

# Cuban Research in Current International Journals

The following selection—alphabetical by title—reflects Cuban medical publishing in international journals over the last quarter on an array of topics. Links to these journal articles may be found at [www.medicc.org/mediccreview](http://www.medicc.org/mediccreview).

**A method to study global spatial patterns related to sensory perception in scalp EEG.** Ruiz Y, Pockett S, Freeman WJ, González E, Li G. *J Neurosci Methods*. 2010 Aug 15;191(1):110–8.

Prior studies of multichannel ECoG from animals showed that beta and gamma oscillations carried perceptual information in both local and global spatial patterns of amplitude modulation, when the subjects were trained to discriminate conditioned stimuli (CS). Here the hypothesis was tested that similar patterns could be found in the scalp EEG human subjects trained to discriminate simultaneous visual-auditory CS. Signals were continuously recorded from 64 equispaced scalp electrodes and band-pass filtered. The Hilbert transform gave the analytic phase, which segmented the EEG into temporal frames, and the analytic amplitude, which expressed the pattern in each frame as a feature vector. Methods applied to the ECoG were adapted to the EEG for systematic search of the beta-gamma spectrum, the time period after CS onset, and the scalp surface to locate patterns that could be classified with respect to type of CS. Spatial patterns of EEG amplitude modulation were found from all subjects that could be classified with respect to stimulus combination type significantly above chance levels. The patterns were found in the beta range (15–22Hz) but not in the gamma range. They occurred in three short bursts following CS onset. They were non-local, occupying the entire array. Our results suggest that the scalp EEG can yield information about the timing of episodically synchronized brain activity in higher cognitive function, so that future studies in brain-computer interfacing can be better focused. Our methods may be most valuable for analyzing data from dense arrays with very high spatial and temporal sampling rates.

**Antioxidant and immunomodulatory effects of Viusid in patients with chronic hepatitis C.** Gomez EV, Perez YM, Sanchez HV, Forment GR, Soler EA, Bertot LC, et al. *World J Gastroenterol*. 2010 Jun 7;16(21):2638–47.

**Aim** To investigate the efficacy of Viusid, a nutritional supplement, as an antioxidant and an immunomodulator in patients with chronic hepatitis C. **Methods** Sixty patients with chronic hepatitis C who were non-responders to standard antiviral treatment were randomly assigned to receive Viusid (3 sachets daily,  $n = 30$ ) or placebo ( $n = 30$ ) for 24 wk. The primary outcome was the change in serum malondialdehyde and 4-hydroxyalkenals (lipid

peroxidation products). Secondary outcomes were changes in serum tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interferon- $\gamma$  (IFN- $\gamma$ ) and interleukin-10 (IL-10). **Results** Statistically significant reductions in serum 4-hydroxyalkenals and malondialdehyde levels were observed in both groups in comparison with pretreatment values, but the patients who received Viusid showed a more marked reduction as compared with the control group ( $P = 0.001$ ). TNF- $\alpha$  levels significantly increased from 6.9 to 16.2 pg/mL ( $P < 0.01$ ) in the patients who received placebo in comparison with almost unchanged levels, from 6.6 to 7.1 pg/mL ( $P = 0.26$ ), in the patients treated with Viusid ( $P = 0.001$ ). In addition, IL-10 levels were markedly increased in the patients treated with Viusid (from 2.6 to 8.3 pg/mL,  $P = 0.04$ ) in contrast to the patients assigned to placebo (from 2.8 to 4.1 pg/mL,  $P = 0.09$ ) ( $P = 0.01$ ). Likewise, the administration of Viusid markedly increased mean IFN- $\gamma$  levels from 1.92 to 2.89 pg/mL ( $P < 0.001$ ) in comparison with a reduction in mean levels from 1.80 to 1.68 pg/mL ( $P = 0.70$ ) in the placebo group ( $P < 0.0001$ ). Viusid administration was well tolerated. **Conclusion** Our results indicate that treatment with Viusid leads to a notable improvement of oxidative stress and immunological parameters in patients with chronic hepatitis C.

**A program for the reduction of occupational injuries and changes in safety culture among stevedores at Port of Havana, Cuba.** Robaina C, Partanen TJ, Ávila I. *Int J Occup Environ Health*. 2010 Jul–Sep;16(3):312–9.

