

Cuban Research in Current International Journals

Adjuvants and myeloid-derived suppressor cells: Enemies or allies in therapeutic cancer vaccination.

Fernández A, Oliver L, Alvarez R, Enrique L, Lee KP, Mesa C. Hum Vaccine Immunother. 2014 Nov 1:e29847. [Epub ahead of print]

Adjuvants are a critical but largely overlooked and poorly understood component included in vaccine formulations to stimulate and modulate the desired immune responses to an antigen. However, unlike in the protective infectious disease vaccines, adjuvants for cancer vaccines also need to overcome the effect of tumor-induced suppressive immune populations circulating in tumor-bearing individuals. Myeloid-derived suppressor cells (MDSC) are considered to be one of the key immunosuppressive populations that inhibit tumor-specific T cell responses in cancer patients. This review focuses on the different signals for the activation of the immune system induced by adjuvants, and the close relationship to the mechanisms of recruitment and activation of MDSC. This work explores the possibility that a cancer vaccine adjuvant may either strengthen or weaken the effect of tumor-induced MDSC, and the crucial need to address this in present and future cancer vaccines.

Antioxidant effects of JM-20 on rat brain mitochondria and synaptosomes: Mitoprotection against Ca(2+)-induced mitochondrial impairment.

Núñez-Figueroa Y, Pardo-Andreu GL, Ramírez-Sánchez J, Delgado-Hernández R, Ochoa-Rodríguez E, Verdecia-Reyes Y, et al. Brain Res Bull. 2014 Oct;109:68–76.

Because mitochondrial oxidative stress and impairment are important mediators of neuronal damage in neurodegenerative diseases and in brain ischemia/reperfusion, in the present study, we evaluated the antioxidant and mitoprotective effect of a new promising neuroprotective molecule, JM-20, in mitochondria and synaptosomes isolated from rat brains. JM-20 inhibited succinate-mediated H₂O₂ generation in both mitochondria and synaptosomes incubated in depolarized (high K⁽⁺⁾) medium at extremely low micromolar concentration and with identical IC₅₀ values of 0.91 μM. JM-20 also repressed glucose-induced H₂O₂ generation stimulated by rotenone or by antimycin A in synaptosomes incubated in high sodium-polarized medium at extremely low IC₅₀ values of 0.395 μM and 2.452 μM, respectively. JM-20 was unable to react directly with H₂O₂ or with superoxide anion radicals but displayed a cathodic reduction peak at -0.71V, which is close to that of oxygen (-0.8V), indicating high electron affinity. JM-20 also inhibited uncoupled respiration in mitochondria or synaptosomes and was a more effective inhibitor in the presence of the respiratory substrates glutamate/malate than in the presence of succinate. JM-20 also prevented Ca⁽²⁺⁾-induced mitochondrial permeability transition pore opening, membrane potential dissipation and cytochrome c release, which are key pathogenic events during stroke. This molecule also prevented Ca⁽²⁺⁾ influx into synaptosomes and mitochondria; the former effect was a consequence of the latter because JM-20 inhibition followed the patterns of carbonyl cyanide p-trifluoromethoxyphenyl hydrazone (FCCP), which is a classic mitochondrial uncoupler. Because the mitochondrion is considered an important source and target of neuronal cell death signaling after an ischemic insult, the antioxidant and protective effects of JM-20 against the deleterious effects of Ca⁽²⁺⁾ observed at the mitochondrial level in this study may endow this molecule with the ability to succeed in mitochondrion-targeted strategies to combat ischemic brain damage.

Approaches to refining estimates of global burden and economics of dengue.

Shepard DS, Undurraga EA, Betancourt-Cravioto M, Guzmán MG, Halstead SB, Harris E, et al. PLoS Negl Trop Dis. 2014 Nov 20;8(11):e3306.

