cleavage assays for Morpholino modified, 2'-O-Methyl modified and not modified sgRNAs when complexed with Cas9 protein and reacted with PCR amplified target gene.

Figure B: Cy3 labelled sgRNAs delivered to the HEK 293T cells through lipofection after complexed with Cas9 protein.

Biography :

The presenter, **Saheli Ganguly**, completed her PhD from Calcutta University , India on Applied Chemistry and have 5+ years of research experience in fast paced research labs/start-up in USA recognizing the application of biomolecules in cellular biology and bionanomaterials with extensive experience in 3D in vitro tumor models, cell-based assays, primary cell culture. Currently the author is working as Senior research Associate in University of Colorado, Boulder, USA on CRISPR -CAS genome editing with chemically modified guide RNAs.

Anti-pan AAV – New versatile antibody for the detection of various AAV serotypes including novel capsids

Authors: Kaja Betts, Joshua Baal, Christina Querfurth, Lea Hupe, Rita Lacher, Klaus-Ingmar Pfrepper, Maik Lander, Martin März, Dana Holzinger

PROGEN Biotechnik GmbH, Germany

Abstract:

Recombinant adeno-associated virus (AAV) vectors have become leading tools for viral gene therapy. However, some biological mechanisms are still not completely understood. Different AAV serotypes are employed in gene therapy development, each offering unique tissue tropism depending on the specific serotype. Additionally, the field is witnessing a surge in the development of novel, engineered AAV serotypes with optimized properties to address diverse therapeutic needs. In this context, antibodies capable of specifically detecting conformational epitopes on AAV capsids—thereby recognizing only intact and fully assembled particles—are indispensable for the accurate quantification of AAV titers. These specialized antibodies are essential for establishing stringent quality control standards, ensuring robust and precise evaluation of AAV gene therapy products. By enabling accurate titer determination, these antibodies contribute significantly to the therapeutic efficacy and safety of AAV-based gene therapies.

PROGEN offers an extensive portfolio of AAV antibodies tailored to bind the specific serotypes. However, certain research applications can benefit from using a single antibody that recognizes a broad spectrum of serotypes. Additionally, with the increasing use of novel capsid variants and shuffled vectors, commercially available antibodies often fall short. To address this need, PROGEN has developed a new recombinant antibody that exhibits robust binding reactivity to intact particles of various AAV serotypes.

Here we present comprehensive characterization data for the new anti-pan AAV antibody. We introduce several variants of this antibody and demonstrate its cross-reactivity and high sensitivity against multiple AAV serotypes, including new variants and shuffled vectors. We provide data supporting its applicability across a range of research needs. Specifically, we illustrate its effectiveness as a neutralizing antibody, its compatibility with ELISA test systems, and its utility in fluorescence-based applications requiring labelled antibodies. Due to this multifaceted usability, the anti-pan AAV antibody displays a valuable tool in AAV research and therapeutic development.

Biography:

Katja Betts is a strategic leader in gene therapy research, currently at PROGEN Biotechnik, where she drives innovation in AAV, LNP, and diagnostics through ISO 13485–certified in-house analytical tool production. With expertise in international marketing, contract negotiations, and cross-cultural team management, she also serves on the Strategic Advisory Board of the BioRN Life Science Cluster Rhine-Neckar, advancing collaborations across academia, biotech, and pharma.

Closing the Final Steps in Hematopoietic Stem Cell Therapy Manufacturing: An FDA-Supported Approach to Process Automation and Closure

M. Tauras*; K. Klinkowski; L. Zhou; Y. S. Makhija; A. McCreary; D. Tingley; A. Thurmond; B. Nguyen; L. Deems; F. Norman; J. Hu; T. Chakraborty

Vor Bio Inc, MA , USA

Abstract:

The manufacturing of gene-edited hematopoietic stem cell (HSC) allografts requires aseptic, scalable processes to ensure product quality and patient safety. The final steps—harvest, formulation, fill, and finish (H/F/F/F)—are at high risks of contamination, variability, and inefficiencies such as extended manufacturing time, manual handling risks, and impurity removal challenges. Despite advances in cell therapy manufacturing, there is limited data on comparing manual to automated H/F/F/F processes for HSCs, creating uncertainty in their implementation and optimization. The Cytiva Sepaxä system offers an automated, closed alternative that integrates washing, formulation, and batch tracking while minimizing manual intervention.

Here, we compare the manual process with a semi-automated Sepax-based H/F/F/F approach. Both methods resulted in comparable post-thaw cell recovery, viability, and *in vitro* differentiation potential, but the Sepax-based approach demonstrated superior impurity removal. Furthermore, automation improved efficiency by reducing processing time, maintaining sterility and phenotype integrity.

Transitioning to a closed system preserved key readouts while addressing manufacturing inefficiencies and standardization challenges. By automating the final processing steps, Sepax reduces manual handling risks, shortens manufacturing time, and ensures a reproducible workflow. These findings support the feasibility of a fully closed H/F/F/F system, facilitating final drug product formulation while enabling regulatory compliance and scalability for clinical and commercial applications.

Biography:

Matthew Tauras is a Principal Associate Scientist at Vor Bio, specializing in cell therapy process development. He earned a Bachelor's in Biology and a Master's in Business and Analytics from the University of Massachusetts Amherst. Since joining Vor Bio in 2021, he has focused on developing scalable, GMP-compliant manufacturing processes for hematopoietic stem cell (HSC) and CAR-T therapies. His experience includes process automation, closed-system integration, technology transfer, and the development of protocols for upstream and downstream processing, formulation, and cryopreservation to support clinical and commercial manufacturing.

Overcoming Challenges of Gene-Edited Hematopoietic Stem Cell Manufacturing: Enhancing Yield Through Donor Mobilization Regimen and Cell Culture Conditions

Kylee Klinkowski*, M. Tauras, G. Zarraga, D. Tingley, J. Ferrucio, F. Norman, G. Angelini, J. Hu, T. Chakraborty

Vor Bio, MA, USA

Abstract:

Gene-edited hematopoietic stem cell (HSC)-based therapies offer promising treatments for hematological disorders, including genetic diseases, malignancies, and immune deficiencies. Achieving the required therapeutic dose with desired cell health and phenotype hinges on both the quality and quantity of donor HSCs, as well as an optimized manufacturing process. Geneedited HSC manufacturing involves multiple steps - cell washing, isolation, gene editing, culturing, harvesting, cryopreservation, and thawing - posing a risk of both cell loss and reduced cell stemness, which could compromise the graft fitness and engraftment.

Donor variability presents a significant challenge, as differences in baseline HSC frequency and stemness can impact both expansion potential and final product quality. Compounding this, HSCs do not expand efficiently in culture; critical subpopulations that support engraftment, such as long-term HSCs (LT-HSCs), begin to differentiate over time. culture optimization are essential to ensure dose attainment and maintain drug quality. To overcome these limitations, we investigated the impact of mobilization regimens used to recruit donor HSCs from bone marrow, and *ex vivo* culture conditions, including cell seeding density and culture duration. In an N = 2 donor-matched full-scale process development study, we found that dualmobilized starting material (G-CSF and Plerixafor) produced at least twice the number of HSCs and four times the number of LT-HSCs compared to single-mobilized material (G-CSF only) - both before processing and throughout culture, while maintaining high cell viability. Additionally, for each mobilization regimen, reducing the culture seeding density by half increased HSC and LT-HSC yields at all culture time points with high cell viability. As expected, HSC and LT-HSC frequency decreased with each culture day. These findings demonstrate that dual-mobilization and optimized culture density significantly enhance cell yield while maintaining a desirable phenotype, but also reinforces the delicate balance between cell yield and phenotype. By refining donor mobilization strategies and culture conditions, we can improve gene-edited HSC manufacturing efficiency and success rates, ensuring sufficient cell numbers for effective transplantation.

Biography :

Kylee Klinkowski is a Senior Process Development Engineer at Vor Bio, specializing in cell and gene therapy treatments for acute myeloid leukemia (AML). With expertise in process optimization, cell therapy equipment, CDMO collaboration, technology transfer, GMP manufacturing support, Design of Experiment (DoE), Failure Modes and Effects Analysis (FMEA), and risk assessments**,** Kylee plays a key role in advancing HSC-based gene therapies. Prior to working in Process Development at Vor Bio, Kylee worked in Discovery Research**,** focusing on antibody-drug conjugates (ADCs) at ImmunoGen (now AbbVie), and small molecule screening at Novartis Institute for Biomedical Research (NIBR)**,** gaining experience in early-stage drug development. Kylee is a Chemical Engineer, with a Biochemical Engineering focus and a minor in Chemistry via the University of Massachusetts Amherst.

