21st World Congress and Exhibition on

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Posters






Vaccines World 2017

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

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

Biography

Ida Cristina Gubert completed her Bachelor degree in Biological Sciences from Universidade Federal do Paraná (1975); Master's Degree in Genetics from Universidade Federal do Paraná (1986); PhD in Biochemical and Molecular Pharmacology from Universidade Federal de Minas Gerais (2005) and; Post-doc in Bioethics in Clinical Research (Facultad Latinoamericana de Ciências Sociales, FLACSO, Argentina). She has experience in Immunology, focusing on Applied Immunology.

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Notes:

Ingo Nagler, Virol Res J 2017, 1:4

PATfixTM - At-line monitoring of impurities and critical quality attributes in biopharmaceutical up- and downstream processes using HPLC fingerprinting

Ingo Nagler, Aleš Štrancar[1], Sebastijan Peljhan[1], Tomas Kostelec[1], Romina Žabar[1], Blaž Goričar[1], Vid Skvarča[1], Valentin Steinwandter[3], Patrick Sagmeister[3] and **Vignesh Rajamanickam[2]**
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The most commonly used gene transfer vectors are adeno- associated viruses, vaccinia viruses, adenoviruses, lentiviruses, retroviruses and pDNA. Due to their large size and sensitivity to pH, temperature and shear forces, purification is challenging and time-consuming. Consequently a fast and efficient downstream processing purification method is required to isolate sufficient amounts of vectors with the final purity and state that conforms to stringent regulatory demands. Convective interaction media (CIM) monolithic columns provide a robust platform for the purification of viral particles for vaccines and gene therapy. Pores are replaced by large channels allowing unrestricted flow of large biomolecules, eliminating diffusion and allowing flow-independent resolution and dynamic binding capacity. These properties, along with low back- pressure, lead to higher purity, recovery and efficiency in the downstream process. The poster presents multiple examples where monolithic chromatographic column are used as capture or polishing step in a process. Viruses (Adenovirus, Lentivirus), vaccines (Influenza A H1N1) and pDNA are shown as case studies for their respective downstream processes. The properties of monolithic columns allow their use both as capture step where high flow rates are required to capture and concentrate the particles, as well as polishing. Characterized by very high resolving power, monoliths can separate empty and full capsids of Adeno-associated virus and discriminate between pDNA isoforms (supercoiled, linear, open- circular).

Biography

BIA Separations is the leading developer and manufacturer of Convective Interaction Media (CIM) monolithic columns for fast purification of biomolecules. Our goal is to provide the best solutions in downstream processing and analytics, with the goal of saving our customers valued time and costs during the production of their desired biomolecules. We have over 20 years' experience in chromatographic purification of large biomolecules including viruses, VLPs, phages, pDNA, antibodies (IgM, IgG), proteins, as well as removal of viral particles, endotoxins and proteins from different biological matrices. We provide products that range from small analytical columns to large industrial prep-scale columns (including cGMP and disposable units in IEX, HIC, affinity and customized formats) as well as method development services.

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Anne Thomas, Virol Res J 2017, 1:4

Protection of horses from West Nile virus lineage 2 challenge following immunization with a whole, formalin-inactivated WNV lineage 1 vaccine

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Over the last years West Nile Virus (WNV) lineage 2 has spread from the African to the European continent. This study was conducted to demonstrate efficacy of an inactivated, lineage 1-based, WNV vaccine (Equip WNV) against intrathecal challenge of horses with a recent isolate of lineage 2 WNV. Twenty horses, seronegative for WNV, were enrolled and were randomly allocated to one of two treatment groups: an unvaccinated control group (T01, n=10) and a group administered with Equip WNV (T02, n=10). Horses were vaccinated at day 0 and 21 and were challenged at day 42 with WNV lineage 2, Nea Santa/Greece/2010. Personnel performing clinical observations were blinded to treatment allocation. Sixty percent of the controls had to be euthanized after challenge compared to none of the vaccinates. A significantly lower percentage of the vaccinated animals showed clinical disease (two different clinical observations present on the same day) on six different days of study and the percentage of days with clinical disease was significantly lower in the vaccinated group. A total of 80% of the non-vaccinated horses showed viremia while only one vaccinated animal was positive by virus isolation on a single occasion. Vaccinated animals started to develop antibodies against WNV lineage 2 from day 14 (two weeks after the first vaccination) and at day 42 (the time of onset of immunity) they had all developed a strong antibody response. Histopathology scores for all unvaccinated animals ranged from mild to very severe in each of the tissues examined (cervical spinal cord, medulla and pons), whereas in vaccinated horses 8 of 10 animals had no lesions and two had minimal lesions in one tissue. In conclusion, Equip WNV significantly reduced the number of viremic horses, the duration and severity of clinical signs of disease and mortality following challenge with lineage 2 WNV.

