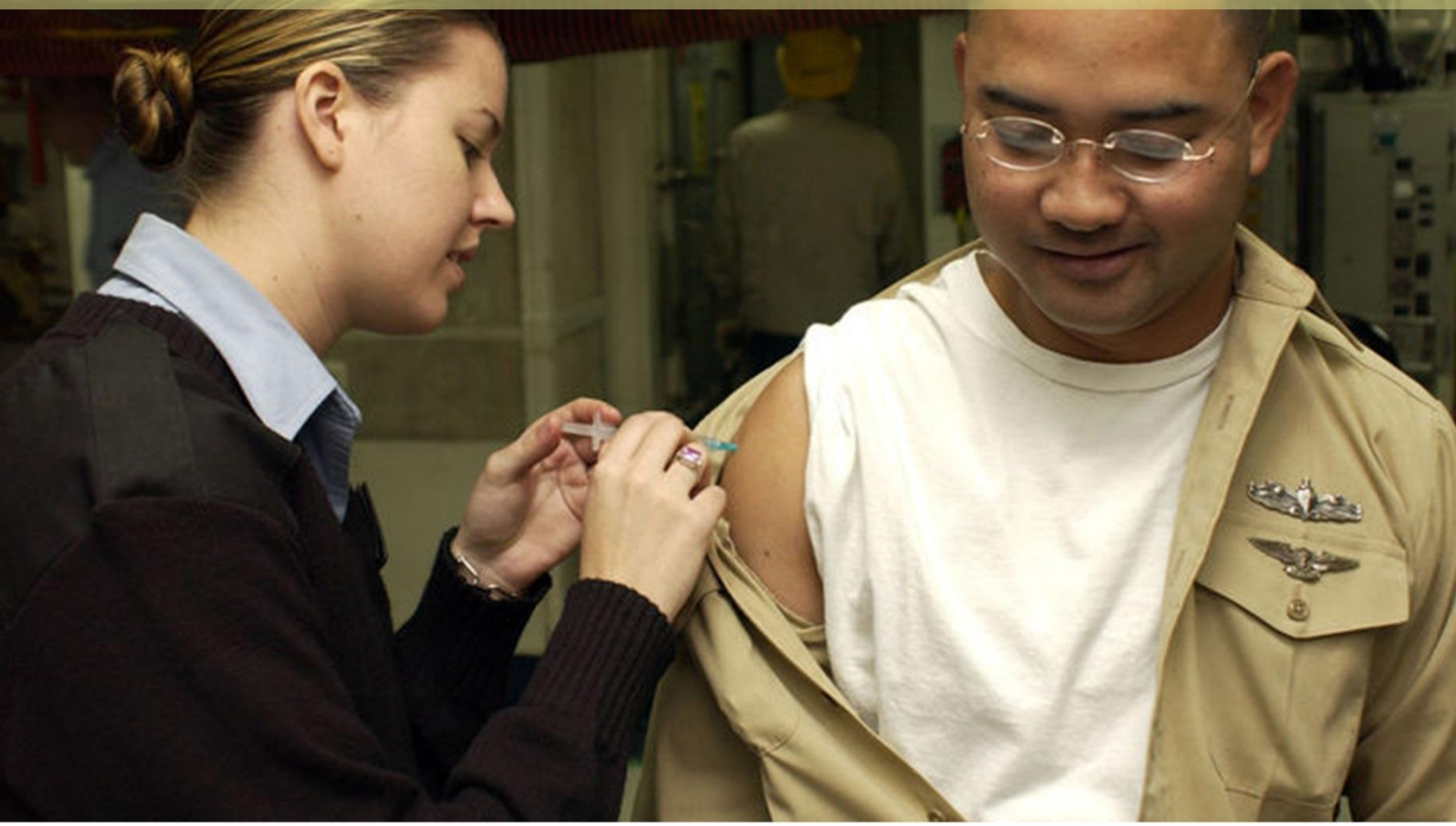
THE 2015 VACCINE SUMMIT

ABSTRACTS



13th - 15th October 2015
London, UK

EuroSciCon

Now in its third year, this international interdisciplinary event is an open forum for discussion of all scientific and clinical aspects of vaccine development and vaccinations. Using a multi-professional and inter-specialty approach this event offers plenty of opportunity for networking and debate, and will bring you up to date with current research and thinking.

This event has CPD accreditation

Hashtag: #Vac2015

This abstract book will be finalised two weeks before the event

www.regonline.co.uk/Vac2015

Table of Contents

Invited Speakers Abstracts

Clostridium difficile Vaccine- C diffense Study

Dr Amit Arora, Consultant physician and Geriatrician, University Hospital of North Midlands, Stoke on Trent, United Kingdom

Clostridium difficile associated diarrhea is a serious condition often associated with antibiotic treatment speically on frail older hospitalized patients. The first vaccine for this condition is being investigated at present at seven UK centres. This talk gives a brief overview of the illness, treatment and prevention options available at present.

Oral vaccines for the control of poultry diseases

Professor Anthony Amaechi ATTAMA, Drug Delivery and Nanomedicines Research Unit, Department of Pharmaceutics, University of Nigeria, Nsukka, Enugu State, Nigeria

There is an enormous challenge for the development of oral vaccines for man and animals. Liposomes and niosomes containing vaccines and antigens for use in poultry management were formulated and evaluated with good results. The enhancement of immune response of fowls to Newcastle disease (ND) vaccine encapsulated in 1,2-dioleoyl-3-trimethylammonium propane (DOTAP)-based liposomes was evaluated together with Span 20-based niosome loaded with ND vaccine. Oral liposomal formulations of fowl typhoid vaccine were also evaluated in fowls with appreciable boost in the level of immunity.

