The vaccine segment is anticipated to be one of the fastest growing one of the healthcare industry and several leading firms have stepped up vaccine investments in recent years. Unlike therapeutic agents, vaccines are administered to healthy individuals only once or very infrequently during a life time. Vaccines generate well-documented positive externalities, yet their poor awareness and acceptability among vaccine end-users may contribute to resurgence of transmissible diseases and consequently trigger governmental interventions such as mandating vaccination.

In addition to technical and clinical development per the highest quality standards, bringing new vaccines to market requires carefully orchestrated programs targeting the multiple types of stakeholders along the entire value chain and addressing their respective purchasing behavioral drivers.

Against a backdrop of anti-vaccination buzz and vaccine fatigue, successful global launch and sustainable usage of a vaccine requires the development of a multi-pronged strategy addressing all aspects in relation to acceptability (e.g. the motivation to immunize despite the quasi-disappearance of the disease), accessibility (e.g. supply chain services), availability (e.g. mechanisms ensuring reliability of supply) and affordability (e.g. tiered pricing policy taking country differences in per capita income into account). Leveraging novel technological advances can positively influence the ability to activate these levers successfully.

**BIOGRAPHY**

Pierre A. MORGON is CEO of MRGN Advisors and Regional Partner for Switzerland at Mérieux Développement. He is also Chairman of the Board of Virometix, as well as Non-Executive Director to the Boards of Theradiag, of Eurocine Vaccines, of Alma Biotherapeutics and of Vaccitec. Pierre has over 30 years of experience in the global life science industry, especially with vaccines and immunotherapy, at the helm of international operations, in C-level positions at global level and as CEO of start-ups. He is a lecturer in several MBA programs in world-class business schools and in life science conferences. He holds a Doctorate of Pharmacy, a Master in Business Law and a MBA. He is also an alumnus of INSEAD and IMD.
International Conference on

VACCINES AND IMMUNOLOGY

June 28-29, 2018 | Amsterdam, Netherlands

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CHARACTERISTICS OF MONTANIDE™ ISA 51 VG ADJUVANT DESIGNED FOR THERAPEUTIC CANCER VACCINES

Maria Lazaro
France

Therapeutic cancer vaccines are one interesting alternative to treat cancer by active immunotherapy. The use of well defined overexpressed tumor antigens is linked with weak and short term immune response. In order to improve the immune response induced antigens may be associated with enhancers such as adjuvants. Water-in-oil (W/O) emulsions such as Montanide TM ISA 51 VG represent an interesting option for immunotherapy vaccines for which potent adjuvants are required. CIMAVAX-EGF vaccine to treat cancer has already been authorized in Cuba and many others Latin American countries, it’s also in late state in Europe and Asian countries which efficacy has been largely proven in patients suffering from lung cancer (NSCLC).

Vaccines based on Montanide™ ISA 51 VG interestingly enhance the immune response thanks to a depot effect conferred by this kind of adjuvant at the injection site. This renders a danger signal that increases and prolongs the interaction with antigen presenting cells. These interactions lead to an enhanced CD8+ and CD4+ activation and promote production of IFN, TNF, IL-2. Additionally, the use of adjuvant enhance the memory T-cells, in particular the central memory T-cells. Taken together, these results show that vaccines based on Montanide™ ISA 51 VG can induce a potent specific cytotoxic T response and a significant increase in antibody titers with the development of polarized Th1 responses.
THE INTESTINAL MICROBIOME AND ORAL VACCINE IMMUNOGENICITY

Vanessa Catherine Harris
Netherlands

Rotavirus (RV) is a leading cause of serious childhood gastroenteritis. Rotavirus vaccines (RVV) have lower effectiveness in developing countries. Many other live attenuated and inactivated viral and bacterial oral vaccines also have diminished effectiveness in developing country settings. We have shown that the intestinal microbiome correlates with RVV immunogenicity. The study presented in this talk evaluates if intestinal microbiome modulation improves RVV immunogenicity. In an open-label, proof-of-principle, randomized-control trial healthy men, aged 18-35 were enrolled. Subjects were randomized: 7-days broad-spectrum (oral vancomycin, ciprofloxacin, metronidazole), narrow-spectrum (oral vancomycin), or no antibiotics, and then vaccinated with RVV (RotarixTM), polysaccharide-pneumococcal (Pneumo 23), and tetanus-toxoid vaccines. The primary study endpoint was 28 days-post-vaccination anti-RV IgA level difference. Secondary endpoints were proportion of day 7 anti-RV IgA boosting (>2-fold increase), absolute and proportion of RV-antigen shedding, anti-RV, pneumococcal, and anti-tetanus IgG, and microbiome correlations with outcomes.

Baseline anti-RV IgA was high in all groups. There were no 28-day anti-RV IgA differences, but anti-RV IgA boosting was higher in narrow-spectrum subjects (8/21 vs. 1/21 each, RR=0.125, 95%CI:0.02-0.67, p=0.021). Higher proportions of subjects shed RV in narrow and broad-spectrum groups (8/21 each vs. 1/21, RR 8, 95%CI:1.5-47.4, p=0.02) and narrow-spectrum had higher OD-shedding overall (p= 0.0027). There were no anti-RV, tetanus or pneumococcal IgG differences. Both antibiotic treatments decreased Bacteroidetes; only vancomycin reduced Firmicutes and expanded Proteobacteria abundance. Despite the negative primary endpoint, this study shows targeted intestinal microbiota alteration boosts RVV response in sero-positive adults and supports a role for microbiome manipulation in improving RVV immunogenicity in developing countries.
PANORAMA OF THE DEVELOPMENT OF VACCINES AGAINST HIGH-IMPACT ARBOVIRUS INFECTIONS IN MEXICO

Ernesto Torres-Lopez
México

Viral infections that use arthropods as a vector have become more relevant in recent years. Among these, the most important are those caused by the Dengue virus (DENV), Chikungunya virus (CHIKV) and Zika virus (ZIKV). The World Health Organization (WHO) estimates 50 to 100 million new cases reported annually of DENV infections. CHIKV infections present annual variations, taking in 2017 an estimated 123,087 confirmed cases according to the WHO. In the case of ZIKV infections, the WHO estimates a total of 223,477 confirmed new cases between 2015 and 2018. Infection by one of the four serotypes of DENV confers lasting protection against homotypic reinfection, but only transient protection against a secondary heterotypic infection which is associated with an increased risk of severe disease. The development of the dengue vaccine focuses on the generation of a tetravalent vaccine designed to provide long-term protection against all serotypes of the virus. Currently several candidate vaccines are in the developmental stages.

