INTERNATIONAL EGE-AGEM VACCINE SYMPOSIUM

September 1-2, 2022

Ege University Vaccine Development Application and Research Center

Bornova/İzmir, Turkiye

ABSTRACT BOOK

Organized by Ege University Vaccine Development Application and Research Center

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SCIENTIFIC PROGRAMME OF INTERNATIONAL EGE-AGEM VACCINE SYMPOSIUM

September 1-2, 2022

September 1

09:00-09:30 Registration

09:30-10:00 Opening Talks
Adnan Yüksel GÜRÜZ, Ph.D., Prof.
Director of EGE-AGEM

10:00-10:15 Coffee Break

10:15-11:30 *Moderators: Adnan Yüksel GÜRÜZ, M.D., Ph.D., Prof.*

10:15-10:30 History of Vaccine Technology
Adnan Yüksel GÜRÜZ, M.D., Ph.D., Prof.
Ege University Faculty of Medicine, Department of Parasitology
Ege University Vaccine Development Application and Research Center

10:30-10:45 COVID-19 DNA Vaccine Platform
Mert DÖŞKAYA M.D., Ph.D., Assoc. Prof.
Ege University Faculty of Medicine, Department of Parasitology
Ege University Vaccine Development Application and Research Center

10:45-11:00 DNA vaccines against Parasitic Infections
[1,2]Muhammet KARAKAVUK (Ph.D., DVM) and [2,3]Hüseyin CAN (Ph.D., Assoc. Prof.)
[1]Ege University Odemis Vocational School
[2]Ege University Vaccine Development Application and Research Center
[3]Ege University Faculty of Science Department of Biology Molecular Biology Section

11:00-11:15 Devolopment of DNA Vaccines against SARS-CoV-2
Aytül GÜL, MSc
Ege University Faculty of Engineering Department of Bioengineering
Ege University Vaccine Development Application and Research Center

11:15-11:30 mRNA Vaccines against Parasitic Infections
Hüseyin CAN, Ph.D., Assoc. Prof.
Ege University Faculty of Science Department of Biology Molecular Biology Section,
Ege University Vaccine Development Application and Research Center

11:30-12:00 Coffee Break

12:00-13:15 *Moderator: Gülten KANTARCI Ph.D., Prof.,*

12:00-12:15 Potential of extracellular vesicles as vaccines
Mustafa KOTMAKÇI Ph.D., Assoc. Prof.
Department of Pharmaceutical Biotechnology, Faculty of Pharmacy, Ege University

12:15-12:30 The Role of the Resident Memory T-cells in Immune Response and Vaccine Studies
Hasan AKBABA, Ph.D., Assoc. Prof.
Department of Pharmaceutical Biotechnology, Faculty of Pharmacy, Ege University

12:30-12:45 Formulation and Stabilty Aspects of the BioNTech Vaccine comirnaty
Yücel BAŞPINAR, Ph.D., Assoc. Prof.
Department of Pharmaceutical Biotechnology, Faculty of Pharmacy, Ege University

12:45-13:00 Immune Checkpoint Gene Knockout Phenomenon as a Potential Anticancer Vaccine
Gülşah EREL AKBABA, Ph.D., Assoc. Prof.
Department of Pharmaceutical Biotechnology, Faculty of Pharmacy, Izmir Katip Çelebi University

13:00-13:15 Cancer Vaccines
Bilge DEBELEC BÜTÜNER, Ph.D., Assoc. Prof.
Department of Pharmaceutical Biotechnology, Faculty of Pharmacy, Ege University

13:15-14:45 Lunch

14:45-16:00 *Moderator: Cemal ÜN, Ph.D., Prof.*

14:45-15:00 Biostatistics techniques used in vaccine development
Şengül CAN, Ph.D.
Computer Research and Application Center, Manisa Celal Bayar University, Manisa, Turkey

15:00-15:15 Transmission-blocking antigens in the development of vaccines against arthropod vector-borne diseases
Ahmet Efe KÖSEOĞLU, Ph.D., Asst. Prof.
Biruni University, Faculty of Engineering and Natural Sciences, Department of Molecular Biology and Genetics, Istanbul, Turkey

15:15-15:30 Strains and plasmids commonly used in vaccines based on Saccharomyces cerevisiae
Tuğba KARAKAVUK, BSc
Ege University, Institute of Science, Department of Biotechnology,
Ege University Vaccine Development Application and Research Center

15:30-15:45 Immune response induced by vaccines against parasitic agents
Aysu DEĞİRMENCİ DÖŞKAYA M.D., Ph.D., Assoc. Prof.
Ege University Faculty of Medicine, Department of Parasitology
Ege University Vaccine Development Application and Research Center

15:45-16:00 COVID-19 Vaccines
Seren KAPLAN, BSc
Ege University Vaccine Development Application and Research Center

September 2

10:15-11:00 *Moderator: Mert DÖŞKAYA, M.D., Ph.D., Assoc. Prof.*

10:15-10:30 Anti-Vaccination: History and Reasons
Sedef ERKUNT ALAK, Ph.D.,
Ege University Vaccine Development Application and Research Center

10:30-10:45 Backbone of Plasmid DNA vaccines
Ceren GÜL, BSc
Ege University, Institute of Science, Department of Biotechnology, Ege University
Ege University Vaccine Development Application and Research Center

10:45-11:00 RNA Vaccines
[1]İrem YAVUZ and [2]Ülcan MANAV
[1]Trakya University, Faculty of Engineering, Genetics and Bioengineering Department,Edirne, Turkey
[2]Ege University, Faculty of Science, Biology Department, Bornova, Izmir, Turkey

11:00-11:45 Coffee Break

11:45-12:30 *Moderator: Hüseyin CAN, Ph.D., Assoc. Prof.*

11:45-12:00 DNA Vaccines
[1]Öykü KERİMOĞLU and [1]Ece OKUR
[1]Ege University Faculty of Engineering Department of Bioengineering

12:00-12:15 Importance of Bioinformatics in Vaccine Development
Ege AMİRAK
Uludağ University Faculty of Science Department of Biology Molecular Biology Section

12:15-12:30 Virus-Like Particle (VLP)-based Vaccines
[1]Dila ÇINAR and [1]Berfin ULUÇ
[1]Ege University Faculty of Engineering Department of Bioengineering

12:30–14:00 Lunch

14:00-13:45 *Moderator: Muhammet KARAKAVUK, Ph.D., DVM*

14:00-14:15 Protein Based Vaccines
[1]Simge BURGAZ and [2]Beyza AKAL
[1]Ege University, Faculty of Science, Biology Department, Bornova, Izmir, Turkey
[2]Uşak University, Faculty of Science, Molecular Biology and Genetics, Uşak, Turkey

14:15-14:30 Use of Lipid-Based Formulations in Vaccines
[1]Esra ERSEVEN and [1]İpek Sena KOÇ
[1]Ege University Faculty of Engineering Department of Bioengineering

14:30-14:45 Adeno-viral vector vaccines
[1]Bengisu ÇELİK and [1]Fatma Rabia ÇAKICI
[1]Izmir University of Economics, Faculty of Engineering, Genetics and Bioengineering

