Cuban Research in Current International Journals

Arterial Blood Pressure Is Closely Related to Ascites Development in Compensated HCV-Related Cirrhosis. Vilar E, Torres A, Calzadilla L, Yasells A, Sánchez Y, Pérez YM. PLoSOne. 2014 Apr 22;9(4):395736.

Background Arterial blood pressure (BP) is a reliable marker of circulatory dysfunction in cirrhotic patients. There are no prospective studies evaluating the association between different levels of arterial BP and ascites development in compensated cirrhotic patients. Therefore, we evaluated the relationship between arterial BP and ascites development in compensated cirrhotic patients. **Materials and methods**A total of 402 patients with compensated HCV-related cirrhosis were prospectively followed during 6 years to identify ascites development. At baseline, patients underwent systolic, diastolic and mean arterial pressure (MAP) measurements. Any history of arterial hypertension was also recorded. The occurrence of events such as bleeding, hepatocellular carcinoma, death and liver transplantation prior to ascites development were considered as competing risk events. **Results** Over a median of 156 weeks, ascites occurred in 54 patients (13%). At baseline, MAP was significantly lower in patients with ascites development (75.9 mm/Hg [95%CI, 70.3-84.3]) than those without ascites (93.6 mm/Hg [95% CI: 86.6-102.3]). After adjusting for covariates, the 6-year cumulative incidence of ascites was 40% (95%CI, 34%-48%) for patients with MAP<83.32 mm/Hg. In contrast, cumulative incidences of ascites were almost similar among patients with MAP values between 83.32 mm/Hg and 93.32 mm/Hg (7% [95% CI: 4%-12%]), between 93.32 mm/Hg and 100.31 mm/Hg (5% [95% CI: 4%-11%]) or higher than 100.31 mm/Hg (3% [95% CI: 1%-6%]). The MAP was an independent predictor of ascites development.**Conclusions** The MAP is closely related to the development of ascites in compensated HCV-related cirrhosis. The risk of ascites development increases in 4.4 fold for subjects with MAP values <83.32 mm/Hg.

Biodosimetry estimation using the ratio of the longest: shortest length in the premature chromosome condensation (PCC) method applying autocapture and automatic image analysis. González JE, Romero I, Gregoire E, Martin C, Lamadrid AI, Voisin P, et al. J Radiat Res. 2014 Apr 30.

The combination of automatic image acquisition and automatic image analysis of premature chromosome condensation (PCC) spreads was tested as a rapid biodosimeter protocol. Human peripheral lymphocytes were irradiated with 60Co gamma rays in a single dose of between 1 and 20 Gy, stimulated with phytohaemaglutinin and incubated for 48 h, division blocked with Colcemid, and PCC-induced by Calyculin A. Images of chromosome spreads were captured and analysed automatically by combining the Metafer 4 and CellProfiler platforms. Automatic measurement of chromosome lengths allows the calculation of the length ratio (LR) of the longest and the shortest piece that can be used for dose estimation since this ratio is correlated with ionizing radiation dose. The LR of the longest and the shortest chromosome pieces showed the best goodness-of-fit to a linear model in the dose interval tested. The application of the automatic analysis increases the potential use of the PCC method for triage in the event of massive radiation causalities.

Brain morphometry of Dravet Syndrome. Pérez A, García-Pentón L, Canales-Rodríguez EJ, Lerma-Usabiaga G, Iturria-Medina Y, Román FJ, et al.

The aim of this study was to identify differential global and local brain structural patterns in Dravet Syndrome (DS) patients as compared with a control subject group, using brain morphometry techniques which provide a quantitative whole-brain structural analysis that allows for specific patterns to be generalized across series of individuals. Nine patients with the diagnosis of DS that tested positive for mutation in the SCN1A gene and nine well-matched healthy controls were investigated using voxel brain morphometry (VBM), cortical thickness and cortical gyrification measurements. Global volume reductions of gray matter (GM) and white matter (WM) were related to DS. Local volume reductions corresponding to several white matter regions in brainstem, cerebellum, corpus callosum, corticospinal tracts and association fibers (left inferior fronto-occipital fasciculus and left uncinate fasciculus) were also found. Furthermore, DS showed a reduced cortical folding in the right precentral gyrus. The present findings describe DS-related brain structure abnormalities probably linked to the expression of the SCN1A mutation.

