WORLD VACCINES AND IMMUNOLOGY CONGRESS

July 23-24, 2018 | Osaka, Japan

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KEYNOTE FOURM
The existing vaccines are mainly limited to the microorganisms we are able to culture and produce and/or to those whose killing is mediated by humoral response (antibody mediated). It has been more difficult to develop vaccines capable to induce functional cellular response needed to prevent or cure chronic diseases.

New strategies should be taken into account in the improvement of cell-based immune responses in order to prevent and control the infections and eventually clear the virus.

This work present preclinical and clinical results with vaccine candidates against dengue virus, HBV and HIV based on virus like particles (VLPs) and virus like nucleoparticles (VLNs) able to stimulate mucosal as well as systemic immunity. Particles based on envelope or nucleocapsid viral proteins induce a strong immune response after mucosal or systemic administration in mice, non-human primates and humans. In addition, the immune response obtained was biased in a Th1 sense.
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EPITOPE-BASED PEPTIDE VACCINE DESIGN AGAINST MOKOLA RABIES VIRUS GLYCOPROTEIN G UTILIZING IN SILICO APPROACHES

Arwa Abdelhalim Mohammed
Sudan

Lyssavirus is considered as a neglected, zoonotic and tropical virus. Among all the lyssavirus species known to exist today, Mokola virus is unique and appears to be exclusive to Africa. This virus is responsible for a meningoencephalomyelitis in mammals therefore; in silico prediction of epitopes of appropriate protein residues is important to produce a peptide vaccine with powerful immunogenic and minimal allergic effect. The aim of this study was to design a vaccine for Mokola virus using its glycoprotein peptides as an immunogen to stimulate protective immune response.

Methods and Materials: Glycoprotein G Sequences of Mokola was explored from NCBI then the sequences were aligned to obtain conserved regions. The nominees epitopes from Immune Epitope Database were analyzed by different prediction tools for B-cell, T-cell MHC class II and I. Then sequences aligned with the aid of ClustalW implemented in the BioEdit program.

Results and Conclusions: For Bepipred test of B-cell the total number of conserved epitopes was 85. For Emini surface accessibility prediction, 36 conserved epitopes were passing the default threshold 1.0. In Kolaskar and Tongaonkar antigenicity, 36 conserved epitopes gave score above the default threshold 1.045. However, there are only three epitopes that pass the three tests (LYTIPEK, LAHQK, YPSVPS). The reference glycoprotein strain was analyzed using IEDB MHC-I binding prediction tool to predict T cell epitope. Twenty conserved peptides were predicted to interact with different MHC-I alleles. For MHC-II binding prediction there were 47 conserved epitopes found to interact with MHC-II alleles. The peptides GQILIPEMQ, FRRLSHFRK and FVGYVTTF had the affinity to bind the highest number of MHC-II alleles. World Population coverage for MHC-I most promising 3 peptides FVDLHMPDV, FVGYVTTF and RLFDGTVWS was 67.42%, while the world population coverage for most promising MHC-II peptides was 99.77%, for the binding to MHC-I and MHC-II, The peptide FVG TTTF world population coverage was 99.31%.
Title

ANTI-FIBROTIC AND ANTIOXIDANT EFFECTS OF TUNISIAN ARBUTUS UNEDO LEAVES AQUEOUS EXTRACT AGAINST BLEOMYCIN-INDUCED LUNG FIBROSIS IN RAT

Name & Country

Anouar ABIDI
Tunisia

Abstract

Introduction: The present study aimed to investigate the protective effect of Tunisian Arbutus unedo leaves aqueous extract (AuE) against bleomycin (BLM)-induced lung fibrosis as well as the involvement of oxidative stress in such protection.