The candidate vaccines against CHIKV have been developed through multiple technologies, however, only two have successfully completed Phase I clinical trials. One of these vaccines is based on VLPs, which contain particles structurally equal to CHIKV but without nucleic acids, which after being administered stimulates the appearance of neutralizing antibodies. The other vaccine uses chimeras based on measles virus which contains genes encoding envelope glycoproteins and viral capsid proteins, producing an immune response and high antibody titers. In the case of ZIKV it has been difficult to define its physiopathology in humans, however, there are multiple vaccines in development including DNA vaccines that express prM-E genes, inactive purified vaccines and messenger RNA vaccines. Currently the most promising use live attenuated virus simulating the natural cycle of infection producing long-lasting immune responses with the appearance of high titers of neutralizing antibodies and specific antiviral cytokines.
VACCINES TO TACKLE ANTIMICROBIAL RESISTANCE

Ivana Haluskova Balter
France

Bacteria, viruses, parasites and fungi that are resistant to drug cause 700,000 death each year. By 2050 superbugs inured to treatments could cause up to 10 million deaths annually and costs the global economy US$100 trillion. (1) AMR (antimicrobial) resistance is regarded nowadays as a major threat to global public health. The issue is receiving high-level political attention (G7 and G20 in 2017 for first time). Pandemics, drug resistance and neglected diseases framing health as a “global security issue”. The list was drawn up in a bid to guide and promote research and development (R&D) of new antibiotics, as part of WHO’s efforts for AMR (27th Feb 2017) Tuberculosis (MDR/XDR) and latent tuberculosis represent a major issue to tackle attracts global attention as witnessed by recent WHO and inter-ministerial meeting in November 2017 in preparation of high level UN meeting in 2018. Problem of resistance get worsened due declining number of new antibiotics and limited number of new classes (2). Multifaceted strategy to promote and prioritize highly potential alternatives to tackle AMR like vaccines development is required. Vaccines like diphtheria and tetanus did not prompt resistance. In 1980 the smallpox vaccine had eradicated the naturally circulating virus worldwide without generating resistance. Additionally, introduction of live vaccines like measles and BCG has been associated with much larger reduction of morality than can be explained by the prevention of the targeted infections and recent research like LATV pertussis (3) highlights importance of “off target” effects to be evaluated in depth. Thoughtful and innovative vaccines development taking into account host microbiota “superorganism” and immune crosstalk - Immune system training linked with several inflammatory/autoimmune diseases open large avenue for future development. (4) Accurate diagnostic and surveillance with better understanding of genetic and immunologic background of host specific response and pathogen evolution drives successful country adapted vaccine research. Vaccines, as highly potent tool and valuable alternative from long term perspective being clearly recognized as a major tool for public health already. Further strong support to promote them as highly potential tool to tackle antibiotic resistance need joint endorsement including regulatory and economic stakeholders along with necessary partnership at Global level.
Title

HIV/AIDS, MALARIA AND EBOLA VACCINES AND IMMUNOLOGY RESEARCH IN TANZANIA AND EAST AFRICA

Name & Country

Mariam Makame
Tanzania

Abstract

Vaccine production in developing countries is a challenging subject that requires attention. Tanzania is one of the developing countries in sub-Saharan Africa that strive to overcome the dilemma. These shortfalls lead to vaccine production under performance. Several issues were studied and analyzed during development and production of veterinary vaccines in the Tanzania and East Africa for the years. For now, the goals is to conduct health research, and the vision is to expound more on Clinical and Biomedical Research that are currently being conducted. The majority of the research being done was mainly concentrated on Malaria and HIV. However, after the outbreak of Ebola in West and Coastal Africa, most of the research agencies included Ebola and related infections in most of their research.

Biography

MARIAM IDD MAKAME is currently the Managing Director of Meshurap African Handmade and the Executive Director of Usaidizi Orphans Organization (Lushot, Tanga, Tanzania. Duly recognized by the Tanzania National NGO Coordination (TNNC) Cert. No. ooNGO/08297). Usaidizi Orphans Organization (UOO) is dedicated to providing Food, FREE Health-care, Tuition FREE Education and Shelter to HIV/AIDS infected and/or affected Children. UOO is not limited to supporting only HIV&AIDS Orphans. In our care, we have widows and/or single-mothers, the elderly, and the handicapped and/or disabled members of our community.
Viral infections that use arthropods as a vector have become more relevant in recent years. Among these, the most important are those caused by the Dengue virus (DENV), Chikungunya virus (CHIKV) and Zika virus (ZIKV). The World Health Organization (WHO) estimates 50 to 100 million new cases reported annually of DENV infections. CHIKV infections present annual variations, taking in 2017 an estimated 123,087 confirmed cases according to the WHO. In the case of ZIKV infections, the WHO estimates a total of 23,477 confirmed new cases between 2015 and 2018.

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**Title**

IMMUNOMICS TECHNOLOGIES USING PROTEIN AND PEPTIDE MICROARRAYS – FOR ANTIBODY PROFILING

**Name & Country**

Andreas Weinhäusel

Austria

**Abstract**

An individual’s antibody profile or immunome is stable over years but can change in respect to pathological changes as well as these changes can be triggered by vaccination/immunization or different therapeutic intervention. Antibody profiling on high density protein and peptide arrays has been shown to elucidate pathophysiological alterations in various indications like auto-immune, cancerous, and neurological disease, as well as in allergy and infectious disease.

Protein-arrays are usually generated using recombinant expression, and have limited flexibility – but can be customized when proteins are available. Peptide-arrays can be easily customized to present proteins deduced from sequences, without the need of protein-expression. We have setup immunomics discovery technologies using protein-and peptide-microarrays (presenting 32000 spots or up to 6 mio peptides, respectively) as well as targeted multiplexed technologies for validation of findings.

These are all customizable and affordable even when discovery studies are done with a small number of samples. In line with the different technologies we have established and optimized bioinformatics and laboratory methods and can provide complete workflows from design, experimental setup and sample analysis till data-analysis. This is also true when we have lower multi-plexed technologies available providing targeted micro-arrays (presenting hundreds - thousands antigens) as well as bead-arrays in an up to 500-plexed format for marker-refinement and confirmation.

