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Poly-caprolactone: A promising biodegradable polymer

Asma Al Hosni

The University of Manchester, UK

Degradable plastic have received extensive attention because of their faster degradation in the environment. Among these degradable polymers is Poly-Caprolactone (PCL), which has attracted interest as a substitute for conventional polymers because of its properties as a synthetic polymer that is biodegradable. PCL was tested for its degradation with three different polymer forms: discs, film and powder. The results showed that PCL discs could be fully degraded under controlled environmental conditions after 91 days at 50 °C under compost conditions. Moreover, PCL film showed a significant reduction in tensile strength with time when measured after incubation in compost under four different temperatures. Finally, for distributed polymer samples such as powders, the reduction in residual polymer was significant. Moreover, Fungi from the surface of the polymer discs were isolated, identified and tested for its ability to degrade PCL. Therefore it can be confirmed that PCL degradation rate increases with time and as we move to higher temperatures.

Biography

Asma Al Hosni is pursuing PhD at the University of Manchester. She is working on the microbial degradation of biopolymers. She has completed her MSc from Nottingham University in UK in 2008. She is working as a Lecturer at the Higher College of Technology in the Sultanate of Oman.

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Highly bioactive porous 3D Cu-MOFs against MRSA

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Metal-Organic Frameworks (MOFs) are a group of highly porous crystalline materials consisting of metal clusters interconnected with organic linkers. Owing to their high porous and regular structure properties, MOFs has been expanded in biology and medicine as well as gas storage, purification and catalysis. Transition metal ions and metal nanoparticle containing Cu, Zn, Co and Ag have gained prominence as substitutes for new antibacterial agent to effect on bacteria. However, it is known excessive metal ions leached from metal nanoparticle would be harmful to the normal tissue as well as to bacteria. To solve these leakage problems, many researchers tried to trap the metal ion in MOF through coordination of bio active metal ion to organic ligands. New antimicrobial material composed of robust and porous Cu-MOFs are designed in consideration of the inherent characteristics of the metal and organic ligand such as oxidation number, counter ion, the coordination mode, the size and bridging property of the ligand. Bioactive porous three-dimensional Cu-MOFs representing high selective gas sorption were synthesized by hydrothermal reaction. Cu-MOFs containing Cu₂ di-nuclear units connected by flexible glutarate and bipyridyl ligands are formulated as [Cu₂(Glu)₂(μ -L)] \bullet x(H₂O) (Glu=glutarate, L: bpy=1,2-bis(4-pyridyl) (1), bpa = 1,2-bis(4-pyridyl)ethane (2), bpe = 1,2-bis(4-pyridyl)ethene (3), bpp = 1,2-bis(4-pyridyl)propane (4)). The single crystal X-ray study showed that Cu-MOFs contain paddle-wheel Cu₂ di-nuclear units connected by glutarates to form two-dimensional (2D) sheets and these sheets were bridged by bipyridyl ligand to form three-dimensional (3D) frameworks. The number of solvent water molecules in MOF was calculated from elemental analysis and TGA. The solvent-free MOFs 1, 2, 3 and 4 indicated 18.9%, 26.5%, 27.7% and 30.8% of void volumes, respectively, based on the PLATON analysis and contain well-defined 1D channel. Porous 3D Cu-MOF exhibited high selective sorption of quadrupolar CO₂ over N₂ and H₂. Antibacterial activities of Cu-MOFs against MRSA will be discussed.

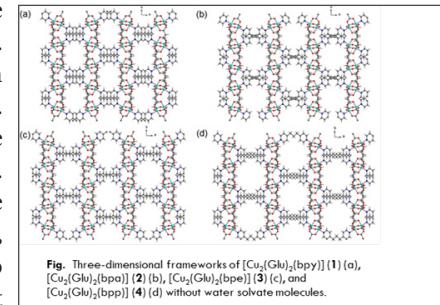


Fig. 2. Three-dimensional frameworks of [Cu₂(Glu)₂(bpy)] (1) (a), [Cu₂(Glu)₂(bpa)] (2) (b), [Cu₂(Glu)₂(bpe)] (3) (c), and [Cu₂(Glu)₂(bpp)] (4) (d) without water solvate molecules.