Dengue presents a formidable and growing global economic and disease burden, with around half the world's population estimated to be at risk of infection. There is wide variation and substantial uncertainty in current estimates of dengue disease burden and, consequently, on economic burden estimates. Dengue disease varies across time, geography and persons affected. Variations in the transmission of four different viruses and interactions among vector density and host's immune status, age, pre-existing medical conditions, all contribute to the disease's complexity. This systematic review aims to identify and examine estimates of dengue disease burden and costs, discuss major sources of uncertainty, and suggest next steps to improve estimates. Economic analysis of dengue is mainly concerned with costs of illness, particularly in estimating total episodes of symptomatic dengue. However, national dengue disease reporting systems show a great diversity in design and implementation, hindering accurate global estimates of dengue episodes and country comparisons. A combination of immediate, short-, and long-term strategies could substantially improve estimates of disease and, consequently, of economic burden of dengue. Suggestions for immediate implementation include refining analysis of currently available data to adjust reported episodes and expanding data collection in empirical studies, such as documenting the number of ambulatory visits before and after

hospitalization and including breakdowns by age. Short-term recommendations include merging multiple data sources, such as cohort and surveillance data to evaluate the accuracy of reporting rates (by health sector, treatment, severity, etc.), and using covariates to extrapolate dengue incidence to locations with no or limited reporting. Long-term efforts aim at strengthening capacity to document dengue transmission using serological methods to systematically analyze and relate to epidemiologic data. As promising tools for diagnosis, vaccination, vector control, and treatment are being developed, these recommended steps should improve objective, systematic measures of dengue burden to strengthen health policy decisions.

Comparing the usefulness of the 1997 and 2009 WHO dengue case classification: a systematic literature review.

Horstick O, Jaenisch T, Martinez E, Kroeger A, See LL, Farrar J, et al. *Am J Trop Med Hyg.* 2014 Sep 3;91(3):621–34.

The 1997 and 2009 WHO dengue case classifications were compared in a systematic review with 12 eligible studies (4 prospective). Ten expert opinion articles were used for discussion. For the 2009 WHO classification studies show: when determining severe dengue sensitivity ranges between 59–98% (88%/98%: prospective studies), specificity between 41–99% (99%: prospective study) - comparing the 1997 WHO classification: sensitivity 24.8–89.9% (24.8%/74%: prospective studies), specificity: 25%/100% (100%: prospective study). The application of the 2009 WHO classification is easy, however for (non-severe) dengue there may be a risk of monitoring increased case numbers. Warning signs validation studies are needed. For epidemiological/pathogenesis research use of the 2009 WHO classification, opinion papers show that ease of application, increased sensitivity (severe dengue) and international comparability are advantageous; 3 severe dengue criteria (severe plasma leakage, severe bleeding, severe organ manifestation) are useful research endpoints. The 2009 WHO classification has clear advantages for clinical use, use in epidemiology is promising and research use may at least not be a disadvantage.

Cryptococcus and Cryptococcosis in Cuba. A minireview.

Illnait-Zaragozi MT, Martínez-Machín GF, Fernández-Andreu CM, Perurena-Lancha MR, Hagen F, Meis JF. *Mycoses.* 2014 Dec;57(12):707–17.

Cryptococcosis has emerged as an important public health problem in Africa, Asia and the Americas due to the increasing numbers of persons at risk of this infection and the adaptation of its aetiological agents to new environments. The proper management requires early recognition of *Cryptococcus neoformans/C. gattii* species complex infection, familiarity with the use and limitations of diagnostic tests and knowledge of the available treatment options. This review will address these issues with the goal of providing sufficient information to suspect, diagnose and treat patients with cryptococcosis based on Cuban data and review of the literature.

Evaluation of commercially available diagnostic tests for the detection of dengue virus NS1 antigen and anti-dengue virus IgM antibody.

Hunsperger EA, Yoksan S, Buchy P, Nguyen VC, Sekaran SD, Enria DA, et al. *PLoS Negl Trop Dis.* 2014 Oct 16;8(10):e3171.