Biography

Anne Thomas is DVM and PHD from University of Liège (Belgium). She has also a PostDoc from the same university. She joined Pfizer Animal Health in 2006 and works in Zoetis-VMRD from 2011.

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Immunological evaluation of HCV core and its alternative reading frame protein vaccine prototypes

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Hepatitis C remains a serious healthcare problem and there is no prophylactic or therapeutic vaccine currently available, although many candidates are in clinical trials. One of the attractive targets is the nucleocapsid protein (core). HCV core (aa 1-191) is highly conserved among HCV genotypes. It binds and packages viral genomic RNA and regulates its translation. The 5' terminus of HCV genome also encodes core+1/ARF protein. This protein possibly participates in HCV morphology or replication, it can be important in gene regulation and it can affect immune response mechanisms. A set of plasmids for eukaryotic and prokaryotic expression carrying different in length variants of the 5' terminus of HCV genome were constructed. Obtained DNA and proteins were purified and used in immunization of BALB/c mice in different schemes of immunization by protein and naked DNA (*in vivo* electroporation). Specific immune response was determined and immunization with HCV core aa 1-159 and full length ARFP proteins expressed in E. coli induced the specific immune response. The antibody titers against HCV core reached 104 and maximum antibody titers against ARFP reached 103. Immunization with HCV core and ARFP genes also induced the specific immune response. Both natural and mutated HCV core genes with prohibited frame-shift provide the same levels of specific cellular responses. Thus, a higher expression of HCV core from the mutated or optimized genes compared to the wild type sequence could not provide for its better immunogenicity. Efficacy of ARFP expression by the natural ribosome frameshift mechanism was low and obviously insufficient to induce a specific immune response. Thus, anti-ARFP immune response is not competing with that against HCV core, and cannot explain low immunogenicity of core in DNA-immunization performed with the virus-derived genes. The immunization by DNA-prime and protein-boost seems to combine the advantages of both approaches and improve the immune response.

Recent Publications

- Sominskaya I, Jansons J, Dovbenko A, et al (2015) Comparative immunogenicity in rabbits of the polypeptides encoded by the 5' terminus of hepatitis C virus RNA. J Immunol Res. http://dx.doi.org/10.1155/2015/762426.
- Dishlers A, Skrastina D, Renhofa R, et al (2015) The hepatitis B virus core variants that expose foreign C-terminal insertions on the outer surface of virus-like particles. Mol Biotechnol. 57(11-12):1038-49.
- Ivanov A V, Smirnova O A, Petrushanko I Y, et al (2015) HCV core protein uses multiple mechanisms to induce oxidative stress in human hepatoma Huh7 cells. Viruses 7(6):2745-70.
- Sominskaya I, Skrastina D, Petrovskis I, et al (2013) A VLP library of C-terminally truncated hepatitis B core proteins: correlation of RNA encapsidation with a Th1/Th2 switch in the immune responses of mice. PLoS One. 8(9):e75938.
- Skrastina D, Petrovskis I, Petraityte R, et al (2013) Chimeric derivatives of hepatitis B virus core particles carrying major epitopes of the rubella virus E1 glycoprotein. Clin Vaccine Immunol. 20(11):1719-28.

Biography

Irina Sominskaya has completed her Doctor of Biology Degree from Latvian University, Riga, Latvia in 1992. She is the Head of Viral hepatitis group of Latvian Biomedical Research and Study Center, Riga, Latvia. Using a multidisciplinary approach, including molecular biology, cell biology, and immunology technologies, the objective of group research is to gain a deeper understanding of virus-host interactions at a fundamental level. She has 25 publications and was a project Leader of several Latvian and international projects. She was supervisor of four doctoral degree students.

