
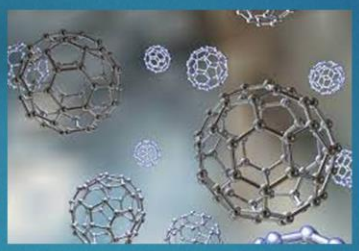





# 2nd INTERNATIONAL EGE-AGEM VACCINE SYMPOSIUM, September 7-8, 2023

EGE UNİVERSİTY VACCİNE DEVELOPMENT APPLİCATİON AND RESEARCH CENTER
BORNOVA/İZMİR, TURKİYE

# 2nd INTERNATIONAL EGE-AGEM VACCINE SYMPOSIUM

***September 7-8, 2023***

***Ege University Vaccine Development Application and Research Center***

***Bornova/İzmir, Türkiye***

# *ABSTRACT BOOK*

***Organized by Ege University Vaccine Development Application and Research Center***

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# ABSTRACTS

***OP-1***

# Recent Advances in Preclinical Vaccine Development to Accelerate Vaccine Development

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Vaccine antigen selection and design, vaccine prototype development, preclinical immunogenicity, and challenging studies, GMP grade scale up and pilot production (quality control), and toxicity studies (non-GLP, GLP) are the five main subtopics that compose up preclinical vaccine development. Selecting and designing the vaccine antigen is the initial step, and it is crucial because a poor choice made here could set back vaccine development for years. Preclinical vaccine development has recently benefited from the increased use of computational techniques like immunoinformatic approaches combined with artificial intelligence (AI), which allow researchers to sift through large amounts of data and narrow the field down to a small number of candidates for additional testing. Data from computational approaches must be comparable with data from in vitro and in vivo screening platforms in this step. The choice of sophisticated vaccination platforms, such as mRNA, DNA, or recombinant protein/VLP, which offer benefits like quick development, scalability, and inducing potent immune responses, is what determines the second step in the development of a prototype vaccine. Adjuvants that can boost vaccination efficacy and give long-lasting immunity, such as toll-like receptor agonists, oil-in-water emulsions, and nanoparticle-based adjuvants, become more significant in this step. To assess the efficacy of prospective vaccines in clinical trials, human volunteers are voluntarily infected with a mutant pathogen in a controlled setting using Controlled Human Infection Models (CHIMS), which have recently been established. Once the third step of the vaccine development pipeline is completed with very strong immunogenicity responses, the vaccine candidate moves on to TRL-4, which entails non-GLP toxicity studies in suitable animal models to evaluate safety. The next stage is to produce your vaccine in a GMP setting, but first you need to maximize your bioprocess's scale-up. AI is being employed in this step to expedite the optimization process. Upstream and downstream bioprocesses must be carried out in tandem with quality requirements during pilot GMP production. These requirements include characterization studies of vaccine components like adjuvant, antigen, and preservatives, as well as analysis of impurities and contaminants, stability studies to assess shelf life and storage conditions, process validation to guarantee consistency and reproducibility between vaccine batches, evaluation of critical process parameters, and confirmation that the finished product satisfies quality specifications as specified by regulatory bodies (TITCK, EMA, or FDA). To determine whether the finished product is safe for use in clinical trials, a GLP-grade toxicity study must be carried out. Overall, time-to-market for vaccines is being shortened by recent developments in preclinical vaccine research, including the use of computational methods, the incorporation of sophisticated animal models and CHIMs, and the use of AI in decision-making.

***OP-2***

# Expected immune response in parasites vaccines

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The main goal in vaccine development is to 'train' the immune system by using a version of the pathogen or an antigenic fragment of the pathogen that will not harm the body. For an immune response to occur, the vaccine antigen must first be recognized as "foreign" by the immune system. The vaccine components are taken up by phagocytic cells in peripheral tissue that express pattern recognition receptors (PRRs) that recognize pathogen-associated molecular patterns (PAMPs). Activated antigen-presenting cells migrate to the nearest lymph node. Inside the lymph nodes, antigen processed by antigen-presenting cells is presented to lymphocytes, thus activating an antigen-specific acquired immune response. In the B cell-mediated response, antibodies specifically recognize the target pathogen and bind to its surface so that pathogens can be marked for destruction by other immune cells or their ability to bind and enter host cells can be inhibited. In the T cell-mediated immune response, CD4+ T cells produce signaling molecules called cytokines and chemokines to mobilize and coordinate other immune cells at the site of infection, while CD8+ cytotoxic T cells can recognize and kill virus-infected cells to prevent the pathogen from multiplying and spreading. After the first vaccination, memory B cells are formed with the help of T cells. Memory B cells do not produce antibodies until they encounter antigen again and differentiate into antibody-producing plasma cells. The reaction after the second vaccination is much faster than the immune response after the first vaccination. The immune response to any parasite is no different from the response of any other microorganism. All parasites elicit both humoral and cellular immune responses. Factors that make parasites difficult to control by the host include their size, the complexity of their life cycle, the diversity of their antigenic content, and their various immune escape mechanisms. In extracellular parasites such as helminths, IL-4-mediated Th2 and Ig E-dominated antibody responses play a more active role. Th1, CD8+ T cells and macrophages are predominantly involved in the immune response against intracellular parasites formed by protozoa. In the early stages of the immune response, IL-12 is produced by phagocytic cells and induces IFN-γ production by natural killer (NK) cells and T cells. IFN-γ production rapidly activates.