Coxsackievirus A6 and enterovirus 71 causing hand, foot and mouth disease in Cuba, 2011-2013. Fonseca MC, Sarmiento L, Resik S, Martínez Y, Hung LH, Morier L, et al. Arch Virol. 2014 Apr 10. [Epub ahead of print]

Hand, foot and mouth disease (HFMD) is usually caused by coxsackievirus A16 or enterovirus 71 (EV71).

Between 2011 and 2013, HFMD cases were reported from different Cuban provinces. A total of 42 clinical specimens were obtained from 23 patients. Detection, identification and phylogenetic analysis of enterovirus-associated HFMD were carried out by virus isolation, specific enterovirus PCR and partial VP1 sequences. HEV was detected in 11 HFMD cases. Emerging genetic variants of coxsackievirus A6 and EV71 were identified as the causative agents of the Cuban HFMD cases.

Cuba: exploring the history of admixture and the genetic basis of pigmentation using autosomal and uniparental markers. Marcheco-Teruel B, Parra EJ, Fuentes-Smith E, Salas A, Buttenschøn HN, Demonti D, et al. PLoS Genet. 2014 Jul 24;10(7):e1004488.

We carried out an admixture analysis of a sample comprising 1,019 individuals from all the provinces of Cuba. We used a panel of 128 autosomal Ancestry Informative Markers (AIMs) to estimate the admixture proportions. We also characterized a number of haplogroup diagnostic markers in the mtDNA and Y-chromosome in order to evaluate admixture using uniparental markers. Finally, we analyzed the association of 16 single nucleotide polymorphisms (SNPs) with quantitative estimates of skin pigmentation. In the total sample, the average European, African and Native American contributions as estimated from autosomal AIMs were 72%, 20% and 8%, respectively. The Eastern provinces of Cuba showed relatively higher African and Native American contributions than the Western provinces. In particular, the highest proportion of African ancestry was observed in the provinces of Guantánamo (40%) and Santiago de Cuba (39%), and the highest proportion of Native American ancestry in Granma (15%), Holguín (12%) and Las Tunas (12%). We found evidence of substantial population stratification in the current Cuban population, emphasizing the need to control for the effects of population stratification in association studies including individuals from Cuba. The results of the analyses of uniparental markers were concordant with those observed in the autosomes. These geographic patterns in admixture proportions are fully consistent with historical and archaeological information. Additionally, we identified a sex-biased pattern in the process of gene flow, with a substantially higher European contribution from the paternal side, and higher Native American and African contributions from the maternal side. This sex-biased contribution was particularly evident for Native American ancestry. Finally, we observed that SNPs located in the genes SLC24A5 and SLC45A2 are strongly associated with melanin levels in the sample.

Current status of prenatal diagnosis in Cuba: causes of low prevalence of Down syndrome. Méndez LA, Hechavarría D, de la Torre ME, Pimente H, Hernández J, Pérez B, et al. Prenat Diagn. 2014 May. [Epub ahead of print]

Objective To analyze trends in cytogenetic prenatal diagnosis in Cuba and to analyze possible causes leading to a low Down syndrome prevalence in a country where the triple test is not available. **Method**An analysis of the Cuban program in prenatal cytogenetic diagnosis from 1984 to 2012 was conducted. Results are described, with particular emphasis on indications, abnormal results, types of invasive procedures, and terminations of pregnancy. **Results** 75 095 cytogenetic prenatal diagnostic analyses were conducted; maternal age was the indication for 77.9 % of the amniocenteses and chorionic villi samplings. The detection rate of chromosomally abnormal pregnancies was 2.3% for maternal age and increased to 8 to 9% for other indications. When a chromosomal abnormality was identified, 88.5% terminated the pregnancy. In 2002 the live birth prevalence of Down syndrome was 8.4 per 10 000 live births and in 2012, 7 per 10 000. **Conclusion** Prenatal diagnosis in Cuba has contributed to a significant reduction in chromosomal aberrations. The impact increased due to the demographic trends of the population, the high index of terminations of pregnancy and the establishment of a network of cytogenetic laboratories throughout Cuba.

Delineating the functional map of the interaction between nimotuzumab and the epidermal growth factor receptor. Tundidor Y, García CP, Pupo A, Infante YC, Rojas G. MAbs. 2014 Apr 23;6(4).