14:45-15:00 Use of nano-formulations in vaccines
[1]Nefise YILMAZ and [2]Sude ŞARU
[1]Ege University, Faculty of Science, Department of Biochemistry, İzmir, Turkey
[2]Ege University, Faculty of Engineering, Department of Bioengineering, İzmir, Turkey

15:00-15:15 Immunoinformatics in Vaccine Development
[1]Hasan Doruk BİÇER and [2]Selin KOÇ
[1]Ege University, Vaccine Development Application and Research Center, Izmir, Turkey
[2]Izmir University of Economics, Faculty of Engineering, Genetics and Bioengineering

15:15-15:30 Coffee Break

15:30-16:00 Award Ceremony and Closing

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OP-1: History of Vaccine Technology

Adnan Yüksel GÜRÜZ

OP-2: COVID-19 DNA Vaccine Platform

Mert DÖŞKAYA

OP-3: DNA Vaccine against Parasitic Infections

Muhammet KARAKAVUK and Hüseyin CAN

OP-4: Development of DNA Vaccines against SARS-CoV-2

Aytül GÜL

OP-5: mRNA Vaccine against Parasitic Infections

Hüseyin CAN

OP-6: Potential of Extracellular Vesicles as Vaccines

Mustafa KOTMAKÇI

OP-7: The Role of the Resident Memory T-cells in Immune Response and Vaccine Studies

Hasan AKBABA

OP-8: Formulation and Stability Aspects of the BioNTech Vaccine Comirnaty

Yücel BAŞPINAR

OP-9: Immune Checkpoint Gene Knockout Phenomenon as A Potential Anti-Cancer Vaccine

Gülşah EREL AKBABA

OP-10: Cancer Vaccines

Bilge DEBELEC BÜTÜNER

OP-11: Biostatisitcs Techinques Used In Vaccine Development

Şengül CAN

OP-12: Transmission-blocking antigens in the development of vaccines against arthropod vector-borne diseases

Ahmet Efe KÖSEOĞLU

OP-13: Strains and plasmids commonly used in vaccines based on Saccharomyces cerevisiae

Tuğba KARAKAVUK

OP-14: The immune response that must be induced by vaccines against parasitic agents

Aysu DEĞİRMENCİ DÖŞKAYA

OP-15: COVID-19 Vaccines

Seren KAPLAN

OP-16: Anti-Vaccination: History and Reasons

Sedef ERKUNT ALAK

OP-17: Backbone of Plasmid DNA vaccines

Ceren GÜL

OP-18: RNA VACCINES

İrem YAVUZ and Ülcan MANAV

OP-19: DNA vaccines

Öykü KERİMOĞLU and Ece OKUR

OP-20: Importance of Bioinformatics in Vaccine Development

Ege AMİRAK

OP-21: Virus-Like Particle (VLP)-based Vaccines

Dila ÇINAR and Berfin ULUÇ

OP-22: Protein Based Vaccines

Simge Burgaz and Beyza AKAL

OP-23: Use of Lipid-Based Formulations in Vaccines

Esra ERSEVEN and İpek Sena KOÇ

OP-24: ADENO-VIRAL VECTOR VACCINES

Fatma Rabia ÇAKICI and Bengisu ÇELIK

OP-25: The Use of Nano-Formulations in Vaccines

Sude ŞARU and Nefise YILMAZ

OP-26: Immunoinformatics in Vaccine Development

Hasan Doruk BİÇER and Selin KOÇ

ABSTRACTS

OP-1

History of Vaccination

[1,2]Adnan Yüksel GÜRÜZ

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Vaccines are safe, and one of the most effective ways of protecting humankind and animals against harmful diseases, before come into contact with them. It uses host's body's natural defenses to build resistance to specific infections and makes the immune system ready for a challenge. Vaccines teaches the immune system to create antibodies, by the same way when it's exposed to a microorganism, without causing infection or complication.

If we time travel in mile stones of vaccination, we may found ourselves in a Buddhist Monastery where the Buddhist monks drank snake venom to confer immunity to snake bite and variolation (smearing of a skin tear with cowpox to confer immunity to smallpox) in 17th century China. Then our next stop will be Istanbul, Ottoman Palace Lady Mary Montagu (1689-1762), the wife of a British ambassador, wrote to her friends in Britain (1717-1721) about a procedure called "vaccination" (variolation) against smallpox. Lady Montagu (herself and her family members inoculated in this Ottoman method against smallpox), and upon her return to Britain she campaigned to popularize the procedure there. Her letters are the oldest documentation of vaccines and vaccination in Turkey and Europe.

Our very important stop is in Britain, where Edward Jenner, who is considered the founder of vaccinology in the West in 1796. He inoculated a 13 year-old-boy with vaccinia virus (cowpox), and demonstrated immunity to smallpox, made him the most popular person in the history of modern vaccination. Since 1798 (the development of first smallpox), with the systematic implementation of mass smallpox immunisation culminated in its global eradication in 1979.

Now we are in 19th century, where we proudly announce Dr. Louis Pasteur who developed live attenuated cholera vaccine and inactivated anthrax vaccine in humans, 1897-1904, respectively, followed by Plague vaccine, invented in the late 19th Century. Between 1890-1950, bacterial vaccine development proliferated, like the Bacillis-Calmette-Guerin (BCG) vaccination, which we still use effectively.

As we moved forwar to 20th century in 1923, Alexander Glenny inactivated tetanus toxin with formaldehyde and developed a perfect tetanus vaccine. With the same method diphtheria vaccine was introduced in 1926. Followed by Pertussis vaccine, the first whole cell vaccine in 1948.

As we moved to the 20th century development in viral tissue culture methods (1950-1985), open a new approach to develop the Salk (inactivated) polio vaccine and the Sabin (live attenuated oral) polio vaccine. Mass polio immunisation has now eradicated wild polio virüs

from 99% of the world. Then scientists did not stop, they knew thet there will be more diseases to endanger human health. They develop many vaccines in the last 50 years either by modifiying the available methods or introducing new platforms technologies. These novel techniques have shortened the time needed to design, produce and impliment the vaccines from years to months with a lower cost.

With the COVID-19 pandemic, all novel platforms are in use to over come SARS-CoV-2 and probable new emerging diseases.

OP-2

COVID-19 DNA Vaccine Platform

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The success of DNA vaccines in preclinical studies in the first years paved the way for clinical studies. They are not viable which eliminates the risk of infection in the vaccinated individual.

