Lipid Nanoparticle Technology to Enable Nucleic Acid Therapeutics and Vaccines

An AstraZeneca – NMIN CRS Industry Educational Workshop

as part of the Controlled Release Society Annual Meeting

Wednesday, July 28th, 2021

12:00 – 4:00 pm & 5:00 – 9:00 pm EDT

AstraZeneca and the Nanomedicines Innovation Network (NMIN) are pleased to host this CRS Industry Educational Workshop as part of the 2021 CRS Virtual Annual Meeting, exploring the clinical translation of nucleic acid-based therapeutics.

PROGRAM

Part I: LNP Basics and Future Aspects

Chairs: Dominik Witzigmann / Terry Allen

Times are given in EDT.

12:00–12:10 ***Introductory remarks: The Importance of the Scientific Entrepreneur for the Translation of Academic Discoveries Into the Commercial World***
Pieter Cullis, Research & NanoCore Leader, NMIN

12:10–12:40 ***Let's talk about the importance of lipid nanoparticle design***
Dominik Witzigmann & Jayesh Kulkarni, NanoVation

12:40–1:20 ***Development of broadly protective influenza virus vaccines using nucleoside-modified mRNA***
Norbert Pardi, U Penn

1:20–1:50 ***Off-the-shelf delivery system for RNA-based nanomedicines***
Raymond Schiffelers, UCM Utrecht

1:50–3:20 **SHORT TALKS**

- ***The importance of the biomolecular corona for LNP delivery***
  Valentina Francia, UMC Utrecht & UBC
- ***Optimization of nanoparticle-mediated genome editing for genetic diseases: Towards direct comparison with viral mediated gene augmentation approaches***
  Colin Ross, UBC
- ***Self-amplifying RNA: the next generation of messenger RNA***
  Anna Blakney, UBC
- ***LNP technology for modulating blood clotting***
  Christian Kastrup, UBC

- ***Modular LNP-prodrug platform technology***
  Roy van der Meel, Eindhoven University of Technology
- ***Leveraging LNPs for in situ gene editing in skin***
  Sarah Hedtrich, UBC
- ***Highly selective targeting of RNA to leukocytes using conformation LNPs***
  Dan Peer, Tel Aviv University

3:20–4:00 **PANEL DISCUSSION**

LNP technology is ready for prime time – what is the next breakthrough?

Part II: Clinical Translation and Regulatory Aspects

Chairs: Marianne Ashford / Sanya Puri

Times are given in EDT.

5:00–5:25 ***LNP technology enabling clinical translation of mRNA therapeutics and vaccines***
Thomas Madden, Acuitas Therapeutics

5:25–5:50 ***Design and optimization of novel lipids and formulations for systemic delivery***
Mark Cornebise, Moderna

5:50–6:15 ***Manufacturing of Lipid Nanoparticle-based mRNA therapeutics***
Patrick Baumhof, CureVac

6:15–6:40 ***Comparison of different platform technologies for delivering RNA***
Heinrich Haas, BioNTech

6:40–7:05 ***Scale up, process development and manufacturing of clinical mRNA-LNPs***
Pierrot Harvie, Precision Nanosystems

7:05–7:30 ***Analytical characterisation of mRNA & Lipid Nanoparticles (LNPs)***
Gunilla Nilsson, AstraZeneca

7:30–7:55 ***Regulatory considerations and experience in EU***
Dolores Hernan, EMA Europe

7:55–8:30 **PANEL DISCUSSION**

Lessons learned and the future path for LNP-based gene therapies and vaccines

SPEAKERS, CHAIRS & MODERATORS *in alpha order*

Terry Allen is a Professor Emerita of Pharmacology and Oncology at the University of Alberta and a visiting professor at the University of British Columbia. She is a fellow of the Royal Society of Canada and a Fellow of the Controlled Release Society. She has been active in the drug-delivery field for over 35 years, and has made important contributions to the development of long-circulating liposomes and ligand-targeted nanomedicines for anticancer drugs and gene medicines.