For broader validation and clinical studies we have both micro- and bead-array technologies established for analyzing large series of samples in 96-well microwell-plates in medium-plexed assays. We have established and optimized different methods and combined these to a full workflow for providing modules as well as the entire pipeline for antibody-based analysis and diagnostics, which can be conducted with 10µl amounts of serum or plasma as well as using other body fluids like saliva.
PROTEINS SELECTED IN LEISHMANIA (VIANNIA) BRAZILIENSIS BY AN IMMUNOPROTEOMIC APPROACH APPLIED AS POTENTIAL VACCINE AND DIAGNOSIS TARGETS AGAINST LEISHMANIASIS

Thaís Teodoro de Oliveira Santos
Brazil

Leishmaniasis is a vector-borne disease caused by protozoan parasites of the Leishmania genus. The treatment presents problems, which have made it necessary to develop alternative control measures, such as vaccination. In this work, an immunoproteomic approach was performed to identify antigens in protein extracts of promastigote and amastigote-like forms of Leishmania (Viannia) braziliensis, the main species causing tegumentary leishmaniasis (TL) in the Americas, by using TL patients sera. Proteins recognized by sera samples (western-blot) were separated by two-dimensional electrophoresis (2DE) and identified by mass spectrometry. With the purpose of reduce the cross-reactivity, spots recognized by TL patients sera, but also by antibodies present in healthy individuals patients or by Chagas disease patients sera were discarded. Some proteins, such as enolase, initiation factor 5a and hypothetical proteins were later evaluated to validate the results of the immunoscreening. For this, their coding regions were cloned and the corresponding recombinant proteins were purified and evaluated for the serodiagnosis and as vaccine in BALB/c mice against Leishmania sp. infection.

The antigens showed sensitivity and specificity values ranging from 95.4 to 100%, and 82.5 to 100%, respectively. An in vivo experiment in BALB/c mice was developed, since these animals were immunized with the recombinant proteins plus saponin, and later challenged with Leishmania promastigotes. The results revealed that the vaccines induced high levels of Th1 cytokines evaluating by a capture ELISA and flow cytometry, which were associated with nitrite production and specific IgG2a isotype antibodies.

This pattern was associated with protection, which was characterized by significant reductions in the parasite load in several organs of the animals. This study represents a significant contribution not only in identifying stage-specific L. braziliensis proteins, but also in revealing the expression of new hypothetical proteins, providing new molecules to be tested as diagnostic antigens and vaccine candidates against leishmaniasis.
INVESTIGATIONS ON ACIDIC SERINE PROTEASE V2 (APrV2) OF DICHELOBACTER NODOSUS AS A POTENTIAL VACCINE CANDIDATE AGAINST VIRULENT FOOTROT

Aasim Habib  Wani
India

Dichelobacter nodosus, a Gram negative anaerobe secretes extracellular proteases involved in digestion of the hoof and underlying soft tissue of ruminants causing footrot. Various whole cell and fimbriae based, monovalent and multivalent vaccines have been used, but they fail to provide cross protective immunity against different serogroups. Among the proteases, APrV2 has been considered most important virulence factor and is conserved across different D. nodosus serogroups.

Considering the role of APrV2 in footrot pathogenesis this study measured the immunogenic potential of APrV2 in sheep. APrV2 gene was amplified from a virulent D. nodosus that was characterized using genotypic and phenotypic methods. APrV2 was expressed in E. coli and purified through affinity chromatography. Safety and potency test were carried out using rAPrV2 in combination with FCA and IFA in sheep. Immune response comparison of rAPrV2 vaccinated sheep (group I) was made with whole cell vaccinated (group II) and control sheep (group III). Indirect ELISA revealed a significant increase in rAPrV2 specific (P < 0.05) IgG immune response in group I and group II sheep. IgG titres of 320 were measured at day 15 and 45 in group I sheep while group II sheep revealed titres of 5120 and >10240 at 15 and 45 days respectively.

PBMCs (2×106 cells/well/ml) from each sheep on each time point were stimulated with rAPrV2 (25 μg), heat killed D. nodosus (10 μg) and Concanavalin A (5 μg) as a positive control for 4 hours and monitored for measuring early Th1 (IFN-γ and TNF-α) and Th2 (IL-4 and IL-6) response. It was observed that in group I sheep, significant (P < 0.05) elevation was seen in IL-4 and IL-6 on 15th day when stimulated with rAPrV2 and only IL-6 on 15th and 45th day when stimulated with heat killed D. nodosus in comparison to control sheep. In group II sheep IL-4, TNF-α and IFN-γ were significantly (P < 0.05) elevated on 15th day and only IFN-γ on 45th day when stimulated with rAPrV2 while on stimulation with heat killed D. nodosus, IL-6 and TNF-α were elevated significantly (P < 0.05) on 15th day while IL-6, TNF-α and IFN-γ were significantly (P < 0.05) low on day 45 when compared to control animals. Intra-group comparison of group I sheep to day 0 revealed that only TNF-α was significantly (P < 0.05) elevated at 45th day when stimulated with heat killed D. nodosus. Intra-group comparison of group II sheep revealed significant (P < 0.05) elevation in all four cytokines on 15th and 45th day when stimulated with rAPrV2, when stimulated with heat killed D. nodosus, TNF-α and IFN-γ were significantly (P < 0.05) elevated on day 15 and IL-6 and TNF-α on 45th day. In general only IL-4 levels were elevated on 45th day than observed on 15th day in rAPrV2 vaccinated sheep however insignificant. In conclusion vaccination with rAPrV2 induced superior humoral antibody response (IgG) and Th2 type cell mediated response (IL-4).
T cell vaccination is a technique of immunotherapy already applied to Multiple Sclerosis. It consists in identifying cytotoxic autoimmune T cells responding to auto-antigens, cultivating and expanding them in the laboratory. They are then re-injected into the patient after inactivation by glutaraldehyde or X-rays.

The rationale is thus to use them as a vaccine to trigger an immune response by the patient against his/her own cytotoxic autoimmune cells. An autoimmune component of the physiopathology induced by HIV infection, was suspected to be responsible for part of CD4 cell death that cannot be accounted for by the sole direct killing effect of the virus. Accordingly, we have identified anti-CD4 T cells in HIV infected patients, pointing towards an anti-CD4 autoimmune activity associated with the viral infection.