Therapeutic Use of Vaccine for Treatment of Chronic Hepatitis B: From Bench to Bedside

Dr. Sheikh Mohammad Fazle Akbar, MBBS, MD, PhD, Principal Investigator, Toshiba General Hospital, Tokyo, Japan

'Vaccine', an amicable weapon to prevent infectious diseases, has been applied for centuries. But, little has been explored about the role of vaccine as a therapeutic approach. Studies in mice provided insights about the nature of therapeutic vaccine and a therapeutic vaccine was applied in hepatitis B virus (HBV) transgenic mice, normal volunteers and patients with chronic hepatitis B (CHB) to assess its safety and efficacy. Finally, a phase III clinical trial has been accomplished in 151 patients with CHB that compared the efficacy of therapeutic vaccine over pegylated interferon, the most costly drug available to treat CHB.

HIV-1 Vaccines: The Yin and Yang of Viral Entry Where We Keep Getting It Wrong

Dr Cynthia L. Bristow, Chief Executive Officer, Alpha-1 Biologics, New York, USA

We recently determined that thymopoiesis requires VLDLR-induced cellular locomotion that is dependent on the abundant protein α1proteinase inhibitor (α1PI, α1 antitrypsin) that is expressed by hepatocytes and lymphocytes. We previously demonstrated the presence of 3F5 monoclonal antibody in the blood of HIV-1 infected individuals and that in the absence of viral particles, 3F5 binds to and inactivates human, but not chimpanzee α1PI. The presence of 3F5 produces acquired α1PI deficiency in humans resulting in reduced thymopoiesis. We observed that in these individuals, CD4+T cell counts rebounded to normal levels following 2 weeks of receiving weekly α1PI replacement therapy.

Pseudotype-based neutralisation assays for influenza: a systematic analysis

George Carnell, Viral Pseudotype Unit, School of Pharmacy, University of Kent, UK

Assays utilizing influenza pseudotypes, chimeric viruses bearing influenza glycoproteins, have been shown to be highly efficient for the measurement of homosubtypic and heterosubtypic broadly neutralising antibodies, making them ideal serological tools for the study of cross-protective responses against multiple influenza subtypes with pandemic potential. In this talk, we will compare literature involving the production of influenza pseudotypes with particular emphasis on their use in serum antibody neutralisation assays. This will enable us to establish the parameters required for optimisation and propose a consensus protocol to be employed for the further deployment of these assays in influenza vaccine immunogenicity studies.

Oncolytic activity of attenuated Measles virus against mesothelioma

Dr Jean-François Fonteneau, Chargé de recherche INSERM, INSERM UMR892, CNRS UMR6299, Institut de Recherche en Santé de l'Université de Nantes, France

Attenuated vaccine strains of Measles virus (MV) are evaluated as oncolytic virus for the treatment of different cancers in clinical trials. Recently, we screened the oncolytic activity of this virus against 22 mesothelioma tumor cell lines and 4 types of healthy primary cells. We observed that 15 tumor cell lines were sensitive, whereas the other tumor cell lines and the healthy cells were not. We then observed that the oncolytic activity depends on defects in the antiviral type I Interferon response in the sensitive tumor cell lines. Our study shed light on how the attenuated strain of MV exerts its oncolytic activity.

Why do parents who usually vaccinate their children hesitate or refuse? General good vs. individual risk

Dr Anat Gesser-Edelsburg, Head of Health Promotion Department, School of Public Health, University of Haifa, Israel

This study examines vaccination hesitancy or refusal following the 2013 polio outbreak in Israel.
It employed a questionnaire survey (n = 197) and content analysis of parents' discussions in blogs, Internet sites, and Facebook pages (n = 2499).
The findings indicate that some parents who normally give their children routine vaccinations decided not to give them OPV due to lack of faith in the health system, concerns about vaccine safety, reasons specific to the polio outbreak in Israel, while some vaccinated due to a misunderstanding.
We conclude that high attention should be given to the public's risk perception context-dependent analysis.

State of the art of VLP-based vaccines against influenza virus- commercial and scientific approach

Dr Beata Gromadzka. Department of Recombinant Vaccines, Intercollegiate Faculty of Biotechnology, University of Gdansk, Medical University of Gdansk, Poland

The development of new technologies for production of vaccines, including the vaccines against influenza, is one of the biggest concerns of public health. The 20th century gave start to a new trend in vaccinology focused on the use of protein components of particular pathogens ensuring the safety of protective preparations. A comprehensive study on the recombinant sub-unit vaccines has provided new opportunities and founded a new branch of science dealing with the use of virus-like particles (VLPs) as potential, next generation vaccines.
This presentation is aimed at describing the limitations of available influenza vaccines and summarising the current scientific trends using classic influenza virus VLPs and innovative nano-structures which are potential vaccine against influenza.

Realising the Potential of Viral Vectored Vacccines

Dr. Sarah Gilbert, University of Oxford, Jenner Insitute, Oxford, United Kingdom

Replication-deficient viral vectored vaccines have been used in many clinical studies. They are an exciting platform technology with an excellent safety profile and the potential to facilitate rapid vaccine development for outbreak pathogens. Recent work in using this technology for several different applications will be presented.

Plant-Made Vaccines for Developing Countries

Dr Kathleen Hefferon, University of Toronto, Canada

Plant-produced vaccines offer enormous potential for providing relief to developing countries by reducing the incidence of infant mortality caused by infectious diseases. Vaccines derived from plants have been demonstrated to effectively elicit strong immune responses. These plant-made biopharmaceuticals are inexpensive to produce, require fewer purification steps, and can be stored at ambient temperatures for prolonged periods of time. As a result, plant-produced vaccines have the potential to be more accessible to the rural poor. This presentation will provide an overview of plant-produced biopharmaceuticals that are under development to target infectious diseases including human immunodeficiency virus, malaria and Ebola virus.