She has over 200 peer-reviewed publications and is an inventor on several patents. The product Doxil, the first anticancer nanomedicine approved in the world, came out of pioneering research in her laboratory at the University of Alberta. She has also been active in the area of new drugs from natural product, which has resulted in two drugs proceeding into Phase II clinical trials. Her recent work in developing ligand-targeted therapeutics for small molecule therapeutics and gene medicines is at the leading edge of this exciting new field and the methods she developed are widely used throughout the field.

Marianne Ashford is Senior Principal Scientist of Advanced Drug Delivery, Pharmaceutical Sciences, R&D, in AstraZeneca. She is responsible for applying drug delivery approaches which have the potential to enable the progression of innovative medicines. She has been instrumental in introducing nanomedicines into the AstraZeneca portfolio, and initiated several key collaborations, building internal capability in nanomedicines and drug targeting. She holds a PhD in oral drug delivery to the colon, and a degree in Pharmacy from the University of Manchester. She has published over 55 peer reviewed papers and six book chapters, is an Honorary Professor at the University of Nottingham and serves on numerous academic and industrial scientific committees and advisory boards in the field of drug delivery.

Patrick Baumhof is Vice President Formulation and Delivery at CureVac AG. Trained in Chemistry, at the University of Leipzig, his scientific expertise includes chemistry, pharmaceutical sciences and immunology. He joined CureVac in July 2007 when he was responsible for the development and preclinical testing of new formulations for mRNA vaccines and therapeutics. He is inventor of several patents and he co-authored several publications on mRNA technology.

Anna Blakney is an Assistant Professor at the University of British Columbia in the Michael Smith Laboratories and School of Biomedical Engineering. She completed her BS in Chemical & Biological Engineering at the University of Colorado, a PhD at the University of Washington in Bioengineering and postdoctoral training in immunology at Imperial College London. Her laboratory seeks to understand the immune mechanisms of RNA and biomaterials to engineering next generation vaccines and therapeutics. She is also passionate about vaccine literacy and public engagement and runs a TikTok account that now has >200,000 followers and >17M views.

Mark Cornebise is an Associate Scientific Director in the Platform Chemistry group at Moderna working on delivery technologies for mRNA therapeutics. He has extensive experience in small molecule drug discovery, having contributed to anti-inflammatory, antibacterial and antiviral programs, among others. Prior to joining Moderna five years ago he held positions at Biogen Inc., Vertex Pharmaceuticals, and AstraZeneca plc. He is (co)author on 16 peer-reviewed journal articles and is an inventor on eight granted US patents. He received a BA in Chemistry from the University of North Carolina at Chapel Hill and an MS in Organic Chemistry from New York University.

Pieter R. Cullis, (Ph.D., FRSC, FNAI [USA]) was the founding Scientific Director of the NanoMedicines Innovation Network (NMIN), the leader of NMIN's Gene Therapy Research Theme and of its NanoCore core facility, Professor of Biochemistry and Molecular Biology at the University of British Columbia and Founding Director of the Centre for Drug Research and Development.

Dr. Cullis' laboratory has been responsible for fundamental advances in the generation, loading and targeting of liposomal systems for intravenous delivery of conventional and genetic drugs. This work has led to two products that have been approved by regulatory agencies in the U.S. and Europe for the treatment of cancer and its complications, one that is in late stage (Phase III) clinical trials and two more that are about to enter Phase I studies. From 1987 to 1991, Dr. Cullis was President and Director of The Canadian Liposome Company Inc. (CLC), a company he co-founded. CLC was a subsidiary of The Liposome Company Inc. (TLC, Princeton , NJ). Dr. Cullis has also played a founding role in Inex Pharmaceuticals Corp. (Director and CSO 1992-2004), Lipex Biomembranes Inc. (Director and Chairman, 1985-2000), Northern Lipids Inc. (Director and Chairman, 2005 onwards) and Protiva Biotherapeutics Ltd. (Director 2001-2005 and Chairman, Scientific Advisory Board). He has published over 300 scientific articles and is an inventor on over 30 patents.

