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1st International mRNA Health Conference

October 23-24, 2013 - Tübingen, Germany

Programme

www.mrna-conference.com

CUREVAC
the RNA people®

In memoriam Friedrich Miescher
(August 13, 1844 – August 26, 1895)

Imprint

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Summary

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Greetings from the Initiators

Dear colleagues,

It is my exquisite pleasure to welcome you to the 1st International mRNA Health Conference in Tübingen. This is a premiere and we are fully confident that the Conference - and the city around it - will surpass your expectations.

Messenger RNA (mRNA)-based gene transfer presents several remarkable advantages over traditional gene therapy methods: by entirely avoiding the danger of insertional mutagenesis, the *in vivo* manipulation of cells with mRNA is considered to be a valuable and safe alternative.

Recently, we and others have shown that by incorporating nucleotide modifications into therapeutic mRNA, rare as well as more prevalent diseases could be treated in respective mouse models. This demonstrates the fascinating potential of the delivery of modified mRNA for the treatment of inherited diseases, especially for those in which no other treatment options are currently available.

We believe that modified mRNA is a viable alternative to current and developing protein or gene therapies and certainly will pave the way for further therapeutic developments.

We are delighted to have you here in Tübingen and we wish you fruitful discussions and a wonderful time.

Michael Kormann
University of Tübingen

Dear colleagues,

We would like to welcome you to the 1st International mRNA Health Conference.

Messenger (m) RNA is a universal biomolecule with tremendous potential for many therapeutic applications. In the 90s, DNA was regarded as a revolutionary approach for gene therapy, but its promise was never realized. Meanwhile, mRNA, the forgotten biomolecule, remained the research focus of a certain group of scientists, including those at CureVac, a University Tübingen spin off.

This continuous research has led to fabulous progress in the field and has deepened our understanding of the unique properties of mRNA. We have overcome many of mRNA's limitations, such as instability, and today, we have not only learned how to stabilize and manipulate mRNA, we are actually transforming mRNA into an entirely new class of therapeutic molecule with wide-ranging applications.

In fact, we have recently seen the first successful human proof-of-concept studies for mRNA as a cancer immunotherapeutic.

We are looking forward to a successful conference that will set the course for new, fruitful collaborations and the establishment of a novel biotechnology sector. The foundation will be set here in Tübingen, where Friedrich Miescher did his groundbreaking work on nucleic acids in 1869.

Ingmar Hoerr
CEO and Co-founder of CureVac

Conference Program

Wednesday, October 23, 2013

8:00 am — Opening registration and reception

9:00 am — Welcome remarks by
Herbert Müther, Prorector of Research, University of Tübingen

Boris Palmer, Lord Mayor of Tübingen

Michael Kormann, University of Tübingen, Initiator of the Conference

Ingmar Hoerr, CEO and Co-founder of CureVac, Initiator of the Conference

Introductory Session: Principles and impact of mRNA as a therapeutic biomolecule

9:45 am — Chair Introduction by Hans-Georg Rammensee, University of Tübingen

9:50 am — Katalin Kariko, University of Pennsylvania
Nucleoside-modified mRNA for therapy

10:20 am — Karsten Henco, HS LifeSciences
Principles and impact of mRNA as a therapeutic biomolecule

10:50 am — Coffee break (20 minutes)

Lecture Session 1: mRNA based therapeutic vaccines in the field of oncology

11:10 am Chair Introduction by Christian Mandl, Novartis, and Ugur Sahin, BioNTech

11:15 am Peter Brossart, University of Bonn
Development of RNA based vaccines

11:45 am Ugur Sahin, BioNTech
mRNA for personalized oncology

12:15 am Kris Thielemans, University of Brussels
Dendritic cell based immunotherapy of melanoma: the Brussels' experience

12:45 am ***Lunch break (60 minutes)***
Exclusively sponsored by TriLink

1:45 pm Benjamin Weide, University of Tübingen
mRNA-based vaccination in malignant melanoma

