Anatomic and functional connectivity relationship in autistic children during three different experimental conditions. Machado C, EstÃ©vez M, RodrÃguez R, Leisman G, Melillo R, Chinchilla M, et al. Â Brain Connect. 2015 Sep 18. [Epub ahead of print]

A group of 21 autistic children were studied for determining the relationship between the anatomic (AC) versus functional (FC) connectivity, considering short-range and long-range brain networks. AC was assessed by the DW-MRI technique and FC by EEG coherence calculation, in three experimental conditions: basal, watching a popular cartoon with audio (V-A), and with muted audio track (VwA). For short-range connections, basal records, statistical significant correlations were found for all EEG bands in the left hemisphere, but no significant correlations were found for fast EEG frequencies in the right hemisphere. For the V-A condition, significant correlations were mainly diminished for the left hemisphere; for the right hemisphere, no significant correlations were found for the fast EEG frequency bands. For the VwA condition, significant correlations for the rapid EEG frequencies mainly disappeared for the right hemisphere. For long-range connections, basal records showed similar correlations for both hemispheres. For the right hemisphere, significant correlations incremented to all EEG bands for the V-A condition, but these significant correlations disappeared for the fast EEG frequencies in the VwA condition. It appears that in a resting-state condition, AC is better associated with functional connectivity for short-range connections in the left hemisphere. The V-A experimental condition enriches the AC and FC association for long-range connections in the right hemisphere. This might be related to an effective connectivity improvement due to full video stimulation (visual and auditory). An impaired audiovisual interaction in the right hemisphere might explain why significant correlations disappeared for the fast EEG frequencies in the VwA experimental condition.

Anti-NeuGcGM3 reactivity: a possible role of natural antibodies and B-1 cells in tumor immunosurveillance. RodrÃguez-Zhurbenko N, Rabade-Chediak M, Martinez D, GriÃ±an T, Hernandez AM. Ann N Y Acad Sci. 2015 Jul 27. DOI: 10.1111/nyas.12827. [Epub ahead of print]

While not naturally expressed in normal human tissues, N-glycolylated (NeuGc) gangliosides are overexpressed in several tumors and have immunosuppressive capacity, which contributes to cancer progression. Naturally occurring antibodies against NeuGcGM3 exist in healthy donors that specifically recognize and kill tumor cells expressing the antigen by complement-dependent and -independent mechanisms, the latter resembling an oncotic necrosis-type of cell death. Both the levels of anti-NeuGcGM3 antibodies in the sera of healthy donors and the percentage of donors with these natural antibodies decrease with age. Our work has shown that anti-NeuGcGM3 antibodies are not detected in the sera of non-small cell lung cancer (NSCLC) patients, compared to age- and sex-matched healthy donors, which have anti-NeuGcGM3. Interestingly, the level of serum total IgM, but not IgG, was significantly lower in cancer patients than in healthy donors. Screening of immortalized mouse splenic and peritoneal-derived hybridomas showed that peritoneal B-1 cells secrete anti-NeuGcGM3 with tumor cytotoxic capacity. Defects in the natural surveillance against tumor antigens could increase the risk of elderly donors developing cancer and affect the capacity of cancer patients to effectively fight against tumor cells.

Association of status redox with demographic, clinical and imaging parameters in patients with Huntingtonâ€™s disease. PeÃ±a-SÃ¡nchez M, RiverÃ³n-Forment G, ZaldÃvar-Vaillant T, Soto-Lavastida A, Borrero-SÃ¡nchez J, Lara-FernÃ¡ndez G, et al. Clin Biochem. 2015 Jul 22. pii: S0009-9120(15)00250-7. DOI: 10.1016/j.clinbiochem.2015.06.014. [Epub ahead of print]

Huntington's disease (HD) is an autosomal dominant, progressive neurodegenerative disorder, caused by an expanded trinucleotide CAG sequence of the huntingtin (Htt) gene, which encodes a stretch of glutamines in the Htt protein. The mechanisms of neurodegeneration associated with the accumulation of Htt aggregates still remains unclear.