Biography

Do Nam Lee has received her BS and MS from Yonsei University in Chemistry. She has earned her PhD from Yonsei University (1992) under the supervision of Prof. Chang Hwan Kim and completed Postdoctoral study as a member of the groups of Prof. Robert West at University of Wisconsin-Madison. She has worked as visiting scholar at Peking University. She is currently an associate professor at Kwangwoon University, Republic of Korea and mostly focusing on researches of synthesis and application of coordination complexes, functional metal organic frameworks and polymers.

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Dissecting the regulation of the three tandem promoters of the *Escherichia coli* kps gene cluster at chromosomal level

Esraa Aldawood and Ian Roberts

University of Manchester, United Kingdom

There are three tandem promoters (PR1-1, PR1-2 and PR1-3) within the PR1 regulatory region of *Escherichia coli* kps capsule gene cluster. In this study, we dissect out the regulation of the PR1 promoters in the chromosome and examine the effect of global regulators known to regulate transcription of the kps gene cluster such as IHF, HNS and slyA. Several constructs were made in UTI89 and UTIP1lacZ strains with mutations in the -10 of the selected promoter using gene doctoring followed by K1 phage sensitivity assay and FACS analysis in UTI89 strain and measuring the transcriptional response using chromosomal lacZ reporter fusion assay in UTIP1lacZ strain. The mutation of PR1-2 UTIP1lacZ reduced β -galactosidase activity by 50% indicating that PR1-2 is a functional promoter. In contrast mutation of PR1-1 abolished transcription from the whole PR1 promoter indicating that both PR1-2 and PR1-3 are dependent on PR1-1. These data were mirrored by K1 capsule production as detected by sensitivity to K1-specific bacteriophage and FACS analysis. Mutation of PR1-2 reduced the capsule production by half whereas mutation of PR1-1 hindered capsule formation. Moreover, three different mutations in ihf, hns and slyA were made in those promoter constructs and showed a reduction in the β -galactosidase activity in PR1-2 mutant, where it has PR1-1 acing, indicating that these regulators may act in PR1-1 specifically. Overall, these results demonstrate the importance of PR1-1 promoter in the PR1 regulatory region and the complex interplay between multiple promoters. Going forward I intend to study the individual role of each promoter during infection of particular cell line.

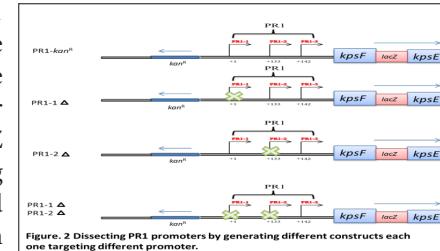


Figure. 2 Dissecting PR1 promoters by generating different constructs each one targeting different promoter.

Biography

Esraa Aldawood is pursuing PhD in Molecular Microbiology at the University of Manchester, UK

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The role of TGF- β 1 in the development of Fetal Alcohol Syndrome (FAS)

Zhanna Malakhova

Baltic Federal University, Russia

The poor results of all anti-alcohol programs create a chain of other problems. However, none of them is as burning as female alcoholism and, consequently, the development of FAS in their children. The study aimed at identifying possible differences in the TGF- β 1 content in the blood serum of pregnant women who abuse alcohol and who do not. Twenty-nine pregnant women were examined. Of these, 1st group (the main group) included 8 women (with a history of alcohol addiction), and 2nd (control) group of 21. The determination of the TGF- β 1 level was performed during 11th-14th weeks of pregnancy. Due to the peculiarities of the examined women pregnancy period (gestosis, extragenital pathology and gynecological diseases), a parallel study of TGF- β 1 in rats was conducted. The investigations were carried out in the autumn-winter period on 26 1-2-month-old Wistar rats, weighing 280-300g. They were divided into two groups: 1 - main (13 animals receiving 15% alcohol solution instead of water for 1 month before pregnancy and during the entire pregnancy), 2 - control (13 intact rats). To determine TGF- β 1, a heterogeneous solid-phase enzyme-linked immunosorbent assay (Rat-TGF- β 1 ELISA test system BMS623 and BMS623TEN, Bender medsystems, Austria) was used. The number of TGF- β 1 in the 1st group of women was 71.7 ng/ml, 8.8 ng / ml (t = 1.94, p <0.05) in the second. The reference values of TGF- β 1 0 - 3.46 ng/ml. The experiment on rats also resulted in statistically significant TGF- β 1 value differences: in the experimental group M = 187.9 ng / ml, in the control group m = 129.7 ng / ml, t = 2.68, p <0.02. An increase in TGF- β 1 concentration in women who took alcohol during pregnancy and a similar trend in alcoholized pregnant rats allow to say that the existing receptor block to the growth factor is associated with ethanol influence. Based on these provisions, it becomes possible to explain the complex of clinical data peculiar to newborns with FAS: intrauterine growth retardation, facial deviations, changes in the central nervous system.