This study describes the structure, process, and impact of a comprehensive sixteen-month safety enhancement program among stevedores at the Port of Havana, Cuba. Our objective was to reduce occupational injury risk and improve safety conditions by enhancing hazard knowledge and identification as well as improving safety behavior. The target group for the training program consisted of 185 male stevedores in one port terminal. A comparison group of 105 male stevedores was included from another terminal where the program was not implemented. Other personnel were included in the program. The training covered a number of safety procedures and used various training methods. As contrasted with the comparison group, injury incidence decreased in the intervention group, accompanied by significant improvements in safety knowledge and behavior and injury hazard identification. The practices of the program led to safety enhancements in the port and are being considered for adoption in other ports in Cuba.

**Asymptomatic dengue infection in a Cuban population confirms the protective role of the RR variant of the Fc $\gamma$ RIIIa polymorphism.** García G, Sierra B, Pérez AB, Aguirre E, Rosado I, González N, et al. *Am J Trop Med Hyg*. 2010 Jun;82(6):1153–6.

The role of human Fc $\gamma$  receptors (Fc $\gamma$ R) has been recognized considerably over the last years. These receptors vary in their affinity for IgG subclasses and the intracellular signals elicited by them. Allelic variants of Fc $\gamma$ R genes may influence the biological phagocyte activity, accounting for an inherited pre-disposition to disease. The specific Fc $\gamma$ RIIIa (CD32) contains a polymorphic variant (H/R131) that has been associated to a reduced risk for developing dengue hemorrhagic fever (DHF). Here, we investigated the role of this polymorphism in a very well-characterized group of Cuban individuals with antecedents of DHF, dengue fever (DF), or subclinical dengue infection. The HH131 genotype was significantly associated with dengue disease, either DF ( $*P = 0.016$ ; odds ratio = 4.425; 95% confidence interval = 1.10–20.52) or DHF ( $P = 0.00018$ ; odds ratio = 10.56; 95% confidence interval = 2.33–54.64) with respect to the subclinical infection.

**Evaluation of colorimetric methods using nicotinamide for rapid detection of pyrazinamide resistance in Mycobacterium tuberculosis.** Mirabal NC, Yzquierdo SL, Lemus D, Madruga M, Milián Y, Echemendía M, et al. *J Clin Microbiol*. 2010 Aug;48(8):2729–33.

The direct detection of pyrazinamide resistance in Mycobacterium tuberculosis is sufficiently difficult so that many laboratories don't attempt it. Most pyrazinamide resistance is caused by mutations that inactivate the pyrazinamidase enzyme needed to convert the prodrug pyrazinamide to its active form. We evaluated two newer and simpler methods to assess pyrazinamidase activity—the nitrate reductase and malachite green microtube assays—using nicotinamide in place of pyrazinamide. A total of 102 strains were tested by these methods and the results compared with those obtained by the classic Wayne assay. Mutations in the *pncA* gene were identified by sequencing the *pncA* gene from all isolates in which pyrazinamide-resistance was detected by any of the three methods. Both the nitrate reductase and malachite green microtube assays showed sensitivities of 93.75% and specificities of 97.67%. Mutations in the *pncA* gene were found in 14 of 16 strains that were pyrazinamide resistant, and in 1 of 4 strains that were sensitive by the Wayne assay. Both of

these simple methods, used with nicotinamide, are promising and inexpensive alternatives for the rapid detection of pyrazinamide resistance in limited-resource countries.

**Ictal extension (dorsiflexion) of the toes in a patient with temporal lobe epilepsy: A new ictal lateralizing sign.** Machado RA, Mila RA. *Epilepsy Behav.* 2010 Aug;18(4):481–4.

Neurologists have analyzed the clinical behaviors that occur during seizures for many years. Several ictal behaviors have been defined in temporal lobe epilepsy (TLE). Ictal behaviors are especially important in the evaluation of candidates for epilepsy surgery. We propose a new ictal lateralizing sign originating from the nondominant hemisphere: extension (dorsiflexion) of the toes (Babinski's, Chaddock's, and Moniz' signs). Our patient is a 16-year-old woman. Her epileptogenic foci were localized to the right neocortical temporal region after noninvasive presurgical investigations. Cranial MRI revealed a right insular lesion compatible with focal cortical dysplasia or cortical tumor. We observed progressive movement of the left leg and, when the patient touched the lateral aspect of the foot to the bed, dorsiflexion of the great toe (Babinski's sign). In other seizures, the patient started a progressive movement of the left leg, rubbing the external border of the left foot on the bed and provoking dorsiflexion of the great toe (Chaddock's sign). The Brissaud reflex component was also observed when the movement was accompanied by internal rotation of the leg and recruitment of the tensor fascia lata, making dorsiflexion more likely to be a reflex response and not voluntary. We also observed forceful passive plantar flexion at the ankle in association with dorsiflexion of the great toe (Moniz' sign). All of these signs were contralateral to ictal seizure onset and to the cerebral epileptogenic lesion. These signs may occur as a result of ictal activation of a specific brain region in this hemisphere.

