VANCOUVER NANOMEDICINE DAY

2025 Program and Abstract Booklet

VANCOUVER NANOMEDICINE DAY

November 12, 2025

All talks are in auditorium 1101 / overflow in auditorium 1201 / posters and breaks in lobby

	Session 1		**Chair: Miffy Cheng**
9:00 AM	Joel Finbloom / Miffy Cheng	Welcome to the 10th Vancouver Nanomedicine Day 2025	UBC Pharmaceutical Sciences
9:10 AM	Anna Blakney	Next-Generation RNA Vaccines & Therapies	UBC SBME and MSL
9:45 AM	Omar Khan	The First Nanomedicines Created from the Dark Transcriptome	University of Toronto
10:20 AM	Muhammad Muzamil Khan	Lymph node targeted Lipid Nanoparticles for Vaccine Delivery Applications	UBC Biochemistry
10:35 AM	Belal Tafech	Optimized CRISPR-Loaded Lipid Nanoparticles for Efficient Gene Editing in Cystic Fibrosis Lung Models	UBC SBME and Pharm Sci
10:50 AM		Coffee Break	
	Session 2		**Chair: Sarah Hedtrich**
11:20 AM	Stephanie Willerth	3D Bioprinted Tissues as a Tool for Studying Nanotherapeutics	University of Victoria
11:55 AM	Hagar Labouta	On-Chip Innovation for Nanoparticle Design and Testing	University of Toronto
12:30 PM	Jolene Phelps	Stem Cell-Derived Extracellular Vesicles to Reverse Inflammatory Damage to the BBB in Alzheimer's Disease	University of Victoria
12:45 PM	Taniya Adak	Untangling the Analytical Complexities of Targeted Lipid Nanoparticles (tLNPs)	Cytiva
1:00 PM		Lunch Break	
1:30 PM		Poster Session	
	Session 3		**Chair: Urs Hafeli**
3:00 PM	Panel Discussion on Entrepreneurship in Nanomedicine		Moderated by Linh Le
4:00 PM	Tatsuhiro Ishida	Immunological Responses Against PEGylated Materials	Tokushima University
4:35 PM	Shyh-Dar Li	Polymer-Lipid Nanoparticles for Enhanced RNA Delivery	UBC Pharmaceutical Sciences
5:10 PM	Victor da Silva	Machine Learning-Guided Optimization of Bioinks for Neural Tissue Engineering	University of Victoria
5:25 PM	Jad Kaj	Self-Assembled Fluorescent Supra-J-Aggregate Nanoparticles For Targeted Bioimaging	UBC Chemistry
5:40 PM	Joel Finbloom / Miffy Cheng	Poster Prizes and End of Nanomedicine Day	UBC Pharmaceutical Sciences

VANCOUVER NANOMEDICINE DAY

November 12, 2025

Dear Participants,

It is our great pleasure to welcome you to **Vancouver Nanomedicine Day 2025**. It's truly an honour to organize this fantastic symposium for its **10th meeting**, with over 300 people registered from across the Vancouver area and beyond. We are especially proud that this conference attracts a mix of academic and industry scientists to discuss their work and learn about new approaches to nanomedicine.

Nanomedicine Day 2025 will feature 12 talks, a panel discussion, and 32 posters highlighting the discoveries and innovations in nanomedicine that are contributing to global progress in acute, chronic and orphan disease treatment and management. Nanomedicine has allowed us to deliver drugs directly to disease sites, to dramatically improve their efficacy and reduce their toxicity, and to enable gene therapies with the potential to treat most human diseases. Diagnostics and imaging agents based on nanotechnology will help us to detect disease earlier and to more accurately monitor the effectiveness of therapy. Lastly, nanomaterials are being engineered as novel *in vitro* models to better study disease states and develop next generation therapeutics. In all of these areas, revolutionary developments are ongoing, at enormous speed.

Please use this day not only to learn about new research, but also as a chance to network with each other in order to spark new ideas and foster collaborations between clinicians, basic researchers, engineers, trainees, research partners, life science, pharma, and biotechnology companies, and beyond.

Thank you for attending and we look forward to an exciting day of science!

Sincerely,

Joel Finbloom

Miffy Cheng

Co-Chairs, Nanomedicine Day 2025
Faculty of Pharmaceutical Sciences, University of British Columbia

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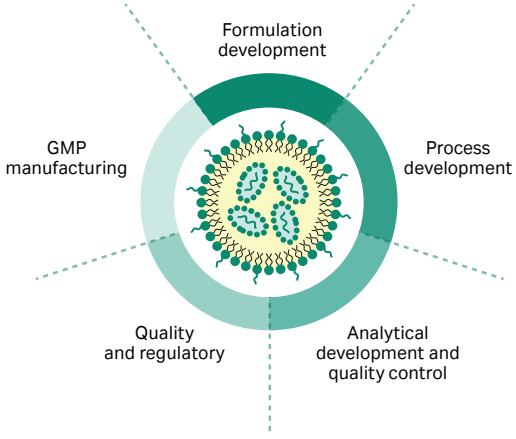

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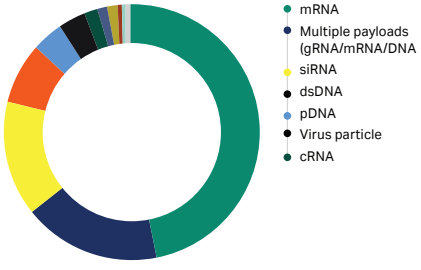
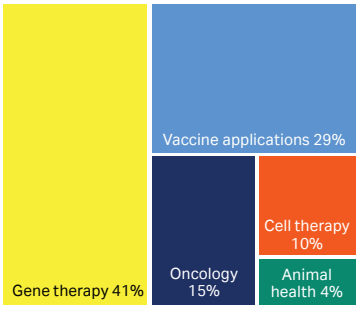
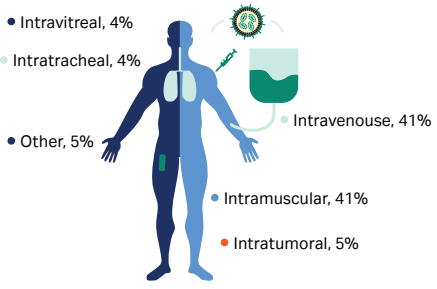


Applications



Delivery methods



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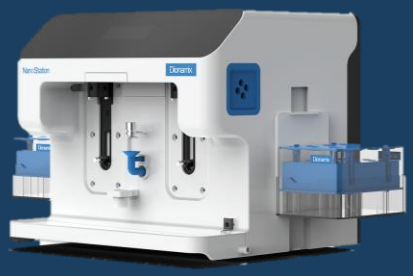
UNLOCK THE FUTURE OF LIPID NANOPARTICLE RESEARCH



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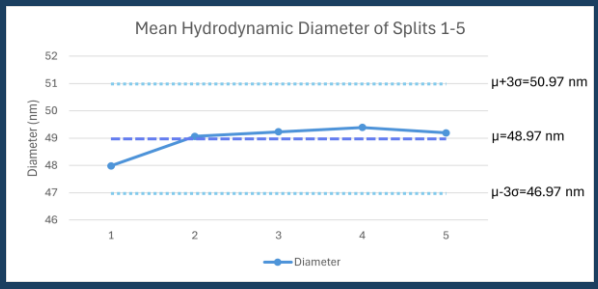

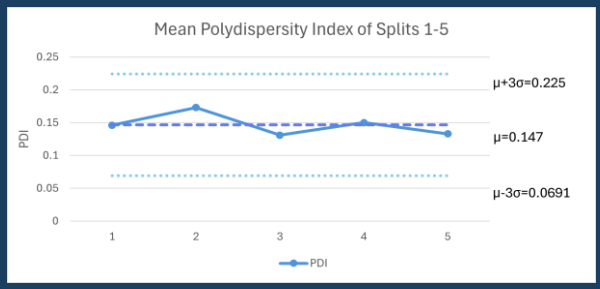

Tight control of empty LNP characteristics
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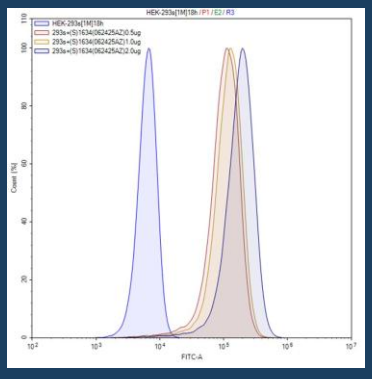
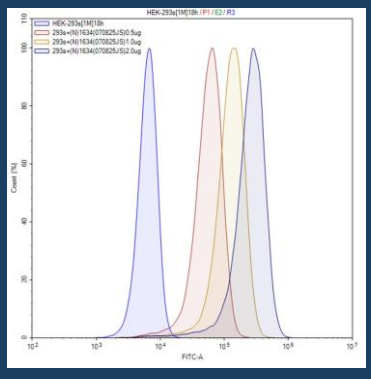
Competitor



NanoStation



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About the Invited Speakers

Anna Blakney, University of British Columbia
Michael Smith Laboratories and School of Biomedical Engineering

Dr. Anna Blakney is an Assistant Professor in the Michael Smith Laboratories and School of Biomedical Engineering at UBC. She received her Bachelor of Science in Chemical & Biological Engineering from the University of Colorado at Boulder, and her PhD in Bioengineering from the University of Washington. She completed a postdoctoral fellowship at Imperial College London on the development of molecular and biomaterial engineering strategies for delivery of self-amplifying RNA. Her lab uses bioengineering, molecular biology and immunology approaches to develop the next generation of RNA vaccines and therapies. She is also a passionate science communicator and runs a TikTok channel dedicated to educating the public about RNA biotechnology, which now has 250,000 followers and 18M views

Omar Khan, University of Toronto
Institute of Biomedical Engineering

Professor Khan is the Canada Research Chair in Nucleic Acid Therapeutics. He earned his B.A.Sc. and Ph.D. in Chemical Engineering and Applied Chemistry from the University of Toronto, and his academic supervisor was Professor Michael V. Sefton. He later joined the laboratories of Professors Daniel G. Anderson and Robert Langer as a Postdoctoral Associate in the Massachusetts Institute of Technology. Professor Khan was also the Scientific Founder and Chief Scientist of Tiba Biotech, a Boston-area company spun out from his postdoctoral research. He has also co-founded the OFK Lab spinout Azane Therapeutics with his graduate students. As an mRNA nanotechnology and vaccine expert, he is regularly featured in television, radio and print news.