Biography

Zhanna Malakhova has completed his Graduation from the Pediatric Faculty of the Ural State Medical Institute in 1992. From 1996 he worked like Assistant of the Department of Children's Diseases of the Medical Faculty of the Ural medical University. Since 2015 he has been working at the Baltic Federal University (Kalininograd) as a Professor of the Department of therapy.

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Undifferentiated adult human Mesenchymal Cells (ahMSCs) response on a novel graphene coated – nurse's a phase bio-ceramic

Ruben Rabadan-Ros¹, Belén Gil-Muñoz², Clara Meseguer-Ortiz³, Dra Piedad N de Aza⁴ and Luis Meseguer-Olmo¹

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It is well known that Si- Ca-P bio-ceramics are promising bioactive materials for bone tissue engineering, particularly for bone repair. Recently, it has been reported that graphene can be used as an additive to improve the properties of composites due to its biocompatibility and it has been proposed for a number of biomedical applications. Graphene has remarkable mechanical properties, which makes it potentially a good reinforcement in ceramic composites. It also has unique electrical and thermal properties, which makes it attractive filler for producing multifunctional ceramics for a wide range of applications. It has been shown that Graphene Oxide (Go) and reduced graphene oxide (r-Go) can promote biological interactions due to its many surface functional groups and serve as a carrier for drugs and other biomolecules. In addition, Go regulates the proliferation and differentiation of cultured mesenchymal stem cells. In this work, we have optimized the graphene coating of a Si-Ca-P bioceramic, obtaining scaffolds totally covered by a thin layer of graphene oxide and reduced graphene oxide. *In vitro* assays with adult human mesenchymal stem cells (ahMSCs) showed that A-Go stimulates cellular proliferation more than A-Gr the first days of culture. This could support the theory of other researchers that indicates that Go mainly stimulates cell proliferation, while r-Go favors cell differentiation.

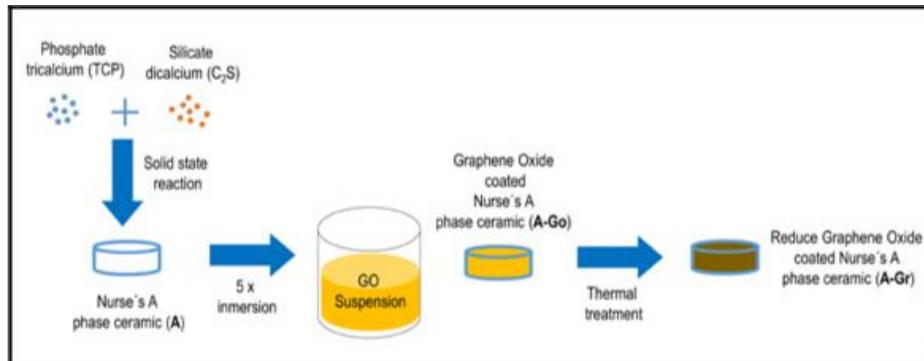


Figure: Synthesis of graphene coated Nurse's A phase

Biography

Ruben Rabadan Ros is a Post-doctoral Researcher who has his expertise in Tissue Repair and passion in improving the health by the study of Organ and Tissue Regeneration. In his short career, he has focused in bone, ligament and cartilage regeneration, and he has helped to develop scaffolds based on the C₂S-TCP phase diagram and combination bio-ceramics with fibroin, specially testing their biocompatibility and osteointegration by *in vitro* and *in vivo* studies.