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Ingo Nagler, Virol Res J 2017, 1:4

Downstream processing of gene therapy vectors and vaccines using monolithic columns

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Production of high value biological therapeutics usually involves complex manufacturing processes with high process variability. Additionally, development of robust and reliable bioprocesses can be challenging. PAT aims to enhance bioprocess understanding and implies a holistic approach to ensure that quality is built into products by design. Efficient PAT therefore calls for fast and robust analytical techniques which enables to asses high quality information about critical quality attributes and key performance indicators as parallel as possible to the manufacturing process. PATfix™ is unique HPLC system for routine gradient separations that enables every analytical task. Equipped with bio-inert ceramic pump heads is deliberately tailored to meet the demands of analytical applications covering wide range of biomolecules. Highly sensitive and fast multi-wavelength detector enables to detect component peaks even in very fast gradients.

Recent Publications

- E LIMONTA, Miladys, et al. "Comparison of CIM® C4 HLD monolithic column with Sartobind phenyl membrane column for pIDKE2 purification." Chinese Journal of Chromatography 1028: 1036.
- Vincent, David, et al. "The development of a monolith-based purification process for Orthopoxvirus vaccinia virus Lister strain." Journal of Chromatography A (2017).
- Lesch, H. P., et al. "Production and purification of lentiviral vectors generated in 293T suspension cells with baculoviral vectors." Gene therapy 18.6 (2011): 531-539.

Biography

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Accepted Abstracts






Vaccines World 2017

Virol Res J 2017, 1:4

Nature and fear: Two distinct mechanisms that shape pediatric vaccine-refusal in the US

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Statement of the Problem: Low childhood immunization rates and frequent outbreaks of vaccine-preventable diseases threaten the health and well-being of our nation's children. While access to affordable vaccination plays a role in the current immunization state, most data point to parental vaccine-hesitancy and vaccine refusal. The United State and other countries have expended significant funding showcasing vaccine safety and disproving widely publicized links to health concerns such as autism. Despite these efforts, as many as 50% of parents consider themselves vaccine-hesitant. The purpose of this study is to describe parents' decision-making process as they choose to reject, delay or defer vaccination decisions for their children age 6 and under.

Methodology & Theoretical Orientation: In a qualitative field study, we elicited parents' vaccine associations as well as deep-rooted and complex vaccine stories to uncover the flawed causal knowledge parents possess about the safety and need of vaccines, their reasoning biases, and main decision-making paths.

Findings: All parents were driven in their no-vaccine decisions by a strong desire to protect their children. However, two distinct decision-making paths emerged – a visceral fear mechanism that overrides or influences cognition and places parents in a state of anxiety and concern; and a rule-based, "nature knows best" mechanism, which veils parents in an unfounded optimism and perceived well-being.

Conclusion & Significance: Parents refusing or delaying vaccination represent a heterogeneous group, guided by distinct decision-making paths which instill different affective states. Effective communication of vaccine safety information should be affectively customized to the two groups of parents.

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Virol Res J 2017, 1:4

Strategies for enhancing the safety and efficacy of recombinant vaccines and technology transfer to developing nations

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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. Finally, the ILMB has facilitated and implemented the transfer of technologies in molecular biology to developing countries in Africa that has led to self-sufficiency.