Factors Influencing the Recommendation of the Human Papillomavirus Vaccine by South African Doctors

Dr Muhammad Hoque, University of KwaZulu-Natal (Westville Campus), Durban, South Africa

The objective of this study was to investigate factors contributing to recommend HPV vaccines to the patients. This was a cross-sectional study was conducted among 320 doctors, using a self-administered anonymous questionnaire. Results indicated that doctors overall level of knowledge regarding HPV infections and HPV vaccine was poor. But the majority intended to prescribe the vaccine to their patients. There was knowledge gap regarding HPV infection and HPV vaccine among the doctors. For HPV vaccination program to be successful in the country, there is an urgent need to educate the doctors on this matter.

Effect of oil adjuvants on integrity of foot-and-mouth disease virus vaccine antigens

Dr. Michiel M. Harmsen, Scientist, Central Veterinary Institute Wageningen UR, Division Virology, Lelystad, The Netherlands

Many vaccines are prepared by emulgation of antigens with an oil adjuvant and contain the antimicrobial agent thiomersal. This talk focusses on the effect of oil emulsification and thiomersal addition on the stability of foot-and-mouth disease virus (FMDV) vaccines. Both thiomersal and oil emulsification result in more rapid decrease in FMDV vaccine potency upon prolonged storage. We could further show that this decrease was due to dissociation of virions into discrete subvirion particles. Addition of BSA and sucrose strongly decreased virion dissociation in a synergistic manner. This study shows the importance of analysing integrity of vaccine antigens after oil emulsification.

Approaches for inducing an immune response against tumor antigens

Dr Jonathan Lewis, Boston, United States

Humans can mount a mutation-specific or tumor-specific T cell response to cancers. Various synthetic DNA and cell engineering approaches are enabling immune responses to cancers. Examples include engineering T cells with CAR- T (chimeric antigen receptors), stimulating antigen presentation and collapse of tumor stroma with controllable, directed IL-12, and controlled production of bispecific antibodies by genetically-modified allogeneic stem cells.

Designing new vaccines to safeguard global poliovirus eradication

Dr Andrew Macadam, NIBSC, Herts, United Kingdom

New poliovaccines will be needed to safeguard global eradication: Sabin strains are known to evolve into essentially wild-strains so their long-term use is incompatible with eradication; inactivated vaccines do not prevent transmission and are currently made from wild polioviruses so present a significant biosecurity risk. We have developed safer seed strains for IPV production and genetically stable live-attenuated strains designed for use in outbreak control. The capsid proteins of poliovirus have been engineered to produce VLPs which are stable enough to allow vaccine production using recombinant expression, ideal for the post-eradication world.

Overview of assays for influenza vaccines immunology evaluation and correlates of protection

Professor Emanuele Montomoli, Dept. of Molecular and Developmental Medicine, University of Siena, Italy

Correlates of protection against influenza viruses have not been fully defined, it is widely believed that protection against influenza can be conferred by serum haemagglutinin (HA) antibodies. The immune response to injected influenza vaccine are routinely assessed by titrating serological HA antibodies which can be detected in serum 3-4 weeks after primary infection or vaccination. The most commonly used serological assays used for influenza viruses include hemagglutination inhibition (HI), single radial haemolysis (SRH), microneutralization (MN), ELISA and Western blot. Recently, ELISA tests have been improved, thanks to the clarification of the structure of HA. HI and SRH remain the most commonly applied methods, while the latter is being increasingly replaced by MN.

Development of a Lentivirus-Based Reference Material for Zaire Ebola Virus Nucleic Acid Amplification Assays

Dr Giada Mattiuzzo, NIBSC-MHRA, Potters Bar, United Kingdom

Nucleic acid amplification technology assays were the main diagnostic test during the recent Ebolavirus outbreak. A standard is needed to evaluate the efficiency and sensitivity of these assays. We have developed a safe, stable Zaire Ebolavirus RNA standard (HIV-EBOV) by encapsidating the negative strand viral RNA into a HIV-1 like particle. This HIV-EBOV standard was tested in different assays showing good efficiency and linearity, and stability at high temperature allowing the shipping of the material worldwide. These results support the evaluation of the HIV-EBOV in an International collaborative study for the establishment of the 1st International Standard for Ebolavirus RNA

Human HCMV-specific antibody responses generated following immunisation with a subunit gB vaccine

Dr Gary R McLean, Imperial College London & London Metropolitan University, London, UK

Human cytomegalovirus (HCMV) is a pathogen with serious consequences during pregnancy, transplantation and for the immunosuppressed. An experimental subunit vaccine composed of a recombinant HCMV glycoprotein B (gB) has recently been undergoing clinical trial. This presentation will outline the HCMV-specific antibody responses generated from a phase 2 randomised placebo-controlled trial following vaccination of transplant recipient patients. In particular the antibody responses to the important neutralising epitope AD-2 will be focussed on.

Integration of biology and mathematical modelling towards a better understanding of pathogen behaviour and rational design of improved bacterial vaccines

Dr Piero Mastroeni, Reader in Infection and Immunity, University of Cambridge, United Kingdom

Due to difficulties in the implementation of hygiene measures and to increases in antimicrobial resistance, vaccination remains the most feasible means to counteract bacterial infections. Using salmonelloses as a paradigm for invasive bacterial infections we have studied the interaction between pathogen behaviour and immune responses in the context of vaccination. The analysis of molecularly tagged bacterial subpopulations in vivo has revealed that live attenuated vaccines are superior to non-living preparations to control bacteraemia during a secondary challenge and to restrain growth and inter-organ spread of the bacteria in the systemic organs.

