21st World Congress and Exhibition on

VACCINES, VACCINATION & IMMUNIZATION

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Scientific Tracks & Abstracts

Day 1






Vaccines World 2017

Major Sessions:

Novel Vaccines - Research and Development | Cancer Vaccines | Chikungunya vaccine | Vaccines Discovery, Development & Formulation | DNA vaccines

Session Chair
Andreas Meinke
Valneva Austria GmbH, Austria

Session Co-Chair
Youness Cherradi
Merck Life Science, Belgium

Session Introduction

Title: **Antigen-coupled immune cells serve as antigen-delivery carriers for cancer vaccine**
Chang Qing Xia, University of Florida, USA

Title: **Ethical issues in the production, design and clinical trials of new vaccines for emerging diseases in low income countries**
Ida Cristina Gubert, Federal University of Parana, Brazil

Title: **Measles vector vaccine platform as an effective tool to prevent chikungunya virus infection**
Matthias Müllner, Themis Bioscience GmbH, Austria

Title: **Universally protective vaccines: A revolution in modern vaccinology**
Geert Vanden Bossche, German Center for Infection Research (DZIF), Germany

Title: **Live-recombinant measles virus vaccine to prevent zika virus infection**
Sabrina Schrauf, Themis Bioscience GmbH, Austria

Title: **A novel mechanism linking memory stem cells with innate immunity in protection against HIV-1 infection**
Thomas Lehner, Kings College London, UK

Title: **Challenges and dilemmas about vaccines against Epstein Barr virus and the other herpesviruses**
Emmanuel Drouet, University of Grenoble-Alpes, France

Title: **Development of a production and purification platform for virus like particles (VLP) and adenovirus vector vaccine candidates: Two case studies**
Youness Cherradi, Merck Life Science, Process Solutions, Belgium

Title: **Harnessing the immunogenicity of viral proteins for designing novel cancer DNA vaccines**
Gaëlle Vandermeulen, Louvain Drug Research Institute - University of Louvain, Belgium

Chang Qing Xia et al., Virol Res J 2017, 1:4

Antigen-coupled immune cells serve as antigen-delivery carriers for cancer vaccine

Chang Qing Xia[1], **Qunfeng Wu**[2], **Xiaoli Chang**[3], **Yixian Guo**[3] and **ChenLiu**[2]
[1]University of Florida, USA
[2]Rutgers University, USA
[3]Xuanwu Hospital - Capital Medical University, China

Cancer immunotherapy has achieved extraordinary clinical outcomes over the last several years, particularly, chimeric antigen receptor (CAR) T cell therapy and immune checkpoint blockade therapy. An additional promising approach is to develop effective tumor vaccines for cancer prevention and treatment. The most common vaccine approach is inoculation of soluble antigens combined with adjuvants. Although this vaccine approach is most commonly employed worldwide, it has several disadvantages such as, a relatively large dose of antigen is required, an adjuvant is usually required, and only antigen-specific T cells in the local draining lymph nodes can be activated even if multiple injection sites are chosen. In this report, we took advantage of the lymphoid tissue homing property of immune cells to develop high-efficient antigen-delivery system to stimulate all antigen-specific T cells in the body. We wisely employed "click" chemistry method to efficiently couple the antigens to mouse spleen cells, then intravenously injected those antigen-coupled spleen cells into recipient mice and potently induced antigen specific CD4 and CD8 T cell response with heightened IFN-g producing capability. When we tested tumor antigen-coupled spleen cells in triggering anti-tumor immunity in melanoma and hepatocyte cancer mouse models, we found that this approach induced very strong anti-tumor immunity in both prophylactic and therapeutic experimental settings, and the animal survival was significantly improved. Immunological investigation showed that this approach induced both enhanced humoral and cellular immunity against tumor. Recently, we found that antigen-coupled allogeneic spleen cell injection induced equivalent, if not stronger, antigen-specific immune responses in contrast to injection of antigen-coupled syngeneic spleen cells, which could lead to off-the-shelf cell products for tumor vaccine. Our novel and unique approach is utilizing the homing nature of immune cells to distribute tumor antigens throughout the entire immune system and subsequently elicit strong anti-cancer immunity. Additional advantages over other vaccine approaches are minimal number of antigens required (only the antigens coupled to the cell membrane) and no adjuvant needed. Therefore, our approach holds high potential for clinical translation just like blood transfusion but without concerning about red blood cell type.