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Influence of topography of porous-Nurse's A phase bioceramic on metabolic activity of adult human mesenchymal stem cells

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It is well known that Si-Ca-P bioceramics are promising bioactive materials for bone tissue engineering, particularly for bone repair¹. Silicon incorporation to these ceramics may be fundamental to skeletal development stimulating mesenchymal stem cells proliferation and differentiation to osteoblasts ^{2,3}. An important characteristic of a bioceramic designed for bone reconstruction is its open porosity with a high area / volume ratio that facilitates the initial circulation of biological fluids, cell migration and vascular invasion after bone implantation ^{4,5}. In this work, we have processed a Si-Ca-P ceramic using a Q-switched Nd:YAG laser, obtaining biocompatible ceramics with 70 μ m and 350 μ m homogeneously distributed interconnected pores. *In vitro* assays using *ahMSCs* showed that cells seeded onto the top of these scaffolds could proliferate, cross the small pores and enter into big pores. So, if we use these bioceramics *in vivo*, we could probably observe how the cells penetrate into the bioceramics through the pores, improving the cellular and vascular colonization of the biomaterial and allowing initial circulation of the body fluids from the first moment of implantation, increasing the bioceramic biodegradability.

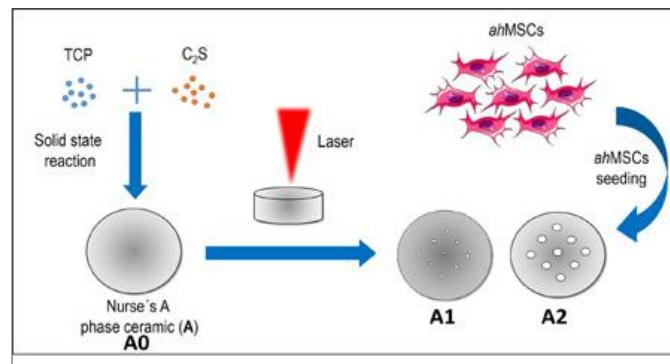


Figure: Synthesis of porous Nurse's A phase and ahMSCs seeding

Biography

Ruben Rabadan (PhD) is a post-doctoral researcher who has his expertise in Tissue Repair, and passion in improving the health by the study of Organ and Tissue Regeneration. In his short career, he has focused in bone, ligament and cartilage regeneration, and he has helped to develop scaffolds based on the C₂S-TCP phase diagram and combining bioceramics with fibroin, specially testing their biocompatibility and osteointegration by *in vitro* and *in vivo* studies.

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Bio-efficiency of *Cinnamomum verum* loaded niosomes and its microbicidal and mosquito larvicidal activity against *Aedes aegypti*, *Anopheles stephensi* and *Culex quinquefasciatus* (Diptera: Culicidae)

Asaithambi Kalaiselvi¹, Michael Gabriel Paulraj², Savarimuthu Ignacimuthu² and Ekambaram Nakkeeran¹

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The emergence of mosquito vector borne diseases is considered as a perpetual problem globally in tropical countries. Outbreak of several diseases such as chikungunya, zika viral infection and dengue fever has created a massive threat towards living population. Frequent usage of synthetic insecticides like DDT eventually had its adverse harmful effects on humans as well on the environment. Since there are no perennial vaccines, prevention, treatment or drugs available for these pathogenic vectors, WHO is more concerned in eradicating their breeding sites effectively without any side effects on humans and environment by approaching plant derived natural eco-friendly bio-insecticides. The aim of this study is to investigate the larvicidal potential *Cinnamomum verum* essential oil (CEO) loaded niosomes were prepared using trans-membrane pH gradient method using cholesterol and surfactant variants of Span 20, 60 and 80 and treated against II to IV instar larvae of *Aedes aegypti*, *Anopheles stephensi* and *Culex quinquefasciatus*. The synthesized CEO loaded niosomes were characterized by zeta potential, particle size, Fourier Transform Infrared Spectroscopy (FT-IR), GC-MS and SEM analysis to evaluate charge, size, functional properties, composition of secondary metabolites and morphology. The Z-average size of the formed niosomes was 1870.84 nm and had good stability with zeta potential -85.3 meV. The entrapment efficiency of the CEO loaded niosomes was determined by UV-Visible Spectrophotometry. Evaluation of synthesized niosomes against gram-positive (*Bacillus subtilis*) and gram-negative (*Escherichia coli*) bacteria and fungi (*Aspergillus fumigatus* and *Candida albicans*) at various concentrations were assessed for its bio-potency. The larvicidal activity was evaluated at various concentrations for 24 h and LC50 and LC90 values were calculated. The results exhibited that CEO loaded niosomes has greater efficiency against mosquito larvicidal property and also the results suggest that niosomes could be used in various applications of biotechnology and drug delivery systems with greater stability by altering the drug of interest.

