IECV 2024 Conference

The 2nd International Electronic Conference on Vaccines

27–29 November 2024 | Online

Program and Abstract Book

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The 2nd International Electronic Conference on Vaccines

27–29 November 2024 | Online

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Table of Contents

Welcome from the Chair

We are pleased to announce the 2nd International Electronic Conference on Vaccines (IECV 2024), which will be held online and promoted by the open access MDPI journal Vaccines (ISSN 2076-393X, IF 5.2).

There are currently major challenges to developing new vaccines and improving existing platforms for both infectious diseases and cancer. Novel methods of vaccine delivery for both human and different animal species are required. Advances in vaccine design to give broad protection to mitigate against the mutation of antigens and to provide both good humoral and cellular immunity are a priority. For flaviviruses, particularly dengue, there are major hurdles to producing vaccines, which not only cover all the serotypes but also prevent the induction of antibody-dependent enhancement. Inactivated and subunit vaccines need to be combined with effective long-acting adjuvants to optimise their potential. In all cases, novel assays, in particular omics-based approaches, are necessary to evaluate in-depth and early responses to vaccination.

The IECV 2024 invites researchers from academia, as well as vaccine practitioners, to contribute original findings, novel ideas, scientific concepts, and new technologies and experiences to deal with immunology mechanisms, animal models for immunologic diseases, viral immunology, immunopathogenesis, vaccine development and efficacy evaluation, immune responses to vaccines, vaccine technology, vaccine vectors, adjuvants, and immunomodulators, with reference to the following topics:

Cancer vaccines, immunotherapy, and immunoprevention;
Challenges of developing a dengue vaccine;
Vaccine adjuvants;
mRNA vaccines;
Advancement in vaccine design for broad protection;
Novel assays for evaluating responses to vaccination.

The conference will be held entirely online, allowing people from all around the world to participate without any concerns about travel or related expenses. An electronic conference offers a platform for quick and direct exchanges of the latest research findings and innovative ideas.

The vaccine scientific community's support and enthusiasm are greatly appreciated, as you play a crucial role in ensuring the success of this 2nd edition of IECV. Your contribution will pave the way for many more successful editions in the future.

Professor Sara Louise Cosby
Conference Chair
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2. Virology, Veterinary Sciences Division, Agri-Food and Biosciences Institute, UK

vaccines

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Vaccines (ISSN 2076-393X) is an international, peer-reviewed open access journal focused on laboratory and clinical vaccine research, utilization and immunization. Vaccines publishes high quality reviews, regular research papers, communications and case reports. Our aim is to encourage scientists to publish their experimental and theoretical results in open access form in as much detail as possible. The full experimental details must be provided so that the results can be reproduced and computed data or files regarding the full details of the experimental procedure can be deposited as supplementary material.

Journal Webpage: https://www.mdpi.com/journal/vaccines

Keynote Speakers

Professor Eva Sevick

University of Texas Health Science Center's Institute of Molecular Medicine (IMM), Austin, USA

Prof. Dr. Martin F. Bachmann

1. Department of Immunology, University of Bern, Bern, Switzerland,
2. Nuffield Department of Medicine, Jenner Institute, University of Oxford, Oxford, UK

Dr. Byron Martina

Erasmus MC, Rotterdam, Netherlands

Dr. Antonio Di Lorenzo

Interdisciplinary Department of Medicine, University of Study of Bari, General Hospital, Piazza Giulio Cesare 11, 70124 Bari, Italy

Invited Speakers

Professor Roger Geiger

Institute of Research in Biomedicine, Universita della Svizzera italiana, Lugano, Switzerland

Dr. Paul Engeroff

Department of Immunology, University of Bern, Bern, Switzerland

Dr. Gerald Barry

School of Veterinary Medicine, University College Dublin, Dublin, Ireland

Program at a Glance

	Day 1	Day 2	Day 3
Morning	**Session 5.** Advancement in Vaccine Design for Broad Protection	**Session 3.** Vaccine Adjuvants	-
Afternoon	**Session 1.** Cancer Vaccines, Immunotherapy, and Immunoprevention **Session 5.** Advancement in Vaccine Design for Broad Protection	**Session 6.** Novel Assays for Evaluating Responses to Vaccination	**Session 2.** Challenges of Developing a Dengue Vaccine & **Session 4.** mRNA Vaccines

IECV 2024 Program

27th November 2024 (Wednesday)

Session 5. Advancement in Vaccine Design for Broad Protection

Time: 9:00 (CET, Basel) | 03:00 (EDT, New York) | 16:00 (CST Asia, Beijing)

CET Time	Speaker	Title
09:00–09:15	**Professor Sara Louise Cosby** Event Chair	**Welcome from the Event Chair**
09:15–09:45	**Prof. Dr. Martin Bachmann** Keynote Speaker	Companion animals as link for the development of therapeutic vaccines in humans
9:45–10:00	**Dominik Rothen** Selected Speaker	Preclinical evaluation of novel sterically optimized VLP-based vaccines against all four DENV serotypes
10:00–10:15	**Gianmarco Ferrara** Selected Speaker	An Evaluation of the humoral response following two doses of a Coxiella burnetii vaccine in water buffalo
10:15–10:30	**Xinyue Chang** Selected Speaker	Virus-like particle-derived vaccine induces broad neutralising antibodies against porcine epidemic diarrhea virus (PEDV)
10:30–10:45	**Victoria Jane Smyth** Selected Speaker	Evaluation of Chicken Astrovirus Breeder Vaccine Candidate
10:45–11:00	**Zilu Ma** Selected Speaker	Lysosome-Associated Membrane Protein Targeting Strategy Improved Immunogenicity of Glycoprotein-Based DNA Vaccine for Hantaan virus
11:00–11:15	**Dudnikova Ekaterina Nikolaevna** Selected Speaker	The dynamics of the incidence of vaccine-controlled infections in the southern federal district of the russian federation from 2010 to 2023
11:15–15:00	BREAK	

Session 1. Cancer Vaccines, Immunotherapy, and Immunoprevention
Session 5. Advancement in Vaccine Design for Broad Protection

Time: 15:00 (CET, Basel) | 09:00 (EDT, New York) | 22:00 (CST Asia, Beijing)

CET Time	Speaker	Title
15:00–15:15	**Prof. Dr. Mona O. Mohsen** Session Chair	**Welcome from the Session Chair**
15:15–15:45	**Professor Roger Geiger** Invited Speaker	Metabolic modulation of tumors with engineered bacteria for cancer immunotherapy
15:45–16:15	**Prof. Dr. Eva Sevick** Keynote Speaker	Improving checkpoint blockade immunotherapy with vaccination and lymphatic delivery
16:15–16:30	**Romano Josi** Selected Speaker	Intranasal administration of a tetravalent nanovaccine inhibits growth of HPV-associated head and neck orthotopic tumors in a murine model
16:30–16:45	**Arnau Solé Casaramona** Selected Speaker	Cutting-Edge: Unleashing the Potential of γδ T Cells with Novel Nanoparticles for Cancer Immunotherapy Applications
16:45–17:00	**Silvia A. Sousa** Selected Speaker	Exploiting surface-exposed proteins to develop new therapeutic strategies against Bcc and Pseudomonas aeruginosa infections
17:00–17:15	**Araceli Veronica Marquez-Escobar** Selected Speaker	Synthesis and characterization of zein nanoparticles for antigen delivery

28th November 2024 (Thursday)

Session 3. Vaccine Adjuvants

Time: 9:00 (CET, Basel) | 03:00 (EDT, New York) | 16:00 (CST Asia, Beijing)

CET Time	Speaker	Title
09:00–09:10	**Prof. Dr. Silvio Tafuri & Dr. Srinivasa Reddy Bonam** Session Chairs	**Welcome from the Session Chairs**
09:10–09:40	**Dr. Antonio Di Lorenzo** Keynote Speaker	TBA
09:40–09:55	**Fusako Mitsunaga** Selected Speaker	Efficacy, Safety, and Molecular Mechanism of Sublingual Poly(I:C)-Adjuvanted Vaccine Formulated with SARS-CoV-2 RBD or Influenza HA Antigen in Non-Human Primates, Macaque Monkeys
09:55–10:10	**Kishore Alugupalli** Selected Speaker	Turbo: an adjuvant platform for bacterial glycoconjugate vaccines
10:10–10:25	**Xinliang Kang** Selected Speaker	Overcoming Aging-Associated Poor Influenza Vaccine Responses with CpG 1018 Adjuvant
10:25–14:00	**BREAK** Selected Speaker	

Session 6. Novel Assays for Evaluating Responses to Vaccination

Time: 14:00 (CET, Basel) | 08:00 (EDT, New York) | 21:00 (CST Asia, Beijing)

CET Time	Speaker	Title
14:00–14:10	**Prof. Dr. Seth Pincus & Dr. Tan Yee Joo** Session Chairs	**Welcome from the Session Chairs**
14:10–14:30	**Dr. Tan Yee Joo** Session Chair	**Establishing surrogate assays to measure antibodies inhibiting multiple subtypes of influenza A virus**
14:30–15:00	**Dr. Paul Engeroff** Invited Speaker	Allergy Immunotherapy: Considering Immune Complexes
15:00–15:15	**Milagros Virhuez Mendoza** Selected Speaker	Distinguishing the antibodies induced by the live attenuated vaccine (LC16m8) and orthopoxvirus infections
15:15–15:30	**Valeria Perniola** Selected Speaker	Covid-19, influenza, and pneumococcus vaccinal status among hospitalized patients during the Covid-19 pandemic era
15:30–15:45	**Zilu Ma** Selected Speaker	Immunoreactivity Analysis of MHC-I Epitopes Derived from the Nucleocapsid Protein of SARS-CoV-2 via Vaccination
15:45–16:00	**Alvaro Munaylla** Selected Speaker	In silico design of a vaccine candidate against Oropouche virus based on a multi-epitope protein

29th November 2024 (Friday)

Session 4. mRNA Vaccines
Session 2. Challenges of Developing a Dengue Vaccine

Time: 14:00 (CET, Basel) | 08:00 (EDT, New York) | 21:00 (CST Asia, Beijing)

CET Time	Speaker	Title
14:00–14:10	**Dr. Jorge H. Leitão & Dr. Srinivasa Reddy Bonam** Session Chairs	**Welcome from the Session Chairs**
14:10–14:40	**Professor Gerald Barry** Invited Speaker	Analysis of bovine coronavirus sequences circulating in Ireland and development of a prototype, species specific, mRNA vaccine, targeting this virus
14:40–14:55	**Rabaï Bouderhem** Selected Speaker	Regulating the use of AI in mRNA vaccine development through policy coherence
14:55–15:10	**Noe Juvenal Mendoza-Ramírez** Selected Speaker	DNA immunization with a plasmid that codifies O-SN SARS-CoV-2 fusion protein induced effective humoral and cellular immune response in a preclinical model
15:10–15:55	**Dr. Henry Puerta-Guardo & Dr. Bapi Pahar** Session Chairs	**Welcome from the Session Chairs**
15:15–15:35	**Dr. Henry Puerta-Guardo** Session Chair	**TBA**
15:35–16:05	**Dr. Byron Martina** Keynote Speaker	**TBA**
16:05–16:20	**Hector Hernando Gutierrez Barbosa** Selected Speaker	A comparison of Humanized mice models using NOD-derived strains for Dengue virus infection
16:20–16:35	**Arturo Linan-Torres** Selected Speaker	Development of a dual vaccine candidate against dengue and zika viruses by presenting a mimotope on the capsid of adeno-associated virus serotype 8

Session 1. Cancer Vaccines, Immunotherapy, and Immunoprevention

sciforum-104701: An attractive vaccine candidate based on AP205 VLPs fusing with an RBM domain of a new porcine deltacoronavirus strain in China