One of the concerns over the use of live vaccines is their potential residual virulence, especially in areas of the world where immunodeficiences are rife. We therefore used a global approach based on Transposon Directed

Insertion-site Sequencing (TraDIS) to search for Salmonella mutants that retain attenuation in immunodeficient individuals. One of the mutants has been further tested in immunocompromised hosts and has shown increased safety and good protective ability against virulent bacteria.

Reference materials and standards for serological assays in vaccine evaluation

Dr Mark Page, National Institute for Biological Standards & Control, Potters Bar, UK

Reference materials are used to assure the quality of medicines worldwide. By using a biological reference material or standard of known activity or potency, bioassay results can be compared and calibrated to give a consistent result, both between and within laboratories over time. For diagnostic tests, the use of control samples of known activity allows the sensitivity and specificity of the test system to be monitored and quality assured. Collaborative studies between laboratories to assess candidate standards are the method of choice; examples of these studies will be presented to demonstrate their utility for serological assays as applied to vaccines.

Poor responders to equine influenza immunisation: independent impact of age and maternal-derived antibodies on short and mid-term protective antibody levels in Thoroughbred foals

Dr Romain Paillot, Animal Health Trust, Kentford, Newmarket, UK

Every year, several Equine Influenza (EI) epizooties are reported worldwide, which have important welfare/economic consequences. EI vaccination is one of the most efficient methods of prevention. However, not all horses develop protective immunity. Serological surveillance was used to identify poor responder to primary EI vaccination in 118 thoroughbred foals. All foals were immunised with a recombinant canarypox-based EI vaccine. Results showed that independently of the presence of MDA, the age of foals at first immunisation plays an important role in the establishment of adequate antibody levels, and highlights the benefit provided by serological surveillance to identify poor vaccine responder.

Optimisation of influenza pseudotyped lentivirus production

Dr Simon Scott, Lecturer, University of Kent, Chatham, United Kingdom

Pseudotyped viruses (PVs) provide flexible, safe tools for fundamental virological studies and antibody/antiviral screening assays. PVs consist of the 'core' of one virus (e.g. lentivirus) and 'envelope' of the study virus (e.g. influenza virus haemagglutinin, HA). Generation of PVs involves co-transfection of producer cells with plasmids encoding essential viral components. Two enzymes are crucial for infectivity of influenza viruses and their PVs; HA-cleaving cellular proteases and neuraminidase. The type and quantities of all these DNA and enzymatic components should be optimised for each to maximise PV titre, enhancing consistency in large-scale studies. Results from such optimisation experiments will be presented.

Sublingual vaccination and vaccine delivery systems

Mr. Jaroslav Turánek, Head of Department of Immunology and Immunotherapy, Veterinary Research Institute, Czech Republic

Sublingual region is a favourable site for inducing the specific immune response or tolerance towards antigens and allergens, respectively. Contrary to nasal administration, there is no risk of invading the olfactory nerve by the nanoparticles. Sublingual immunisation represents safe and easy way for vaccine administration which can induce specific immune response on all mucosal surfaces as well as systemic one.

We bring together the technology of electrospinning and the technology of mucoadhesive oral films to develop new dosage form for effective delivery of nanoparticles into sublingual mucosa in unidirectional manner. This system is used for construction of mucosal vaccines.

Immunochemical and protective activity of pneumococcal protein-containing compounds in the experiment

Dr Denis Vorobyev, Federal State Budgetary Scientific Institution "I. Mechnikov Research Institute of Vaccines and Sera", Moscow, Russia

Streptococcus pneumoniae is one of the leading causes of diseases such as pneumonia, bacteremia and otitis media. The existing pneumococcal polysaccharide and conjugate vaccines reduces diseases among the elderly and children. However protein-based pneumococcal vaccines are considered as alternative vaccine candidates. The main reason for this approach is the cross-reactivity of pneumococcal proteins. We used strains of S. pneumoniae serotypes 3, 6B, 10A, 14, 19F and 36R for obtain of pneumococcal protein-containing compounds. The studied pneumococcal protein-containing antigens induced interspecies cross-reactivity that was confirmed in experiments in vitro and protected mice from heterologous challenge strain of S. pneumoniae, serotype 3.

Aβ immunotherapy with single chain variable fragments for Alzheimer's disease

Dr Sandra Villegas, Universitat Autónoma de Barcelona (UAB), Barcelona, Spain

Alzheimer's Disease (AD) is considered to be a 2first century pandemic. Aβ-immunotherapy, especially passive immunotherapy, is a promising approach to treat AD. However, albeit several monoclonal anti bodies have been tested in clinical trials none of them has passed Phase III. Single-chain antibodies (scFv), devoid of the Fc fragment, are becoming an attractive therapeutic strategy as they provide an alternative, non-inflammatory, approach to facilitate Aβ clearance. ScFv-h3D6, a bapineuzumab derivative, has been proved efficient at the behavioral, cellular and molecular levels in the 3xTg-AD mouse model. The engineering of such a scFv to improve its properties is presented.

Patient Safety: Using technology to select the right vaccine, right person, right schedule

Dr Adrienne Willcox, Health Team Ltd., Glos, UK

As vaccines increase in number and complexity, so does the need to prevent administration errors. Decisions on whether to vaccinate require knowledge of vaccinology and individual SPCs too vast to commit to memory. Clinicians performing vaccination often do so as part of a wider role in general practice or pharmacy, facing significant time pressures on consultations. This talk describes how technology can intelligently prevent vaccination errors and alert practioners to cautions, contraindications and advisory messages prior to vaccination. A case is made for technology as an essential aid to patient safety and the clinical and cost-effective vaccine consultation.