Objectives To determine oxidative stress biomarkers in HD patients and their relationship with clinical, demographic and neuroimaging parameters. Design and methods Fourteen patients and 39 controls paired by age and sex participated in this study. Oxidative damage was assayed in blood by measuring malondialdehyde (MDA) and advanced oxidative protein products (AOPPs). Antioxidant status was determined by activities of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GR), reduced glutathione (GSH), protein thiols and total antioxidant capacity (FRAP). The Unified Huntington Disease Rating Scale (UHDRS) and neuroimaging studies were also employed. Results MDA, AOPP and GPx were significantly increased in HD patients with respect to the control group, while GR activity was decreased. FRAP correlated with age of disease onset, AOPP with motor severity (UHDRS score), age of patients and age of disease onset. Caudate atrophy was associated with lower plasma concentrations of GSH. Conclusions These findings point to a redox imbalance in HD patients. GR activity could be a potential biomarker for symptom onset in asymptomatic gene carriers, while plasmatic GSH could be useful in monitoring the progression of neurodegeneration - as an expression of caudate atrophy - during the course of the disease.

Decay of Sabin inactivated poliovirus vaccine (IPV)-boosted poliovirus antibodies. Resik S, Tejeda A, Fonseca M, Sein C, Hung LH, Martinez Y, et al. Trials Vaccinol. 2015;4:71â€“4. Trials Vaccinol. 2015;4 :71â€“4.

Introduction We conducted a follow-on study to a phase I randomized, controlled trial conducted in Cuba, 2012, to assess the persistence of poliovirus antibodies at 21â€“22 months following booster dose of Sabin-IPV compared to Salk-IPV in adults who had received multiple doses of oral poliovirus vaccine (OPV) during childhood. Methods In 2012, 60 healthy adult males aged 19â€“23 were randomized to receive one booster dose, of either Sabin-inactivated poliovirus vaccine (Sabin-IPV), adjuvanted Sabin-IPV (aSabin-IPV), or conventional Salk-IPV. In the original study, blood was collected at days 0 (before) and 28 (after vaccination), respectively. In this study, an additional blood sample was collected 21â€“22 months after vaccination, and tested for neutralizing antibodies to Sabin poliovirus types 1, 2 and 3. Results We collected sera from 59/60 (98.3%) subjects; 59/59 (100%) remained seropositive to all poliovirus types, 21â€“22 months after vaccination. The decay curves were very similar among the study groups. Between day 28 and 21â€“22 months, there was a reduction of â©¾87.4% in median antibody levels for all poliovirus types in all study groups, with no significant differences between the study groups. Conclusion The decay of poliovirus antibodies over a 21â€“22-month period was similar regardless of the type of booster vaccine used, suggesting the scientific data of Salk IPV long-term persistence and decay may be broadly applicable to Sabin IPV.

Drug Development in Conformational Diseases: A Novel Family of Chemical Chaperones that Bind and Stabilise Several Polymorphic Amyloid Structures. SablÃ³n-Carrazana M, FernÃ¡ndez I, Bencomo A, Lara-MartÃnez R, Rivera-Marrero S, DomÃnguez G, et al. PLoS One. 2015 Sep 1;10 (9):e0135292. DOI: 10.1371/journal.pone.0135292. eCollection 2015.

The increasing prevalence of conformational diseases, including Alzheimer's disease, type 2 Diabetes Mellitus and Cancer, poses a global challenge at many different levels. It has devastating effects on the sufferers as well as a tremendous economic impact on families and the health system. In this work, we apply a cross-functional approach that combines ideas, concepts and technologies from several disciplines in order to study, in silico and in vitro, the role of a novel chemical chaperones family (NCHCHF) in processes of protein aggregation in conformational diseases. Given that Serum Albumin (SA) is the most abundant protein in the blood of mammals, and Bovine Serum Albumin (BSA) is an off-the-shelf protein available in most labs around the world, we compared the ligandability of BSA:NCHCHF with the interaction sites in the Human Islet Amyloid Polypeptide (hIAPP):NCHCHF, and in the amyloid pharmacophore fragments (AÎ²17-42 and AÎ²16-21):NCHCHF. We posit that the merging of this interaction sites is a meta-structure of pharmacophore which allows the development of

chaperones that can prevent protein aggregation at various states from: stabilizing the native state to destabilizing oligomeric state and protofilament. Furthermore to stabilize fibrillar structures, thus decreasing the amount of toxic oligomers in solution, as is the case with the NCHCHF. The paper demonstrates how a set of NCHCHF can be used for studying and potentially treating the various physiopathological stages of a conformational disease. For instance, when dealing with an acute phase of cytotoxicity, what is needed is the recruitment of cytotoxic oligomers, thus chaperone F, which accelerates fiber formation, would be very useful; whereas in a chronic stage it is better to have chaperones A, B, C, and D, which stabilize the native and fibril structures halting self-catalysis and the creation of cytotoxic oligomers as a consequence of fiber formation. Furthermore, all the chaperones are able to protect and recondition the cerebellar granule cells (CGC) from the cytotoxicity produced by the hIAPP20-29 fragment or by a low potassium medium, regardless of their capacity for accelerating or inhibiting in vitro formation of fibers. In vivo animal experiments are required to study the impact of chemical chaperones in cognitive and metabolic syndromes.