Molecular details of epidermal growth factor receptor (EGFR) targeting by nimotuzumab, a therapeutic anti-cancer antibody, have been largely unknown. The current study delineated a functional map of their interface, based on phage display and extensive mutagenesis of both the target antigen and the Fv antibody fragment. Five residues in EGFR domain III (R353, S356, F357, T358, and H359T) and the third hyper variable region of nimotuzumab heavy chain were shown to be major functional contributors to the interaction. Fine specificity differences between nimotuzumab and other anti-EGFR antibodies were revealed. Mapping information guided the generation of a plausible in silico binding model. Knowledge about the epitope/paratope interface opens new avenues for the study of tumor sensitivity/resistance to nimotuzumab and for further engineering of its binding site. The developed mapping platform, also validated with the well-known cetuximab epitope, allows a comprehensive exploration of antigenic regions and could be expanded to map other anti-EGFR antibodies.

Development of four sandwich ELISAs for quantitation of capsular polysaccharides from Neisseria meningitidis serogroups A, C, W and Y in multivalent vaccines. Reyes F, Otero O, Cuello M, Amin N, García L, Cardoso D, et al. J Immunol Methods. 2014 May;407:58–62.

Neisseria meningitidis is a Gram negative bacterium that has been classified in 13 serogroups according to the biochemical composition of the capsular polysaccharide (CP). However, invasive infections are most frequently caused by six of these serogroups: A, B, C, W, X and Y (MenA, MenB, MenC, MenW, MenX, MenY). Individual CP quantitation in multivalent meningococcal CP-based vaccines is required for quality control testing of these products. In this regard, four sandwich enzyme-linked immunosorbent assays (ELISAs) were developed for the quantitation of CP. The quantitation and detection limits of the four ELISAs were below 1ng/mL. The assays showed good reproducibility and repeatability as calculated for each point of the standard curve (CV<15%). In addition, five multivalent meningococcal CP-based vaccines were evaluated and the proposed ELISAs showed that these vaccines were found into the accepted range (±30%) of CP content. These assays are suitable for screening multiple plain or conjugated meningococcal CP-based vaccines and could be useful for monitoring lot-to-lot consistency and stability analysis.

Evaluation in mice of the immunogenicity and protective efficacy of a tetravalent subunit vaccine candidate against dengue virus. Lazo L, Izquierdo A, Suzarte E, Gil L, Valdes I, Marcos E, et al. Microbiol Immunol. 2014 Apr;58(4):219–26.

A dengue vaccine must induce protective immunity against the four serotypes of the virus. Our group has developed chimeric proteins consisting of the protein P64k from Neisseria meningitidis and the domain III from the four viral envelope proteins. In this study, the immunogenicity of a tetravalent vaccine formulation using aluminum hydroxide as adjuvant was evaluated in mice. After three doses, neutralizing antibody titers were detected against the four viral serotypes, the lowest seroconversion rate being against dengue virus serotype 4. One month after the last dose, immunized animals were challenged with infective virus, and partial but statistically significant protection was found to have been achieved. Based on these results, further studies in mice and non-human primates using this tetravalent formulation in a prime-boost strategy with attenuated viruses are strongly recommended.

First dengue hemorrhagic fever epidemic in the Americas, 1981: insights into the causative agent. Rodríguez-Roche R, Hinojosa Y, Guzmán MG. Arch Virol. 2014 Aug 5. [Epub ahead of print]

Historical records describe a disease in North America that clinically resembled dengue haemorrhagic fever during the latter part of the slave-trading period. However, the dengue epidemic that occurred in Cuba in 1981 was the first laboratory-confirmed and clinically diagnosed outbreak of dengue haemorrhagic fever in the Americas. At that time, the presumed source of the dengue type 2 strain isolated during this epidemic was considered controversial, partly because of the limited sequence data and partly because the origin of the virus appeared to be southern Asia. Here, we present a molecular characterisation at the whole-genome level of the original strains isolated at different time points during the epidemic. Phylogenetic trees constructed using Bayesian methods indicated that 1981 Cuban strains group within the Asian 2 genotype. In addition, the study revealed that viral evolution occurred during the epidemic - a fact that could be related to the increasing severity from month to month. Moreover, the Cuban strains exhibited particular amino acid substitutions that differentiate them from the New Guinea C prototype strain as well as from dengue type 2 strains isolated globally.

Hearing screening using auditory steady state responses obtained by simultaneous air- and bone-conduction stimuli. Mijares E, Báez L, Cabrera L, Pérez MC, Torres A. Acta Otorrinolaringol Esp. 2014 Apr 21. doi: 10.1016/j.otorri.2014.02.006. English, Spanish.