Harnessing Non-Coding RNAs for the Advancement in Gene Therapy

J. Coleman*, N. Chandel, and P. Pande.

Enzo Life Sciences, NY, USA

Abstarct:

Gene therapy encompasses methodologies aimed at altering or regulating genetic material within an individual's cells to address or prevent disease. This technique works by introducing, removing, or altering genetic material within a cell. Regulatory non-coding RNAs (ncRNAs) are pivotal molecules in gene regulation and the preservation of cellular homeostasis. In the context of gene therapy, ncRNAs significantly impact gene expression control and cellular mechanisms. They are integral to target specificity, immune modulation, and drug resistance and serve as biomarkers for disease diagnosis and treatment monitoring.

Non-coding RNAs are comprised of long non-coding RNAs (lncRNAs), microRNAs (miRNAs), small interfering RNAs (siRNAs), piwi-interacting RNAs (piRNAs), small nuclear RNAs (snRNAs), and small nucleolar RNAs (snoRNAs). In this study, we used AMPIVIEW® RNA probes for *in situ* hybridization targeting regulatory ncRNAs as a proof of principle for detecting its expression with fluorescence signal. We selected a few ncRNAs that are interconnected through their roles in regulating key cellular processes such as epithelial-to-mesenchymal transition (EMT), cell proliferation, apoptosis, and differentiation, making them significant in the context of cancer and other diseases. Non-coding RNA activated by DNA damage (NORAD) is crucial for maintaining genomic stability; the microRNA 200 (miR-200) family is known to regulate EMT; miR-Let-7 is involved in cell differentiation and proliferation; miR-410 regulates cell proliferation and apoptosis; miR-140 plays a role in regulating the TFG-β signaling pathway; and miR-30a is involved in regulating stem cell differentiation and various signaling pathways relevant to cell reprogramming.

Identifying ncRNAs is crucial for advancing gene therapy due to their regulatory role in gene expression and cellular processes. The *in situ* hybridization detection method facilitates the visualization of ncRNAs within their native cellular location, thereby elucidating their spatial distribution and functional roles. This detection method is essential for understanding the roles of ncRNAs in this field.

Biography:

Jack Coleman is an accomplished biochemist with extensive experience in both academia and industry. Serving as the Director of Biochemistry at Enzo Life Sciences International, Inc. since 1996, Coleman directs research across multiple sites and focuses on the development of innovative products. Previously, Coleman held the position of Assistant Professor at LSU Health Sciences Center, where research centered on lipid and lipopolysaccharide biosynthesis in bacteria, along with teaching responsibilities for various student groups. Early in the career, Coleman conducted postdoctoral research at the University of Wisconsin-Madison, investigating lipopolysaccharide biosynthesis in Escherichia coli. Coleman earned a Ph.D. in Molecular Biology/ Biochemistry from Stony Brook University and a B.S. in Chemistry and Biology from Frostburg State University.

Favorable Complement Profile of AAVrh10: Clinical Monitoring Experience from Three Gene Therapy Studies across two programs

Aubert G.[1], Khan A.[1], Rosales X.[1], See Tai S.[1], Adler E.[1], Crystal R. [2]

[1]Lexeo Therapeutics, NY, USA

Abstract :

Background: Complement activation is a key safety consideration in adeno associated virus (AAV) gene therapy, especially with systemic administration at high doses. Activation of complement pathways can trigger inflammatory responses such as thrombotic microangiopathy or capillary leak syndrome, that have resulted in fatal outcomes. A systematic understanding of complement activation in AAV trials is essential to inform safety monitoring and risk mitigation. Across two clinical programs using systemic AAVrh10, including studies in Friedreich ataxia cardiomyopathy (FA-CM) and PKP2 associated arrhythmogenic cardiomyopathy (ACM), prospective complement monitoring was implemented to assess systemic immune activation following vector administration.

Methods: Complement levels are being evaluated in three, ongoing clinical studies using AAVrh10. Two studies investigate AAVrh10-hFXN gene therapy in FA-CM: an investigator sponsored study at Weill Cornell Medical College (WCM, NHLBI HL151355) and the multi-site Lexeo Therapeutics sponsored SUNRISE FA study. Both use corticosteroids as immunosuppression for 3 months following dosing and complement components C3 and C4 are monitored during the early post dosing period, with extended longitudinal follow up in the WCM study. Patients receive doses of $1.8x10^{11}$, $5.6x10^{11}$, or $1.2x10^{12}$ gc/kg.

The third study evaluates AAVrh10-hPKP2 gene therapy in PKP2-ACM at doses of $2x10^{13}$ and $6x10^{13}$ gc/kg. Complement markers (C3, C4, soluble C5b 9, Factor I, Factor H, ADAMTS13, CH50) are assessed from screening to day 28. Patients receive prednisone and sirolimus for 3 months following dosing.

Results: Across both studies in FA-CM, out of 16 patients dosed, two patients showed a concurrent decrease in C3 and C4 below normal limits on day 16 at a dose of $5.6x10^{11}$. These findings were not associated with thrombocytopenia or other clinically significant laboratory abnormalities and returned to normal without intervention. No clinically significant changes in complement values were observed in any other patients during the monitored period following AAVrh10-hFXN administration.

In the PKP2-ACM study with 6 patients dosed, two patients, one per dose cohort, showed transient increases in soluble C5b-9 between day 10 and day 28, without changes in other complement markers. One additional patient had a decrease in C4 below normal, also without other associated changes. None of these findings were linked to clinical symptoms or significant laboratory abnormalities.

Conclusion: Across three clinical studies to date using systemically administered AAVrh10, complement activation was infrequent, transient, and not clinically significant across doses from $1.8x10^{11}$ to $6x10^{13}$ gc/kg.

Biography:

Xiomara Rosales is a medical doctor and clinical development expert with over 20 years of experience in gene therapy and rare neuromuscular disorders. Currently the Director of Gene Therapy, Clinical Development at Lexeo Therapeutics, she previously held leadership roles at Neurogene Inc. and served as a Clinical Investigator at both Columbia University Medical Center and Nationwide Children's Hospital. Her work focuses on mitochondrial and neurodegenerative diseases, lysosomal storage disorders, and natural history studies. She holds an M.D. from Universidad de los Andes and an MPH from Columbia University, and has received executive training from Harvard. Dr. [Last Name] is fluent in English and Spanish and has contributed extensively to advancing gene therapy clinical programs for rare diseases.

Session: Scaling Up CGT: Manufacturing Innovation, Commercialization Strategies & Global Accessibility

From Development to commercialisation: what is the key to success?

A. De Riva* Corresponding author

Advent Bioservices Ltd, UK

Abstract:

Each stage of drug development has its own challenges. This is even more pronounced in cell therapy because of the intrinsic nature of this type of product. The complex biological and immunological mechanisms on which cell therapy is based require innovative solutions in development, manufacture, operations and a pragmatic approach to regulations to address the new challenges that this therapeutic field have thrown at the industry. In addition the considerations associated with facility design and maintenance, raw materials, bespoke equipment and personnel are several fold enhanced compared to the requirements for small molecules or biologics. While the industry is progressing in the pursuit of an allogenic approach that will allow resolution of many of the manufacturing hurdles of cell therapy, answers to personalised medicine have been found such as the development of the concept of 'scale-out' as an alternative to the traditional 'scale-up', now supported more and more by rapid advances in automation.

Inevitably all this requires a level of investment not seen before in the industry. For this reason, cell therapy demands a high level of scrutiny of all aspects of drug product development, together with a strategic vision that allows developers to 'get it right first time' to avoid wasting time and resources re-engineering not-fit-for-purpose processes down the line. Hence, applying the principles of 'Quality by Design' in a holistic fashion to cell therapy has become a must for developers in order to put themselves in the best position to take products to market. This principle is often referred to as 'starting with the end in mind'. Due to the complexity of cell therapy products, this is not trivial. The consequence of not getting it right the first time can be catastrophic, not only for the survival of a company, but also for patients due to the potential loss of access to life changing therapies. This is observed in what it is referred to as the 'valley of death', the deep loss of progression observed between pre-clinical research and pivotal clinical trials. When every single decision has implications that can significantly impact timelines and ultimately cost, it is paramount that companies get ahead of the game and acquire from the beginning all the skills, knowledge and experience required to deliver the product to the bedside. People are always at the core of human activities, and here too having the right people with the experience, knowledge and strategic vision really fulfils the mantra 'starting with the end in mind'.