2:15 pm Ulrike Gnad-Vogt, CureVac
Vaccination with self-adjuvanted mRNA vaccines (RNActive®) targeting multiple antigens for the treatment of prostate cancer and non-small cell lung cancer

Lecture Session 2: mRNA based protein therapeutics – Part 1

2:45 pm Chair Introduction by Katalin Kariko, University of Pennsylvania, and Stephane Bancel, Moderna Therapeutics

2:50 pm Michael Kormann, University of Tübingen
In vivo delivery of chemically modified mRNA

3:20 pm Carsten Rudolph, ethris
Stabilized non-immunogenic messenger RNA (SNIM® RNA) for transcript therapy

3:50 pm ***Coffee break (30 minutes)***

4:20 pm Gregory Cost, Sangamo BioSciences
Zinc-finger and TALE nuclease mRNA effect animal transgenesis and human therapy

4:50 pm Stephane Bancel, Moderna Therapeutics
Challenges of building a biotech company with a new drug modality

5:20 pm Igor Splawski, Novartis Institutes for BioMedical Research
In vivo expression of modified mRNA for the correction of inherited disorders

5:50 pm ***Coffee break (20 minutes)***

6:10 pm **Panel Discussion: Establishing the field and industry**
Chaired by: Friedrich von Bohlen, dievini
Panellist: Karsten Henco, HS LifeSciences
Igor Splawski, Novartis Institutes for BioMedical Research
Stephane Bancel, Moderna Therapeutics
Brad Guild, Pfizer
Valérie Lecouturier, Sanofi Pasteur

8:00 pm - 11:00 pm **Networking Evening in the Hohentübingen Castle**
Exclusively sponsored by Thermo Fisher Scientific

Thursday, October 24, 2013

8:00 am Opening reception

9:00 am Welcome remarks to the second conference day by the initiators

Lecture Session 2: mRNA based protein therapeutics – Part 2

9:10 am Chair Introduction by Michael Kormann, University of Tübingen, and Gregory Cost, Sangamo BioSciences

9:15 am Ian MacLachlan, Tekmira Pharmaceuticals
Lipid Nanoparticle-Mediated Delivery of Messenger RNA

9:45 am Frank DeRosa, Shire
Messenger RNA Therapy (MRT) Platform: Protein Therapy for Multiple Therapeutic Categories

10:15 am Pierrot Harvie, PhaseRx
SMARTT Polymer Technology® Targets and Delivers mRNA to the Liver

10:45 am Coffee break (20 minutes)

Lecture Session 3: mRNA based vaccines for infectious diseases and allergy

11:05 am Chair Introduction by Josef Thalhamer, University of Salzburg, and Kris Thielemans, University of Brussels

11:10 am Stefaan de Koker, Ghent University
Type I IFN in mRNA based vaccination: an unusual suspect?

11:40 am Christian Mandl, Novartis
Alphavirus-Vectored Vaccines: From VRP to SAM® RNA vaccines

12:10 am Annette Vogel, Federal Research Institute for Animal Health Germany
Protective efficacy of mRNA vaccines against influenza A virus infection

12:40 am Lunch break (40 minutes)
Exclusively sponsored by TriLink

1:20 pm Josef Thalhamer, University of Salzburg
mRNA vaccines: The save way to immunize against type I allergy

1:50 pm Ulrich Kalinke, Twincore
RNAdjuvant® is a novel immune enhancer which induces local cytokine responses that augment anti-viral protection

Lecture Session 4: Production and regulatory aspects

2:20 pm Chair Introduction by Benjamin Weide, University of Tübingen

2:25 pm Florian von der Mülbe, CureVac
GMP manufacturing of RNA – a knowledge-based platform production process

2:55 pm Thomas Hinz, Paul-Ehrlich-Institute
Regulatory Requirements for Recombinant RNA-Based Therapies

3:25 pm Coffee break (20 minutes)