High EGFR and low p-Akt expression is associated with better outcome after nimotuzumab-containing treatment in esophageal cancer patients: preliminary clinical result and testable hypothesis. Wang CY, Deng JY, Cai XW, Fu XL, Li Y, Zhou XY, et al. Oncotarget. 2015 Jul 30;6 (21):18674â€“82.

The epidermal growth factor receptor (EGFR) is widely overexpressed in esophageal squamous cell carcinoma (ESCC) and it results is associated with a poor prognosis. Identifying the subgroup of ESCC patients who are sensitive to EGFR-targeted therapy is a key point to facilitate its medical use.We retrospectively analyzed 32 ESCC patients treated with the combination of nimotuzumab (h-R3) and radiotherapy (RT) or chemoradiotherapy (CRT). Expression of EGFR and phosphorylated proteins associated with EGFR signaling pathway, i.e. p-Akt and p-Erk, were assessed with immunohistochemistry (IHC) for all patients. Correlations between these proteins' expression levels and overall survival (OS) were assessed.High expression of EGFR, p-Akt and p-Erk was detected in 53.1% (17/32), 54.8% (17/31) and 59.4% (19/32) of tumors respectively. No significant differences in OS were found between high EGFR, p-Akt and p-Erk expression groups and their respective counterparts. Of note, significantly better overall survival was observed in patients with coexistence of high EGFR expression and low p-Akt expression (p = 0.030).Our data allowed us to put forward a hypothesis that high EGFR and low p-Akt expression may predict a clinical benefit of EGFR antagonists such as nimotuzumab combined with RT or CRT. This can be discussed in the terms of oncogene addiction and synthetic lethality concepts. This hypothesis can be further tested in larger groups of patients.

Lipopolysaccharide aggregates in native agarose gels detected by reversible negative staining with imidazole and zinc salts. RodrÃguez C, Hardy E. Anal Biochem. 2015 Sep 15;485:72-80. DOI: 10.1016/j.ab.2015.06.020. Epub 2015 Jun 19.

We investigated the use of imidazole and zinc salts for the detection of lipopolysaccharide (LPS) aggregates separated by native agarose gel electrophoresis (NAGE). As a result, a new staining procedure was established by which as little as 1.5 Î¼g of Escherichia coli O55:B5 LPS aggregates were detected by means of inducing a clear, transparent pattern, contrasted against an opaque background. E. coli O55:B5 LPS preparations treated with nucleases and proteinase K proved that the reverse-stained LPS pattern is not related to any potential artifacts caused by unrelated biomolecules (e.g., nucleic acids, proteins). After this, we showed that the procedure is applicable to two-dimensional LPS separation using NAGE/SDS-PAGE, while at the same time confirming that real polydisperse LPS aggregates are represented by the stained profile. Also, we demonstrated the general applicability of this stain to the detection of different NAGE-separated LPS aggregates (e.g., from E. coli 026:B6, E. coli 0111:B4, Salmonella minnesota Re595). Finally, using lysozyme as a model protein, we found that imidazole-zinc may be combined with Coomassie Brilliant Blue R-250 into a double-staining process to enable the use

of NAGE for investigating the interaction of cationic proteins and LPS aggregates and protein or LPS concentration effects on protein-LPS binding.

Male sex is independently associated with faster disability accumulation in relapse-onset MS but not in primary progressive MS. Ribbons KA, McElduff P, Boz C, Trojano M, Izquierdo G, Duquette P, et al. PLoS One. 2015 Jun 5;10(6):e0122686. DOI: 10.1371/journal.pone.0122686. eCollection 2015.

Background Multiple Sclerosis is more common in women than men and females have more relapses than men. In a large international cohort we have evaluated the effect of gender on disability accumulation and disease progression to determine if male MS patients have a worse clinical outcome than females. Methods Using the MSBase Registry, data from 15,826 MS patients from 25 countries was analysed. Changes in the severity of MS (EDSS) were compared between sexes using a repeated measures analysis in generalised linear mixed models. Kaplan-Meier analysis was used to test for sex difference in the time to reach EDSS milestones 3 and 6 and the secondary progressive MS. Results In relapse onset MS patients (n = 14,453), males progressed significantly faster in their EDSS than females (0.133 vs 0.112 per year, P<0.001,). Females had a reduced risk of secondary progressive MS (HR (95% CI) = 0.77 (0.67 to 0.90) P = 0.001). In primary progressive MS (n = 1,373), there was a significant increase in EDSS over time in males and females (P<0.001) but there was no significant sex effect on the annualized rate of EDSS change. Conclusion Among registrants of MSBase, male relapse-onset patients accumulate disability faster than female patients. In contrast, the rate of disability accumulation between male and female patients with primary progressive MS is similar.