***OP-3***

# *In vitro* synthesis of non-replicating ROP6 coding mRNA transcripts: an approach of EGE-AGEM

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mRNA vaccination is one of the recombinant vaccine approaches (such as DNA, recombinant protein and viral vector vaccines) in which in vitro produced mRNAs that can encode the targeted antigen are used. It has been stated that there are some advantages of mRNA vaccines over other recombinant vaccine approaches such as simple and rapid in vitro production of mRNAs, not-being infectious, not-possible of integration into the host genome and degradation within cell. There are four important parts in a synthetic mRNA structure: from 5' end to 3' end, the 5' cap, the UTRs on either side of the open reading frame (ORF), the ORF that will encode the antigen of interest, and the poly A tail. During mRNA design, modified 5' cap, α or β globin UTRs, a poly A tail with length of 64-150 nucleotides, and modified nucleotides such as pseudouridine are used to increase the expression level and the stability of the *in vitro* mRNAs. In this study, it was aimed to synthesize in vitro mRNAs coding ROP6 protein that was detected to be antigen by microarray methods (Döşkaya et al., 2018). During the design of the mRNA transcripts coding ROP6 protein, Anti-Reverse Cap Analog (ARCA) which is a modified cap analog was preferred as 5' cap. The ARCA carries –OCH3 replaced with the 3' OH group (closer to m7G) and this modification forces ARCA incorporation in the forward orientation unlike transcripts synthesized with conventional cap analog. An internal ribosome entry site (IRES) element of Encephalomyocarditis virus (EMCV) which promotes high-level translation of mRNAs was selected as the 5' UTR. As 3' UTR, an alpha 3' UTR in length of 20 nucleotide, called as complex minimal region and showing protection against RNAse activity was used. For poly A tail, enzymatic approach capable of up to 150 base poly (A) tail was preferred. Furthermore, the codon optimized ROP6 protein coding gene along with 5' and 3' UTRs was synthetized within a plasmid by service procurement and used during the *in vitro* expression of ROP6 coding mRNA transcripts as template. For the synthesis of non-replicating ROP6 coding mRNA transcripts, a commercial kit (mMESSAGE mMACHINE® T7 Ultra Kit) yielding approximately 20–30 µg of RNA in each reaction was used. Also, after the obtained ROP6 protein coding mRNAs were purified, transfection of the mRNAs was performed to the HEK293 cell line to show the translation of the recombinant ROP6 protein. According to the results obtained, both agarose gel electrophoresis and nanodrop results showed that non-replicating ROP6 coding mRNA transcripts was successfully produced in levels which indicated in the mRNA expression kit. Moreover, the presence of the recombinant ROP6 protein was showed using the fluorescence microscopy and Western blotting. In conclusion, since the synthetic mRNA design was successfully produced the ROP6 protein, it was thought that the design can be also used for expression of another antigenic proteins.

***OP-4***

# Cyclic AMP signalling in the acute tachyzoite stage of *Toxoplasma gondii*

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Cyclic adenosine monophosphate (cAMP) is a universal second messenger which regulates crucial cellular processes through signalling pathways. cAMP is produced by adenylate cyclases (ACs), and its downstream impact is mediated by ion channels, cAMP-dependent protein kinases (PKAs) or exchange proteins activated by cAMP (EPACs) in mammalian cells. In *Toxoplasma gondii*, a widespread obligate intracellular protozoan parasite infecting almost all vertebrates including human, cAMP signalling has been described to be important for the switch between fast-replicating tachyzoite (acute infection agent) and dormant bradyzoite (cyst forming causative agent of chronic infection) stages of the parasite. Besides, it is known to be regulating motility-dependent invasion event in tachyzoites. Although four ACs (ACα1-3, ACβ) are encoded from the genome of *T. gondii*, only ACα3 and ACβ are expressed in the tachyzoite stage of the parasite. While ACα3 shows a punctual distribution within the cytosol, ACβ is located in the special region of the secretory organelle Rhopty at the invasive apical pole of the parasite. Genetic deletion of ACα3 doesn't change the growth of the parasite; however, the fitness during lytic cycle significantly impaired in ACβ-knockout mutant, which is arisen from disrupted invasion ability of their host *in vitro*. These phenotypic profile has been shown to be regulated through *Tg*PKA, as an only mediator of the cAMP signalling pathway in *T. gondii*. Recently, the existence of an EPAC protein has been proposed as a regulator of a non-canonical signalling pathway in the malaria parasite *Plasmodium falciparum* although it's role remained elusive in the parasite. The ortholog of *Pf*EPAC in *T. gondii* was found to be localized in the pointed conoidal end, which implies its potential role to control invasion of the parasite. The special localizations of both *Tg*ACβ and *Tg*EPAC and their potential functions make them promising vaccine candidates to fight against toxoplasmosis.