His early career focused on the creation of three dimensional organoid models and engineered tissue substitutes. This work evolved to include the development of nucleic acid-based platform technologies and novel biomaterials to study the genetic mechanisms of diseases and create RNA-based therapies. Now, Professor Khan endeavors to contribute to Canada’s growing research-to-translation ecosystem by creating new regenerative medicine-enabling technologies, and training highly qualified personnel capable of addressing diverse local and global bioengineering needs.

Stephanie Willerth, University of Victoria
Department of Mechanical Engineering and Division of Medical Sciences

Dr. Willerth is a full professor in Biomedical Engineering at the University of Victoria. She has dual appointments in the Department of Mechanical Engineering and the Division of Medical Sciences. She also holds an appointment with the School of Biomedical Engineering at the University of British Columbia.

She recently founded the start-up company Axolotl Biosciences that sells high quality bioinks for bioprinting human tissue models. She is an active member of the steering committee of the BC Regenerative Medicine Initiative and the Stem Cell Network. She also serves as a staff scientist at Creative Destruction Lab. Dr. Willerth served as the acting director of UVic's Centre for Biomedical Research and the Biomedical Engineering undergraduate program from 2018-2021 and as the president of Canadian Biomaterials Society from 2018-2019. She was elected to the Royal Society of Canada's College of New Scholars in 2021. Engineers and Geoscientists of B.C. awarded her their teaching award of excellence in the same year.

Hagar Labouta, University of Toronto
Faculty of Pharmacy

Dr. Hagar Labouta is a Scientist at Unity health Toronto and Assistant Professor at University of Toronto at Leslie Dan Faculty of Pharmacy and Institute of Biomedical Engineering. She has research experience in nanomedicine, drug delivery, and biomedical engineering. Before joining University of Toronto, she was an Assistant Professor at the University of Manitoba.

She got her Ph.D. in pharmaceutical nanotechnology from Saarland University (Germany) and completed several Postdocs at Helmholtz institute (Germany), and University of Calgary (Canada). Her team is using microfluidics to design lipid-based nanoparticles for the aim of breaching biological barriers with special focus on applications related to Women's Health. To ensure clinical translation of the novel therapies designed in her lab, her team develops humanized organ-on-a-chip models for preclinical evaluation of nanoparticles. Her lab is well-funded by national and international funds. Dr. Labouta has a strong publication record and is a co-inventor on an international patent for the development of nanosystems for intracellular targeting. She has also worked with the WHO on two health-related projects.

She has won several awards and fellowships including Member of the Year Award from the Controlled Release Society (USA), Interstellar Award from New York Academy of Sciences (USA), Innovation and Career Development Award by the Biomedical Engineering Society (USA), Apotheker Jacob Prize (Germany) and curriculum award for the Nanoscience Minor Program (Canada). Dr. Labouta serves as an Associate Editor for Drug Delivery and Translational Research (DDTR) and is on the editorial board of Journal of Controlled Release.

Shyh-Dar Li, University of British Columbia
Faculty of Pharmaceutical Sciences

Dr. Shyh-Dar Li received his BSc in pharmacy from National Taiwan University in 1998 and PhD in pharmaceutical sciences from the University of North Carolina at Chapel Hill in 2008. He finished his postdoctoral training at Moores Cancer Center at the University of California, San Diego in 2009. He is now the Tong Louie Chair Professor in Pharmaceutical Sciences and the Chair of Nanomedicine and Chemical Biology at UBC Faculty of Pharmaceutical Sciences.

Dr. Li has won several international and national research awards, including 2014 AFPC New Investigator Award, 2013 AAPS New Investigator Award in Pharmaceutics and Pharmaceutical Technologies, 2013 CIHR New Investigator Award, 2013 CSPS Early Career Award, and 2012 Prostate Cancer Foundation Young Investigator Award.

Dr. Li's research focuses on developing innovative drug delivery systems to enable novel therapies with biological drugs including peptides, proteins, antibodies, and nucleic acids. His research program has been supported by CIHR, NSERC, and MITACS.

Tatsuhiro Ishida, University of Tokushima
Department of Pharmacokinetics and Biopharmaceutics

Professor Tatsuhiro Ishida graduated from Tokushima University, Japan, in 1993 and then received his Master degree in 1995 and his PhD in 1998 from the Faculty of Pharmaceutical Sciences, Tokushima University. From 1998 to 2000, he was a postdoctoral fellow at the University of Alberta, Canada (Prof. T.M. Allen’s laboratory). In 2000, he became an Assistant Professor in Faculty of Pharmaceutical Sciences at Tokushima University, and was promoted to an Associate Professor in 2003.

He has been a full Professor there since 2014. He has published 205 peer-reviewed papers, 22 review articles, and 16 book chapters. He has given 36 presentations as an invited speaker at international conferences. He is interested in delivery of nucleic acids and anti-cancer therapeutics. He is also interested in immunological responses to PEGylated therapeutics, namely PEG, and the mechanisms behind such anti-PEG responses.

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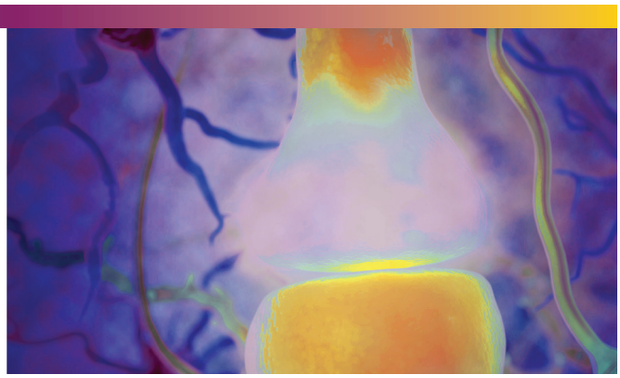

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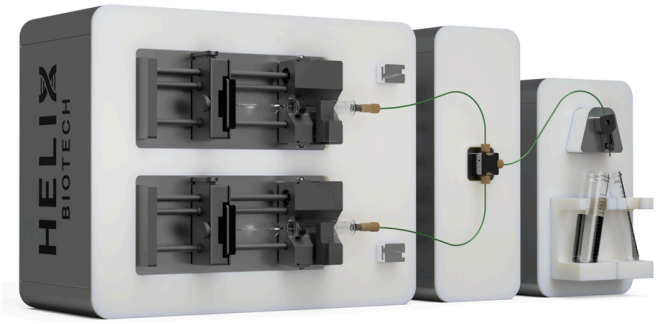

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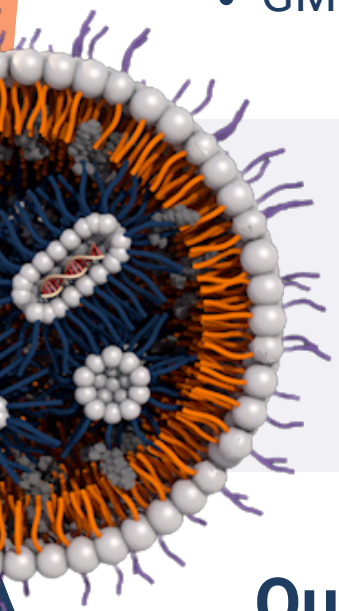

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Oral Presentations from Submitted Abstracts

Lymph node targeted Lipid Nanoparticles for Vaccine Delivery Applications

Muhammad Muzamil Khan[1], Ehsan Ansari Dezfouli[1], Cedric Brimacombe[2], Kevin fox[1], Taehyun Kim[3], Anthony Wong[3], Olga Pacios Santamaria[1], James Russell[4] and Pieter Cullis[1]
Department of Biochemistry and Molecular Biology, University of British Columbia[1], Polymorphic Bioscience Inc[2], School of Biomedical Engineering, University of British Columbia[3], Faculty of Medicine, University of British Columbia[4]

Introduction: Lipid Nanoparticles (LNPs) have emerged as a promising vehicle for safe and effective delivery of mRNA based vaccines(1). Lipid nanoparticles are effective in protecting mRNA from nuclease degradation, and endosomal escape to reach to the targeted cell(2).Targeting the antigen presenting cells (APCs) within the Lymph nodes (LN) is promising strategy to improve vaccine efficacy(3). In this study, we prepared Lipid Nanoparticles for the Lymph node targeted delivery of mRNA-LNP based vaccines. Importantly, we did not add a fifth component to organic phase, rather it was mixed with aqueous phase to interact with lipid components and form LN targeted lipid nanoparticles.

Hypothesis: The Lymph node targeted lipid nanoparticles will have better transfection in lymph nodes after intramuscular injection and provide a platform for vaccine delivery applications

Methods: The Lipid Nanoparticles were prepared using T-mixing methods. Ionizable Lipids (D-LIN-MC-3-DMA/ALC-0315) along with DSPC, Cholesterol and DMG-PEG were mixed in Ethanolic phase and mRNA was mixed in 100mM Sodium acetate buffer with or without lymph node targeting agent. The size and Zeta potential was measured using Malvern (UK) Zeta Sizer and Encapsulation efficiency was measured using Quant-it Ribogreen assay. The images were analyzed using Cryo-EM. The i*n vitro* transfection was evaluated using Dendritic cells lines (DC2.4) and Bone marrow dendritic cells (BMDCs). The *in vivo* transfection was evaluated by IM injecting luciferase mRNA containing LNPs in CD-1 mice. The images were taken using IVIS after 3 hours and 24 hours and major organs such as lymph nodes, spleen, muscle and liver were collected and homogenized for further evaluation using luciferase assay.