Introduction and Objectives Minimising false positives rates is an important goal of universal newborn hearing screening programmes. An adequate way for reaching that goal could be differentiating between transient conductive hearing losses (false positives) and permanent sensorineural hearing impairments (true positives) by means of a methodology that studies electrophysiological responses obtained using both air- and bone-conduction stimuli. Our objective was to evaluate the efficiency of an automated hearing screening test based on auditory steady state responses obtained using simultaneous air- and bone-conduction stimuli. **Methods** A sample of 80 high-risk babies under 2 months old [English corrected, Eds.] were screened using the automatic screening test. A confirmatory clinical and electrophysiological evaluation was used as the gold standard. **Results** The estimated diagnostic efficiency of this screening test was equivalent (100% sensitivity and 97.7% specificity) to the efficiency reported for otoacoustic emissions and automated auditory

brainstem responses. The introduction of bone conduction in the screening reduced the false positive rate from 13.3% to 2.2%. The test duration was 5.3 (±1.9) min. In 34% of babies only one repetition of the test was needed to raising the result. **Conclusions** The screening test performed quite well in this initial clinical trial, differentiating transient conductive hearing losses from permanent neurosensory impairments and improving the diagnostic efficiency of auditory steady state responses.

Management of chronic Giardia infection. Escobedo AA, Hanevik K, Almirall P, Cimerman S, Alfonso M. Expert Rev Anti Infect Ther. 2014 Jul 25:1–15. [Epub ahead of print]

Advances in our understanding of chronic giardiasis (CG) may improve our care of patients in this stage of the disease. This review proposes a new concept of CG and highlights the recent advances in our understanding and management of this condition. According to this review, management requires, initially, an accurate diagnosis, which may exclude several conditions that can mimic CG. Optimal treatment requires a tailored approach which includes the recognition of the known modifiable causes of this health condition, assessment of symptoms and potential complications, their treatment utilizing, if necessary, a multidisciplinary team, and an ongoing monitoring for the effect of therapy - weighing the efficacy of individual drugs - all of these together may lead to a successful treatment of CG.

Nuclear medicine in the management of patients with heart failure: guidance from an expert panel of the International Atomic Energy Agency (IAEA). Peix A, Mesquita CT, Paez D, Pereira CC, Felix R, Gutierrez C, et al. Nucl Med Commun. 2014 Apr 28. [Epub ahead of print]

Heart failure is increasing worldwide at epidemic proportions, resulting in considerable disability, mortality, and increase in healthcare costs. Gated myocardial perfusion single photon emission computed tomography or PET imaging is the most prominent imaging modality capable of providing information on global and regional ventricular function, the presence of intraventricular synchronism, myocardial perfusion, and viability on the same test. In addition, I-mIBG scintigraphy is the only imaging technique approved by various regulatory agencies able to provide information regarding the adrenergic function of the heart. Therefore, both myocardial perfusion and adrenergic imaging are useful tools in the workup and management of heart failure patients. This guide is intended to reinforce the information on the use of nuclear cardiology techniques for the assessment of heart failure and associated myocardial disease.

Pilot study of a novel combination of two therapeutic vaccines in advanced non-small-cell lung cancer patients. Herrera ZM, Ramos TC. Cancer Immunol Immunother. 2014 Jul;63(7):737–47.

Cancer vaccines contain tumor antigens in a pro-inflammatory context with the purpose to generate potent antitumor immune responses. However, tumor cells develop different immunosuppressive mechanisms that limit the effectiveness of an anticancer immune response. Therefore, therapeutic vaccine treatment alone is usually not sufficient to generate tumor regression or survival improvement, especially in the advanced disease scenario in which most clinical studies have been conducted. Combining cancer vaccines with different anticancer therapies such as chemotherapy, radiotherapy and other immunotherapeutic agents has had different levels of success. However, the combination of cancer vaccines with different mechanisms of action has not been explored in clinical trials. To address this issue, the current review summarizes the main clinical and immunological results obtained with two different therapeutic vaccines used in advanced non-small-cell lung cancer patients, inducing an immune response against epidermal growth factor (CIMAvax-EGF) and NGcGM3 ganglioside (racotumomab). We also discuss preliminary findings obtained in a trial of combination of these two vaccines and future challenges with these therapies.