Biography

Chang Qing Xia received his MD and PhD degree in China, and have been working at US for almost two decades. He is currently an Assistant Professor in the Department of Pathology, Immunology and Laboratory Medicine at University of Florida. His research is focused on dendritic cells and development of antigen-specific immunotherapies for autoimmune diseases and malignant tumors.

xia@pathology.ufl.edu

Notes:

Ida Cristina Gubert, Virol Res J 2017, 1:4

Ethical issues in the production, design and clinical trials of new vaccines for emerging diseases in low income countries

Ida Cristina Gubert
Federal University of Parana, Brazil

Statement of the Problem: Since first developed by Jenner and Pasteur vaccines have shown to be an important tool for the eradication (cow pox) and prevention of communicable diseases with high morbidity and mortality rates, and became one component of public health policies. However, good quality housing, appropriate disposal of sewage, nutrition, education and adequate sanitary conditions have also been an important determinant in health promotion. In this way, upper level societies have witnessed a significant reduction of diseases such as zoonosis, communicable diseases and vector born infections. Nevertheless, populations in low income countries still face poor sanitary and living conditions which contribute to the emergence of new diseases. Recently countries in Latin America witnessed the epidemics of a vector borne viral infection that resulted in microcephaly to the fetuses born from infected women.

Purpose: The purpose of this text is to present a reflection on the life conditions of these populations, their vulnerability, the need for new vaccines, the public health policies to be implemented and the ethical issues to be considered in this reality.

Methodology: An analysis on the ethical issues concerning the development of new vaccines and their trials in low income countries.

Conclusion & Significance: It is undeniable all benefits that have been reached in health promotion through immunization protocols worldwide. However insufficient supply, the rationale of use and distribution of vaccines in low income countries, the health condition of the participants in the trials, inclusion and exclusion criteria, the comparative arm, the inclusion of pregnant women, risks and benefits, the availability of the final product once trial is finished and the voluntary or compulsory character of immunization are some of the ethical issues that deserve consideration in the development and distribution of vaccines as a part of public health policies in low income countries.

Recent Publications :

- GUBERT, I. C.. Conflitos e abordagem bioética de crianças com distúrbios do desenvolvimento sexual. Revista Pistis Praxis, v. 4, p. 33-40, 2012.
- GUBERT, I. C.; SANCHES, M. A. (Org.) . bioética e vulnerabilidades. 1a. Ed. Curitiba: Editora Champagnat e Editora da UFPR, 2012. v. 1. 220p.
- GUBERT, I. C.; ROCCO, C. S. . GENÉTICA E VULNERABILIDADE. In: Ida Cristina Gubert e Mário Antônio Sanches. (Org.). Bioética e Vulnerabilidade. 1ed. Curitiba: Editora Champagnat e Editora UFPR, 2012, v. 1, p. 31-51.
- GUBERT, I. C.; MIRANDA, M. C. M. ; MALCA, E. Q. . La investigación en vacunas y enfermedades desatendidas:un aspecto relegado en la ética de la investigación?. In: Francisco Javier Leon Correa e Patrícia Sorokin. (Org.). Bioética y Salud Pública en y para America Latina. 1ed. Chile: FELAIBE, 2015, v. , p. 8-492.
- GUBERT,I.C et.al. INVESTIGACIÓN DE VACUNAS EN PEDIATRÍA: PERSPECTIVAS BIOÉTICAS Y DE SALUD PÚBLICA. Available in Research Gate. DOI: 10.13140/RG.2.1.3839.6567 • 10/2015
- ROCCO,C.S.;GUBERT,I.C..INTERVENÇÃODIETÉTICA NAS DOENÇAS NEUROLÓGICAS NA INFÂNCIA: conflitos éticos e bioéticos.. In: Caroline Filla Rosaneli. (Org.). Contextos, conflitos e escolhas em Alimentação e Bioética. 1ed.Curitiba: EDITORA UNIVERSITÁRIA CHAMPAGNAT, 2016, v. 1, p. 125-140.
- CARLA SENZ C, ALGER J, BECA JP, BELIZÁN JM, CAFFERATA ML, CANARIO GUZMÁN JA et al. Un llamado ético a la inclusión de mujeres embarazadas en investigación. Rev Panam Salud Publica. 2017;41:e13.