Results: The Prepared LNPs were 60-70nm in range and with the coating of lymph node targeting agent the size was around 90nm. The encapsulation efficiency was above 90% for all prepared LNPs. The Cryo-EM analysis shows ALC-0315 LNPs with bleb-like structures and with the coating of LN-targeting agents they have a bleb inside with targeting agent outside. The LN-targeted LNPs have better transfections using DC2.4 cell lines and transfection efficiency was significantly improved in bone marrow dendritic cell lines. The IVIS image analysis shows LN-targeted LNPs were drained towards lymph nodes and have significantly higher transfection compared to other LNPs.

Conclusion: The results concluded that the LN-targeted Lipid Nanoparticles have potential to target Lymph nodes and can be exploited vaccine delivery applications. Further, In-vivo immune response studies are needed to validate the efficacy of Hyaluronic acid coated Lipid Nanoparticles.

Acknowledgement: The authors acknowledge the funding from Canada Biomedical Research Fund and/or Bioscience Research Infrastructure fund. The Author also acknowledge Clair Atikson for Crto-EM services.

References:

1. Tenchov R, Bird R, Curtze AE, Zhou Q. Lipid Nanoparticles─From Liposomes to mRNA Vaccine Delivery, a Landscape of Research Diversity and Advancement. ACS Nano. 2021;15(11):16982-7015.
2. Hou X, Zaks T, Langer R, Dong Y. Lipid nanoparticles for mRNA delivery. Nature Reviews Materials. 2021;6(12):1078-94.
3. Jiang H, Wang Q, Sun X. Lymph node targeting strategies to improve vaccination efficacy. Journal of Controlled Release. 2017;267:47-56.

Optimized CRISPR-Loaded Lipid Nanoparticles for Efficient Gene Editing in Cystic Fibrosis Lung Models

Belal Tafech[1,2], Tiffany Carlaw[1,2], Tessa Morin[2], Jerry Leung[3], Kevin An[4], Colin Ross[2], Jay Kulkarni[4], Pieter R. Cullis[3,4], Sarah Hedtrich*[1,2,5,6]

[1] School of Biomedical Engineering, University of British Columbia, Vancouver, BC, Canada

[2] Faculty of Pharmaceutical Sciences, University of British Columbia, 2405 Wesbrook Mall, Vancouver V6T 1Z3, BC, Canada

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[5] Center for Biological Design, Berlin Institute of Health @ Charité, 13125 Berlin, Germany

[6] Centre for Blood Research & Life Science Institute, University of British Columbia, Life Sciences Centre, Vancouver, British Columbia, Canada.

Abstract:

Cystic fibrosis (CF) is a monogenic disease characterized by debilitating lung dysfunction due to mutations in the *CFTR* gene, with CRISPR-based gene editing offering a promising corrective therapy. However, efficient delivery and gene editing in airway epithelial cells face significant challenges due to mucosal and immune barriers. In this study, we optimized CRISPR delivery and gene editing using lipid nanoparticles (LNPs) through strategies including fine-tuning Cas9:sgRNA ratios, chemically modifying sgRNAs, and enhancing endosomal escape. Notably, by refining the ionizable lipid composition, we identified an optimized formulation, LNP-H. Integrating optimized sgRNA modifications into LNP-H resulted in ~50% editing in patient-derived CF bronchial epithelial cells. In 3D CF bio-engineered models pretreated with dornase alfa, LNP-H achieved ~12.7% editing. Additionally, LNP-H enabled ~12% gene correction in patient-derived cells with the CFTR^R1162X mutation. These findings are potentially clinically relevant, as previous studies indicate that ~5-10% normal CFTR expression is sufficient for normal lung function.

Therapeutic potential of mesenchymal stem cell-derived extracellular vesicles in reversing inflammatory damage to the blood-brain barrier in Alzheimer's disease

Jolene Phelps[1,2,3], Farnoosh Kalantarnia[1,3], Katherine S. Elvira[3,4], Stephanie M. Willerth[1,2,3]

1. *Department of Mechanical Engineering, University of Victoria*
2. *Division of Medical Sciences, University of Victoria*
3. *Centre for Advanced Materials and Technology, University of Victoria*
4. *Department of Chemistry, University of Victoria*

Mesenchymal stem cell-derived extracellular vesicles (MSC-EVs) have shown promise in reducing neurodegeneration and cognitive deficits in Alzheimer's disease (AD). This study investigated whether MSC-EVs can restore blood-brain barrier (BBB) function in AD. Human induced pluripotent stem cells (hiPSCs) with the PSEN2 N141I mutation (familial AD) and isogenic controls were differentiated into brain microvascular endothelial cells (iBMECs) and healthy controls were differentiated to mesenchymal stem cells (iMSCs). EVs isolated from healthy iMSC expended culture medium were characterized and added to inflammatory-induced control and AD iBMECs exposed to lipopolysaccharide (LPS). Permeability and expression of BMEC markers (ZO-1, VE-cadherin, GLUT-1) were assessed. No significant differences in permeability were found, but LPS reduced ZO-1 in AD iBMECs and increased GLUT-1 in all groups. Notably, MSC-EVs restored GLUT-1 and ZO-1 levels in LPS-treated AD iBMECs. These findings suggest AD iBMECs are more vulnerable to inflammation, and MSC-EVs may help preserve BBB integrity under inflammatory conditions.

Untangling the Analytical Complexities of Targeted Lipid Nanoparticles (tLNPs)

Taniya Adak[1], Adam Crowe[1], Hailey Kim[1], Reka Geczy[2], Zach Ngkaion[2], Ariel Zhang[1], Gemma Ryan[1], Andrew Kondratowicz[1], Pierrot Harvie[2], and Jagbir Singh[1]

[1]Biopharma Services, Nucleic Acids and Nanomedicines, [2]R&D 1055 Vernon Dr., Vancouver, BC, Canada
Cytiva Nanomedicine

Targeted lipid nanoparticles (tLNPs) represent a promising advancement in Cell and Gene Therapies by enabling cell-specific delivery and overcoming limitations of conventional LNPs, such as hepatic accumulation and dependence on endogenous protein mediated uptake mechanisms. Nevertheless, the translation of tLNPs to clinical and commercial applications is hindered by challenges in scalable manufacturing and the lack of robust analytical tools. Herein, we present a suite of orthogonal analytical methods developed to optimize manufacturing of an anti-CD3-IgG coated, mRNA tLNPs. Chromatographic techniques such as size-exclusion chromatography with fluorescence detection (SEC-FLR), reverse-phase HPLC-FLR and LC-MS were employed to identify optimum conjugation conditions, characterization of conjugated species, and quantification of ligand-to-LNP ratios. *In vitro* potency *assays* demonstrated receptor-mediated uptake and selective transfection in primary T cells, confirming the targeting efficacy of the anti-CD3 IgG tLNPs. These findings highlight the critical role of integrated analytical workflows in ensuring reproducibility, functionality, and scalability in tLNP manufacturing.

From Mechanical Properties to Biology: Machine Learning-Guided Optimization of Bioinks for Neural Tissue Engineering

Victor Allisson da Silva (PhD. Candidate, University of Victoria); Stephanie Willerth (Supervisor, University of Victoria).

Introduction: 3D bioprinting presents a promising avenue for creating biomimetic tissues with applications in regenerative medicine and disease modeling. However, the development of ideal bioinks remains challenging due to a predominant reliance on trial-and-error approaches. As cells are highly responsive to the mechanical properties of their environment—a phenomenon governed by mechanosensing and mechanotransduction —this study hypothesizes that tuning the mechanical properties of biocompatible bioinks can enable the prediction and optimization of cellular behavior, including viability, proliferation, and functionality [1, 2].

Methods: A bioink library was formulated by varying concentrations of fibrin and alginate to achieve a wide range of mechanical characteristics. Each formulation was assessed for stiffness, viscosity, storage modulus, loss modulus, printability, swelling behavior, and degradation rate. Neural progenitor cell (NPC) viability was quantified via LDH assays at Day 1 (D1), Day 7 (D7), and Day 15 (D15). Proliferation was measured by PicoGreen assays, and functionality was evaluated through membrane depolarization using voltage-sensitive dyes. To correlate mechanical properties with biological outcomes, both traditional (Multiple Linear Regression - MLR) and machine learning (Lasso, Ridge, Elastic Net, and Support Vector Regression—SVR) models were developed.

Results: Tuning bioink formulations generated a broad distribution of mechanical properties, with no clear visual correlation to printability. Increased stiffness correlated with reduced degradation rates and elevated swelling behavior. Biologically, the formulations produced a wide range of outcomes, including both favorable and unfavorable effects on viability and proliferation. Among all models, SVR demonstrated superior predictive accuracy, particularly under conditions of limited data or nonlinear relationships. Critically, the model's performance was validated using an independent and diversified dataset comprising bioinks from plant-based, animal-derived, and synthetic sources. The SVR model maintained robust predictive capabilities across these varied compositions, indicating its strong generalizability and potential for broader application in bioink development.

Discussion: These findings confirm that mechanical properties serve as reliable predictors of cellular behavior in 3D bioprinted constructs. The lack of association between visual printability and performance reinforces the need for quantifiable, data-driven parameters in bioink design. SVR's ability to manage small datasets and minimize the impact of outliers makes it particularly well-suited for biological applications where data variability is common. The successful cross-validation using distinct bioink types further underscores the model's adaptability and translational relevance.

Conclusion: Bioink design can be significantly enhanced through the use of machine learning models that integrate mechanical properties as predictive inputs. This approach shifts development from empirical testing to informed prediction, improving reproducibility and accelerating optimization. Future work will focus on expanding model validation to additional cell types and integrating chemical property analyses to further refine predictive power and applicability across diverse tissue engineering applications.