Molecular and histological tools to diagnose an imported case of American cutaneous leishmaniasis in Cuba. Montalvo AM, De Armas Y, Fraga J, Blanco O, MenÃ©ndez R, Montoto V, et al. Int J Dermatol. 2015 Jun 12. DOI: 10.1111/ijd.12915. [Epub ahead of print]

Background Leishmaniasis represents a polymorphous group of diseases caused by around 20 different species of Leishmania parasite. Increases in the number of cases of leishmaniasis reported as a consequence of the growth in travel and migration are of concern to epidemiologists and are diagnostically challenging in non-endemic areas. Methods Molecular and histological analyses of a paraffin-embedded skin biopsy were used in parallel to detect Leishmania parasites in a Cuban woman with suspicious lesions arriving in Cuba from Venezuela. Primers based on the 18S fragment of ribosomal ribonucleic acid (rRNA) and heat shock protein 70 genes (hsp70) were used for molecular detection. Results Histological studies detected the presence of the parasite. A small fragment of Leishmania DNA was amplified by polymerase chain reaction (PCR) targeting the 18S fragment using, for the first time, nucleic acid obtained from paraffin-embedded tissue as a template. Amplification of a larger fragment from the hsp70 gene did not occur. Conclusions The detection of Leishmania DNA from paraffin-embedded tissue by means of 18S-targeted PCR is a feasible approach to diagnosis. In combination with classical methods such as histology, the molecular detection of the parasite was demonstrated to be useful in confirming Leishmania infection in a traveler

Molecular Epidemiology of Tuberculosis in Havana, Cuba, 2009. GonzÃ¡lez DÃaz A, Battaglioli T, DÃaz RodrÃguez R, Goza ValdÃ©s R, GonzÃ¡lez Ochoa E, Van der Stuyft. Trop Med Int Health. 2015 Jul 24. DOI: 10.1111/tmi.12569. [Epub ahead of print]

Objectives To estimate the proportion of tuberculosis cases attributable to recent transmission and the risk factors possibly associated with tuberculosis clustering. Methods Population-based study combining information from epidemiological investigation of tuberculosis cases notified to the National Tuberculosis Control Program in Havana, Cuba, in 2009 with the results of genotyping of Mycobacterium tuberculosis isolates with variable number tandem repeat of mycobacterial interspersed repetitive units (MIRU-VNTR) typing. Results Of 186 cases, 61 were genotyped: 33 patterns and five

clusters with 19, 7, 3, 2 and 2 cases were found. The proportion of cases due to recent transmission was 45% (95% confidence interval 33-58%). Routine contact investigation failed to identify a substantial number of epidemiological links. A history of living in a closed setting was strongly associated with clustering. Conclusions The proportion of cases due to recent transmission in Havana in 2009 is high. The existing control measures in closed settings should be strengthened. A study on a larger number of cases and for a longer time period should be carried out to obtain more precise estimates. Further studies on the utility and cost-effectiveness of the addition of molecular epidemiology techniques to support the progress towards tuberculosis elimination in Cuba, a low-incidence resource-limited setting, are also needed.

More than a pore: the interplay of pore-forming proteins and lipid membranes. Ros U, GarcÃa-SÃ¡ez AJ. J Membr Biol. 2015 Jun;248(3):545â€“61.

Pore-forming proteins (PFPs) punch holes in their target cell membrane to alter their permeability. Permeabilization of lipid membranes by PFPs has received special attention to study the basic molecular mechanisms of protein insertion into membranes and the development of biotechnological tools. PFPs act through a general multi-step mechanism that involves (i) membrane partitioning, (ii) insertion into the hydrophobic core of the bilayer, (iii) oligomerization, and (iv) pore formation. Interestingly, PFPs and membranes show a dynamic interplay. As PFPs are usually produced as soluble proteins, they require a large conformational change for membrane insertion. Moreover, membrane structure is modified upon PFPs insertion. In this context, the toroidal pore model has been proposed to describe a pore architecture in which not only protein molecules but also lipids are directly involved in the structure. Here, we discuss how PFPs and lipids cooperate and remodel each other to achieve pore formation, and explore new evidences of protein-lipid pore structures.

