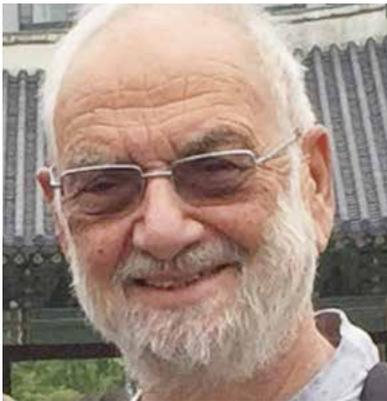


SPEAKERS DEBATE 1, JULY 8, 2021



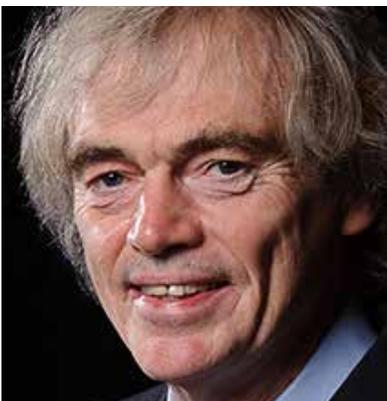
**Prof. Dr. Yechezkel
Barenholz**



**Professor Dr. Sir
David Baulcombe FRS**



Dr. Patrick Baumhof



Prof. Dr. Pieter Cullis



**Prof. Dr. med.
Patrick Hunziker**



Dr. Michael Keller



Dr. med. h.c. Beat Löffler, MA



Prof. Dr. Melissa Moore



Dr. Andreas Wagner

This Webinar is in zoom and at the same time in live stream for quality reasons. During the meeting, you can write your questions that reach the chair of the CLINAM-Debate who passes them to the speakers. (Possibility to stay after the meeting for further oral debate in a zoom room) This Debate is open for up to 400 participants. **The participation is free however, registration in order to get the link is mandatory.** Please go to the [registration contact page](#) on our website.

CLINAM

European Foundation for Clinical Nanomedicine
Switzerland

THE FIRST CLINAM DEBATE (1/2021)

July 8, 2021 / 4 hours 16.15 -20.15 (CEST Time)

Accelerating the RNA- Revolution in Medicine

After the Virtual CLINAM Summit in last October with 560 delegates, we decided to bring urgent topics within the goals of the Foundation to our community with Debates, inviting speakers of excellence. The topic to be discussed in the first debate is the RNA revolution in medicine, which make clinical use of RNA, RNAi, mRNA, ncRNA and siRNA. This revolution was enabled by concomitant development and maturation of three achievements:

1. Means to produce at large scale stable RNA for the highly sensitive RNA as well as methods to modify mRNA so it would reduce immune activation and increase gene expression.
2. The development of unique lipids and lipid composition that with the RNA will produce lipid nano-particles (LNP) that enable RNA productive delivery that results in silencing for specific liver enzyme by siRNA and protein production for mRNA.
3. Developing methods that enable scale-up of a GMP production of LNP as productive carriers of RNA.

Different types of products are now in clinical use.

The Patisiran (Onpattro) the first siRNA-LNP nano-drug which was developed by Alnylam (1995-2012): to treat hereditary amyloid transthyretin (hATTR) amyloidosis LNP siRNA program: gene silencing in the liver.

The BNT162b2 mRNA-LNP vaccine (2012-2020) one of the two first mRNA nano-drugs and developed by BioNTech/Pfizer as a COVID-19 vaccine. At the same time, Moderna developed its mRNA-1273 COVID-19 Vaccine.

Many other mRNA-based vaccines have been developed previously for different infections such as mRNA-1893 Zika-Vaccine; NA flu and HIV vaccines are in development (HBV); Dengue Virus DENV1 prM/E mRNA-LNP vaccine; and many others. In addition, RNAi treatment candidates for hepatitis B virus are in development. All these are based on lipid nano-particles (LNP) as the carrier of the specific RNA.

RNA-technology is a booster for the future of medicine in many fields. The progress in the last years in purification, stabilization and intracellular drug delivery of RNA has enabled the development of RNA-based therapeutics for a broad spectrum of applications.