They can be easily produced for clinical studies, and stable in room temperature which makes them easily shipped to remote areas. The protein DNA vaccines synthesizes is exactly the same as its natural and thus can stimulate both arms of the immune response. They enter the nucleus of the transfected cell and as a result, the induced immune response is durable for many years. Moreover, they can be used without the use of toxic adjuvants and it has been shown in over 400 clinical studies to be non-toxic to humans. They are cost-effective and can be produced under GMP conditions. During the COVID-19 pandemic several DNA vaccines targeting SARS CoV-2 has been developed and passed to clinical studies. During this pandemic ZyCoV-D vaccine developed in India is the first DNA vaccine to receive emergency use approval in humans which is another milestone for DNA vaccines. There are also some Licenced veterinary DNA vaccines which are against, West Nile virus infection in horses, Infectious hematopoietic necrosis disease in salmon, melanoma cancer in dogs, Pancreatic infection in salmon, and Avian influenza in chickens (H5N1). In our DNA vaccine platform, we define a process of DNA vaccine development from TRL-1 to TRL-5 including prototype GMP production in 42 days. The first step is the design step including epidemiological screening, in silico analysis, and docking which takes 2 days. The second step is the development of the DNA vaccine within a week including confirming on agarose gel electrophoresis and restriction enzyme digestion. The next step is *In vitro* transfection, Western blot and IFA to show the vaccine antigen protein expression which takes approximately 3-4 days. Steps 4 and 5 includes vaccine administration to mice and immunogenicity analyses which takes approximately 28 days. Step 6 is the high scale DNA vaccine production in bioreactor which is amenable with GMP conditions and takes about 48 hours. Overall, the DNA vaccine platform defined herein can develop a DNA vaccine against future pathogen X in 42 days.

OP-3

DNA Vaccines of Parasitic Infections

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Plasmid-based DNA vaccines may prove to be promising immunization tools in this area because vectors can be designed to integrate several antigens from different stages of the parasite life cycle or different subspecies; vaccines, formulations and immunization protocols can be tuned to match the immune response that offers protective immunity; and DNA vaccination is an affordable platform for developing countries. Partial and full protective immunity have been reported following DNA vaccination against the most significant parasitic diseases in the world.

Parasitic infections are one of the most devastating causes of mortality and morbidity worldwide. While immunization against these infections is an ideal solution, the development of effective vaccines is not taking place due to the particular challenges posed by parasitic pathogens. Many parasites are multicellular organisms, follow complex life cycles, exhibit impressive antigenic variability, and use ingenious mechanisms to evade the influence of the immune system, so vaccine development remains challenging.

Research on the development of DNA vaccines has also targeted parasitic diseases. One of the most challenging tasks in the development of vaccines against these pathogens is the choice of the most promising candidates. Since many of the antigens exposed to the immune system are polymorphic or show antigenic variation, they are not suitable candidates for vaccine development. On the other hand, invariant components may be poorly immunogenic or ineffective at eliciting protective immunity. Nevertheless, the simplicity with which DNA vaccines can be designed allows a rapid screening and testing of the multitude of antigens that can be identified in the complex life cycle of these pathogens. It is thought that the problems will be solved by using antigens that are critical for the infection process or located on the surface of the parasite and therefore exposed to the host immune system.

Keywords: DNA vaccine; Parasites; Antigens

OP-4

Development of DNA Vaccines against SARS-CoV-2

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which emerged unexpectedly in late December 2019, has caused over 590 million cases and over 6 million deaths worldwide[1]. The rapid spread of the virus all over the world has made the development of vaccines a biomedical priority. There are eight vaccine strategies developed against SARS-CoV-2: virus vaccines (inactivated vaccines), nucleic acid vaccines (DNA and RNA vaccines), viral vector vaccines (non-replicated), and protein-based vaccines (subunit vaccines and virus-like particles)[2,3]. DNA vaccines provide several advantages over other vaccine strategies, including being straightforward, easy to manufacture, dependable, affordable, and having higher stability[4]. DNA vaccines may be ideal for rapid, inexpensive, and large-scale preparation of SARS-CoV-2 vaccines. The development of DNA vaccines includes three main steps: antigen selection and design; demonstration of *in vitro* expression; and assessment of immunogenicity by *in vivo* studies. All DNA vaccines now undergoing clinical trials employ the spike (S) protein, the surface protein of SARS-CoV-2, as their antigen. Recognition of the prefusion state on the virus surface by the immune system is crucial for generating an effective immune response. Prefusion stabilized S protein designs are favored as vaccine antigens because the S protein is metastable in the prefusion state[5]. The engineered S protein is cloned into vaccine vectors and followed by *in vitro* studies demonstrating the expression of the vaccine protein in human cells. Animal models are vaccinated, and cellular and humoral response assessed after vaccination. If it has sufficient immunogenicity, the vaccine will move towards clinical trials. Currently, there are 16 candidate SARS-CoV-2 DNA vaccines in clinical trials that could combat the pandemic, according to World Health Organization reports.

Keyword: SARS-CoV-2; DNA Vaccine; Antigen design; Protein expression; Immunogenicity.

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OP-5

mRNA Vaccines against Parasitic Infections

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mRNA vaccine is one of the recombinant vaccine approaches using in vitro produced mRNAs that can encode the targeted antigen. mRNA vaccines have some advantages over other recombinant vaccine approaches due to their relatively simple and rapid in vitro mRNA production, the lack of the possibility of mRNAs being infectious or integrated into the host genome, and their degradation within the cell after a certain period of time. In a synthetic mRNA structure, there are four important parts. From the 5' end to the 3' end of the mRNA, these parts consist of the 5' cap, the UTRs both sides of the open reading frame, the open reading frame (ORF) that will encode the antigen of interest, and the poly A tail. During mRNA design, the use of modified 5' caps, the use of α or β globin UTR sequences, the addition of a 64-150 nucleotide poly A tail, and the use of pseudouridine instead of uridine increased the mRNA expression level and stability, and prevented excessive inflammatory response, which is considered a vaccine side effect formation. On the other hand, in the delivery of mRNAs into the cell, a carrier system such as lipid nanoparticles is used to increase their uptake potential and prevent mRNA degradation. One of the first studies in the development process of mRNA vaccines was carried out in 1993 against influenza virus. In this study, mRNAs encoding nucleoprotein as antigens were administered subcutaneously or intravenously in cholesterol/phosphatidylcholine/phosphatidylserine. As a result, it was reported that the antigen-specific cytotoxic T cell response developed. The other study was carried out two years later, and it was shown that antigen-specific antibody response developed as a result of intramuscular administration of mRNAs encoding carcinoembryonic antigen (CEA) twice a week without combining with any delivery system. The study, which is considered to be the first clinical study, was carried out in 2007. In this study, after the mRNAs encoding luciferase were produced in accordance with human applications, they were administered subcutaneously and luciferase activity was demonstrated in biopsy samples taken from the injection site within 1-2 hours. In the following years, a large number of clinical studies have been carried out aiming to develop mRNA vaccines against different types of cancer, such as skin, kidney, prostate, lung, brain and breast cancer. In addition to cancer studies, there are clinical studies on the development of mRNA vaccines against HIV as well as rabies, Zika and influenza viruses. Also, the mRNA vaccine developed by Pfizer-BioNTech against COVID-19 became the first COVID-19 vaccine to receive full approval from the FDA (American Food and Drug Administration). A limited number of mRNA vaccine studies have been performed in the field of parasitology. The first mRNA vaccine study was conducted against T. gondii in 2016. In this study, mRNA transcripts encoding *T. gondii* GRA6, ROP2A, ROP18, SAG1, SAG2A and AMA1 were produced, and then a total of 40 µg mRNA transcript was administered to mice without using any delivery system. After a single dose of mRNA vaccine, protection was analyzed in mice infected with *T. gondii* PRU strain at a lethal dose. According to the results, all of the mice in the control group died before the 25th day, while all the mice in the vaccinated experimental group survived. No death was observed even on the 175th day. The second study was similarly conducted to develop an mRNA vaccine against *T. gondii*. In this study, mRNAs encoding nucleoside