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Self-Assembled Fluorescent Supra-J-Aggregate Nanoparticles For Targeted Bioimaging

Jad Kaj, Subin Kim, Jasmine Bernal-Escalante, Elisa Leicht, Christine Traaseth, W Russ Algar

Department of Chemistry, University of British Columbia

A particular type of molecular dye aggregates, J-aggregates, feature exciting photophysical properties such as very narrow emission bands and high brightness. Despite the clear potential of J-aggregates as fluorescent labels for targeted bioanalysis and imaging, the non-trivial engineering of bioconjugates of these materials has made their adoption scarce. Here, we present the simple preparation of self-assembled J-aggregate-based nanoparticles, termed (Supra-J)-Dex. The assemblies were characterized both physically and photophysically, where the (Supra-J)-Dex had an average hydrodynamic diameter of 133 nm and exhibited brighter emission than J-aggregates prepared in bulk solution. Tetrameric antibody complexes were used to simply and successfully immunolabel SK-BR3 cancer cells with (Supra-J)-Dex with very high fluorescence contrast. The cells were also successfully imaged by two-photon excitation fluorescence. Overall, the (Supra-J)-Dex nano-assemblies show great potential as a material for bioanalysis and imaging, and the simplest and most effective method reported to date for bright cellular immunofluorescent labelling using J-aggregates.

POSTER PRESENTATIONS (P1-P16)

P1	Agnes Szwarczewski	Investigating the Cytosolic Delivery and Measurement of Quantum Dot-based Concentric FRET Probes Toward Intracellular Sensing	UBC Chemistry
P2	Alaleh Yourdkhani	Stimuli-Responsive Nanocomplexes for Targeted Antibiotic and Enzyme Codelivery to Treat Chronic Biofilm Infections	UBC Pharmaceutical Sciences
P3	Angela Subin Kim	Expanded Strategies for the Bioconjugation of Super-Quantum Dot Assemblies	UBC Chemistry
P4	Armin Faghihi	Designing Lipid Nanoparticle-Based Tools to Engineer Macrophages In Vivo	UBC Faculty of Medicine and UBC Biochemistry
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P10	Haruka Takata	An in vivo inflammatory microenvironment targeting system with amine-terminated PEG modified nanoparticles	Tokushima University
P11	H. Yazdani Ahmadabadi	Proprietary non-PEG stabilizer lipids for nucleic acid lipid nanoparticles	Cytiva
P12	Janell Ko	Advancing Lipid Nanoparticle Characterization Through Super-Resolution Single-Molecule Localization Microscopy	UBC Pharmaceutical Sciences
P13	Jasmine Bernal Escalante	Tetrazine ligation for QD-Antibody conjugates	UBC Chemistry
P14	Jerry Leung	Increased particle fusion and blebbing decreases lipid nanoparticle potency	UBC Biochemistry and MSL
P15	Jordon Tom	Optimizing LNP and Proteinase mRNA to Remodel Tumour Extracellular Matrix	UBC Pharmaceutical Sciences
P16	Kathy G. Wong	Optimizing Conditions for Single Step, High Yield circRNA Manufacturing	UBC MSL

POSTER PRESENTATIONS (P17-P32)

P17	Kelly Rees	Comparison of Cellular Immunolabelling Between Dextran-Functionalized Quantum Dots (QDs), Supra-QD Assemblies, and Super-QD Assemblies	UBC Chemistry
P18	Kevin Fox	Expanding the Lipid Toolkit Towards Targeted Delivery of RNA Therapeutics	UBC Biochemistry and Pharmaceutical Sciences
P19	Leanna Yee	Neoantigen-based personalized cancer vaccine: LNP-mediated delivery of multi-epitope mRNA extends survival in aggressive melanoma cancer model	Cytiva
P20	Meenakshi Swaminathan	Lipid Nanoparticles Enable High Efficiency CRISPR HDR Mediated Gene Insertions in Primary Human T Cells	Cytiva
P21	Michael Nguyen	Microfluidic Tangential Flow Filtration Optimizations for Liposomes and Lipid Nanoparticles	UBC Pharmaceutical Sciences
P22	Nastaran Davilu	Optimizing Lipid Nanoparticle–Mediated CRISPR/Cas9 Gene Editing in Bioengineered Lung Models of Cystic Fibrosis	UBC SBME
P23	Nuthan Vikas Bathula	Formulation and Administration Timing of Lipid Derivatized JAK-Inhibitor and Corticosteroid Modulate saRNA-LNP Inflammation and Expression	UBC SBME and MSL
P24	Patrick Francis	Fed-Batch IVT mRNA synthesis using the BioLector XT and ReadyToProcess™ WAVE™ 25	Cytiva
P25	Rachel Li	Helper Lipid Re-Design Blocks Recycling and Supercharges mRNA Delivery with Lipid Nanoparticles	UBC Pharmaceutical Sciences
P26	Seth Keenan	Prototype Smartphone-Based Device for Flow Cytometry	UBC Chemistry
P27	Sree Gayathri Talluri	TFF in RNA workflow: process optimization for RNA and LNP manufacturing	Cytiva
P28	Tiffany Carlaw	Non-viral in situ gene editing effectively and safely rescues congenital ichthyosis-causing mutations in human skin	UBC Pharmaceutical Sciences
P29	Vincent Halim	Optimizing CRISPR-Cas9 mRNA for Epithelial Skin and Lung Gene Editing	UBC Biochemistry and Pharmaceutical Sciences
P30	Yao Zhang	Increasing mRNA loading capacity of lipid nanoparticles	UBC Biochemistry, SBME, and MSL
P31	Yihao Wang	Ultra-Bright Luminescent Lanthanide Nanoparticles for Time-Gated Bioanalysis and Imaging	UBC Chemistry
P32	Zhengyu Chen	Advancing mRNA therapeutics: Lipid nanoparticles demonstrate favorable safety and efficacy profile with repeated mRNA administration in normal and tumor-bearing mice.	Cytiva

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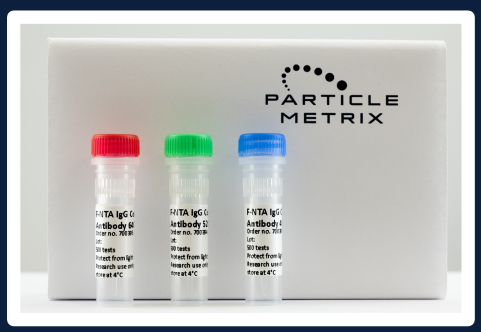

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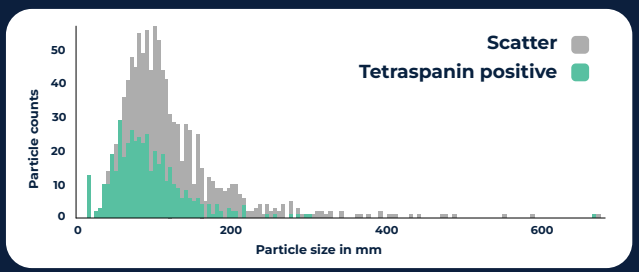

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Poster Presentations from Submitted Abstracts

P1

Investigating the Cytosolic Delivery and Measurement of Quantum Dot-based Concentric FRET Probes Toward Intracellular Sensing

Agnes Szwarczewski1, Jasmine Bernal Escalante1, W. Russ Algar1*

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Förster resonance energy transfer (FRET)-based probes are potentially powerful tools for bioanalysis. Concentric FRET (cFRET) is a design strategy that enables a single probe to detect multiple biomolecular targets simultaneously through a network of energy transfer pathways [1].
This network is formed via the conjugation of multiple copies of multiple dye acceptors to a central quantum dot (QD) donor through biomolecular linkers (e.g. peptides). Presently, the multiplexed sensing capabilities of cFRET have been limited to in vitro detection [2]. cFRET probes are promising tools for studying important cellular processes involving multiple biomarkers and multistep pathways; however, translating cFRET detection from test tubes to the intracellular environment introduces several new levels of complexity.
Here, we present ongoing efforts to advance cFRET probes towards intracellular sensing, including cytosolic delivery and measurement. We designed and characterized a new cFRET combination that combines a yellow-emitting QD donor with red-emitting Atto 594 and deep-red-emitting Atto643 fluorescent dye acceptors. Then, using microinjection as a direct cellular delivery method, the cytosolic distribution and stability of the photoluminescence (PL) for these materials were studied in live lung cancer cells. Temporal changes in the cytosolic QD and dye PL signals were investigated via fluorescence microscopy to assess the timescale and limiting factor for cFRET probe viability within cells. Overall, these results provide an essential foundation for the future applicability of cFRET probes for cellular analysis.

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P2

Stimuli-Responsive Nanocomplexes for Targeted Antibiotic and Enzyme Codelivery to Treat Chronic Biofilm Infections

Alaleh Yourdkhani, Chinekwu S. Nwagwu, Sara Jamshid-Nezhad, Joon H. Lee, and Joel A. Finbloom*

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Biofilms create complex barriers that protect bacteria from antibiotics and the immune system, making infections harder to treat. The negatively charged extracellular polymeric substances (EPS) within biofilms trap positively charged antibiotics like tobramycin (TOB), reducing their efficacy. To address this, we developed pH-responsive nanocomplexes (NCs) for the co-delivery of TOB and DNase, an EPS-degrading enzyme. The NCs were prepared by combining TOB and DNase with polycationic and polyanionic polymers under varying conditions and assessed for particle size, PDI, surface charge, encapsulation efficiency, and drug release. The optimized NCs showed uniform particles (~340 nm, PDI ~0.2) with encapsulation efficiencies above 80% for TOB and 40% for DNase. Under acidic conditions mimicking biofilm environments, they swelled to >2 μm, suggesting stimulus-responsive behavior. These findings highlight the potential of NCs to enhance drug delivery, disrupt biofilms, and improve therapeutic outcomes.

