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.

Altered oxidative stress indexes related to disease progression marker in human immunodeficiency virus infected patients with antiretroviral therapy. Gil L, Tarinas A, Hernández D, Riverón BV, Pérez D, Tápanes R, et al. Biomed Pharmacother. 2010 Sep 25. [Epub ahead of print]

Background It is generally accepted that oxidative stress (OS) is implicated in immunological and metabolic abnormalities during HIV infection. The acting mechanism used by Highly Active Antiretroviral Therapy (HAART) comes to add metabolic alterations. **Method** This is an observational study assessing the effect of two HAART combinations on redox indicators and on progression markers of disease. A cohort of 84 healthy and 84 HIV+ subjects were followed for 6 months. Fifty-six HIV+ subjects were distributed in group I (AZT, 3TC, IND) and group II (D4T, 3TC, NEV) according to drug combination. Peroxidation potential (PP), glutathione (GSH), malondialdehyde (MDA), total hydroperoxides (HPO), superoxide dismutase (SOD), catalase (CAT), advanced oxidation protein products (AOPP), percent of DNA fragmentation (% FDNA), CD4+, CD38+, CD95+ T lymphocytes subsets, viral load and body mass index (BMI) were measured at baseline and at 6 months. **Results** After HAART started, CAT values for both groups receiving treatment did not showed [*sic*] significant difference. For group II, all other OS indexes were significantly higher than those for group I and the HIV+ not treated group ($p<0.05$), except for GSH values in group II ($p<0.05$) which was lower than group I values. These data suggest poor prognostic for group II. Not significant differences were found between treatment groups respect CD4+, CD8+, CD38+, CD95+ T cell subset count, viral load and BMI. **Conclusions** The findings suggest that increased OS occurs additionally to persistent redox imbalance associated to HIV infection during apparently successfully HAART. This conclusion does not only underline HAART associated toxicity but it may be also methodologically important for the follow-up of further clinical studies.

Chronic Vaccination with a Therapeutic EGF-Based Cancer Vaccine: A Review of Patients Receiving Long Lasting Treatment. González G, Crombet T, Lage A. Curr Cancer Drug Targets. 2010 Nov 10. [Epub ahead of print]

Therapeutic vaccines continue to be one of the most active fields in cancer research. However, despite clear evidence of antitumor effect in laboratory animals, and despite the ability of current vaccine candidates to elicit tumor specific antibodies and T-cells in humans, objective responses in the clinical trials are rare. The role of therapeutic vaccines in advanced cancer patients, if any, would be to decrease the rate of disease progression and to increase survival and quality of life. Due to the redundant regulatory loops contracting the immune response to antigens that cannot be eliminated, such a role would require chronic vaccination, which is at first sight at odds with the classic experience of vaccinology. During the last decade our team has been developing a therapeutic vaccine for advanced lung cancer, which consists in human recombinant Epidermal Growth Factor (EGF) chemically conjugated to a carrier protein from Neisseria meningitides. Several clinical trials have been carried out, showing increase in anti-EGF antibody titers, decrease in plasma EGF concentration and survival advantage in vaccinated patients. In the present paper we review data from 58 patients who were vaccinated monthly for more than one or two years. Long term vaccination was feasible and safe, and there was no evidence of cumulative toxicity. Patients kept high anti-EGF antibody titers during all the time of vaccination, without evidence of immune response exhaustion. Continued vaccination increased the probability to get a high antibody response, which has been previously shown to be, in turn, associated with a better survival. Observations done in this series of patients suggest that long term therapeutic vaccination is a feasible strategy, worth to be further explored in the aim of transforming advanced cancer into a chronic disease.

Detection of Markers of Cardiovascular and Renal Risk in Cuba: Isle of Youth Study (ISYS). Herrera R, Almaguer M, Chipi J, Toirac X, Martínez O, Castellanos O, et al. Nephron Clin Pract. 2010 Nov 12;117(4):c353–c62.