Xinyue Chang, Zhenyuan Zhang, Fei Fei, Yilian Chen, Minghui Zhang and Xuelan Liu

College of Animal Science and Technology, Anhui Agricultural University, Hefei 230036, China

Swine coronaviruses (SeCoV) have become a major concern in pig farming and have caused enormous economic losses all over the world. Porcine deltacoronavirus (PDCoV) is a newly emerged SeCoV, which was able to infect avians as well as humans. Therefore, developing efficient vaccines against PDCoV is not only important to pork production, but also contributes to public healthcare. In this study, we identified a new PDCoV strain, CHN/GD/2023, which was isolated from a diarrheal piglet colon. After a thorough sequence analysis of the Spike gene, CHN/GD/2023 was found to be closely related with other PDCoV viruses that have recently been isolated in China. Next, a VLP-based vaccine candidate, AP205-RBD, was produced by genetically fusing the receptor-binding domain (RBD) of CHN/GD/2023 to the C-terminus of the AP205 gene. The purified AP205-RBD successfully displayed RBD on the surface and exhibited a spherical particle structure with a diameter of 51 nm. The agarose gel image demonstrated that ssRNA from *E. coli* was packaged inside the AP205-RBD particle. In addition, AP205-RBD demonstrated potent immunogenicity in mice, as highly RBD-specific IgG titers were detected. Importantly, these antibodies were able to neutralize CHN/GD/2023 PDCoV in vitro, suggesting that the AP205-RBD vaccine is capable of protecting against viruses. Moreover, we surprisingly found that AP205-RBD elicited antibodies that could neutralize another strain of PDCoV that was previously isolated in China, implying that AP205-RBD could potentially protect animals from different PDCoV strains. In summary, a new PDCoV strain was isolated and identified in this study, and an effective vaccine candidate, AP205-RBD, was reported, which could induce broad antibody protection responses in mice.

sciforum-107166: An Evaluation of the humoral immune response generated by the inoculation of a multi-peptide-based vaccine prototype derived from tumoral antigens of breast cancer in Balb/C mice

Edgar Hurtado-Ortega [1,*], María Lilia Nicolás-Morales [1], Amalia Vences-Velázquez [1], Juan Miguel Mendoza-Bello [2], Mónica Espinoza-Rojo [2] and Karen Cortés-Sarabia [3]

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[2] 2 Laboratorio de Biología Molecular y Genómica, Facultad de Ciencias Químico Biológicas. UAGro. Chilpancingo de los Bravo, Guerrero. México
[3] Universidad Autónoma de Guerrero

Introduction: Breast cancer is the most diagnosed type of cancer in women and the leading cause of death by cancer worldwide. In recent years, active immunotherapy using vaccines has been raised as a novel approach to conventional treatments. Peptide-based vaccines are developed using overexpressed proteins in the tumor, commonly known as tumor antigens, that can stimulate the humoral immune response. Objective: To evaluate in Balb/c mice the production of antibodies induced by inoculation with doses of 30, 50, and 100 µg of the multi-peptide-based vaccine prototype derived from tumoral antigens. Material and methods: The vaccine prototype included the peptides derived from the following proteins: mammaglobin-α, NY-ESO-1, PLAC-1, Syntenin-1, and MAGE-A3. These were selected by in silicio analysis. Peptides were mixed with Freund incomplete adjuvant and inoculated subcutaneously during days 1, 15, 45, and 60 in twelve Balb/C mice classified into four experimental groups (three experimental groups and a placebo group). The mice were bled during days 0, 40, and 80, and serum samples were used to detect the presence of antibodies (IgM, IgG1, IgG2a, IgG2b, and IgG3) and the recognition of each individual peptide by assays of Indirect ELISA and Dot blot. Results: We observed the production of IgM and subclasses of IgG in the three experimental groups (30, 50, and 100 µg), mainly the subclasses IgG2a and IgG2b. In the Dot blot, we observed that immunized mice produce antibodies against all the peptides; particularly, the peptides derived from Syntenin-1, PRAME, mammaglobin-α, and PLAC-1 were the most immunogenic. Conclusion: The multi-peptide-based vaccine prototype induced antibody production against each peptide. The results can contribute to the development of future in vivo experiments focused on the effect of the administration of peptides on avoiding tumoral growth.

sciforum-098541: An in silico and in vivo analysis of a novel multi-epitope peptide vaccine against hepatocellular carcinoma

Yusra Zarlashat [1,*] and Hassan Mushtaq [2]

[1] Government College University, Faisalabad
[2] Health Biotechnology Division, National Institute for Biotechnology and Genetic Engineering (NIBGE-C), Faisalabad, Pakistan

Hepatocellular carcinoma (HCC) is becoming more prevalent, making it one of the most serious worldwide health challenges. Several studies have focused on designing effective multi-epitope peptide vaccines against HCC in recent years. An in silico approach was used in prior investigations to create a multi-epitope peptide vaccine against HCC. Glypican-3 (GPC-3), melanoma-associated antigen-C2 (MAGE-C2), aspartyl-β-hydroxylase (ASPH), and New York esophageal squamous cell carcinoma 1 (NY-ESO-1) are four overexpressed antigens in HCC patients that we used in the vaccine's design. A multi-epitope peptide vaccine against HCC was designed through in silico antigen selection, physicochemical characterization, epitope prediction, structural analysis, cloning optimization, immune simulation, bacterial expression, protein purification, and immunological evaluation in rats. Four B-cells, nine MHC-I restricted, and eleven MHC-II restricted epitopes were selected based on their antigenicity score >0.5 and non-allergenicity with an adjuvant that included a segment of the microbial heat shock protein (HSP70) peptide 407-426 for vaccine construction. The relevant linkers were used to link each of the vaccine components and the cloned-in vector. This vector was successfully transformed into the Escherichia coli strain to further evaluate itsimmunological response and efficacy. The primary aim of this study is to design a vaccine and subsequently conduct laboratory experiments to evaluate its efficacy and safety profiles. It covers 90% of the global population, hence it is very effective. The vaccine's easily soluble nature was shown by its physicochemical properties, such as its hydropathicity index (-0.457) and aliphatic index (75.63). The vaccine has a high probability of being soluble in E. coli, with a solubility of 0.680. The ongoing results will provide insights into the efficacy of the vaccine against HCC.

sciforum-103741: Comprehensive Review on Vaccination Approaches in Triple-Negative Breast Cancer

Nishant Mahendra Patel [1,*], Zubair Saghir Ahmed Shaikh [2], Sulbha G Patil [2], Amitkumar Dhankani [3] and Palak Mahendra Patel [4]

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[2] Department of Pharmaceutics, P.S.G.V.P.M'S College of Pharmacy, Shahada, 425409, India
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[4] KM Shah Dental College and Hospital, Sumandeep Vidyapeeth, Vadodara, 391760, India

Triple-Negative Breast Cancer (TNBC) represents a formidable subtype of breast cancer, characterized by the absence of estrogen receptors, progesterone receptors, and HER2 protein. This phenotype presents significant treatment challenges due to its aggressive nature and lack of targeted therapies. Consequently, there has been an intensified focus on novel therapeutic strategies, including vaccination approaches, which hold promise in eliciting robust anti-tumor immune responses. This review provides a comprehensive analysis of current vaccination strategies employed in the management of TNBC. It explores various vaccine platforms, such as peptide-based, dendritic cell-based, viral vector-based, and virus-like nanoparticle (VLP)-based vaccines, highlighting their mechanisms of action. Furthermore, this review examines the role of neoantigen vaccines, which leverage tumor-specific mutations to enhance immune specificity and efficacy, and combination strategies that integrate vaccines with other modalities, including immune checkpoint inhibitors and conventional chemotherapies, to potentiate anti-tumor responses and overcome immunosuppressive tumor microenvironments. Emerging trends, such as personalized vaccination approaches tailored to individual patient tumor profiles, are evaluated for their potential to revolutionize TNBC treatment paradigms. Additionally, we address the challenges and limitations faced in vaccine development, including antigen selection, delivery methods, and the heterogeneity of TNBC. This review concludes with future perspectives on optimizing vaccine-based therapies and their integration into standard TNBC treatment regimens. By synthesizing current research and clinical advancements, this review aims to provide a detailed understanding of vaccination strategies in TNBC, underscoring their potential to improve patient outcomes and contribute to the ongoing battle against this aggressive cancer subtype.

sciforum-096094: Cutting-Edge: Unleashing the Potential of γδ T Cells with Novel Nanoparticles for Cancer Immunotherapy Applications

Arnau Solé Casaramona [1,*], Romano Josi [2], Anete Ogrina [3], Ina Balke [3], Sanjana Marar [4], Simone Danielle de Brot [5], Eva Sevick [6] and Mona O.Mohsen [4]

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Introduction: Recent research demonstrates that specific variants of gamma delta (γδ) T cells possess innate properties, previously deemed only adaptative. Our understanding of the innate-like behavior of γδ T cells upon encountering virus-like nanoparticles (VLPs) remains limited. Exploring the interaction between γδ T cells and VLPs presents an intriguing avenue for research, offering insights into how VLPs can serve as an effective platform to enhance their expansion and activation. Methods: We created novel plant-derived VLPs, engineered to incorporate TLR ligands to effectively stimulate the innate immune system. This study encompasses in vivo and in vitro assays, FC analysis and RNA sequencing. Results: Our findings demonstrate the robust uptake of our novel VLPs by γδ T cells, leading to significant expansion in draining lymph nodes upon subcutaneous injection. Interestingly, in mice lacking TLR7 or C3, γδ T cell expansion was reduced, suggesting their involvement in the immune response triggered by our VLPs. Subsequent analysis of γδ T cell Vγ1 and Vγ4 subtypes post-VLP administration revealed substantial expansion and distinct activation profiles. Ongoing RNA sequencing will unveil activation pathways, shedding light on the molecular mechanisms underlying their response to our innovative VLPs. Conclusion: Our novel data reveal the innate-like response of γδ T cells to our VLPs, loaded with different innate stimuli. This highlights the rapid and crucial role of γδ T cells in early immune responses, offering insights for potential immunotherapeutic strategies against cancer.

sciforum-106550: Development of Nanobodies Targeting TIGIT for Cancer Immunotherapy

Shipeng Wang *, Jixiang Gu, Chunhui Li, Huimin Ma, Xiangyu Xie, Wenxiao Sun, Xinyue Chang and Lisha Zha

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TIGIT, a T-cell immunoreceptor with Ig and ITIM domains, has been recognized as a critical inhibitory receptor on T cells and natural killer (NK) cells. It plays an important role in immune suppression mediated by tumors. Tumor cells express CD155, which engages TIGIT and hampers T cell or NK cell activation to perform cytotoxicity, thus facilitating tumor progression. Releasing TIGIT on immune cells from CD155 binding to target tumor cells is one promising strategy for cancer immunotherapy. To this end, TIGIT-specific nanobodies were generated by immunizing camels with the TIGIT protein, from which a library of nanobodies was built. Then, Monoclonal nanobodies were screened by phage display, and high-affinity nanobodies for TIGIT were identified. Competitive ELISA assays were performed to demonstrate that nanobodies effectively inhibited the binding of TIGIT to CD155. Furthermore, the cytotoxicity activities of NK-92MI cells were significantly enhanced by adding TIGIT antibodies; meanwhile, higher cell degranulation was determined. At the same time, the viability of tumor cells after mixing with NK-92MI cells was detected, showing that the viabilities of K562 cells were as high as 90%, suggesting the limited cytotoxicity of NK-92MI cells. In contrast, the viabilities of K562 cells were significantly reduced when the nanobodies were added, indicating that nanobodies effectively block TIGIT on NK cells from binding to CD155 on tumor cells. These findings suggest that the screened nanobodies have promising potential for further evaluation in tumor-bearing mouse models. These nanobodies might offer significant benefits in clinical settings by improving patient selection and therapeutic outcomes in cancer immunotherapy.

sciforum-096101: Intranasal administration of a tetravalent nanovaccine inhibits growth of HPV-associated head and neck orthotopic tumors in a murine model

Romano Josi [1,*], Arnau Solé Casaramona [2], Sanjana Marar [2], Simone De Brot [3] and Mona Mohsen [2]

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[3] COMPATH, Institute of Animal Pathology, University of Bern, Bern, Switzerland

Introduction: The incidence of human papillomavirus 16 (HPV16)-associated head and neck squamous-cell carcinoma (HNC) is steadily rising. Intranasal neoadjuvant vaccines against HNC are a novel and potentially highly effective approach in cancer immunotherapy to directly induce broad humoral and cellular mucosal immunity.