***OP-5***

# Adenoviral Vector Vaccines

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Vaccination is one of the common and efficient techniques used for developing immunity against infectious diseases. Through accumulated research and development over the years, many types of vaccines have been developed, including inactivated vaccines, live-attenuated vaccines, messenger RNA (mRNA) vaccines, subunit vaccines, recombinant vaccines, polysaccharide vaccines, conjugate vaccines, toxoid vaccines, and viral vector vaccines.

Viral vector vaccines are among those that have been spotlighted with the outbreak of the COVID-19 pandemic. Viral vector technology is based on delivering genetic material into the recipient's cells by modified harmless viruses. The transportation of genetic material targets the transcription of a protein, antigen or prompting an immune response without causing infection within the recipient's host cells.

The most prevalent vectors used in vaccination are adenoviruses, due to their high nuclear transfer efficiency, large tissue tropism and low pathogenicity. Adenoviruses are non-enveloped viruses possessing a double-stranded DNA genome that cause ocular, gastrointestinal epithelium and upper respiratory tract infections in humans. Adenoviral vector genomes typically range in size from 26 to 45 kb, which may include early genes like E1, E3, and E4. Deletion of these regions and the potential insertion of foreign genes enable modifications to the virus's replication characteristics. Hence, adenoviral vectors are capable of efficient gene transfer to both dividing and non-dividing cells. Nevertheless, they exhibit short-lived expression due to remaining episomal, and in the systemic usage misexpressions occur in non-targeted tissues.

Overall, despite the limitations inherent in adenoviral vector vaccines, the benefits they provide are indisputable. In environments where infectious diseases like COVID-19 are prevalent, vaccines have played a pivotal role in safeguarding human health through the provision of immunity. Ongoing research and development studies suggest that combining adenoviruses with other technologies may offer a more reliable range of solutions.

**Keywords:** human adenovirus, viral vector vaccines, vaccination, COVID-19, infection

***OP-6***

# DNA Vaccines for Veterinary Medicine

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Next approaches to the prevention and treatment of numerous diseases are provided by DNA vaccines, which are referred to as next generation vaccines and a quickly evolving technology. It took forty years to successfully transfect mammalian cells in vivo after pure DNA was injected. Its potential was largely unknown until Wolf and colleagues demonstrated in 1990 that a reporter gene producing an enzyme protein could be produced in mouse skeletal muscle in vivo.

Vaccinations for animals are crucial for both economic output and the avoidance of zoonotic diseases, in addition to preventative medicine. Veterinary vaccinations account for the majority of vaccines administered globally and in our nation. Consequently, in the production of veterinary vaccines, the significance of biotechnology vaccines is growing.

The FDA (U.S. Food and Drug Administration) has approved the plasmid Pvax-1, one of the DNA vaccine vectors, for use in humans and animals that are appropriate for human consumption. The H5N1 avian influenza DNA vaccine for chickens was the first commercially available DNA vaccine, and it was released in 2017. Additionally, licenses have been granted for DNA vaccines created to prevent the West Nile virus in horses, infectious hemopoietic necrosis disease, pancreatic illness in salmon, and melanoma in dogs.

***OP-7***

# DNA Vaccine Transfection Systems

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DNA vaccine is a platform that utilizes plasmid DNA (pDNA) to trigger an immune response against a specific pathogen. These vaccines offer several advantages: they stimulate both arms of the immune system, boast a short production time with low costs, eliminate the risk of pathogen conversion, and provide extended shelf life and reduced transportation expenses due to their stability. Furthermore, they serve as a safety platform against various diseases because they do not provoke anti-vector or non-target acquired immunity in the vaccine recipient. DNA vaccines can be administered through five primary routes: intramuscular (IM), subcutaneous (SC), intradermal (ID), intravenous (IV), and intranasal (IN). Additionally, various methods have been developed to enhance the transfection rate and efficiency of pDNA delivery, including electroporation, needle-free jet injectors, gene guns, and microneedle arrays. In gene gun-based delivery, a biolistic system is employed to directly deliver DNA-coated microparticles to the skin. Needle-free jet injectors utilize both spring-activated and compressed gas (CO2; carbon dioxide) mechanisms to generate high-pressure flows, eliciting robust cellular immune and antibody responses. The ZyCoV-D vaccine, the first DNA vaccine authorized for emergency use against the SARS-CoV-2 virus in India, performed this method. In the microneedle array-based delivery method, the vaccine is injected directly into and controlled within the living skin layers. Electroporation is a delivery method that enhances DNA uptake by creating temporary pores in cell membranes through the application of electric pulses. DNA vaccines offer a promising and versatile approach to immunization, harnessing the power of plasmid DNA to trigger robust immune responses while presenting multiple administration options and innovative delivery methods that enhance their efficacy. Previous studies have shown that DNA vaccines employing these methods generate a more potent immune response than those that do not.