triphosphate hydrolase-II were produced and purified in vitro and administered to mice (10 µg mRNA transcripts). The second dose was administered 3 weeks later. According to the results obtained, as the protection was analyzed with the use of *T. gondii* PRU and RH strains, it was reported that partial protection, prolonged lifespan and a decrease in the number of brain tissue cysts were observed in the experimental group mice. The third study was conducted in 2018 against *Plasmodium* spp. In this study, mRNAs encoding *Plasmodium* macrophage migration inhibitory factor (PMIF) were administered to mice (15 µg mRNA transcripts). The second dose was administered 3 weeks later. According to the results obtained, it was reported that PMIF specific CD4+ response increased, anti-PMIF IgG titer increased 4-fold, and when protection analysis was performed with *P. berghei*, complete protection against re-infection was obtained. The last study was conducted against *L. donovani* in 2018. In this study, mRNA transcripts encoding 3 different proteins (LEISH-F2) were administered to mice (10 µg mRNA transcripts). The second dose (5 µg of recombinant LEISH-F2 protein formulated with 5 µg glucopyranosyl lipid A) was administered 3 weeks later. According to the results obtained, it was reported that antigen-specific Th1 response was observed in addition to strong IFN-gamma response and in the protection analysis performed with *L. donovani*, a significant decrease in parasite load was detected in the livers of the experimental group mice. As a result, the data obtained from these studies show that the mRNA vaccine model can also be applied against parasites, and an effective protection can be achieved by performing mRNA designs encoding specific antigens.

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OP-6

Potential of Extracellular Vesicles as Vaccines

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Extracellular vesicles (EVs) have gained considerable interest in the biomedical arena for treatment and diagnosis of several diseases. In addition to their potential in diagnostics and therapeutics development, they also possess remarkable potential for use as immunotherapeutics and vaccines. EVs are cell-released lipid encapsulated vesicles with nano- to micro-sized dimentions. Several subpopulations of these vesicles are characterized, namely exosomes, microvesicles and apoptotic bodies. Each of these cell-deirved EV subtypes carry a number of cell specific molecules (proteins, lipids, DNA, RNA etc.). The protein cargo of these vesicles which is source-cell-specific makes them suitable candidates for vaccine development. Indeed, several bacterial outer membrane-derived vesicle (OMV) vaccines have been licensed for management of meningitis outbreaks in several parts of the world. Moreover, because they are non-replicating structures, they are deemed to be more safe as compared to conventional attenuated bacterial vaccines. Currently, the potential of different EVs as anticancer, antiparasitic and antiviral vaccines are being investigated.

OP-7

The Role of the Resident Memory T-cells in Immune Response and Vaccine Studies

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The immune system must defend the host at the most likely sites of pathogen encounter. Recent data demonstrate that a population of memory T cells (TRM) resides long-term within peripheral tissues and provides a first line of host defense from pathogens that cause local infection (Hill, 2015). Defining mechanisms that control TRM precursor localization and persistence within skin will be important for optimizing vaccines to provide local protection as well as therapies to prevent unwanted inflammation. In this study we investigated the mechanisms that direct the interstitial migration, persistence and response of cutaneous TRM. While the local cytokine microenvironment is known to direct TRM formation, factors that inhibit TRM differentiation/persistence are unknown. We also investigated the promotion or inhibition of TRM formation depending on the local cytokine microenvironment (Cheuk et al., 2017). Lastly, although TRM have been identified at sites of cutaneous inflammatory disease, targeting TRM is an untested therapeutic approach. We used a mouse model of vitiligo with preclinical application to investigate that autoreactive TRM maintain depigmentation, and that depletion of autoreactive TRM will prevent and/or ameliorate disease.

Keywords: Resident memory T cell, vitiligo, CD49a, cytokine microenvironment, prime and pull,

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OP-8

Formulation and Stability Aspects of the BioNTech Vaccine Comirnaty

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Regarding the fact that the approval for release of a drug or vaccine takes approximately 10-12 years, it is remarkable that the BioNTech vaccine (Tozinameran; comirnaty) was available in less than one year. The R&D concept of BioNTech startet on 16th and 29th January 2020, respectively, the active Research was initiated on 29th January 2020. The coordination of Development process/programm with PEI (Paul-Ehrlich-Institute), which is responsible for vaccines and sera in Germany, startet stepwise on 6th March, following 20th February and 8th April 2020, respectively. The vaccine candidates for clinical trials were determined based on GLP toxicity and tolerability tests, proof of strong vaccine activity for animal studies (antibodies, T-cells) and GMP manufacturing of testing preparations with appropriate quality. Afterwards, the first clinical trial was proposed on 9th and 18th April 2020 at PEİ and EK of the state. Here, this approval was accelarated from 3 months to only 3 days, given on 21st April 2020. Phase I clinical trial of 4 vaccine candidates startet 23rd April 2020 (Germany) and 5th May 2020 (USA), respectively. Here, BNT162b2 showed the best safety profiles. Phase II startet July 2020 and Phase III on November 2020. At that point, the collaborations with Pfizer (USA) and Fosun Pharma (China) startet. After obtaining the first results the "Rolling-Review" approval process startet October 2020, leading to the proposal for the approval on 1st December 2020. Only 20 days later EMA approved the vaccine.
However, even the clinical trials were performed very quickly, for the approval for the finished vaccine detailed documents about the final vaccine are required, İncluding stability studies. Here, some guidelines like "Guidelines On Stability Evaluation of Vaccines, WHO/BS/06.2049" and/or "ICH Harmonised Tripartite Guideline Quality of Biotechnological Products: Stability Testing Of Biotechnological/Biological Products Q5c" should be followed.
Due to the fact the stability of the final vaccine have to be tested, this tests are more sophisticated, the more complex the final vaccine is. There are some requirements for vaccines, besides the active, like a carrier/delivery system, compounds appropriate pH and tonicity, aqueous solvant, adjuvants, preservatives etc.
The more complex the final vaccine formulation is, the more test are required. BioNTech have chosen not to use an adjuvant, preservative and a ready-to-use carrier/delivery system for accelarating the approval process. Here, a two stage vaccine was developed: First, a powder form for an easier storage, transport, stability, and second a dilution step with NaCl solution before the final application by injection. However, a carrier is required due to the fact that "naked" nucleic acid are enzymatic degradated after their application/injection. The following components were used: mRNA, the ionized lipid ALC-0315 = (4-Hydroxybutyl)azandiyl)bis (Hexan-6,1-diyl)bis(2-hexyldecanoat), the PEG-lipid ALC-0159 = 2-[(Polyethylenglykol)-2000]-N,N-ditetradecylacetamid, the co-lipids 2-Distearoyl-sn-glycero-3 phosphocholin and Cholesterol, the salts potassium chloride, monobasic potassium phosphate, sodium chloride and dibasic sodium phosphate-dihydrate, the cryoprotectan sucrose and the

solvant water for injections. Here, by adding/diluting the formulation with NaCl solution, the lipids and mRNA together are forming in situ lipid nanoparticles, acting as carrier. No adjuvant, preservative and carrier/delivery system was used, so no tests were required for them. Thus, only tests were performed for the vaccine in dry powder form, because this form is stored.
Due to the fact that before the injection the powder vaccine is diluted with NaCl solution, no tests are required for the solution, because this solved vaccine is injected, not stored.
The lack of an adjuvant and a ready-to-use carrier/delivery system facilitated and accelarated the stability tests among others and finally the approval.