Prevalence, Incidence and Associations between APOE Genotype, Cardiovascular Risk Factor and Dementia in Cuban Populations (I10-1.005). Llibre JJ, Guerra M, Llibre JC, Llibre JJ. Neurology. 2014 Apr 8;82(10 Suppl).

Background We estimate the prevalence, incidence and correlates of dementia among older Cubans; assess the effects of apolipoprotein E genotype on dementia prevalence and estimate the association between cardiovascular risk factors, apolipoprotein E genotype on dementia incidence. **Methods** A one phase survey (baseline) of all over 65 year old residents of seven catchment areas in Cuba (n=2944) during 2003 to 2005. Dementia diagnosis was established according to DSM-IV and 10/66 criteria. APOE genotype was determined

in 2 520 participants. Baseline data was used to estimate prevalence and the effect of apolipoprotein E genotype on dementia prevalence. An incidence wave was conducted 4.5 years after cohort inception in order to estimate incidence and cardiovascular risk factors associations. **Results** The prevalence of DSM-IV dementia was 6.4% and 10.8% according to the 10/66. Both dementia outcomes were associated with older age, less education, a family history of dementia, shorter leg length and smaller skull circumference. The incidence rate of 10/66 dementia was 21 per 1000/pyear (95% CI, 17.6-23.5). APOE genotype was associated cross-sectionally with dementia prevalence, but the effect on the incidence of dementia was much attenuated, and only apparent among those in the youngest age group. There were no associations between hypertension, diabetes, lipid profile, smoking and the incidence of dementia. **Conclusion** The prevalence and incidence of dementia in the older Cuban population studied is high, and the rate increases with age. These findings underscore the need to improve our understanding of risk factors associated with dementia in specific populations, as well as the need for public health programs for both patients and caregivers in a population that is currently undergoing rapid demographic ageing and epidemiological transition.

Prolonged Use of Nimotuzumab in Children with Central Nervous System Tumors: Safety and Feasibility. Cabanas R, Suarez G, Alert J, Reyes A, Gonzalez MC, Pedrayes JL, et al. Cancer Biother Radiopharm. 2014 May;29(4):173–8.

Primary brain tumors constitute the most frequent solid tumor of childhood. High expression of the epidermal growth factor receptor (EGFR) protein has been associated with tumor progression and enhanced tumorigenicity in adult and children gliomas. Nimotuzumab is a humanized antibody that targets the EGFR and has proven efficacy in adult and children gliomas. To provide a new therapeutic option for patients with active, poor prognosis central nervous system (CNS) tumors and to evaluate the feasibility and safety of long-term nimotuzumab therapy in children with diverse CNS tumors, an expanded access program was launched at the Juan Manuel Marquez hospital. Patients were required to be 18 or younger and have one CNS tumor: low-grade glioma (LGG) or high-grade glioma (HGG), brainstem glioma (BSG), ependymoma or primitive neuroectodermal tumor (PNET), and a Lansky or Karnofsky performance status ≥40. Treatment consisted of weekly nimotuzumab administered at 150 mg/m2 for 12 weeks, continuing every 14 days in the absence of severe condition worsening or unacceptable toxicity. Nimotuzumab was administered alone or in combination with radiotherapy, chemotherapy, or both, depending on the tumor type, stage, and previous treatment. Eighty-eight patients, 39 with BSG, 25 with HGG, 9 with progressive LGG, 9 with anaplastic ependymomas, and 6 with other tumor types, including PNET, neuroblastoma, meduloblastoma, and thalamic tumors, were treated with the antibody. The mean number of nimotuzumab doses was 36, from 1 to 108. The most frequent adverse events were mild to moderate skin rash, mucositis, vomiting, seizures, hypothermia, hyperthermia, and paleness. One patient had a grade 3 mucositis, while the other had a grade 3 bleeding on surgery. Sixteen children stopped treatment after at least 2 years with stable disease, partial or complete response. All children were able to maintain the best response achieved on treatment after a 3-year interruption. In summary, this study shows the feasibility of very prolonged administration of nimotuzumab together with the lack of rebound effect after treatment cessation.

Recombinant dengue 2 virus NS3 protein conserves structural antigenic and immunological properties relevant for dengue vaccine design. Ramírez R, Falcón R, Izquierdo A, García A, Alvarez M, Pérez AB, et al. Virus Genes. 2014 May 23. [Epub ahead of print].