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***OP-8***

# The Role of *Saccharomyces cerevisiae* in Advancing Next-Generation Recombinant Protein Vaccines

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Recombinant proteins are often produced in prokaryotic organisms such as *Escherichia coli* in expression systems. However, eukaryotic organisms are preferred as hosts due to their ability to perform post-translational modifications that can affect the activity and stability of the target protein.[1] Besides their ability to perform post-translational modifications, they are considered safe platforms for recombinant protein production. On the other hand, *E. coli* cell wall components contain endotoxins which can lead to various side effects. Therefore, the presence of endotoxins in *E. coli* raises concerns for safety, whereas yeasts are free from endotoxin risk.[2]

To ensure the biological consistency of vaccine studies, it is imperative to determine and meticulously document the quantity and profiles of host cell proteins expressed. Choosing the suitable host organism for vaccine production is crucial. For example, the vaccines for hepatitis B and HPV are made using *S. cerevisiae*, and it's been recognized that these vaccines may contain up to 5% yeast protein. However, studies show that allergic reactions to yeast protein are rare.[3,4,5] Studies have indicated that certain cell wall components in *S. cerevisiae and Pichia pastoris* may stimulate the immune system, leading to an enhanced vaccine response. Consequently, researchers are currently exploring the potential of using whole yeast to develop oral vaccine formulations.[6]

Besides the safety of its vaccine platform, *S. cerevisiae* presents further advantages as a host organism for the industrial-scale production of proteins. *S. cerevisiae*'s resistance to adverse osmotic conditions, low pH tolerance, and genetic manipulability make it an ideal model organism for biotechnological applications.[7] Also, when it comes to large-scale production, certain strains of yeast are preferred due to their human-like glycosylation pathways, which make them more cost-effective than other complex organisms. These yeasts are advantageous because they can quickly achieve high cell densities, and they do not contain pyrogens, pathogens, or virus inclusions.[8]

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***OP-9***

# mRNA vaccine: A potential therapeutic candidate in vaccinology

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mRNA vaccine has emerged as a promising approach to deal with infection disease and cancer in recent years. The reason is that it can be produced cost effectively, large scale and in a short amount of time. In addition to that, there is no possibility of random mutations in chromosomal DNA when mRNA enters into cytoplasm. Likewise, mRNA molecule does not contain any antibiotic resistance gene to change human's microbiota. Additionally, mRNA can degrade easily to eliminate toxicity of the vaccine. On the other hand, In terms of challenges, the major problem is that they easily degregade by RNase because of their single strand structure. The other concern is optimization of mRNA molecule stability to be able to increase vaccine efficiency. Delivery system can support to overcome stability issues to increase both humoral and cellular response. However, it causes anaphylaxis, myocarditis, myopericarditis, cerebral venous thrombosis and cytokine release syndrome. The reason for this, most lipid nanoparticles contain Polyethylene glycol (PEG) which extends circulation time of the nanoparticle in blood stream. Besides all these, even though certain percentage of the population have shown health concerns, there is no doubt that mRNA vaccines will help to eradicate future outbreaks and save human lives. To sum up, The new mRNA vaccine technology can be future's therapeutic candidate in vaccinology, or we might be opening a Pandora's Box of new diseases.

***OP-10***

# DNA VACCINES

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DNA vaccines have attracted considerable attention in the fields of medicine and biotechnology in recent years. These vaccines offer several advantages over traditional vaccines. DNA vaccines involves use of genetic material to encode target proteins, thereby triggering an immune response in the body. One of the main advantages of DNA vaccines is their rapid and adaptable production. Traditional vaccine production can be time-consuming, whereas DNA vaccines speed up the manufacturing process by containing the genetic code for the target protein. This translates into a rapid response capability, which is particularly advantageous in emergency vaccine situations. DNA vaccines also have the potential to induce strong and long-lasting immune responses. They allow the target protein to be produced in vivo, potentially protecting the body for long periods of time. However, the long-term safety and efficacy of DNA vaccines are still under investigation and require further research. Nevertheless, DNA vaccines have their own set of challenges. Technical hurdles include issues related to delivery and the stability of the genetic material. Ethical and safety concerns also need to be addressed. In conclusion, DNA vaccines could play an important role in the future of healthcare, but further research and development is essential. With their rapid production and potential for robust immune responses, these vaccines represent a promising area of medical research.