Method: We utilized our previously reported Qβ-HPVag consisting of virus-like particles loaded with CPG and chemically coupled to four elongated HPV16-derived E6/E7 MHCI peptides for intranasal administration in an orthotopic murine model. Our study encompasses a range of in vivo and in vitro experiments, as well as tissue imaging mass cytometry (ongoing), to evaluate the immune cell populations within the tumor microenvironment.

Results: Our preliminary results indicated that intranasal administration of Qβ-HPVag impeded orthotopic tumor growth and enhanced the infiltration of tumor-infiltrating lymphocytes in the tumor. Assessment of vaccinated mouse lungs showed an increased CD8 T cell population, suggesting a protective potential of the intranasal vaccine. Moreover, our findings demonstrated improved tumor-free survival in the treated group after primary tumor dissection, indicating the efficacy of the neoadjuvant approach.

Conclusion: Our preliminary findings demonstrate the effectiveness of intranasal vaccination using Qβ-HPVag in an orthotopic murine model of aggressive head and neck cancer. These promising outcomes pave the way for novel clinical development strategies in HNC immunotherapy, suggesting a potential transformative impact on treatment paradigms.

Session 2. Challenges of Developing a Dengue Vaccine

sciforum-105071: A comparison of Humanized mice models using NOD-derived strains for Dengue virus infection

Hector Hernando Gutierrez Barbosa [1,*], Sandra Medina-Moreno [1], Federico Perdomo-Celis [2], Harry Davis [1], Joel Chua [1] and Juan C Zapta [1]

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Dengue, a major public health issue in tropical and subtropical regions, currently has no specific treatment and only one licensed vaccine, with limited use in endemic areas. The lack of antiviral drugs and the challenges in understanding dengue's pathophysiology stem from the absence of an effective animal model that mirrors human infection in terms of viraemia peaks, clinical presentation, and immune response. Humanized mouse models have been useful in viral disease research, but dengue studies often use NOD-scid IL2R gamma null (NSG) immunodeficient mice, which focus on preventing graft rejection rather than fully developing human hematopoiesis. In this study, we compare four humanized mouse models derived from NOD mice expressing human cytokines, which were xenotransplanted and infected with DENV-2 (New Guinea C) intravenously. The models (Hu-NSG, hu-EXL, hu-SGM3) received xenotransplants of CD34+ fetal cord blood, while one model (Hu-SGM3-PBMCs) was transplanted with human PBMCs. We found that models expressing human cytokines had higher viremia compared to the NSG model. All the models showed infectious virus during viremia, confirmed by means of indirect plaque assays. The Hu-SGM3-PBMCs model, in particular, developed a severe infection with signs of bleeding and intestinal necrosis, leading to the death of all mice by day 18 post-infection, with viremia levels twice as high as in the other models according to RT-qPCR. The models using hCD34+ cells showed low or undetectable levels of human proinflammatory cytokines during infection, measured by means of flow cytometry Bead Arrays. In contrast, the hu-mice model with human PBMCs exhibited detectable and decreasing levels of IFN-g, IL-10, IP10, and TNF, which is consistent with the immune modulation seen in DENV-2 New Guinea C strain infections. These results indicate that humanized mice models derived from NOD mice expressing human cytokines enhance viremia and offer a relevant platform for studying dengue and potential treatments.

sciforum-106548: Development of a Dual Vaccine Candidate Against Dengue and Zika Viruses by Presenting a Mimotope on the Capsid of Adeno-associated Virus Serotype 8

Arturo Linan-Torres *, Esmeralda Cuevas-Juarez, Ana Ruth Pastor, Cesar Millan-Pacheco, Octavio T. Ramirez and Laura A. Palomares

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Pre-existing dengue virus (DenV) immunity is a risk factor for severe dengue mediated by antibody-dependent enhancement (ADE), which occurs when a seropositive DenV patient is re-infected with a DenV of a different serotype. DenV and Zika virus (ZikV) are highly similar, and ADE has been observed between them. As DenV and ZikV co-circulate in many regions of the world, a vaccine that provides protection against both viruses without inducing ADE is needed. The main objective of this work was to determine the potential as a vaccine candidate of a mimotope of the shared epitope EDE of DenV and ZikV, displayed in the capsid of adeno-associated virus serotype 8 (AAV-8).

AAV-8 capsids that display the EDE mimotope (chimeric VLP) and native control capsids (native VLP) were produced. The VLPs were purified using iodixanol gradients and characterized by Western blot, dot blot, transmission electron microscopy, and cryo-electron microscopy, showing that the chimeric VLPs were recognized by a monoclonal antibody specific for DenV and ZikV, and not for AAV-8, and that the chimeric protein assembled into AAV-8 capsids with typical morphologies. Groups of BALB/c mice were subcutaneously or intramuscularly immunized with chimeric VLP, native VLP, or controls. Serum samples were collected to evaluate the humoral immune response through the ELISA test. Mice immunized with chimeric VLP produced antibodies that recognized DenV serotype 2 and ZikV. In silico biophysical studies were performed to analyze the interaction between the mimotope and the antibody against DenV and ZikV. We then evaluated the function of the chimeric VLP as a viral vector. The chimeric VLP could encapsidate the eGFP gene and transduce the HEK-293 and CHO cells, showing that the function of the AAV vector was retained after modification.

This work represents a new strategy for the development of a vaccine against DenV and ZikV based on a mimotope.

Session 3. Vaccine Adjuvants

sciforum-098011: Efficacy, Safety, and Molecular Mechanism of Sublingual Poly(I:C)-Adjuvanted Vaccine Formulated with SARS-CoV-2 RBD or Influenza HA Antigen in Non-Human Primates, Macaque Monkeys

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The sublingual vaccine introduced in this study induces mucosal antibody-mediated protection against SARS-CoV-2 and influenza viruses, which infect via the upper respiratory tract, mouth, and nose. Poly(I:C) is an adjuvant used to activate TLR3-mediated immune responses, but it remains unapproved due to its proinflammatory side effects. The mucosae of the oral cavity are the primary target of the sublingual vaccination, although this poses a practical limitation due to the inhibitory mucin barrier.

We developed a sublingual SARS-CoV-2 vaccine using the SARS-CoV-2 RBD antigen and Poly(I:C) adjuvant, as well as an influenza vaccine including the HA antigen. These vaccines were tested in non-human primates, macaque monkeys, utilizing N-acetyl cysteine to disintegrate the mucus layer. The sublingual Poly(I:C)-adjuvanted vaccine (SPAV) elicited mucosal and systemic immune responses, including antigen-specific secretory IgA in saliva and nasal washing, as well as specific IgA and IgG in blood. These antibodies neutralized SARS-CoV-2, suggesting that the SPAV protects against the SARS-CoV-2 virus.

SPAV appeared to be safe judging from the results of the blood tests, the plasma inflammatory cytokines, the gene expression of the proinflammatory factor in the WBC, and a direct comparison to AddaS03, which is an emulsion adjuvant viewed as being safe. In mice, an intranasally administrated Poly(I:C)-adjuvanted vaccine had a potent unfavorable effect in the olfactory bulb, causing the upregulated expression of nine proinflammatory genes, but the same was not true in monkeys. Thus, the previously reported detrimental effects of Poly(I:C)-adjuvanted vaccines in mice are overstated due to differences in nose structure and function, as well as immune response, between mice/rodents and macaques/primates.

DNA microarray analysis revealed that the SPAV mediates atypical up- or down-regulated gene expression associated with immune suppression/tolerance, leading to incomplete Treg differentiation and T-cell exhaustion. Possibly, the PASV could induce previously unknown effects on balancing stimulation and inhibition, like the “Yin and Yang" concept, in immune responses.

sciforum-104984: Enhancing adjuvant efficacy with dispersed Ascorbyl Palmitate (ASC16)

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Today, an ideal adjuvant must meet several essential criteria: it must be safe, biocompatible, and capable of directing the immune response and enhancing antigen presentation. ASC16 (GRAS and FDA Inactive Ingredients Database) is a derivative of vitamin C that can form viscoelastic hydrogels or act as a toxin inhibitor depending on whether it is present at high or low concentrations, respectively. For these reasons, we proposed to evaluate the effect of dispersed ASC16 (low concentration; Mo) as an additive in a hydrogel (high concentration; Pa40) to produce experimental antivenom. For the formation of the hydrogel, first, ASC16 (25 mg) and PEG_{400} solution (0.750 mL) were mixed and heated to 63 °C until complete solubilization. Then, this dispersion was cooled to 40 °C, and then it was incorporated into 0.250 mL of PBS solution with or without dispersed ASC16 (120 µM) and finally venom proteins (6-10 µg/mice). Afterward, BALB/c mice were inoculated with hydrogel in the absence or presence of additive (Pa40 and Pa40Mo). Fourteen days after the inoculation, skin and blood samples were taken for histological analysis of local injury and to determine the titre and specificity of the antibodies by ELISA and Immunoblotting tests. We used t-tests for two independent samples to verify whether there were significant differences. Our results show that Pa40Mo induced the highest titres (3.75) and had the highest Western blot signal, followed by Pa40 (3.27), with significant differences ($p \leq 0.05$). Histological analyses indicate that both formulations caused tissue alterations by the observation of regenerating muscle cells. This study shows that both formulations provide evidence of acute injury and that formulations with dispersed ASC16 as an additive induce higher antibody titres and have greater specificity than formulations without the additive. However, future studies are needed to determine the signalling mechanism of dispersed ASC16.

sciforum-104723: Overcoming Aging-Associated Poor Influenza Vaccine Responses with CpG 1018 Adjuvant

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Introduction: Immunosenescence significantly reduces the efficacy of influenza vaccines in the elderly. This study explores the use of a clinically approved CpG 1018 adjuvant, an oligonucleotide-based adjuvant, to enhance influenza vaccine-induced immune responses to the influenza vaccine in aged mice, approximating the response in humans in their late 50s to early 60s.

Methods: Aged and young adult mice were immunized with the 2009 H1N1 pandemic influenza vaccine, with and without the CpG 1018 adjuvant. Serum antibody titers and cellular immune responses were evaluated. Mice were challenged with a lethal dose of mouse-adapted homologous viruses to evaluate the protective efficacy.

Results: In aged mice, CpG 1018 significantly increased influenza vaccine-induced serum antibody titers and Th1-biased CD4+ T cell responses and stimulated cytotoxic T lymphocytes. The CpG 1018-adjuvanted aged mice exhibited improved survival and reduced morbidity after the viral challenges as compared to those vaccinated without the adjuvant. In comparison, the non-adjuvanted vaccine induced more potent immune responses in the young adult mice.

Conclusions: Our data support the addition of CpG 1018 to influenza vaccines to enhance its immunogenicity and protective efficacy in aged mice. These findings advocate for the use of the CpG 1018 adjuvant in influenza vaccines for the elderly to enhance both humoral and cellular immune responses, thereby improving health outcomes in this vulnerable population.

sciforum-105080: Turbo: an adjuvant platform for bacterial glycoconjugate vaccines

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Introduction. The activation of the adaptive immune system requires the engagement of co-stimulatory pathways in addition to primary antigen receptor signaling, and adjuvants play a central role in this process. Surprisingly, many bacterial polysaccharide vaccines, including typhoid Vi polysaccharide and quadrivalent meningococcal conjugate (MCV4) vaccines, do not incorporate adjuvants, and induce highly variable antibody responses. We found that Toll-Like Receptor 4 ligands present in typhoid vaccines account for the immunogenicity of typhoid vaccines. Based on this rationale, we developed a non-toxic TLR4 ligand, a monophosphoryl lipid A-based adjuvant formulation called Turbo.