Dr. Cullis was awarded the Ayerst Award by the Canadian Biochemical Society in 1986, the B.C. Science Council Gold Medal for Health Sciences in 1991, the Alec D. Bangham Award for contributions to liposome science and technology in 2000, the B.C. Biotechnology Association award for Innovation and Achievement in 2002, was elected a Fellow of the Royal Society of Canada in 2004 and was awarded the Barre award for contributions to Pharmaceutical Sciences by the University of Montreal in 2005. Dr. Cullis also received the UBC Alumni Award for Research in Science and Medicine in 2005. In 2011, Dr. Cullis won the prestigious Prix Galien Canada award and the Bill and Marilyn Webber Lifetime Achievement Award.

Valentina Francia is a joint postdoctoral fellow between the Cullis Lab at the University of British Columbia (Canada) and the Schiffelers lab at UMC Utrecht (Netherlands). Her research focuses on the investigation of the biomolecular corona of lipid nanoparticles as a targeting strategy for siRNA delivery. Dr. Francia obtained a PhD in pharmacology from the University of Groningen (Netherlands) where she studied the endocytosis of nanomedicines. Dr. Francia is a board member and social media coordinator of the BeNeLux & France and Canadian Chapters of the CRS and is NMIN's Research Theme 2 KTEE Accelerator.

Heinrich Haas has more than 20 years of experience in academic research and industrial pharmaceutical development. His professional focus is on colloidal/nanoparticulate formulations for targeted drug delivery with therapeutic and diagnostic applications. Since joining BioNTech RNA Pharmaceuticals GmbH in 2010, he has helped build the formulation development and analytics unit, which develops formulations for delivery of RNA and small molecules.

Dr. Haas received his Ph.D. in physical chemistry. He was subsequently responsible for a variety of projects in biopharmaceutical research and development, ranging from the exploration of novel colloidal therapeutic and diagnostic carriers to up-scaling and development of market-compliant manufacturing methods for liposome products. He has an active record of publications in peer-reviewed journals and patent applications in the field of drug delivery.

Pierrot Harvie is currently Clinical Manufacturing Manager at Precision NanoSystems. He has 20 years' experience working as a formulation / process scientist in the biotech industry. Previously, he was a Senior Scientist at Genevant Sciences (Vancouver, BC), an Associate Director at PhaseRx, (Seattle WA) & a formulation scientist at Marina Biotech (Bothell, WA), Celator Pharmaceuticals (Vancouver, BC) & Targeted Genetics Corporation (Seattle, WA). He is the author of 7 U.S. patents & 20 peer-reviewed papers. He holds a Ph.D. in Microbiology & Immunology from Laval University.

Sarah Hedtrich obtained her PhD in Pharmacology & Toxicology from the Freie Universität Berlin in Germany in 2009. During her postdoc, she moved to the Ludwig-Maximilians-University in Munich and Tufts University in Boston, USA. After returning to Berlin 2013, she headed a junior research group and was appointed an assistant professor in 2015. She relocated her lab to the U of British Columbia in 2019. She co-/authored over 70 peer-reviewed journal articles in high impact journals including the Journal of Controlled Release, Small, Nature Reviews Materials, and Theranostics. Her research focuses on inflammatory and genetic diseases of human epithelia, the development of novel therapeutic approaches and tissue engineering of complex, human-based organ models aiming for valid and predictive test systems for preclinical and fundamental research.

Christian Kastrup is an Associate Professor in the Department of Biochemistry and Molecular Biology and a member of the Centre for Blood Research (CBR) at the University of British Columbia. His cutting-edge research is primarily concerned with understanding mechanisms of blood clot formation and degradation. More recently, he has become interested in developing nanoparticle therapies for hemostasis and thrombosis. Dr. Kastrup is co-leader of NMIN's Theme 2: Gene Therapy research area and its NanoCore facility.

Jayesh Kulkarni is a nanomedicine scientist with academic and industry experience in the field of lipid-based drug delivery systems for small molecule therapeutics, proteins, and genetic drugs. He has contributed to the design and development of lipid nanoparticles (LNP), describing the biophysical processes of LNP formation, the mechanism by which these particles form, and the numerous factors that can affect this process. Dr. Kulkarni is an NMIN Postdoctoral Fellow and is CSO of NanoVation Therapeutics.