Biography:

Alessandra brings over 20 years of experience in R&D, PD, CMC and regulatory affairs gained in the private and academic sectors in cell and gene therapy, immune-oncology and immunology. Alessandra holds a PhD in Molecular Immunology obtained at the National institute for Medical Research and sponsored by UCL (UK), and studied Biological Sciences at the University of Padova (Italy).

Alessandra has authored several papers, reviews, and posters and has spoken at numerous conferences and webinars.

Digital and Automation: Accelerating innovation in CGT industrialisation

Daniel Gibson

Cell and Gene Therapy, Catapult, United Kingdom

Abstract:

The integration of digital and automation technologies is essential for driving the next phase of industrialisation in the CGT sector. As demand for advanced therapies grows, the industry faces significant challenges in scaling manufacturing capabilities efficiently, while maintaining quality and compliance. The adoption of cutting-edge automation and digital platforms is pivotal in transforming these production processes, enhancing both the pace of innovation and the scale of operations.

Automation technologies can drastically reduce manual interventions, enabling higher throughput, reduced costs, and improved data integrity. This approach not only ensures consistent product quality but also supports faster time-to-market for therapies, addressing critical patient needs. Digital platforms, on the other hand, provide real-time data management, traceability, and process optimisation, allowing manufacturers to monitor and adapt workflows dynamically. Together, these advancements foster a more agile, scalable, and sustainable CGT manufacturing ecosystem.

By embracing digital and automated solutions, the CGT industry can unlock significant improvements in productivity, environmental sustainability, and regulatory compliance, ensuring that life-saving therapies can reach a broader population more efficiently.

Biography:

A strategic leader and change agent with over a decade's experience in process development and clinical delivery. With extensive experience within the Cord Blood banking and Cell and Gene Therapy industries with a track record for delivery and creating innovative solutions. Dan provides overall leadership and direction for the cell and gene therapy service at Anthony Nolan. Through his career working in the cord blood banking and cell & gene therapy area he has amassed expertise in cell sourcing, cell processing and the associated logistics. Dan draws on this knowledge to help build and deliver scalable solutions to meet growing industry needs.

Key Considerations for Successfully Commercialization a Cell & Gene Product

Cassandra Perkins

Syneos Health, NC, USA

Abstract:

Casey Perkins, a commercial leader in Cell & Gene Therapy, will bring her expertise drawing on the successful launch of the first $2.1M gene therapy product in the US. She will also provide a roadmap for success, pain points to overcome, the important decisions that affect a successful launch in the CGT space. She will also delve into the the importance of patient - product journey roadmap and key considerations that impact a CGT products success. As a valued member of the Syneos Health CGT Consulting team, Casey continues to provide manufacturers with CGT strategy, launch, and lifecycle management.

Biography:

Casey Perkins is a highly respected industry leader with extensive expertise in trade and channel management, market access, reimbursement, and patient services. Known for developing and executing innovative strategies, Casey has played a key role in the successful launch and lifecycle management of multiple complex therapies, most notably Zolgensma—the first $2.1 million gene therapy—guiding it from pre-launch through commercialization and ensuring access for over 1,500 U.S. patients. Casey has led cross-functional teams across national trade relations, reimbursement support, channel design, strategic partnerships, and patient services.

Throughout their career, Casey has earned numerous awards and honors, including the Novartis Gene Therapies Impact Award (2021), AveXis Corporate Values Award (2019), Depomed President's Club and Create Great Award, as well as recognition from industry partners such as McKesson, Cardinal Health, and the Healthcare Distribution Alliance. They have served on key industry councils, including the HDA Industry Council and World Courier Advisory Council.

Their expertise spans a wide range of therapeutic and product categories—including rare, orphan, specialty, complex, small molecule, and biologic drugs—across diverse reimbursement channels such as commercial insurance, Medicare, Medicaid, buy-and-bill, white bagging, and 340B. Casey has a strong command of distribution models including specialty pharmacy, wholesale, and third-party logistics, and brings deep experience in compendia, contracting, diagnostics, and direct/indirect procurement. With a consistent focus on patient-centric access strategies and operational excellence, Casey Perkins continues to be a driving force in advancing care in the biopharma and CGT sectors.

Innovative Platforms, Strategies and a Peek into the Commercial Future

Stefan Sandström *

Biosector Ltd., JAPAN

Abstract:

Gene therapy is transitioning from its experimental adolescence into a complex and high-stakes commercial reality. As AAV, CAR-T, mRNA-based and other therapies evolve, the industry must confront the stark commercial thresholds that lie ahead. Key among them: cost and cytokine storms. The price tag of many current modalities limits accessibility, challenging the whole ecosystem to reimagine value chains, manufacturing innovation, and business models.

Across major markets, commercial readiness varies widely. In the U.S., investor appetite and structured fast-track pathways often accelerate time-to-market. In the EU, gene therapies fall under the ATMP designation, where harmonized central regulation often meets friction at the national reimbursement level. Japan's regenerative medicine law allows for conditional approvals, which can enable early launch if paired with deep post-marketing surveillance and uncompromising quality control.

These regulatory and strategic contrasts require companies to adapt not only their technologies but their go-to-market models. Platform innovation must now align with manufacturing scalability, reimbursement feasibility, and a differentiated value proposition for each region. The commercialization blueprint cannot be an afterthought.

To reimagine value chains demand a fundamental shift away from traditional centralized production towards agile, distributed manufacturing networks. This involves strategic investments in modular, scalable facilities, including potential point-of-care models to minimize logistical complexities and ensure product integrity. Embracing AI-driven automation and digital twins for real-time process control and predictive analytics is crucial for optimizing manufacturing, ensuring consistent quality, and reducing costs.

Manufacturing strategies must be tailored to address the unique challenges of niche indications and small patient populations without sacrificing economic viability, requiring flexible platforms and cost-effective technologies. Sustainable business models will rely on value-based contracts, milestone-linked pricing, and robust public-private collaborations that share risk and incentivize long-term value creation, ensuring patient access and industry sustainability.

As autologous manufacturing shifts to the hospital setting, new revenue streams are forming. Hospitals could evolve into hybrid treatment-manufacturing centers, generating income from on-demand production, patient-specific logistics, and quality services. This shift invites a service-oriented pricing logic, making hospitals stakeholders not only in treatment but in therapeutic production.

Meanwhile, regulatory expectations are evolving fast. Innovation and compliance are no longer separate concerns—successful players embed regulatory fluency into every stage of product design and market preparation.

This talk presents a forward-leaning commercial perspective on gene therapy's trajectory, with insights tailored to leaders navigating global complexity.

Biography:

Stefan Sandström is a senior commercialization advisor with a dual background in chemical engineering and medicine. He has held multiple CEO roles in Swedish companies expanding internationally, and for nearly two decades has lived in Japan, where he specializes in guiding biotech and pharma companies into the Japanese market. Stefan currently leads Biosector Ltd., working at the intersection of advanced therapies, regulatory strategy, and market access. His expertise lies in bridging global innovations with the nuanced demands of Japan's pharmaceutical ecosystem: facilitating strategic partnerships, commercialization roadmaps, and successful entry into one of the world's most highly regulated markets.

Bringing Biopharma Processing To Life

Rob Blackman

Parker, CA, USA

5 Key words:

1. Leak-free
2. Overmolded
3. Automation
4. Filtration
5. Bioreactor

Biography:

In my role at Parker PureTain, I provide single-use assemblies for biologics manufacturing – from upstream seed-trains to sampling rigs, incipient & ingredient frozen storage and downstream Final Fill-Finish needle lines in isolator bags. In my career I've represented lab supplies, equipment, reagents, kits, furniture and services with several companies for over 30 years and the Parker organization stands out to me as being exceptionally ethical, entrepreneurial and responsive.