RNA therapeutics imply a fast-developing row of drugs that already today change possibilities of healthcare for many diseases and broadens the pathway towards personalized medicine. RNA-based drugs are cost effective and can target previously undruggable diseases. It is a revolutionary therapeutic technology: Biotech startups and academic groups and clinicians at the hospitals can very fast develop personalized (i.e. for individual cancer patients) and/or precision (for group of patients having a similar disease) RNA constructs.

Seven Speakers will elucidate the topic, followed by questions. This event aims to discuss how we can improve the world of RNA and how different classes of RNA-based therapeutics can be developed to shorten the time to get to clinical trials and then to vaccines and drugs to be used with high therapeutic index for the benefit of patients.

Welcome:

Dr. med. h.c. Beat Löffler, MA, CEO of the European Foundation for Clinical Nanomedicine, Basel, Switzerland (5')

Chair of the Session:

Prof. Dr. Yechezkel Barenholz, Hebrew University, Hadassah Medical School, Jerusalem, Israel (10')

Speakers (20' intervention and 5' Questions)

The Onpattro Story and the Clinical Translation of Nanomedicines Containing RNA-based Drugs

Prof. Dr. Pieter Cullis, Professor Biochemistry, University of BC (UBC) Co-founder of Acuitas Therapeutics, Lipid Nanoparticle Technology, Vancouver, Canada (20' +5')

mRNA -Vaccines on the Fast Track – How Polymun Contributed to Tackle the Pandemic

Dr. Andreas Wagner, Head Liposomal Formulation, Polymun Scientific Immunbiologische Forschung GmbH, Klosterneuburg, Austria (20' +5')

mRNA Based Therapeutics

Dr. Patrick Baumhof, Vice President Formulation & Delivery, CureVac AG, Tübingen, Germany (20' +5')

Lessons from Plants for RNA-based Anti-viral Strategies in Animals and People

Professor Dr. Sir David Baulcombe FRS, Regius Professor of Botany, Royal Society Research Professor and Head of the Department of Plant Sciences, The Cambridge Conservation Initiative (CCI), University of Cambridge, Cambridge, United Kingdom (20' +5')

Some Learnings Made from Preclinical Concept to Clinical Translatability in Nanomedicinal approaches

Dr. Michael Keller, Senior Principal Scientist, Pre-Clinical CMC Pharma Research and Early Development, Roche Innovation Center Basel, Basel (20' +5')

The mRNA Research Platform at Moderna Therapeutics

Prof. Dr. Melissa Moore, Moderna Therapeutics, Chief Scientific Officer, Research Platform Moderna, Cambridge, MA, USA (20' +5')

Vaccination Strategies in Constrained Vaccine Availability Settings

Prof. Dr. med. Patrick Hunziker, Deputy Head of the Intensive Care Unit, University Hospital Basel, President of the International Society for Nanomedicine, Basel, Switzerland (20' +5')

Further Questions (30')

Debate in Zoom room after Meeting possible (45')

End of CLINAM-Debate 1

Time Conversion

European CEST Time 04.15 pm - 20.15 pm

Vancouver Time 07.15 am - 11.15 am

Cambridge Time 10.15 am - 2.15 pm

London Time 03.15 pm - 07.15 pm

Israel Time 05.15 pm - 09.15 pm

Registered participants will receive their link too access one week before the meeting



Yechezkel Barenholz

Professor Emeritus Yechezkel (Chezy) Barenholz is head of the Liposome and Membrane Research Lab at the Hebrew University-Hadassah Medical School, Jerusalem, Israel and is also the Daniel G. Miller Professor in Cancer Research at Hebrew University of Jerusalem. He has been on the faculty at Hebrew University since 1968 and has been a visiting Professor at leading Universities around the world.

His current research focuses on the development of drugs and nano-drugs based on drug delivery systems (DDS) best exemplified by the anticancer Doxil®, the first liposomal drug as well as the first nano-drug approved by the FDA (1995) with over 700,000 cancer-patients treated so-far world-wide. Few of the liposomal drugs he and his team developed are now at different stages of pre-clinical and clinical stages. Professor Barenholz is an author of >420 scientific publications, cited >35,500 times, with h-index 93 Barenholz is a co-inventor in > 55 approved patent families >50% of them licensed. He is a founder of four 6 start-ups, NasVax (now Therapix) Moebius, PolyPid, LipoCureRX, RebioticsRX, and Ayana Pharma. He received many National and International awards including Honorary Doctorate degree from the Technical University of Denmark (2012) and the 2012 founders award of the International Controlled Release Society.