Therefore we were able to transpose the T cell vaccination technique to HIV infected patients with low CD4 cell counts not responding to HAART. In a first stage clinical trial, anti-CD4 T cells from BPMC were stimulated and expanded by exposition to recombinant CD4 molecule and inactivated before being re-injected in 15 patients as an autologous vaccine.

No adverse effect whatsoever was observed. CD4 cell counts were improved in seven patients. A controlled second stage clinical trial on more patients is necessary to assess the efficacy. In parallel we have identified some peptides in the CD4 molecule as epitopes for the anti-CD4 autoimmunity, which may allow for a simplification of the technique.
THE HALLMARKS OF TUBERCULOSIS AND THEIR CLINICAL SIGNIFICANCE

Zlatko Dembic
Norway

Abstract

Introduction: Heritable susceptibility to tuberculosis (TB) is complex and polygenic in nature. Only five to ten percent of humans that come in contact with the bacterium Mycobacterium tuberculosis (Mt) will manifest the disease, provided no acquired- or congenital immunodeficiency were present. We still lack a viable explanation for the observed epidemiologic fact. Background: Activation of macrophages via pro-inflammatory cytokines IFN-γ and Interleukin (IL)-17 can kill intracellular bacteria such as Mt. Instead, macrophages stimulated by the Toll-like receptor (TLR)-10 agonists show an anti-inflammatory effect. The TLR-10 acts by inhibiting the TLR-2 signaling from the cell membrane. The TLR-2 is the Mt-binding protein by which activated macrophages can internalize (and kill) Mt. Inactivation of the TLR-2 protein might convey a risk for developing the disease. This was supported by our finding that TLR2 gene polymorphisms, which either inactivate the TLR2 gene product or have a dominant-negative role in TLR-2-signaling are associated with elevated risk for tuberculosis in the Croatian Caucasian population.

Findings: The genome-wide study found that three single nucleotide polymorphisms (SNPs) within the HLA class II loci were significantly associated with TB (Nat Gen, 2016) suggesting that adaptive immunity is of paramount importance for defense against TB. In our studied population, an SNP in the TLR10 gene was associated with risk for TB, analyzed by the dominant model of inheritance, however, this was contrasted by the fact that SNPs in the IL17A and F genes were not.

Conclusion and Significance: Studying genetic risk by association analyses or genome-wide screening led us propose that clinical manifestation of TB is a state above certain “riskthreshold”. Threshold is reached by accumulation of seemingly minor susceptibilities divided between the hallmarks of the disease (we suggest there are 5 hallmarks). The model suggests that every human population has its own mosaic of genetic risks for TB.
Recrudescence of Yellow Fever in Southeastern Brazil: Possible Impacts of Recent Changes in Immunization Policies for Yellow Fever Control in Endemic Countries.

Guilherme Côrtes Fernandes
Brazil


The prevention of sylvatic and urban cases of yellow fever (YF) depends on high vaccination coverage. In Brazil, after control of urban YF in the first half of the 20th Century, and the ensuing progressive reduction in the risk of acquiring the disease in the Southeast region of the country, YF vaccination was restricted to the North and Central regions. In the last two decades there was evidence of higher YF virus circulation in the Southeast, which prompted the expansion of areas with YF vaccination recommendation. However, a simultaneous increase in concerns over vaccine reactogenicity limited the reach of such expansion. Vaccination coverage remained low in the Southeast, allowing for the occurrence of the largest YF outbreak in decades in 2017-2018, with a daunting risk of reintroduction of YF in densely populated urban areas infested with Aedes aegypti. On the verge of having to vaccinate millions of people in a short timeframe, and taking into account the risk of vaccine shortage, the Brazilian Ministry of Health started reactive vaccination campaigns in areas where the vaccine was not previously recommended.

It also changed the recommendation from 2 doses for children, followed by a booster dose at 10-year intervals, to the WHO recommendation of a single dose for life. In regions with suboptimal vaccination coverage undergoing outbreaks, such as the state of Minas Gerais, there were restrictions to access for children and adults with history of vaccination, and, as such, a broad reactive vaccination was not implemented. Broad, non-restrictive reactive vaccination was only offered in areas without prior recommendation for YF vaccination. On the first 2 months of the current outbreak, 11 confirmed cases of YF were reported in individuals with history of vaccination in the state of Minas Gerais. A review was done of available evidence on immunogenicity, reactogenicity and duration of humoral and cellular immunity of YF vaccines in adults and children to assess issues related to the current strategies and public policies adopted by the Brazilian Immunization Program to control the disease.
LEPTOSPIROSIS AND “ONE HEALTH”. PREVENTION AND CONTROL THROUGH EFFECTIVE VACCINES

Jessica Petrakovsky
Argentina

The concept of "One Health" starts from the awareness of the important possibilities that exist to protect public health through policies aimed at preventing and controlling the pathogens present in animal populations, acting at the interface between people, animals and the environment.

Leptospirosis is a zoonosis to be controlled because it is extremely difficult to eradicate. This microorganism can be housed and expelled in the urine of many animals, perpetuating among themselves like the carrier state. The prevention of animal leptospirosis directly impacts the incidence / prevalence of the human disease.

The infection of people can occur indirectly, through the environment (by water or mud contaminated with the urine of animals with leptospires) or directly (in dairy farms, domestic canines, etc.). The main control measures in veterinary medicine are vaccination, hygienic-sanitary measures and epidemiological surveillance.

The best method of prevention is a systematic vaccination. The vaccines are mainly destined to cattle, swine and canines. There is a variety of vaccines containing different serovars of Leptospira, combined or not with viral and / or bacterial agents. The serovars used in the formulation always has to be local. Theoretically, any mammal is capable of being infected by any serovar, but in practice a few serovars are enzootic in a region.