Methods. The adjuvanticity of Turbo was tested with WHO-prequalified or FDA-approved typhoid and MCV4 vaccines, as well as a haptenated antigen system (NP-CGG) in several inbred and outbred strains of mice of all ages. The methodology employed included transgenic mouse systems, challenge models, serum bactericidal assays, ELISA, ELISpot, flow cytometry, and immunohistochemistry.

Results: Turbo promoted antibody responses across all ages and eliminated or minimized the booster requirement. In contrast to the commonly used adjuvant alum, Turbo promoted a superior germinal center response accompanied by affinity maturation and class switching to all four IgG isotypes. The magnitude of these IgG responses was sustained for more than one year in mice, which is concurrent with long-lived plasma cells present in bone marrow. Unlike alum, Turbo adjuvanticity is not dependent on canonical or non-canonical inflammasome activation or pyroptosis. Turbo upregulated the expression of the co-stimulatory molecules CD86 and CD40 on B cells, and Turbo adjuvanticity is dependent primarily on the TLR4-MyD88 axis and is lost in mice deficient in CD86 or CD40.

Conclusion: Turbo efficiently engages the required co-stimulatory pathways and promotes long-lasting antibody responses across all ages. Therefore, Turbo can be incorporated into a wide range of mono and multivalent polysaccharide vaccines to enhance immunogenicity and maximize efficacy.

Session 4. mRNA Vaccines

sciforum-105220: The Efficacy, Safety, and Immunogenicity of mRNA-1345 for Respiratory Syncytial Virus Prevention in Adults: A Systematic Review

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Background: Respiratory syncytial virus (RSV) is a major pathogen that causes respiratory illness in adults and most commonly affects populations with additional comorbidities or the elderly. RSV poses a significant risk for severe respiratory infections among adults. The mRNA-1345 vaccine utilizes advanced mRNA technology. While mRNA vaccines have demonstrated considerable success in other infectious disease contexts, detailed evidence on the efficacy, safety, and immunogenicity of mRNA-1345 specifically for RSV among adults remains scarce. Objective: We aimed to evaluate the effectiveness and safety profile of the mRNA-1345 vaccine in preventing RSV infections in adult populations. Method: A search was conducted through PubMed and the Cochrane Library to identify randomized controlled trials examining the efficacy and safety of the mRNA-1345 vaccine against RSV. The review was conducted adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Results: The mRNA-1345 vaccine demonstrated an overall efficacy of 68.4% against RSV- associated respiratory illness (ARI) and 83.7% against RSV-associated lower-respiratory-tract disease (LRTD) with at least two signs or symptoms in individuals aged 60 and older. Concerning RSV-associated respiratory illness (ARI), the vaccine provided 78.5% protection against RSV-A and 51.7% against RSV-B strains. The vaccine's safety profile was comparable to a placebo, with mild to moderate adverse events like injection-site pain and fever. Adverse events were rare and equally distributed between the vaccine and placebo groups. Conclusion: The mRNA-1345 vaccine has demonstrated significant benefits in preventing RSV-associated LRTD and ARI in adults aged 60 and older. Additionally, it has proven to have an acceptable safety profile across age groups, particularly in those aged 18-49 and 60 and above. The vaccine also elicited a robust immune response, with clear evidence of immunogenicity. Overall, the mRNA-1345 vaccine emerges as a promising candidate for adult vaccination.

sciforum-106319: DNA immunization with a plasmid that codifies O-SN SARS-CoV-2 fusion protein induced effective humoral and cellular immune response in a preclinical model

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DNA vaccines have been developed against viruses for many years. For COVID-19, acid nucleic immunization has been evaluated. A few preclinical studies have shown that the combination of the spike and nucleocapsid proteins of SARS-CoV-2 induced a robust immune response. In this work, we designed a plasmid that codifies for fusion proteins and evaluated its ability to elicit an immune response in a mouse model. Using in silico approaches, we determined the most immunogenic regions of the spike (S) and nucleocapsid (N) proteins of the SARS-CoV-2 Omicron strain. Once the sequences were selected, we generated the structure of this fusion protein in AlphaFold and determined its physicochemical and immunogenic properties on several platforms. The sequence was cloned in pcDNA3.1 and named pcDNA3.1/O-SN. The expression of plasmid was evaluated by Western blot and immunofluorescence. Then, BALB /c mice were immunized with 25 µg of pcDNA3.1/O-SN and parental vector pcDNA3.1. Three doses at 20-day intervals were administrated. After immunization, bleedings were performed, serum samples were obtained, and the humoral response was determined. Splenocytes were obtained from the immunized mice, and the cellular T-cell response was analyzed by flow cytometry. Finally, a cross-reaction with RBD from different SARS-CoV-2 variants of concern was evaluated. Specific antibody responses of IgM and IgG against N and S1 proteins from SARS-CoV-2 were observed in pcDNA3.1/O-SN-immunized mice. Furthermore, these antibodies exhibited neutralization activity, and production of IFN-γ was detected in CD4+ and CD8+ cells from the pcDNA3.1/O-SN-immunized mice. Additionally, a sera cross-reaction was observed with different VOCs. Our results indicate that DNA vaccination with the pcDNA3.1/O-SN generated by our working group is capable of inducing a specific humoral and cellular immune response.

sciforum-096272: Regulating the use of AI in mRNA vaccine development through policy coherence

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Artificial intelligence (AI) has become a game-changer in advancing mRNA vaccine development, bringing unparalleled speed and efficiency to research. AI-driven tools play a crucial role in enhancing vaccine potency and stability by optimizing gene sequences. This results in vaccines that provoke stronger immune responses and are more resistant to degradation. Such progress could enhance health equity and global vaccine distribution, especially in areas lacking adequate cold storage facilities. However, integrating AI into vaccine development poses several technical, ethical and regulatory challenges. One significant hurdle is accurately identifying antigens that can trigger effective immune responses. Additionally, the swift pace of AI-driven research often surpasses current regulatory frameworks, necessitating a delicate balance between innovation and oversight. Ethical issues such as data privacy, algorithmic bias, safety, explainability and transparency in decision-making processes must be tackled to maintain public trust. Regulatory agencies are addressing these obstacles by formulating guidelines covering data authenticity, reliability, transparency,and real-world patient monitoring. A risk-based AI regulation approach is being explored, requiring robust governance structures and collaborative efforts among global regulatory bodies. While AI shows great potential in transforming mRNA vaccine development, concerted efforts are crucial to navigate challenges and ensure the safe and equitable realization of its benefits worldwide.

sciforum-088320: The important role of the booster among patients with COVID-19 who were previously vaccinated against SARS-CoV-2

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In many countries, a booster dose against COVID-19 is recommended to reduce the risk of complications and death. A prospective epidemiological study of patients with COVID-19 who were previously vaccinated against the disease was conducted to compare those with a booster dose and those without. We analyzed 390 patients with COVID-19, hospitalized in various structures of the University Hospital "St. George”, in the city of Plovdiv, between October 2021 and April 2022, previously vaccinated against SARS-CoV-2. Only 12.1% (n=390) of all patients with COVID-19 (n=2835) were vaccinated. Onset of illness and hospitalization were, on average, 5.6 months after a full vaccination course. The average age of hospitalized vaccinated patients was 64.8 years (+-standard deviation 16.2) with a median of 69 years and a range of 15-95 years. The number of those with booster doses was 61 (15.6%). The data on fatal cases showed that 91.4% were unvaccinated and 8.6% were fully vaccinated. The average age of deceased vaccinated patients was 74 years, and they had 2.21 accompanying diseases. The booster dose reduces the risk of death by 2.5 times compared to the full vaccination course. The present epidemiological study confirms the importance of vaccination and revaccination against SARS-CoV-2. The ratio between vaccinated and unvaccinated hospitalized patients shows that the available vaccines against the disease in Bulgaria protect against severe complications and death.

Session 5. Advancement in Vaccine Design for Broad Protection

sciforum-103599: Green Routes: Exploring Protein-Based Virus-like Nanoparticle Transport and Immune Activation in Nicotiana benthamiana for Biotechnological Applications

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Introduction: Viral, bacterial, fungal, and nematode infections can cause significant losses and damage to crops. Treatment options remain limited in agriculture. Accordingly, novel immune activators are required to strengthen plant defense systems and enhance protection against pathogens. Virus-like nanoparticles (VLPs) have been extensively used in developing prophylactic and therapeutic vaccines in animals and humans. However, their potential use in plants is scarce. Hence, they may serve as a promising candidate for novel agricultural solutions and for advancing plant nanotechnology.

Methods: We synthesized protein-based VLPs derived from the bacteriophage Qβ-VLPs encapsulating non-replicative ssRNA. We fluorescently labeled Qβ-VLPs for visualization in Nicotiana benthamiana plants utilizing confocal microscopy. To assess the potential of our nanoparticles to induce an immune response in treated plants, we evaluated the upregulation of the key genes responsible for leaf defense mechanisms against pathogens.

Results: We demonstrate that the fluorescence of the icosahedral 30 nm Qβ-VLPs can be effectively visualized within the intercellular space of (N. benthamiana) one hour post infiltration. Furthermore, infiltration with Qβ-VLPs led to an upregulation in key defense genes (NbPR1a, NbPR5, NbNPR, NbERF1, NbMYC2, and NbLRR2) in treated plants. Using RT-qPCR, a significant increase in the relative expression levels of defense genes was observed, with sustained high levels of NbERF1 and NbLRR2 even after 24 h. Taken together, the data suggest that Qβ-VLPs have a significant capacity to upregulate genes pivotal to leaf defense mechanisms against pathogens in N. benthamiana plants.

Conclusion: We conclude that the dispersal of our protein-based nanoparticles in the intercellular space of N. benthamiana leaves, loaded with ssRNA, initiates a PAMP-triggered immunity. This activation launched a series of signaling cascades, culminating in the enhanced expression of genes associated with various defense mechanisms.

sciforum-106474: Identification of neutralizing epitopes in avian leukosis virus

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Neoplasms and reduced productivity in chickens caused by avian leukosis viruses (ALVs) have led to significant economic losses in the poultry industry. Due to the frequent genomic mutations that give rise to new viral variants, traditional whole-virus vaccines have demonstrated inadequate protection. With the high prevalence of ALV in farms in China, it is urgent to develop novel vaccines to control ALV. The capsid protein p27 is highly conserved across all current ALV subtypes, and studies have shown that p27-specifc antibodies in ALV-infected chickens were able to neutralize ALV, making it a promising target for vaccine design. We screened anti-p27 monoclonal antibodies using phage display technology from antibodies 111C and 86C that could neutralize ALVs. To identify neutralizing epitopes, antibody–antigen docking simulation was first used to predict epitopes that might interact with neutralizing antibodies. Then, the predicted peptides were generated, which were then identified by ELISA and Western blot to bind to neutralizing monoclonal antibodies. The affinities of the neutralizing antibodies in binding to the identified epitopes were as high as 10^{-9} M, validating the neutralizing epitopes were correct. These epitopes were found to be highly conserved among most ALV variants and could be displayed on virus-like particles (VLPs) to form vaccine candidates. These vaccines will be tested in chickens to assess both their immunogenicity and protection against ALVs. The reverse vaccinology used in this study provides an excellent paradigm for the development of protective vaccines against ALV, with broader implications for future vaccine research.

sciforum-107419: Lysosome-Associated Membrane Protein Targeting Strategy Improved Immunogenicity of Glycoprotein-Based DNA Vaccine for Hantaan virus

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Background and Aims

Hemorrhagic fever with renal syndrome (HFRS) is a viral zoonotic disease primarily caused by the Hantaan virus (HTNV). This illness is prevalent in over 70 countries worldwide, posing a significant public health challenge due to its high endemicity. The glycoprotein (GP) of HTNV is a key structural protein that is crucial for triggering both humoral and cellular immune responses, making GP-specific immunoprophylaxis a promising therapeutic approach for HFRS.