David Baulcombe

Dept. Plant Sciences, University of Cambridge, Downing Street, Cambridge CB2 3EA

PROFESSIONAL MEMBERSHIPS

Society for Experimental Biology, Society for General Microbiology, Biochemical Society, Genetics Society, Royal Society, National Academy of Sciences USA

HONOURS AND AWARDS

- Major Awards and recognition
- Gruber Genetics Prize (2014) Gruber Foundation USA (shared with Ambros and Ruvkun)
- Balzan Prize (2012) (for epigenetics) Balzan Foundation, Rome
- Wolf Prize for Agriculture (2010) Wolf Foundation Israel
- Knight Bachelor, (Queens Birthday Honours list 2009)
- Albert Lasker Award for Basic Medical Research (2008) Lasker Foundation (shared with Ambros and Ruvkun)
- Royal Medal (2006) The Royal Society
- Foreign Associate Member of the National Academy of Sciences (USA) (elected 2005)
- Fellow of the Royal Society (elected 2001)

CURRENT RESEARCH INTERESTS

Since 1973, when I started my research career, I have thought that one of the major challenges in biology is understanding of gene regulation in plants and animals. Genes are switched on and off during development and in response to the environment so that biology at molecular, organismal and population levels would be informed by knowledge about gene regulation. It has been the underlying theme throughout my research career. I work on plants but the general concepts and many of the mechanisms are common to all parts of the tree of life and my work has had impact in diverse areas including agriculture and biomedicine.



Patrick Baumhof

Vice President Formulation & Delivery 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. Currently he is heading the department for Product design an formulations and is Program manager for the RNAoptimizer Program.

RECENT PUBLICATION

- Proximity Ligation Assays for In Situ Detection of Innate Immune Activation: Focus on In Vitro-Transcribed mRNA Emmeline L. Blanchard, Kristin H. Loomis, Sushma M. Bhosle, Daryll Vanover, Patrick Baumhof, Bruno Pitard, Chiara Zurla, Philip J. Santangelo Mol Ther Nucleic Acids. 2019 Mar 1; 14: 52–66. PMID
- Unmodified mRNA in LNPs constitutes a competitive technology for prophylactic vaccines; Johannes Lutz, Sandra Lazzaro, Mohamed Habbadine, Kim Ellen Schmidt, Patrick Baumhof, Barbara L. Mui, Ying K. Tam, Thomas D. Madden, Michael J. Hope, Regina Heidenreich, Mariola Fotin-Mleczek; NPJ Vaccines. 2017; 2: 29
- Sequence-engineered mRNA Without Chemical Nucleoside Modifications Enables an Effective Protein Therapy in Large Animals; Andreas Thess, Stefanie Grund, Barbara L Mui, Michael J Hope, Patrick Baumhof, Mariola Fotin-Mleczek, Thomas Schlake; Mol Ther. 2015 Sep; 23(9): 1456–1464.
- A novel, disruptive vaccination technology: Self-adjuvanted RN-Active® vaccines; Karl-Josef Kallen, Regina Heidenreich, Margit Schnee, Benjamin Petsch, Thomas Schlake, Andreas Thess, Patrick Baumhof, Birgit Scheel, Sven D Koch, Mariola Fotin-Mleczek; Hum Vaccin Immunother. 2013 Oct 1; 9(10): 2263–2276



Pieter R. Cullis

Scientific Director and CEO, NanoMedicines Innovation Network
Professor, Department of Biochemistry and Molecular Biology - UBC