Biography

Bachelor degree in Biological Sciences from Universidade Federal do Paraná (1975), masters Degree in Genetics from Universidade Federal do Paraná (1986) and PhD in Biochemical and Molecular Pharmacology from Universidade Federal de Minas Gerais (2005) and Post-Doc in Bioethics in Clinical Research (Facultad Latino Americana de Ciências Sociales, FLACSO, Argentina). Has experience in Immunology, focusing on Applied Imunology, acting on the following subjects: Immunology and Public Health. Chair Ethics Commitee in Research at Universidade Federal do Paraná and member of Group of Studies in Bioethics (NEB) , Curitiba, PR.

gubert@ufpr.br

Matthias Müllner Xia et al., Virol Res J 2017, 1:4

Measles vector vaccine platform as an effective tool to prevent chikungunya virus infection

Matthias Müllner, Katrin Ramsauer, Andrea Pfeiffer, Raimund Vielnascher, Christa Firbas and **Erich Tauber**
Themis Bioscience GmbH, Austria

Themis' is developing a safe, effective and affordable preventive vaccine platform against priority pathogen diseases that have the potential to cause epidemics such as Chikungunya or Zika virus infection by using a "plug-and play" vaccine technology. This technology is based on a measles vaccine vector (MV) that can be easily genetically modified to express immunoprotective proteins for designated emerging infectious pathogens. This delivery platform technology has already demonstrated proof of principle in humans through a Phase 1 clinical trial in 42 healthy volunteers with a recombinant measles vaccine against Chikungunya virus (MV-CHIK). We showed that the vaccine was well tolerated. One immunization induced functional, neutralizing antibodies in up to 90% of immunized subjects, a second immunization induced 100% seroconversion. Importantly, immunogenicity was independent of pre-existing anti-vector (measles) immunity. We show here a Phase 2 clinical trial to demonstrate the vaccine vector safety and immunogenicity in up to 300 subjects. Preliminary findings point at excellent safety and immunogenicity profile in the two doses tested. Data are currently under final evaluation and auditing, and will be presented here.

Biography

Matthias Müllner holds a Master's degree in Molecular Biology from the University of Vienna and completed his Doctoral studies in 2010 at the Department of Virology and Biomedicine at the Veterinarian University of Vienna. He joined Themis Bioscience in 2011 and in his function as Head of CMC, he was responsible for the development of a stable and robust manufacturing process for Themis' Measles based live virus vaccine platform technology. The respective process was successfully used to manufacture phase 1 and/or phase 2 clinical batches for vaccines against Chikungunya Virus (MV CHIK), Dengue Virus (MV DEN) and Zika Virus (MV ZIKA). Currently, the process is optimized for commercial vaccine production.

Matthias.Muellner@themisbio.com

Notes:

Geert Vanden Bossche, Virol Res J 2017, 1:4

Universally protective vaccines: A revolution in modern vaccinology

Geert Vanden Bossche
German Center for Infection Research (DZIF), Germany

To eliminate safety risks related to infectivity, inactivated pathogens and, more suitably, well-characterized pathogen-derived antigens (Ags) have increasingly been used as immunogens in 'modern' vaccines. The selection of these Ags is usually based on their capacity to induce immune responses that 'correlate' with natural protection. These Ags, however, are composed of antigenically variable or conformation-dependent epitopes (e.g., B cell epitopes) and/or subject to immunogenetic restriction (e.g., linear, T cell epitopes). In addition, the immunogenicity of conventional vaccinal Ags is largely dependent on memory CD4+ T helper cells. However, activation of the latter upon natural infection or foreign Ag exposure of genetically predisposed subjects can occasionally lead to immune pathology. On the other hand, pathogens have evolved to incorporate into their arsenal of peptides self-mimicking motifs that are highly conserved and vulnerable as they are exposed on the surface of infected or pathologically altered host cells. These Ags, however, are either not immunogenic or subvert the host immune system. Hence, they are not used as vaccinal Ags in contemporary vaccines. We consider that new vaccines enabling immune targeting of these Ags by MHC-unrestricted memory NK cells are the new Holy Grail in modern vaccinology.