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Virol Res J 2017, 1:4

Strengthening maternal immunization to improve the health of mothers and infants

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The reduction in mortality of children less than five years of age has been faster than for maternal mortality. Additionally, the reduction in post neonatal mortality has been faster than the decrease in neonatal mortality resulting in an increase in the percentage of U5 deaths that currently occur in the neonatal period to ~45%. Maternal immunization (MI) has the potential to decrease serious morbidity and mortality not only in the mother, but also the fetus, neonate and young infant that are not yet able to immunologically respond to most vaccines. Currently, we are only beginning to unlock the potential of using vaccines this way. The tetanus and influenza vaccines are recommended in pregnancy not only to prevent diseases causing serious morbidity and mortality in the mother, but also in neonates and young infants. Recently, the yellow fever vaccine has been recommended for use in pregnant women in outbreak settings and a phase 3 trials with a hepatitis E vaccine is currently ongoing in Bangladesh. Vaccines are also available or under development that could be given to pregnant women not to specifically prevent disease in them, but rather in their fetus or young infant. The acellular pertussis vaccine has recently been recommended for use in pregnant women in countries that have documented increasing numbers of deaths in young infants due to pertussis. Examples of vaccines currently being specifically developed to give to pregnant women for protection of their unborn child and/or infant include those designed to prevent respiratory syncytial virus and group B streptococcus disease. This lecture will discuss the current status of the MI program and various implementation issues that need to be addressed (e.g., vaccine hesitancy in pregnant women and their families as well as healthcare workers and government officials).

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Virol Res J 2017, 1:4

TRPV4 calcium-permeable channel is a novel regulator of oxidized LDL-induced macrophage foam cell formation

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Cardiovascular disease is the number one cause of death in developed world, and atherosclerosis, a chronic inflammatory arterial disease, is the most dominant underlying pathology. Macrophages are thought to orchestrate atherosclerosis by generating lipid-laden foam cells and by secreting inflammatory mediators. Emerging data support a role for a mechanical factor, e.g., matrix stiffness, in regulation of macrophage function and atherogenesis. We have obtained evidence that TRPV4, an ion channel in the transient receptor potential vanilloid family and a known mechanosensor, is the likely mediator of oxidized low-density lipoprotein (oxLDL)-dependent macrophage foam cell formation, a critical process in atherogenesis. Specifically, we found that genetic ablation of TRPV4 or pharmacologic inhibition of TRPV4 activity by a specific antagonist blocked oxLDL-induced macrophage foam cell formation, and TRPV4 deficiency prevented matrix stiffness or scratch-induced exacerbation of oxLDL-induced foam cell formation. Mechanistically, we found that plasma membrane localization of TRPV4 was sensitized to the increasing level of matrix stiffness, and TRPV4 activity regulated oxLDL uptake but not its internalization in macrophages. Altogether, these findings identify a novel role for TRPV4 in regulating macrophage foam cell formation by modulating uptake of oxLDL.

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Virol Res J 2017, 1:4

Vaccines against infectious diseases

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A vaccine is a biological preparation that improves immunity to a particular microorganism. Accurate diagnostic and surveillance with better understanding of genetic and immunologic background of host specific response and pathogen evolution drives adapted vaccine research. AMR (antimicrobial) resistance is regarded nowadays as a major threat to global public health. The issue is receiving high-level political attention (G7 summit and upcoming G20 for first time). Pandemics, drug resistance and neglected diseases framing health as a global security issue. WHO made a list to promote research and development (R&D) of new antibiotics (27th Feb 2017) underlining gram-negative bacteria. Although initially omitted from the list, tuberculosis and latent tuberculosis represent still a major issue to tackle. XDR tuberculosis has evolved in several tuberculosis endemic countries to drug incurable or programmatically incurable tuberculosis. BCG vaccine successfully helped to interrupt transmission cycle and along with antibiotic discovery to decrease mortality. However, its efficacy remains controversial. HIV/AIDS has known link with tuberculosis but other risk factors have also emerged in recent years as important determinants of the TB epidemic, one of which is diabetes mellitus. Risk or new emerging and re-emerging pathogens originated from animals after having crossed the species barrier (e.g., Ebola) and re-appearance of old diseases like pertussis, measles and known limitations of drugs underline need for innovative vaccines as highly potent tool to tackle resistance and valuable alternative from long term perspective being clearly recognized as a major tool for public health.