3:45 pm **Panel Discussion: Regulatory aspects and classification of mRNA**

Chaired by: Karl Josef Kallen, CureVac
Panellist: Thomas Hinz, PEI
Christian Mandl, Novartis
Ulrich Kalinke, Twincore
Michael Heartlein, Shire
Carsten Rudolph, ethris

4:45 pm Wrap-up by the initiators

5:00 pm End of the conference
Optional: CureVac company visit

Short abstracts to the lectures

Introductory Session: Principles and impact of mRNA as a therapeutic biomolecule

October 23 – 9:50 am
Katalin Karikó, University of Pennsylvania
Nucleoside-modified mRNA for therapy

In vitro-transcribed mRNAs encoding therapeutic proteins have great potential for clinical applications. Incorporation of naturally modified nucleosides, such as pseudouridine, into mRNA confers enhanced biological properties. Pseudouridine-containing mRNAs are non-immunogenic and translate with higher efficiency than unmodified mRNAs. We recently demonstrated that delivering submicrogram quantities of erythropoietin-encoding mRNA into mice caused a significant increase in reticulocyte counts and hematocrits, thus demonstrating the clinical potential of in vitro transcribed mRNA for protein replacement therapy. Nucleoside-modified mRNA offers a new platform for expressing proteins currently in clinical practice with expansion to intracellular proteins that can't be generated with existing therapy.

October 23 – 10:20 am
Karsten Henco, HS LifeSciences
Principles and impact of mRNA as a therapeutic biomolecule

„Gene therapy without genes" seems to be a learning session from the setbacks of gene therapy experienced over the recent decade. The mRNA molecule and its derivatives surprisingly proved its potency as drug candidates, vaccines or protein substitutes upon transfection. The lack of any retro-transcription of mRNAs in normal tissue overcomes any concern of genome-integration mediated activation of e.g. cancer

inducing genes. Modifications of mRNA reduce reactions of the innate immune system to below a detectable level. Nevertheless, successful mRNA application requires as a second technology platform a potent transfection, if possible a tissue related transfection platform. Nobody wants to run the next cycle of RNA-based frustration of potent biomolecules such as siRNA failing due to inefficient cellular uptake in a functional form. With all this being in place, the pharma world seems to face a completely new class of drugs for a large number of unmet medical needs.

Lecture Session 1: mRNA based therapeutic vaccines in the field of oncology

October 23 – 11:15 am
Peter Brossart, University of Bonn
Development of RNA based vaccines

In several preclinical studies we were able to demonstrate that ivtRNA can generate antigen specific CTL that recognize multiple TAA derived epitopes presented on different HLA molecules. Furthermore, in addition to CD8+ responses this approach elicits antigen specific CD4+ T lymphocytes against HLA class II peptides derived from cytosolic antigens as a result of autophagy. We previously finished a clinical trial in patients with metastatic RCC using the intra dermal application of ivtRNA coding for several TAAs. In this clinical trial we were able to show that this approach elicits TAA specific cytotoxic and T-Helper lymphocytes in vivo and results in an improved overall survival of patients responding to the treatment. These vaccine induced T cells recognized several epitopes deduced from the used TAAs and lysed HLA matched tumor cells.

October 23 – 11:45 am
Ugur Sahin, BioNTech
mRNA for personalized oncology

We at BioNTech (Biopharmaceutical New Technologies, Mainz) develop entirely individualized immunotherapies for the tailored treatment of numerous cancers and other diseases with high medical need. BioNTech´s optimized mRNA GMP drug platform (Ribological) was iteratively optimized for more than one decade to deliver any type of mRNA therapeutics with optimal potency, activity and pharmacokinetic properties in vivo. The immunotherapy pipeline includes mRNA cocktails targeting a combination of commonly expressed shared tumor-associated antigens (TAAs) as well as genomics customized treatments tailored to the antigen repertoire and mutations of the patient´s tumor.