Chronic vascular diseases constitute a growing global health problem. **Objectives** To (a) determine marker positivity for renovascular damage in the total adult population of the Isle of Youth, Cuba; (b) describe marker association with common risk factors for renal and related chronic vascular conditions, and (c) identify best predictors of renovascular damage. **Methods** Previous informed consent was obtained, the population studied was 55,646, and subjects were aged ≥20 years. Blood pressure, weight and height were measured and a questionnaire applied. Urine markers for renovascular damage (hematuria, proteinuria and microalbuminuria) were also determined. **Results** Positive markers were detected in 21.3%: hematuria (12.6%), microalbuminuria (6.8%), proteinuria (0.9%), and proteinuria + hematuria (0.9%). Risk factors were highly prevalent: 15.1% were aged ≥60 years; 32.3% overweight, 13.9% obese, and 25.1% smokers. Prevalence of high blood pressure (30%), diabetes mellitus (5.4%) and cardiovascular disease (5%) was also high, while cerebrovascular disease registered 0.9%. Markers were more prevalent in older people and in those suffering from diabetes mellitus, high blood pressure, cardiovascular and cerebrovascular disease, overweight or obesity. Risk factor regression tree analysis identified hypertension as the best predictor of renovascular damage. **Conclusions** Adult population-wide screening revealed hidden morbidity and permitted better risk stratification. Results serve to inform community-based multidisciplinary and intersectoral disease prevention and management.

Early Interferon-Based Treatment After Detection of Persistent Hepatitis C Virus Infection: A Critical Decision. Amador-Cañizares Y, Dueñas-Carrera S. J Interferon Cytokine Res. 2010 Nov;30(11):817–24.

Approximately 170 million people are infected with the hepatitis C virus (HCV) worldwide. Infection with this pathogen is persistent in more than 80% of cases, frequently developing severe forms of liver damage such as cirrhosis and hepatocellular carcinoma. No preventive vaccine is available against HCV, and current treatment based on the combination of pegylated interferon and ribavirin is effective in ~55% of patients infected with genotype 1, the most prevalent genotype. This review analyzes several factors influencing the achievement of a sustained virological response, namely undetectable HCV RNA at 6 months after conclusion of therapy. Particularly, the relevant issue of age and duration of infection is discussed in detail. Indeed, the final decision for starting treatment should be a case-by-case point. However, the cost-benefit analysis seems to indicate that in patients who are motivated and without contraindications, starting the treatment as early as possible is probably the best choice for success.

HCMV seroprevalence and associated risk factors in pregnant women, Havana City, 2007 to 2008. Correa CB, Kourí V, Verdasquera D, Martínez PA, Álvarez A, Alemán Y, et al. Prenat Diagn. 2010 Sep;30(9):888–92.

Objective To prenatally identify pregnant women at risk of developing congenital infection due to human cytomegalovirus (HCMV). **Methods** One thousand one hundred and thirty-one pregnant women from three municipalities from Havana City were serologically screened for HCMV infec-

tion (IgM/IgG, IgG avidity) from January 2007 to January 2008. Demographical, epidemiological, and clinical variables were correlated to serologic status to identify predictors of seroconversion in pregnancy. **Results** The majority of women were seropositive to HCMV (92.6%); 27 women (2.4%) developed HCMV active infection during pregnancy, defined by the detection of IgG+ and IgM+ (7 women), IgM+ and IgG- (2 women), and IgG seroconversion (18 women). Susceptibility of active HCMV infection during pregnancy was associated with maternal age < 20 years and nulligravidity. Primary infection was detected in 20 pregnant women (1.8%), whereas 7 patients (0.6%) had active non-primary infection. **Conclusion** Although pregnant women in Cuba have high seroprevalence rates for HCMV, those younger than 20 years and nulligravidae are at risk of acquiring infection during pregnancy.

Heart rate variability in type 2 spinocerebellar ataxia. Montes-Brown J, Sánchez-Cruz G, García AM, Báez ME, Velázquez-Pérez L. Acta Neurol Scand. 2010 Nov;122(5):329–35.