**Induction of  $\gamma$ -H2AX foci in human exfoliated buccal cells after in vitro exposure to ionising radiation.** González JE, Roch-Lefèvre SH, Mandina T, García O, Roy L. *Int J Radiat Biol.* 2010 Sep;86(9):752–9.

**Purpose** To test the  $\gamma$ -H2AX (Histone 2AX phosphorylation of serine 139) foci assay for the detection of ionising radiation-induced DNA damage in buccal exfoliated cells. **Materials and methods** Buccal mucosa cells from five individuals (three females, two males, aged 26–47 years) were exposed to 0, 0.5, 1, 2 and 4 Gy of gamma-rays. DNA damage and DNA damage removal were measured using the  $\gamma$ -H2AX foci assay. Lymphocytes from one donor and the nuclear antigen H2B were used as a positive control to test the staining protocol. **Results** In the absence of radiation exposure, no

significant differences for both H2B and  $\gamma$ -H2AX signals were detected when comparing buccal cells and lymphocytes. The  $\gamma$ -H2AX foci rate per cell in non-irradiated buccal cells was  $0.08 \pm 0.02$ . The number of  $\gamma$ -H2AX foci increased linearly with ionising radiation dose in the interval from 0–4 Gy, and reached a foci rate per cell of  $0.82 \pm 0.22$  at 4 Gy. Incubation experiments after in vitro gamma irradiation revealed that the number of  $\gamma$ -H2AX foci did not show a significant decrease 5 h post exposure under the experimental conditions used. **Conclusion** Data suggest that it is possible to apply the  $\gamma$ -H2AX foci assay for the detection of ionising radiation-induced DNA damage in buccal exfoliated cells. The low removal of ionising radiation induced  $\gamma$ -H2AX foci in buccal cells is a potential advantage for a biological dosimetry application.

**Large-scale application of highly-diluted bacteria for Leptospirosis epidemic control.** Bracho G, Varela E, Fernández R, Ordaz B, Marzoa N, Menéndez J, et al. *Homeopathy.* 2010 Jul;99(3):156–66.

**Background** Leptospirosis is a zoonotic disease of major importance in the tropics where the incidence peaks in rainy seasons. Natural disasters represent a big challenge to Leptospirosis prevention strategies especially in endemic regions. Vaccination is an effective option but of reduced effectiveness in emergency situations. Homeoprophylactic interventions might help to control epidemics by using highly-diluted pathogens to induce protection in a short time scale. We report the results of a very large-scale homeoprophylaxis (HP) intervention against Leptospirosis in a dangerous epidemic situation in three provinces of Cuba in 2007. **Methods** Forecast models were used to estimate possible trends of disease incidence. A homeoprophylactic formulation was prepared from dilutions of four circulating strains of Leptospirosis. This formulation was administered orally to 2.3 million persons at high risk in an epidemic in a region affected by natural disasters. The data from surveillance were used to measure the impact of the intervention by comparing with historical trends and non-intervention regions. **Results** After the homeoprophylactic intervention a significant decrease of the disease incidence was observed in the intervention regions. No such modifications were observed in non-intervention regions. In the intervention region the incidence of Leptospirosis fell below the historic median. This observation was independent of rainfall. **Conclusions** The homeoprophylactic approach was associated with a large reduction of disease incidence and control of the epidemic. The results suggest the use of HP as a feasible tool for epidemic control, further research is warranted.

**MCP-1 and MIP-1 $\alpha$  expression in a model resembling early immune response to dengue.** Sierra B, Pérez AB, Vogt K, García G, Schmolke K, Aguirre E, et al. *Cytokine.* 2010 Jul 21. [Epub ahead of print]

Dengue virus has become endemic in most tropical urban areas throughout the world, and DHF has appeared concomitantly with this expansion. The intensity of dengue virus replication during the early stages of infection could determine clinical outcomes; therefore, it is important to understand the impact of dengue virus infection on the earliest immune defense against microbial infection, which also strongly regulates the adaptive immune responses. This study was aimed at evaluating the expression of the CC-chemokines MIP-1 $\alpha$ /CCL3 and MCP-1/CCL2 in peripheral blood leukocytes using an *ex vivo* model resembling dengue infection *in vivo*, in subjects with a well characterized dengue immune background, due to the exceptional Cuban epidemiological situation in dengue. The expression of IFN $\gamma$ , TNF $\alpha$  and IL10 was also evaluated, giving insight about the role of MCP-1 and MIP-1 $\alpha$  in the interplay between innate and adaptive immunity. From individuals with different dengue immune background after dengue virus challenge, increased and different expression of the chemokines and cytokines studied was verified in peripheral blood mononuclear cells, thus demonstrating that the previous immunity to a dengue virus serotype has a strong influence on the early immune response after dengue re-infection.