October 23 – 12:15 am
Kris Thielemans, University of Brussels
Dendritic cell based immunotherapy of melanoma: the Brussels' experience

Electroporation of DCs with mRNA encoding the full-length tumor antigens should lead to presentation of many epitopes by the patient's unique set of HLA molecules. Moreover, electroporation of DC with mRNA also allows the functional modification of the cellular vaccine. To this goal, we provide three different molecular adjuvants to immature, monocyte derived DCs through electroporation with mRNA coding for CD40L, CD70 and caTLR4 or socalled TriMix mRNA. At our institution, clinical trials in pretreated advanced melanoma patients are being performed. These patients are treated with TriMixDCMEL, a mixture of TriMixDC colectroporated with mRNA encoding a fusion of DC.LAMP and 1 of 4 melanoma associated antigens (gp100, tyrosinase, MAGE-C2 or MAGE-A3).

October 23 – 1:45 pm
Benjamin Weide, University of Tübingen
mRNA-based vaccination in malignant melanoma

Three consecutive investigator-initiated clinical trials were performed since 2003 to treat melanoma patients at the Department of Dermatology, Tübingen. In the first study the vaccine was applied by intradermal injections of autologous amplified tumor-mRNA. In the second trial we used protamine-stabilized mRNA coding for defined melanoma-associated antigens and in the third approach mRNA was applied also by intranodal injections. Target antigens in this latest study were selected based on their expression profile in autologous tumor from a pool of 9 mRNAs. Vaccinations were safe and feasible. Anti-melanoma immune-responses as well as clinical responses were detected in a subset of patients.

October 23 – 2:15 pm
Ulrike Gnad-Vogt, CureVac
Vaccination with self-adjuvanted mRNA vaccines (RNActive®) targeting multiple antigens for the treatment of prostate cancer and non-small cell lung cancer

The RNActive® technology allows generating messenger RNA based vaccines against a variety of protein antigens. Antigens of choice are encoded by a sequence engineered messenger RNA that is translated into proteins after intradermal injection. RNActive® vaccines are self-adjuvanted and activate TLR 7. Phase I/IIA clinical trials demonstrated the safety and immunogenicity of RNActive® vaccines encoding a variety cancer antigens in patients with advanced prostate cancer and non-small cell lung cancer. In these trials immune responses against all encoded antigens could be induced, comprising cellular as well as humoral responses. Further trials, including a randomized placebo controlled phase IIb trial in prostate cancer, are ongoing to test the clinical efficacy of RNActive® vaccination.

Lecture Session 2: mRNA based protein therapeutics

October 23 – 2:50 pm
Michael Kormann, Universitiy of Tübingen
In vivo delivery of chemically modified mRNA

Chemically modified mRNA has recently shown promise as an alternative to traditional gene therapy approaches. We have demonstrated the successful utilization of modified mRNA in both rare and high prevalence lung disease models. First, mRNA encoding for Surfactant Protein B (SP-B) showed life-saving efficacy in a murine model of SP-B deficiency. Secondly, modified Foxp3 mRNA was able to rebalance T helper cell responses and protect against airway hyperresponsiveness and tissue inflammation in a murine model of Th2-driven allergic asthma. mRNA is a promising therapeutic tool for the treatment of diseases where intermittent bursts of gene expression or repeated dosing are favored.

October 23 – 3:20 pm
Carsten Rudolph, ethris
Stabilized non-immunogenic messenger RNA (SNIM® RNA) for transcript therapy

Ethris SNIM® RNA is an enabling platform for „Transcript Therapies“ in a broad variety of medical indications, from hereditary or acquired metabolic diseases to regenerative medicine. SNIM® RNA circumvent TLR activation and thus enables repeated administration of mRNA. Because of its precursor function, SNIM® RNA yields sustained protein production within the body and overcomes short duration effects of recombinant proteins. Ethris has developed proprietary delivery systems for pulmonary, systemic and local SNIM® RNA administration and will present preclinical results from its pulmonary program. Efficient delivery systems and non-immunogenicity are the keys for making mRNA therapeutics reality beyond oncology applications.