My research interests concern the roles of lipids in biological membranes and the development of nanomedicines using lipid nanoparticle (LNP) technology to deliver small molecule drugs and macromolecular “genetic” drugs *in vivo*. Studies on the roles of lipids concern the ability of membrane lipids to adopt non-bilayer structures (including the roles of such structures in processes such as membrane fusion) and transport processes across bilayer lipid systems induced by trans-bilayer ion gradients. My interests in nanomedicines are first: development of nanomedicines employing LNP delivery systems containing small molecule drugs, particularly drugs used in cancer chemotherapy, with the aim of increasing potency and reducing toxicity by enhancing drug delivery to, and release at, sites of disease such as tumours and second: designing nanomedicines based on LNP technology that enable the therapeutic use of macromolecular genetic drugs such as small interfering RNA (siRNA), antisense oligonucleotides, mRNA and plasmids for gene therapy, including gene editing. These efforts have led to four nanomedicines that have been approved for clinical use by regulatory agencies such as the US Food and Drug Agency (FDA), the European Medicines Agency and Health Canada. Seven other nanomedicines are in clinical testing (see Table below). Of particular note is the drug Onpattro, a gene therapy that was approved (August 2018) by the FDA to treat a disease known as

hereditary amyloid transthyretin (hATTR) amyloidosis. Onpattro is the first RNAi-based drug to be approved by the FDA and employs an LNP delivery system developed in collaboration with Alnylam Pharmaceuticals (Boston), my UBC laboratory and two spin-offs that I co-founded (Arbutus Biopharma and Acuitas Therapeutics). Onpattro delivers an siRNA to silence the TTR gene in the liver. A remarkable feature of Onpattro is that it appears able to not only stop further progression of this hitherto untreatable disease (which usually leads to death within five years of diagnosis), but also to reverse the neuropathies and cardiovascular issues associated with hATTR.

(LNAs), with a particular focus on disruptive concepts to enable enhanced delivery of LNA.



Patrick Hunziker

Patrick Hunziker has studied Medicine at the University of Zurich, Switzerland. He received a doctoral degree based on thesis work in experimental immunology from the University of Zurich and did further research in experimental haematology at University Hospital in Zurich, Switzerland. He earned specialist degrees in Internal Medicine, Cardiology and Intensive Care Medicine. As a fellow at the Massachusetts General Hospital, Harvard Medical School, worked on cardiac imaging in a joint project with the Massachusetts Institute of Technology, Cambridge. 2008 Patrick Hunziker became professor for Cardiology and Intensive Care Medicine at the University of Basel. His professional activities in Europe, the U.S., Africa and China gave him a broad insight into the needs for the medicine of the future in a variety of settings. Hunziker became involved in medical applications of Nanoscience in the late nineties and has been the pioneer physician in Nanomedicine in Switzerland since then. With improved prevention, diagnosis and cure of cardiovascular disease as his main research topic, he worked in the nanoscience fields of atomic force microscopy, nanoptics, micro/nanofluidics, nanomechanical sensors and polymer nanocarriers for targeting. He is the co-founder of the European Society of Nanomedicine, co-founder of the European Foundation for Clinical Nanomedicine and co-initiator of the European Conference for Clinical Nanomedicine and is clinically active as deputy head of the Clinic for Intensive Care Medicine at the University Hospital Basel, Switzerland. After being founding president of the European Society for six years he was elected as President of the International Society for Nanomedicine, which is uniting members from all continents in the world and realizes regular Summer schools on Nanomedicine.



Michael Keller

Michael Keller studied Chemistry & Biochemistry at the ETH Zürich from 1989-1994. The award of the ETHZ-Imperial College London exchange scholarship 1994 enabled him to pursue a MSc/DIC in Chemical Research at Imperial College London, before joining the Research group of Professor Manfred Mutter at the University of Lausanne where he carried out a PhD in Bioorganic Chemistry. After a year as lecturer at the same Institute, he joined Imperial College London Genetic Therapies Centre as Academic Visitor specializing in nonviral delivery systems for nucleic acids. He co-founded the Anglo/Japanese Biotech company IC-Vec Ltd. in 2002 developing novel cationic lipids and nanomedicines for siRNA delivery, before joining Novartis Pharma AG Basel to build up siRNA formulation in Technical Research & Development. He was awarded the Novartis Leading Scientist Award in 2009 for his work on siRNA delivery. In late 2017 he joined the preclinical CMC unit at Hoffmann-La Roche Ltd. Basel to work on locked nucleic acids