Methods

Lysosome-associated membrane protein 1 (LAMP1) has the ability to target antigens to lysosomes and endosomes, thereby enhancing the immunogenicity of nucleic acid vaccines. In this study, we developed a recombinant DNA vaccine for HTNV GP that utilizes LAMP1 to direct the vaccine to the major histocompatibility complex (MHC) class II compartment. We conducted thorough computational analyses to evaluate the properties of the vaccine molecule and its potential immune responses in the body. Initial animal studies confirmed the effectiveness of GP-derived Th epitopes and multi-epitope vaccines.

Results

We designed two vaccines based on Gnc molecules and optimized them using a LAMP-targeting approach. Following three immunizations, mice receiving the pVAX-LAMP/Gnc vaccine exhibited increased splenocyte-specific IFN-γ secretion and higher serum antibody titers, particularly in terms of neutralizing activity. Furthermore, the efficacy of these molecular therapies was supported by preliminary in silico findings and laboratory animal experiments. By facilitating lysosomal trafficking and antigen presentation, the LAMP1 targeting strategy significantly enhanced both humoral and cellular immune responses specific to EBOV-GP.

Conclusions

Our research expands the strategic framework for improving DNA vaccine design and presents a promising candidate for HFRS prevention, establishing a foundation for future antiviral vaccine strategies.

sciforum-106564: Synthesis and characterization of zein nanoparticles for antigen delivery

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Zein has been used in pharmaceutical applications, including the synthesis of nanoparticles applied as delivery systems for drugs and antigens. Zein nanoparticles (ZNPs) are classified as organic nanoparticles withdesirable characteristics, such as safety, biodegradability, low toxicity, and high loading capacity. The aim of this work was to obtain ZNPs by a simple and low-cost method and assess their potential as nanocarriers for the delivery of antigens, enhancing immunogenicity. ZNPs were produced by the nanoprecipitation method, showing a mean hydrodynamic size of 220 nm, a low polydispersity index (0.13± 0.15), and negative zeta potential (-8.9 ± 0.89). The adsorption-mediated antigen loading capacity of the obtained ZNPs was assessed using bovine serum albumin (BSA) as a model antigen. Different mass ratios of ZNPs: BSA were evaluated in the absorption experiments (1:0.5, 1:1, and 1:2), and samples were analyzed by TEM to determine size and particle morphology. The best adsorption efficacy was observed at a 1:2 mass ratio, with 63% efficacy, and a two-fold increase in particle size wasobserved upon BSA adsorption (424nm ± 36). To improve BSA adsorption, different adsorption buffers (Tris or Citrate buffer) at different pH values (5.5 or 7.4) were tested. The adsorption was improved using a Tris buffer at pH 5.5 during the adsorption step, while storage was set by using a Tris buffer at pH 7.4. In conclusion, a simple method to produce monodisperse ZNPs and bioconjugates based on such carriers was achieved, and its application in developing vaccine prototypes is guaranteed.

sciforum-106569: A virus-like-particle-derived vaccine induces neutralizing antibodies against novel duck reovirus (NDRV）

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Novel duck reovirus (NDRV) causes high morbidity in ducklings, and the recovered individuals often show stunted growth. There is currently no commercial vaccine available for effectively controlling NDRV. The capsid protein σC in NDRV is responsible for virus–cell attachment and thus plays a key role in viral infection. In this study, we aimed to develop a new vaccine candidate presenting σC on the virus-like particle AP205 according to specific binding with SpyCatcher and SpyTag. Firstly, σC-SpyTag was expressed in *E. coli* and purified, which was then coupled to AP205-SpyCatcher to generate AP205-σC. Then, AP205-σC was characterized, and the results demonstrated that it remained intact and had a homogenous viral particle structure, which packaged prokaryotic ssRNA inside. After immunizing ducklings with it, AP205-σC induced σC-specific IgY antibodies that could effectively recognize NDRV. Importantly, these antibodies were able to block the virus from infecting duck embryo fibroblasts in vitro, suggesting the vaccine successfully elicited neutralizing antibodies in ducklings. Consistently, the clinical pathologic features like lesions or listlessness in the AP205-σC-immunized ducklings were drastically reduced compared to those in the control group. Moreover, the viral loads in the AP205-σC-immunized ducklings were strikingly reduced, indicating that the vaccine contributed to viral clearance. These results suggested that AP205-σC exhibited excellent immunogenicity and posed protection against NDRV infection in ducks. In conclusion, AP205-σC has the potential to induce neutralizing antibody responses against NDRV and is worthwhile to develop for large-scale application.

sciforum-096016: An Evaluation of the humoral response following two doses of a Coxiella burnetii vaccine in water buffalo

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Ruminants, both domestic and wild, are the primary sources of Q fever, a zoonosis that causes reproductive abnormalities in animals and acute (self-limiting flu-like syndromes) and chronic (pneumonia, hepatitis, and endocarditis) conditions in people. The disease affects people and domestic ruminants globally, with vaccination being the primary method of control and management. Coxevac is the only approved vaccine for preventing Q fever in ruminants. This phase I vaccination greatly decreases the risk of miscarriage and shedding. Vaccination against Q fever has not been shown to be effective in buffalo, despite their extensive farming in several countries. This study used phase-specific ELISAs to assess the humoral response and its impact on abortion rates in buffalo. A total of 35 water buffalo were inoculated with two doses of a commercial vaccine and screened for phase I and II antibodies. Seroreactivity increased significantly between t0 and t1, and decreased somewhat between t1 and t2. Seroconversion did not differ substantially by age or natural infection status. At t1 and t2, naturally pre-infected animals showed somewhat greater reactivity than negative animals, but no significant differences were found. Animals over 20 months demonstrated higher seroreactivity at t1 compared to younger animals, but the difference was not statistically significant. Herd research found that immunization lowered miscarriage and placenta retention rates. The impact of immunization on miscarriage rates was reported regularly. In June, herd research showed 19 placenta retentions and 3 miscarriages due to Coxiella burnetii, which was detected using specialized real-time PCR. After five months after immunization, only five placenta retentions and one miscarriage occurred. Preliminary evidence suggests that vaccination can be effective in buffalo, even in seropositive animals. However, further research is needed to fully understand the dynamics of seroconversion in this species.

sciforum-106630: Challenges in Developing Universal Influenza Vaccine: Progress and Hurdles in Creating Broad Protection Against the Rapidly Mutating Virus

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Influenza remains a persistent global threat, with the rapid mutation of its surface proteins, particularly hemagglutinin (HA), challenging the effectiveness of seasonal vaccines. Universal vaccination seems to be a promising way of combatting the influenza virus's rapid mutation rate. The concept of a universal vaccine aims to provide broad protection against diverse strains by targeting conserved viral epitopes. In this review, I explored some of the major hurdles in achieving this goal, focusing on antigen selection, immunodominance, and the challenges posed by nanoparticle-based and T-cell-mediated vaccine platforms. The pursuit of a universal influenza vaccine faces numerous challenges despite advancements in the identification of conserved antigens and innovative technologies. Different types of vaccines have been put into clinical trials, such as viral vector and mRNA-based vaccines, non-replicating viral vector vaccines, and broadly neutralized antibodies (bnAbs), which have been proven to meet the research demands of the universal influenza vaccine. While promising, these approaches face significant barriers, including issues of antigen stability, delivery, and struggles of eliciting durable cross-reactive immune responses in mucosal tissues. Novel platforms like mRNA vaccines and viral vector vaccines show promise in providing broad protection against virus mutations. Breakthroughs in vaccine design continue to be made, aiming to enhance cross-protective efficacy and defense against potential pandemics. The results highlight that although significant progress has been made, overcoming the scientific, technical, and regulatory challenges is essential for achieving a truly universal influenza vaccine. In conclusion, ongoing global collaboration and innovative research are crucial for overcoming these barriers. However, the mutation rate of the influenza virus presents a significant obstacle in the path towards a commercially available universal vaccine.

sciforum-104764: Comparative immunogenicity of 10 µg versus 20 µg of Hepatitis B vaccine booster dose in healthcare workers

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Healthcare workers (HCWs) are at increased risk of occupational exposure to hepatitis B virus (HBV) infection, even if they have received a complete immunization schedule of three doses of hepatitis B vaccine in infancy. According to our Hospital Immunization Program, Hepatitis B surface (anti – HBs) antibody serum levels were determined in all HCWs at the time of hospital admission in order to investigate the HBV immunity state. HCWs with low anti-HBs serum levels (10 mIU/mL) usually received a booster dose of 20 µg/1 ml Engerix B (GlaxoSmithKline Biologicals, Belgium) vaccine. However, due to a temporary shortage of the 20 µg Engerix B vaccine, we wondered if 10 µg/0,5 ml (pediatric dose) could be equally effective to elicit the immunogenicity in our HCWs. For this reason, we conducted a pilot study on forty homogeneous HCWs with a non-immune level of anti HBs antibody (10 mIU/ml) who were previously vaccinated in infancy. Twenty HCWs (Group A) received a booster dose of Engerix B vaccine 10 µg/0,5 ml, and twenty HCWs (Group B) received the standard dose of 20 µg/1 ml of Engerix B vaccine. One month after the vaccination, the anti-HBs antibody serum levels in all participants in the study were determined. The results showed a significant increase in anti-HBs antibody serum levels both after 10 micrograms and 20 micrograms of Engerix B vaccine. All but two healthcare workers were immunized after their booster dose; no statistically significant difference was found in the mean of anti-HBs antibody serum levels between groups A and B. If confirmed in a large clinical trial, the use of 10 micrograms Engerix B booster dose in adults could represent a preferred choice in terms of cost efficacy, particularly in specific situations, for example in vaccination programs in low-income countries.

sciforum-104255: Comprehensive Evaluation of Immunoreactivity and Immunoinformatics of 9 Epitopes on CCHFV glycoprotein C

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Crimean–Congo hemorrhagic fever virus (CCHFV) is a geographically widespread tick-borne virus that causes severe hemorrhagic fever. Increasing numbers of people are at risk of infection as vectolactivity expands. Cellular immunity (e.g., CD8 T cells) against CCHFV structural antigens plays an important protective role. Among the structural proteins, the Gc protein mediates the fusion of viral and host cell membranes, which are major immune targets and play a key role in anti-infection immunization and antiviral intervention. The aim of this study was to evaluate and screen CCHFV Gc proteins for major histocompatibility complex class I (MHC-I)-restricted epitopes using state-of-the-art evaluation strategies. The combination of five database algorithms generated 133 human HLAclass I-restricted Gc high-affinity epitopes and 41 mouse H2-restricted Gc high-affinity epitopes. Twenty-one conserved epitopes with high affinity and strong immunogenicity were further screened by immunogenicity, as well as interspecies and intraspecies conservation assessments. Meanwhile, molecular docking simulations further determined that these 21 epitopes dock well with MHC I. In BALB/*c* and SI mice, these 21 epitopes were able to induce anti-Gc specific cellular immune responses according to wet-lab Elispot results. These epitopes were further characterized, and 15 of them were considered low-risk in terms of toxicity and sensitization with 98.55% somatic coverage of the HLA population, and analysis of the highly mutated loci showed that the mutation results did not affect the affinity. Unlike other epitope studies, we performed a bidirectional hierarchical cluster analysis of CCHFV Ges and MHC I haplotypes from different genetic backgrounds to explore the relationship between peptides and MHC from a holistic perspective. The results of this study not only provide insights for the design and development of vaccines against CCHFV epitopes, but also provide insights into the immune reactivity of CCHFV Gcs with pan-MHC class I molecules. It is expected to provide an important reference for the control of CCHFV transmission.

sciforum-106631: Designing a novel multi-epitope cocktail vaccine candidate for Lymphatic Filariasis: An immuno-informatics approach

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Background: Lymphatic filariasis is a neglected tropical disease (NTD) affecting more than 863 million people in 47 countries across the world. A multi-epitope prophylactic/therapeutic vaccination targeting filarial defense proteins would be invaluable in achieving the current goal of LF elimination.