**Modeling secondary level of HIV contact tracing: its impact on HIV intervention in Cuba.** Hsieh YH, Wang YS, de Arazoza H, Lounes R. *BMC Infect Dis.* 2010 Jul 1;10:194.

**Background** Universal HIV testing/treatment program has currently been suggested and debated as a useful strategy for elimination of HIV epidemic in Africa, although not without practical issues regarding the costs and feasibility of a fully implemented program. **Methods** A mathematical model is proposed which considers two levels of detection of HIV-infectives through contact tracing of known infectives in addition to detections through other means such as random screening. Simulations based on Cuban contact tracing data were performed to ascertain the potential impact of the different levels of contact tracing. **Results** Simulation studies illustrate that: (1) contact tracing is an important intervention measure which, while less effective than random screening, is perhaps less costly and hence ideal for large-scale intervention programs in developing countries with less resources; (2) the secondary level of contact tracing could significantly change the basic disease transmission dynamics, depending on the parameter values; (3) the prevalence of the epidemic at the time of implementation of contact tracing program might be a crucial factor in determining whether the measure will be effective in preventing disease infections and its eventual eradication. **Conclusions** Our results indicate that contact tracing for detection of HIV infectives could be suitably used to remedy inadequacies in a universal HIV testing program when designing timely and effective intervention measures.

**Reibergram of intrathecal synthesis of C4 in patients with eosinophilic meningitis caused by *Angiostrongylus cantonensis*.** Padilla-Docal B, Dorta-Contreras AJ, Bu-Coifu-Fanego R, Rodríguez-Rey A, Gutiérrez-Hernández JC, de Paula-Almeida SO. *Am J Trop Med Hyg.* 2010 Jun;82(6):1094–8.

*Angiostrongylus cantonensis* produces eosinophilic meningitis in humans and is endemic in Thailand, Taiwan, China, and the Caribbean region. During infection with this parasite, it is important to know if the complement system may be activated by the classical or lectin pathway. Cerebrospinal fluid and serum samples from 20 patients with meningitic angiostrongyliasis were used to quantify C4 levels and albumin. Results were plotted on a C4 CSF/serum quotient diagram or Reibergram. Twelve patients showed intrathecal synthesis of C4. Antibody-dependent complement cytotoxicity should be considered as a possible mechanism that destroys third-

stage larvae of this helminth in cerebrospinal fluid of affected patients.

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**Relationship of type 1 diabetes to ancestral proportions and HLA DR/DQ alleles in a sample of the admixed Cuban population.** Díaz-Horta O, Cintado A, Fernández-de-Cossio ME, Nazabal M, Ferrer A, Roca J, et al. *Ann Hum Biol.* 2010 Jun 22. [Epub ahead of print]

**Background** Incidence of type 1 diabetes varies widely around the world, probably due to ethnic differences across populations among other factors. **Aims** To determine whether there is an association between disease and ancestry proportions; and to control disease-HLA associations for possible confounding by admixture or population stratification. **Subjects and methods** 100 cases and 129 controls participated in the study. Ancestry informative markers, which have considerable differences in frequency between European,

West African and Native American populations were used. Type 1 diabetes associated HLA susceptibility/protection alleles were ascertained by PCR using specific primers. Statistical analyses were conducted using STRUCTURE 2.1, ADMIXMAP 3.7, SPSS 16.0 and STRAT 1.0 packages. **Results** The results of logistic regression implemented in ADMIXMAP 3.7 indicated that European ancestry was associated with type 1 diabetes mellitus with an odds ratio of 5.7 corresponding to one unit change in European admixture proportion. Association was found between HLA alleles and disease, DQA1\*0501, \*0301 DQB1\*0201 and DRB1\*0301, \*0401 being susceptibility alleles and DRB1\*1501, DQA1\*0102/3 and DQB1\*0602 being protective alleles. **Conclusions** We found an association between European ancestry and type 1 diabetes in our sample, indicating the contribution of ethnicity to incidence differences. Previously reported associations of HLA DR/DQ alleles with disease are confirmed for the admixed Cuban population. 