Objectives To explore cardiovascular autonomic regulation in Spinocerebellar ataxia type 2 (SCA2) patients, using heart rate variability (HRV) analysis and neurophysiologic autonomic reflex tests, and determine relations and causal related factors of dysautonomia in SCA2. **Materials and Methods** Heart rate variability indices for 5 min series of RR intervals were analyzed in 97 SCA2 patients, assessed quantitatively for somatic and autonomic nervous system complaints applying the International Cooperative Ataxia Rating Scale and Scales for Outcomes in Parkinson's disease (SCOPA-AUT), respectively. Autonomic testing included: resting control, standing, Valsalva maneuver and deep breathing. **Results** Mean RR, long- and short-term variability indices and spectral density power (LF, HF) indices were lower in the patients group, whereas LF/HF ratio and LF (nu) were higher. Highly [*sic*] differences between groups were observed for seven diagnostic autonomic test indices. Significant correlations were found between different clinical and demographic indices and between clinical indices and some HRV indices. **Conclusions** We confirm the presence of cardiovascular autonomic dysfunction in a large group of SCA2 patients.

Immunogenicity and safety of a NeuGcGM3 based cancer vaccine: Results from a controlled study in metastatic breast cancer patients. Mulens V, de la Torre A, Marinello P, Rodríguez R, Cardoso J, Díaz R, et al. Hum Vaccin. 2010 Sep 14;6(9):736–44.

Increased levels of NeuGc-containing gangliosides have been described in human breast cancer. A controlled Phase II clinical trial was conducted in patients with metastatic breast cancer to evaluate immunogenicity, safety and to identify evidences of biological activity of a cancer vaccine composed by NeuGcGM3 in a proteoliposome of *Neisseria meningitidis* together with Montanide ISA 51 as adjuvant. After first line chemotherapy, 79 women were randomized 1:1 to receive the vaccine candidate or best supportive care. All patients achieved at least stable disease to the first line therapy for the metastatic condition. Treatment consisted on 5 vaccine doses every 2 weeks and then, monthly re-immunization to complete 15 doses. Vaccination with the NeuGcGM3 based vaccine was safe and the most frequent adverse events consisted on injection site reactions, fever, arthralgia and chills. The vaccine was immunogenic and a sustained increase of both IgG and IgM antibody titers against NGcGM3 was observed after the second vaccination month. Antibodies were able to recognize the NeuGcGM3$^+$ murine tumor cell line L1210 and the myeloma cell line P3X63. Humoral response was specific since vaccination did not result in Neu-Acetyl GM3 or GM2-antibody response. Hyperimmune sera from vaccinated patients were able to prevent the NeuGcGM3 mediated CD4 down-modulation on T lymphocytes. In the intent to treat analysis, there was a trend toward a survival advantage for the vaccine group and this effect was significant for women bearing non-visceral metastasis. Two phase III clinical studies with this vaccine candidate are ongoing.

Influence of maternal redox status on birth weight. Osorio JC, Cruz E, Milanés M, Ramírez Y, Sierra M, Cruz M, et al. Reprod Toxicol. 2010 Oct 8. [Epub ahead of print]

The aim of this study was to determine the influence that maternal redox status, between 30 and 36 weeks of healthy human pregnancy, has on birth weight. Ferric reducing potential (FRP), extracellular superoxide dismutase (ecSOD) activity and erythrocyte reduced glutathione (eGSH) concentration were measured as antioxidant indicators, and serum malondialdehyde (MDA) concentration as a lipoperoxidation indicator. Consumption of dietary micronutrients with antioxidant capacity was recorded. We observed a direct correlation between birth weight and ecSOD activity and eGSH concentration. An interaction between eGSH with FRP and serum ecSOD activity also correlated directly with birth weight. Other correlating factors included maternal thiamine consumption and interactions between vitamins C and E and carotenoids and vitamin E intake. These findings support the notion that antioxidant status has a positive influence on birth weight.

Kaposi's sarcoma-associated herpes virus load in asymptomatic contacts of Cuban epidemic KS patients. Kourí V, Martínez PA, Blanco O, Capó V, Rodríguez ME, Dovigny MD, et al. Arch Virol. 2010 Dec;155(12):1971–6.