Method: In this study, a combination of immunomics and immune-informatics was applied to construct a multi-epitope vaccine candidate. The antigenic proteins were identified by immune blotting against different categories of *Wuchereria bancrofti*-infected LF sera.

Result: The major antigenic proteins were heat shock protein 70, Tubulin beta chain, Enolase, Galectin, and 14-3-3 zeta. The five antigens were combined together to construct a multi-epitope vaccine after predicting the linear B-cell and T-cell epitopes of individual antigens. A three-dimensional model of the candidate vaccine was predicted, followed by refinement, and was validated using RAMPAGE and PROCHECK servers. A Toll-like receptor (TLR) agonist, a 50S ribosomal subunit of *Mycobacterium tuberculosis,* was included in the candidate vaccine to enhance vaccine immunogenicity. The docking of the chimeric peptide vaccine against the TLR5 resulted in high binding efficiency for the docked complex. The in silico immune simulation provided a significant increase in $CD4^+$ T-cell and $CD8^+$ T-cell populations.

Conclusion: In summary, the recombinant putative vaccine showed high immunogenicity which could be experimentally validated in the future for the development of a potent LF vaccine. Furthermore, by employing multi-epitope structures and constructing a cocktail vaccine for LF, this study has the potential to represent an important milestone in the development of an anti-filarial vaccine.

sciforum-096229: Evaluation of Chicken Astrovirus Breeder Vaccine Candidate

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Introduction: Chicken astrovirus (CAstV) is a ubiquitous agent infecting global broiler production, mainly affecting embryos and neonates, with some highly pathogenic (hp) strains causing hatchery losses (up to 69%) and fatal kidney disease with visceral gout. There are two serogroups of CAstV, A and B; most diseases have been associated with the B serogroup, which is subdivided into subgroups via capsid gene genotyping.

Methods: The CAstV-11672 (subgroup Bi) strain was administered to in-lay broiler breeder hens as a live breeder vaccine candidate. Sera were monitored weekly for seroconversion via ELISA. Eggs were collected from seroconverted and control hens, and were synchronised and incubated to hatch. Hatchlings in isolators were challenged with one of three hp strains belonging to subgroups Bi, Biii and Biv. The chicks were visually monitored for disease development; their CAstV levels were monitored by real time RT-qPCR; and their weight and development of kidney lesions by days four and ten (termination) were monitored.

Results: Thelevels of CAstV seroconversion in hens were low after oral inoculation but increased significantly after intramuscular inoculation. The levels of anti-CAstV antibodies detected in egg yolks were approximately half that of the hens. The weights of chicks with maternally-derived antibodies (matABs) were significantly higher at day 10 after being challenged with hp strains from the Bi and Biii subgroups. The chicks with matABs showed no kidney lesions at day 4 from any of the hp strains, whereas the chicks without matABs had substantial numbersof kidney lesions at day 4, which were statistically significant by day 10.

Conclusions: The CAstV-11672 strain elicited a strong immune response in adult birds, with successful the transmission of matABs that protected the hatchlings from challenges with hp strains of CAstV, resulting in the prevention of kidney damage and higher body mass compared to chicks without anti-CAstV matABs. CAstV-11672 appears to be a successful candidate for a CAstV breeder vaccine.

sciforum-106791: Exploiting surface-exposed proteins to develop new therapeutic strategies against Bcc and *Pseudomonas aeruginosa* infections

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Respiratory infections caused by *Burkholderia cepacia* complex (Bcc) and *Pseudomonas aeruginosa* remain life-threatening to Cystic Fibrosis (CF) patients. Immunotherapies are attractive alternatives to protect CF patients against these infections. In order to identify new targets for the development of immunoprotective therapies, we used a surfomics approach to find putative surface-exposed proteins. This methodology combined with immunoinformatics tools allowed the identification of surface-exposed proteins containing B-cell epitopes [1]. The OmpA-like protein BCAL2645 was chosen and demonstrated by Western blotting and ELISA assays to be immunoreactive against sera from CF patients with a record of Bcc infections. The protein was characterized as multifunctional and important in the infection process. An anti-BCAL2645 polyclonal antibody was produced and was found to decrease the number of adhered and invading *B.cenocepacia* bacteria to human cells in vitro by more than 70% [2]. A cross-effect against *P.aeruginosa* and *B.multivorans* using this antibody was also observed, strongly decreasing the adhesion and invasion of these species to the human bronchial epithelial cell line CFBE41o-[3]. Using the animal model *Galleria mellonella,* the antibody was found to confer protection against these infections. These results highlight the potential of anti-BCAL2645 antibodies for passive immunization therapies to prevent infections against two of the most problematic bacterial species infecting CF patients. Preliminary results from passive immunization strategies under study using anti-BCAL2645 antibodies will be presented.

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[3] Seixas, AMM; etal. A Polyclonal Antibody against a *Burkholderia cenocepacia* OmpA-like Protein Strongly Impairs *Pseudomonas aeruginosa* and *B.multivorans* Virulence. *Vaccines* **2024**, *12*,207. https://doi.org/10.3390/vaccines12020207

sciforum-105201: Exploring the oral route of vaccine delivery using recombinant secretory IgA as a vehicle to boost immune responses against tuberculosis in BCG-primed mice

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An improved vaccine against tuberculosis (TB) is urgently needed to enhance the impact of TB immunisation offered by BCG, the only licensed TB vaccine, which is currently unable to substantially reduce the number of TB cases globally. Most new TB vaccine candidates use the parenteral and invasive route of immunisation without showing significant superiority to BCG. Wide-ranging vaccination strategies should be considered to improve the chances of finding an ideal TB vaccine. Here, we explore the potential of treating TB with a non-invasive immunisation route, specifically looking at the oral route of vaccination as a potential strategy for developing a new TB vaccine, which is arguably the most preferred route of vaccination due to its ease of administration at a lower cost compared to injectable vaccines. The downstream hostile gut environment poses a major challenge to oral vaccine development. Several strategies for overcoming this challenge have been studied, such as using live-attenuated vectors and nanoparticles. Our group is at an early stage of developing an oral TB vaccine candidate based on a chimeric secretory IgA-Ag85B subunit vaccine constructed to withstand the gut environment and reach the mucosal immune cells to initiate immune responses. We are currently evaluating the immunogenicity of the vaccine candidate as a booster to BCG in a mouse model to further assess its potential. BALB/c mice primed with BCG were given the vaccine candidate orally, with subsequent collection of samples from the euthanised mice 4 weeks post-booster to determine the T-cell responses in the spleen using flow cytometry and the anti-Ag85B IgG levels in serum and the anti-Ag85B IgA levels in bronchoalveolar lavage using ELISA. The findings from this study can offer new knowledge regarding oral immunisation using a recombinant secretory IgA construct that could potentially become a candidate vaccine for future TB vaccine development.

sciforum-106469: Flagellin-Displayed HBc virus-like particles for hemagglutinin Stem-Based Universal Influenza Vaccine Development

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Influenza vaccination faces challenges due to viral mutagenicity, necessitating a shift towards universal vaccine approaches. Many current vaccinations target the globular head region of the hemagglutinin (HA) surface protein of the Influenza virus. However, despite the widespread use of this technique, it does not offer broad protection against possible mutations or variations that naturally occur in the Influenza virus. Our study focuses on creating a broadly effective influenza vaccine by targeting the conserved hemagglutinin stem using virus-like particles (VLPs). Through innovative Spy Catcher/Spy Tag technology, we engineered VLPs presenting the HA stem on their surface adjuvanted with the VLP composition containing the Hepatitis B core protein and Flagellin, enhancing immunogenicity. The virus-like particle is made up of two components. The first component is the core of the particle, in which the HBc-flagellin particle assembles into a spherical particle, displaying the Spy Catcher protein on the surface of this particle. This is then combined in solution with a custom HA stem peptide, conjugated with Spy Tag to complete the VLP, with the HA stem displayed on the surface. Preliminary results demonstrating the successful assembly of VLPs into spherical particles visualized by transmission electron microscopyproved the remaining ability of Spy Tag binding to the virus core, and completed gene cloning for the HA stem protein. This project offers insights into universal vaccine design and holds promise for advancing influenza prevention strategies, as well as a theoretical platform for other virus-like particle vaccines.

sciforum-104999: Immunogenicity study in Development of Mucosal Vaccine Against Tuberculosis using Chimeric Secretory IgA: TB Multi-epitopes Protein in Milk samples

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Introduction: Tuberculosis (TB) remains one of the leading infectious diseases worldwide. The Bacillus Calmette-Guérin (BCG) vaccine, the only currently available TB vaccine, offers limited protection in adults. Therefore, it is critical to develop new effective vaccines. Considering Mycobacterium tuberculosis (Mtb) primarily infects the lungs, mucosal vaccines may be a promising strategy, as they can stimulate both systemic and mucosal immunity. This study explores the development and evaluation of a novel mucosal TB vaccine utilizing TB multi-epitopes by producing a recombinant chimeric protein in the mammary gland of goat, and in vivo mucosal immunization by utilizing the stable properties of the chimeric protein.

Methods: An AAV vector carrying TB multi-epitopes and secretory IgA-J chain were co-transduced into the mammary gland of goat, and milk was collected daily. The chimeric protein containing the TB multi-epitopes antigen and secretory components in milk was detected by Western blot against anti-His and anti-Ag85b. The protein was then purified from the milk using the Akta Prime purification system. The mice were immunized using purified protein intranasally, and their immunogenicity responses were evaluated by flow cytometry.

Results: In milk containing chimeric protein, bands corresponding to murine secretory component (75 kDa) and multi-epitopes Antigen Fc-alpha (75 kDa) could be detected against anti-His and anti-Ag85b, respectively. After the chimeric protein was purified, a purity of 95% of chimeric protein was obtained and detected at 75 kDa. Mice immunized with the vaccine candidate were shown to elicit immune response by producing a higher level of activated and memory T cells compared to the control group.