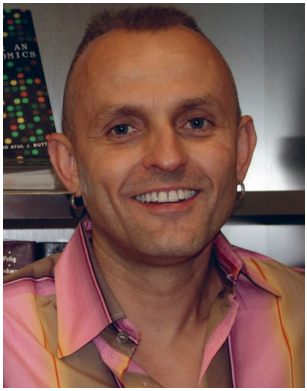
October 23 – 4:20 pm
Gregory Cost, Sangamo BioSciences
Zinc-finger and TALE nuclease mRNA effect animal transgenesis and human therapy

DNA is the traditional nucleic acid for the delivery of exogenous genetic information. We find however, that mRNA is a superior choice for some applications as it produces a short, transient period of higher-level expression with a very low chance of genomic integration. From the creation of genetically engineered cell lines and transgenic animals to the development of genetically modified-cell therapies, mRNA is emerging as a preferred method of gene delivery.

October 23 – 4:50 pm
Stephane Bancel, Moderna Therapeutics
Challenges of building a biotech company with a new drug modality

The biotech sector is filled with companies that never make it. The challenges are compounded when building a biotech company that is trying to develop drugs with a brand new, raw technology. Stephane Bancel, moderna Therapeutics's founding CEO will share his thoughts as well as the actions moderna is taking to increase its odds to bring innovative drugs to patients.

October 23 – 5:20 pm
Igor Splawski, Novartis Institutes for BioMedical Research
In vivo expression of modified mRNA for the correction of inherited disorders



Many inherited diseases result from loss-of-function mutations in one gene, and therapy is often inadequate. Our objective is to develop modified synthetic mRNA therapy for treatment of severe disorders caused by inherited protein deficiency. We encapsulated modified and purified mRNA encoding mouse erythropoietin

(mEPO) in cationic lipid nanoparticles. We achieved high mEPO levels after a low intravenous dose. Subcutaneous or intramuscular administration of identical dose elicited ~10-fold lower levels. Two intravenous doses were sufficient to increase hematocrit. The formulation elicited no cytokine response. We are currently focused on in vivo mRNA expression of therapeutically relevant secreted, intracellular and transmembrane proteins.

October 24 – 9:15 am
Ian MacLachlan, Tekmira Pharmaceuticals
Lipid Nanoparticle-Mediated Delivery of Messenger RNA

Seven products based on Tekmira's lipid nanoparticle (LNP) delivery platform have entered clinical trials providing increasingly robust proof of clinical activity in multiple disease areas using small interfering RNA as the active pharmaceutical ingredient. We have recently applied the LNP technology to the efficient encapsulation and delivery of chemically modified mRNA in preclinical models demonstrating robust expression in numerous tissues and tumours following intravenous administration. These encouraging results, orders of magnitude greater than that achieved using previously published, commercially available delivery agents, suggest that there may be numerous opportunities for the development of mRNA therapeutics using LNP delivery.

October 24 – 9:45 am
Frank DeRosa, Shire
Messenger RNA Therapy (MRT) Platform: Protein Therapy for Multiple Therapeutic Categories

Messenger RNA (mRNA) Therapy is a technology that holds the promise of organs acting as factories to produce proteins for local or systemic therapy. Previous work has shown that mRNA has therapeutic potential; however efficient delivery to required tissue has been difficult to achieve. We present here, successful delivery of mRNA to various regions of the body including the liver, kidney and other tissues

and organs; achieving preclinical proof-of-concept for systemic and local delivery. Examples of supra-physiologic protein production with favorable pharmacokinetics and demonstration of efficacy in various disease models will be discussed.