Needle-free jet injector intradermal delivery of fractional dose inactivated poliovirus vaccine: Association between injection quality and immunogenicity. Resik S, Tejeda A, Mach O, Sein C, Molodecky N, Jarrahian C, et al. Â Vaccine. 2015 Jul 17. pii: S0264-410X(15)00872-5. DOI: 10.1016/j.vaccine.2015.06.071. [Epub ahead of print]

Introduction The World Health Organization recommends that as part of the polio end-game strategy a dose of inactivated poliovirus vaccine (IPV) be introduced by the end of 2015 in all countries currently using only oral poliovirus vaccine (OPV). Administration of fractional dose (1/5 of full dose) IPV (fIPV) by intradermal (ID) injection may reduce costs, but its conventional administration is with Bacillus Calmette-Guerin (BCG) needle and syringe (NS), which is time consuming and technically challenging. We compared injection quality achieved with BCG NS and three needle-free jet injectors and assessed ergonomic features of the injectors. Methods Children between 12 and 20 months of age who had previously received OPV were enrolled in the Camaguey, Cuba study. Subjects received a single fIPV dose administered intradermally with BCG NS or one of three needle-free injector devices: Bioject Biojector 2000Â® (B2000), Bioject ID PenÂ® (ID Pen), or PharmaJet TropisÂ® (Tropis). We measured bleb diameter and vaccine loss as indicators of ID injection quality, with desirable injection quality defined as bleb diameter â‰¥5mm and vaccine loss <10%. We surveyed vaccinators to evaluate ergonomic features of the injectors. We further assessed the injection quality indicators as predictors of immune response, measured by increase in poliovirus neutralizing antibodies in blood between day 0 (pre-IPV) and 21 (post-vaccination). Results Delivery by BCG NS and Tropis resulted in the highest proportion of subjects with desirable injection quality; health workers ranked Biojector2000 and Tropis highest for ergonomic features. We observed that vaccine loss and desirable injection quality were associated with an immune response for poliovirus type 2 (P=0.02, P=0.01, respectively). Conclusions Our study demonstrated the feasibility of fIPV delivery using needle-free injector devices with high acceptability among health workers. We did not observe the indicators of injection quality to be uniformly associated with immune response.

Objective measurements of image quality in synchrotron radiation phase-contrast imaging versus digital mammography. Ruiz-GonzÃ¡lez Y, PÃ©rez-DÃaz M, MartÃnez-Ã guila D, DÃaz-Barreto M, Fleitas I, Mora-Machado R, et al. Int J Comput Assist Radiol Surg. 2015 Jun 20. [Epub ahead of print]

Purpose Phase-contrast mammography with synchrotron radiation is an innovative X-ray imaging practice that improves the identification of breast lesions. Previous studies have proven the superiority of the mammography images taken in the phase-contrast modality using synchrotron radiation beams as compared with images taken in conventional mammography by subjective analyses. However, to our knowledge, no previous study has compared different acquisition systems in order to quantify this improvement by means of objective robust indicators. In this research, we intend to quantify the superiority of phase-contrast imaging by means of objective metrics of image quality. Methods Images from the American College of Radiology Mammographic Accreditation Phantom were obtained at hospitals, in two digital mammography equipment and at the Elettra synchrotron radiation facility (Trieste, Italy), using free space propagation phase-contrast modality. Regions of interest were selected to analyze image quality at the fibers (phase object) and masses (area object) simulated on the phantom by means of the signal-to-noise ratio, the figure of merit, the contrast and the edge visibility. Results The image contrast and edge visibility were significantly higher at the phase-contrast modality as compared with digital mammography equipment. The figure of merit using phase-contrast modality was higher for the fibers and comparable for the masses. Conclusion The results showed an improvement of the contrast and edge visibility in phase-contrast images. These improvements may be important in the detection of small lesions and details.

Recombinant AAV-mediated in vivo long-term expression and anti-tumour activity of an anti-ganglioside GM3(Neu5Gc) antibody. Piperno GM, LÃ³pez-Requena A, Predonzani A, Dorvignit D, Labrada M, Zentilin L, et al. Gene Ther. 2015 Jul 16. DOI: 10.1038/gt.2015.71. [Epub ahead of print]