Commercially available diagnostic test kits for detection of dengue virus (DENV) non-structural protein 1 (NS1) and anti-DENV IgM were evaluated for their sensitivity and specificity and other performance characteristics by a diagnostic laboratory network developed by World Health Organization (WHO), the UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) and the Pediatric Dengue Vaccine Initiative (PDVI). Each network laboratory contributed characterized serum specimens for the panels used in the evaluation. Microplate enzyme-linked immunosorbent assay (ELISA) and rapid diagnostic test (RDT formats) were represented by the kits. Each ELISA was evaluated by 2 laboratories and RDTs were evaluated by at least 3 laboratories. The reference tests for IgM anti-DENV were laboratory developed assays produced by the Armed Forces Research Institute for Medical Science (AFRIMS) and the Centers for Disease Control and Prevention (CDC), and the NS1 reference test was reverse transcriptase polymerase chain reaction (RT-PCR). Results were analyzed to determine sensitivity, specificity, inter-laboratory and inter-reader agreement, lot-to-lot variation and ease-of-use. NS1 ELISA sensitivity was 60–75% and specificity 71–80%; NS1 RDT sensitivity was 38–71% and specificity 76–80%; the IgM anti-DENV RDTs sensitivity was 30–96%, with a specificity of 86–92%, and IgM anti-DENV ELISA sensitivity was 96–98% and specificity 78–91%. NS1 tests were generally more sensitive in specimens from the acute phase of dengue and in primary DENV infection, whereas IgM anti-DENV tests were less sensitive in secondary DENV infections. The reproducibility of the NS1 RDTs ranged from 92–99% and the IgM anti-DENV RDTs from 88–94%.

Exploring the "weight" of food cravings and thought suppression among Cuban adults.

Rodríguez-Martín BC, Gil-Pérez P, Pérez-Morales I. *Eat Weight Disord.* 2014 Nov 7. [Epub ahead of print]

Purpose The current study aimed to analyze individual differences on foodcravings, intrusive-related thoughts and its suppression between normal weight and overweight/obese Cuban adults. **Methods** Participants were 1,184 individuals from general population, aged between 18 and 64 years ($M = 32.89$; $SD = 12.87$), with 69.1% females. All participants answered a set of questionnaires and provided demographic, anthropometric and clinical data. **Results** Overweight/obese individuals had higher mean scores than normal weight individuals on foodcravings (including its nine dimensions) and food and body weight/shape thoughtsuppression. Large effect sizes were found for body weight/shape thoughts suppression and lack of control over eating, where overweight and obese individuals showed the highest scores. This trend was also found for food thoughts suppression, foodcravings trait, cue-dependent eating, preoccupation with food and guilty feelings, with effect sizes from medium to large. Finally, medium effect sizes were observed for intention to eat and negative affect. **Conclusion** Overweight/obese individuals experienced more foodcravings and food and body weight/shape thoughtsuppression than normal weight individuals among Cubanadults.

Haematopoiesis radioprotection in Balb/c mice by an aqueous mycelium extract from the Basidiomycete Pleurotus ostreatus mushroom.

Llauradó G, Morris HJ, Tamayo V, Lebeque Y, Beltrán Y, Marcos J, et al. *Nat Prod Res.* 2014 Nov 25:1–5. [Epub ahead of print]

The study examined the radioprotective activity of an aqueousextract from Pleurotusostreatusmycelium administered to Balb/cmice. Male mice were whole-body irradiated on day 0 (^{60}Co , at 0.43 Gy/min) and divided into two groups. The extract was administered intraperitoneally to one group (100 mg/kg) on days - 10 to - 6 and - 2 to +1 with respect to the irradiation. The irradiated-control group was injected with saline solution; non-irradiated mice were used as negative controls. The radioprotective effect was evident by increases in bone marrow cellularity ($5.1 \times 10^6/\text{femur}$ vs. $1.1 \times 10^6/\text{femur}$ in saline-control mice, $p < 0.05$), leucocyte counts ($10.5 \times 10^9/\text{L}$ vs. $4.5 \times 10^9/\text{L}$, $p < 0.05$), and spleen cellularity ($11.2 \times 10^7/\text{spleen}$ vs. $6.2 \times 10^7/\text{spleen}$, $p < 0.05$). The extract stimulated macrophage phagocytic activity as judged by a faster rate of carbon clearance in terms of absorbance ratios (1.62 vs. 2.01 , $p < 0.05$). Therefore, this extract may be a candidate therapeutic agent with radioprotective activity for haematopoiesis damage, particularly to cells involved in immune function.

High frequency of antiviral drug resistance and non-b subtypes in HIV-1 patients failing antiviral therapy in Cuba.

Kourí V, Alemán Y, Pérez L, Pérez J, Fonseca C, Correa C, et al. *J Int AIDS Soc.* 2014 Nov 2;17(4 Suppl 3):19754. doi: 10.7448/IAS.17.4.19754.