Conclusion: The protein complex formed by TB multi-epitopes-Fc alpha and the murine secretory component can be obtained, purified and detected in milk samples, provided that the mammary gland acts as a potential bioreactor for the production of the recombinant vaccine candidate. The immune response was shown to be induced by the protein complex in mice by producing more activated and memory T cells.

sciforum-104948: Novel Tuberculosis (TB) Oral Vaccine Candidate: Enhancing Mucosal Immunity with Recombinant Secretory IgA (SIgA) in Goat Milk

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The Bacillus Calmette–Guérin (BCG) vaccine, the only licensed tuberculosis (TB) vaccine, has limited effectiveness in preventing pulmonary TB in adults. Our study explores using the mammary gland of non-transgenic goats to produce an oral vaccine candidate, combining secretory IgA (SIgA) with epitopes from TB. This approach aims to enhance mucosal immunity and provide comprehensive protection across different stages of TB infection. The vaccine candidate was developed by engineering recombinant epitopes including Antigen 85b (Ag85b) for active TB, alpha-crystallin (Acr) for latent TB, and resuscitation-promoting factor E (RpfE) for reactivated TB combined with SIgA. We evaluated the immunological response by administering goat milk containing the recombinant protein directly as oral immunization. Five groups of Balb/C mice (n=5) were categorized as follows: recombinant milk (RM), normal milk (NM), BCG prime with RM boost (BCG-RM), BCG prime with NM boost (BCG-NM), and BCG alone (BCG). The RM and NM groups received daily oral immunizations with RM or NM for two weeks. The BCG-primed groups received booster doses of RM or NM daily for two weeks, one month after the initial BCG vaccination. Two weeks after the final immunization, the mice were sacrificed, and IgA levels in the saliva and lung lavage were measured using enzyme-linked immunosorbent assay (ELISA). Mice immunized with recombinant vaccine-containing milk, especially those primed with BCG, showed a significant increase in IgA levels in the saliva and lung lavage compared to the normal milk and BCG-only groups. These results indicate that the recombinant vaccine-containing milk can effectively induce a strong mucosal immune response against TB. The significant increase in IgA levels in mice, particularly in BCG-primed groups, highlights the potential of this vaccine as a booster candidate with BCG priming.

sciforum-106628: Peptides from PfEMP1 interacting with cytoadherence receptor gC1qR may provide broader protection against severe malaria

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Malaria is a major public health problem. Estimates suggestthat there were over 249 million cases of malaria in the year 2022. Most of the severe malaria cases and almost all the malaria-related deaths are caused by malaria parasite *Plasmodium falciparum*. The malaria parasite *P. falciparum* has unique cytoadherence properties through which it sequesters in the host's microvascular endothelial cells. The *P. falciparum*-infected erythrocytes can bind to the host's microvascular endothelial cells, platelets, uninfected erythrocytes and other immune cells, such as dendritic cells, and sequester in the host's blood vasculature. The cytoadherence of *P. falciparum*-infected erythrocytes in the brain and placenta has been associated with severe malaria disease. Cytoadherence to microvascular endothelial cells causes obstruction in blood flow, endothelial cell activation, and the release of proinflammatory cytokines. Studies have also shown that the gC1qR-mediated cytoadherence of *P. falciparum*-infected erythrocytes to dendritic cells can lead to the inhibition of the dendritic cells and therefore may contribute to the immune suppression of the innate immune system of the host. Cytoadherence is mediated by specific receptor–ligand interactions. Earlier, we identified a novel receptor gC1qR for cytoadherence to brain microvascular endothelial cells and platelets. The P. falciparum-infected erythrocytes can bind to dendritic cells, platelets and brain microvascular endothelial cells via gC1qR as a receptor. Cytoadherence to gC1qR has been implicated in the pathogenesis of severe malaria by several studies. We have also mapped the interacting domain of PfEMP1 interacting with gC1qR. Since gC1qR has an important role in severe malaria pathogenesis and the inhibition of dendritic cells have a role in innate and adaptive immunity, a vaccine targeting gC1qR and its PfEMP1 ligand interaction will likely have a broader protection, eliciting a longer-lasting immunity against *P. falciparum* infections.

sciforum-102014: Preclinical evaluation of novel sterically optimized VLP-based vaccines against all four DENV serotypes

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Over the past few decades, dengue fever has become a significant threat to global health, mainly in tropical regions but more lately also in regions with moderate climates. Since the currently approved vaccines have significant practical limitations, there is a strong need for a dengue vaccine that is safer and more effective. In this study, we introduce novel vaccination candidates covering all four Dengue virus (DENV) Serotypes based on virus-like particles (VLPs). VLPs are traditional vaccine platforms which are already implemented on the market for several diseases. They are considered safe and efficient because they have a highly organized and repetitive surface and lack any replication-competent genetic material. Due to the high thermostability of VLPs used here, distribution and administration in DENV endemic zones would be simplified and facilitate vaccination programs. To design such vaccine candidates, the Dengue virus envelope protein domain III (DV) of the serotypes 1, 2, 3, or 4, which represents the major target of DENV-neutralizing antibodies, was selected to be either genetically fused or chemically coupled to bacteriophage-derived AP205-VLPs. To facilitate the incorporation of the relatively large EDIII domain, AP205 monomers were dimerized, resulting in a VLP with 90 rather than 180 N- and C-termini. The generated vaccines induced high antibody titers of high affinity/avidity in mice, indicating a protective potential of the vaccine candidates. This was confirmed by the ability to neutralize the different Dengue virus serotypes in an in vitro neutralization assay. The administration of a tetravalent vaccine simultaneously induced high neutralizing titers against all four serotypes. Importantly, no enhancing antibodies were induced, at least not against the tested DENV2. In conclusion, the vaccine candidates, especially when administered in a combined fashion, exhibit intriguing properties for potential use in the field, and exploring the possibility of conducting a clinical trial would be a logical next step.

sciforum-105086: The Dynamics of the Incidence of Vaccine-Controlled Infections in the Southern Federal District of the Russian Federation from 2010 to 2023

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Introduction. An uncontrolled flow of migration and powerful anti-vaccination propaganda have led to an outbreak of vaccine-controlled infections among the Russian population in recent years.

The purpose of this study is to assess the dynamics of the incidence of whooping cough, measles, and rubella among the population in the Southern Federal District of the Russian Federation in the period of 2010 to 2023.

Methods. Thi study is based on data from the federal statistical observation form "Information on the number of diseases registered in patients living in the service area of a medical organization" for the period of 2015 to 2023.

Results. Between 2010 and 2023, the number of whooping cough cases amounted to 9199. The lowest number of whooping cough cases in the Southern Federal District was registered in 2021 and amounted to 15 (0.16%). The largest number of whooping cough cases was registered in 2023 and amounted to 4511 (49.04% of all detected cases since 2010). Krasnodar had the highest number of cases (2027—24.7%), followed by Rostov in second place (635 cases—6.9%) and Volgograd in third place (473 cases—5.14%).

The number of cases of rubella in the period from 2010 to 2023 in the Southern Federal District amounted to 108. The smallest number of cases was 0, and this was registered in the period from 2017 to 2023. The largest number was 30 cases, and thiswas registered in 2013 (27.78% of all detected cases since 2010). In first place for the number of cases of rubella was Krasnodar (23 cases—21.3%) in 2013, in second place was Volgograd (13 cases—12.04%) in 2010, and in third place was Astrakhan (12 cases—11.11%) in 2014.

Conclusions. During the studied period, the largest number of cases of whooping cough and rubella was registered in the Krasnodar region. The lowest number of cases of all nosologies was registered in 2020--2021, which was probably due to social isolation during the COVID-19 pandemic.

sciforum-106575: Therapeutic effects of neutralizing antibodies to protect chickens from fowl adenovirus serotype 4 (FAdV-4) infection

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Fowl adenovirus serotype 4 (FAdV-4), leading to Hepatitis-hydropericardium syndrome (HHS) in chickens, has caused huge economic losses to the poultry industry in China since 2015. Therefore, effective therapeutic approaches to prevent FAdV-4 is critical for HHS control. In this study, we identified two monoclonal antibodies, 27A-5 and 42A-10, to specifically bind to and neutralize FAdV-4 viruses in vitro. Pre-incubation of both antibodies with FAdV-4 hindered the viruses from infecting LMH cells, with the complete blocking concentrations being 33.3 μg/mL for 27A-5 and 16.6 μg/mL for 42A-10. In addition, whether these antibodies pose viral neutralization abilities in vivo was determined, as was whether they could be used as therapeutic antibodies in the future. In chickens, the survival rates were 100% after administration with both antibodies (10 mg/kg), while the fatality rates of untreated chickens were 100%. In addition, a low dose (5mg/kg) of the 27A-5 antibody could save all animals. Moreover, pathologic changes such as pericardial sac liquid and liver damages in survivors were remarkably reduced. Further analysis demonstrated that inflammation caused by FAdV-4 infection was decreased in antibody treated animals. More importantly, the viral loads in treated chickens were almost cleared, indicating that the antibodies were effectively neutralizing the FAdV-4 viruses in vivo. In conclusion, the two antibodies could neutralize FAdV-4 in vitro and in vivo, which means that they have the potential to be therapeutic antibodies for HHS treatment. This study lays a foundation for the development of safe and effective therapeutic methods against FAdV-4.

sciforum-104957: Versatile and scalable nanoparticle vaccine as a scaffold against newly emerging influenza viruses

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Introduction:

Influenza viruses present a serious threat to public health by causing highly contagious respiratory illnesses that impact hundreds of thousands of people each year. Current vaccines primarily work by generating neutralizing antibodies that target the hemagglutinin (HA1) head. However, the emergence of new strains, particularly avian influenza, highlights the growing need for new vaccines. The global spread of these new strains also endangers not only biodiversity but also the agricultural industry, as migratory birds can transmit the virus to animals such as sea lions, poultry and pigs.

Methods:

In this study, we assessed the immunogenicity and effectiveness of a novel influenza vaccine candidate based on virus-like particles (AP205-VLPs) that display the HA1 head domain from A/PR8/H1N1. This was achieved by genetically linking the HA1 head domain to the N-terminus of dimerized capsid proteins. A major benefit of this approach is the potential to produce the vaccine in bacteria, which could significantly lower costs and improve accessibility.

Results:

Our findings revealed that intranasal (i.n.) and subcutaneous (s.c.) administration of HA1-AP205dim induced similar levels of specific IgG and IgA antibodies in the serum of vaccinated mice. These vaccination-induced antibodies were capable of neutralizing the virus in vitro. Furthermore, both administration routes provided strong protection against a lethal dose of the A/PR8/H1N1 virus.

Conclusion:

In conclusion, the i.n or s.c application of HA1-AP205dim represents a promising influenza vaccination approach. This opens the door for future HA1-AP205dim vaccine development for both human and animal health, as these vaccines can potentially be produced on a large scale through bacterial expression for widespread immunization programs.

sciforum-104190: Virus-like particle-derived vaccine induces broad neutralising antibodies against porcine epidemic diarrhea virus (PEDV)

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Although vaccines against porcine epidemic diarrhea viruses (PEDVs) are available, PED outbreaks still occur in many countries due to the emergence of new variants. Therefore, more work is required to develop efficient and broadly protective vaccines. To this end, we present here a new vaccine candidate, AP205-S1, which could effectively elicit systemic and mucosal antibody responses in mice and pigs. The vaccine was generated by coupling the S1 protein of PEDV-KB2013-130 with AP205-VLP via SpyCatcher/SpyTag bonding. AP205-S1 demonstrated an intact and homogenous viral particle structure and packed ssRNA. Upon administration in mice, AP205-S1 induced high amounts of S1-specific IgG antibodies in sera as well as in gastrointestinal tracts, especially after the booster. Importantly, these antibodies were able to neutralize PEDV KB2013-130 in vitro, indicating that the vaccine protects against PEDV infection. Of note, AP205-S1-elicited antibodies exhibited cross-neutralizing potencies against AH-2018 strains, belonging to the G-I group. Last but not least, S1-specific IgG antibodies were stimulated in pigs after AP205-S1 immunization, which could recognize and block PEDV from infecting Vero cells in vitro. The viral loads in AP205-S1-immunized pigs were strikingly reduced compared to AP205-SpyCatcher-immunized pigs. In conclusion, AP205-S1 exhibited excellent immunogenicity in mice and pigs and posed protection against PEDV infection in pigs.