Cytocentric Conditions for Decentralized Biomanufacturing

A. D. Henn, PhD MBA *, S. Darou, T. Lee, R. Yerden, S.A. Mustafa

BioSpherix,, NY, USA

Abstract:

As capabilities for human therapeutics advance, disparities in access to them increase. To improve access to cell therapies and reduce transportation, the manufacture of live cell products needs to be near the donors and the patients. A decentralized cell production system, the blood products system, has over a thousand cell processing sites in the US alone. To ensure that the quality of therapeutic treatments across a distributed network of sites for cell therapies remains high, all processing should be closed, controlled, and reproducible across all locations. The Xvivo System® X2 is a modular, closed cell incubation and handling system that provides full-time Cytocentric® environments, designed to be optimal for cells. The Xvivo System uses HEPA-filtered compressed gases rather than filtered room air found in traditional isolators, and temperatures in each module can be controlled to optimal conditions for cells. Research has shown that constant physiologic temperature and oxygen is beneficial for human bone marrow MSC cultures. Studies previously demonstrated that controlling relative humidity to low levels in cell processing modules prevents microbial growth and spread, a novel mechanism for reducing microbial risks in cell processing. Five problem microbes were used to assess the fate of microbes in Xvivo conditions including *P. aeruginosa, C. albicans, S. aureus, A. brasiliensis, and B. subtilis*. The microbes don't grow or spread under desiccating conditions. Conditions that are optimized for cells and desiccating for microbial control can be monitored remotely, enabling a decentralized model of cell therapeutic production easier to be managed with AI and Digital Twins. Fully optimized, controlled, and verifiably reproducible processes for cell manufacturing are essential for widespread access to advanced therapeutics. Cytocentric conditions can uniquely streamline cell therapy production, bringing it closer to donors and patients everywhere.

Biography:

Alicia D. Henn PhD MBA is Chief Scientific Officer for BioSpherix, Ltd. Previously, Dr. Henn was a researcher at the Center for Biodefense Immune Modeling at University of Rochester. Dr. Henn also owns the In Vitro Reproducibility and Physiologic Cell Manufacturing groups on LinkedIn, promoting clonable, physiologically relevant cell environments for scientific reproducibility and translatability.

Enhancing Cell & Gene Therapy Manufacturing with BatchLine Lite MES: A Collaborative Success Story with Vector BioMed

Carlo de Vera, Manufacturing Director for Vector BioMed
Neil Wetherall, Managing Director of BatchLine

Vector BioMed: 910 Clopper Road, 200S, Gaithersburg, MD 20878
BatchLine: Tech Incubator, Manchester Technology Centre, 103 Oxford Road, Manchester M1 7ED

Abstarct:

As the Cell & Gene Therapy sector continues to grow, the adaptation of modern manufacturing solutions becomes crucial. This presentation shares the experiences of Vector BioMed (VBM) in implementing the Lite Manufacturing Execution System (MES), focusing on their journey and its impacts on manufacturing practices.

Vector BioMed, specializes in providing rapid access to optimized-by-design Lentiviral vectors for clinical development and commercialization, collaborated with us to integrate the Lite MES into their production processes.

Our discussion will explore the practical challenges and solutions encountered during this transition, providing an honest account of the implementation and operational impact.

Key aspects include:

1. **Implementation Journey**: A look into the stages of implementing Lite MES within VBM's operations, emphasizing the hands-on experience and adjustments made along the way.
2. **Operational Impact**: Insight into the real-world changes Lite MES brought to VBM, particularly in workflow optimization, traceability enhancements, and maintaining compliance within the demanding framework of Cell & Gene Therapy production.
3. **Reflections and Learnings**: Sharing what VBM learned through this process, including unexpected benefits and areas for future improvement.

We invite you to learn from VBM's experience with BatchLine Lite MES, and to discuss the evolving landscape of manufacturing solutions in this innovative therapeutic field.

Biography:

Carlo de Vera is a results-driven biopharmaceutical leader and currently serves as Manufacturing Director at Vector BioMed. He brings extensive experience in cGMP biologics and lentiviral vector manufacturing, with a deep understanding of late-stage process development, validation, and the full product lifecycle.

Carlo has a proven track record in quality and compliance, complemented by strong problem-solving and troubleshooting skills. His leadership style emphasizes teamwork, continuous improvement, and operational excellence. He has successfully led both clinical and commercial manufacturing teams, ensuring strict compliance with cGMP regulations and safety standards.

His expertise also includes process automation, data management, and system lifecycle management. Known for innovative thinking and strong interpersonal skills, Carlo consistently drives performance and efficiency across manufacturing operations.

Biography:

Neil is the Managing Director of BatchLine. He supports industry and our clients across all continents. Neil has extensive experience in operations and supply chain management in a top-tier pharma company and has also led the IT strategy for supply chain and manufacturing, implementing enterprise-wide technology programs across all continents.

Shipping Validation 101: A Phase-Appropriate Approach for Cell and Gene Therapies

Carson Dickey

Modality Solution, TX, USA

Abstract:

This presentation will

- Define supply chain validation and its role in supporting pivotal studies and commercial products
- How to generate robust data to demonstrate shipping hasn't affected your therapy's CQAs
- Strategies for ensuring minimal material use for testing to reduce cost and supply burdens

Submissions

Carson is an expert in cold chain engineering and biopharmaceutical shipping validation and is passionate about developing risk-based validation strategies, qualifying thermal packaging, and designing transport studies. He has been involved in regulatory submissions for commercial approval of biopharma products worldwide and has received over 30 approvals for products where he was responsible for developing shipping validation strategies, including CGT products. Carson serves as the co-chair of the Cold Chain Logistics and Management Working Group within the International Society of Cell and Gene Therapies (ISCT). Through this experience and his work at Modality Solutions, Carson has expertise in cold chain validation and operations for cell and gene therapy supply chains. Additionally, he co-authored the ISTA supply chain risk assessment guidance whitepaper that provides industry guidance on conducting supply chain risk assessments.

Biography:

As Director of Engineering Solutions, **Carson Dickey** specializes in the qualification and validation of combination medical devices within the biopharmaceutical cold chain. He leads design and validation engineering efforts, including thermal packaging design and qualification for temperature-sensitive drug products. Carson also develops simulation testing strategies for drug product transport, conducts risk assessments, and creates validation protocols. Serving as a key technical liaison to development teams, he ensures robust and compliant engineering solutions. He holds a Master of Engineering in Biomedical Engineering and a certification in Quality Engineering for Regulated Technologies from Texas A&M University.

Developing an Advanced Sterility Assay for CGT Products on the QIAcuity dPCR Platform

Frederick Kweh

KWEHEALTH, LLC, FL, USA

Abstract:

Sterility testing is a critical bottleneck in cell and gene therapy (CGT) manufacturing, with traditional methods requiring 14 days and struggling with limited sample volumes and complex matrices. KWEHEALTH's Digital Sterility Assay (DSA), powered by QIAGEN's QIAcuity digital PCR platform, aims to transform this landscape by delivering rapid, sensitive, and reliable contamination detection in under 24 hours. This innovative assay multiplexes antibody-based detection of bacterial proteins with 16S rRNA gene amplification, ensuring comprehensive coverage without the need for lengthy growth steps. Tailored for CGT products, it addresses key challenges—small sample volumes, matrix interference, and urgent timelines—while maintaining femtomolar sensitivity. Join us to explore how the QIAcuity-enabled Digital Sterility Assay can accelerate product release, enhance patient safety, and streamline GMP workflows, with insights into its validation and broader biopharma applications.

Biography:

Dr. Frederick Kweh is a seasoned biomedical scientist with over 20 years of experience in basic, translational, and clinical research across gene therapy, monoclonal antibodies, metabolic disorders, cancer genetics, and viral vaccines. He has held leadership roles at Resilience Inc., Thermo Fisher Scientific, and Ology Bioservices, where he spearheaded the development of advanced analytical technologies and assays to support viral vectors, cell therapies, and biologics. A Ph.D. graduate from the University of Florida, Dr. Kweh is widely published and recognized with multiple awards for his research on Prader-Willi syndrome and obesity. His strengths lie in innovation, team leadership, regulatory compliance, and a deep commitment to advancing science and therapeutic development.

Can Data-Driven Manufacturing Fuel Global Access for Cell Therapies?

N.K. *Pike

Catalent Pharma Solutions, NJ, USA

Abstract:

Cell therapies through their curative potential offer life-changing treatment options to patients with previously incurable diseases. Cell therapies have achieved unprecedented success as evidenced by the growing numbers of commercial approvals and clinical trials across the globe. Despite this success, cell therapy developers continue to face many challenges including manufacturing complexities, costs, scalability, and regulatory compliance. One strategy to overcome these barriers and make such therapies more accessible, is the adoption of data-driven manufacturing along with advanced analytics. Data-driven manufacturing enables developers to acquire, analyze and optimize data related to cell health and behavior, and build predictive models for process optimization. Advanced analytics is the backbone of process optimization and quality control, as it allows for observation of trends, mitigation of problems in real-time and enables informed decisions for successful manufacturing.