P3

Expanded Strategies for the Bioconjugation of Super-Quantum Dot Assemblies

Angela Subin Kim, W. Russ Algar

Department of Chemistry, University of British Columbia

Fluorescent materials conjugated to antibodies and other biomolecular affinity probes enable specific cellular labeling and imaging, and the development of molecular diagnostic tools. Quantum dots (QDs) are of interest for bioanalysis due to their resistance to photobleaching, broad absorption and narrow emission spectra, and high brightness. To enable more demanding applications, ultra-bright fluorescent materials have been prepared by assembling many individual QDs into nanoparticle assemblies on the order of 100 nm in diameter. These “super-QDs” are particularly suitable for smartphone-based fluorescence imaging due to their exceptional brightness and retention of the other unique optical properties of individual QDs. To date, options for the bioconjugation of super-QDs have been limited to tetrameric antibody complexes (TACs).

This poster presents new bioconjugation strategies for super-QDs. One approach uses digoxigenin as a molecular adapter to enable the use of TACs to conjugate affinity probes other than antibodies to super-QDs. The second approach uses the strongest known protein-ligand interaction—the avidin-biotin system—to enable conjugation with various affinity probes. In this case, the amphiphilic dextran used in the preparation of super-QDs was further modified with biotin. The avidin-binding activity of the biotinylated super-QDs was confirmed and characterized, and labeling of breast cancer cells using these materials with biotinylated anti-HER2 antibodies was demonstrated. The new methods for super-QD conjugation will facilitate the development of smartphone-based diagnostic tools for point-of-care applications.

P4

Designing Lipid Nanoparticle-Based Tools to Engineer Macrophages In Vivo

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Abstract
Tumor-associated macrophages (TAMs) are programmable targets for in vivo cancer immunotherapy. We engineered lipid nanoparticles (LNPs) to selectively favor macrophage transfection while minimizing hepatic uptake, enabling delivery of mRNA/siRNA payloads to induce CAR expression and disarm inhibitory pathways. Fifty LNPs varied cholesterol (5–46%), ionizable lipid ALC (20–46%), helper lipids (DSPC ± PS/PE/PG at 10–60%), and fixed DMG-PEG (1.5%). All used firefly luciferase mRNA at N/P 6 and were screened in RAW, bone-marrow–derived macrophages (BMDMs), dendritic cells (DCs), and HepG2 hepatocytes; the Pfizer ALC formulation served as control. A PS-containing top performing LNP achieved ~20-fold higher luciferase in BMDMs versus control, ~8-fold lower in HepG2, and 1.5-fold lower in DCs, indicating macrophage selectivity. In the other hand, PE-enriched LNPs increased expression ~10-fold in both BMDMs and HepG2. These data show helper-lipid chemistry tunes cell tropism; PS adds macrophage bias while substantially reducing hepatic delivery. For next steps, top PS-LNP candidates will be evaluated for in vivo delivery using Fluc bioluminescence to define organ tropism, followed by GFP mRNA dosing and flow cytometry to quantify uptake in TAMs and other immune cell subsets.

Keywords: macrophages; lipid nanoparticles; mRNA; immunotherapy

P5

Polyvinyl Alcohol-Based Silver-Releasing Hydrogels for Accessible Wound Dressings

Boray He, Jun Gao

University of British Columbia

Simple and accessible wound care solutions are of growing interest, especially in low-resource settings where advanced commercial dressings may not be available. The common and accessible polymer polyvinyl alcohol (PVA) is being studied in this project as a matrix for silver-based wound dressings. To investigate structure–function relationships, PVA samples were evaluated both with and without crosslinking. After crosslinking, silver ions ($AgNO_3$ immersion) were added. Silver release was quantified using a platinum nanoparticle (PtNP)-based colorimetric assay, where PtNPs mimic peroxidase activity to oxidize TMB with H_2O_2 into a blue product, inhibited by Ag^+ at 652 nm. While uncrosslinked films dissolved easily in aqueous solution, crosslinked films demonstrated enhanced stability and extended silver release. Ethanol-assisted casting and chitosan blending were also explored to enhance mechanical and antibacterial properties.

P6

Comparative study of lipid nanoparticle mixing technologies for early development of nucleic acid medicines at bench scale

Daniel F.G. Costa[1], Evan Fuini[1], Drake Dunaway[1], Kendra Bayne[1], Molly Brennan-Smith[1], Zahra Merchant[2], Andrea Engel[1]

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Background: Lipid nanoparticles (LNPs) have emerged as the main drug delivery system for nucleic acid medicines post COVID-19 pandemic. Novel lipid excipients and payload modalities continue to be developed for improved tissue targeting, higher drug product potency, and expansion of therapeutic use beyond vaccines. In parallel, alternative mixing technologies have hit the market with the promise of optimizing LNP manufacturing and reducing downstream processing challenges for scaling up production.

Methods: We evaluated the ability of mixing systems of contrasting technologies to produce lipid nanoparticles carrying an array of nucleic acid payloads. Co-injection, microfluidics, impingement jet and tee-mixing were compared. Dynamic Light Scattering was used for particle size characterization. Nucleic acid encapsulation was determined by Ribogreen assay. In vitro potency was tested on HEK293 and A549 cell culture.

Results: All technologies produced LNPs with quality control profile comparable to clinically validated drug products, including particle size ≤ 100 nm, PDI ≤ 0.2 and nucleic acid encapsulation ≥ 90%. Moreover, the selection of nucleic acid type did not significantly impact the quality of LNPs formulated on impingement jet mixer, a gold-standard technology for commercial batch manufacturing of LNP vaccines. mRNA (1-2k NTs), saRNA (>10k NTs) and sgRNA + mRNA were successfully formulated. In vitro evaluation of the LNPs on HEK293 and A549 cell culture showed over 10 times stronger luminescence signal after treatment with FLuc saRNA in comparison to its mRNA counterpart, confirming functionality of the formulations.
Conclusion: The mixing technologies tested efficiently produced lipid nanoparticles at bench scale (1.5 mL batch), regardless of the type of nucleic acid payload evaluated. Scaled-down versions of systems suited for GMP manufacturing are now available for early research activities to ease technology transfer challenges during scale-up and commercialization stages.

P7

Optimizing mRNA delivery with porphyrin-lipid nanoparticles

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Lipid nanoparticles (LNP) have achieved great clinical success in nucleic acid delivery through COVID-19 vaccines, but inefficient endosomal escape remains a major challenge for therapeutic efficacy. LNPs with porphyrin-lipids have shown to enhance endosomal escape of siRNA by generation of reactive oxygen species upon near-infrared irradiation. We hypothesize that such mechanism could facilitate more efficient endosomal escape and improve cell transfection of mRNA as the cargo.
To develop a transfection potent formulation of porphyrin-LNPs, we investigated various lipid compositions and mixing methods. We characterized the resulting particles based on their physiochemical properties, including absorbance, fluorescence, size, and polydispersity index, and evaluated *in vitro* transfection profile by firefly luciferase assay. Successful incorporation of porphyrin into LNPs was confirmed by the expected red shift in the absorbance spectrum and fluorescence quenching. Notably, the porphyrin-LNPs demonstrated transfection potency in HepG2 cells, which provides a strong potential for photosensitive enhancement of mRNA endosomal escape.

P8

Biodegradable polymers with tertiary amines enhance mRNA delivery of lipid nanoparticles via improved endosomal escape

Feng Zhao [a], Shyh-Dar Li [a]

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Lipid nanoparticles (LNPs) have recently gained prominence as a safe and effective delivery vehicle for RNA-based therapy. However, the endosomal release efficiency of standard LNPs has been shown to be poor, limiting the transfection efficiency. Here, we explored incorporating a biodegradable polymer which only contains tertiary amines as a pH-sensitive functional group into LNPs, aiming to introduce the proton sponge effect to facilitate the endosomal release. Our results demonstrated that the polymer-modified LNPs (*p*-LNPs) maintained small particle size, neutral surface charge and high mRNA encapsulation efficiency, along with increased pKa value and pH buffering capacity. The optimal *p*-LNP enhanced the endosomal escape efficiency from 20 % to 80 % compared to the standard LNPs. Upon intravenous administration, the optimal *p*-LNP loaded with luciferase mRNA significantly increased the transgene expression evidenced by more than 100-fold increase in luciferin bioluminescence from the liver compared to the standard LNPs.[1]

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P9

Versatile Lipid Nanoparticle Platform for Efficient CRISPR-Cas9 Gene Editing in Primary T Cells and CD34+ Hematopoietic Stem Cells

Hannah Ly*, Reka Geczy#, Aruna Balgi#, Stella Park#, Meenakshi Swaminathan#, Mana Novin, Rita Zhao, Angela Zhang, Nikita Jain, Anitha Thomas and Samuel Clarke
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Lipid nanoparticles (LNPs) offer a promising, non-viral approach for efficient gene editing in hard-to-transfect cells like human primary T cells and CD34+ hematopoietic stem cells (HSCs). In this study, a library of innovative ionizable lipids and LNP compositions was developed and screened using the NxGen™ platform, enabling direct delivery of CRISPR-Cas9 components. Optimized protocols achieved up to 90% double knockout of TCR and CD52 in T cells, and up to 90% knockout of CD33 and CD45 in HSCs, all while maintaining high cell viability and robust proliferation. Colony-forming assays confirmed preserved differentiation capacity in HSCs. Media type, supplements, and treatment kinetics significantly influenced editing efficiency. The protocol was scaled from well-plates to G-Rex® bioreactors, demonstrating the scalability of LNPs and their potential for clinical application as a platform for gene delivery in T cells and HSCs.