Introduction Emergence of HIV-1drugresistance may limit the sustained benefits of antiretroviral therapy (ART) in settings with limited laboratory monitoring and drug options. The objective is to implement the surveillance of drugresistance and subtypes in HIV-1patientsfailing ART in Cuba. **Methods** This study compiled clinical and genotypic drugresistance data 588 ART-experienced HIV-1patients attending a clinical center in Havana in 2009-2013. Drugresistance testing was performed as part of routine clinical care. Drugresistance mutations and levels were determined using Rega version 8.0.2. **Results** Eighty-three percent received solely ART containing at least three drugs. Patients from 2009 to 2010 were longer treated (median: 4.9 vs 2.7 years) and exposed to more ART regimens (median: 4 vs 2 regimens) compared to patients from 2011-2013. Nucleoside reverse transcriptase inhibitor (NRTI), non-nucleoside RTI (NNRTI) and PI mutations were present in 83.5, 77.4 and 52.0%. Full-class resistance (FCR) to NRTI, NNRTI, PI and multidrug resistance (MDR) were detected in 25.0, 33.7, 11.4 and 6.3%. FCR to NRTI, NNRTI, PI and MDR were present in 12.8, 28.7, 0 and 0% after first-line failure (164 patients) and in 23.1, 34.6, 3.8 and 3.1% after second-line failure (130 patients). Subtype B (32.5%), BG recombinants (19.6%) and CRF19_cpx (16.2%) were the most prevalent genetic forms. Subtype distribution did not change significantly between 2009-2010 and 2011-2013, except for BG recombinants that increased from 12.2 to 21.3% ($p=0.002$). **Conclusions** Our study found a high prevalence of drugresistance and supports the need for appropriate laboratory monitoring in clinical practice and access to drug options in case of virological failure.

Novel treatment approaches in hypertensive type 2 diabetic patients.

Castro Torres Y, Katholi RE. *World J Diabetes.* 2014 Aug 15;5(4):536–45.

Type2 diabetes mellitus (T2DM) and hypertension represent two common conditions worldwide. Their frequent association with cardiovascular diseases makes management of hypertensivepatients with T2DM an important

clinical priority. Carvedilol and renal denervation are two promising choices to reduce plasma glucose levels and blood pressure in hypertensive patients with T2DM to reduce future complications and improve clinical outcomes and prognosis. Pathophysiological mechanisms of both options are under investigation, but one of the most accepted is attenuation in sympathetic nervous system activity which lowers blood pressure and improves insulin sensitivity. Choice of these therapeutic approaches should be individualized based on specific characteristics of each patient. Further investigations are needed to determine when to consider their use in clinical practice.

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, Páez D, Pereira CC, Félix R, Gutiérrez C, et al. Nucl Med Commun. 2014 Aug;35(8):818–23.

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-¹²³I-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.

Opinion Toward Living Liver Donation of Hospital Personnel From Units Related to Organ Donation and Transplantation: A Multicenter Study From Spain and Latin-America.

Rios A, Ayala García MA, Sebastián J, Abdo Cuza A, Martínez Alarcón L, Ramírez EJ, et al. Hepat Mon. 2014 Dec;14(12):e15405.

Background Hospital personnel of services related to donation and transplantation process play a fundamental role in the development of transplantation. **Objectives** The aim of this study was to investigate the attitude toward living liver donation (LLD) among hospital personnel from services related to donation and transplantation in hospital centers in Spain and Latin America. **Materials and methods** Eight hospitals within the "International Donor Collaborative Project" were selected, three in Spain, three in Mexico and two in Cuba. The study was performed in transplant related services, using a randomized sample, which was stratified by the type of service and job category. **Results** In total, 878 workers were surveyed of which 82% (n=720) were in favor of related LLD, 10% (n=90) were against and 8% (n=68) undecided. Attitudes toward related LLD were more favorable in the following groups: the Latin Americans (86% in favor vs. 77% among the Spanish; P=0.007); younger people (37 vs. 40 years, P=0.002); those in favor of either deceased donation (P<0.001) or living kidney donation (P<0.001); those who believed that they might need a transplant in the future (P<0.001); those who would accept a liver from a living donor (P<0.001); those who discussed the subject of donation and transplantation with their families (P=0.040); and those whose partner was in favor of donation and transplantation (P=0.044). **Conclusions** Personnel from donation and transplantation-related units had a favorable attitude toward LLD. This attitude was not affected by psychological factors, although it was influenced by factors directly and indirectly related to the donation and transplantation process.