Adoption of data-driven manufacturing with predictive modelling and advanced analytics is vital in propelling these "living therapies" without compromising safety and efficacy. As more cell therapy assets are being developed, it is imperative to streamline manufacturing and reduce costs so more patients can benefit from them. The manufacturing space can benefit from advanced analytics tools such as predictive modeling, data management and mining, AI, and machine learning to better understand critical quality attributes and critical-process parameters and help build efficient workflows, thus making these life-changing therapies more accessible.

Biography:

Nirupama (Rupa) Pike is a seasoned leader with over two decades of experience in regenerative medicine, bringing deep expertise across R&D, GMP manufacturing, technology transfer, process development, and commercial operations in the cell and gene therapy space. She is passionate about building and scaling innovative cell therapy programs, driving strategic partnerships, and developing high-performing teams. Rupa's work is fueled by a sincere commitment to making a meaningful impact in the lives of patients facing difficult-to-treat diseases.

Session: Optimizing AAV Manufacturing: Engineering, Processing, Analysis and Quality Control

Keynote:

Viral Vector Innovation: Improving Quality, Productivity, and Gene Size Capacity

Sebastien Ribault

Oxford Biomedica, United Kingdom

Biography:

Dr. Sébastien Ribault is the Chief Commercial Officer at Oxford Biomedica (OXB), bringing over 25 years of experience in the biotechnology and CDMO sectors. Prior to joining OXB in 2022, he served as Vice President and Head of Biologics and Viral Vector CDMO at Merck Life Science, where he led the company's CDMO expansion and played a key role in establishing the Life Science Services business unit. Earlier in his career, he held scientific roles at Transgene and Hemosystem. Dr. Ribault holds a PhD in Molecular and Cellular Biology from the University of Strasbourg.

Novel Cell Engineering Platform for High-Yield AAV Production and Improved Manufacturability via Engineered HEK-293 Cells

***Larry Forman; K. Ngo**

CHO Plus, CA, USA

Abstract:

Adeno-associated virus (AAV) has emerged as a significant therapeutic modality in gene therapy. Challenges such as poor yield and variable product quality persist in the viral vector manufacturing space and we are addressing these problems using our cell engineering technologies.

Our cell engineering platform for improved AAV manufacturing addresses the 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 CQAs, can significantly bolster the efficiency and cost-effectiveness of gene therapy manufacturing, and can accelerate current development timelines.

We used a directed-evolution approach based on repeated cell fusions to shuffle the cell genome, and to amplify whole chromosomes of HEK-293 host cells. Engineered clones enriched for 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 inducible system that maximizes the 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 10^{17} viral particles/L (vp/L)—at least 10-fold higher than current industrial manufacturing processes. Selection 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 10^{16} 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. We further propose a model regarding the role of mitochondria for enhancing capsid percent-full. Taken together, our several related platform technologies provide solutions for meeting current—and future—gene therapy manufacturing challenges.

Biography:

Larry Forman is a biologist by training. He worked at Genentech from 1980-1996 where his focus was mammalian cell culture process development. After Genentech, Larry worked for other pharmaceutical companies involved with the production of human therapeutic proteins via mammalian cell culture. In 2014 Larry founded CHO Plus to (successfully) develop cell-engineering methods for significantly increasing the specific productivity of mammalian cells used for biomanufacturing: engineered CHO cells for improved recombinant therapeutic protein production; engineered HEK-293 cells for improved AAV production.

The Need for an Unbiased Assay to Detect and Quantify Replication Competent AAV in Clinical Vector Products

F.Dorange; P-A Vinot; B. Erout; B. Gachet; C. Breuleux; G.A. Ramirez; M Gasmi*

SparingVision, France

Abstract:

Replication-competent AAVs (rcAAV) are gene therapy product-related impurities that could have associated safety risks for patients. rcAAVs are conventionally detected in cell-based assays consisting of successive rounds of amplification in the presence of an adenovirus with a qPCR readout on viral gene sequences. The absence of rcAAV detection in 1E+08 vg has generally been used as an acceptance criterion.

Our data show that this cell-based method can yield significantly different results between testing facilities using different assay protocols. Moreover, we show that positive or negative results are highly dependent on the capacity of serotypes to infect the permissive cell line in vitro, which could be quite different from what is observed in vivo.

An analytical method that allows the unbiased detection and quantification of rcAAVs is thus needed. We have developed a method based on a multiplex digital PCR (dPCR) that targets 3 junctions specific to rcAAV genomes: ITR-Rep, ITR-Cap and Rep-Cap. It accounts for the presence of potential exogenous sequences and it takes advantage of the partitioning of the dPCR to isolate particles containing triple positive genomes. Several recombinant AAV vector batches of various serotypes, positive or negative for rcAAV in the cell-based assay showed similarly extremely low levels of triple positive genomes (less than 0.00008% of genomes quantified by qPCR) in comparison to wild type (wt)AAV. Interestingly the latter showed that only 3% to 7% of their genomes were triple positive. Results were independent of the HEK293/transfection manufacturing protocol. However, no triple positive entities were found in baculovirus-generated preparations likely due to the modifications in constructs of the vector system.

Our data suggest that there are likely no HEK293/transfection-derived vector AAV preparations devoid of rcAAV genomes. In this context our efforts constitute the first step toward the goal of changing the way rcAAVs are detected and quantified. More results from other sponsors using AAV vectors are needed to solidify our preliminary data set and to engage in a field-wide discussion, including regulators, on how to generate specifications and acceptance criteria for this novel analytical method. This will help to better reflect on and provide mitigation strategies for potential safety risks associated with rcAAVs until means to eliminate them from vector batches have been identified.

Biography:

Pierre-Axel Vinot brings over 10 years of experience in preclinical research, clinical trials, and CMC management, particularly in the field of cell and gene therapies. He holds a Pharm.D. from the University of Paris and a Ph.D. from Sorbonne University and completed a specialized residency in biotech product development within AP-HP, the Europe's largest hospital group. His career spans academic research, public hospitals, and biotech companies, where he has worked on advancing innovative therapies. Currently, Dr. Vinot leads the CMC portfolio at SparingVision, focusing on the development and manufacturing of gene therapy solutions for retinal degeneration.

Transformative Advances in Viral Vector Manufacturing: Unlocking Commercial Scalability, Consistency and Cost-effectiveness with Tet-Off PCL Innovation

S. D'Costa, Genezen

Genezen, IN, USA

Abstract:

Genezen is a boutique viral vector CDMO dedicated to advancing gene and cell therapies by providing manufacturing solutions and services specializing in lentiviral (LVV), retroviral (RVV), and adeno-associated virus, AAV viral vector process development and manufacturing to support clients in preclinical, clinical and commercial product development.

AAV and LVV serve as efficient tools for delivering therapeutic transgenes into both dividing and nondividing cells, facilitating sustained gene expression. While several platforms exist for their production, transient transfection of naïve production cells (preferably HEK293 cells) to produce vector is the most popular and quickest platform. However, challenges in processes utilizing transient transfection methods include batch-to-batch variability and heightened costs associated with manufacturing. These challenges contribute to the overall high production costs of these Cell and Gene Therapy (CGT) products.

In response to these challenges, Genezen is exploring alternatives to traditional plasmid DNA from E. coli including synthetic DNA. Specifically, for LVV production, Genezen has implemented a proven Tet-off Producer Cell Line (PCL) system to overcome the limitations of traditional production methods. Through meticulous evaluation, we have successfully adapted a PCL that consistently achieves raw IU titers exceeding 6e6/mL in four 200L productions across two distinct VSVG enveloped Transgenes of Interest (TOIs). This innovative approach demonstrated superior titers with better residual profile in a comparative study with one of the TOIs tested. The Tet-off PCL system offers numerous advantages, including improved Downstream Processing (DSP) with enhanced overall recoveries, a superior residual profile, and the ability to generate multiple sublots that can be combined into a super lot with titers surpassing 5e8 IU/mL.

By eliminating the requirement for cGMP-grade E. coli plasmids in vector production, Genezen's approach holds the promise of significantly reduced costs, improved commercial scalability, and consistent batch yields when compared to current industry-standard manufacturing processes. This innovation represents a substantial step forward in the field of gene and cell therapy, with the potential to enhance patient access to medicines based on these vectors.