Session 6. Novel Assays for Evaluating Responses to Vaccination

sciforum-104560: Immunoreactivity Analysis of MHC-I Epitopes Derived from the Nucleocapsid Protein of SARS-CoV-2 via Vaccination

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SARS-CoV-2 has spread worldwide since 2019, causing the devastating COVID-19 pandemic. As of June 23, 2024, the cumulative number of infections worldwide has exceeded 705 million. As the structural protein of SARS-CoV-2, nucleocapsid (N) protein plays a key role in the viral lifecycle and participates in various activities during virus invasion, including interaction with the host immune system. In this study, we used computational methods to predict the MHC-I dominant epitopes, which brought about 282 dominant epitopes restricted to the human HLA-I superfamilies and mouse H-2 haplotypes. Further analysis of immunogenicity and conservation yielded the "preferred epitopes". Among them, KTFPPTEPK, LSPRWYFYY, SPRWYFYYT and NTASWFTAL have been validated by other laboratories in one or two dimensions in terms of their antigenic profiles. Through our multi-disciplinary research, we also screened out and obtained four unproven "preferred epitopes". Docking simulations were conducted with the corresponding MHC-I alleles. Then, two-way hierarchical clustering revealed the principles on immunoreacitivities between NP peptides and pan-MHC-I haplotypes. We propose a state-of-the-art epitope exploitation strategy that integrates multiple tools and approaches and provides prospects for the development and application of epitope-based immunotherapy in viral epidemics. Our study also provides insight into extensive protective mechanisms between different variants, providing guidance for the development of highly protected epitope vaccines in the future.

sciforum-104394: Post-vaccination COVID-19 Spike-Specific IgA antibody levels in vaccinee nasopharyngeal samples

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Increased COVID-19-specific secretary IgA antibody levels in the respiratory tract are required for inhibiting early COVID-19 virion particle attachment to ACE-2 receptors and primary virus replication. Because all COVID-19 vaccines are administered parenterally, it has been thought that the vaccine might not elicit sufficient mucosal immunity (1). The purpose of this study was to determine the level of IgA antibodies in respiratory samples from vaccinees. Twenty-ninenasopharyngeal swabs were collected from healthy participants who had received at least two doses of a different COVID-19 vaccination. Rt-PCR confirmed that all samples were negative for COVID-19. A quantitative ELISA kit with defined calibrators (0-25) ng/ml coated with recombinant 2019-nCoV Spike protein (antigen) was used to measure IgA antibody concentrations per sample. The results revealed that COVID-19 spike IgA was present at a lower level in the majority of the samples (86.2%), with a mean IgA level of 0.01 ng/ml. Only four samples had higher IgA levels, which accounted for 13.8%. (Fig. 1). Three subjects had elevated IgA levels, ranging from 0.5 to 1.5 ng/m. One individual had a boosted IgA level of 3.4 ng/ml, which retested negative in COVID-19 Rt-PCR and appeared to be a recently recovered asymptomatic COVID-19case. The result explains why COVID-19 vaccines failed to prevent virus transmission and infection, because the vaccines failed to elicit protective mucosal immunity in the form of highly protective secretary IgA antibodies in vaccinees. This is because the current COVID-19 vaccines are administered parentally rather than through the mucosal portal via oral immunization or nasal spray delivery. Thus, there is a need for second or third mucosal (nasal/oral) COVID-19 vaccine doses which might imitate natural infection by boosting mucosal IgA levels. This would help in reducing the number of healthy carriers and, in the long run, in eradicating the existing circulating virus.

sciforum-104656: COVID-19, Influenza, and Pneumococcus Vaccinal Status Among Hospitalized Patients During the COVID-19 Pandemic Era

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Background: Little is known about the impact of COVID-19, influenza, and pneumococcus vaccinal status on hospital stays in patients admitted to internal medicine units during and after the COVID-19 pandemic.

Methods: Data on adult patients admitted to the internal medicine division (99% from the emergency care unit), Regional Hospital, Bari, Italy, between June 2020 and December 2023 were extracted from the hospital information system. Vaccine status, medical history, demographic data, and clinical outcomes were analyzed using a multiple linear regression model to determine the factors influencing the length of hospitalization.

Results: A total of2,008 patients were included (F/M = 767/1241; mean age = 73.5±SEM0.3 yrs). Overall, their mean hospital stay was 10±0.2 days and was similar between sexes. The prevalence of patients vaccinated against COVID-19 was 82.6% (doses 1, 2, 3, 4, and 5, respectively = 2.4%, 14.4%, 43.3%, 17.8%, and 4.8%); against influenza, it was 69.6% (doses 1, 2, 3, 4, and 5, respectively = 16.0%, 14.2%, 13.7%, 13.8%, and 11.9%); and against pneumococcus, this was 14.2% (doses 1 and 2, respectively = 12.1% and 2.1%), with no gender difference. The hospital stays before and after any vaccine dose were comparable. Multiple linear regression showed that among all factors (age, sex, and vaccine type and doses), only age was positively correlated with hospital stay (R^2 0.04, P= 0.01). The prevalence of patients admitted for severe non-COVID-19 pneumonitis was 4.7%, and those vaccinated against COVID-19 had a shorter average hospital stay than unvaccinated patients (8.7 vs 11.3 days, P=0.03).

Conclusions: Vaccinations are preventive tools for decreasing hospital stays in internal medicine wards. COVID-19 vaccination effectively reduces the hospital stay of patients with severe (non-COVID-19) pneumonitis.

sciforum-104806: Distinguishing the antibodies induced by the live attenuated vaccine (LC16m8) and orthopoxvirus infections

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[Introduction] The vaccinia virus (VACV) LC16m8 strain is a highly attenuated vaccine against smallpox and mpox, licensed in Japan. Unlike its parental strain (LC16mO) or ancestral vaccines, the B5R protein of the LC16m8 strain has a frameshift mutation, resulting in a truncated B5R protein.

[Objective] Our objective was to determine the B5R protein antigenic domains and develop an assay to distinguish LC16m8 vaccine-induced antibodies from orthopoxvirus infections.

[Methods] Four recombinant proteins, located at the N-terminal and C-terminal region of the B5R, were expressed in *E.coli*, and their antigenicity was examined by immunoblot analysis. They were then used to produce polyclonal antibodies in SPF rabbits. Next, the sensitivity of the anti-B5R antibodies was evaluated by immunofluorescence assay using orthopoxvirus-infected cells, or by expressing their B5R homologous regions. Furthermore, a Luminex bead-peptide assay was developed to target the B5R domains, and its specificity was evaluated using anti-orthopoxvirus antibodies. Finally, we screened the sera of 45 healthy human donors and 5 Mpox patients.

[Results] The expressed B5R N-terminal and C-terminal proteins were specifically recognized by anti-LC16mO B5R antibodies. The anti-B5R N-terminal antibodies cross-reacted with orthopoxvirus-infected cells or their expressed B5R homologous region. Nonetheless, the C-terminal antibody cross-reacted with infected cells of VACV, monkeypox and cowpox virus, but did not with the LC16m8 strain or the expressed LC16m8 B5R protein. Both B5R peptides showed cross-reaction with antibodies against VACV and monkeypox virus (Clade I, IIa & IIb). Furthermore, seven human serum samples showed neutralizing antibodies against VACV, from which two human donors and one Mpox patient showed affinity to the C-terminal peptide and recognized the full-length-B5R protein.

[Conclusion] The expressed B5R proteins, anti-B5R antibodies and Luminex bead-peptide assay might be useful for detecting orthopoxvirus infections among the LC16m8-vaccinated population.

sciforum-106638: In silico design of a vaccine candidate against Oropouche virus based on a multi-epitope protein

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Oropouche virus (OROV) is the pathogen that causes Oropouche fever, an endemic disease in Amazonian regions, whose symptomatology could include complications in the nervous and blood systems, and for which there are no specific treatments or vaccines. The development of vaccines has been supported by advances in areas such as immunoinformatics and the introduction of new vaccination platforms such as viral vectors for the delivery of pathogen antigens. The aim of the present work was to design a vaccine against the Oropouche virus based on a multi-epitope protein and using immunoinformatics. A consensus proteome of OROV was generated from the alignment of sequences stored in databases. Based on this proteome, CD8+ T cell, CD4+ T cell and B cell epitope prediction programs were used to identify peptides with epitope potential. The epitopes to be included in the vaccine were then selected based on the following criteria: high promiscuity towards HLA-I and HLA-II alleles that are prevalent in the countries most affected by the virus, conservation of the peptide among the different OROV strains, non-homology of the peptide with the human proteome, and the absence of toxicity and allergenicity of the peptide. After the filtering and selection process, eleven T cell epitopes, which allowed for a total coverage of the most frequent HLA alleles among OROV-exposed countries, and three B cell epitopes were selected. The chosen epitopes were concatenated by linkers to generate a multi-epitope protein, which also contains the sequence of the β-defensin 3 as an adjuvant. The multi-epitope protein will be evaluated by molecular docking analysis against TLR4 to identify its potential to activate the immune system. This study proposes a vaccine candidate against the Oropouche virus that will be tested in preclinical models in the next phase of this project.

sciforum-104953: Th1-dominant immune response induced by foot-and-mouth disease vaccine confers protection in cattle

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Introduction: Foot-and-mouth disease (FMD) is a highly contagious viral infection affecting cattle, pigs, and other cloven-hoofed animals. The disease, caused by FMD virus (FMDV), poses a severe threat to the livestock industry due to its ability to spread rapidly and cause high productivity losses. In India, to prevent outbreaks and safeguard animal health and productivity, a trivalent vaccine containing the inactivated virus antigens of three serotypes (O, A, and Asia-1) is employed. While humoral immunity, characterized by antibody production, is essential for defending against FMDV, a comprehensive understanding of protection also requires an investigation of cell-mediated immune (CMI) responses.

Methods: Indian cattle aged 6 to 9 months were immunized with a trivalent FMD vaccine in a water-in-oil-in-water (W/O/W) formulation. We evaluated the virus neutralizing antibody and CMI responses following vaccination. The cattle were challenged with homologous FMDV serotype O at six months post vaccination.

Results: The vaccine elicited potent humoral and cellular immune responses. The vaccine-induced virus-neutralizing antibody response peaked around two to four weeks post-vaccination and was maintained for up to six months. Elevated IFN-γ and reduced IL-4 cytokine levels by 14 days post-vaccination (dpv) and the dominance of the IgG2 isotype antibody at 30 dpv suggested a predominantly Th1-type cellular immune response. Interestingly, IFN-γ and IL-4 expression exhibited inverse patterns of regulation, highlighting the precise regulation of Th1 and Th2 responses. The challenging of vaccinated cattle with the homologous FMDV serotype O at six months post-vaccination showed 100% protective efficacy.

Conclusions: The study findings demonstrated that humoral, as well as CMI, responses with a predominant Th1 immune response contributed to the vaccine's efficacy against the FMDV challenge in cattle.

sciforum-105056: The COVID-19 Vaccine Anxiety Scale Teen Version: A Mental health screen for Covid-19 Vaccine-Related Anxiety among Teenagers in Egypt

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Introduction: The Covid-19 pandemic has had huge effects on the physical life and psychological health of people worldwide. Not only have adults been affected, but children and adolescents have also suffered. The hope of a return to normal life was raised with the development of vaccines, but misinformation and insufficient knowledge of authentic science about the effectiveness and safety of the vaccines have created another psychological phenomenon, namely, anxiety over the vaccinations themselves. Children are more likely to be affected by such fears and anxieties. To **address this problem**, a unique scale was developed to measure anxiety among teenagers regarding Covid-19 vaccines, and the scale's psychometrics (validity and reliability) were evaluated.

Methods: The Scale items were developed, and after arriving at 30 total items, item pooling and division of the items into five subscales was performed. These subscales measure Emotional, Cognitive, Physiological, Behavioral, and Emotion Regulation dimensions. Data was collected from 1296 participants with an age range of 12--18. To check the psychometrics of the scale, Exploratory Factor Analysis, Variance, Rotated Factor Matrix, Construct Reliability and Validity, and Confirmatory Factor Analysis were performed.

Results: For the five dimensions that were developed, the Cronbach's alpha reliability coefficients were as follows: Emotional Dimension, 0.797; Cognitive Dimension, 0.857; Physiological Dimension, 0.951; Behavioral Dimension, 0.769; and Emotion Regulation, 0.900.

Conclusions: The developed scale is reliable and valid for measuring vaccination anxiety among teens. Future research should follow up on this study with a more expansive population worldwide.

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