Methods: In this respect, adult rats were used and divided into three groups of twenty each: control (NaCl, 0.9%), BLM and BLM (2 mg/kg b.w.) + AuE (250 mg/kg/day). The rat pulmonary fibrosis model (PF) was established by intratracheal instillation of BLM, and the effect of 250 mg/kg AuE treatment once daily observed. Animals were pretreated for 30 days before the induction of fibrosis by BLM and 20 days after the induction of fibrosis. The effect of the treatment was studied using 1H RMN analysis on the broncho alveolar lavage fluid (Balf) of the rats. Histopathological (inflammation and fibrosis) and immunohistochemical (TGF-β1 density) changes were evaluated.

Results: BLM Administration followed by AuE reduced BLM-induced weight loss, increased proline, glucose, and glycerid rates in Balf. In vivo, our data demonstrated that AuE administration protected against BLM-induced fibrosis by decreasing TGFβ immunostaining in lungs alveoli, histiocytes and inflammatory infiltrate. We also showed that acute bleomycin induced fibrosis was accompanied by an oxidative stress status in lung tissue as assessed by the increase of lipid peroxidation as well as antioxidant enzyme activities depletion such as superoxide dismutase (SOD) and catalase (CAT). More importantly, AuE treatment reversed all BLM-induced oxidative stress parameters disturbances (reduced superoxide dismutase and catalase).

Conclusion: These findings provide an insight into the preventive and therapeutic potential of AuE in the treatment of PF.

Biography

Anouar ABIDI has completed his PhD at the age of 32 years from Carthage University, Tunisia. He is the professor of High Institute of Health and Paramedical Sciences, Tunisia. He has many publications in International Journals.
ISSUES IN AFFORDABILITY AND ACCESS TO VACCINES AND THE ROLE OF THE VACCINE INDUSTRY

K V Balasubramaniam, holds a graduate degree in Mechanical Engineering from the Madras University (1979) and doctoral degree in Management from the University of Hyderabad. He has over 35 years' experience in managing industrial enterprises, with nearly 30 years in the pharmaceutical industry. He is the former Managing Director of India's leading vaccine manufacturer- Indian Immunologicals Ltd (IIL) and was instrumental in establishing IIL as the No 1 animal vaccine player, India.

Access to vaccines and their affordability are prime concerns in developing countries. While much has been done to address these critical determinants of immunization by multi-lateral agencies, there are many aspects related to the character and structure of the industry which are still to be effectively addressed. Chief among these are the non-egalitarian mission of vaccine companies, the oligopolistic character of the industry, lack of focus on vaccines for neglected diseases and pursuit of profit maximization. Compounding this at the field level are issues related to health system preparedness, delivery infrastructure, programme errors, and to some extent the negative social and religious influence. It is imperative on the vaccine industry to shed its reticence and play a pro-active and egalitarian role to foster shared value with governments and the society, and thereby make immunization affordable and accessible to all.
Vaccines used for vaccination of pregnant women, data related to safety

Merita Kucuku
Albania

The vaccine can protect the pregnant women directly against vaccine preventable infections and also potentially protect the fetus and infant via specific antibodies transferred from the mother during pregnancy. The publications have evidence about the risk of influenza disease, particularly in the second and the third trimester and the safety and effectiveness of immunization with inactivated influenza vaccines. If the influenza vaccination particularly given in the second or third trimester demonstrated benefits for mother and newborn for seasonal and pandemics flue.

Tetanus toxoid vaccine: Tetanus toxoid vaccine (TT) is recommended for use in pregnancy for elimination of maternal and neonatal tetanus in developing countries. WHO estimates that there were 59000 neonatal tetanus deaths in 2008, a 92% reduction from the late 1980s and an indicator how widely maternal TT immunization is being used. By Feb. 2012, 34 countries had still not eliminated maternal and neonatal tetanus. It is well established the effectiveness of TT vaccination of pregnant women in preventing neonatal tetanus deaths, and a WHO position paper on tetanus, published in 2006.