Biography

Geert Vanden Bossche obtained his DVM at the Veterinary Faculty of Ghent and his PhD in Virology at the University of Hohenheim, Stuttgart. Following his Postdoctoral training in Virology, Immunology and Molecular Biology at the Free University of Berlin and the University of Hohenheim (Germany), he was given the Venia Legendi and subsequently held adjunct faculty appointments at the University of Hohenheim (Germany), the University of Leuven (Belgium) and the European Faculty for Environmental Sanitation at the University of Ghent (Belgium). He then transitioned to the Vaccine Industry to serve various senior roles in both early and late vaccine development (GSK, Novartis, Solvay). In 2008, he joined the Bill & Melinda Gates Foundation in Seattle to serve as Senior Program Officer in Vaccine Discovery for Global Health. Furthermore, he also founded UNIVAC LLC, a start-up vaccine company, and coordinated the Ebola Vaccine Program on behalf of GAVI. He is now the Head of Vaccine Development Office at the German Center for Infection Research (DZIF) in Germany. He is board certified in Virology and Microbiology, the author of over 30 publications, and inventor on a patent application for universal vaccines. He has presented vaccine- and adjuvant-related topics at multiple international congresses.

geert.vandenbossche@live.be

Notes:

Sabrina Schrauf et al., Virol Res J 2017, 1:4

Live-recombinant measles virus vaccine to prevent zika virus infection

Sabrina Schrauf, Katrin Ramsauer, Raimund Vielnascher, Alexander Kort, Matthias Müllner, and **Erich Tauber**
Themis Bioscience GmbH, Austria

Zika virus is an emerging mosquito-borne *flavivirus*. The virus emerged in the past 70 years only sporadically with self-limiting small outbreaks. In 2013, a large outbreak in French Polynesia resulted in over 30,000 cases. Since early 2015 Zika virus spread in the Americas and to date caused autochthonous, vector-borne transmission in 48 countries and territories. This rapid emergence of the previously unknown pathogen raised the urgent need for a vaccine that can be rapidly produced in response to a newly emerging pathogen. Themis took the challenge and developed a vaccine candidate from design to Phase 1 clinical trial within 14 months. The MV-ZIKA vaccine candidate is a live attenuated recombinant viral vectored vaccine for the prophylaxis of Zika virus infection. The measles virus (MV) Schwarz vaccine strain was used as the backbone into which nucleotide sequences encoding Zika virus structural proteins glycoprotein precursor (prM) and the Envelope (E) were inserted to produce the MV-ZIKA. In measles virus susceptible mice, single or multiple vaccinations with MV-ZIKA induced a robust protective immunity, as shown by the induction of ZIKV E protein specific antibodies. The immunization of Cynomolgus macaques resulted in the induction of Zika virus neutralizing antibodies in all vaccinated animals. To evaluate the optimal dose of MV-ZIKA regarding immunogenicity, safety, and tolerability we initiated a double blinded, randomized, placebo-controlled, multi-center, phase 1 trial in 48 healthy volunteer subjects. The subjects will receive one or two vaccinations. The immunogenicity as confirmed by the presence of functional antibodies will be determined on day 28 after the second immunization. The clinical trial is currently ongoing and preliminary data will be presented here.

Biography

Sabrina Schrauf graduated as PhD from the University of Vienna in the field of Virology where she worked on Flavivirus biology including Tick-borne encephalitis virus and West Nile virus. She joined Themis in 2015 to coordinate preclinical development of vaccines-vaccine design and testing.

sabrina.schrauf@themisbio.com

Notes:

A novel mechanism linking memory stem cells with innate immunity in protection against HIV-1 infection

Thomas Lehner[1], Yufei Wang[1], Trevor Whittall[1], Stuart Neil[2] and **Mukesh Mistry[1]**
[1]Mucosal Immunology Unit, Kings College London, UK
[2]Kings College London, UK