OP-9

Immune Checkpoint Gene Knockout Phenomenon As A Potential Anti-Cancer Vaccine

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Engagement of programmed death 1 receptor (PD-1) and its ligand PD-L1/2 induces a signal transduction pathway that inhibits the activity of tumor-infiltrating cytotoxic T lymphocytes and promotes tumor growth and metastasis. PD-L1 gene knockout can restore antitumor T cell responses and cause long-term remission in a subset of cancer patients with advanced or refractory tumors. The lack of safe and effective delivery across the blood-brain barrier and the profound immune suppressive microenvironment are two main hurdles to glioblastoma (GBM) therapies. Extracellular vesicles (EVs) could been used as therapeutic delivery vehicles to GBM but with limited efficacy. We hypothesized that EV delivery to GBM can be enhanced by (i) modifying the EV surface with a brain-tumor-targeting cyclic RGDyK peptide (RGD-EV) and (ii) using bursts of radiation for enhanced accumulation. In addition, EVs were loaded with small interfering RNA (siRNA) against programmed cell death ligand-1 (PD-L1) for immune checkpoint blockade. We show that this EV- based strategy dramatically enhanced the targeting efficiency of RGD-EV to murine GBM, while the loaded siRNA reversed radiation-stimulated PD-L1 expression on tumor cells and recruited tumor-associated myeloid cells, offering a synergistic effect. The combined therapy significantly increased CD8+ cytotoxic T cells activity, halting tumor growth and prolonging animal survival (1). The selected cell source for EVs isolation and the presented functionalization strategy are suitable for large- scale production. These results indicate a promising avenue for future research in the quest for cancer vaccine design.

Keywords: glioblastoma, immunotherapy, extracellular vesicles, radiation therapy, targeted delivery

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OP-10

Cancer Vaccines

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Cancer vaccines in use include preventive vaccines against infectious agents associated with cancers and therapeutic vaccines used as immunotherapy agents to treat cancers. The goal of therapeutic cancer vaccines is to induce tumor regression, eradicate minimal residual disease, establish immunological memory for long-lasting tumor control and avoid non-specific or adverse reactions. Although vaccination strategy against cancer has been a breakthrough, challenges in cancer therapy still need to be solved. Limitations in developing cancer vaccines include heterogeneity within and between cancer types and intrinsic genetic instability of tumor cells. However, aberrant and novel tumor antigens can be expressed and serve as potential targets for cancer immunotherapy. Thus, personalized cancer vaccination strategy can be a potent approach to trigger a broad-based antitumor response. Future of effective novel cancer vaccines depend on screening and identification of appropriate tumor-specific antigens and the choice of vaccine delivery platforms in order to overcome various mechanisms of resistance posed by the tumor.

OP-11

Biostatisitcs Techinques Used In Vaccine Development

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Vaccines are biological substances that provide protection against infections by stimulating the immune system in humans and animals. Statistical techniques are needed for different stages of the vaccine studies. In the past, biostatistics was first used in the evaluation of vaccine protection in vaccine development studies. Statistical methods used in vaccine studies range from analyzing a small sample to field trials. For this reason, statistics has become an indispensable component of the vaccine development process by using modern technology. Vaccine efficacy and safety are generally evaluated in randomized and well-controlled clinical trials before the vaccine is licensed. Experimental and control group participants are included in these studies. These groups are followed periodically and the cases in both groups are tabulated. In this study, the efficacy of protection will evaluated in patients divided into experimental and control groups using SPSS package program. For this, information will be given about the SPSS package program and then the analysis that will be applied will be determined. Later, further analyses including data definition, data entry and suitability of the data will be performed in the SPSS program. In conclusion, a general evaluation will be performed on the case study by explaining how to interpret the results.

OP-12

Transmission-blocking antigens in the development of vaccines against arthropod vector-borne diseases

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Arthropod vector-borne diseases are increasing as emerging and re-emerging potential zoonotic threats by affecting nearly 3.5 billion people at risk worldwide and becoming problematic especially in tropical countries. The most famous of these is malaria, a mosquito-borne disease caused by *Plasmodium*, which was revealed to be transmitted by *Anopheles* mosquito vectors at the end of the 19th century, causing the deaths of more than 600,000 people a year, primarily children. There are also mosquitoes such as *Aedes* species, which alone transmit pathogens that cause many arboviral diseases including dengue, chikungunya, Zika, and yellow fever, which cause serious health problems and deaths for humanity worldwide. Flea-borne diseases include diseases such as plague (*Yersinia pestis*) and murine typhus (*Rickettsia typhi*), which have caused very important health problems and deaths both in the past and today, as well as recently emerged human pathogens (*Bartonella henselae* and *Rickettsia felis*). Tick-borne diseases are also increasing in suitable ecological habitats with the spread of ticks due to the temperature rise driven by global warming, threatens animal and human health as well as causes great economic loss in the livestock industry. Because insecticides and acaricides are used to control mosquito-borne, flea-borne, and tick-borne diseases, genetic resistance has evolved to a great extent. Although vaccine studies against pathogens are increasing day by day, in recent years, transmission-blocking antigens targeting arthropod vectors that transfer pathogens instead of targeting individual pathogens have come to the fore in vaccine studies against vector-borne diseases. For example, the fibrinogen-like (FBG) domain of the fibrinogen-related protein 1 (FREP1) located in the mosquito midgut, which facilitates the transmission of *Plasmodium falciparum*, was found to be conserved with a similarity rate of more than 90 percent among *Anopheles* mosquitoes in different parts of the world, and anti-FBG antibodies against malaria have been found to block the transmission in all *Anopheles* species. Another example is the application of vaccines developed for BM86, HAA86, Salp25D, and SUB transmission-blocking antigens, which are secretory and surface proteins found in different tick species (*Rhipicephalus microplus*, *Hyalomma anatolicum*, and *Ixodes scapularis*) that transmit various pathogens, resulting in reductions in tick infestations and pathogen infections, and the protective roles of these antigens have been emphasized in many studies. In conclusion, transmission-blocking antigens are promising vaccine candidate antigens in the future for veterinary and human medicine, especially in the prevention and reduction of vector-borne diseases caused by pathogens transmitted by mosquitoes, fleas, and ticks.