Biography:

Susan D'Costa is a molecular virologist spanning 25 years of experience in virology. Over the past ten years she has been actively involved in viral vector analytics, process development, manufacturing, and building successful teams. She is currently the Chief Technical and Commercial Officer at Genezen, a leading gene and cell therapy CDMO. Prior to Genezen, Susan was CTO at Alcyone Therapeutics, a biotechnology company pioneering next-generation CNS precision gene-based therapeutics for complex neurological conditions. At Alcyone, she was responsible for viral vector CMC, device development operations and partnering on new technologies for both gene therapy and precision delivery. Dr. D'Costa has also held leadership roles of increasing responsibility at Thermo Fisher Scientific, Viral Vector Services and its predecessor companies – Brammer Bio and Florida Biologix, working with different viral vectors, liaising with diverse biotech clients and building teams with scientific and operational excellence. Susan holds a Ph.D. in biology, specializing in molecular virology, from Texas Tech University; an MS in biochemistry from Mumbai University (Grant Medical College) and a BS in microbiology/biochemistry also from Mumbai University (St. Xavier's College).

An AAV GMP Manufacturing Solution for Large Clinical Demand Indications

Timothy Fenn

Lexeo Therapeutics, CT, USA

Abstract:

The high cost of goods (COGs) and low yields of current AAV manufacturing processes preclude development pipelines from considering indications with large patient and/or dose demands due to the significant capital required to supply the clinic and to commercialize the drug product. The combination of costly manufacturing and small number of patients has driven up the price of AAV therapies to record-setting heights, further limiting patient access and under-serving many patient populations.

We have developed a highly reproducible and scalable 200L GMP AAV production process using the Sf9-baculovirus system. The process is relatively simple – there is no need for costly plasmids, time-intensive generation of producer cell lines, intensification, or large-scale production of recombinant baculovirus, and purification is a straightforward 2-column process. The overall process delivers over 1E15 vg/L of purified AAVrh.10 product that contains less than 25% empty capsids. A 200L GMP batch can yield approximately thirty (30) 6E13 vg/kg doses for LEXEO's LX2020 PKP2 program. Produced this way, Lexeo's AAV drug substance has shown consistent potency from *in vivo* and IND-enabling studies through GMP production of clinical-grade material and is currently supplying LEXEO's clinical-stage programs.

The current state of AAV manufacturing has significantly limited the progression of AAV gene therapy to successful commercial viability. The universal problem of high COGS and low yield has not allowed gene therapy to have the deep impact on healthcare that it has the potential to do. Lexeo's manufacturing process and overall CMC strategy can dramatically expand patient access and transform the gene therapy field.

Biography:

Timothy Fenn is a dedicated professional in the field of gene therapy, currently contributing to the advancement of innovative treatments at Lexeo Therapeutics in Connecticut, USA. With a strong background in translational science and therapeutic development, he plays a vital role in the progression of clinical-stage programs aimed at addressing genetic disorders. His work supports Lexeo's mission to deliver transformative gene therapies to patients with high unmet medical needs.

High-Efficiency, Single-Use Chromatography Solutions for Scalable Viral Vector Purification

Sanjeev Saxena, Vinit Saxena (Corresponding Author)

Sepragen Corporation, CA, USA

Abstract:

Sepragen has developed a compact, low-flow, automated single-use chromatography system combined with high-flow, low-cost resins packed in a radial flow column design for the efficient purification of viral vectors such as AAV and lentivirus. This platform maximizes throughput, minimizes pressure drop, and enhances scalability, all while reducing contamination risks and cleaning validation needs. The system's single-use automation streamlines process development and clinical-to-commercial scale-up. This technology offers a robust solution for gene therapy manufacturing, supporting rapid development timelines and compliance with cGMP standards in viral vector production

Biography:

Sanjeev Saxena CCO, Sepragen Corporation

Sanjeev Saxena is the Chief Commercial Officer at Sepragen Corporation, where he leads the development and commercialization of innovative purification technologies for gene therapy manufacturing. With a strong background in chromatography systems, Sanjeev focuses on delivering high-efficiency, scalable solutions for viral vector production, ensuring alignment with cGMP standards and accelerating time-to-market for emerging therapies.

Development of Next-generation Xcite® AAV Stable Producer Cell Lines

G. Li[1]; N. Knowles[1]; C. Li[1]; F. Lugo[1]; T. Duong[1]; P. Le[2]; *Boning Gu[1]

Lonza Houston Inc., TX, USA

Abstract:

Recombinant adeno-associated viruses (AAV) are increasingly used in gene therapy to treat human genetic diseases, however, the low productivity and high cost of current AAV manufacturing process limit markedly the access of these revolutionary therapies to patients. Here we report the development of our high-performing, helper virus-free, Xcite® AAV stable producer cell lines (PCL). The technology stably integrates DNA cassettes of helper, rep-cap, and therapeutic gene into the genome of HEK293 cells, which allows the robust induction of AAV production via tightly controlled, inducible promoters. The PCL platform delivers over 1E12 vg/mL titer and 30% full capsid in crude harvest across thirty cell passages. In addition, using a clinically relevant transgene and an engineered capsid provided by our partner, we confirmed the robust AAV PCL development process from stable pools to selected single cell clones, which produces over twenty times higher titer than the transient transfection process. In summary, our Xcite® AAV stable PCL represents a next-generation technology to industrialize scalable AAV manufacturing at significantly reduced cost and complexity.

Biography:

Bingnan Gu, Senior Director, R&D, Viral Vector and Cell Therapy, Lonza Bingnan has over twenty years research and development experience in academia and industry, focused on stem cell regulation, cell line and vector engineering, and cell and gene therapy (CGT) manufacturing process and analytics innovation. He authors over twenty peer-reviewed articles in leading journals and eight patent applications in CGT manufacturing technologies and analytics. He leads the group of R&D scientists for the development of Lonza's proprietary AAV, lentivirus, and cell therapy manufacturing platforms. Bingnan earned his PhD degree in molecular medicine from the University of Texas Health Science Center at San Antonio, MBA from the University of Texas at Austin, and Bachelor in life sciences from Fudan University in China.

How to Enhance AAV Yield with a Single Clone Producer Cell Line, Optimized Plasmid Design, and the TESSA® Production Platform

Mark Davis

Minaris Advanced Therapies, PA, USA

Abstract:

As gene and cell therapy pipelines expand, the demand for high-purity, high-yield viral vectors—particularly AAV—continues to grow. To address this, we have developed an integrated approach that combines a genetically uniform, high-yield single-clone producer cell line, a reengineered packaging plasmid, and the TESSA® (Tetracycline-Enabled Self-Silencing Adenovirus) platform.

Our proprietary RepCap plasmid design features Cap expression under a strong CMV promoter, while Rep expression is modulated via an EMCV internal ribosome entry site (IRES), enabling improved control of Rep levels and significantly enhancing viral titer. In parallel, the TESSA® platform offers a non-transfection-based production method that delivers increased yield, infectivity, consistency, and scalability—supporting clinical-scale manufacturing.

This platform was further validated with fit-for-purpose downstream processes across multiple AAV serotypes and both transient transfection and TESSA®-based production. Together, these innovations offer a robust and reproducible solution to accelerate AAV-based therapeutic development.

Biography:

Mark Davis is a dedicated Scientist specializing in downstream process development at Minaris Advanced Therapies. With a strong foundation from Drexel University, he began his career at Eurofins and joined Minaris Advanced Therapies in 2022 and has been focused on optimizing bio-manufacturing processes on behalf of our clients. Passionate about precision and innovation, Mark plays a key role in refining therapeutic production workflows to ensure quality, reproducibility, and scalability.

Optimizing Technology Transfer and Federal Partnerships to Advance Cell and Gene Therapy Innovation

CF Silverthorn*

Foundation for the National Institutes of Health MD, USA

Abstract:

The Bespoke Gene Therapy Consortium (BGTC), a pre-competitive public-private partnership managed by the Foundation for the National Institutes of Health (FNIH) as part of the National Institutes of Health's (NIH's) Accelerating Medicines Partnership® (AMP®) program, is an initiative bringing together the resources and expertise of multiple NIH institutes, pharmaceutical companies, biotechnology companies, professional organizations and patient advocacy groups to demonstrate manufacturing, pre-clinical, and regulatory frameworks that will accelerate the development of Adeno-Associated Virus (AAV) gene therapies for rare diseases. In May of 2023 the BGTC announced the selection of eight rare diseases for its clinical portfolio. Standardized critical quality attributes for manufactured product, standardized pre-clinical testing and clinical trial protocols, and standardized regulatory submission templates will be used to advance each therapy into a Phase 1 clinical trial, demonstrating the replicability of various processes. The BGTC published its first version of a publicly accessible regulatory playbook in February of 2023; future updates will incorporate learnings and outcomes from the manufacturing and pre-clinical processes. This session will discuss various tech transfer issues that the BGTC has encountered and how the pre-competitive public-private partnership framework has guided the navigation of these issues.