***OP-11***

# Protein Based Vaccines

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Protein-based vaccines have emerged as a promising vaccination strategy, offering a more reliable and highly customizable approach to struggling against infectious diseases. These vaccines, also called subunit vaccines, are prepared either by isolating a specific protein from the pathogen and presenting it as an antigen on its own, or by cloning the antigen in a vector such as virus, bacteria, yeast, using genetic engineering technology. These vaccines are designed to selectively target the pathogen's most immunogenic and antigenic proteins to induce a protective response against the pathogen without causing disease.

During the development of recombinant protein vaccines, there are many factors to be considered in the process of making suitable proteins to be used. For example, in this process, the appropriate expression system should be selected and processes such as fermentation and purification should be optimized very well.

Protein-based vaccines also have many advantages over other types of vaccines. Because they do not contain live or inactive pathogens, they are generally safer and have fewer side effects. They can also be used effectively in immunocompromised individuals who cannot be administered live vaccines. In addition, protein-based vaccines can be produced more easily and quickly than other types of vaccines. This makes them an attractive option for quick solutions against possible new outbreaks or pandemics. It also has several advantages such as high specificity, low toxicity, and the ability to trigger both humoral and cellular immunity. In addition to having many advantages like these, they also have disadvantages such as needing booster dose and requiring the use of adjuvant.

Human papilloma virus (HPV), hepatitis B virus (HBV) and acellular pertussis vaccines are representatives of this group. Although protein-based vaccines have several advantages and are promising for the future, there are still challenges to be overcome in terms of providing broad protection and maintaining stable antigenicity.

***OP-12***

# Immunoinformatics

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The sequencing of genomes in humans and other model organisms has led to the accumulation of a substantial amount of data related to immunology research. Additionally, considerable clinical and epidemiological data is being deposited in diverse scientific publications and clinical records. This accumulation of information serves as a valuable resource for researchers investigating the mechanisms of immune function and the development of diseases. Consequently, managing this swiftly expanding immunological dataset has given rise to the emerging field known as immunoinformatics. A special use of immunoinformatics is in reverse vaccinology. In the conventional process of developing vaccines, scientists frequently use pathogens that have been weakened or inactived. Reverse vaccinology entails studying a pathogen's DNA to locate possible antigens that could stimulate an immune response. Without employing the entire pathogen, unlike in the conventional vaccines, these antigens are then created and evaluated to see if they could trigger an immune response. A particular area on an antigen's surface where antibodies or immune receptors can attach is known as an epitope, also known as an antigenic determinant. For B cells, the epitopes that are both nonlinear and linear are required. For T cells the epitopes should attach with MHC 1 and MHC2. Epitopes possess specific physicochemical attributes like antigenicity, size, binding affinity, structural stability, solubility, etc. Immunoinformatics databases serve as repositories of vast biological data and computational tools, enabling researchers to predict, catalog, and analyze epitopes efficiently, and to design vaccines with targeted immune responses.

**Keywords:** Immunoinformatics; Reverse vaccinology; Epitopes

***OP-13***

# Bioinformatics in Vaccine Development

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Vaccine is described as a biologic preparation that helps the immune system, strengthens immunity, and protection against a severe microbial infection. The practice of immunization against smallpox was formalized in Western medicine by Edward Jenner in 1796, who utilised infected material isolated from cows (vaca in Latin) and coined the term "vaccine". For centuries, vaccines have been utilized to fight various contagious illnesses, effectively reducing the impact of these diseases. Considering the recurring global threat of infectious disease pandemics, vaccination has become a highly promising approach to save countless lives and decrease infection rates. According to the World Health Organization, immunization annually safeguards three million individuals. The logic in conventional vaccines is to isolate, inactivate, and inject, while second-generation vaccines have emerged with the development of science and technology. With the contributions of genetics, genomics and proteomics, the method followed in second-generation vaccines is to isolate a protein from the pathogen and present it as an antigen by itself or to prepare it by cloning the antigens in a vector such as virus, bacteria, yeast. Components that stimulate the immune system are produced. Reverse vaccinology, which is called the 3rd generation, has emerged with the increasing vaccine studies. Unlike these two vaccine methods, reverse vaccinology basically aims to develop a potential vaccine against it by examining the genetic sequence of a virus or bacteria. In these vaccines, the genome of the pathogen is scanned with immunoinformatic and bioinformatic analyzes, and possible antigens and epitopes are selected. These analyzes are used to select potential vaccine candidates. Bioinformatics tools used in reverse vaccinology are constantly being developed and renewed, and they give us faster and more precise results compared to traditional vaccine methods. Multi epitope peptide vaccines are also considered as 3rd generation vaccines and are innovative vaccines. Multiple epitopes are used to elicit an immune response against one or more pathogens. These vaccines can be designed much more specifically. With the development of a new generation vaccine, bioinformatics programs are also developing. Some of them; for data analysis: NCBI and UniProt, for variation analysis: MEGA, for protein structure prediction RaptorX and I-Tasser, for docking simulation analysis: ClusPro v2.0, for codon optimization and molecular cloning: JCat, for 3D model refinement and validation GalaxyRefine module.