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Virol Res J 2017, 1:4

Tumor liberated protein (TLP) as potential vaccine for lung cancer patients

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Tumor liberated protein (TLP) has been previously described as a TAA (complex) present in the sera from lung cancer patients with early stage disease. Since early detection improves overall survival in lung cancer, identification of screening biomarkers for patients at risk for the development of this disease represents an important target. Starting from the peptide epitope RTNKEASI previously isolated from TLP complexes, we generated a rabbit anti-RTNKEASI serum. This antiserum detected and immunoprecipitated a 55 kDa protein band in the lysate of the lung cancer cell line A549. This protein band was identified as aldehyde dehydrogenase isoform 1A1 through mass spectrometry, revealing the molecular nature of at least one component of the previously described TLP complex. Next, we screened a cohort of 29 lung cancer patients (all histologies), 17 patients with non-neoplastic lung pathologies and nine healthy donors for the presence of serum ALDH1A1 and global serum ALDH by enzyme-linked immunosorbent assay. This analysis indicated that the presence of ALDH was highly restricted to patients with lung cancer. Interestingly, the global ALDH test detected more lung cancer patients compared to the ALDH1A1-specific test, suggesting that other ALDH isoforms might add to the sensitivity of the assay. Our data suggest that ALDH levels may therefore be evaluated as part of a marker panel for lung cancer screening. Finally, the ability of the immune system to recognize a TAA, enables the development of a vaccine approach for preventive and therapeutic application and represents a main target of this field of research.

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Virol Res J 2017, 1:4

Measles vaccination: Threat from related veterinary viruses and need for continued vaccination post measles eradication

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Measles virus (MV) is the only human virus within the morbillivirus genus of the Paramyxoviridae. The virus can cause severe complications such as measles giant cell pneumonia and acute post measles encephalitis. More rarely fatal infections of the CNS, sub-acute sclerosing panencephalitis (SSPE) and in immunosuppressed individuals measles inclusion body encephalitis (MIBE) occur. The World Health Organization (WHO) has set goals towards the complete eradication of MV in at least five WHO regions by 2020. This presents potential problems as the closely related veterinary members in the genus share common cell entry receptors raising the risk of zoonotic infection. MV is thought to have evolved from the eradicated cattle morbillivirus, rinderpest, and to have entered the human population during cattle domestication. Lessons have also been learned from other animal to human virus transmission i.e. human immunodeficiency virus (HIV) and more recently avian influenza, severe acute respiratory syndrome (SARS) and Middle Eastern Respiratory Syndrome (MERS). This highlights the potential consequences of complete withdrawal of MV vaccination after eradication. The measles vaccine is live attenuated and has very low risk of reversion but is still unlikely to be acceptable in a MV free world raising the need for alternative approaches. A formalin fixed MV vaccine was used for a period in the 1960's but provided short lived and non-complete immunity with an altered immune response and death of some children following later infection. This has encouraged research into recombinant vaccines for MV or the closely related veterinary viruses using other virus vector systems.

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Virol Res J 2017, 1:4

Cost-benefit analysis of a projected national HPV vaccination program in Lebanon

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Background: HPV vaccination is believed to be a determining factor in preventing cervical cancer (CC). The introduction of HPV vaccination in the national EPI program has been under debate in Lebanon for several years, in the absence of compelling cost-benefit evidence. This analysis compares the potential cost of such a decision to the cost of cervical cancer treatment, with the aim of contributing some evidence to the national debate.

Methods: The cost of HPV vaccination for all 11-year old girls in a given year was calculated and compared to the yearly cost of CC treatment. The first part of the equation was estimated based on the current price for the cheapest available vaccine in Lebanon (Cervarix®). The cost of cancer treatment was estimated for 100 cases, which is the average incident case-load registered nationally over several years, while weighing for the proportional distribution of non-invasive cases versus more expensive invasive ones. The analysis was conducted under the favorable assumption that the vaccine will provide lifelong protection against all cervical cancers, that the incidence of CC will not increase and that treatment will be successful for all diagnosed cancers.

Results: The cost of two recommended doses of the vaccine with a current price of 70.8 USD per dose, administered to an estimated population of 38,000. 11-year old girl was estimated around 5 million USD. In comparison, the weighted cost of treating 100 cases of CC was about 1,650,000 USD in total. Thus, the ratio of expected cost of vaccination to that of CC treatment in a given year was 3.3/1. To break-even, the price of one vaccine dose would have to be dropped to about 5 USD, which is considered highly unlikely as long as the vaccine has not fallen in the public domain, an event expected within 10 years. A break-even point may also occur if cancer treatment costs continue to rise. The cost was accrued annually by 15.6%, based on increases in cancer drug costs recorded by the Ministry of Public Health. Even at year 10, the cost difference would remain substantial.