Keywords: Transmission-blocking antigen, vector-borne disease, arthropod, vaccine

OP-13

Strains and plasmids commonly used in vaccines based on *Saccharomyces cerevisiae*

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Saccharomyces cerevisiae is a non-pathogenic yeast species primarily used in brewing and bread making. Historically, it has been frequently used in understanding basic cellular processes in eukaryotes and in vaccine studies. It has important advantages such as ease of manipulation, low cost, and easy design (1). Moreover, they are safe as they do not contain pathogens, viral inclusions, or pyrogens in their structure. They grow rapidly in simple environments and secrete recombinant proteins and modify them for eukaryotic organisms (2). Generally, INVSc.1 and EYB100 are the most commonly used yeast strains in vaccine studies. These strains are preferred for protein expression because they grow fast and are easy to use (3,4). Vectors used in the transformation of S. cerevisiae host strains are generally generated by hybridization with yeast-derived bacterial strains. It contains the bacterial ori and a sequence that confers resistance to a specific antibiotic such as ampicillin and the material necessary for plasmid replication in an Escherichia coli host. Yeast similarly contains genes for the selection of yeast transformants such as LEU2 or URA3. The pYES and pYC vectors were designed for high expression of recombinant proteins in S. cerevisiae. pYES vectors have two replication origins and are episomally maintained in high copy. It also contains components of the 2µ yeast plasmid. In addition, they replicate independently of chromosomal DNA with the ARS sequence and STB locus. pYC vectors carry the CEN6/ARSH4 origin and maintain the copy number of the desired gene similar to that of wild-type genes. The use of pYE-type plasmids is common in most production systems. Typically, they contain 30 copies or more. YIp type vectors do not contain ARS sequences and are integrated into chromosomes. They are quite stable but exist in low copy numbers (2,5,6).

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OP-14

Immune response induced by vaccines against parasitic agents

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Protection through vaccines is quite complex. Many of the classic vaccines currently in use have been developed largely empirically, with little or no knowledge of how they activate the immune system. Today, there are many studies on this subject and even vaccine designs and new vaccine models are created in line with immune response screening studies (1). In order for an immune response to a vaccine to occur, the vaccine antigen must first be perceived as "foreign" by the immune system. When the vaccine antigen enters the body for the first time, it first activates the innate immune system and is recognized through receptors that allow the immune system to perceive the structure that it considers "foreign". The antigen-specific immune response induced after vaccination basically occurs in two ways as humoral (secretory) immune response (B cell response) and cellular immune response (T cell response). B and T cell responses specific to the vaccine antigen given to the body after vaccination begin with the recognition of the antigen by the antigen presenting cells, especially the dendritic cells. After vaccination, vaccine antigens attract freely circulating dendritic cells, macrophages and neutrophils to the scene. The vaccine antigen is perceived as foreign, then macrophages and dendritic cells are activated. Afterwards, the surface receptors of the dendritic cells change and they migrate to the lymph nodes. Activation of T and B lymphocytes occurs in lymph nodes. B cells are stimulated with vaccine antigens coming to secondary lymph tissues, cytokines secreted from activated dendritic cells or vaccine antigens reaching B cells by diffusion. Vaccine antibody responses fall below the protective level over time, unless there are repeated antigens and live vaccines are not used. After the first vaccination, memory B cells are formed with the help of T cells. Memory B cells cannot produce antibodies until they encounter the antigen again and differentiate into antibody-producing plasma cells. The second post-vaccination reaction occurs much faster than the immune response that occurs with the first vaccination. T cell responses develop in parallel with B cell responses with the help of activated dendritic cells. Except for polysaccharide vaccines, all vaccines stimulate the CD4+ T cell response. Th1 and Th2 cells support B cell or CD8+ T cell differentiation. In

addition, live vaccines directly stimulate the CD8+ T cell response involved in killing infected cells (2, 3).

The immune response against any parasite is not different from the response for other microorganisms. For all microorganisms that infect the host, the response begins with the immune system cells recognizing these organisms. Parasites are difficult to control by the host because of their three characteristics based on their size, complexity of life cycles, and differences in their antigenic content. All parasites elicit both humoral and cellular immune responses. IgM, IgG, IgA and IgE class specific antibodies are secreted, indicating that the parasite antigens are recognized by the host. However, the correlation between the humoral and cellular immune response and the relationship to the protection of the host may be low. Parasites express different antigens at different times during their life cycle. This leads to very different antibody-dependent and independent responses (4).

To summarize the immune mechanisms specific to parasites, the immune response can be approached from two aspects as intracellular and extracellular parasites. While Th1, CD8+ T cells and macrophages are effective against intracellular parasites, Th2 and antibody responses seem to play an active role against extracellular parasites. IgE and mast cells play an active role in cestode and nematode infections. If we look at the subject in terms of Toxoplasma gondii, IgA response is observed in the transmission via the gastrointestinal tract. Both humoral and cellular immune responses are observed against T. gondii. However, protective immunity was best observed in the response associated with the IFN-gamma secreting CD8+ T cell. In addition, tumor necrosis factor alpha is one of the important cytokines in the immune response (4-6).

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screening sera of murine model infected orally with oocysts and tissue cysts. Parasit Vectors. 2018, 11(1):393. doi: 10.1186/s13071-018-2934-1.

OP-15

COVID-19 Vaccines

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Developments in the field of structural biology and vaccine studies have allowed the molecular structure of the virus to be determined quickly in the event of a pandemic and ensured that reliable vaccine candidates take their place in the market. With the emergence of the pandemicsituation, many countries have included studies on Covid-19 vaccines. Among these vaccine strategies, besides conventional vaccine techniques, new generation vaccine technologies are also included.

Vaccine techniques used in the Covid-19 pandemic are inactivated virus vaccine, protein subunit vaccine, viral vector-based vaccine, mRNA vaccine, and DNA vaccine. For example, Sinovac vaccine produced by Coronovac is inactivated vaccine, BioNTech and Moderna vaccines are mRNA vaccines, vaccine produced by AstraZeneca is non-coding viral vector vaccine, vaccine known as ZyCoV-D is DNA vaccine, and NVX-CoV2373 vaccine, also known as Novavax, is protein subunit vaccine.

In addition to these vaccine techniques, there are vaccines using adjuvant technology and usinglipid nanoparticles. Adjuvant use is a technology used to increase vaccine efficacy. The purpose of using nanoparticles such as lipid nanoparticles used in nucleic acid vaccine formulations is to provide protection against endogenous enzymes and to facilitate cellular uptake and intracellular release.

In addition to the studies carried out around the world, vaccine studies for Covid-19 are also carried out in Turkey. Turkovac vaccine, an inactivated vaccine, was approved for emergency use in Turkey on 22 December 2021. In addition, many universities and institutions continue their preclinical studies, and conventional and new technology vaccine studies are carried out in our country.

OP-16

Anti-Vaccination: History and Reasons

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Anti-vaccination started in the 18th century with the introduction of the smallpox vaccine produced by the English scientist Edward Jenner against smallpox.[1] Vaccine hesitancy and anti-vaccination are different from each other, and according to the definition of the World Health Organization, vaccine hesitancy means delay in accepting or not allowing the administration of some vaccines even though the vaccine is available. On the other hand, anti-vaccination means rejecting all vaccines without any hesitation. Due to the rapid increase in anti-vaccination cases in the world in recent years and reaching dangerous levels, the World Health Organization established a group called the Working Group on Vaccine Hesitancy.[2] Also in 2019, anti-vaccination was reported as one of the 10 main reasons that endanger global health, listed by the World Health Organization.[3]