Thomas Madden is President and CEO of Acuitas Therapeutics and a world-renowned expert in the area of nanotechnology. Dr. Madden obtained his BSc. and Ph.D. in Biochemistry from the University of London, U.K. He has held several senior academic and industry positions including Assistant Professor in Pharmacology at the University of British Columbia and Senior Director, Technology Development and Licensing at Tekmira Pharmaceuticals (formerly INEX Pharmaceuticals). Dr. Madden founded Acuitas Therapeutics in February 2009 and has guided the company to a leadership position in the application of lipid nanoparticle (LNP) technology for the delivery of nucleic acid therapeutics. Dr. Madden has over 60 publications in peer-reviewed journals relating to LNP technology and the development of pharmaceutical products, including recent publications in Nature. In 2020, Dr. Madden was made a Fellow of the American Institute for Medical and Biological Engineering in recognition of his contributions to the field of nucleic acid delivery.

Gunilla Nilsson holds a Master of Science from Chalmers University, Gothenburg. After graduation, she joined AstraZeneca where she has held various roles within analytical chemistry and drug product development. In 2014 she transitioned to the New Modalities research area, working mainly with analytical development and strategies in the mRNA field. Her expertise is analytical science with focus on separation techniques such as liquid chromatography and capillary electrophoresis. In her current position as Team leader in Advanced Drug Delivery, AstraZeneca, Gunilla is responsible for the CMC analytical development of biomolecules such as oligonucleotides, mRNAs and peptides in early clinical phase.

Norbert Pardi holds a Ph.D. in biochemistry and genetics. He has been working at the University of Pennsylvania since 2011. His research interest is the development of mRNA-based therapeutics with particular focus on new generation vaccines. He explored the development of a novel vaccine platform using nucleoside-modified mRNA in lipid nanoparticles (LNPs) and used it to generate highly effective vaccines targeting various pathogens. Dr. Pardi is a pioneer of the nucleoside-modified mRNA vaccine technology and published milestone papers in the field. He is regularly invited to give lectures at prestigious scientific meetings.

Dan Peer is a Professor and the Director of the Laboratory of Precision NanoMedicine at Tel Aviv University (TAU). He is also the Vice President for Research and Development in Tel Aviv University, the biggest university in Israel. From 2016 -2020, he was the Chair of Tel Aviv University Cancer Biology Research Center, which includes 17 affiliated hospitals and from 2017, he is the Founding and Managing Director of the SPARK program, Center for Translational Medicine at TAU.

Prof. Peer's work was among the first to demonstrate systemic delivery of RNA molecules using targeted nanocarriers to the immune system and he pioneered the use of RNA interference (RNAi) as drug discovery tools in immune cells. In addition, his lab was the first to show systemic, cell specific delivery of modified mRNA to cells to induce therapeutic gene expression of desired proteins within the immune system that has enormous implications in cancer, inflammation and infection diseases and the first to show systemic, cell specific and high efficiency therapeutic genome editing in cancer.

Prof. Peer has more than 120 pending and granted patents. Some of them have been licensed to several pharmaceutical companies and one is currently under registration as a new drug for inflammatory bowel disease and blood cancer. In addition, based on his work, four spin-off companies were generated aiming to bring innovative personalized medicine into clinical practice. Prof. Peer is a scientific advisory board member in more than 15 companies and on the scientific advisory board of more than 20 journals. He is a past President of the Israeli Chapter of the Controlled Release Society, and a Member of the Board of the Israel Young Academy of Science.

Sanya Puri is Associate Director, Advanced Drug Delivery, Pharmaceutical Sciences, R&D, in AstraZeneca. She holds a PhD from the University of Nottingham in designing polymeric nanoparticles for tumour targeting, with her first degree in Pharmacy from India. She joined AstraZeneca in 2008, working on the formulation of clinical products for inhalation, and moved into the Pharmaceutical Development team in 2010 to work extensively in the field of advanced nanomedicines and new modalities for oncology therapeutics. She progressed to the role of Associate Principal Scientist in 2013 and became involved in driving innovative science and implementing clinical development strategies applied to nanomedicines and nucleic acid-based therapeutics. In 2017 she became team leader of the Advanced Drug Delivery team and established a team of multidisciplinary scientists from leading drug delivery groups with expertise in drug delivery sciences and cell biology.