Conclusions: Despite WHO recommendations, the current epidemiological situation of Lebanon is not favorable to the adoption of universal mandatory HPV vaccination. Our analysis shows, even under the debatable assumption of life-long protection, HPV vaccination is not cost-beneficial and will remain so for at least 10 years to come.

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Virol Res J 2017, 1:4

The immunization status of children of 1st grade in elementary schools of city of Trikala, Greece in 2016-17

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The purpose of this survey was to assess the immunization status of children in the 1st grade of elementary school in Trikala city in Greece and to write down the percentage of coverage of each vaccine that is included in the national immunization program and also to record the vaccination coverage and to compare it with previous records at national and global level. The size of the sample was 667 students of 30 schools in the city of Trikala. Of the 667 students, 618 students participated (92.65% participation). Percentage of vaccination DTP-Polio (Diphtheria-Tetanus-Pertussis-Polio) is low at 84.30%. The full 2-dose MMR vaccination rates are low, of 89.64%. Hepatitis B: vaccination coverage 98.06%; Haemophilus type B: coverage rate is very high 99.51% and Meningitis C: very high vaccination coverage rate. A significant increase is recorded in relation to 2012 rates of 98.71% versus 15%. Pneumococcus: very high vaccination coverage. A significant increase is recorded in relation to the rates of 2012, 89.71% versus 4% chickenpox: high vaccination coverage 92.88% hepatitis A: High vaccination coverage rate 92.56% Influenza: The vaccination rate is low, just 16.99%, as according to the national vaccination program only children of high risk are vaccinated. Meningococcus B: this much-discussed vaccine is recorded at low rates, 16.34% as the cost of the vaccine is high and not covered by the insurance funds. Rotavirus: It is a restricted vaccine as it is strictly given at certain times, so if it is not done in the first infancy, it is not recommended to use it later. This in combination with the partial insurance coverage does not favor broad vaccination.

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Virol Res J 2017, 1:4

Veterinary vaccines: Oriented approaches for intracellular and extracellular pathogens

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Statement of the Problem: We work on two relevant cattle pathogens such as *Mycobacterium bovis,* agent of bovine TB and *Escherichia coli* O157:H7, the main member of the Enterohemorrhagic *E. coli* (EHEC) group, is the agent of uremic hemolytic syndrome. *M. bovis* and EHEC are both zoonotic pathogens. But while M. bovis is pathogenic to both cattle and humans, producing tuberculosis; EHEC do not provoke an illness in cattle (being cattle a reservoir) but causing a severe disease in human infants. In turn, *M. bovis* is an intracellular pathogen and EHEC is not an invasive pathogen.

Methodology & Theoretical Orientation: We reasoned that to combat an intracellular pathogen, we need a live attenuated vaccine deleted in genes related to the virulence for that we designed a *M. bovis* wild type deleted in *mce* genes, additionally and for safety, another gene (*phoP*) was deleted. The vaccine probed to be effective in mice, guinea pig and cattle experimentally challenged. In the case of EHEC, we used recombinant proteins (rAgs) from the type 3 secretion systems and sometimes additional proteins. rAgs were emulsified in an adjuvant that promotes mucosal IgG response. Animals were challenged with an EHEC inoculum and a protection reducing the bacterial shedding and the number of excreting animals was observed.

Conclusion & Significance: The rational design of vaccines is based in selecting the adequate approach to induce the adequate protective immune response for a given pathogen. In our case, results were promissory and prompt us to improve the current vaccine formulations to obtain efficient vaccines.

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Virol Res J 2017, 1:4

Dendrimeric peptides can confer protection against foot-and-mouth disease virus in cattle

