

# Advancing Vaccines in the Genomics Era

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## 1033 Attitudes towards the swine influenza vaccination of multi-nationality parents in Saudi Arabia

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In late March 2009, an outbreak of a respiratory illness later proved to be caused by novel swine-origin influenza A (H1N1) virus was identified in Mexico. In late December 2009, the number of laboratory-confirmed cases in Saudi Arabia was 15850, with 124 deaths. During this infection outbreak, it is important to study the concerns, knowledge, attitudes and behavior of the public. Such information can be crucial to the improvement of communication efforts by public health officials and clinicians. The aim of this study was to identify attitudes towards the swine influenza vaccination of multi-nationality parents in Saudi Arabia. A total of 900 survey sheets were distributed in 13 provinces of Saudi Arabia and 469 (52.1%) were completed. Of the total respondents, 122 (26%) were Saudi, 288 (61.4%) did not indicate their nationalities and 59 (12.6%) were other Arabs; 36 (61%) were Jordanian, 23 (39%) were Egyptian. Of the total respondents, 422 (90%) report that the swine influenza vaccination was not safe with fear of side effects believed to be the most likely reason as the survey sheet does not require a justification for the rejection and 47 (10%) report that the influenza vaccine was important. In a multivariate analysis, the following factors were important in choosing vaccinations, therefore, feeling at risk of influenza, and not using any vaccine alternatives, and that the vaccine is important for self and children's protection, were statistically important factors ( $P \leq 0.01$ ). Thus, efforts to increase the acceptance rates should take these factors in consideration.

## 1035 Recombinant Influenza Viruses as Vaccine Vectors against Infectious Diseases – Proof of Concept against *Trypanosoma cruzi*

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Recombinant viruses emerge as promising tools for testing heterologous prime-boost vaccination protocols. Reverse genetics technique allows manipulation of negative strand RNA viruses, such as Influenza, which arise in this context as interesting vaccine vectors. Chagas disease, caused by the protozoan *Trypanosoma cruzi*, is a good vaccine model since it has described susceptibilities in mice, and known immunodominant epitopes present in ASP2 protein, which elicits a strong protective CD8 response. We generated and evaluated recombinant influenza viruses carrying sequences coding for polypeptides corresponding to different portions of ASP2. Those recombinant viruses were used in heterologous prime-boost regimen in sequential immunization with recombinant adenovirus encoding ASP2. We found a strong specific anti-ASP2 cellular immune response in vaccinated mice that was protective against infection with Y strain in susceptible C3H/He mice. The heterologous prime-boost protocol elicited more CD8+ T cells specific for the immunodominant epitope expressing polyfunctional effector profile. In a model of chronic infection using Colombian strain-infected C57BL/6 mice with signs of heart injury, we tested this regimen. The same improvement of Immunodominance and polyfunctional CD8 response was detected, even though vaccination did not reverse cardiomyopathy. As perspective, combined drug therapy with vaccination regimen will be tested. Overall, we demonstrated the usefulness of influenza viruses as vaccine vectors against Chagas disease. Grants: CNPq, FAPEMIG, INCTV

## 1034 Identification of novel physiological effect of oral administration of ferulic acid on hepatic gene expression in stroke-prone spontaneously hypertensive rats

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Ferulic acid (FA, 4-hydroxy-3-methoxycinnamic acid) is the most abundant hydroxycinnamic acid in the plant kingdom. FA is essentially found in the bran of grain and hence it is a suitable raw material for the production of FA. FA is known to be a high antioxidant, an effective scavenger of free radicals, and it lowers blood glucose level in streptozotocin-induced diabetic rats and blood pressure (BP) in spontaneously hypertensive rats. This study was aimed to investigate the effects of single oral administration of FA to reduce BP and improve lipid levels in stroke-prone spontaneously hypertensive rats (SHRSP). Male 12-week-old of SHRSP was administered FA or distilled water (control) via a gastric tube. The BP was measured before and 1, 2, 4, and 6 h after the administration. After 5 days, the rats were administered again with the same procedure and were sacrificed 2 h after the administration. The DNA microarray technique was used to identify novel physiological effect of FA on hepatic gene expression. Hypotensive effect was observed after 1, 2 and 4 h, and back to the basal condition after 6 h; with the lowest value at 2 h. Decrease of the angiotensin-1 converting enzyme (ACE) activity in plasma corresponded well to the reduction of BP 2 h after the oral administration. Plasma total cholesterol and triglyceride levels were lower after 2 h the administration. The mRNA expression of genes involved in the lipid, glucose, and drug metabolisms were down-regulated in FA group. These results suggested that oral administration of FA appears to have a beneficial activity to improve hypertension and hyperlipidemia.

## 1036 Immunological analysis of cutaneous melanoma patients treated with CSF470 therapeutic vaccine in a Phase II-III trial.

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Cutaneous melanoma (CM) incidence is increasing very fast and due to the lack of effective treatments, the development of new therapies is intensively searched. We have developed the therapeutic vaccine CSF470, composed of allogeneic irradiated CM cells plus BCG and GM-CSF, currently being tested vs IFN- $\alpha$ 2b in a phase II-III trial on stage IIB, IIC, III CM patients (NCT01729663). In an effort to decipher immunologic events on the afferent and efferent arms of the immune response associated with CSF470 treatment, we analysed *in situ* and peripheral immune status on patients during vaccination. As an example, we present here two clinical cases. Patient RMD had a biopsy of the vaccination site 45 days after inoculation. We observed an inflammatory response, with CD11c<sup>+</sup> dendritic cells (DC) isolated or conforming dense structures in direct contact with melanoma Ag deposits, surrounded by CD8+, CD4+ and B lymphocytes. Patient MBB, at the end of the two-year study, developed a s.c. metastasis, in which brisk infiltration by CD8+ and CD4+ cells with cytolytic activity on tumor cells was observed. No remarkable changes in peripheral blood CD4+, CD8+, Tregs and NK cells were observed in the same patient. These results suggest that CSF470 vaccine recruits antigen presenting cells to the vaccination site, where tumor Ags are deposited and directly contact CD8+ and CD4+ T cells, probably initiating the antitumor immune response. In one of the vaccinated patients, we evidenced the presence of tumor cytolytic CD8+ T cells in the tumor.

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