P10

An in vivo inflammatory microenvironment targeting system with amine-terminated PEG modified nanoparticles

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One of the hallmarks of tumor tissues and inflamed tissues is the increased permeability of the blood vessels. Therefore, impressive accumulation of nanomedicines with long circulating property was observed in both tissues. [1, 2] These effects are widely utilized for passive targeting of nanomedicines. However, despite a lot of studies on the ligand-modified nanoparticles have been attempted, only a few have been entered into clinical trials, and all were terminated or halted mainly due to the heterogeneity of receptor expression. As a common feature of both cancer and inflammation, it is known that these lesional tissues are acidic by Warburg effect and/or hypoxia. So, we hypothesized that amine-terminated PEG-modified liposomes (NH_2-PEG-Lip), which exhibit a positive charge at an acidic environment, may be retained in those acidic tissues compared to non-charged methoxy-terminated PEG-modified liposomes (CH_3O-PEG-Lip). In this study, therefore, we investigated the distribution of amine-terminated nanoparticles (NH_2-PEG-Lip) to solid tumors, fibrotic kidney, and psoriatic lesional skin.

The zeta-potential of NH_2-PEG-Lip was approximately - 4.0 mV at a neutral environment (pH 7.4) and approximately + 4.3 mV at an acidic environment (pH 6.5). Colon 26 tumor-bearing mouse model, unilateral ureteral obstruction (UUO)-induced renal fibrosis mouse model, and imiquimod-induced psoriasis-like mouse model were injected intravenously with DiI or DiR-labeled NH_2-PEG-Lip or CH_3O-PEG-Lip. After 24 hours, the fluorescence in the target tissues were observed under fluorescence microscopy or IVIS. In the tumor tissues, CH_3O-PEG-Lip were distributed into the edge region, which may have rich angiogenic vessels, while NH_2-PEG-Lip were distributed not only in the edge but also in the central region. In the fibrotic kidney, NH_2-PEG-Lip were further distributed in the ligated ureter kidney than CH_3O-PEG-Lip. In the psoriatic lesional skin, NH_2-PEG-Lip were more widely distributed than CH_3O-PEG-Lip. Interestingly, i.v. injection with siRNA-loaded NH_2-PEG-lipid nanoparticle (LNP) including siRNA against CD40 (for renal fibrosis) or IL-23 (for psoriasis) attenuated each disease progression better than CH_3O-PEG-LNP.

In this study, we found that NH_2-PEG modification to the surface of NPs may provide a novel and efficient drug delivery system which is able to target the acidic microenvironment in the legional tissues.

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P11

Proprietary non-PEG stabilizer lipids for nucleic acid lipid nanoparticles

H. Yazdani Ahmadabadi, K. Paulson, H. Son, L. Yee, A. Thomas

Affiliation: Cytiva

Introduction: Polyethylene glycol (PEG)-lipids play a critical role in lipid nanoparticle (LNP) formulations by preventing aggregation during manufacturing, storage, and systemic circulation. However, PEG-lipids present notable challenges, including immunogenicity, hypersensitivity reactions, limited structural tunability, and decreased LNP loading capacity. These drawbacks constrain their utility in genomic medicine. In contrast, non-PEG stabilizers offer a promising alternative, with reduced immunogenicity and enhanced flexibility in chemical design to support broader applications in therapeutic delivery.
Methods: We designed and synthesized a diverse library of non-PEG stabilizers. LNPs were formulated using our NanoAssemblr™ microfluidic platform and proprietary ionizable lipids. Size and polydispersity index (PDI) were assessed via dynamic light scattering, and encapsulation efficiency (EE) was determined using Ribogreen assay. In vivo efficacy was evaluated in two murine models: (1) a vaccine model using SARS-CoV-2 self-amplifying RNA (saRNA) administered intramuscularly (two doses on days 0 and 28, sera collected on days 21 and 42); and (2) a protein therapy model using erythropoietin (EPO) mRNA administered intravenously (sera collected at 6 and 24 hours post-injection). Ex vivo activity was assessed using primary T cells treated with varying doses (0.5 – 4 µg/million cells), followed by flow cytometry detection for viability and gene editing efficiency.

Results: We successfully developed multiple non-PEG stabilizers with diverse chemistries, molecular weights, and architectures. Several candidates produced LNPs with optimal critical quality attributes (CQAs): particle size < 150 nm, PDI < 0.2, and EE > 90%. These results held across a range of payloads (gRNA, mRNA, and saRNA) and lipid compositions. Unlike PEG-lipids (e.g., PEG-DMG), which exhibit poor CQAs beyond 3 mol%, select non-PEG stabilizers retained favorable CQAs at higher mol%, enabling applications that require long circulation or targeted delivery.
In vivo – several non-PEG LNP formulations matched or outperformed PEG-DMG benchmarks in both mRNA and saRNA models. The lead candidates demonstrated robust performance across multiple payloads and lipid architectures, and varied administration routes (intravenous (IV), intramuscular (IM), and subcutaneous (SC).).
Ex vivo – several non-PEG LNPs enabled efficient gene editing of primary T cells, with >90% T cell receptor (TCR) knockout efficiency at low, non-toxic doses, surpassing PEG-lipid benchmarks and offering a safer route for T cell engineering ex vivo.

Conclusion: Our study establishes non-PEG stabilizers as a great alternative to PEG-lipids in LNP design, offering enhanced biocompatibility, formulation flexibility, and delivery efficiency across in vivo and ex vivo applications. These findings represent a significant step toward safer and more adaptable LNP systems for genomic medicine and cell therapy.

P12

Advancing Lipid Nanoparticle Characterization Through Super-Resolution Single-Molecule Localization Microscopy

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Lipid nanoparticles (LNP) have shown immense potential for gene therapy and vaccine applications, enabling efficient delivery of nucleic acid drugs. While commonly employed techniques for formulation characterization such as electron microscopy and dynamic light scattering can provide structural insights at the nanoscale level, more detailed and quantifiable imaging is needed to better inform formulation optimization. Here, we propose the use of single-molecule localization microscopy techniques (SMLM), using direct Stochastic Optical Reconstruction Microscopy (dSTORM) to achieve nanometer-level resolution of LNP physicochemical properties at the molecular level. Using this platform, we have optimized a protocol for analyzing LNP-mRNA formulations with morphologies including oil core, blebs, and liposomal LNPs by evaluating parameters such as size, cargo loading efficiency, and PDI. This work will lead to the development of an imaging workflow to better assess LNP properties, ultimately guiding formulation optimization for more effective therapeutic applications.

P13

Tetrazine ligation for QD-Antibody conjugates

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Quantum dots (QDs) are highly promising materials for biological applications due to their small size and unique fluorescence properties. The success of QDs in these applications depends on optimized surface and bioconjugate chemistries. Antibodies remain the gold standard for specific binding to target biomarkers; however, the effective and reproducible preparation of QD-antibody conjugates remains non-trivial. Challenges include unwanted aggregation or crosslinking between QDs, inconsistency in the number of antibodies per QD, and low retention of antibody activity. The features of click chemistry are promising for addressing these challenges.
Among available click chemistries, tetrazine ligation is an attractive option due to its bioorthogonality and fast reaction kinetics. Here, we explored multiple strategies to implement tetrazine click chemistry with QDs, including surface chemistries based on amphiphilic polymers, small-molecule ligands, and polyethylene glycol (PEG) and dextran ligands. Both trans-cyclooctene (TCO) and norbornene (Nb) derivatives of these chemistries were also evaluated as the click partner for tetrazine. In total, eight different approaches were investigated. Although all of the derivatives were reactive on their own, most became unreactive when functionalized on the surface of a QD, which appeared to induce substantial hindrance. Ultimately, the tetrazine derivative of an amphiphilic polymer was the only chemistry that was active for ligation. Altogether, this research highlights the challenges in optimizing the tetrazine ligation with QDs and provides insight into the most effective strategies to implement this chemistry.

P14

Increased particle fusion and blebbing decreases lipid nanoparticle potency

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The ionizable lipid in lipid nanoparticle (LNP) mRNA systems significantly govern particle morphology and potency. We have found that LNP displaying “bleb” structures generally exhibit improved transfection potencies, where blebs can be induced by formulating in high ionic strength buffers. It is not known, however, whether this phenomenon extends to LNP mRNA systems containing other ionizable lipids of vastly different characteristics. Here we demonstrate that LNPs containing ionizable lipids with a higher fusogenic propensity in fact display poorer characteristics when formulated under high ionic strength buffers, triggered by increased fusion. Such LNPs exhibited increased particle size and substantially reduced mRNA encapsulation; a greater number and size of blebs per particle; and notably, a >15-fold decrease in liver transfection *in vivo*. Increased blebbing and particle fusion therefore do not necessarily confer improved potency, suggesting that the ionizable lipid and formulation buffer must be carefully considered to achieve optimal particle properties.

P15

Optimizing LNP and Proteinase mRNA to Remodel Tumour Extracellular Matrix

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Immunotherapies such as checkpoint inhibitors and cell therapies have emerged as promising treatments for cancer patients. Yet, some patients with solid tumours see little to no effect from these treatments. One factor behind these inefficacies is the tumour extracellular matrix (ECM) which physically blocks interactions with the tumour. Among the proteins within the ECM, collagen is most abundant protein.
In this project, we propose remodeling collagen levels within the ECM using lipid nanoparticles to deliver mRNA to relevant 3D spheroid models and demonstrate the feasibility of Matrix Metalloprotease 8 (MMP8). We formulated LNPs with up to a 52-fold increase in transfection potency when compared to Onpattro formulations in spheroids. Additionally, we designed an MMP8 mRNA sequence which elevated expression by 282 times over baseline expression and achieved up to 40% cleavage of collagens. Our findings demonstrate MMP8 as a viable adjuvant to immunotherapy, improving patient outcomes in solid tumours.