To evaluate the pathogenic mechanisms and transmission routes involved in KSHV infection in 22 Cuban individuals who maintained close contact with epidemic KS patients, real-time PCR was used to quantify KSHV-DNA in clinical samples of plasma, saliva and peripheral blood mononuclear cells (PBMC). KSHV-DNA was detected in 72.7% (16/22) of the contacts. The highest levels of KSHV load were detected in saliva, followed by PBMC (average log copies/100 ng DNA = 1.28 and 1.12), while significantly lower levels were detected in plasma (average log copies/ml = 0.37). Two of three intra-domiciliary and two serodiscordant sexual contacts of AIDS-KS patients were infected with KSHV. The rate of KSHV-DNA detection in saliva and PBMC samples in men who have sex with men (MSM) was significantly higher than in heterosexuals (HT) (p=0.014). MSM were more likely to harbor KSHV-DNA in saliva when compared with HT individuals (OR 4.33; 95% CI 1.117–16.8). These results emphasize that, in Cuba, KSHV horizontal transmission through saliva may occur, although homosexual behavior may predispose an individual to KSHV acquisition. Even in the absence of disease, KSHV could cause an asymptomatic systemic infection in individuals who maintain close contact with AIDS-KS patients.

Kinetics of dengue virus NS1 protein in dengue 4-confirmed adult patients. Vázquez S, Ruiz D, Barrero R, Ramírez R, Calzada N, del Rosario Peña B, et al. Diagn Microbiol Infect Dis. 2010 Sep;68(1):46–9.

In this work, the presence of NS1 protein as a possible early marker of dengue infection was studied in serum samples from confirmed adult patients with a primary and secondary dengue 4 infection. A total of 209 serum samples collected from day 2 up to day 7 of fever onset from 71 patients were tested by Platelia NS1 antigen capture ELISA kit (BioRad, Marnes-la-Coquette, France), and the results were compared with those obtained by capture antidengue virus IgM (MAC)-ELISA and ELISA inhibition method tests. The 83.3% of primary cases and 96.4% of secondary cases were NS1 positive. The kinetics of NS1 protein showed the highest values in optical density mean ratio or in percentage of positives between days 2 and 4. The results obtained in this study show the utility of the NS1 protein as a virologic early marker of dengue infection. Prospective studies should be carried out to confirm its utility as a prognostic marker of severe illness.

Modification in redox status of diabetes mellitus type 1 patients after insulin transition. Gil-Del Valle L, de la C Millian L, Toledo A, Ávila J, Tápanes R, Llera I, et al. Biomed Pharmacother. 2010 Oct 26. [Epub ahead of print]

Aims To determine and compare an extensive array of biochemical redox indices before and after insulin type change in diabetes mellitus (DM) patients' type 1. **Methods** Glutathione, malondialdehyde, peroxidation potential, superoxide dismutase, catalase, total hydroperoxide and advanced oxidation protein products in relation to

blood glucose and glucose indicators control such as glycosylated haemoglobin and fructosamine were measured in 40 patients before and after 2 months since pork insulin was changed to human insulin in type 1 diabetic patients. These data was compared to sex and age-matched healthy control. **Results** After 2 months of changing, all indicator measured were favorably evolved and were significantly modified ($P<0.05$) except activity of erythrocyte enzymes superoxide dismutase and catalase. Adverse reactions (hypoglycaemic events) were observed in seven patients with 0.7% of incidence. It was related to concomitant use of captopril, clortalidone and nitropental for hypertension treatment. Simultaneous beneficial change in glucose, glucose control indices and redox markers were noted in 27 (68%) of total patients of study. **Conclusion** These results contribute to both evidences that transition process from animal to human insulin could be beneficial to DM type 1 patients and an integral overview about metabolic events involved could be valid for evaluate treatment effects. The results contribute to evidences that transition to human insulin can improve the antioxidant status of diabetic patients.

Oxidative stress in aging: Theoretical outcomes and clinical evidences in humans. Gildel Valle L. Biomed Pharmacother. 2010 Sep 25. [Epub ahead of print]

Oxidative damage accumulation in macromolecules has been considered as causative of cellular damage and pathology. Considering early observations of Gershman that oxygen free radicals exist *in vivo* in the 1950s Denham Harman proposed seminal [*sic*] that reactive oxygen species are a cause of aging (free radical theory of aging). The goal of this review is to analyze recent findings related Harman's theory. In this regard, we have focused primarily on theoretical analyses of oxidative stress and their biological impact. It is not the only theorem proposed to explain the mechanism(s) involved in aging at the molecular level. We also discuss how this theory is related to other areas of research specifically, the mitochondrial hypothesis of aging, molecular and cell basis to chronic inflammation and disease appearance, caloric restriction experiments and the most recent clinical studies in healthy human's populations. We reviewed evidences of alterations in biological events likely account for the age-related decline in the ability of cells to respond oxidant stimuli, which compromises homeostasis, increases vulnerability to OS and contribute to senescence. [*sic*] Clearly further studies will be needed to contribute to strategies elucidation such could offer significant benefits for the aged humans.