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Foot-and-mouth disease virus (FMDV) causes a highly contagious disease in cloven-hoofed animals. A synthetic vaccine candidate consisting of dendrimeric peptides harboring two copies of a B-epitope [VP1(136-154)] linked to a T-cell epitope [3A(21-35)] of FMDV confers protection to type O FMDV challenge in pigs. Herein, we show in cattle that novel dendrimeric peptides bearing a T-cell epitope [VP1(21-40] and two or four copies of a B-cell epitope [VP1(135-160)] from type O1 Campos FMDV (termed B2T and B4T, respectively) elicited FMDV specific immune responses to similar levels to a commercial vaccine. Animals were challenged with FMDV and 100% of vaccinated cattle with B2T or B4T were protected to podal generalization. Moreover, bovines immunized with B4T were completely protected against FMDV challenge (with no clinical signs), which was associated with titers of viral neutralizing antibodies in serum higher than those of B2T group ($p<0.05$) and levels of opsonic antibodies similar to those of animals immunized with FMDV commercial vaccine. Bovines vaccinated with both dendrimeric peptides presented high levels of IgG1 anti FMDV in sera and in mucosa. When IgA in nasal secretions was measured, 20% or 40% of the animals in B2T or B4T groups respectively, showed anti-FMDV IgA titers. In addition, B2T and B4T peptides evoked similar consistent T cell responses, being recognized in vitro by lymphocytes from most of the immunized cattle in the proliferation assay, and from all animals in the IFN-γ production assay. Taken together, these results support the potential of dendrimers B2T or B4T in cattle as a highly valuable, cost-effective FMDV candidate vaccine with DIVA potential.

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Influence of genetically modified mosquitoes in dengue epidemic network

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There are many examples of complex systems in the world from different domains of life. For example, the social contacts includes, the social networks of friendship, a covert network of terrorists, sexual contact network, and scientific collaboration network are all complex networks. Complex networks play a significant role in the research of epidemic diseases and in their modeling such as HIV/AIDS. The dengue epidemic is a dynamic and complex phenomenon which has gained much attention due to its harmful effects that sometimes becomes a cause of death of a person. According to WHO, it is estimated that approximately 3.6 billion people are living in the dengue affected part of the world. It has become an emerging challenge to health authorities and legislators, as there are presently no authorized antibodies or particular therapeutics for its treatment. The dengue fever is caused by a mosquito of specific specie named as *Aedes aegypti*. It is important to discuss here that only female *Aedes aegypti* is the dengue vector that is also the super spreader of ZIKA virus. The dataset (obtained from MOH Selangor, Malaysia) showed the results that proved the dengue epidemic as a scale-free network (SFN) instead of random network. The scale-free feature is very important in the treatment of epidemic diseases. Here, we observe the influence of Genetically Modified Mosquitoes (GMM) in a complex network of the dengue epidemic. The results showed that GMM technique is much suitable in SFN and can suppress the wild population of *Aedes aegypti*. The results are important for the researchers and policy makers who deal with the arbovirus epidemic diseases like ZIKA virus.

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Antibody against synthetic peptide of prolactin-inducible protein homologue precursor (PIP-HP) of Bali cattle (Bos javanicus) saliva: A potential biomarker for immunoassay development

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Background: We have successfully identified sequence of a Prolactin-Inducible Protein Homologue Precursor (PIP-HP) in Bali cattle (*Bos javanicus*) saliva by matrix-assisted laser desorption ionization-time-of-flight-mass spectrometry (MALDI-TOF-MS). PIP-HP as one of salivary proteins that might potentially altered in disease and could serve as novel diagnostic biomarkers. Antibody against PIP-HP hence needs to be produced.

Methods: A synthetic amino acid sequence of the PIP-HP was developed and then conjugated to bovine serum albumin and was used to immunize Indonesian local rabbits. Serum antibody that specific to the PIP-HP was purified sequentially by ammonium sulfate precipitation and protein A affinity methods. Purified antibody was then used to analyze the presence of PIP-HP in the ruminants' saliva by means of dot blot and western blot. A preliminary study on the development of immuno lateral assay using the purified anti-PIP.HP antibody as the biomarker has also been carried out.

Results: Specific antibody was successfully produced against a synthetic amino acid sequence fragment of PIP-HP of Bali cattle saliva. The antibody can be used to analyze the presence of PIP-HP not only in the saliva but also in other fluids including semen fluids of large ruminants (cattle and buffalo). The antibody was also able to be used to develop immuno lateral assay kits. In addition, we also found that the antibody was able to inhibit the growth of E. coli culture, but did not to *S. aureus*. The findings in this study need to be explored further especially in the relationship with the potential of anti-PIP-HP as biomarker for animal diseases biomarker.

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