Beat Löffler

Born in Basel. After a study visit in the USA, he studied Philosophy, Communication Sciences and Politics at Free University in Berlin, (Master of Arts, magna cum laude.) He further developed his skills in Biology and Medicine absolving the training of the European Center of Pharmaceutical Medicine. 2014 he received an MD h.c. from the University Basel. In 1984 he co-founded an Agency for New Media. From 1988 to 1994 he was Head of the International Hightech Forum Basel organizing congresses on new technologies in mobility, energy, CFD and medical technology. 1994 he founded his own company „L & A concept engineering“ for translation of science-based visions and establishment of worldwide networks (mission and strategy for realizing visions). Six years Secretary General/coach of the trinational BioValley Promotion Team, (Upper-Rhine Biotechnology network). 2003-06 mandated by NEC Hightech Performance Computing in charge of the Life Sciences Business Development in Biology/ Medicine. 2007 founded with Prof. Patrick Hunziker, MD the European Foundation for Clinical Nanomedicine. He launches the annual SUMMITS, the European Journal of Nanomedicine, (new open access Journal CLIN-AM Precision Medicine). He cofounded the European Society and the International Society for Nanomedicine. He is head of dissemination in several framework programme projects and in the EU-flagship Application Team DigiTwins for the chapter Nanomedicine. New are the virtual Debates that replace seminars and summer schools during the pandemic. Nanomedicine, (ISNM) which realizes every year a Nanomedicine Summer school.



Melissa Moore

In her role as Chief Scientific Officer, Platform Research, Dr. Melissa Moore is responsible for leading mRNA biology, delivery and computation science research at Moderna. She joined Moderna in 2016 from the University of Massachusetts Medical School (UMMS), where she served as Professor of Biochemistry & Molecular Pharmacology, Eleanor Eustis Farrington Chair in Cancer Research and a long-time Investigator at the Howard Hughes Medical Institute (HHMI). Dr. Moore was also a founding Co-Director of the RNA Therapeutics Institute (RTI) at UMMS, and was instrumental in creating the Massachusetts Therapeutic and Entrepreneurship Realization initiative (MasSTERi), a faculty-led program intended to facilitate the translation of UMMS discoveries into drugs, products, technologies and companies. Dr. Moore is an elected member of the National Academy of Sciences (2017) and a Fellow of the American Academy of Arts and Sciences (2019). Dr. Moore holds a B.S. in Chemistry and Biology from the College of William and Mary, and a Ph.D. in Biological Chemistry from MIT, where she specialized in enzymology under Prof. Christopher T. Walsh. She began working on RNA metabolism during her postdoctoral training with Phillip A. Sharp at MIT. During her 23 years as faculty member, first at Brandeis and then at UMMS, her research encompassed a broad array of topics related to the roles of RNA and RNA-protein (RNP) complexes in gene expression, and touched on many human diseases including cancer, neurodegeneration and preeclampsia.



Andreas Wagner

Dr Andreas Wagner is currently the Head of Liposome Technology at Polymun Scientific GmbH in Klosterneuburg, Austria. He has significant expertise in development and optimization of liposomal drug products. Over the last 15 years, his group guided approx. 15 different liposomal drug products into clinical trials. He studied Biotechnology in Vienna,

Austria and earned his Master and Ph.D. degrees in the field of liposomology at the Institute of Applied Microbiology supervised by Prof. Hermann Katinger and Prof. Karola Vorauer-Uhl. Dr Andreas Wagner is listed as inventor on several patents, like the liposome technology and some product patents of liposomal formulations and he has published several peer reviewed articles dealing with liposomes, the technology, products thereof and their application in preclinical and clinical studies. Since 2001, he built up the liposome technology unit at Polymun Scientific GmbH.

Polymun Scientific is a private Austrian company, located in Klosterneuburg, offering contract development and manufacturing of biopharmaceuticals as well as development and production of liposomal formulations. Its patented liposome/LNP technology allows efficient manufacturing of constantly high quality in small and large scale. Over the last 10 years, Polymun has guided more than 15 liposomal formulations into clinical trials, amongst them DNA and different kinds of RNA formulations. Polymun is an FDA- and EMA-inspected manufacturer conducting several own R&D projects. For more information, please visit www.polymun.com

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