Day 1:

Oral Presentation Abstracts

Oral presentations will be added after the submission deadline

VACCINE-INDUCED PITYRIASIS ROSEA AND PITYRIASIS ROSEA-LIKE ERUPTIONS: A REVIEW OF THE LITERATURE

G Ciccarese, F Drago, S Javor, A Parodi
Dermatology Department, University of Genoa, Largo Benzi 10, Genoa, 16132 Italy

Pityriasis rosea (PR) is an exanthematous disease due to the endogenous systemic reactivation of human herpesvirus-6 (HHV-6) and/or -7 (HHV-7). PR and PR-like eruptions (PR-LE) have rarely been described after vaccinations. The Authors reviewed the cases of vaccine-induced PR reported in literature differentiating typical PR from PR-LE and trying to explain the pathogenetic mechanisms that underlie these conditions.

From 1947 to date, 29 cases of PR/PR-LE have been reported after vaccinations and the smallpox one was responsible for most of the eruptions. The data concerning the patient's age, the average time lapse between vaccination and eruption onset and the average exanthem duration in PR and PR-LE are in agreement with the different clinical features of these manifestations. The pathogenetic mechanism leading to PR after a vaccination is unknown. It could be hypothesized that the vaccine, eliciting a specific immune response against a definite infectious agent may distract the T-cell immunosurveillance on the latent infections, as HHV-6/7, which may reactivate.

Conversely, PR-LE may occur as a hypersensitivity delayed response to a vaccine. Another possible mechanism is the molecular mimicry with a viral epitope that could result in a T-cell mediated skin reaction resembling PR. To distinguish between PR and PR-LE is of paramount importance especially in cases of multi-dose vaccines. In fact, when a vaccine-induced PR is diagnosed, the patient may cautiously receive the other vaccine doses whereas in cases of vaccine-induced PR-LE it is preferable to avoid administration of other vaccine doses since more dangerous reactions may develop.

Day 2:

Oral Presentation Abstracts

THE COMPLEXITY OF CHICKEN VACCINATION AGAINST LP AIV H9N2 IN VIEW OF PHYLOGENETICS, ANTIGENIC CARTOGRAPHY AND THE CHALLENGE DOSES

Davidson Irit
Division of Avian Diseases, Kimron Veterinary Institute, Bet Dagan, P.O.Box 12, Israel 50250

Avian influenza viruses, H9N2 subtype, are widespread worldwide, but became endemic in Asia and the Middle East. Israeli AIV H9N2 are low pathogenic according to their cleavage site and belong to the G1 lineage.

Five major phylogenetic clades were described since the year 2000: Clades I, II and III originated in the Far East and co-populated Israel, Jordan and Lebanon, clade IV resembled Egyptian, Jordan and Lebanon AIV H9N2 strains, while clade V resembled strains isolated in Saudi Arabia and Persian Gulf countries. A dynamic phylogenetic evaluation of the AIV H9N2 HA showed by the time to the most recent common ancestor that the first detection of H9N2 in Israel occurred soon after its introduction in the country. However, the H9N2 early detection did not prevent virus circulation, evolution and re-emergence. The virus population Skyline dynamics of genetic diversity revealed two peaks (years 2003-2004 and 2008), corresponding to clades III and IV and introduction of the two vaccines. The mean evolution rate was 6.123 E-3 substitutions/site/year, as in countries that use AIV vaccination.

The influence of the genetic differences between clades on the vaccination efficacy was evaluated in experimental vaccination and challenge trials in SPF chicks. Vaccines were prepared with Montanide adjuvant (Seppic, Inc. France) including AIV old or new strains of clades I+II and V. When challenged with old and new AIV strains, the extent of protection between old and new clades was related to the phylogenetic distances and to the challenge doses.

Acknowledgment
We thank Drs. A. Panshin, S. Perk, A. Lublin, L. Simanov, E. Lapin and I. Shkoda, for AIV diagnosis and sequencing at KVI and to Mrs. A. Al-Toury, N. Osidze and I. Reibshtein for devoted assistance. The study was supported by grant US-4379-11 from USA-Israel Agricultural Research & Development Fund (BARD).

POLYION COMPLEX (PIC) NANOPARTICLES AS A NOVEL AND BIODEGRADABLE ADJUVANT FOR POTENT INDUCTION OF ADAPTIVE IMMUNITY

M. Baba, T. Uto, T. Akagi, M. Akashi
Center for Chronic Viral Diseases, Kagoshima University, Kagoshima 890-8544, Japan

Development of effective vaccines is desired for prophylaxis and treatment of a variety of infectious diseases and cancers. Several lines of evidences suggest that an appropriate adjuvant strongly enhances the immunogenicity of antigens. We have investigated biodegradable nanoparticles (NPs) composed of poly(γ-glutamic acid)-graft-L-phenylalanine ethylester (γ-PGA-Phe). The NPs carrying various antigens are capable of inducing antigen-specific humoral and cellular immunity. However, there is an obstacle to developing this type of NPs as a vaccine adjuvant for clinical use, because they are likely contaminated with a small amount of an organic solvent, such as dimethyl sulfoxide, during their production process. To circumvent this problem, we have recently created novel polyion complex (PIC) NPs as a vaccine adjuvant. PIC NPs can be prepared by mixing γ-PGA-Phe polymer with cationic polymer in saline. We examined the efficacy of PIC NPs for their antigen delivery and immunostimulatory activity in vitro and in vivo. PIC NPs enhanced antigen-uptake by dendritic cells (DCs) and subsequently induced maturation of DCs. The immunization of mice with antigen-carrying PIC NPs could induce potent and antigen-specific cellular and humoral immunity. Since PIC NPs can be created in the absence of any organic solvents, PIC NPs may have great potential as a novel candidate for an effective antigen carrier and vaccine adjuvant.