No data for any signal of AEFI for pregnant women after TT immunization and this support the vaccine use. Case series in the USA and several European countries, and studies in Latin America and the Islamic Republic of Iran and Canada which used MMR and MR vaccines provide indirect evidence of the safety of these vaccines for pregnant women but this is not enough information to exclude a risk.
Title

USING RADIATION TO TURN THE TUMOR INTO AN "IN SITU" VACCINE FOR LUNG CANCER

Name & Country

James Welsh
Texas, USA

Abstract

For the last 100 years radiation has been used solely for location control, but now with the advent of immunotherapy, we have the potential to expand the benefit of radiation to systemic disease. Our laboratory has generated the model of PD1 resistant to lung cancer and using this model we are testing several new immunotherapies to produce abscopal systemic responses in combination with radiation. We have recently completed three trial with 100 patient each of testing the safety and efficacy of combing immunotherapy with radiation for lung cancer. This talk will educate the audience about the biological rationale of using immunotherapy with antigen release from radiation along with the most up to date data on where the field is at, along with new approaches for the future.
Title
THE ACCESS TO PRODUCE COMPATIBLE VIRAL VACCINES FOR INDIVIDUALITY

Name & Country
Tirasak Pasharawipas
Thailand

Abstract
With a thought of safety reason to prevent side effects, subunit viral vaccine becomes the major choice for manufacturing viral vaccine. However, many kinds of viral vaccines could not reach their accomplishment. The success to use subunit viral vaccine to prevent a particular viral infection is limit. This is different from the time when Cowpox virus was originally used for vaccination to prevent the smallpox epidemic over a thousand years ago in China and then more scientific approved by Edward Jenner over two century ago. However, there is a question why viral vaccines cannot be effective for everybody. Accordingly, we need to revise our knowledge and manipulate an alternative direction to produce viral vaccine. To prevent viral infection, a body must produce a protective antibody to prevent the particular viral agent to attach the viral receptor on a target cell.

Theoretically, adaptive immunity needs induction not only by a particular antigen but also our cellular molecule called major histocompatibility complex (MHC) to form a complex molecule with its appropriate epitope to activate a specific receptor of T cell. There are two classes of MHC molecules called class I and class II. MHC class I is required for inducing cytotoxic T cell while MHC class II is for helper T cell. Helper T cell plays a key role to induce an effective stage of acquired immunity including an antibody. To produce the viral specific antibody, MHC class II plays a key role to induce helper T cell and then B cell to synthesize a specific antibody. Since the MHC gene alleles are highly polymorphic so the possibility that individuals have the same gene alleles might be one in a million which, mostly, can be found in those who are an identical twin. Accordingly, a subunit viral vaccine, which contains a limit number of epitopes, would reduce a capacity of an antigen presenting cell, such as a dendritic cell, to process some epitopes to induce the particular helper T cell clones. Subsequently, in some people, the corresponding B cell clones cannot synthesize the antibody to neutralize the particular infectious viral agent. Accordingly, this presentation will present an approach to develop the viral vaccine for everybody.
APPLICATION OF SINGLE STRAND RNA AS ADJUVANT FOR HUMAN PAPILLOMA VIRUS VACCINE