Reverend Edmund Massey, in his 1772 sermon "The Dangerous and Sinful Practice of Vaccination", stated that vaccines were demonic operations and condemned it as an attempt to resist God's punishments on man for his sins.[4] In addition to the theological reasons for anti-vaccination, political and legal reasons also led to anti-vaccination after the passage of laws mandating parents to vaccinate their children in the mid-19th century in England. As a result of this, activists established the Anti-Vaccination League in London.[5] Anti-vaccination is made on the grounds such as vaccines do not have reliable ingredients, there are many side effects that are not disclosed by companies, childhood vaccines cause autism, vaccination is an individual decision, vaccines are used as biological weapons and similar reasons.[6]

The use of social media is one of the most important factors in the spread of anti-vaccination, which also emerged in a major way during the COVID-19 pandemic. During the pandemic the sharing of news of unknown origin by unreliable people and the belief of people without adequate knowledge of these news increased the opposition to vaccination.[7] The fact that COVID-19 is a disease encountered for the first time all over the world and the new discovery of vaccines has made it easier for people to manage their ideas. In order to prevent this situation, it is very important to raise awareness of the society about scientific literacy, to listen to expert advice and to share the information with known sources by the media.[8]

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OP-17

Backbone of Plasmid DNA vaccines

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DNA vaccination is a platform provide for treating human and animal diseases with gene-based materials. DNA plasmids combining two different types of sequences are typically used in DNA vaccines. These are a region from the bacterial genomic sequence that is required for replication and selection in bacteria, combined with a region from the eukaryotic sequence that is required for the expression of the encoded transgene in mammalian cells. It also contains multiple cloning sites into which the target antigen sequence will be inserted, and an antibiotic resistance gene[1]. The eukaryotic sequence region contains the promoter upstream, and the polyadenylation sequence downstream of the target gene. The promoter region is responsible for transcription of mRNA during transfection into the nucleus. The polyA signal mediates mRNA cleavage and polyadenylation, which results in effective cytoplasmic export of mRNA. The Kozak consensus sequence, including the start codon of the transgene, is recognized by ribosomes, enabling efficient translation to occur[2]. Additionally, the eukaryotic promoter's subsequent post-translational modification of the expressed antigen results in a native protein structure that can go through the appropriate processing and immunological presentation. Because of the different codon usage of bacteria and mammalian cells, codon optimization is generally required for efficient expression of pathogen-derived proteins in mammalian cells[3]. Furthermore, these vaccines have a reduced manufacturing time and lower cost because they require only single-step cloning into plasmid vectors. The DNA vaccine platform has advantages, including no risk of conversion to infectious form because it does not contain the pathogen itself, stimulation of both B and T cell responses, easier production methods, physical stability, and storage without a cold chain. Due to the lack of anti-vector immunity or non-target acquired immunity against DNA in the vaccine recipient, DNA vaccines are a safe platform against diseases[4,5].

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OP-18

RNA VACCINES

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RNA molecules have been used as therapeutic and research tools for over two decades. It prevents or treats any disease characterized by a deficiency of one or more of the key proteins. The scope of such diseases is wide; It includes genetic and infectious diseases as well as cancers. The RNA (mRNA) vaccine is based on the principle that mRNA is an intermediate messenger to be translated into an antigen after being delivered to host cells by various routes. mRNA vaccines have come to the forefront as the technology used by many companies in the development of vaccines during the COVID-19 pandemic.

While mRNA vaccines have advantages such as being easy and fast to produce, having much higher biosecurity than DNA-based vaccines, not interacting with the host genome, and having the molecule in the cytoplasm in the mRNA vaccine; The storage and transportation of mRNA vaccines requires ultra-low temperatures, which can also be considered as a disadvantage. He classifies mRNA vaccines into two types: non-replicating and self-replicating (also known as replicons) mRNA vaccines.

In the past COVID-19 pandemic, Pfizer/BioNTech (BNT162b2) and Moderna (mRNA-1273) COVID-19 vaccines are both mRNA vaccines and use the LNP platform.

Keywords: RNA vaccines, COVID-19, Pfizer/BioNTech, Moderna

OP-19

DNA Vaccines

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The study on DNA vaccines first began in the 1990s, when the plasmid DNA is injected into the skin or muscle was reported to induce antibody responses to antigens. Data from preclinical studies using DNA vaccine technology have received a lot of attention as the platforms generate protective immunity against a wide variety of virus families. After the first DNA vaccines were developed in cattle, human studies revealed that the DNA was well tolerated and perfectly safe. Also DNA vaccines seem to be more harmless and more stable than ordinary vaccines. Plasmids are non-viable and do not multiply, and therefore have a low risk of developing secondary disease and infection. The main concern about their potential DNA vaccines has been integrated into the host genome and generated immune responses to agent anti-DNA. Extensive surveys have found little evidence of integration, and the merger risk appears to be less than normal mutation.

Recent research has generated new clues from fundamental research on insert design, RNA structure, diversity in codon usage, and leader sequence optimizations. The need for improvements and continuous optimization in this technology has been revealed.

New formulations such as lipids and polymers, as well as new delivery devices such as gene gun, skin delivery devices, and more recently electroporation technology, appear promising in preclinical models and clinical research is still being closely monitored.

In the last three years, four DNA vaccines or immunotherapy products have been approved in the veterinary field for various species, including salmon, pig, dog and equine. These products represent the first validation of the commercial viability of the DNA vaccine platform and represent significant advances in this area.

The development of the DNA platform will continue to be an exciting and highly productive adventure, demonstrating the best in academic and translation science and collaboration between industry, regulatory authorities, funding bodies and academics.

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OP-20

Importance of Bioinformatics in Vaccine Development

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Bioinformatics, as a nexus of computer science, mathematics and biotechnology, is one of the newest scientific fields involved in biological issues. Bioinformatics approaches present useful results from large amounts of raw data (Romano et al. 2011).

Vaccine design is the most critical and time-consuming step in the entire process of vaccine development. An effective subunit vaccine consists of the epitope, linker, and adjuvant.

Bioinformatics plays a vital role in vaccine design by identifying and predicting the essential components of the vaccine, such as target antigen, B and T epitope, and suitable linker. Besides, computational approaches, such as molecular modeling, protein–protein docking, molecular dynamics simulations, etc., help in predicting the vaccine construct properties in a short period and allow a researcher to move further for its experimental studies.

The raw data have been extensively used to analyze gene and protein expression and predict structural, immunogenicity and general features of proteins. Study and comparison of the physical, chemical and immunogenicity characteristics of proteins can increase our knowledge regarding them and help the researchers select the proper epitopes for DNA vaccine investigations.

Keywords: Bioinformatics, Vaccines, DNA vaccines

OP-21

Virus-Like Particle (VLP)-based Vaccines

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VLPs are protein structures that structurally mimic the virus and cannot replicate because they do not carry the genetic material of the virus. Because viral capsids designed to be expressed are conformationally virus-like, their interaction with cellular receptors also mimics the virus. [1]. Since VLPs do not carry any genetic material, they are considered a safe method for vaccine development, as they cannot replicate. VLP-based vaccines against human papillomavirus (HPV) and hepatitis B virus (HBV) infections have been approved by the FDA and are used for prophylactic protection. Along with being used as a preventive vaccine, they can also be used in cancer immunotherapy, autoimmunity, allergy and addiction treatments. They stimulate both humoral (MHC-II) and cellular-based immunity (MHC-I) [2].