Proteomic Profile Regulated by the Anticancer Peptide CIGB-300 in Non-Small Cell Lung Cancer (NSCLC) Cells. Rodríguez-Ulloa A, Ramos Y, Gil J, Perera Y, Castellanos-Serra L, García Y, et al. J Proteome Res. 2010 Oct 1;9(10):5473–83.

CIGB-300 is a proapoptotic peptide-based drug that abrogates the CK2-mediated phosphorylation. This peptide has antineoplastic effect on lung cancer cells *in vitro* and *in vivo*. To understand the mechanisms involved on such anticancer activity, the NCI-H125 cell line proteomic profile after short-term incubation (45 min) with CIGB-300 was investigated. As determined by 2-DE or 2D-LC-MS/MS, 137 proteins changed their abundances more than 2-fold in response to the CIGB-300 treatment. The expression levels of proteins related to ribosome biogenesis, metastasis, cell survival and proliferation, apoptosis, and drug resistance were significantly modulated by the presence of CIGB-300. The protein translation process was the most affected (23% of the identified proteins). From the proteome analysis of the NCI-H125 cell line, novel potentialities for CIGB-300 as anticancer agent were evidenced.

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 Nov;37(6):778–88.

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.

Research Priorities for Neglected Infectious Diseases in Latin America and the Caribbean Region. Dujardin JC, Herrera S, do Rosario V, Arevalo J, Boelaert M, Carrasco HJ, et al. PLoS Negl Trop Dis. 2010 Oct 26;4(10): e780.

Global priorities for research in neglected infectious diseases (NIDs) can be assessed in different ways, but it is important to realize that regional priorities may significantly differ one from another. The region of Latin America and the Caribbean (LAC) is—along with Africa and Asia—more affected by NIDs than other regions of the world. Some of the Latin American NIDs are common to other continents, while others are very specific or disproportionately affect the Latin American region. Because of its huge ecological diversity, ongoing environmental changes, and massive migrations, LAC is also a catalyst for the (re-)emergence and spreading of NIDs, both inside and outside the subcontinent. Following a colloquium on NIDs in LAC held in Lima, Peru, between 12 and 14 November 2009, a thematic workshop was organized with the support of the European Commission (EC). It involved 29 scientists (16 from the Americas, two from the Democratic Republic of Congo and India, respectively, and nine from Europe) working on different NIDs and representing several research areas from basic to applied. This report summarizes the consensus comments of the expert group after oral and written consultation. It is envisaged that this document should stimulate a debate within the scientific community and serve as a recommendation for future actions by international or regional funding agencies in the area of NIDs in LAC.

Subtle rapid eye movement sleep abnormalities in presymptomatic spinocerebellar ataxia type 2 gene carriers. Rodríguez-Labrada R, Velázquez-Pérez L, Ochoa NC, Polo LG, Valencia RH, Cruz GS, et al. Mov Disord. 2010 Oct 19. [Epub ahead of print]

Rapid eye movement (REM) sleep disorders are commonly associated to patients with spinocerebellar ataxia type 2 (SCA2); however, these abnormalities have not been studied in presymptomatic gene carriers. To determine whether the REM sleep pathology is detectable before clinical manifestation of SCA2 and evaluate it as a preclinical biomarker, we studied 36 presymptomatic SCA2 individuals and 36 controls by video-polysomnography (VPSG) and sleep questionnaires. Presymptomatic subjects showed significant decrease of REM sleep percentage, REMs density, total sleep time, and sleep efficiency. Aging effect on REM sleep percentage was significant in both groups. There was no correlation between cytosine-adenine-guanine (CAG) repeat length and REM sleep. Our findings identified the REM sleep pathology as a prominent herald sign of SCA2, conferring a special importance to VPSG as a sensitive neurophysiological tool to detect early changes associated with SCA2, which contributes to the understanding of disease pathophysiology and the development of therapeutic trials focused on the preclinical disease stage.