**Key words:** vaccination, new generation vaccinology, reverse vaccinology, bionformatic tools

***OP-14***

# Anti vaccination: Attitudes during COVID-19

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The smallpox vaccination developed by English scientist Edward Jenner against smallpox in the 18th century marked the beginning of the anti-vaccination movement. The World Health Organization defines vaccine hesitation as the delay in accepting or refusing to allow the administration of certain vaccines, even while the vaccine is accessible. This is distinct from anti-vaccination sentiment. Conversely, being anti-vaccination means that one refuses to consider any vaccines at all. The World Health Organization formed the Working Group on Vaccine Hesitancy in response to the alarming rise in anti-vaccination cases that has occurred globally in recent years. The World Health Organization classified anti-vaccination as one of the top 10 factors endangering world health in 2019.

In his sermon "The Dangerous and Sinful Practice of Vaccination," delivered in 1772, Reverend Edmund Massey denounced vaccinations as a demonic activity and denounced vaccination as an attempt to thwart God's retribution on man for his crimes. Apart from theological objections, anti-vaccination sentiments were also influenced by political and legal factors following the enactment of laws in England in the mid-19th century requiring parents to vaccinate their children. This led to the founding of the Anti-Vaccination League by activists in London. Arguments against vaccination include those that claim vaccines contain unreliable components, have numerous unreported negative effects, induce autism in children, are personal choices, or are utilized as biological weapons, among other similar claims.

Distinguished one of the main causes of the anti-vaccination movement, which also became prominent during the COVID-19 pandemic, is the usage of social media. The spread of untrusted individuals' reports during the epidemic and the belief of those who lacked sufficient information about it led to a rise in anti-vaccine sentiment. People's ability to regulate their ideas has improved because COVID-19 is a disease that is being discovered for the first time worldwide and the recent development of vaccines. It is crucial to educate the public about scientific literacy, to heed professional advice, and to share knowledge with reputable sources through the media in order to avert this circumstance.

***OP-15***

# The Significance of Bioinformatics and Immunoinformatic in COVID-19 Vaccine Discovery

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In the beginning of 2020, several people suffered from the pandemic caused by the Sars-CoV-2 virus, which became a significant public health issue. With the global spread of this virus and the implementation of pandemic conditions, the scientific community made substantial efforts to research the virus and develop a vaccine. The *in silico* approach, known as reverse vaccinology (RV), which utilizes genome sequences translatable into proteins, expedited the identification of vaccine candidates. The utilization of the RV in-silico approach is crucial because it offers predictions for the antigenicity, epitope regions of B and T cells, as well as other parameters such as signal peptide, subcellular localization, and solubility for targeted proteins. Results obtained from *in silico* predictions are of utmost importance for preventing potential failures that can occur at the end of wet lab studies or even in the late stages of clinical trials. In the context of our laboratory, during the *in silico* analysis of the COVID-19 DNA vaccine we developed, the entire genome of SARS-CoV-2 was analyzed. For this purpose, spike, envelope, and membrane proteins were targeted as vaccine candidates. During the in-silico analyses, physico-chemical parameters, secondary structure, subcellular localization, transmembrane helices, antigenicity, and signal peptide were predicted for 27 proteins from the reference Wuhan genome. Later, for structural proteins and proteins with a signal peptide, allergenicity, BetaWrap motifs, similarity with host proteins, post-translational modifications (PTMs), and B/T cell epitopes were predicted. Selected epitopes were then docked with receptors of MHC-I/II alleles. Finally, the effects of variations frequently occurring in structural proteins and in proteins predicted to have a signal peptide on antigenicity, signal peptide, solubility, BetaWrap motifs, PTMs, and epitope regions were investigated.

***OP-16***

# DNA Vaccine Vectors

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DNA vaccines serve as a platform for treating human and animal diseases using gene-based materials. Generally, DNA vaccine vectors consist of two different types of regions: prokaryotic and eukaryotic regions. The former refers to a region derived from the bacterial genomic sequence, necessary for replication and containing an antibiotic resistance gene, which is essential for selection in bacterial hosts. The latter is a region obtained from the eukaryotic sequence, crucial for expressing the encoded transgene in mammalian cells. In this eukaryotic region, there is a multiple cloning site where the relevant gene is inserted, a promoter located upstream of this region that initiates transcription, leading to the formation of mRNA transcripts, a Kozak sequence recognized by ribosomes to initiate translation, and a signal peptide that allows the protein to be expressed outside the cell. Downstream of the target gene, there is a polyadenylation signal that facilitates efficient mRNA transfer to the cytoplasm by mediating polyadenylation. DNA vaccine vectors are classified into three generations based on modifications to the vector backbone. In the first generation of DNA vaccine vectors, the prokaryotic region comprises at least one antibiotic resistance gene, derived from the bacterial replication origin that enables replication in E. coli, and functions as a selectable marker in bacterial culture. However, first-generation DNA vaccine vectors containing antibiotic resistance genes raise safety concerns due to the potential for antibiotic allergies and the development of antibiotic resistance through horizontal gene transfer in bacteria. Additionally, these genes increase the plasmid size, leading to reduced transfection efficiency. To address these disadvantages, second-generation DNA vaccine vectors have been developed using RNA-based, toxin-antitoxin-based, auxotrophic, or operator-repressor titration selection markers instead of antibiotic resistance markers. Third-generation DNA vaccine vectors have been developed by replacing the pUC origin, which causes a decrease in expression levels in the prokaryotic region, with a 300 bp mini-origin to mitigate this reduction. DNA vaccines represent a versatile platform for combatting human and animal diseases through the use of gene-based materials, with various generations of vaccine vectors designed to enhance safety and efficiency while harnessing the power of both prokaryotic and eukaryotic regions for therapeutic benefit.