The ganglioside GM3(Neu5Gc) has gained increasing attention as therapeutic target because of its selective expression in various human tumours, such as melanoma, breast and lung cancer. 14F7 is a mouse IgG1 with specific reactivity to GM3(Neu5Gc)-positive tumours. The therapeutic activity of 14F7 has also been demonstrated in vivo, through its repetitive passive administration in tumour-bearing animals. In this work we used an alternative strategy to deliver recombinant 14F7 in vivo and analysed the therapeutic efficacy of this approach. We engineered a recombinant adeno-associated vector to direct the expression of secretable recombinant 14F7 in BALB/c animals. A single administration of the rAAV induced efficient production and secretion of the antibody in the bloodstream, with an expression level reaching plateau at âˆ¼3 weeks after injection and persisting for almost a year. Strikingly, upon challenge with GM3(Neu5Gc)-positive X63-AG8.653 myeloma cells, tumour development was significantly delayed in animals treated with rAAV-14F7 with respect to animals treated with a control rAAV codifying for an irrelevant antibody. Finally, no significant differences in survival proportion were detected in animals injected with rAAV-14F7 or treated by standard administration of repetitive doses of purified monoclonal antibody 14F7.

Recombinant streptokinase vs hydrocortisone suppositories in acute hemorrhoids: A randomized controlled trial. HernÃ¡ndez-Bernal F, Castellanos-Sierra G, Valenzuela-Silva CM, CatasÃºs-Ã lvarez KM, MartÃnez-Serrano O, Lazo-Diago OC, et al. World J Gastroenterol. 2015 Jun 21;21 (23):7305â€“12.

Aim To compare the efficacy and safety of recombinant streptokinase (rSK) vs hydrocortisone acetate-based suppositories in acute hemorrhoidal disease. Methods A multicenter (11 sites), randomized (1:1:1), open, controlled trial with parallel groups was performed. All participating patients gave their written, informed consent. After inclusion, patients with acute symptoms of hemorrhoids were centrally

randomized to receive, as outpatients, by the rectal route, suppositories of rSK 200000 IU of one unit every 8 h (first 3 units) and afterwards every 12 h until 8 administrations were completed (schedule A), one unit every 8 h until 6 units were completed (schedule B), or 25 mg hydrocortisone acetate once every 8 h up to a maximum of 24 administrations. Evaluations were performed at 3, 5, and 10 d post-inclusion. The main end-point was the 5th-day response (disappearance of pain and bleeding, and â‰¥ 70% reduction of the lesion size). Time to response and need for thrombectomy were secondary efficacy variables. Adverse events were also evaluated. Results Groups were homogeneous with regards to demographic and baseline characteristics. Fifth day complete response rates were 156/170 (91.8%; 95% CI: 87.3-96.2), 155/170 (91.2%; 95%CI: 86.6%-95.7%), and 46/170 (27.1%; 95%CI: 20.1%-34.0%) with rSK (schedule A and B) and hydrocortisone acetate suppositories, respectively. These 64.6% and 63.9% differences (95%CI: 56.7%-72.2% and 55.7%-72.0%) were highly significant (P < 0.001). This advantage was detected since the early 3rd day evaluation (68.8% and 64.1% vs 7.1% for the rSK and active control groups, respectively; P < 0.001) and was maintained even at the late 10th day assessment (97.1% and 93.5% vs 67.1% for rSK and hydrocortisone acetate, respectively; P < 0.001). Time to response was 3 d (95%CI: 2.9-3.1) for both rSK groups and 10 d (95%CI: 9.3-10.7) in the hydrocortisone acetate group. This difference was highly significant (P < 0.001). All subgroup stratified analyses (with or without thrombosis and hemorrhoid classification) showed a statistically significant advantage for the rSK groups. Thrombectomy was necessary in 4/251 and 14/133 patients with baseline thrombosis in the rSK and hydrocortisone acetate groups, respectively (P < 0.001). There were no adverse events attributable to the experimental treatment. Conclusion rSK suppositories showed a significant advantage over a widely-used over-the-counter hydrocortisone acetate preparation for the treatment of acute hemorrhoidal illness, as well as having an adequate safety profile.

Stability Studies of a Freeze-Dried Recombinant Human Epidermal Growth Factor Formulation for Wound Healing. Santana H, GarcÃa G, Vega M, BeldarraÃn A, PÃ¡ez R. PDA J Pharm Sci Technol. 2015 Mayâ€“Jun;69(3):399â€“416.
DOI: 10.5731/pdajpst.2015.01052.