Day 3:

Oral Presentation Abstracts

Oral presentations will be added after the submission deadline

THE VIRAL VECTOR VACCINE VSV-GP BOOSTS THE IMMUNE RESPONSE UPON REPEATED APPLICATIONS

J. Kimpel[1], R. Tober[1], M. Krismer[1], S. Schneider[1], T. Hofer[1], A. Bresk[1], Z. Banki[1], L. Egerer[1], D. von Laer[1]
[1]Division of Virology, Medical University of Innsbruck, Peter-Mayr-Str. 4b, Innsbruck, Austria

Background: Vesicular stomatitis virus (VSV) is a potent candidate vaccine vector for various diseases. However, VSV's inherent neurotoxicity has limited its clinical application. Additionally, VSV induces neutralizing antibodies rapidly and is thus ineffective upon repeated applications. Our group has recently shown that VSV pseudotyped with the glycoprotein (GP) of the lymphocytic choriomeningitis virus, VSV-GP, is not neurotoxic. Here, we evaluated the potential of VSV-GP as a vaccine vector.

Methods: We used Ovalbumin (OVA) as a model antigen and analyzed immunogenicity of GP-pseudotyped and wild-type VSV expressing OVA (VSV-GP-OVA and VSV-OVA) in vitro and in vivo in mouse models. Furthermore, we introduced antigens from a pathogen or luciferase as marker gene into VSV-GP.

Results: Both VSV-OVA and VSV-GP-OVA induced functional OVA-specific CTLs and anti-OVA antibodies upon single immunization of mice. However, boosting with the same vector was only possible for the GP-pseudotype but not for wild-type VSV. The efficacy of repeated immunization with VSV-OVA was most likely limited by the high levels of neutralizing antibodies, which we detected after the first immunization. In contrast, no neutralizing antibodies against VSV-GP were induced even after seven boost immunizations. CTL responses induced by VSV-GP-OVA were as potent as those induced by an adenoviral state-of-the-art vaccine vector. Additionally, immunization with both vectors completely protected mice in a bacterial challenge model. Antigens from pathogens were expressed in VSV-GP infected cells and immunization of mice with VSV-GP vectors containing HIV envelope induced high titers of HIV-specific antibodies which were boosted upon repeated immunization.

Conclusion: Taken together, VSV-GP is non-neurotoxic, induces potent immune responses, enables boosting and thus is a promising novel vaccine vector.

Poster Presentation Abstracts

Poster abstracts will be finalised weeks before the event

SERUM MICRORNAS AS POTENTIAL BIOMARKERS FOR EARLY DIAGNOSIS OF HEPATITIS C VIRUS-RELATED HEPATOCELLULAR CARCINOMA

Tarek K. Motawi[1], Olfat G. Shaker[2], *Shohda A. El-Maraghy*[1], and Mahmoud A. Senousy[1*]
[1]Biochemistry Department, Faculty of Pharmacy, Cairo University, Cairo, Egypt
[2]Medical Biochemistry and Molecular Biology Department, Faculty of Medicine, Cairo University, Cairo, Egypt

Abstract

Circulating microRNAs are deregulated in liver fibrosis and hepatocellular carcinoma (HCC). We investigated the potential usefulness of serum microRNAs; miR-19a, miR-296, miR-130a, miR-195, miR-192, miR-34a, and miR-146a, as novel diagnostic biomarkers for hepatitis C virus (HCV)-related HCC. We also explored their serum profiles during fibrosis progression in HCV-associated chronic liver disease (CLD) and whether they could serve as fibrosis progression markers to HCC. 112 Egyptian HCV-HCC patients, 125 non-malignant HCV-CLD patients, and 40 healthy controls were included. CLD patients were subdivided according to Metavir fibrosis scoring. Serum microRNAs were measured by qRT-PCR custom array. Studied miRNAs were deregulated in HCC versus controls, and except miR-130a, they were differentially expressed between HCC and CLD patients. Studied microRNAs distinguished HCC from other groups by receiver-operating-characteristic analysis with higher sensitivity than alpha-fetoprotein (42%). miR-34a was superior to discriminate HCC from controls (sensitivity:100%, specificity:89.2%), whereas miR-19a (sensitivity:92.5%, specificity:75%) and miR-146a (sensitivity:96.4%, specificity:73.9%) to discriminate HCC from CLD and advanced fibrosis (F3-F4) subgroup, respectively. miR-146a was a significant predictor of being diagnosed with HCC in CLD group by logistic regression analysis. Serum microRNAs were fibrosis-stage independent, however, miR-19a was significantly downregulated during liver fibrosis (F1-F3) progression to cirrhosis (F4) to HCC. Studied microRNAs were positively correlated in HCC. miR-19a and miR-34a were correlated with portal vein thrombosis and HCC staging,

respectively. Studied microRNAs, but not miR-130a, could serve as potential biomarkers for early HCC detection in high-risk groups, with miR-19a as a biomarker for liver fibrosis progression to HCC.