To guarantee the quality of the biologics, all the series of vaccines that are commercialized in Argentina must be approved by the National Service of Animal Health and Agroalimentary Quality (SENASA). The following quality controls are carried out on each of the series produced: sterility, safety, inactivation, pH and efficacy in hamsters. Leptospirosis is a global public health problem in tropical and subtropical regions. The situation of the disease in developing economies propose a great challenge since humans and animals often live in a close association.
Title

SIMULTANEOUS INTEGRATION OF INFLUENZA VACCINE AND CHITOSAN NANOPARTICLES WITHIN CPG NUCLEOTIDES OLGODODESI AND CHECK ITS EFFICIENCY IN REDUCING THE DOSE OF INFLUENZA VACCINE IN THE MOUSE MODEL

Name & Country

Seyed Farid Sadati

Turkey

Abstract

New formulations are needed to improve the efficacy of influenza vaccines. Lack of efficient delivery systems for transporting antigenic molecules to the cytosol of antigen presenting cells presents a major obstacle for antigen uptake by immune cells. To this end, influenza Whole Inactivated Virus (WIV) vaccines were formulated with chitosan nanoparticles and Cpg oligonucleotide as a biodegradable delivery system and a Th1-specific adjuvant, respectively. Inactivated Influenza virus vaccine with CpG and Chitosan was injected intradermally to female Balb/C mice. Injections were single dose in high and a reduced valium. Thirty days after injection, cell proliferation assay (MTT), IFN-gamma and IL-4 Elispot assays were carried out. Sera samples were collected 21 days after immunization to measure IgG1 and IgG2a levels. In addition, the mice challenged with mouse adapted virus, were monitored for weight loss. The results of analyzing the stimulation of cellular and humoral immune systems and weighting the mice show a significant stimulation of both humoral and cellular immunities; also weight gain and a decrease in mortality in the mice receiving both dosages of inactivated influenza virus vaccines with CpG and Chitosan coating were observed (Fig. 1). This finding demonstrated that CpG-chitosan low-dose vaccine was less costly than high-dose and helps in production of more vaccine despite the limited production required virus. Based on our results, it can be concluded that formulation of inactivated Influenza virus with CpG and its delivery by Chitosan as low-dose in return of high-dose with the same results as balanced between cellular and humeral immune responses can make enormous saving in manufacturing vaccine.
Title

PHYSICOCHEMICAL AND IMMUNOLOGICAL STUDIES ON METHYLGLYOXAL MODIFIED IMMUNOGLOBULIN G: IMPLICATION FOR DIABETES TYPE 2

Name & Country

Sidra Islam

India

Abstract

Methylglyoxal (MG), a highly reactive endogenous α-oxoaldehyde is a deceptively small molecule formed during the metabolism of biological macromolecules namely glucose, fatty acids and protein. It is an intermediate of maillard reaction and is a potent glycating agent showing 20,000 times more glycating potential than glucose. It reacts rapidly with proteins forming hydroimidazolone derivatives, hence making them highly immunogenic. Increased protein-MG adducts have been reported in various pathological states such as diabetes and rheumatoid arthritis. In the present study, MG mediated structural alterations in IgG were characterized by various physicochemical techniques. Further, the immunogenicity of native and MG treated IgG was probed in female rabbits. The results revealed hyperchromicity in UV spectroscopy and AGE specific fluorescence, quenching in tyrosine fluorescence, tertiary structural change in near-UV CD, increase in hydrodynamic radii in DLS, aggregate formation in thioflavin T and congo red staining assay and increase in molecular mass in MALDI-TOF MS. The modified IgG was highly immunogenic inducing high titre antibodies. From the results, it can be concluded that MG modification of IgG generate neo-epitopes on the molecule making it immunogenic. The results point towards a possible role of MG-IgG in the complications associated with diabetes type 2.
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The vaccine segment is anticipated to be one of the fastest growing one of the healthcare industry and several leading firms have stepped up vaccine investments in recent years. Unlike therapeutic agents, vaccines are administered to healthy individuals only once or very infrequently during a life time. Vaccines generate well-documented positive externalities, yet their poor awareness and acceptability among vaccine end-users may contribute to resurgence of transmissible diseases and consequently trigger governmental interventions such as mandating vaccination.

In addition to technical and clinical development per the highest quality standards, bringing new vaccines to market requires carefully orchestrated programs targeting the multiple types of stakeholders along the entire value chain and addressing their respective purchasing behavioral drivers.

Against a backdrop of anti-vaccination buzz and vaccine fatigue, successful global launch and sustainable usage of a vaccine requires the development of a multi-pronged strategy addressing all aspects in relation to acceptability (e.g. the motivation to immunize despite the quasi-disappearance of the disease), accessibility (e.g. supply chain services), availability (e.g. mechanisms ensuring reliability of supply) and affordability (e.g. tiered pricing policy taking country differences in per capita income into account). Leveraging novel technological advances can positively influence the ability to activate these levers successfully.
The role of Auto ZelK Bridge Software, Hardware, and Bioelectronics in Biomedical and Space Science Advanced Research and New Vaccine and Drug Discovery and Development

Zelalem Kiros Bitsue
Ethiopia

Modern biomedical, space science research and health care are provided by multidisciplinary teams in which biomedical engineers contribute to the advancement of knowledge equally as medical professions. Biomedical engineering represents one of the most rapidly growing branches of industry in the developed world. Main Objective: To develop Software, Hardware, and Bioelectronics devices (machine) and identify and determine the effective potential in biomedical and space science researches. Methods: The software development methods to be use formal, informal, approaches, and various forms of prototyping methods, are of interest in this work.

Result and Discussion: Having a crossdisciplinary approach, the project will have the potential to discover whole new soft wares, hard wares, and bioelectronics devices openings in the area of the biomedical and space science research. This research project enhances the prospects of the economy as a whole as it improves the capabilities and competitive advantage of the soft wares, hard wares, and bioelectronics devices development at university.

Bioassay

Asst Professor Zelalem was born in Ethiopia. He earned a Ph.D. in Immunology, MBBS Degree in medicine and surgery, a bachelor’s degree in Nursing and Health administration, a bachelor’s degree in Theology and Leadership; a diploma in advanced research proposal writing, research report writing, methods, grant proposal writing. He is Ass. Professor at the Addis Ababa Institute of Technology and Owner, Founder and General Director at United States of African Health Organization "US-AHO". Zelalem is an energetic, motivating and highly skilled consultant specializing in biomedical research particularly in Immunological research and leadership at United States of Africa Health Organization "US-AHO".