Parkinson's disease severity levels and MDS-Unified Parkinson's Disease Rating Scale.

Martínez-Martín P, Rodríguez-Blázquez C, Alvarez M, Arakaki T, Arillo VC, Chaná P, et al. Parkinsonism Relat Disord. 2014 Nov 5. [Epub ahead of print]

Background Severity of PD is usually assessed by means of the motor and disability-based Hoehn and Yahr staging (HY), or clinician and patient global perceptions. Scores of more detailed assessments, as the MDS-UPDRS, have not been translated to a grading that allows assignment of score sections to severity levels. The objective of the present study is to determine cut-off points for PD severity levels based on the MDS-UPDRS. **Methods** International, observational study. Applied assessments were: HY, MDS-UPDRS, Clinical Impression for Severity Index, and Clinical and Patient Global Impression of Severity. The coincidence in severity level (mild, moderate, severe) of at least two clinical classifications plus the patient's gradation was considered "the criterion of severity". Cut-off values for each MDS-UPDRS subscale was determined by triangulation of: 1) percentile 90 of the subscale total score; 2) receiver operating characteristic (ROC) analysis; and 3) ordinal logistic regression (OLR) model. **Results** Sample was composed of 452 consecutive PD patients without dementia, 55.3% males, age 65.1 ± 10.7 years and PD duration 8.7 ± 6.3 years. All HY stages were represented. The "criterion", classified 275 patients (60.8% of the sample) as: mild PD, 149

(54.2%); moderate, 82 (29.8%); and severe, 44 (16%). The following MDS-UPDRS cut-off points between mild/moderate and moderate/severe levels were found: Part 1: 10/11 and 21/22; Part 2: 12/13 and 29/30; Part 3: 32/33 and 58/59; and Part 4: 4/5 and 12/13. **Conclusion** Cut-off points to classify PD patients as mild, moderate, or severe on the basis of their MDS-UPDRS scores are proposed.

Plasmodium falciparum M1-Aminopeptidase: A Promising Target for the Development of Antimalarials.

González-Bacero J, Fando R, Monte-Martinez AD, Charli JL, Chávez ML. *Curr Drug Targets*. 2014;15(2):1144–65.

Malaria is a devastating human parasitic disease that receives enhanced attention due to the emergence of resistance to traditional drugs. Thus, the search for new molecular targets is a major goal. PfAM1 is an aminopeptidase from *Plasmodium falciparum*, William H. Welch 1897, belonging to the M1 family of metalloproteases, which is a promising target of inhibitors to block the intra-erythrocytic stages of the parasite. Since its identification in 1998, many efforts have been done to validate PfAM1 as an appropriate target of antimalarials. The present work is a critical review of the main structural, functional and kinetic characteristics of PfAM1, as well as a summary of the effects of key inhibitors at molecular and cellular levels. The systematization of experimental results should contribute to a better understanding of the properties of PfAM1 as a target of antimalarials and promote research projects focused on the development of PfAM1 inhibitors.

Preclinical immunogenicity study of trivalent meningococcal AWX-OMV vaccines for the African meningitis belt.

Tunheim G, Naess LM, Acevedo R, Fieldheim AK, Bolstad K, García L, et al. *Vaccine*. 2014 Oct 8;32(49):6631–8.

In the recent decade, epidemic meningitis in the African meningitis belt has mostly been caused by *Neisseria meningitidis* of serogroups A, W and X (MenA, MenW and MenX, respectively). There is at present no licensed vaccine available to prevent MenX meningococcal disease. To explore a trivalent MenAWX vaccine concept, we have studied the immunogenicity in mice of MenX outer membrane vesicles (X-OMV) or MenX polysaccharide (X-PS) when combined with a bivalent A-OMV and W-OMV (AW-OMV) vaccine previously shown to be highly immunogenic in mice. The vaccine antigens were produced from three representative wild type strains of MenA (ST-7), MenW (ST-11) and MenX (ST-751) isolated from patients in the African meningitis belt. Groups of mice were immunized with two doses of X-OMV or X-PS combined with the AW-OMV vaccine or as individual components. All vaccine preparations were adsorbed to Al(OH)₃. Sera from immunized mice were tested by ELISA and immunoblotting. Functional antibody responses were measured as serum bactericidal activity (SBA) and opsonophagocytic activity (OPA). Immunization of mice with X-OMV, alone or in combination with AW-OMV induced high levels of anti-X OMV IgG. Moreover, X-OMV alone or in combination with the AW-OMV vaccine induced high SBA and OPA titers against the MenX target strain. X-PS alone was not immunogenic in mice; however, addition of the AW-OMV vaccine to X-PS increased the immunogenicity of X-PS. Both AWX vaccine formulations induced high levels of IgG against A- and W-OMV and high SBA titers against the MenA and MenW vaccine strains. These results suggest that a trivalent AWX vaccine, either as a combination of OMV or OMV with X-PS, could potentially prevent the majority of meningococcal disease in the meningitis belt.