October 24 – 10:15 am
Pierrot Harvie, PhaseRx
SMARTT Polymer Technology® Targets and Delivers mRNA to the Liver

PhaseRx SMARTT Polymer Technology® has previously been shown to effectively deliver siRNA to hepatocytes in the liver using an N-acetylgalactosamine targeting group. For mRNA delivery, a similar targeted multi-domain polymer has been developed. The mRNA and polymer self-assemble into a 70 nm nanoparticle. The mRNA condensation assessed by SYBRGold assay showed that 26% of the mRNA is dye inaccessible, indicating a strong interaction between the polymer and the mRNA. The mRNA formulation is freeze-thaw stable and imparts serum stability to the mRNA. Mice injected intravenously with polymer formulated FLUC mRNA showed luciferase expression specific to the liver 2-3 logs above background.

Lecture Session 3: mRNA based vaccines for infectious diseases and allergy

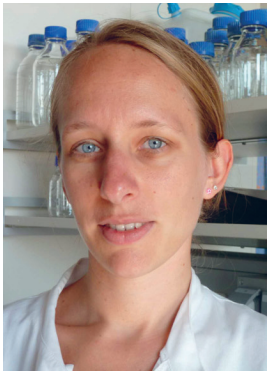
October 24 – 11:10 am
Stefaan de Koker, Ghent University
Type I IFN in mRNA based vaccination: an unusual suspect?

mRNA-lipoplexes are capable of inducing cytotoxic T cells (CTL) following subcutaneous immunization. Transfection of dendritic cells with mRNA-lipoplexes is accompanied by a strong induction of type I IFNs. Remarkably, these type I IFNs decrease the strength of the evoked response, as evidenced by an over tenfold increase in CTL numbers in IFNaR-/- mice. Although type I IFN have positive effects on the quality

of the immune response following immunization with protein antigens, they negatively interfere with the strength of mRNA based vaccination by imposing an antiviral status upon the dendritic cell, resulting in inhibition of antigen translation and diminished antigen presentation.

October 24 – 11:40 am
Christian Mandl, Novartis
Alphavirus-Vectored Vaccines: From VRP to SAM® RNA vaccines

Viral-vectored vaccines mimic viral infections thus providing for an in vivo expression of the antigen, stimulation of the innate immune response and induction of a broad cellular and humoral adaptive response. Alphaviruses have been studied extensively as viral vectors and are characterized by a high antigen expression level. Virus-like replicon particles (VRPs) have been successfully tested in the clinic. We took the system a step further by delivering the alphaviral self-amplifying messenger RNA with synthetic delivery systems. SAM vaccines have achieved immune responses comparable to VRP vaccines in various animal models.



October 24 – 12:10 am
Annette Vogel, Federal Research Institute for Animal Health Germany
Protective efficacy of mRNA vaccines against influenza A virus infection

Influenza A viruses (IAVs) have a segmented genome and effective vaccination is challenging. Especially the reassortment points out the need for a new technology that allows rapid adaptation of vaccines. In this context, mRNA vaccines for prophylactic vaccination against IAVs were designed. In mice, immunogenicity and/or protective efficacy were analyzed. The mRNA vaccines induce protective immunity, elicite B and T cell–dependent protection and target multiple antigens, including the highly conserved viral nucleoprotein, indicating its usefulness as a cross-protective vaccine. Thus, mRNA vaccines could address substantial medical need in the area of influenza prophylaxis and extend the field of anti-infective vaccinology.

October 24 – 1:20 pm
Josef Thalhamer, University of Salzburg
mRNA vaccines: The save way to immunize against type I allergy

The prevalence of type I allergic diseases within the populations of industrialized countries has reached about 25%. The only approved therapeutic approach, specific immunotherapy (SIT), solely transiently mitigates allergic symptoms, and harbours frequent side effects, altogether leading to a poor patient compliance.
These facts have changed the attitude towards protective anti-allergic approaches, and gene vaccines turned out to be ideal candidates to prevent from allergic sensitization. Among the nucleic acid-based vaccines, mRNA proved to be highly effective and superior with respect to the stringent safety criteria required for allergy prophylaxis.