His background includes more than 15 years of experience as an educator, clinician, Leadership and advanced biomedical research in all settings in which biomedical research is provided. Zelalem is an Owner, founder, General Director and serves as, General Director of the United States of African Health Organization "US-AHO". Publications he has made 120+ publications, he is corresponding / first author on 112+ Publications as well as over 44,000 citations.
ENHANCING ANTIBODY SERODIAGNOSIS ON PEPTIDE MICROARRAYS USING A CONTROLLED MULTIPRESENTATION STRATEGY

Marina Cretich
Italy

Here we present a workflow enabling the rapid delivery of efficient immunoassays for different diagnostics contexts which expands the current limits of peptide-based serodiagnosis on microarrays. Our strategy starts from the use of computational tools for accurate immune-reactive peptide design; exploit chemo-selective strategies for optimal probes presentation on sensing surfaces by the use of clickable polymeric coatings and finally generate peptide chips for fluorescence microarrays and SPR imaging. We will show how the rigorous control of probe design, orientation and surface density enabled by our platform positively impacts the diagnostic accuracy of antibody detection in serum of Burkholderia infected patients. Furthermore, we will compare different strategies of peptide multiple presentation to increase immunoreactivity in the context of allergy screening and for functional mimicking of discontinuous epitopes of NS1 protein for Zika virus diagnosis.
STRATEGIES FOR ENHANCING THE SAFETY AND EFFICACY OF LIVE RECOMBINANT VACCINES

Tilahun Yilma
USA

We have taken a number of approaches to improve the safety and efficacy of recombinant vaccines for use in humans and animals, including: choice of the strain of vaccinia virus (VACV) used as a vector, insertional inactivation of virulence and immunoregulatory genes of VACV, and expression of cytokine genes that attenuate the vector by more than a million-fold without reduction in immunogenicity. These strategies are illustrated by providing examples of recombinant VACV (rVACV) vaccines we have developed for rinderpest, vesicular stomatitis, simian immunodeficiency virus, smallpox, and Rift Valley fever. Additionally, we have exploited the advantages of recombinant vaccines and developed diagnostic kits that permit one to distinguish between vaccinated and infected individuals. We constructed rVACVs expressing an interferon gamma (IFNγ) and lacking the immune-modulating genes B8R, B13R, and B22R. IFNγ is a Cytokine with potent Immunoregulatory, antineoplastic, and antiviral properties. These rVACVs replicated to high titers in tissue culture, yet were avirulent in both immunocompromised and immunocompetent mice with no detectable viral replication in these animals. A single immunization elicited potent humoral, T-helper, and cytotoxic T-cell immune responses in mice despite the absence of any detectable virus replication in vivo. IFNγ co-expression and the inactivation of one or more VACV immune-modulating genes provide an optimized method for increasing the safety while maintaining the efficacy of rVACV vaccines for use in humans and animals.
GOLD NANOCAGES FOR THE DELIVERY OF VACCINES IN VITRO

Emine Yavuz
Turkey

In order to increase the immune modulation capacities of vaccines different adjuvant systems have been studied. Especially nanoparticle-based carriers are being widely investigated. Biocompatible and bioinert gold nanoparticles have been commonly used as potential delivery vehicles. It has also been shown that of Au nanoparticles with different structural properties may lead to different immunological responses. Recently, gold nanocages (AuNCs), a special design with ultra thin porous walls and hollow interiors, have shown a promising potential in the fields of image-guided delivery of antigens. In this project our aim is to use the AuNCs for the delivery of Hepatitis B antigen for vaccination purposes (infectious diseases vaccine) in vitro. Here, Au nanocages were used to explore their effect on the internalization of HBsAg into antigen presenting cells (i.e. macrophages). Following the loading of HBsAg on nanoconstructs via non-covalent approaches, their immune responses were assessed by different techniques such as flow cytometry and ELISA. The in vitro tracking of AuNC-based nanocarrier was performed by confocal microscopy imaging. We believe that construction and characterization of AuNC-based nanovaccines carrying different antigens may increase our understanding of many diseases and highlight its promising potential in nanomedicine research.
THE CENTERS OF PREMELTONS SIGNAL THE BEGINNING AND ENDS OF GENES

Premeltons are examples of emergent structures (i.e., structural solitons) that arise spontaneously in DNA due to the presence of nonlinear excitations in its structure. They are of two kinds: B-B (or A-A) premeltons form at specific DNA-regions to nucleate site-specific DNA melting. These are stationary and, being globally nontopological, undergo breather motions that allow drugs and dyes to intercalate into DNA. B-A (or A-B) premeltons, on the other hand, are mobile, and being globally topological, act as phase-boundaries transforming B- into A- DNA during the structural phase-transition. They are not expected to undergo breather-motions. A key feature of both types of premeltons is the presence of an intermediate structural-form in their central regions (proposed as being a transition-state intermediate in DNA-melting and in the B- to A-transition), which differs from either A- or B- DNA. Called beta-DNA, this is both metastable and hyperflexible – and contains an alternating sugar-puckering pattern along the polymer-backbone combined with the partial-unstacking (in its lower energy-forms) of every other base-pair. Beta-DNA is connected to either B- or to A- DNA on either side by boundaries possessing a gradation of nonlinear structural-change, these being called the kink and the antikink regions. The presence of premeltons in DNA leads to a unifying theory to understand much of DNA physical-chemistry and molecular-biology. In particular, premeltons are predicted to define the 5’ and 3’ ends of genes in naked-DNA and DNA in active-chromatin, this having important implications for understanding physical aspects of the initiation, elongation and termination of RNA-synthesis during transcription. For these and other reasons, the model will be of broader interest to the general audience working in these areas. The model explains a wide variety of data, and carries within it a number of experimental predictions – all readily testable – as will be described in my talk.
Title
VACCINE IN PRIMARY IMMUNODEFICIENCY DISEASES, WHAT WE NEED TO KNOW?

Name & Country
Carmen Carolina Fernandez
Paraguay

Abstract
All the people know the importance of prevention, and the vaccines are the only sufficiently valid tool for that. The fundamental problem with patients who have Primary Immunodeficiency is to formulate the appropriate schemes for each of them. Are more than 300 discovered primary anomalies and increasing every minute, with the new techniques of molecular biology and laboratory that gives us genetic responses to clinical questions.

How we can elaborate vaccine schemes in patients with a compromised immune response, may not respond correctly of them?
How we can recommend protection of nest in the family of a patient with primary immunodeficiency?
Really, be a scheme applicable to all of them? Which are more valid, live bacterial vaccines? Or, inactivated vaccines are better for all?

These questions arise when we are face to face with patients who have an immune deficit. To star we need divided in groups with similarly deficit and response that we know, ANTIBODY DEFICIENCY, MAJOR T-CELL DEFICIENCIES AND DEFECTS IN INTRINSIC IMMUNITY, INNATE IMMUNE DEFICIENCY, SYNDROMIC IMMUNODEFICIENCY and HOUSEHOLD MEMBERS.