Temporal trends of circulating nitric oxide and pro-inflammatory cytokine responses *ex vivo* in intra-abdominal sepsis: results from a cohort study. Ojeda Ojeda M, Larrondo Muguercia H, Magdariaga Figuerola A, Sán-

chez Valdivia A, Rodríguez Alfonso I, Valenzuela Silva C, et al. Inflam Res. 2010 Oct 26. [Epub ahead of print]

Objective and Design To evaluate the association of pro-inflammatory mediators with organ dysfunction and adverse outcome in intra-abdominal sepsis patients. **Subjects** Twenty-one patients admitted to the Intensive Care Unit (ICU) were prospectively included in the study. Only patients with surgical diagnosis of intra-abdominal sepsis were enrolled. **Results** Tumor necrosis factor-α (TNFα) and interleukin (IL)-6 produced *ex vivo* were significantly lower in non-survivors on admission (p=0.021) and day 2 (p=0.013), respectively. Nitric oxide (NO_x) levels were significantly higher in non-survivors from the onset of sepsis and until day 4 after diagnosis (p<0.05). Circulating lymphocyte counts were lower in non-survivors after admission over time, but there was no association with impaired cytokine production in this group of patients during the entire follow-up. All non-survivors developed nosocomial pneumonia concomitantly with multiple organ dysfunction and septic shock. There was a significant correlation between nitric oxide (NO_x) concentrations and the sequential organ failure assessment (SOFA) score at day 2 (r=0.598, p=0.009), and ICU stay (r=0.605, p=0.006). Continuously high NO_x levels correlated with organ failure. The pro-inflammatory mediators TNFα, IL-6 and NO_x, and also the Simplified Acute Physiology Score II (SAPS-II), discriminate survivors from non-survivors. According to logistic regression models, although these parameters are independently associated with the outcome, they do not improve the predictive power of the SAPS-II score for mortality risk. **Conclusions** Disturbances in inflammatory responses and increase in NO_x generation seem to characterize early intra-abdominal sepsis, in which immune suppression is associated with an increased susceptibility to nosocomial infections. Sequential NO_x determinations could be a useful approach for improving the management of patients with intra-abdominal sepsis.

Tumor necrosis factor-alpha, transforming growth factor-β1, and interleukin-10 gene polymorphisms: implication in protection or susceptibility to dengue hemorrhagic fever. Pérez AB, Sierra B, García G, Aguirre E, Babel N, Álvarez M, et al. Hum Immunol. 2010 Nov;71(11):1135–40.

Dengue virus infection has emerged as one of the most important arthropod-borne viral diseases. Some dengue infected individuals develop the severe, life-threatening form of the disease, dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS). Host genetic factors may be relevant and may predispose some individuals to the severe illness. Human leukocyte antigen (HLA), FcγR, tumor necrosis factor (TNF)-α, and dendritic cell-specific intracellular adhesion molecule-3-grabbing nonintegrin (DC-SIGN), among others genes have been associated with the pathogenesis of dengue. Little is known, however, about the predictive value of cytokine genotypes for the clinical outcome of dengue infection. In this study, the TNF-α, interleukin (IL)-6, interferon (IFN)-γ, IL-10 and transforming growth factor (TGF)-β1 gene single nucleotide polymorphisms (SNP) were studied by polymerase chain reaction-sequence-specific primer in a group of individuals with the antecedent of DHF during a secondary infection in the sequence dengue 1/dengue 2. A control group was also included. TNF-α (−308) A allele and IL-10 (−1082/−819/−592) ACC/ATA haplotype were significantly associated with DHF. TNF-α (−308) GG and TGF-β1 (c25) GG genotypes were associated with protection. Our results suggest that genetic predisposition to a high TNF-α production and a low IL-10 production seems to increase the susceptibility to DHF during a secondary dengue 2 infection, whereas TGF-β1 high producers might be protected for developing DHF.