Key words: HCC; HCC diagnosis; microRNAs; microRNA profiling; fibrosis

POTENTIALS OF PLANT PRODUCTS AS ALTERNATIVE TO VACCINATION IN POULTRY PRODUCTION

S. S. Abiola; A. A. Abdurrauf-Babalola; O. O. Sogunle and J. A. Olanite
College of Animal Science and Livestock Production
Federal University of Agriculture, PMB 2240, Abeokuta,
Ogun State, Nigeria

A study was conducted in which leaf meals of Moringa oleifera and Ocimum gratissimum were incorporated in the diets of egg type chickens. A total of four hundred and five (405) 'Isa' strains of day old pullet chicks were used for the study which lasted for 8 weeks. There were nine experimental diets in which Moringa oleifera leaf meal (MOLM) and Ocimum gratissimum leaf meal (OGLM) were incorporated at 0, 5 and 1% levels. Birds on 0% (control) alone were vaccinated against Newcastle and Marek's diseases as at when due. Results of mortality, PCV, Hb and RBC were not significantly different ($P<0.05$) from one another. However, WBC counts showed significant differences ($P<0.05$) across the treatments. Values obtained for Heterophils at levels of inclusion ranged between 32.67-36.56% while results of Lymphocytes ranged between 63.11 and 67.00%. MOLM and OGLM can be included in the diets of egg-type chickens at 1% inclusion level to reduce mortality and cost in poultry production

* Presenting/Corresponding Author.

THE EXPRESSION OF IMMUNOPHENOTYPES IN SUBJECTS AFTER SEASONAL INFLUENZA VACCINE

Shih-Min Wang[1, 2, 3]
[1]Center of Infectious Disease and Signaling Research, National Cheng Kung University, Tainan, Taiwan
Departments of [2]Emergency Medicine and [3]Pediatrics, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan.

ABSTRACT

Seasonal influenza is a serious respiratory illness that causes annual worldwide epidemics resulting in significant morbidity and mortality. The combination of current vaccine efficacy and viral antigenic drifts and shifts necessitates annual vaccination. The efficacy and effectiveness of influenza vaccines depend primarily on the vaccine recipient and the virus similarity to the endemic virus. Regulatory T cells (Tregs) are viable targets to enhance immunogenicity of vaccines. We conducted this study to explore the immunophenotypes, immune mediators, and antibody production after influenza vaccination. The whole blood was collected from healthy subjects before and 10-14 days after influenza vaccine immunization during 2014-2015. The age of enrolled subjects ranged from 24 to 39 years. The cell surface markers, intracellular staining of $Foxp3^+$ Tregs, and Th1/Th2 cytokines were determined. The antibody titer was detected using the hemagglutination inhibition test. The white blood cell count ($5882\pm1184/mm^3$ vs. $6036\pm1254/mm^3$, $p=0.416$) and absolute lymphocyte count ($1764\pm474/mm^3$ vs. $1728\pm521/mm^3$, $p=0.658$) did not change significantly post vaccination. The expression frequency of $CD3^+$, $CD4^+$, $CD16^+CD56^+$, $CD20^+CD25^+$ and $CD20^+CD25^+Foxp3^+$cells were increased significantly post vaccination. However, the expression frequency of CD1C, BDCA-2 and CD141 did not change markedly after vaccination. The plasma level of interleukin (IL)-2, IL-4, IL-5, IL-10, IFN-γ, TNF-α, was not found to increase significantly after vaccination. All enrollees had seropositive of anti-H3N2 and anti-B/Yamagata, and 92% of anti-H1N1 after vaccination. Treg cells seem to participate in the the anti-influenza antibody response post influenza vaccination. Alteration of Treg activity might enhance influenza vaccine antibody responses and efficacy.

DEVELOPMENT OF PH RESPONSIVE CATIONIC AMPHIPATHIC LAH4-L1 PEPTIDE AS A NOVEL DNA VACCINE DELIVERY SYSTEM

Yingying Xu, Jenny K.W. Lam
Department of Pharmacology and Pharmacy, The University of Hong Kong, 21 Sassoon Road, Hong Kong

DNA vaccines use plasmid DNA to encode antigenic proteins to induce both local and systemic immune responses to protect human from infectious diseases. However, the immunogenicity of most DNA vaccines was not satisfactory, mainly due to the poor DNA stability and inefficient DNA delivery, resulting in insufficient antigen presentation and immunity activation. The aim of this project is to develop an efficient non-viral DNA vaccine delivery system, using synthetic amphipathic peptide LAH4-L1 as DNA delivery vector.

In our previous study, LAH4-L1 has been shown as an efficient non-viral gene delivery system due to its ability of protecting nucleic acid from nuclease degradation, enhancing cellular uptake and plasmid expression through

promoting endosomal escape in target cells [Ref 1]. However, its potential in DNA vaccine formulation remains to be investigated.

In this study, the plasmid DNA transfection efficiency of LAH4-L1 on A549 (human alveolar epithelial cancer cells), Calu-3 (human airway epithelial cancer cells), RAW264.7 (mouse macrophages) and JAWSII (mouse immature dendritic cells) were found comparable to the commercial transfection reagent Lipofectamine™ 2000. Furthermore, LAH4-L1 peptide can enhance the hepatitis B antigen plasmid induced immune responses *in vitro*: Firstly, the enzyme-linked immunosorbent assay (ELISA) showed that significant increase of IL-6 and TNF-α secretion was observed after delivering hepatitis B surface antigen encoding plasmid by LAH4-L1 to RAW264.7 macrophages and JAWSII dendritic cells. Secondly, the macrophage phenotype analysis indicated LAH4-L1 could efficiently facilitate the differentiation and maturation of professional antigen presenting cells (APCs) by increasing the expression of CD40, CD80 and CD86 co-stimulatory molecules as maturation markers. These properties make LAH4-L1 a promising DNA vaccine delivery system candidate.