HIV infection affects 37 million people and about 1.7 million are infected annually. Only the RV144 vaccine phase III clinical trial elicited significant protection against HIV-1 acquisition, but the efficacy and immune memory were inadequate. To boost these two critical functions of the vaccine we studied T stem cell memory (TSCM) and innate immunity. TSCM cells were identified by phenotypic markers of CD4+ T cells and they were further characterized into 4 subsets. These consisted of IL-2/IL-15 receptors and APOBEC3G anti-viral restriction factors, which were upregulated, whereas CCR5 co-receptors and α4β7 mucosal homing integrins were decreased. A parallel increase in CD4+ T cells was recorded of the IL-15 receptors, APOBEC3G and CC chemokines, with a decrease in CCR5 expression. We suggest a novel mechanism of dual memory stem cells; the established sequential memory pathway, TSCM →Central →Effector memory CD4+ T cells and the innate pathway consisting of the 4 subsets of TSCM. Both pathways are likely to be activated by endogenous HSP70, the hallmark of cellular stress. The memory stem cells and innate immunity pathways should be optimized to boost the efficacy and immune memory of protection against HIV-1. TSCM are likely to be activated by inducible HSP70, as PES (phenylethynesulphonamide), a small molecular inhibitor induced a dose-dependent inhibition of TSCM. The link between memory stem cells and innate immunity suggests a novel mechanism of inhibiting HIV-1 acquisition, by decreasing CCR5 and α4β7, increasing IL-15/IL-2 receptors and HIV-1 restriction factors.

Recent Publications

- Wang Y, Whittall T, Neil S, Britton G, Mistry M et.al. (2017) A novel mechanism linking memory stem cells with innate immunity in protection against HIV-1 infection. Scientific reports. 7(1):1057.
- Wang Y, Rahman D, Mistry M and Lehner T (2016) The effect of cellular stress on T and B cell memory pathways in immunized and unimmunized BALB/c mice. J. Biol. Chem. 291(39):20707-20717.
- Wang Y, Lavender P, Watson J, Arno M and Lehner (2015) Stress activated DC induce dual IL-15 and IL-b mediated pathways, which may elicit CD4+ T cells and IFN stimulated genes. J. Biol. Chem. 290(25):15595-609.
- Lewis DJM, Wang Y, Huo Z, Gimza R, Babaahmady K et. al. (2014) Effect of vaginal immunization in women with HIVgp140 and HSP70 on HIV-1 replication, innate and T cell adaptive immunity in women. J. Virol. 88(20):11648-11657.
- Wang Y, Whittall T, Rahman D, Bunnik EM, Vaughan R (2012) The role of innate apobec3g and adaptive aid immune responses in HLA-HIV/SIV immunized SHIV infected macaques. PlosOne. 7(4): e34433

Biography

Thomas Lehner is a Professor of Basic and Applied Immunology from London University. He pursued MB, BS London, MD London, FDS RCS, FRC Path, F Med Sci. He has several Prizes and honors to his credit which includes: Besredka Prize of the Pasteur Institute, Lyon, France; Honorary Doctorate, Karolinska Institute, Stockholm, Sweden; Honorary Life President of the International Society for Behcet's Disease; Appointed Commander of the British Empire (CBE) and Honorary Fellow of the Royal Society of Medicine. He has few selected international appointments including: Member of NIH (NIAID), Bethesda US Review Committee Research Grants 1999-2007; Member of Scientific Committee of the International Mucosal Immunology 1997-2006 and Member of the Scientific Committee of the Institute of Virology of the University of Maryland (1998-2002). He has 265 peer-reviewed papers published in scientific journals. Over the past 20 years his research involved animals and humans, preventing HIV and SIV infections, focus on mucosal immunization, generation of CC-chemokines, CCR5 coreceptors stress agents and alloimmunization.

Thomas.lehner@kcl.ac.uk

Emmanuel Drouet, Virol Res J 2017, 1:4

Challenges and dilemmas about vaccines against Epstein Barr virus and the other herpesviruses

Emmanuel Drouet
University of Grenoble-Alpes, France

Human Herpesviruses (HHV1-8) have co-evolved through a persistent infection in the host, spread efficiently to others, generally without causing serious disease. The complex interplay between host and virus has made it difficult to elaborate useful vaccine strategies to protect against the HHV-associated diseases. The Varicella-Zoster vaccine represents the paradigm of a successful Herpesvirus vaccine. This live-attenuated vaccine demonstrates unequivocally that it is possible to develop vaccines against these viruses. Over the years, the development of HHV vaccines has been a story of mixed fortunes, especially for HSV-2 and HCMV. However, studies carried out in various disease settings (i.e. transplant patients or pregnant women), have clearly emphasized the importance of cellular immunity and it is indeed encouraging to see that recent HHV vaccine (i.e. HCMV) development programs have started to incorporate this arm of the immune system. Nowadays, an array of arguments calls for a realistic goal for vaccine strategies which should be preventing HHV disease rather than HHV infection. It is particularly the case for the Epstein-Barr Virus (EBV or HHV4) which is the primary cause of infectious mononucleosis and is associated with epithelial cell carcinomas, as well as lymphoid malignancies. One challenge is that the EBV expresses very different proteins during its lytic and its latent phases. To address this, vaccine candidates have been designed to include proteins from both phases. Here we review the history of EBV vaccine development and the current strategies in the development of new EBV vaccines: As EBV is associated with nearly 200,000 new malignancies each year worldwide, an EBV vaccine to prevent these diseases is really needed. Parallel to this need one could propose priorities for future research: (i) identification of surrogate markers that predict the development of EBV-related malignancies. (ii) definition of a goal for an EBV vaccine and criteria for licensure.