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## *OP-17*

# RNA Vaccines

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An innovative method of vaccination, RNA vaccines have received a lot of interest recently, particularly in light of the COVID-19 pandemic. RNA vaccines use the capacity of messenger RNA (mRNA) to teach cells to produce proteins that stimulate an immune response, as opposed to conventional vaccinations, which use weakened pathogens or protein fragments. Due to their great potential, quick development capability, affordable manufacturing, and possibility for safe delivery, mRNA vaccines represent a viable alternative to conventional vaccination techniques. The rates of antigen expression, the quantity of proteins produced, and the potency of the immune response all depend on the transport and formulation of mRNA vaccines to cells. The most efficient transfer material is created by administering mRNA vaccines to cells in a variety of forms, including lipid nanoparticles, polymers, peptides, and bare mRNA.

This presentation offers a thorough investigation of RNA vaccines, explaining their mechanism of action, advantages, and future perspectives for the development of vaccination strategies. The presentation explores the underlying ideas of RNA vaccines, clarifying how they function in the body to promote immunity. The Pfizer-BioNTech and Moderna COVID-19 vaccines are two well-known examples of RNA vaccines that demonstrate real-world uses and quick development times made possible by this technology.

This presentation covers topics such as safety and long-term effects and aims to clear up misunderstandings and present accurate facts. The potential of RNA vaccine technology extends beyond infectious diseases and includes therapeutic options for illnesses like cancer. We are at the beginning of a new age in vaccination, ready to transform the landscape of global health defenses, by comprehending the revolutionary nature of RNA vaccines.

**Keywords:** RNA vaccine; mRNA; COVID-19

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***OP-18***

# Lipid-Based Formulations in Vaccines

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Due to their capacity to render antigens in vesicular structures, which in turn prevents their enzymatic degradation in vivo, lipid-based vaccine delivery systems such as conventional liposomes, virosomes, bilosomes, vesosomes, pH-fusogenic liposomes, transferosomes, immuno-liposomes, ethosomes, and lipid nanoparticles have attracted remarkable interest in vaccine delivery.Further,by altering the composition of lipids and choosing the best technique for manufacture, such nanocarriers can be made to have the desired properties, such as charge, size, size distribution, entrapment, and site specificity.This ultimately increases its adaptability as a reliable vaccine delivery vehicle. the immunostimulatory potential of lipid-based nanocarriers makes them ideal for effective vaccine delivery.

Using lipid-based drug delivery methods, known as lipid-based formulations (LBF), it is possible to increase the solubility, absorption, and bioavailability of medications that are not highly water soluble. Lipids, surfactants, co-solvents, and occasionally co-surfactants make up LBFs in most cases. To improve medication solubility, surfactants are added to LBF to lower the interfacial tension between the drug and the surrounding aqueous environment. Additionally, they help generate stable micelles or emulsions, which enhances drug absorption. Co-solvents are used to make lipophilic pharmaceuticals more soluble in the lipid phase, which helps in drug dissolution and preserves the medication's solubility during formulation and storage. In order to further stabilize the formulation and improve medication dissolution, co-surfactants are occasionally added to LBF.

**Keywords:** lipid;vaccine;delivery;LBF

***OP-19***

# Vaccines: A solution Against Antimicrobial Resistance

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The introduction of antibiotics into clinical use was arguably the greatest medical breakthrough of the 20th century. They serve as our foremost defense mechanism against bacterial diseases.

Antibiotics employ diverse mechanisms of action to combat microorganisms, including hindering cell wall synthesis, suppressing protein synthesis, disrupting folate synthesis, and interfering with DNA synthesis.

The most recent World Economic Forum Global Risks reports have identified antibiotic resistance as one of the greatest threats to human health. In Europe, it is estimated that 25,000 people die each year as a result of multidrug-resistant bacterial infections, costing the European Union economy €1.5 billion annually. By 2050, the United Nations estimates that up to 10 million deaths could be caused by superbugs and associated forms of antimicrobial resistance.