Biography:

Dr. Courtney Silverthorn is the Vice President for Strategic Alliances and Innovation at the Foundation for the National Institutes of Health, where she is responsible for leading the strategic development and management of the Foundation's business portfolio across multiple departments and overseeing project-restricted fundraising. Prior to joining the FNIH, Courtney was the Acting Director of the Technology Partnerships Office at the National Institute of Standards and Technology, where she led technology transfer activities at the agency and was central to the interagency Lab-to-Market initiative. She also held tech transfer and policy roles at the Office of Science and Technology Policy, the Frederick National Laboratory for Cancer Research, and the National Cancer Institute. Dr. Silverthorn earned a Ph.D. in Pharmacology from The Johns Hopkins University School of Medicine, a M.S. in Leadership from Washington University in St. Louis, and a B.S. in Biochemistry and Molecular Biology from Sweet Briar College.

Successful Commercialization Strategies for Cell and Gene Therapy Products in America's Dynamic Market; Lessons Learned from Recent Product Launches

Kevin Cast, MS

Archbow Consulting, FL, USA

Abstract:

As the Cell and Gene Therapy market continues to grow and expand, many CGT companies are now considering how best to commercialize their novel product(s). CGT products are not well suited to today's US commercial supply chain or payer reimbursement policies. Thus, an experienced supply chain vendor and well tested Provider and Patient Support vendor is mission critical for commercial success.

1. Define the supply chain models available to CGT companies today (Specialty Pharmacy, Third Party Logistics, Specialty Distributors, etc)
2. How to select a best-in-class CGT supply chain partner that meets the specific needs of a high cost ultra frozen CGT product
3. Advise and ideate on novel payment mechanisms that could be relevant for CGT products (Value or Outcome Based Contracts vs Re-Insurance Warranties)
4. Provide strategic insights and market intelligence related to Patient Support Services specific to CGT products

Biography:

Carson Dickey, Director of Engineering Solutions, focuses on qualification and validation of combination medical devices in the biopharmaceutical cold chain. He leads thermal packaging design, transport simulation testing, risk assessment, and protocol development for temperature-sensitive drug products. Carson also serves as a key technical liaison to development teams. He holds a Master's in Biomedical Engineering and a Quality Engineering certification from Texas A&M University.

Navigating Regulatory Success in Cell and Gene Therapy Development

J.C. Mercer*

Facet Life Sciences, PA, USA

Abstract:

Advancements in cell and gene therapy offer groundbreaking possibilities, but unique regulatory challenges can significantly impact timelines and costs. Unlike small molecules or monoclonal antibodies, these therapies require an integrated approach that considers regulatory requirements at every stage. Without strategic planning, companies often overestimate progress, leading to delays and increased expenses.

This presentation provides biotech companies with a roadmap for regulatory success, outlining key considerations from early development to BLA submission. Topics include:

1. **Early FDA Interactions**: When to initiate discussions with the FDA based on developmental milestones, including securing an INTERACT or Type D meeting once the manufacturing process is well-defined and preclinical proof-of-concept data are available.
2. **Pre-IND Milestones**: Common pitfalls in IND preparation, particularly in aligning manufacturing consistency with preclinical data, and strategies to mitigate risks of clinical hold.
3. **Expedited Pathways**: Understanding Fast Track, RMAT, Breakthrough Therapy, and Priority Review designations, when to apply, and how to leverage these programs for regulatory efficiency.
4. **Pivotal Study Readiness**: Ensuring alignment between clinical and CMC development, addressing comparability, potency assay development, patient selection, and FDA expectations for pivotal trial endpoints.
5. **Common BLA Delays**: How misaligned timelines, slow patient recruitment, and incomplete CMC validation can stall approval, and strategies to mitigate these risks.

Real-world case studies will illustrate how early FDA engagement and proactive planning can accelerate development. Companies that integrate regulatory considerations early and leverage expedited pathways can significantly enhance their chances of timely approval.

This session is designed for scientists, chief scientific officers, and academic experts in small biotech companies developing cell and gene therapies. Attendees will gain actionable insights into regulatory strategy, ensuring their programs are well-positioned for success in this competitive and evolving field.

Biography:

Dr. Mercer has over 15 years of experience helping small to medium-sized pharma and biotech companies achieve successful drug and biologic development programs – form idea to approval. Dr. Mercer specializes in designing innovative and creative development strategies that are aligned to company strategic goals; collaborating with the FDA to address unique challenges; and navigating the regulatory complexities inherent in the development of innovative drug and biologic products to ensure efficient development and regulatory approval.

Nonclinical Regulatory Considerations for Cell Therapy Development: Early Development and IND Stage

Ziyan Zhang

Eliquent Life Sciences, NC, USA

Abstract:

Cell therapies represent a groundbreaking advancement in modern medicine, offering the potential for durable, personalized, and disease-modifying treatments across oncology, regenerative medicine, and autoimmune disorders. Unlike traditional pharmaceuticals, these therapies rely on living cells with complex biological functions. Their ability to expand, persist, and interact dynamically with the immune system underlies their therapeutic potential but also introduces significant challenges in nonclinical development. The inherent variability of cell-based products, along with factors such as genetic modifications, further complicates nonclinical assessments. As a result, Investigational New Drug (IND) applications for cell therapies require an integrated and flexible approach, ensuring regulatory compliance while supporting clinical development.

We will focus on key nonclinical considerations for cell therapies at the IND stage, highlighting FDA expectations and best practices for study design. Key topics include species and model selection challenges, biodistribution and persistence, and safety considerations, such as on-target/off-tumor toxicity, cytokine-related toxicity, and tumorigenicity assessments. Additionally, we will discuss the critical coordination between nonclinical testing and CMC strategies to ensure regulatory alignment and accommodate manufacturing changes. Case studies will illustrate recent regulatory feedback on preclinical-to-clinical translation, offering insights into navigating nonclinical safety requirements, engaging in productive pre-IND meetings, and aligning study designs with evolving regulatory expectations.

Given the rapidly evolving regulatory landscape, ensuring compliance with FDA guidelines is essential for advancing cell therapies from research to clinical application. Researchers and biotech companies who wish to bring their products from bench to bedside will gain a deeper understanding of how to align IND-stage nonclinical programs with evolving US regulatory expectations to facilitate a smoother transition into clinical trials.

Biography:

Ziyan Zhang, Ph.D., is a nonclinical consultant at ELIQUENT Life Science, with three years of experience in regulatory affairs. She provides regulatory support for a wide range of therapeutic products, including cell and gene therapies (CGTs), recombinant proteins, antibodies, and small molecules across oncology, genetic and rare diseases, ophthalmology, and other therapeutic areas.

Dr. Zhang has contributed to 15+ regulatory submissions, including IND, FDA meeting packages (Pre-IND, EOPs, and INTERACT), and application for special designations (fast track and orphan drug). Beyond regulatory submissions, she has played a key role in developing nonclinical study strategies, performing gap analyses, and reviewing study reports to support regulatory compliance and alignment.

"Concept to Cure": Integrate Safety/Tox and CMC to Streamline Clinical Development and Commercialization for Advanced Therapies

David Alvarado

Charles River, MA, USA

Abstract:

Charles River is a global leader in contract research, development and manufacturing solutions. This presentation will outline an integrated strategy for streamlining clinical readiness of Advanced Therapies by leveraging our expertise in gene therapy manufacturing, Testing, and pre-clinical services such as Safety Assessment and Toxicology. This strategy has been proven to reduce time to clinic and cost of development.

By combining these critical services under their integrated business model, CRL has re-defined end-to-end service and established a unique and robust pathway to support Cell and Gene Therapy developers from "Concept to Cure".

With over 75 years of experience, Charles River is a trusted partner to drug developers of all sizes and modalities and supports approximately 85% of novel FDA approved drugs per year.