The NS3 protein is a multifunctional non-structural protein of flaviviruses implicated in the polyprotein processing. The predominance of cytotoxic T cell lymphocytes epitopes on the NS3 protein suggests a protective role of this protein in limiting virus replication. In this work, we studied the antigenicity and immunogenicity of a recombinant NS3 protein of the Dengue virus 2. The full-length NS3 gene was cloned and expressed as a His-tagged fusion protein in Escherichia coli. The pNS3 protein was purified by two chromatography steps. The recombinant NS3 protein was recognized by anti-protease NS3 polyclonal antibody and anti-DENV2 HMAF by Western Blot. This purified protein was able to stimulate the secretion of high levels of gamma interferon and low levels of interleukin-10 and tumor necrosis factor-α in mice splenocytes, suggesting a predominantly Th-1-type T cell response. Immunized BALB/c mice with the purified NS3 protein showed a strong induction of anti-NS3 IgG antibodies, essentially IgG2b, as determined by ELISA. Immunized mice sera with recombinant NS3 protein showed specific recognition of native dengue protein by Western blotting and immunofluorescence techniques. The successfully purified recombinant protein was able to preserve the structural and antigenic determinants of the native dengue protein. The antigenicity shown by the recombinant NS3 protein suggests its possible inclusion into future DENV vaccine preparations.

Resistive Cerebral Blood Flow as a Potential Marker of Subclinical Brain Damage in Essential Hypertension. González S, Hernández Z, Quevedo L, Peña M, Fernández R, Menéndez C, et al. World J

Cardiovasc Dis. 2014 Apr;4(4):169–78.

Introduction Subclinical brain damage in essential hypertension is more prevalent than cardiovascular or renal impairment; nevertheless, screening for nervous system involvement is difficult due to the low accessibility and high costs of these techniques. **Objective** To assess the frequency of silent target organ damage in a cohort of asymptomatic hypertensive patients and to evaluate the potential usefulness of carotid ultrasonographic (US) variables as predictors of subclinical brain damage. Patients and **Methods** Thirty four neurologically asymptomatic subjects (mean age 59 years) with essential hypertension were included. Target organ damage was evaluated: degree of hypertensive retinopathy, heart, kidney and brain. Structural and hemodynamical carotid Doppler US parameters were also investigated. **Results** The brain was the most frequently affected target organ (70.6%), followed by the heart (67.9%) and kidney (58.6%). Carotid US parameters showed no association of intima media thickness with brain MRI results; nevertheless, decreased diastolic flow velocity and increased resistive index pointed to a resistive carotid flow pattern in patients with classical brain MRI lesions and predicted subclinical lesions with a sensitivity of 70% and 74% and a specificity of 72% and 80% respectively.**Conclusions** This study supports previous findings that place the brain as the most frequently affected target organ in essential hypertensive patients and sheds more light on the potential usefulness of carotid structure and hemodynamics as imaging biomarkers of subclinical brain lesions.

Role of glutathione S-transferases in the spinocerebellar ataxia type 2 clinical phenotype. Almaguer D, Almaguer LE, Aguilera R, Estupiñán A, González Y, Cuello D, et al. J Neurol Sci. 2014 Jun 15;341(1–2):41–5.

Spinocerebellar ataxia type 2 (SCA2) is a neurodegenerative and incurable hereditary disorder caused by a CAG repeat expansion mutation on ATXN2 gene. The identification of reliable biochemical markers of disease severity is of paramount significance for the development and assessment of clinical trials. In order to evaluate the potential use of glutathione-S-transferase (GST) activity as a biomarker for SCA2, a case-control study in 38 affected, presymptomatic individuals or healthy controls was conducted. An enlarged sample of 121 affected individuals was set to assess the impact of GST activity on SCA2 clinical expression. There was a significant increase in GST activity in affected individuals relative to controls, although sensibility and specificity were not high. GST activity was not significantly influenced by sex, age, disease duration or CAG repeat size and did not significantly influence disease severity markers. These findings show a disruption of in vivo GST activity in SCA2, suggesting a role for oxidative stress in the neurodegenerative process.