Colin Ross is an Associate Professor in the Faculty of Pharmaceutical Sciences at the University of British Columbia and a Scientist at BC Children's Hospital. Dr. Ross's expertise spans pharmacogenetics, genomics, drug development, drug safety, adverse drug reactions, predictive genetics, and genetic/clinical factors of drug response. Ross Lab researchers investigate the genetic basis of disease and severe adverse drug reactions using genomics-guided precision medicine approaches to help make drugs safer, improve disease diagnosis, and develop new, targeted therapeutics.

Dr. Ross's research capitalizes upon national and international collaborations with clinicians, researchers and industry partners. He was instrumental in the establishment of the Canadian Pharmacogenomics Network for Drug Safety (CPNDS), a nation-wide collaborative network of researchers. He currently holds a leadership role on the network's executive steering committee.

Raymond Schiffelers is a translational scientist in the nanomedicine field. He has been active in the field for over 25 years, initially focused on synthetic delivery systems like liposomes and polymers for the delivery of small molecular weight agents and RNA. He received an ERC Consolidator (2010) and ERC PoC (2012) grant to explore EVs as drug delivery systems. The PoC grant formed the basis for the spin-off company Excytex (2014). He is coordinator of two large EU public-private projects on RNA delivery: B-SMART (2016-6M€) and EXPERT (2019-15M€) and vice-chair of the European Technology Platform Nanomedicine. He is (associate) editor of the Journal of *Extracellular Vesicles*, *Journal of Controlled Release* and *International Journal of Pharmaceutics* and serves on the Scientific Advisory Board of *Anjarium Biosciences, Nanocell Therapeutics, 20MED Therapeutics*, and *Alpine Antivirals*. He has been identified by Clarivate Analytics as Highly Cited Scientist.

Roy van der Meel obtained his PhD at Utrecht University under direction of Gert Storm and Wim Hennink. He conducted postdoctoral research in the labs of Raymond Schiffelers at the University Medical Center Utrecht and Pieter Cullis at the University of British Columbia, funded by a Marie Skłodowska-Curie Action from the European Commission and a Veni grant from the Dutch Research Council. Roy is currently appointed Assistant Professor in the Precision Medicine group at the Eindhoven University of Technology. His research is focused on developing RNA-based nanotherapeutics to regulate the immune response in a highly precise manner.

Dominik Witzigmann is recognized for his research on lipid nanoparticle formulations, the fastest growing RNA delivery technology. Dominik is Co-Founder & CEO of NanoVation Therapeutics focusing on the development of nucleic acid therapeutics utilizing lipid nanoparticle systems for treating age-related diseases. Dominik has leadership roles within the NanoMedicines Innovation Network (NMIN), a Canadian Networks of Centres of Excellence in Nanomedicine. Prior to NanoVation, Dominik co-founded NMIN`s NanoCore, leading the development and characterization of advanced lipid nanoparticle technologies, and supporting >30 projects at academic institutions across Canada. He currently serves as a Board Member of the Gene Delivery and Genome Editing focus group of the Controlled Release Society.

About AstraZeneca: AstraZeneca is a global, science-led biopharmaceutical business focused on the discovery, development and commercialisation of prescription medicines in Oncology and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology..

About NMIN: The Nanomedicines Innovation Network (NMIN) is a federal Networks of Centres of Excellence (NCE) that has mobilized a network of experts and organizations from across sectors - academia, healthcare, industry and other not-for-profit enterprises - to strengthen and extend Canada's position as a global leader in developing the next generation of nanomedicines.

This event is supported by:

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Focus Group GENE DELIVERY AND GENE EDITING

PRECISION NANOSYSTEMS

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