Jae-Hwan Nam
Korea

Currently, the human papillomavirus (HPV) vaccine should be administered three times over a period of 6 months to obtain sufficient immunity. The HPV vaccine uses alum as an adjuvant to increase immunity. However, it usually induces a Th2 response, but not Th1 response, which is an insufficient cytotoxic T lymphocytes response. Therefore, in this study, we developed a novel RNA adjuvant, which is single-strand RNA. The plasmid (pCrPV-L1) including type 16 or 18 HPV capsid protein L1 genes under the internal ribosome entry site (IRES) of the cricket paralysis virus (CPV) intergenic region (IGR) was transcribed by T7 RNA polymerase. This type 16 or 18 HPV L1 RNA was treated into bone-marrow-derived dendrite cells (BMDV) cells, which are professional antigen-presenting cells. This RNA adjuvant increased inflammatory cytokines, IL-6, IL-12, TNF-α, and IFN-γ, in BMDC cell supernatants and activated BMDC cells similar to the positive control LPS and poly I:C, indicating that this RNA can function as an adjuvant. To confirm in vitro data, 10 types of HPV capsid protein (L1), which were expressed by insect cell system, were administered intramuscularly to mouse with alum and mixed RNA transcribed from pCrPV-L1 (types 16 and18) (called as RNA adjuvant group). This RNA adjuvant group showed higher IgG1 (indicated Th2 response) and IgG2a (indicated Th1 response) levels compared to 10 types of HPV L1 protein with alum (called as alum adjuvant group). Furthermore, the population of IFN-γ-secreting T cells from splenocytes of the RNA adjuvant group is about two to three times higher than the alum adjuvant group. In addition, the RNA adjuvant group showed higher neutralizing antibody titer than the alum adjuvant group. Taken together, RNA adjuvant may function synergistically with alum adjuvant by reducing the vaccine immunization schedule and antigen amount used.
**Title**
MEASLES INCIDENCE AND SECULAR TREND OVER THE LAST FIVE YEARS, PRE AND POST MASSIVE POPULATION BASED VACCINATION

**Name & Country**
Hamid Yahya. Hussain
Dubai, UAE

**Abstract**

Background: Measles is a highly contagious infection that affects about 20 million people a year, primarily in the developing areas of Africa and Asia. Vaccination has resulted in a 75% decrease in deaths from measles between 2000 and 2013 with about 85% of children globally being currently vaccinated. Objectives: To study measles incidence and trends along the last five years in Dubai, and to study the impact of population based mass immunization intervention on the level of incidence of measles in Dubai.

Methodology: Retrospective records review of the notifiable disease in Dubai (infectious Disease surveillance system) for retrieving secondary data for the year 2013-2014 on measles cases. The output of the mass population MMR vaccination national campaign during 2015 as preventive intervention tool was reviewed. In addition, a cohort of 3-18 years old population was followed for two successive years after mass population immunization campaign.

Results: Number of measles cases in the year 2013 was 38 cases among females and 74 cases among males, with a total of 112 cases. Numbers of students who are covered with measles vaccine during the national measles vaccination campaign, 2015, within their school was 162299 students. Number of measles cases has dropped after the campaign to 26 cases in 2016 and 8 cases in 2017.

Conclusion: Primary prevention intervention strategy proved to be highly effective in reducing measles incidence and cases towards reaching elimination and eradication status. Vaccination coverage significantly linked to cases reporting and identification among target population. Immunization coverage (routine, catch up and national campaign) needs to be maintained on sustainable performance to accelerate reductions of measles cases reporting on long term. Revising national immunization program performance should be always monitored through the cases reporting and disease incidence.
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<th>MATERNAL BOND SCIENTIFIC FINDINGS TO PREVENT CHILD ABUSE</th>
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| **Name & Country** | María Teresa Sotelo  
Mexico |
| **Abstract** | Derived from a meticulous research process, interviewing victimizing mothers, and correlating various medical fact-findings, it is resolved, that the origin of child abuse and homicide, takes place during gestation and lactation, when the mother fails to bond emotionally and conjugates depression or other mental disorder with social risk factors. Antenatal and postnatal timely detection of maternity lack of bond, the risk violence factors, as well, early evaluation of mental illness, are substantial to prevent the baby of violence. Filicide and child abuse is predictable and preventable, by timely alarm signal detection by reinforcing during pregnancy, birth moment, and lactation, the follow up the cases, help counselor assistance and the bonding stimulation, based on new cardio-neural promising research to timely stimulate the mother’s affective connection. |

**Biography**

Maria Teresa Sotelo, President and founder of the non-profit "Foundation En Pantalla Contra la Violencia Infantil". Twenty years of experience on research in various criminal and medical disciplines that delve into the origin of the child abuse and risk factors associated. She developed various initiatives of law, achieving the Mexican government had assumed and considered as the Edict of Law to protect infants from child abuse and abandonment. Pedagogue by profession, other studies in criminal psychology, and investigative journalism. Member of the National of Health Secretariat Commission for Child abused. Guest Member and founder of "Children Research" at the Instituto de Investigaciones Jurídicas, Autonomous University of Mexico. Author of two books, six documentary, five scientific publications.
Title
EFFECT OF CHLORHEXIDINE AND SODIUM HYPOCHLORITE ON STAPHYLOCOCCUS AUREUS BIOFILM