Predictors of neurological deficit after endovascular treatment of cerebral arteriovenous malformations and functional repercussions in prospective follow-up.

Jordan J, Llibre JC, Vázquez F. *Neuroradiol J*. 2014 Dec;27(6):18–24.

Endovascular therapy is a well-established approach to the treatment of cerebral arteriovenous malformations (AVMs). The objective of this study was to determine the predictive factors of neurological deficit following endovascular procedures. Seventy-one patients with cerebral AVMs who underwent 147 embolization sessions from 2006 to 2011 were followed up prospectively (average 31.1 ± 17.5 months). Functional neurological condition was documented by means of the modified Rankin scale. Factors found to be predictors of neurological deficit were the partial obstruction of drainage veins (OR = 197.6; IC = 2.76 - 1416.0; P = 0.015), a positive result in the Propofol test (OR = 50.2; IC = 6.18 - 566.5; P = 0.000), AVM diameter under 3 cm (OR = 21.3; IC: 1.71 - 265.6; P = 0.018), the presence of intranidal aneurysms (OR = 11.2; IC = 1.09 - 114.2; P = 0.042), the absence of post-procedure hypotension (OR = 10.2; IC = 1.35 - 77.7; P = 0.003), deep venous drainage (OR = 7.14; IC = 1.15 - 44.4; P = 0.035), and devascularization in excess of 40% per session (OR = 3.3; IC = 1.11 - 16.8; P = 0.056). Fifty-six patients (78.9%) did not experience changes in their neurological condition after the treatment and 13 patients (18.3%) showed a new neurological deficit related to the treatment; 95.8 % of the patients did not show significant long-term incapacity. Partial obstruction of

drainage veins, small AVMs, intranidal aneurysms, faulty hemodynamic control and extensive devascularization were found to be predictors of neurological deficit. A significant number of patients with neurological deficit improved in the long term.

Racotumomab-alum vaccine for the treatment of non-small-cell lung cancer.

Hernández AM, Vázquez AM. *Expert Rev Vaccine*. 2015 Jan;14(1):9–20. [Epub ahead of print]

Racotumomab-alum vaccine is an anti-idiotypic vaccine able to mimic the tumor-associated antigen NeuGcGM3. Different Phase I clinical trials and compassionate use studies demonstrated its low toxicity and capacity to induce a strong anti-NeuGcGM3 response, able to bind and directly kill tumor cells expressing the antigen. A Phase II/III randomized double-blind clinical trial in advanced non-small cell lung cancer patients showed a significant improvement in overall survival and progression-free survival for racotumomab-alum versus placebo. Patients who developed anti-NeuGcGM3 antibodies capable of binding and killing NeuGcGM3 expressing tumor cells showed significantly longer median survival times. The impact of using racotumomab-alum as switch maintenance followed by second-line therapy is currently being explored in a new randomized, multinational Phase III study.

The impact of globalization on subjectivities in Cuba: A gender perspective.

Vega AP. *Int Rev Psychiatry*. 2014 Oct;26(5):589–94.

Globalization has created great transformations, not only in economics, but also in social and cultural relations, and has influenced political practices and governments. If not critically analyzed, globalization may at first appear positive, but, in parallel with its development, high levels of poverty and exclusion have occurred and these may affect men and women differently. The objective of this article is to reveal the subjective or individual consequences that derive from globalization and the contexts it creates. This analysis centers on a gender perspective within a Cuban context and tries to challenge the prevailing view of the most poor and excluded groups. Psychiatry and psychology have a long way to go in the search for an understanding of the impact of globalization on human well-being, but critical thinking and the social sciences can offer an alternative to the transformation of this constructed order by giving prominence to people's own subjectivities and experiences.