Biography

Emmanuel Drouet is a Professor of Virology at the University of Grenoble-Alps (France), He previously served as a Biomedical Pathologist in the Institut Pasteur (Lyon, France). His research investigates the persisting viruses in human (RNA and DNA viruses) and the balance with our host immune system. He focuses on their effects on humans (both their impact in pathology and their symbiotic relationships in humans). He has an excellent track record in herpesvirus field, and his group is engaged in clinical research in the field of EBV diseases. His current research included the field of Hepatitis C Virus research, leading to elucidation of some aspects of its epidemiology and control.

Emmanuel.Drouet@ibs.fr

Notes:

Youness Cherradi, Virol Res J 2017, 1:4

Development of a production and purification platform for virus like particles (VLP) and adenovirus vector vaccine candidates: Two case studies

Youness Cherradi
Merck Life Science, Process Solutions, Belgium

Case Study 1: Virus-Like Particles (VLP) have received increased attention following their success with marketed vaccines. Whilst clinical candidates have proven efficacy and protection, their large-scale production implies high titer production, high recovery and purity leading to constant process improvement to meet market demand. In this study, a Hepatitis C Virus VLP based vaccine candidate production and purification was evaluated in collaboration with Instituto de Biologia Experimental e Tecnologica (IBET), Portugal. The VLP vaccine candidate was produced in insect cell expression system in a disposable bioreactor technology and cell culture attributes were compared with those from glass stirred tank bioreactor culture. Both systems harvests were subsequently purified to assess the impact of upstream processing on the downstream and the product quality. The downstream train was improved through the selection of appropriate anion exchange resin to reach 70% recovery and a satisfactory Baculovirus log reduction. In addition, appropriate depth filtration and ultrafiltration technologies were assessed and selected. Altogether, this case study lays the foundation for a fully GMP production process that can be easily pilot transferred and implemented for clinical and subsequent commercial production of VLP vaccine candidates.

Case Study 2: Adenoviral vectors (AV) offer a promising new approach to vaccine development due to their easy transgenic coding manipulation, efficient infection of various mammalian cell types and the broad immune response against the target antigen in vaccine recipients. Furthermore, these vectors are known to offer excellent safety profile, in that they can be engineered to be non-replicating in the vaccine recipient and they lack the molecular mechanism for integration into the host genome. AV's are highly amenable to scalable manufacturing processes such as the use of stirred tank bioreactors, high capacity filtration methods, and chromatographic purification procedures. GenVec and Merck have collaborated to evaluate different technologies for potential use in Adenoviral vector (AV) vaccine production. We will present the filter options evaluated on GenVec's AV product candidates, along with the results and filter sizing estimates for the process steps of medium exchange, lysate clarification, post-clarification filtration, concentration/ diafiltration, and post-hold sterile filtration prior to column chromatography.

Biography

Youness Cherradi, PhD is a Process Development Scientist for Merck in EMEA since 2013. He is responsible for customer process development and optimization on various downstream technologies and recently took the responsibility of Global Lead for the Vaccine Process Development team at Merck. He completed Master's Degree in BioEngineering, specializing in Chemical Engineering, Biotechnologies and Applied Genetics from the Université Libre de Bruxelles (ULB, Belgium) as well as a PhD in Molecular Bacteriology from the Medicine Faculty of ULB where he worked and published on virulence mechanisms of Type-3 Secretions Systems.