Name & Country
Wala A Abdallah
Sudan

Abstract
Biofilm is a matrix in which a microorganism encases in it and survive environmental stresses. It help the organisms to resist the antibiotics and disinfectant, chronic biofilm associated infection lead to significant increase in morbidity and mortality especially patient with indwelling medical devices. The objective of this research was to analyze the effectiveness of chlorhexidine, sodium hypochlorite and antimicrobial activity of methicillin and vancomycin against biofilm of isolated strains of Staphylococcus aureus isolated from different clinical samples. The results revealed that most biofilm strains were sensitive to vancomycin, some strains were sensitive some were moderate resist and some were resist to methicillin. In comparing different concentrations (0.3%, 0.2%, 0.15% and 0.075%) of chlorhexidine among time interval (1min, 3min and 5min) concentrations showed significant decrease in biofilm formation in association with time; P value (0.001, 0.001, 0.000, and 0.000 respectively). Different concentrations (5%, 4%, 2.5%, and 1.25%) of sodium hypochlorite also tested through the same time intervals; concentrations showed significant decrease in biofilm in association with time; P value (0.000, 0.000, 0.000 and 0.000 respectively). Conclusions and significance Staphylococcus aureus were sensitive, moderate resist and resist to both Vancomycin and Methicillin, both chlorhexidine and sodium hypochlorite were reduced the biofilm according to concentration and time of contact. Recommendation is to use chlorhexidine and sodium hypochlorite as disinfectant and antibiofilm for longer time.
PERSONALIZING CANCER TUMOR ANTIGENS

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

Immune system can react to cancer cells in two ways, by reacting against tumor-specific antigens, molecules which is unique to cancer cells or against tumor-associated antigens, molecules is expressed differently by cancer cells and normal cells. Immunity to carcinogen-induced tumors in mice is directed against the products of unique mutations of normal cellular genes. These mutant proteins are tumor-specific antigens. Tumors caused by viruses display viral antigens that serve as tumor antigens. Examples are the products of the E6and E7 genes of the human papillomavirus, the causative agent of cervical carcinoma, and EBNA-1. Most recently we have developed evidence for a powerful immunodominance effect that occurs between different tumor antigens and have identified what appears to be a unique mechanism by which at least some forms of immunotherapy induce tumor specific destruction.

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

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

Mark L. Bagarazzi has been Chief Medical Officer at Inovio Pharmaceuticals since 2010 with responsibility for clinical development, biologics manufacturing, regulatory affairs. He previously directed Worldwide Regulatory Affairs, Vaccines/Biologics at Merck where he was responsible for the licensure of RotaTeq and led development for ZOSTAVAX. He was faculty at Drexel College of Medicine and HIV/AIDS director at St. Christopher’s Hospital for Children. He lectures at Perelman School of Medicine at University of Pennsylvania and previously at Johns Hopkins University. He trained at St. Christopher’s Hospital for Children and completed his pediatric infectious diseases fellowship at the Children’s Hospital of Philadelphia.