Vaccination is a potent weapon against antibiotic resistance. Targeting pathogens, vaccines can help prevent the emergence and diffusion of antibiotic resistance by reducing reliance on antibiotics and lowering the prevalence of resistant pathogens.

While vaccines play a pivotal role in combating infections and decreasing the need for antibiotics, challenges and shortcomings are linked to their use against antibiotic resistance. For instance, vaccines offer limited coverage, being specific to certain pathogens and potentially leaving room for other bacterial species to develop antibiotic resistance. This gap allows other resistant bacteria to cause infections.

In conclusion, antibiotic resistance poses a significant challenge endangering the future of humanity. While vaccination is a potent solution to this predicament, relying solely on it proves inadequate. Essential strategies include pursuing novel antimicrobial agents and preventing unnecessary antibiotic usage, both of which are imperative to counteract the emergence of antibiotic resistance.

**Keywords:** Vaccine, antibiotic resistance, antibiotic, bacteria

***OP-20***

# VLP (Virus-liked Particles) Vaccine

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Virus-like particles (VLPs) are virus-derived structures composed of one or more different molecules that have the ability to self-assemble, imitating the shape and size of a virus particle, but cannot infect the virus because they lack genetic material.

The use of virus-like particles to develop vaccines against infectious viral diseases has become an increasingly popular area of study since the success of the HPV vaccine. The increased safety of VLP vaccines, their ability to trigger strong immune responses, their ability to be produced on a large scale and their immunogenicity even at lower doses are the reasons for their increasingly frequent use. There are a variety of widely accepted VLP vaccines on the market, such as the HPV and hepatitis B vaccine, and there has been some success with the VLP malaria vaccine; there are many more types of VLP vaccines targeting other diseases currently under development.

Expression and self-assembly of viral structural proteins can occur in a variety of live or cell-free expression systems, after which viral structures can be assembled and reconstituted. VLPs are highly immunogenic and can elicit both antibody- and cell-mediated immune responses in ways different from those elicited by conventional inactivated viral vaccines. Given that viruses are susceptible to mutation and occasionally render prior immunizations useless, VLPs are also a viable solution to this issue.

**Keywords:** VLP vaccine; Virus-liked-particles; Vaccines

***OP-21***

# Vaccine History

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Vaccines are a safe and very successful means of preventing dangerous diseases from infecting humans or animals before they arise. It strengthens the host's immune system and builds resistance to infections by utilizing the body's natural defenses. Through vaccinations, the immune system is trained to produce antibodies in the same way as it does when it encounters a germ, preventing infection or complications.

If we travel back in time using vaccination milestones, we may find ourselves in a Buddhist monastery in 17th-century China, where the monks used snake venom to protect themselves from snake bites and variolation, which is the process of applying cowpox to a skin tear to protect against smallpox. The Ottoman Palace in Istanbul will be our next destination. The wife of a British ambassador, Lady Mary Montagu (1689–1762), wrote to her friends in Britain (1717–1721) regarding a smallpox immunization known as "variolation." After receiving the smallpox vaccination from this Ottoman approach for herself and her family, Lady Montagu fought to spread the practice back in Britain. The first records of vaccinations and immunization history in Turkey and Europe are found in her letters.

Our most significant stop is in Britain, the home of Edward Jenner, who in 1796 is credited with founding vaccination in the West. As the most well-known figure in the annals of modern vaccination history, he administered a vaccinia virus (cowpox) inoculation to a 13-year-old kid and proved to be immune to smallpox. Since the first smallpox outbreak in 1798, the disease has been systematically eradicated worldwide in 1979 thanks to mass immunization programs.

In the 19th century, we can proudly present Dr. Louis Pasteur as the creator of the live attenuated cholera vaccine and the inactivated anthrax vaccine for humans, which he created between 1897 and 1904, respectively. The plague vaccine was created in the late 19th century. Bacterial vaccine development flourished between 1890 and 1950; one such vaccine is the Bacillus Calmette-Guerin (BCG) immunization, which is still in widespread use today.

Moving forward to 1923, Alexander Glenny created a flawless tetanus vaccination by inactivating the tetanus toxin using formaldehyde. In 1926, the diphtheria vaccine was released using the same methodology. The first whole cell vaccination, the Pertussis vaccine, was introduced in 1948.

The discovery of viral tissue culture techniques in the 20th century (1950–1985) opened up new avenues for the creation of the Salk (inactivated) and Sabin (oral, live-attenuated polio vaccines. Due to widespread vaccination campaigns, wild polio virus has been eliminated in 99% of the world. Scientists continued because they recognized that illnesses will continue to threaten human health. In the past 50 years, numerous vaccinations have been developed through the introduction of new technology or by modifying existing approaches. These cutting-edge methods have reduced the years and costs associated with designing, manufacturing, and implementing vaccinations.

All new platforms are being used in the COVID-19 pandemic to combat SARS-CoV-2 and maybe new, emerging diseases.