Youness.cherradi@merckgroup.com

Notes:

Gaëlle Vandermeulen, Virol Res J 2017, 1:4

Harnessing the immunogenicity of viral proteins for designing novel cancer DNA vaccines

Gaëlle Vandermeulen, Laure Lambricht and **Véronique Préat**
Louvain Drug Research Institute - University of Louvain, Belgium

Harnessing the power of the immune system to destroy or prevent cancers is a highly attractive strategy and a unique approach to cancer therapy. Competitive advantages of cancer vaccines are exquisite specificity, low toxicity, and the potential for a durable treatment effect due to immunologic memory, but their development is challenging due to the low immunogenicity of tumor antigens. As it is the case for cancer, a proper activation of cytotoxic T cells is necessary to clear infection by killing virus-infected cells. For that purpose, the immune system is able to detect and eliminate certain viral threats. We aim to investigate if the expression of specific viral proteins could similarly promote cancer immunization. DNA vaccine is a simple, versatile and clinically applicable method that could greatly benefit from such a strategy. We first demonstrated that the co-administration of a plasmid encoding the HIV-1 Gag viral capsid protein enhanced the efficacy of melanoma DNA vaccine. It favored antigen-specific Th1 immunity, delayed B16F10-OVA tumor growth and improved mouse survival in both prophylactic and therapeutic vaccination approaches. Similarly, a prophylactic DNA immunization against the melanoma-associated antigen gp100 was enhanced. Safety and immunogenicity of pGag have been demonstrated in human in the context of HIV vaccine development. Its use as a genetic adjuvant is thus of particular interest from a translational point of view. We then engineered the vesicular stomatitis virus G glycoprotein as permissive insertion sites allowed T-epitope insertions. Inclusion of either ovalbumin MHC class I or MHC class II restricted epitopes induced the proliferation of specific CD8+ and CD4+ T cells, respectively. The cytotoxic T-cell response was high when the two plasmids were co-delivered allowing a protective therapeutic effect against B16F10-OVA tumor. In conclusion, Gag and VSV-G proteins can be exploited for designing DNA vaccine strategies with promising therapeutic potential in cancer.

Recent Publications

- Lambricht L, Vanvarenberg K, De Beuckelaer A, Van Hoecke L, Grooten J et. al. (2016) Co-administration of a plasmid encoding HIV-1 Gag enhances the efficacy of cancer DNA vaccines. Molecular Therapy. 24(9):1686-1696.
- Lambricht L, Lopes A, Kos S, Sersa G, Préat V, Vandermeulen G (2016) Clinical potential of electroporation for gene therapy and DNA vaccine delivery. Expert Opinion on Drug Delivery. 13(2):295-310.
- Vandermeulen G, Vanvarenberg K, De Beuckelaer A, De Koker S, Lambricht L et. al. (2015) The site of administration influences both the type and the magnitude of the immune response induced by DNA vaccine electroporation. Vaccine. 33(28):3179-3185.
- Vandermeulen G, Uyttenhove C, De Plaen E, Van den Eynde B, Préat V (2014) Intramuscular electroporation of a P1A-encoding plasmid vaccine delays P815 mastocytoma growth. Bioelectrochemistry.100:112-118.
- Vandermeulen G, Athanasopoulos T, Trundley A, Foster K, Préat V, Yáñez Muñoz R J, Dickson G (2012) Highly potent delivery method of gp160 envelope vaccine combining lentivirus-like particles and DNA electrotransfer. Journal of Controlled Release. 159(3):376-83

Biography

Gaëlle Vandermeulen is a senior Postdoctoral Researcher at the University of Louvain. After completing a Master's degree in Pharmacy, she joined the Advanced Drug Delivery and Biomaterials group at the Louvain Drug Research Institute of the University of Louvain (UCL). Her PhD work was part of a European project and she spent several months at the Université Paris Descartes. She completed a PhD on skin DNA electroporation in 2008 and performed a Postdoctoral stay focused on HIV DNA vaccine at the Royal Holloway University of London. She aims to develop novel delivery systems for nucleic acid-based drugs, with a particular focus on DNA vaccines.

gaelle.vandermeulen@uclouvain.be

Notes:

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November 09-10, 2017 Vienna, Austria

Scientific Tracks & Abstracts

Day 2






Vaccines World 2017

Major Sessions:

Novel Vaccines - Development and production | Vaccines formulation

Session Chair
Andreas Meinke
Valneva Austria GmbH, Austria

Session Co-Chair
Youness Cherradi
Merck Life Science, Belgium

Session Introduction

Title: **A live attenuated nasal vaccine against pertussis**
Camille Locht, Center for Infection and Immunity of Lille - Institut Pasteur de Lille, France