VGX-3100 is an immunotherapy designed using SynCon approach to treat HPV-16 and HPV-18 infection and pre-cancerous lesions of the cervix (phase 3) and vulva (phase 2). The immunogenicity and efficacy of VGX-3100 is enabled by the CELLECTRA electroporation delivery system. When VGX-3100 is delivered with the CELLECTRA device it stimulates a specific immune response to HPV-16 and HPV-18 E6 and E7, to clear the infection and eliminate pre-cancerous cells. In a randomized, double-blind, placebo-controlled phase 2b study in 167 adult women with histologically documented HPV-16/18 cervical HSIL (CIN2/3), treatment with VGX-3100 resulted in a statistically significantly greater decrease in cervical HSIL and clearance of HPV infection vs. placebo. The most common side effect was injection site pain, and no serious adverse events were reported. The VGX-3100 approach which utilizes the patient’s own immune system to clear HPV-16 and HPV-18 infection and pre-cancerous lesions without the increased risks associated with surgery, such as loss of reproductive health and negative psychosocial impacts is now being evaluated in a global Phase 3 study. VGX-3100 has the potential to be the first approved treatment for HPV infection of the cervix and the first non-surgical treatment for pre-cancerous cervical lesions.
Bacteria, viruses, parasites and fungi that are resistant to drug cause 700,000 death each year. By 2050 superbugs inured to treatments could cause up to 10 million deaths annually and costs the global economy US$100 trillion. AMR (antimicrobial) resistance is regarded nowadays as a major threat to global public health. The issue is receiving high-level political attention (G7 and G20 in 2017 for first time). The list was drawn up in a bid to guide and promote research and development (R&D) of new antibiotics, as part of WHO’s efforts for AMR (27th Feb 2017) Resistance to antibiotics may arise in a population of susceptible bacteria by the accumulation of mutations (e.g. point mutations in DNA gyrase conferring resistance to quinolones) or by the acquisition of resistance genes that protect the cell against antibiotics. Antibiotic resistance genes can cause phenotypic resistance through a variety of mechanisms, including the enzymatic inactivation of the antibiotic, the modification of the antibiotic target and the prevention of the accumulation of lethal intracellular concentrations of the antibiotic through efflux pumps. Problem of resistance get worsened due declining number of new antibiotics and limited number of new classes direct research to look for alternatives. Additionally, antibiotics shape the ecology of the gut microbiota in profound ways, causing lasting changes to developing and mature microbiotas. The application of next-generation sequencing has enabled detailed views of the side effects these drugs have on commensal populations during treatment of infections. The human gut thus harbours a complex microbial ecosystem, which consists of hundreds of species, collectively termed the gut microbiota. The gut microbiota is relatively stable in healthy adults but the composition of the gut microbiota can change rapidly owing to dietary changes, illness and the use of antibiotics. Importantly, there is and evidence of existing communication between the central and the enteric nervous system, linking emotional and cognitive centers of the brain with peripheral intestinal functions. This interaction between microbiota appears to be bidirectional, namely through signaling from gut–microbiota to brain and from brain to gut-microbiota by means of neural, endocrine, immune, and humoral links. Negative impact on composition and functionality microbiota given existing immune cross-talk including “innate cell immunity training” impact host immune response capacities observed in recent research.imbalances in the gut microbiota can induce inflammation that is associated also with the pathogenesis of obesity, type 2 diabetes mellitus, and Alzheimer’s disease. Therefore in addition to the increased threat of resistance to antibiotics caused by inappropriate use of antibiotics and important side effects on microbiota, it is clear that overuse of broad-spectrum antibiotics must be quickly phased out in favour of more precise approaches and must be complemented by efficient methods to restore the microbiota after injury. Recent advances in the development of narrow–spectrum antivirulence compounds, coupled with a renewed interest in the use of probiotics, FMTs (fecal microbiota transplantation) and phage therapy along with thoughtful development of vaccines and monoclonal antibodies represents paths in multiple approach to tackle AMR considering preservation of microbiota. FMT working principle is to restore the microbiological environment in host intestine similarly as probiotic while administrating live microorganism to confer a health benefit on the host. For both there is a need for standardised clinical protocols to help translation in clinical wider use. Moreover microbiome therapeutics are seen as potential intervention to reduce carriage of resistant pathogens. One should note that vaccines like diphtheria and tetanus did not prompt resistance. In 1980 the smallpox vaccine had eradicated the naturally circulating virus worldwide without generating resistance. Additionally, introduction of live vaccines like measles and BCG has been associated with much larger reduction of morality than can be explained by the prevention of the targeted infections and recent research around LATV highlights importance of “off target” effects to be evaluated in depth. In conclusion, alternative directions considering strongly their role on host microbiota and immune system modulation should be strongly promoted while tackling issue of antibiotic resistance. High potential of vaccines to tackle antibiotic resistance respecting role of gut microbiota as host superorganism gain evidence.
THE OUR BODY ACTS AGAINST FACTS OF PHYSICS IN FEVER