In patients who have antibody deficiency, generally inactivated vaccines considered safe as compared to healthy subjects, in relations to PPSV23, PCV13 is recommend for high-risk individuals, and the timing recommended the interval is 8 week.

Inactivate vaccine can be administrated to CVID and XLA patient even if it could not generate a protective response. In contrast, all available vaccine can administrated to patients with IgA or IgG subclass deficiency. In relations to T-cell deficiency and intrinsic immunity, killed or inactivated vaccines are safe, the response to bacterial conjugate polysaccharide vaccines is likely to be poor and Oral Polio Vaccine should not be administrate to patients or to their household contacts. In patients with Innate Immune, deficiency the BCG vaccine are contraindicate like a Salmonella attenuated Ty21a.
IMMUNOLOGICAL ASPECTS OF SUBLINGUAL AND SUBCUTANEOUS ALLERGEN-SPECIFIC IMMUNOTHERAPY

Nerin N. Bahceciler
Cyprus

Although, allergen specific sublingual (SL) and subcutaneous immunotherapy (SCIT) have been demonstrated to be clinically efficient with similar immunological responses, head to head studies comparing those two modes of allergen administration in terms of onset of clinical improvement along with simultaneous immunological responses and underlying mechanisms of preventive effect is scarce.

Compared to SLIT, SCIT provides a rapid onset of clinical improvement by eliciting a simultaneous surge in production of Th1 and Treg cytokines and blocking antibodies. Similar immunological and clinical responses are evoked quite later, with no effect on IgG4 levels during SLIT. Increases in TGF-beta secretion due to non-relevant allergens during SLIT may explain the preventive effect on new sensitizations.

SLIT and SCIT are both clinically efficient in the treatment of respiratory allergic diseases with slight differences in the early phase in terms of onset of clinical efficacy and simultaneous immunological responses. Both SLIT and SCIT induce similar T cell responses with different dynamics, but specific IgG4 blocking antibody responses are more prevalent following SCIT. Further studies addressing the efficacy and immunological responses multiallergen IT in polysensitized patients are warranted. Updated scientific data on immunological and clinical tolerance of SLIT vs SCIT will be presented.
Membranoproliferative glomerulonephritis (MPGN) is a type of glomerulonephritis caused by deposits in the kidney glomerular mesangium and basement membrane thickening, activating complement and damaging the glomeruli. (MPGN) classified to 3 types according to location of deposits, and based on etiology categorized to secondary and idiopathic.

Objective: The aim of the study is to find the outcome of treatment (remission, partial remission, relapse and progress to end stage renal disease) of idiopathic membranoproliferative glomerulonephritis, among adult Sudanese patients presenting to Omdurman Military Hospital, Renal Unit.

Materials and Methods: A retrospective study of patients with idiopathic MPGN followed up at the clinic. Forty five patients with no identifiable cause of MPGN were included. Idiopathic (MPGN) patients who have high renal profile or nephrotic range treated by three doses of methylprednisolone 0.5 g intravenous in three consecutive days, and of corticosteroid tabs (0.5_1mg/kg/day), slowly withdrawn according to the patient response indicated by spot urine test.

Results: Out of forty five patients the following treatment outcomes were observed, (remission, partial remission, relapsed, and progressed to (ESRD)), (44%, 16%, 18%, 22%) respectively.

Conclusions: In comparison to the similar studies, the remission rate is comparable, but the renal survival rate is different.
Molecular and cellular mechanisms involved in the onset of autoimmunity

Autoimmune diseases are classified into more than 100 different types based on their clinical manifestations. Autoimmunity strikes at different stages of life, but age and/or gender play role in the onset of some of these diseases. The induction of autoimmunity is initiated by the origination of autoantigens, which are the root cause for the development of autoantibodies followed by auto-immunogenicity. Progression of such auto-immunogenicity into autoimmune pathogenesis will be positively regulated by several factors such as viral infection, type I interferons, inflammation, cell death, deoxyribonuclease (DNase), protease enzyme modulations and unregulated T cell activation, whereas induction of anti-idiotypic antibodies and expression of the regulatory T cells (Tregs) suppress autoimmune pathogenesis. Suitable therapies to treat autoimmune diseases are lacking, since mechanisms involved in the onset of these anomalies were poorly understood. Present therapies are limited to symptomatic treatment and come with severe side effects. Therefore, there is an urgent and unmet need for suitable and safer therapies to treat autoimmune diseases. Based on my research findings, I will describe and discuss the role of risk factors, the stepwise molecular and cellular mechanisms involved in initiation and progression of autoimmune pathogenesis and propose better strategies to eliminate and/or minimize the impact of risk factors, modulate molecular and cellular anomalies involved in the onset of autoimmunity. Such focused regimen and/or approaches will help in developing effective and safer ways to prevent and/or control autoimmune pathogenesis for a better quality of life.
INSILICO PREDICTION OF PEPTIDE BASED VACCINE AGAINST FOWLPOX VIRUS (FPV)

Sarah Tag-Elsir
Sudan

Fowlpox virus (FPV) is double stranded DNA virus and a member of Poxviridae family which transmitted via aerosols and insect bite and causes cutaneous and diphtheritic infection in poultry population. This study aimed to design peptide vaccine by selecting all possible epitopes after analyzing of all FPV140 protein sequence reported in NCBI database using insilico approaches. After alignment of retrieved sequence the conserved region applied into IEDB analysis tool to predict B and T cell epitopes, then testing the affinity of predicted epitopes to bind to (BF2*2101) (BF2*0401) chicken receptor for MHC1 molecule, peptides low energy when docked against receptor were suggested as epitopes based vaccine. Peptides (50 PPSPKP 55, 51 PSPKPL 56, 52 SPKPLP 57, 53 PKPLPK 58, 54 KPLPKS 59, 55 PLPSKQ 60, 56 LPKSKQ 61 and 18 RPSSTV 23) were most potential B cell epitopes while (110 YIMDNAEKL 118, 274 FYHRMYYPL 282, 278 MYYPLFSVF 286 231 YVVDNDRYV 239 and 317 LLSGVFLAY 325) docked epitopes suggested to be T cell epitopes because of their good binding affinity especially this overlapped one 110 YIMDNAEKL 118. This study concluded that those predicted epitopes might use to produce good vaccine against FPV after invitro and invivo studies to evaluate its efficiency.
Title

PERSONALIZING CANCER TUMOR ANTIGENS

Name & Country

George Kunudji
Ghana

Abstract

Immune system can react to cancer cells in two ways, by reacting against tumor-specific antigens, molecules which is unique to cancer cells or against tumor-associated antigens, molecules is expressed differently by cancer cells and normal cells. Immunity to carcinogen-induced tumors in mice is directed against the products of unique mutations of normal cellular genes. These mutant proteins are tumor-specific antigens. Tumors caused by viruses display viral antigens that serve as tumor antigens. Examples are the products of the E6 and E7 genes of the human papillomavirus, the causative agent of cervical carcinoma, and EBNA-1. Most recently we have developed evidence for a powerful immunodominance effect that occurs between different tumor antigens and have identified what appears to be a unique mechanism by which at least some forms of immunotherapy induce tumor specific destruction.