Title: **Successfully activating positive behaviors of the stakeholders involved in vaccine purchasing and usage through technological advances**
Pierre A Morgon, Virometix, Switzerland

Camille Locht, Virol Res J 2017, 1:4

A live attenuated nasal vaccine against pertussis

Camille Locht
Center for Infection and Immunity of Lille - Institut Pasteur de Lille, France

Pertussis or whooping cough is making a dramatic comeback in several countries, especially since the switch from the first-generation whole-cell to the more recent acellular vaccines. The reasons for this resurgence are still under debate, but may essentially be due to unexpectedly fast waning of acellular vaccine-induced immunity and insufficient effectiveness of these vaccines to protect against infection by *Bordetella pertussis*, the principal causative agent of whooping cough, even though they protect effectively against *pertussis* disease. To ultimately control pertussis, new vaccines are necessary that protect both against the disease and B. *pertussis* infection. We have developed a live attenuated *pertussis* vaccine that can be administered by the nasal route. This vaccine, named BPZE1, has been shown to be safe in pre-clinical animal models, including severely immunocompromised mice, and to induce strong antibody and T cell responses. A single nasal dose of BPZE1 was able to protect mice against challenge with virulent B. pertussis, and protection was significantly longer lived than that induced by multiple administrations of acellular vaccines. In non-human primates, BPZE1 was also found to be safe and to protect against disease and infection caused by a highly virulent B. *pertussis* clinical isolate. BPZE1 has now successfully completed a phase I clinical trial in humans and was found to be safe in adults, to be able to colonize transiently the human respiratory tract and to induce immune responses in the colonized individuals. The vaccine is now undergoing further clinical development. Interestingly, in the course of the preclinical investigations, unexpected immunomodulatory properties or BPZE1 were uncovered. Without being immunosuppressive, BPZE1 appears to be anti-inflammatory and to protect mice against influenza virus-induced death, against experimental asthma and against experimental hypersensitivity of the skin, most probably linked to innate immune responses induced by the vaccine. Together with the protective effects against B. *pertussis* infection, these anti-inflammatory properties make BPZE1 an interesting tool for the benefit of public health, far beyond the control of pertussis.

Biography

Camille Locht currently holds a position as Research Director at the French National Institute of Health and Medical Research (Inserm) and, since 2010, is the Founding Director of the Center for Infection and Immunity of Lille on the campus of the Institut Pasteur de Lille in France. He has obtained his PhD at the Catholic University of Leuven in Belgium in 1984. After 3-years Postdoctoral stay at the National Institute of Allergy and Infectious Disease in the USA, where he started to work on *pertussis* and cloned the *pertussis* toxin genes, he joined SmithKline – Beecham (now GSK) to help developing acellular *pertussis* vaccines. Since 1989 he is the Head of a research laboratory at the Institut Pasteur de Lille, where he has been the Scientific Director from 2002 to 2013. His research interest is in molecular pathogenesis of respiratory infections, essentially *pertussis* and tuberculosis, with the long-term aim to develop new tools to combat these diseases. He has authored more than 300 international publications, book chapters and patents and has obtained several research awards.

Camille.locht@pasteur-lille.fr

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Successfully activating positive behaviors of the stakeholders involved in vaccine purchasing and usage through technological advances

Pierre A Morgon[1,2]
[1]MRGN Advisors, Switzerland
[2]Virometix, Switzerland

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 as 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 Chief Executive Officer of MRGN Advisors, a consultancy dedicated to the healthcare sector, and Regional Partner for Switzerland at Mérieux Développement, an evergreen investment structure focused on medical devices, *in vitro* diagnostics and patient management services. He is also holding the following board positions: Chairman of the Board of Virometix, a company developing proprietary synthetic nanoparticle platform in vaccines and immunotherapeutic drugs for viral diseases and cancer; Non-Executive Director to the Board of Theradiag, a company focusing on in vitro diagnostics in auto-immunity, infectious diseases and allergy; Non-Executive Director to the Board of Eurocine Vaccines, a company dedicated to developing intra nasal vaccines. He holds a Doctorate of Pharmacy, a Master in Business Law and a MBA. He is also an alumnus of INSEAD, IMD and MCE executive programs.

pm@mrgnadvisors.com

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