We report on the stability assessment of a recombinant human epidermal growth factor (rhEGF) freeze-dried formulation for wound healing by intra-lesional injections. The suitability of packaging material for the light protection of finished dried powder was evaluated after stressed exposure conditions. Degradation kinetics of powder for injection was investigated at concentrations of 25-250 Î¼g/vial and temperatures of 45, 60, and 70 Â°C. The long-term stability was evaluated after storage at 25 Â± 2 Â° C/60 Â± 5% relative humidity (6 months) and 2-8 Â°C (24 months) in the dark and analyzed at several time points. The stability after reconstitution with various diluents was also assessed after 24 h storage at 2-8 Â°C. The rhEGF samples were analyzed for structural integrity by reversed-phase high-performance liquid chromatography (RP-HPLC), size-exclusion HPLC, and sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE). Biological activity was investigated by measuring the cell proliferation in a murine fibroblast cell line. Results show that freeze-dried rhEGF in primary packaging only was photosensitive, as degradation by RP-HPLC that was completely suppressed by the secondary carton package was revealed. An increase in freeze-dried rhEGF stability was observed with the increase in protein concentration from 25 to 250 Î¼g/vial. The long-term stability study showed no significant rhEGF degradation or physical change within the freeze-dried formulations containing 25 or 250 Î¼g/vial of rhEGF. No physical, chemical or biological changes were observed for rhEGF after reconstitution in water for injection or 0.9% sodium chloride during the storage conditions studied.

The human voice areas: spatial organisation and inter-individual variability in temporal and extra-temporal cortices. Pernet CR, McAleer P, Latinus M, Gorgolewski KJ, Charest I, Bestelmeyer PE, et al. Neuroimage. 2015 Jun 24. pii: S1053-8119(15)00555-8. DOI: 10.1016/j.neuroimage.2015.06.050. [Epub ahead of print]

FMRI studies increasingly examine functions and properties of non-primary areas of human auditory cortex. However there is currently no standardized localization procedure to reliably identify specific areas across individuals such as the standard 'localizers' available in the visual domain. Here we present an fMRI 'voice localizer' scan allowing rapid and reliable localization of the voice-sensitive 'temporal voice areas' (TVA) of human auditory cortex. We describe results obtained using this standardized localizer scan in a large cohort of normal adult subjects. Most participants (94%) showed bilateral patches of significantly greater response to vocal than non-vocal sounds along the superior temporal sulcus/gyrus (STS/STG). Individual activation patterns, although reproducible, showed high inter-individual variability in precise anatomical location. Cluster analysis of individual peaks from the large cohort highlighted three bilateral clusters of voice-sensitivity, or "voice patches" along posterior (TVAp), mid (TVAm) and anterior (TVAa) STS/STG, respectively. A series of extra-temporal areas including bilateral inferior prefrontal cortex and amygdalae showed small, but reliable voice-sensitivity as part of a large-scale cerebral voice network. Stimuli for the voice localizer scan and probabilistic maps in MNI space are available for download.

Tobacco seeds as efficient production platform for a biologically active anti-HBsAg monoclonal antibody. HernÃ¡ndez-VelÃ¡zquez A, LÃ³pez-Quesada A, Ceballo-CÃ¡mara Y, Cabrera-Herrera G, Tiel-GonzÃ¡lez K, Mirabal-Ortega L, et al. Transgenic Res. 2015 Jun 25. [Epub ahead of print]

The use of plants as heterologous hosts is one of the most promising technologies for manufacturing valuable recombinant proteins. Plant seeds, in particular, constitute ideal production platforms for long-term applications requiring a steady supply of starting material, as they combine the general advantages of plants as bioreactors with the possibility of biomass storage for long periods in a relatively small volume, thus allowing manufacturers to decouple upstream and downstream processing. In the present work we have used transgenic tobacco seeds to produce large amounts of a functionally active mouse monoclonal antibody against the Hepatitis B Virus surface antigen, fused to a KDEL endoplasmic reticulum retrieval motif, under control of regulatory sequences from common bean (Phaseolus vulgaris) seed storage proteins. The antibody accumulated to levels of 6.5 mg/g of seed in the T3 generation, and was purified by Protein A affinity chromatography combined with SEC-HPLC. N-glycan analysis indicated that, despite the KDEL signal, the seed-derived plantibody bore both high-mannose and complex-type sugars that indicate partial passage through the Golgi compartment, although its performance in the immunoaffinity purification of HBsAg was unaffected. An analysis discussing the industrial feasibility of replacing the currently used tobacco leaf-derived plantibody with this seed-derived variant is also presented

T-Wave Oversensing in Patients with Brugada syndrome - True Bipolar Versus Integrated Bipolar ICD Leads: A Multicenter Retrospective Study. RodrÃguez-MaÃ±ero M, de Asmundis C, Sacher F, Arbelo E, Probst V, Castro-Hevia J, et al. Circ Arrhythm Electrophysiol. 2015 Aug;8 (4):792â€“8.