The fact that VLPs can be applied with formulas that do not contain adjuvants and that they allow faster vaccine production compared to conventional methods constitute their advantages over attenuated viruses that are commonly used for vaccination. These advantages are particularly useful for the treatment of frequently mutating pathogens seen in influenza disease. For example, for influenza vaccine production; With conventional methods, results are obtained 9 months after sequencing of the annual strain, while this period is reduced to 3-12 weeks with VLP production [3]. There are currently licensed VLP vaccines available for HPV, HBV, and malaria. There are also VLP-based vaccine studies with ongoing preclinical and clinical research. [4].

The activation mechanism of VLP vaccines is by increasing the antibody production capacity of the cells by allowing strong activation of B cell receptors after they are injected into the tissue. Moreover, cells infected by an intracellular pathogen present their protein on their outer surface, which can be recognized by cytotoxic T-cells, thereby activating the infected cell to kill [5]. By adding multiple viral structural proteins to VLPs, more virus-specific epitopes are added to the immune system, which can become potential targets for cytotoxic T cells. Production of VLP vaccines can be achieved using mammalian cells, insect cells, bacteria (usually E. coli), yeast and plant cells [6].

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OP-22

Protein Based Vaccines

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Protein based vaccines, use the specific part of the virus that the immune system needs to recognise in order to develop an immune response. They do not contain the whole virus or another virus. Protein based vaccines contain protein fragments made in the laboratory. Their function is allow the immune system to recognise the virus and fight it off if you are infected.

Protein based vaccines have been used for many years, have a good safety profile and relatively easy to produce. The main disadvantage is that due to its low effectiveness, it is necessary to use more than one dose. These vaccines use protein structures of bacteria or viruses that have been purified or obtained by recombinant technology. To work, these vaccines might require adjuvants that immune stimulating molecules delivered alongside the vaccines. Of the more than 150 FDA (U.S. Food and Drug Administration) approved recombinant proteins to date, about 20% are produced in yeast, 30% in *Escherichia coli* and 50% in mammalian cell lines.

The Novavax vaccine is a protein-based vaccines that developed against COVID-19. It is based on the aggregation of spike proteins produced by inserting the SARS-COV-2 spike protein gene region into the Baculovirus gene and entering the Baculovirus moth cell. Novavax, like other protein vaccines, provides an antibody response without entering the cell. Since the production of moth cells is quite easy, it is also possible that their production will become widespread. Also, according to surveys conducted in Germany, opponents of vaccination have shown great interest in this vaccine type.

Keywords: Protein based vaccines; Baculovirus; COVID-19; Novavax

OP-23

Use of Lipid-Based Formulations in Vaccines

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Lipid Nanoparticles (LNP), which emerged in 1991 as an alternative delivery system to conventional colloidal carrier systems, have received increasing attention in recent years.

Lipid Nanoparticles are one of the most advanced pharmaceutical delivery systems. They form a safe and effective delivery system for antigens used in recombinant protein and nucleic acid-based vaccines. They increase the circulation time in the body and help to deliver the antigen to the target area.

Using Lipid Nanoparticles as a delivery system to develop vaccines; high efficiency encapsulation of hydrophilic as well as hydrophobic active ingredients; The benefits include that it can be functionalized with specific ligands to change how the vaccine behaves and which specific cells, tissues and organs it targets. Therefore, Lipid Nanoparticles are an important component of modern vaccine research.

OP-24

Adeno-Viral Vector Vaccines

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Before its highly immunogenic quality were clarified, it was recognized as a vaccine vector thatis able to induce varying immune responses, adenovirus was used as a conveyance vector for particular genes. After its qualities were recognized, it was started to use as a vaccine vector.

[1] Adenoviruses that causes mostly mild self-limited respiratory and ocular infections in humans, are non-enveloped double-stranded DNA viruses. [2] The use of adenovirus as a vectorhas many advantages, firstly since its genome is well understood it is easy to manipulate it. Asa second advantage adenovirus can infect host cells regardless of cell division regarding it has a wide range of host cell tropism. Moreover, it has been identified that the recombinant genome is steadily conserved through permanent passages, and it can be rapidly and considerably produced. Additionally, regarding the mucosal infection is the nature of adenovirus the expectation for efficiency of adenovirus-based vaccines by mucosal direction is high. Therefore, because of their registered immunogenicity and capacity to induce host defense in various species, as well as humans adenoviral vectors have appeared as very encouraging platforms for vaccines. [1] Currently adenoviral vectors are being used to generate various vaccines such as COVID-19, HIV1, Influenza, Ebola vaccines.

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OP-25

The Use of Nano-Formulations in Vaccines

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Nanotechnology is the development of functional materials, devices and systems for the understanding, control, and production of physical, chemical, and biological phenomena at the nanometer scale. Studies such as processing, measuring, modeling, and editing carried out on materials at sizes smaller than 100 nanometers are considered nanotechnological studies. Nanotechnology plays an progressively important role in vaccine development, thanks to nano-carrier-based delivery systems that offer the opportunity to increase cellular and humoral immune responses. Nanoparticle (NP)-based vaccine applications can protect vaccines against premature spoilage, increase stability and have good adjuvant properties.

Nanoparticles provide effective and alternative platforms to traditional vaccine methods with their biodegradable, minimally toxic properties that can be used for the delivery of various antigens to specific tissues and organs. Off-scale materials such as virus-like particles, liposomes, ISCOMs, polymeric, inorganic nanoparticles, and emulsions are attracting attention as potential delivery vehicles that can both stabilize vaccine antigens and act as adjuvants.

The composition of the nanoparticle material has an important role in the transport and pharmacokinetic properties of nanoparticles, release rate and cellular uptake, biodegradability, and biocompatibility. It is thought that nanoparticular vaccines could guide vaccine development in the future for many diseases, including rapidly emerging pandemics such as COVID-19 and cancers that cannot be controlled by vaccination.

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OP-26

Immunoinformatics in Vaccine Development

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The identification of B cell and T cell epitopes is aided by immunoinformatics. When necessary,viruses and bacteria were used in immunoinformatics methods to identify and analyze the potential of diverse B and T cell epitopes. Using information from Leishmania secretory proteins, Khatoon N, et al. discovered and characterized potential B and T cell epitopes. (Khatoon et al., 2017) Additionally, promising chikungunya B and T cell epitopes for the creation of multiple epitope vaccines were discovered and described by Narula A. (Narula et al., 2018) Typically, multi-epitopic vaccine development uses immunoinformatic discovered and defined B and T cell epitopes. (Chakraborty et al., 2021) Reverse vaccinology refers to the use of immunoinformatics in the creation of vaccines. The creation of a multi-epitope vaccine employing several antigenic structures has been sped up by this technique. With the identification of several previously unidentified antigens, immunoinformatics has successfully advanced the creation of vaccines. Immunoinformatic methods are frequently used in reversevaccinology to interpret various antigenic roles. (Chakraborty et al., 2021) Immunoinformatic techniques are a godsend in the field of vaccine production since they help researchers better understand the biology of the pathogen and mutagenesis antigens. The difficulties encountered while addressing viruses with mutagenic antigens might thus be addressed by this next-generation technique. By creating a multi-epitope vaccination with either a mutagenicantigen or a regular antigen, it can offer protection against these infections. (Vivona et al., 2008).

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