P16

Optimizing Conditions for Single Step, High Yield circRNA Manufacturing

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Continuous manufacturing of circular RNAs (circRNAs) is a critical enabler for scalable RNA therapeutics, offering improved reproducibility, efficiency, and integration with next-generation biomanufacturing paradigms. CircRNAs, with their covalently closed structure and innate exonuclease resistance, provide a stable alternative to linear mRNA, but current ribozyme-mediated cyclization methods often require multi-step processing and generate abundant dsRNA by-products. Here, we present a streamlined one-step process that improves circularization efficiency from ~80% to ~90%. This was achieved through rational optimization of ionic conditions, selection of a fit-for-purpose enzyme mutant, and fine-tuned reaction temperature. By eliminating post-IVT processing while enhancing both yield and product quality, our method establishes a foundation to limit dsRNA production via continuous circRNA manufacturing, with potential to simplify commercial-scale production and enable broader adoption of circRNA therapeutics.

P17

Comparison of Cellular Immunolabelling Between Dextran-Functionalized Quantum Dots (QDs), Supra-QD Assemblies, and Super-QD Assemblies

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Cellular immunolabelling with dye-labelled antibodies is an important technique in bioanalysis and imaging; however, there is a need for brighter fluorescent probes in some applications. We have established a series of dextran-functionalized nanoparticles based on semiconductor quantum dots (QDs). These materials include individual dextran-coated QDs (Dex-QDs) and both supra- and super-nanoparticle assemblies of QDs (supra-QDs and super-QDs), which are 1–2 orders of magnitude brighter than Dex-QDs but are larger in size. We have previously demonstrated that all of these materials can be used for extracellular immunolabelling using tetrameric antibody complexes (TACs), but we have not compared them concurrently.

Here, we present a head-to-head-to-head comparison between Dex-QDs, supra-QDs, and super-QDs for cellular immunolabelling, and between the use of TACs and the covalent conjugation of antibodies. Physical characterization data and ensemble and single-particle fluorescence characterization for the materials are also presented. The immunolabelling trends are evaluated and compared to the material characterization data to determine the optimal material and immunolabelling strategy.

P18

Expanding the Lipid Toolkit Towards Targeted Delivery of RNA Therapeutics

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In light of the recent safety concerns with viral vectors, Lipid Nanoparticles (LNPs) should be utilized as a safer, scalable, and affordable alternative whenever delivering gene therapies. Utilization of LNPs has been limited to hepatic and immunological indications due to inherent liver and spleen tropism. Lacking the stealth glycans and targeting capsids of their viral counterparts, LNPs are subject to opsonisation and rapid clearance from circulation. Our rational design of targeted LNPs will incorporate the same glycan and peptide-based strategies to shift biodistribution away from the reticuloendothelial system and towards the target organ. LNPs will be retooled with stealth glycans and targeting peptides, both independently, and in combination, to determine if their functional properties yield an additive effect on biodistribution.

P19

Neoantigen-based personalized cancer vaccine: LNP-mediated delivery of multi-epitope mRNA extends survival in aggressive melanoma cancer model

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Personalized cancer vaccines (PCVs) open new doors for immunotherapy by harnessing the immune system to target tumor specific neoantigens unique to an individual's cancer. Lipid nanoparticle (LNP)-based mRNA vaccines serve as a suitable platform for delivering multi-epitope neoantigen mRNA payloads.
We identified 10 melanoma-specific antigens and synthesized multiple multi-antigen mRNA constructs. We developed proprietary ionizable lipids, encapsulated the various multi-epitope mRNA constructs in LNPs and evaluated their performance within *in vitro* assays and a B16F10 syngeneic mouse melanoma model. Multi-epitope comprising LNPs significantly reduced mean tumor growth rate and extended survival in vaccinated mice compared to controls.
These results demonstrate that our proprietary LNP platform efficiently delivers multi-epitope mRNA LNPs, eliciting potent anti-tumor immune responses in a relevant melanoma model and demonstrating safety of repeated LNP administrations for cancer vaccine applications. This positions our LNP as a promising candidate for further developing PCVs and accelerating new personalized medicine to clinic.

P20

Lipid Nanoparticles Enable High Efficiency CRISPR HDR Mediated Gene Insertions |in Primary Human T Cells

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Stable gene insertion through non-viral delivery is key for advancing safer, more accessible cell and gene therapies. Viral vectors pose manufacturing and safety challenges, while electroporation compromises cell yield and viability. This study demonstrates lipid nanoparticles (LNPs) as a scalable, cost-effective, and gentle alternative for engineering primary T cells. By systematically optimizing critical process parameters—including cell activation, density, nucleic acid dose, and RNA/DNA ratios—LNP-mediated CRISPR delivery achieved an average 31% homology directed repair (HDR), with cell viability remaining high at 96%. The addition of NHEJ inhibitors further increased HDR rates above 50%. Compared to electroporation, LNPs produced similar gene insertion frequencies but yielded significantly more viable edited cells. These findings highlight LNPs' potential for efficient, non-viral gene insertion, offering an adaptable framework for diverse therapeutic targets and supporting the rapid development of next-generation T cell therapies.

P21

Microfluidic Tangential Flow Filtration Optimizations for Liposomes and Lipid Nanoparticles

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Current preclinical studies on lipid nanoparticles (LNPs) provide promising results, yet at the same time, the design of LNPs are becoming increasingly complex. Moreover, the need for production scaling up is required for bringing these agents to clinical testing. The implementation of tangential flow filtration (TFF) to the workflow can offer advantages in both scalability and time. However, maintaining the particles' desired characteristics during the diafiltration process can impact LNP quality attributes. In this study, we explored how microfluidic TFF affects the formation of liposomes and LNPs. We first formulated empty liposomes and LNPs through rapid mixing and examined their sizes and polydispersity (PDI) changes under different transmembrane pressures and shear rates. Subsequently, we found that both liposomes and LNP post-TFF exhibit size and PDI increase compared to dialysis with semi-permeable tubing, which suggests potential aggregation or fusion and the need for further optimization.

P22

Optimizing Lipid Nanoparticle–Mediated CRISPR/Cas9 Gene Editing in Bioengineered Lung Models of Cystic Fibrosis

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The effectiveness of inhalant gene editing therapies for cystic fibrosis (CF) via non-viral delivery methods is currently limited. Our hypothesis is that this low efficiency is due to the dense, viscous mucus that lines patient airways and obstructs delivery to target epithelial cells. This project investigates whether pre-treatment with mucolytic agents can improve the penetration of lipid nanoparticles (LNPs) and enhance CRISPR/Cas9 base editing efficiency in bioengineered 3D CF lung models. These models, developed using primary CF patient–derived bronchial epithelial cells, closely replicate the mucus environment of CF lungs. Various mucolytic conditions were screened prior to LNP transfection with CRISPR/Cas9 mRNA. Editing outcomes were assessed using Sanger sequencing and qPCR. Our findings indicate that certain mucolytics substantially increase editing rates by reducing mucus viscosity and improving nanoparticle diffusion. These results support the development of improved non-viral delivery strategies and highlight the potential of mucolytic pre-conditioning in inhaled CF therapies.

P23

Formulation and Administration Timing of Lipid Derivatized JAK-Inhibitor and Corticosteroid Modulate saRNA-LNP Inflammation and Expression

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Comparing to the traditional mRNA, self-amplifying RNA enables prolonged expression at a much lower dose. However, its clinical translation is hindered by the innate immune activation of saRNA replication. To address this challenge, we investigated lipid-derivatized prodrugs of peficitinib (a pan-JAK inhibitor) and dexamethasone (a corticosteroid) for their ability to modulate the immune response induced by saRNA replication and LNPs. Using both in vitro and in vivo models, we optimized the formulation approach of the prodrug (either co-formulating with saRNA into the LNPs, or separate formulation) and varied timing of administration. Our findings demonstrate that co-formulation of peficitinib exacerbated the endosomal damage signalling and downstream defence pathways, abrogating saRNA replication and expression despite suppressing innate immune activation. By contrast, independent delivery delayed these responses by a few hours, preserving saRNA replication and expression while still mitigating inflammation. Collectively, these results emphasise that the formulation strategy, and timing - not drug identity alone, influence the trade-off between controlling reactogenicity and maintaining transgene expression, offering a refined pathway toward reducing reactogenicity while maximizing the therapeutic potential of saRNA-LNP therapeutics.

P24

Fed-Batch IVT mRNA synthesis using the BioLector XT and ReadyToProcess™ WAVE™ 25

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Affiliation: Cytiva

Introduction & Objectives

RNA-based therapeutics are rapidly transforming modern medicine, offering novel treatment modalities for genetic disorders, infectious diseases, and cancer. As the field matures, the demand for scalable, cost-effective manufacturing solutions continues to grow. Central to RNA therapeutic production is in vitro transcription (IVT), a cell-free, enzymatic process that synthesizes RNA from nucleotide triphosphates (NTPs) using a linear DNA template and polymerase. However, IVT—especially with co-transcriptional capping—remains the most expensive step in RNA manufacturing, posing challenges to the global adoption of RNA therapeutics.

Fed-batch IVT, where NTPs and magnesium salts are added gradually over time, is emerging as a promising strategy to improve RNA yield, reagent usage efficiency, and product quality. This study highlights how the Beckman Coulter BioLector XT microbioreactor and the Cytiva ReadyToProcess™ WAVE™ 25 system provide a powerful platform for process development and scale up of fed-batch IVT.

Materials & Methods

The BioLector XT is a high-throughput, temperature-controlled microbioreactor supporting 48 parallel wells with real-time monitoring of pH, fluorescence, biomass, and dissolved oxygen. Its microfluidic module enables precise, automated, well-specific feeding. These capabilities were leveraged to perform controlled addition of magnesium-NTP feed solution into parallel 0.8 mL IVT reactions to enable rapid optimization of feed rates and stock concentrations. Notably, pH was investigated as a potential in-process indicator of mRNA synthesis, offering a non-invasive method for real-time monitoring of reaction progress.

The optimized process was scaled up into a ReadyToProcess™ WAVE™ 25 system, a GMP-ready, closed bioreactor with integrated pumps and real-time pH and DO monitoring. The WAVE™ 25 supports IVT volumes from 20 mL to 25 L, using either the Cytiva™ Enzyme Micro Reactor Accessory or standard WAVE™ trays. In this study, process development was performed at 0.8mL scales in the BioLector XT and subsequently scaled to 20 mL and 200 mL in the WAVE™ 25.