Background It is thought that compared to integrated bipolar leads, dedicated bipolar are more susceptible to T-wave oversensing. This could be of extreme importance in patients with Brugada syndrome (BrS) since T-wave oversensing in this population is more frequent compared to other ICD recipients without BrS. We aimed to compare the incidence of T-wave oversensing in patients with BrS according to the type of lead (integrated bipolar versus true/dedicated bipolar). Methods and results All BrS patients with an ICD implant in 10 tertiary hospitals between 1993 and 2013. A total of 480 patients were included (mean age 45,6 Â± 14). During a mean follow-up of 74,9 Â± 51,7 months (median 69, range 2-236), 28 patients had T-wave oversensing (5,8%), leading to inappropriate shock in 18 (3,8%). All these events occurred in patients with true bipolar ICD leads (p=0,01) and in two patients it was solved instantaneously by changing the configuration from a dedicated to an integrated bipolar sensing configuration. In the stepwise multivariate models only integrated bipolar ICD leads (HR 0.34; 95% CI

0,171-0,675; p=0,002) was independent predictor of non T-wave oversensing. Conclusions T-wave oversensing is a potential reason of inappropriate shocks in patients with BrS receiving ICDs. In the vast majority it can be solved by reprogramming. However, in some patients it still requires invasive intervention. Importantly, incidence is significantly lower using an integrated bipolar lead system when compared to a dedicated bipolar lead system and hence the latter should be routinely employed in BrS cases.

Usefulness of the Pain Tracking Technique in Acute Mechanical Low Back Pain. Bravo Acosta T, MartÃn Cordero JE, HernÃ¡ndez TÃ¡panes S, Pedroso Morales I, FernÃ¡ndez Cuesta JI, Leyva Serrano M. Pain Res Treat. 2015;2015:512673. DOI: 10.1155/2015/512673. Epub 2015 Jul 9.

Objective To evaluate the usefulness of the pain tracking technique in acute mechanical low back pain. Method We performed an experimental prospective (longitudinal) explanatory study between January 2011 and September 2012. The sample was randomly divided into two groups. Patients were assessed at the start and end of the treatment using the visual analogue scale and the Waddell test. Treatment consisted in applying the pain tracking technique to the study group and interferential current therapy to the control group. At the end of treatment, cryotherapy was applied for 10 minutes. The Wilcoxon signed-rank test and the Mann Whitney test were used. They were performed with a predetermined significance level of p â‰¤ 0.05. Results Pain was triggered by prolonged static posture and intense physical labor and intensified through trunk movements and when sitting and standing. The greatest relief was reported in lateral decubitus position and in William's position. The majority of the patients had contracture. Pain and disability were modified with the rehabilitation treatment in both groups. Conclusions Both the pain tracking and interferential current techniques combined with cryotherapy are useful treatments for acute mechanical low back pain. The onset of analgesia is faster when using the pain tracking technique.

Use of bone marrow-derived cells for regenerative medicine in Cuba.
HernÃ¡ndez P. Bone Marrow Transpl. 2015 Sep 14. DOI: 10.1038/bmt.2015.200. Epub ahead of print.

The Cuban population, like others in North America and Western Europe, is aging. Incidences and prevalence of degenerative diseases such as cardio-vascular diseases, diabetes and stroke are increasing. However, Cuba faces a somewhat unique medical challenge compared with these regions. On the one hand, we have a highly-developed medical education system with about 6.7 physicians/1000 population, a rate more than twice as high as the United States (2.4/1000) and the United Kingdom (2.7/1000). For example, Cuba provides more medical personnel to the developing world than all the G8 countries combined including about 19â€‰000 physicians. We also have highly-developed biomedical research institutions with world-class scientific centers such as the Finlay Institute for Vaccines Research and Production, the Center for Molecular Immunology (CIM) and the Center for Genetic Engineering and Biotechnology (CIGB) and the Latin America School of Medicine (ELAM). However, we lack economic resources for advanced medical interventions. Although our health-care expenditure as percent gross domestic product (GDP, 8.8%) is comparable to most Western European countries, it is far less than the United States (17.1%). More importantly, our per capita GDP ($18â€‰796 USD) is much lower than the United States ($53â€‰042 USD) and Western European countries (about $50â€‰000 USD). Consequently, per capita expenditure on health care in Cuba is only about one-third of Western European countries and of the United States. Because of this limitation we have had to develop innovative approaches to deliver newly-evolving health-care interventions such as regenerative medicine.