October 24 – 1:50 pm
Ulrich Kalinke, Twincore
RNAdjuvant® is a novel immune enhancer which induces local cytokine responses that augment anti-viral protection

Amongst new adjuvants conferring enhance-ment of vaccine-induced anti-viral immunity by inducing a Th1 shift, RNA is a promising candidate. We studied the effect of RNAdju-vant® formulated of non-coding mRNA stabi-lized with a cationic carrier peptide. After i.m. administration of RNAdjuvant® induction of local type I IFN as well as local activation of immune cells was detected only within the draining lymph node. Co-injection of a vaccine together with RNAdjuvant® enhanced virus neutralizing IgG responses as efficiently as the mouse prototype adjuvant poly(I:C). Thus, in the rodent model RNAdjuvant® is an efficacious and locally active adjuvant.

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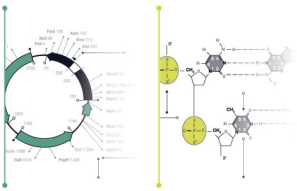

Large Scale and Custom Products for mRNA Synthesis

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- Nucleic Acid Labeling and Detection
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- Custom Packaging, Labeling and Kit assembly

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Lecture Session 4: Production and regulatory aspects

October 24 – 2:25 pm
Florian von der Mülbe, CureVac
GMP manufacturing of RNA – a knowledge-based platform production process

Investments and risks associated with drug development are immense. Especially with regard to production development, high costs are generated at risk at a very early time point, and these are repeated for each drug product. A real platform production process could facilitate drug development. By enhancing product and process understanding, RNA production is able to provide for a variety of products. This could fulfill business needs as well as the expectations of authorities for an increased drug product quality. CureVac has 10 years of experience in RNA manufacture and can build on a multitude of manufactured products. On this basis RNA production can enable a Quality by Design approach.

October 24 – 2:55 pm
Thomas Hinz, Paul-Ehrlich-Institute
Regulatory Requirements for Recombinant RNA-Based Therapies

The clinical development of in vitro transcribed mRNA has been initiated a few years ago in Germany by clinical research groups and biotech-companies. Tumor antigen-encoding mRNA is either transcribed from linearized plasmids or whole tumor cell mRNA is transcribed. The in vitro generated recombinant mRNAs are either directly administered to patients or they are loaded onto antigen-presenting cells ex vivo which are then used as the final medicinal product. The EU and national regulatory environment applicable to mRNA and cell-based medicinal products will be discussed in this presentation.

Panel Discussions

Wednesday, October 23 – 6:10 pm

Panel Discussion: Establishing the field and industry

Chaired by Friedrich von Bohlen, dievini
Panellist: Karsten Henco, HS LifeSciences
Igor Splawski, Novartis Institutes for BioMedical Research
Stephane Bancel, Moderna Therapeutics
Brad Guild, Pfizer
Valerie Lecouturier, Sanofi Pasteur

Nature has always been the place for best drug choices. Proteins and their pathways are the focus for many diseases and their treatment. DNA finally seems to make it – somehow. mRNA, long ignored and underestimated, bears all the advantages to educate the immune system and/or replace defective proteins e.g. to help reconstitute broken pathways. Sounds too good to be true? Not if you look at biology. The missing link was mRNA's stability. This has been overcome and is thus opening a door for seemingly unlimited treatment options and choices. The potential of mRNA therefore looks even broader than it did for antibodies some 35 years ago.

Here are only some of the many questions about the return – or should we better say arrival – of the lost son:

- Where can we expect mRNA in future medicine and therapy?
- Where can mRNA therapy be additive, where disruptive?
- What are the challenges in replacement therapy, what in immunotherapy?
- How safe is mRNA, which safety concerns may come along?
- What can mRNA therapies learn from other platform approaches – and where is it unique?
- What are cost drivers in mRNA production, logistics and application?
- How can we as drivers and players of this emerging field and industry contribute and make it happen? Beyond our individual goals and possible competition?