Tumors of unknown cause which account for most human tumors — express antigens that the immune system can recognize remained in doubt until the development of methods for detecting and isolating them. The advent of hybridism technology led to the development of monoclonal antibodies from mice that were immunized with human tumors. Monoclonal antibodies that reacted specifically with tumor cells were then used to characterize putative human tumor antigens. However, there were doubts that the tumor-specific antigens that mouse monoclonal antibodies could detect would perceive by the human immune system.

The evolution of methods to cultivate human T cells, and in particular tumor-specific T cells from patients with cancer, led to an important breakthrough, the identification of MAGE-1, a melanoma-specific antigen that stimulates human T cells in vitro. With antigen-specific T cells as a reagent, it was possible to clone the MAGE-1 gene. The MAGE-1 studies showed that the human immune system can respond to tumor antigens, and the findings stimulated a productive effort to discover tumor antigens. The result is a long and still-growing list of antigens from a variety of tumors that could serve as targets for treatment.

Bioography

Dr. George Kunudji attained his PhD from the University of Ghana, Legon and postdoctoral studies from University of Ghana Medical School. He is the director of Bikbok Herbal Centre, a reputable herbal organisation that is dispensing services across the country, Ghana and currently discovered herbal antidote to the treatment of cancer tumour. Moreover, he has been serving as the chairman of the health advocacy group of Asuboa Traditional Council and Nifahene (Nifa chief) of Asuboa Traditional Area.
Title

TEMPERATURE DATA ANALYSIS OF THE VACCINE COLD CHAIN SYSTEM IN NORTHERN PART OF THAILAND

Name & Country

Kannika Thiankhanithikun
Thailand

Abstract

Vaccines are temperature-sensitive biological preparations, 2-8 °C or cold chain period were the appropriate range. The change of the temperature during transport system might be effect to vaccines quality assurance. This descriptive study was to analyze the data temperature of vaccine in cold chain system. We aimed to find the factor that effected to the change of vaccine’s temperature before used, such as area of vaccine transport, seasonal and type of health care unit. Temperature data of DPT- HB vaccine that used in National Health Security Office (NHSO) Region 1, included 8 provinces in northern part of Thailand were analyzed. The temperature data were collected by computerized data logger and analyzed by SPSS for window version 17.0 and Logtag analyzer program.

The result showed that, from 323 Health care units in fiscal year 2011, DPT-HB vaccine temperature had lower than 2°C at 86.9% and upper than 8°C at 90.4%. Type of health care unit and seasonal didn’t effect to vaccine temperature control, significantly. In fiscal year 2012, DPT-HB vaccine temperature from 1,399 health care units showed that lower than 2°C at 78.5% and upper than 8°C at 92.5%.

Type of health care unit didn’t effect to vaccine’s temperature control following the World Health Organization criteria but the seasonal had significant effect to vaccine’s temperature control. The study also found that most of the health care worker did not set the computerize data logger follow the handout of the company. Based on the study results adequate equipment, provide training and supervision about new and current computerize data logger were recommended to support to maximize the efficacy and effectiveness of vaccine and cold chain monitoring in health care unit.
A NOVEL MOLECULAR MECHANISM OF INFLAMMATION INVOLVING AP1 TRANSCRIPTION FACTOR

Mirza S. Baig
India

Macrophage plays pivotal roles in pathogen recognition and elimination as well as in the maintenance of tissue homeostasis. Acute inflammatory activation of macrophages by Toll-like and related receptors is characterized by transient activation of AP-1, NF-κB- and IRF-mediated signaling pathways and expression of pro-inflammatory genes. In this study, we have investigated that TIRAP-mediated transactivation of c-Jun regulates AP1 proinflammatory response in macrophages. The structure of AP-1 is a heterodimer composed of proteins belonging to the c-Fos, c-Jun, and ATF families. We have identified that TIRAP-mediated transactivation of c-Jun is essential for its binding with other partners like Fos/ATF2, translocation of AP1 heterodimer to the nucleus and proinflammatory cytokine expression.
Hepatitis B virus can cause cirrhosis of the liver and hepatocellular carcinoma. Due to the lack of sufficient immune response in whole population, several researches are being done to improve the efficacy of Alum based HBV vaccine. Here, Naloxone/Alum mixture as adjuvant was used for the HBsAg vaccine and immune parameters evaluated in immunized mice. In this study the effect of Naloxone/Alum mixture for the HBsAg vaccine has been investigated and compared to Fendrix vaccine. Female Balb/c mice were vaccinated at day 0, 14 and 28 with, Alum based vaccine or Naloxone/Alum mixture vaccine in different doses. Naloxone/Alum vaccine groups received the dose 3, 6 or 10 mg/kg of Naloxone in the vaccine formulation. One group received routine HBsAg Alum vaccine and a group received Fendrix vaccine. Some groups received Naloxone plus HBsAg without Alum and a group received HBsAg without adjuvant. PBS, Naloxone and Alum were also injected into the control groups separately. Finally, the Naloxone/Alum formulated vaccine compared with the Fendrix and routine Alum based vaccine regarding to the levels of total anti-HBS antibody, IFN-γ, IL-4, IgG1 and IgG2a and the level of lymphocyte proliferation. The level of total anti-HBS antibody in Naloxone formulated vaccine was comparable with Fendrix. Meanwhile, IFN-γ/IL-4 ratio level was significantly higher in Naloxone formulated vaccine groups versus mere vaccine group. IgG2a was also higher in the Naloxone formulated vaccine groups. These data showed that Naloxone/Alum mixture has ability to shift the immune response toward Th1 pattern, which more potentiate the immunity against infections.