Safety and preliminary immunogenicity of Cuban pneumococcal conjugate vaccine candidate in healthy children: A randomized phase I clinical trial. Dotres CP, Puga R, Ricardo Y, Broño CR, Paredes B, Echemendía V, et al. Vaccine. 2014 Jul 25. [Epub ahead of print]

A new heptavalent conjugate vaccine (PCV7-TT) is under development in Cuba. PCV7-TT contains 2μg of serotypes 1, 5, 14, 18C, 19F, 23F and 4μg of 6B, each one conjugated to tetanus toxoid (TT). This vaccine was designed with the serotypes that cause most invasive pneumococcal diseases (IPD) worldwide. In the present study, we investigated the safety and explored the immunogenicity of PCV7-TT during a controlled, randomized and double blind clinical trial phase I in 4-5-year-old children. PCV7-TT was well tolerated and as safe as Synflorix used as control vaccine. Following a single-dose vaccination, all individual serotypes included in PCV7-TT induced statistically significant increase of IgG GMC and OPA GMT. These are the first clinical results of PCV7-TT in children and they pave the way toward next clinical trials in children and infants. This clinical trial was published in the Cuban Public Register of Clinical Trials with code RPCEC00000173.

Simultaneous EEG-fMRI: Trial level spatio-temporal fusion for hierarchically reliable information discovery. Dong L, Gong D, Valdes PA, Xia Y, Luo C, Xu P, et al. Neuroimage. 2014 May 20. [Epub ahead of print]

Simultaneous electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) have been pursued in an effort to integrate complementary noninvasive information on brain activity. The primary goal involves better information discovery of the event-related neural activations at a spatial region of the BOLD fluctuation with the temporal resolution of the electrical signal. Many techniques and algorithms have been developed to integrate EEGs and fMRIs; however, the relative reliability of the integrated information is unclear. In this work, we propose a hierarchical framework to ensure the relative reliability of the integrated results and attempt to understand brain activation using this hierarchical ideal. First, spatial Independent Component Analysis (ICA) of fMRI and temporal ICA of EEG were performed to extract features at the trial level. Second, the maximal information coefficient (MIC) was adopted to temporally match them across the modalities for both linear and non-linear associations. Third, fMRI-constrained EEG source imaging was utilized to spatially match components across modalities. The simultaneously occurring events in the above

two match steps provided EEG-fMRI spatial-temporal reliable integrated information, resulting in the most reliable components with high spatial and temporal resolution information. The other components discovered in the second or third steps provided second-level complementary information for flexible and cautious explanations. This paper contains two simulations and an example of real data, and the results indicate that the framework is a feasible approach to reveal cognitive processing in the human brain.

The softening of human bladder cancer cells happens at an early stage of the malignancy process. Ramos JR, Pabijan J, Garcia R, Lekka M. Beilstein J Nanotechnol. 2014 Apr 10;5:447–57.

Various studies have demonstrated that alterations in the deformability of cancerous cells are strongly linked to the actin cytoskeleton. By using atomic force microscopy (AFM), it is possible to determine such changes in a quantitative way in order to distinguish cancerous from non-malignant cells. In the work presented here, the elastic properties of human bladder cells were determined by means of AFM. The measurements show that non-malignant bladder HCV29 cells are stiffer (higher Young's modulus) than cancerous cells (HTB-9, HT1376, and T24 cell lines). However, independently of the histological grade of the studied bladder cancer cells, all cancerous cells possess a similar level of the deformability of about a few kilopascals, significantly lower than non-malignant cells. This underlines the diagnostic character of stiffness that can be used as a biomarker of bladder cancer. Similar stiffness levels, observed for cancerous cells, cannot be fully explained by the organization of the actin cytoskeleton since it is different in all malignant cells. Our results underline that it is neither the spatial organization of the actin filaments nor the presence of stress fibers, but the overall density and their 3D-organization in a probing volume play the dominant role in controlling the elastic response of the cancerous cell to an external force.

XRF analysis of sediments from Nuevitas Bay (Cuba): assessment of current heavy metal contamination. Díaz Rizo O, GelenRudnikas A, Lavin Pérez RD, Arencibia Caraballo G, D'Alessandro Rodríguez K. Nucleus. 2014 Jan–Jun;(55):11–4

Concentrations of chromium, nickel, copper, zinc and lead in surface sediments from six stations located in Nuevitas Bay (Cuba) were estimated by X-ray fluorescence analysis. The Crcontent in sediments shows a strong variation across the studied stations (89-513 mg.kg-1), in contrast with the other elements studied. The application of modified degree of contamination (mCd) classifies as moderate the contamination of Nuevitas Bay. The comparison with Sediment Quality Guidelines and toxicity mean quotients shows that 100 % of the Sediments are associated with the occasional presence of possible adverse effects to human health.