K. M. Yacob, practicing physician in the field of healthcare in the state of Kerala in India for the last 29 years and very much interested in basic research. His field of interest is spread across the fever, inflammation and back pain. He is a writer. He already printed and published nine books in these subjects. He wrote hundreds of articles in various magazines. After scientific studies they have developed 8000 affirmative cross checking questions. Which can explain all queries related with fever.

According to the facts of physics, if temperature increases, thermal expansion of an object is positive it will expand and with decrease of temperature it will shrink. Pressure will increase due to increase of temperature.

On the contrary, during fever we can see blood vessels and skin are shrunk, pressure decreases, body shivers, sleep increases, motion decreases, inflammation increases, body pain increases, blood circulation decreases, dislike cold substances etc., In fever, the firing rate of Warm sensitive neurons decreases, and the firing rate of Cold sensitive neurons increases.

At the same time if we apply hotness from outside by thermal bag or if we drink hot water, our body acts according to the Facts of Physics- increase of temperature will also increase, expands blood vessels and skin, body sweats, motion will increase, inflammation will decrease, body pain will decrease, blood circulation will increase, like cold substances. During fever, why our body acts against Facts of Physics? when disease increases, pressure and temperature will decrease. Blood circulation will decrease due to decrease of pressure. If the essential temperature of the body is going out, essential temperature and pressure will further decrease. This will further endanger the life or action of organ. When disease increase, it is the sensible and discreet action of brain that tends to act against facts of physics to sustain life or protect organ. There is no way other than this for a sensible and discreet brain to protect the life or organ. We will get a clear answer if we find out the purpose of fever, sensible and discreet action of brain. No medical books clarify this one.

During fever, if the temperature of fever is not a surplus temperature or if it is not suppose to be eliminated from the body, the shrinking of skin and blood vessels, shivering of body, dislike towards cold substances etc are a protective covering of the body to increase blood circulation to important organs of the body it is against the facts of physics.
Title
DIRECT EVIDENCE OF VIRAL INFECTION AND MITOCHONDRIAL ALTERATIONS IN THE BRAIN OF FOETUSES AT HIGH RISK FOR SCHIZOPHRENIA

Name & Country
Segundo Mesa Castillo
Cuba

Abstract
There is increasing evidences that favor the prenatal beginning of schizophrenia. These evidences point toward intra-uterine environmental factors that act specifically during the second pregnancy trimester producing a direct damage of the brain of the fetus. The current available technology doesn't allow observing what is happening at cellular level since the human brain is not exposed to a direct analysis in that stage of the life in subjects at high risk of developing schizophrenia.

Methods: In 1977 we began a direct electron microscopic research of the brain of fetuses at high risk from schizophrenic mothers in order to finding differences at cellular level in relation to controls.

Results: In these studies we have observed within the nuclei of neurons the presence of complete and incomplete viral particles that reacted in positive form with antibodies to herpes simplex hominis type I [HSV1] virus, and mitochondria alterations.

Conclusion: The importance of these findings can have practical applications in the prevention of the illness keeping in mind its direct relation to the aetiology and physiopathology of schizophrenia. A study of the gametes or the amniotic fluid cells in women at risk of having a schizophrenic offspring is considered of being observed the same alterations that those observed previously in the cells of the brain of the studied foetuses, it would intend to these women in risk of having a schizophrenia descendant, previous information of the results, the voluntary medical interruption of the pregnancy or an early anti HSV1 viral treatment as preventive measure of the later development of the illness.