Results

Fed-batch IVT conditions developed in the BioLector XT led to considerable improvement in mRNA yield reaching up to 15 g/L of initial reaction volume. This approach enhanced enzyme and DNA template utilization, by enabling more mRNA production from smaller initial volumes. Various feeding strategies were also explored to improve NTP incorporation efficiency and reduce starting DNA template requirements.

A linear relationship between pH and crude mRNA concentration was observed, suggesting a potential pathway for real-time process monitoring. Notably, this relationship was consistent across both the BioLector XT and the scaled-up reactions on the ReadyToProcess™ WAVE™ 25, reinforcing its potential as a scalable process control parameter. The optimized process, when transferred to the ReadyToProcess™ WAVE™ 25, produced approximately 2.8 g of RNA from just 200 mL of starting volume, demonstrating both scalability and robustness of the fed-batch approach.

Conclusion

This study demonstrates that fed-batch IVT strategies can enhance RNA yield and IVT efficiencies. Moreover, it shows the utility of the BioLector XT for IVT process development and further highlights the ReadyToProcess™ WAVE™ 25 as a scalable solution for RNA therapeutics.

P25

Helper Lipid Re-Design Blocks Recycling and Supercharges mRNA Delivery with Lipid Nanoparticles

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A key challenge for lipid nanoparticle (LNP) delivery of nucleic acids is that most particles entering cells are not released into the cytosol but instead recycled back to the cell surface. This inefficient trafficking limits therapeutic potency. To overcome this, we redesigned the LNP helper lipid component, replacing DSPC with alternatives disrupting recycling pathways by altering membrane curvature or interfering with recycling-related GTPases. We identified 12 candidates that reduced recycling from ~80% to ~20% and increased intracellular retention up to ~4.5-fold compared to standard DSPC-LNPs. Mechanistic studies showed that lead formulations lowered Rab11 colocalization, reduced lysosomal degradation, and prolonged residence in pre-lysosomal compartments, creating more opportunities for endosomal escape. Functionally, several modified LNPs boosted reporter gene expression by more than 25-fold in-vitro and 40-fold in-vivo relative to controls. These findings establish helper lipid substitution as a powerful and generalizable strategy to block endosomal recycling and markedly improve mRNA delivery efficiency.

P26

Prototype Smartphone-Based Device for Flow Cytometry

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Many areas of research and healthcare require the ability to detect, enumerate, and classify different cells. Flow cytometry is one of the most widely used methods for this purpose, but the instruments are typically limited to specialized laboratories, resulting in a major barrier to healthcare equity. One possible method for reducing this barrier is the use of a smartphone-based device. With their global proliferation and built-in optoelectronic components, smartphones have excellent potential for laboratory bioanalyses.
Here, we describe development and optimization of a prototype smartphone-based device for flow cytometry. Nuclear and membrane staining on the same cells is quantitatively resolved. Immunoconjugation of ultrabright nanoparticles to cells allows for detection of multiple cell types in the same sample. Potential applications of this device include the identification of cancerous cells from urine or blood samples. The technology described will help improve accessibility to advanced diagnostic health care in resource-limited communities.

P27

TFF in RNA workflow: process optimization for RNA and LNP manufacturing

Sree Gayathri Talluri

Cytiva

Ultrafiltration and diafiltration (UF/DF) via tangential flow filtration (TFF) in RNA and lipid nanoparticle (LNP) downstream processing is typically run at ambient temperature wherein maintaining product quality and minimizing processing time are paramount. We show that 100 kDa regenerated cellulose cassettes can process mRNA and LNPs from bench- (93 cm2) to manufacturing-scale (0.5-1 m2) in less than 2 h with more than 90 % recovery while maintaining product quality.

P28

Non-viral *in situ* gene editing effectively and safely rescues congenital ichthyosis-causing mutations in human skin

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Autosomal recessive congenital ichthyosis (ARCI) refers to a group of rare but highly debilitating skin disorders which significantly impair patients' quality of life and currently lack any effective treatment options.
Here, we report clinically-relevant *in situ* correction of the most common ARCI-causing mutation *TGM1* c.877-2A>G, a splice-site aberration, in human disease models. Targeted skin barrier modulation followed by topical application of the cytosine base editor eTD packaged into lipid nanoparticles yielded functional restoration of ~30% of wild-type transglutaminase 1 enzyme activity in skin tissue.
Toxicity studies demonstrated an excellent safety profile even after repeated application, without systemic distribution of the lipid nanoparticles or the genetic cargo as determined via highly-sensitive methods including DESI metabolic imaging.
This study presents comprehensive preclinical data on the feasibility of *in situ* gene correction of genodermatoses-causing mutations showcasing its therapeutic potential and paving the way for curative next-generation treatments for severe genetic skin diseases.

P29

Optimizing CRISPR-Cas9 mRNA for Epithelial Skin and Lung Gene Editing

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mRNA therapeutics offer a promising strategy for CRISPR-based correction of genetic disorders, with skin and lung diseases such as cystic fibrosis and ichthyosis serving as prime candidates. However, these approaches face challenges including immunogenicity and cell-type specific translation. Therefore, this study aims to establish design rules for Cas9-GFP mRNA that enable efficient editing in epithelial cells. Using FACS-sorted GFP-positive cells, we optimized the transfection dose and timepoint for each cell-type, maximizing gene editing and GFP protein level as a proxy of Cas9 expression. We evaluated key mRNA design strategies, including untranslated regions (UTRs) optimization and incorporation of synthetic 5′ caps. Our findings show that while Cas9 mRNA designs enhance editing in target cells and demonstrate distinct editing efficiencies, lung cells exhibit lower efficacy than skin cells despite increased Cas9 expression in both. These results highlight the potential of rational mRNA design to improve genome editing in a cell-type specific manner.

P30

Increasing mRNA loading capacity of lipid nanoparticles

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Lipid nanoparticle (LNP) mRNA systems are formed under acidic conditions followed by a buffer exchange process to remove organic solvent and to bring the pH to physiological conditions. Here, we explore an alternative formulation process to induce the formation of LNPs with high payload capacity compared to LNPs prepared through the standard formulation procedure. Single-particle characterization of these highly loaded LNPs revealed 6 mRNA copies/LNP while standard LNP formulations only contained 2 mRNA copies/LNP. Further, these highly loaded LNP mRNA systems exhibit improved transfection potencies in vitro, ex vivo, and in vivo when compared to LNP mRNA systems formed from the standard formulation process.

P31

Ultra-Bright Luminescent Lanthanide Nanoparticles for Time-Gated Bioanalysis and Imaging

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Many cells, tissues, and bodily fluids exhibit intrinsic autofluorescence that interferes with fluorescence-based biomarkers detection. Time-gated imaging overcomes this limitation by employing luminescent lanthanide complexes (LLCs) and other emitters with long photoluminescence lifetimes. By introducing a delay between pulsed excitation and signal collection, short-lived autofluorescence decays while LLCs continue to emit. However, the relatively low brightness of LLCs results in poor signal-to-background ratios, limiting their utility in bioanalysis and imaging.

To this end, we developed ultra-bright luminescent lanthanide nanoparticles (NPs) with up to 100-fold enhanced brightness while retaining millisecond-scale lifetimes. Here, we present the NPs synthesis, characterization, and benchmark their performance in multi-biomarkers sensing, point-of-care applications, cellular immunolabeling, and tissue immunohistochemistry using time-gated microscopy. These advances provide sensitive, robust, and broadly applicable tools for biomedical research and clinical diagnostics.

P32

Advancing mRNA therapeutics: Lipid nanoparticles demonstrate favorable safety and efficacy profile with repeated mRNA administration in normal and tumor-bearing mice.

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Introduction:
Lipid nanoparticles (LNPs) have revolutionized mRNA delivery, offering a promising approach for advancing cancer immunotherapy. Effective and safe delivery of tumor antigen-encoding mRNA can stimulate robust anti-tumor immune responses. Here, we developed LNP formulations for delivering ovalbumin (OVA)-encoded mRNA and evaluated their safety, efficacy, and therapeutic potential in the B16-F10-OVA xenograft melanoma mouse model.

Methods:
Novel ionizable lipids were selected for formulating LNPs. OVA-encoded mRNA was encapsulated in LNPs using NxGen™ microfluidic mixing technology on the NanoAssemblr™ platform. The LNPs were characterized for hydrodynamic size, polydispersity index (PDI), loading, and encapsulation efficiency. To assess long-term safety and stability, healthy mice received multiple intramuscular (IM) injections of the LNP formulations at 21-day intervals. Physicochemical stability and toxicity were evaluated through the standard assays and clinical observations. Following this series, B16-F10-OVA tumor-bearing mice were vaccinated intramuscularly with OVA mRNA-loaded LNPs. Clinical symptoms and survival outcomes were monitored and compared to untreated controls.

Results:
OVA mRNA-loaded LNPs were in the desired size range of 60 to 80 nm with a PDI value below 0.2 and an encapsulation efficiency greater than 95%. Long-term stability studies indicated retention of critical quality attributes (CQAs). Repeated IM administration of the proprietary LNPs over an extended period demonstrated stability and tolerability with no detectable toxicity or adverse effects observed in treated animals. Treatment with the OVA mRNA-LNP vaccine improved survival in tumor-bearing mice, significantly extending median survival compared to controls.

Conclusion:
By retaining the CQAs of the drug products, our novel LNP platform efficiently delivers OVA mRNA as a model for protein replacement applications or cancer vaccines. Additionally, repeated IM administrations of these LNPs over an extended period resulted in no detectable adverse events and OVA mRNA LNPs induced potent anti-tumor effects in the B16-F10-OVA model. This favorable safety profile and stability upon repeated dosing underscore LNP suitability for long-term immunization strategies.

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