Biography:

David has worked in biotechnology R&D, diagnostics and commercial roles for over 14 years and has held business development and product leadership positions supporting Cell & Gene Therapy developers as clients at clinical and translational stages for more than 7 years. David has contributed to the development of GMP primary cells and leukapheresis products for cell therapy manufacturing and has most recently joined Charles River's Gene Therapy Manufacturing services team driving external manufacturing partnerships for plasmid DNA, viral vectors and more.

Regulatory, Commercialization and Community Engagement for jCell, an Investigational Allogeneic Cell Therapy for Treatment of Retinitis Pigmentosa

John Sholar

jCyte, CA, USA

Abstract:

jCyte is developing jCell, a gene-agnostic allogeneic cell therapy for the treatment of retinitis pigmentosa, a rare inherited retinal disease that leads to blindness. Critical and unique regulatory and community engagement activities are required in our efforts to commercialize this product and bring an innovative therapy to patients with no meaningful treatments.

Biography:

John has been with jCyte for three years, serving first as General Counsel, then COO, and in 2023 he was appointed as the CEO. John has worked in pharma and biotech for two decades, both in operational roles and as a patent attorney earlier in his career. Prior to his time in law and pharma, John was a naval officer who ran leadership interdiction operations for various oversees conflicts.

Safeguarding Every CGT Sample – An Integrated Stability & Sustainability Outsourcing Model

Ryan Smith

Astoriom Inc, NC, USA

Abstract:

Ensuring the stability, viability and long-term sustainability of sensitive biological samples is particularly complex in cell and gene therapy (CGT), where the margin for error is minimal, and the value of each sample is immeasurable. From autologous cell lines and gene-modified vectors to raw materials and investigational products, CGT research demands rigorous environmental control, cold-chain logistics, and uncompromising quality to protect the integrity of every step across the R&D and manufacturing lifecycle.

This session introduces Astoriom's Integrated Stability & Sustainability Outsourcing Model (ISSOM) – a comprehensive approach to sample protection that addresses the unique demands of CGT programmes. The ISSOM model combines advanced ICH-compliant stability storage with biorepository solutions that support ultra-low, cryogenic and controlled ambient conditions, while also embedding redundancy, regulatory flexibility, and disaster recovery into every element of the storage strategy, supported by our FDA, ICH and other quality credentials.

With a particular focus on preserving highly sensitive and often irreplaceable human-derived samples, this model enables CGT organisations to safeguard against sample degradation, minimise disruption, and accelerate time to clinic. Attendees will explore real-world case studies demonstrating how leading CGT innovators and CROs have leveraged this model to achieve enhanced sample security, ensure GxP compliance, and scale operations without compromising scientific progress.

Key topics will include:

- Building a resilient and flexible stability storage model for CGT pipelines
- Ensuring sample continuity across global CGT trials and manufacturing sites
- Supporting regulatory alignment across FDA, EMA, and local agency requirements
- Integrating disaster recovery planning to prevent loss of high-value human samples
- Achieving operational efficiency while reducing CapEx burden

Biography:

Ryan Smith is the Global Head of Sales at Astoriom. With over 20 years of commercial leadership experience in the life sciences sector, Ryan has led global sales teams and managed strategic partnerships at leading global life sciences service providers, delivering growth across specimen management, capital equipment and outsourced services.

Ryan has a deep understanding of the unique demands of R&D, regulatory compliance, and scaling biopharma operations. At Astoriom, he leads the global sales function, supporting the commercial growth across the company's stability storage, biorepository, and validation services portfolio. Since joining, he has played a key role in aligning sales initiatives with customer needs and advancing the company's mission to safeguard R&D sample assets worldwide, strengthening customer relationships, and supporting expansion efforts.

From Lab to Launch: Case Studies Demonstrating Scalable Solutions for Complex Cell Engineering Workflows

Megan Embrey

MaxCyte Presentation, MD, USA

Abstract:

"Cell-based therapies are transforming the treatment landscape for cancer and other serious diseases, with T cells and NK cells at the forefront of this revolution. However, engineering these immune cells remains a significant challenge due to their sensitivity and resistance to conventional transfection methods. MaxCyte's ExPERT™ electroporation platform addresses these challenges with a highly efficient and scalable solution for delivering a wide range of biomolecules, including mRNA, DNA, and CRISPR-Cas9 RNPs, into hard-to-transfect cells. In this presentation, we will share case studies highlighting the successful engineering of primary human T and NK cells using MaxCyte's optimized workflows. These examples demonstrate high transfection efficiency, robust expression of tumor-targeting receptors (CARs/TCRs), and preservation of cell viability and function. When paired with SequreDx™ for powerful on- and off-target gene editing analysis, MaxCyte empowers scientists with a comprehensive solution for safe, efficient, and scalable cell engineering—streamlining the path from early discovery to clinical and commercial production."

Biography:

Megan Harris Embrey is a Senior Field Application Scientist at MaxCyte, Inc., with over 15 years of hands-on laboratory experience in cellular and molecular biology. She supports and trains users on the MaxCyte ExPERT electroporation platform, enabling applications such as protein production and the development of cell and gene therapies. Her technical expertise includes tissue culture, molecular cloning, transfections, transformations, PCR, CRISPR gene editing, fluorescence and immunofluorescence microscopy, and flow cytometry.

The Future of Cell Culture Media: Pioneering Artificial Human Platelet Lysate for Scalable, Xeno-Free Bioproduction

H. Hemeda*, R. Goetzke, J. Park

PL BioScience GmbH ,Germany

Abstract:

As regenerative medicine and cell-based therapies gain momentum, the demand for safe, high-performance, and ethically produced cell culture supplements continues to intensify. Human Platelet Lysate (HPL) has become a preferred alternative to Fetal Bovine Serum (FBS), offering a xeno-free solution with superior biological performance and reduced risk of animal-borne contaminants. However, the reliance on donor-derived platelets poses ongoing challenges related to supply limitations, batch-to-batch variability, and long-term scalability.

PL BioScience has addressed this challenge by developing the world's first artificial HPL solution based on lab-grown human platelets, representing a transformative leap in cell culture innovation. Developed in collaboration with DewCell Biotherapeutics, PL BioScience led the optimization of a proprietary manufacturing process that converts artificial platelets into a high-performance, GMP-ready supplement. Through extensive process engineering, custom additive development, and rigorous quality control, the resulting artificial HPL not only replicates but enhances the biological activity of natural HPL.

This presentation will explore how PL BioScience's artificial HPL achieves superior consistency, safety, and cell proliferation support compared to both donor-derived HPL and animal-based alternatives. Key insights into growth factor stability, cytokine composition, and performance in stem cell expansion and immunotherapy workflows will be shared, supported by internal data from preclinical studies. Additionally, the xeno-free nature and scalable manufacturing process open the door to reliable, ethical, and future-proof bioproduction at industrial scale.

With a patent filed and manufacturing established in Germany under quality-controlled conditions, PL BioScience is positioned to supply artificial HPL for the full translational pipeline—from research and development to GMP-compliant cell therapy production. This milestone aligns with global regulatory trends favoring animal-free systems and supports the broader mission of building a sustainable and ethically responsible foundation for next-generation biologics.

The artificial HPL solution is not merely a substitute for existing inputs—it is a performance-optimized, clinically viable platform redefining the standard for cell culture media. PL BioScience's innovation marks the beginning of a new era in bioprocessing, where consistency, scalability, and ethical sourcing are no longer trade-offs, but fundamental design principles.

Biography:

Jungsoo Park is Senior Vice President of Global Marketing and Sales at PL BioScience GmbH, where he leads the global strategy for xeno-free human platelet lysate (HPL) technologies supporting cell therapy and regenerative medicine. With a background in life sciences and business administration, he specializes in advancing scientifically robust, commercially scalable solutions that meet the complex demands of clinical cell manufacturing.

His work focuses on bridging the interface between scientific development and therapeutic application—particularly in enabling consistent, safe, and high-performance cell culture systems for stem cell expansion, immunotherapies, and advanced therapy medicinal products (ATMPs). At PL BioScience, Mr. Park has played a central role in the development and launch of the world's first artificial human platelet lysate, a fully synthetic, GMP-compatible supplement designed to overcome the limitations of donor-derived materials.

Committed to accelerating the translation of cell-based innovations into clinical practice, he works closely with partners across the biopharmaceutical sector to ensure that next-generation culture media align with regulatory, ethical, and performance requirements for cell therapy development.

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