Reference

1. Lam K.W., Liang W.L., Lan Y. et al. (2012) *Journal of Controlled Release* 158:293-303.

A BAPINEUZUMAB-DERIVED SINGLE CHAIN VARIABLE FRAGMENT PREVENTS CELLULAR DEATH AND DRECREASES INTRACELLULAR AMYLOID BURDEN

G. Esquerda-Canals, L. Montoliu-Gaya, J. Güell-Bosch, S. Lope-Piedrafita, J. Martí-Clúa & S. Villegas
Protein Folding and Stability Group. Departament de Bioquímica i Biologia Molecular, Unitat de Biociències, Universitat Autònoma de Barcelona. 08193 Bellaterra, Spain. sandra.villegas@uab.cat

Because Alzheimer's disease is considered as a 21st century pandemic, a broad range of therapeutic strategies are currently focused on the prevention or treatment of this overwhelming neuropathology. Successful preclinical approaches in Aβ-immunotherapy have come up against some complications, such as amyloid-related imaging abnormalities (ARIAs), once translated to clinical trials. In order to overcome these adverse effects our group designed scFv-h3D6, a single chain variable fragment derived from bapineuzumab. This anti-Aβ oligomer antibody fragment lacks the constant region of the complete antibody, which promotes microglial activation. In vitro cytotoxicity assays demonstrated that scFv-h3D6 prevents cellular death by withdrawing Aβ oligomers from the amyloid aggregation pathway. 3xTg-AD mice treated with a single intraperitoneal dose of scFv-h3D6 showed, apart from behavioral amelioration, a marked decrease of Aβ oligomers and the recovery apoE and apoJ levels. In the present work, cellular death prevention of those neuronal populations involved in the pathology, along with a dramatic intracellular amyloid burden reduction, are evidenced. On the other hand, and because clinical trials with bapineuzumab showed the adverse effects in those cohorts treated at the highest doses, the molecule has been redesigned to improve thermodynamic stability so that lower doses may show similar effectiveness. The engineered variant, scFv-h3D6-EL, greatly increased the recovery of the viability of neuroblastoma cell-cultures in the presence of Aβ oligomers. Other in vivo experiments to assess the pharmacokinetics and pharmacodynamics of this promising molecule are being performed, as well as a longitudinal study that is being followed by Magnetic Resonance Imaging to discard the occurrence of treatment-related ARIAs. In conclusion, given the positive results obtained with scFv-h3D6-WT treatment and the relevant improvement achieved with the redesign of the molecule, scFv-h3D6-EL becomes a potential therapeutic solution to stop this devastating disease.

Funding: Instituto de Salud Carlos III [FIS-PI113-01330], Generalitat de Catalunya [SGR-GRC-2014-00885] & Generalitat de Catalunya + FEDER (50%) [2014-PROD00032]. PIF-UAB student grants (JGB, GEC & LMG).

GENERATION OF MARKER-FREE RMVA BY HOMOLOGOUS RECOMBINATION USING A 50BP REPETITIVE HOMOLOGOUS SEQUENCE

L FAQIH and TJ Blanchard
The University of Manchester, Oxford Road, Manchester, M13 9PL, UK

Currently, the most frequently used method of generating recombinant poxvirus is by allowing homologous DNA recombination in infected cells. Homologous recombination occurs relatively frequently during poxviral replication. A plasmid-based transfer vector typically directs poxvirus recombination. Homologous recombination into specific sites on the MVA genome is directed by repetitive homologous sequences flanking the transgene with an additional selection marker. Here we describe the design and use of a recombination plasmid that employs transient dominant gpt selection in tandem with beta-galactosidase selection to yield marker-free thymidine kinase deletion mutants containing only the transgene of interest. This is a part of a bigger project held in Dr. Blanchard's lab that focus on developing a rMVA-based HIV vaccine using the natural homologous recombination technique and to understand its immunogenicity. The marker genes are destabilised

by a 50bp repetitive homologous sequence to drive spontaneous intra genomic recombination. Unfortunately, after 11-plaque purification rounds it was apparent that 50bp is not enough to generate a marker-gene-free rMVA. In addition, the recombinant plaques were very small, suggesting that the TK deletion was harmful to the virus.

BACILLUS SUBTILIS ENDOSPORES AS A PLATFORM FOR DISPLAYING INFLUENZA VIRUS ANTIGENS

Tomasz Łęga1, Paulina Weiher2, *Beata Gromadzka2*, Dawid Nidzworski2 1Laboratory of Molecular Bacteriology, Intercollegiate Faculty of Biotechnology, University of Gdańsk and Medical Uni wersity of Gdańsk, Dębinki 1, 80-211 Gdańsk, Poland 2Laboratory of Recombinant Vaccines, Intercollegiate Faculty of Biotechnology, University of Gdańsk and Medical University of Gdańsk, Kładki 24, 80-822 Gdańsk, Poland

The influenza virus is one of the most dangerous pathogens infecting warm-blooded vertebrates worldwide due to its high infectivity and adaptability. Developing effective vaccine against flu virus is a real challenge. In last years a new live antigen carrier system emerged.

Bacterium Bacillus subtilis is a gram-positive bacilli which produce endospores and is generally regarded as safe (GRAS). Spores of Bacillus subtilis are referred to be one of the most resistant life forms. Being metabolically dormant, spores are resistant to many environmental stressors such as UV radiation, desiccation, heat or freezing. Free, mature spores are enclosed in a thick protein envelope called coat which is made of at least 70 different protein species. Spore coat is further divided into inner coat, outer coat and outermost crust. Recent studies show that spores can serve as an antigen carrier by fusing peptide of interest to spore coat proteins. There are evidence that oral or intranasal administration of spores presenting antigens induces a specific, both cellular and humoral immune response which can protect animals from infection. In our study, using a genetic approach we constructed Bacillus subtilis strains producing spores presenting M2eH-A-S-H antigen on their surface. Recombinant spores were orally administrated to mice to evaluate the immunogenic properties of constructs. This work indicates that spores can serve as influenza antigen carrier and induce specific antibody production without use of adjuvants.