Thursday, October 24, 2013 – 3:45 pm

Panel Discussion: Regulatory aspects and classification of mRNA

Chaired by: Karl Josef Kallen, CureVac
Panellist: Thomas Hinz, Paul-Ehrlich-Institute
Christian Mandl, Novartis
Ulrich Kalinke, Twincore
Carsten Rudolph, ethris
Michael Heartlein, Shire

mRNA is emerging as the basis for new prophylactic and therapeutic immunization strategies as well as protein replacement strategies. Nucleotides are the basis of DNA and mRNA. Whilst the former defines genes, carries the genomic information and transmits it to the next generation, the latter only serves to translate the genetic information into proteins. Yet some authorities classify mRNA based approaches as gene therapy, others do not and a third fraction takes a position somewhere in the middle. Moreover, since mRNA only provides a protein code, the same chemical moiety can define very different proteins. This fact can be a challenge, but also an opportunity. Similarly, the production of mRNA based vaccines and therapeutics encounters challenges and opportunities that are different from DNA based drugs, and necessitates the definition of the regulatory requirements surrounding manufacturing. The issues around development and manufacturing of mRNA based vaccines and drugs will be discussed in a round table discussion between experts from regulatory authorities, industry and academia that have propelled the field ahead in recent years.

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Tides Service Technology (TST) Group

Tides Service Technology (TST) was founded in Germany in 2004 by Ludwig Stoeckl.

TST is distributor of Biolytic Lab Performance and PSI Scientific.

Ludwig Stoeckl has a wide experience in the DNA field having previously Co-founded two custom oligo synthesis companies, both who continue to operate successfully. Previously to this he was a field service engineer for ABI, supporting the dna- and peptide instruments.

Other engineers within TST have extensive experience with the „Expedite“, Akta Oligo Pilot, Akta Purifier, Akta Explorer and the Protein Technologies Peptide Synthesizers, complementing the range of oligo and peptide synthesizers supported by TST.

In total Tides Service has a combined experience of over 40 years in the oligo, dna- and peptide applications.

New England Biolabs

New England Biolabs, Inc. is the industry leader in the discovery and production of enzymes for molecular biology applications, and now offers the largest selection of recombinant and native enzymes for genomic research. NEB continues its tradition of providing high quality reagents to support RNA research, and supplies tools for the synthesis, processing, analysis, amplification, cloning and sequencing of RNA molecules. NEB’s expertise in developing and manufacturing products of the highest quality, coupled with best in class technical support makes NEB a first choice for customers demanding optimized reagents for advanced technologies.

TTR
Technologiepark Tübingen-Reutlingen

Kreissparkasse Tübingen

Promotion partner

BioRegio STERN

Initiating Company

CureVac
CureVac is a clinical stage biopharmaceutical company from Tübingen, Germany, that uses its technology platforms for the development of novel therapeutic mRNA vaccines (RNActive®) for cancer and prophylactic vaccines for infectious diseases.

Furthermore CureVac develops adjuvants based on non-coding RNAs (RNAdjuvant®) for enhancing the immune response of other vaccines. The company has successfully completed Phase I/IIa studies with its RNActive® cancer vaccines in prostate cancer and non-small cell lung cancer (NSCLC). Results so far have shown that mRNA-based products are safe and capable of inducing balanced immune responses including humoral and cellular, Th1 and Th2 and effector and memory responses. CureVac is currently running a number of clinical trials with its RNActive® based vaccines, including a large randomized Phase IIb clinical trial in prostate cancer. In addition to developing its own pipeline, CureVac is collaborating with Sanofi Pasteur and In-Cell-Art on a $33.1 million project co-funded by Defense Advanced Research Projects Agency (DARPA) for the development of prophylactic vaccines in infectious diseases utilizing its RNActive® technology platform.

For more information,
please visit *www.curevac.com.*

CUREVAC
the RNA people®