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Safety and effectiveness of nimotuzumab in the treatment of advanced head and neck cancer patients in open population

Aliz M Vega

Center of Molecular Immunology, Cuba

Epidermal Growth Factor Receptor (EGFR) can be overexpressed in Head and Neck Cancer (HNC). Nimotuzumab is a humanized monoclonal antibody (hMab) that binds to the EGFR. A phase IV study was conducted in advanced head and neck newly diagnosed and recurrent cancer patients to evaluate safety and efficacy of nimotuzumab. Four therapeutic schemes were evaluated: Nimotuzumab, nimotuzumab+Chemotherapy (Nimo+CT), nimotuzumab+Radiotherapy (Nimo+RT) and nimotuzumab+Chemo+Radiotherapies (Nimo+CRT). Common toxicity criteria to evaluate Adverse Events (AEs) (version 3.0) was used to classify AEs; Kaplan-Meier curves were compared by the non-parametric Log-rank method and Cox regression was applied for subgroup analyses. A total of 225 patients were included. Most AEs were classified as grade I, AEs related to the product were reported in 36 patients. In this subgroup, most frequent events were anemia, leukopenia, neutropenia, anorexia, nausea, vomiting, asthenia and fever. In the newly diagnosed subset (n=155), although no significant difference was shown in the Intent-to-treat (ITT) analysis, there was a trend toward a benefit in favor of Nimo+CRT, not just related to Progression-Free-Survival (PFS) (22.4 months; p=0.065), but also to Overall Survival (OS) (24.3 months; p=0.089), with higher survival rates at 12 and 24 months for PFS (67.3% and 46.3%, respectively) and OS (70.1% and 50.3%, respectively), compared to the other regimens. Administration of nimotuzumab was safe in the treatment of advanced HNC patients and well tolerated despite the combination with CRT.

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Setting up a methodology for the study of ALK translations by liquid biopsy

Ana Martínez Rodríguez
Spain

Cancer is a generic term for a large group of diseases characterized by the growth of abnormal cells that can then invade and spread to other organs. Lung cancer is one of the most common types. It is also the one with the highest mortality rate in Spain and in the rest of the world. There are two main types of lung cancer: Small-Cell Lung Carcinoma (SCLC) and Non-Small-Cell Lung Carcinoma (NSCLC). The discoveries of Tyrosin Kinase Inhibitors (TKI) that target Anaplastic Lymphoma Kinase (ALK) gene rearrangements have achieved a huge success in the management of patients with ALK-positive NSCLC. The principal TKI for these patients is called Crizotinib. It induces rapid tumor regression and objective responses in the majority of patients whose tumors contain the ALK gene rearrangements. Although a great advance in the treatment of these patients has been achieved, the initial diagnosis remains a challenge since it is confirmed by a tissue biopsy which requires an invasive procedure. Liquid biopsy testing is a new, non-invasive technique, suitable to identify NSCLC patients that can benefit from ALK-targeted therapies. This technology allows the detection of nucleic acids in plasma or serum thanks to the improvement in the Polymerase Chain Reaction (PCR), the digital-PCR. Tumors release fragments of DNA into the bloodstream that can be used to monitor the drug response, allowing much more personalized treatments. This type of genetic material is known as circulating tumor DNA (ctDNA). In addition to ctDNA, exosomal RNA, Circulating Tumor Cells (CTCs) or platelet RNA offer the potential for drug response detection and monitoring by liquid biopsy. The objective of the research is to focus on liquid biopsy using a specific blood component, known as Tumor-educated Blood Platelets (TEPs) and how it can help to detect ALK gene translocations.

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**Screening of crop seedlings to salinity stress tolerance: The case of *Pisum sativum* var. *abyssinicum*
A. Braun in Ethiopia**

Berhane Gebreslassie Gebreegziabher and Berhanu Abraha Tsegay

Bahir Dar University, Ethiopia

Dekoko (*Pisum sativum* var. *abyssinicum*) is one of the most important food legumes grown in south Tigray and north Wollo, northern Ethiopia. It is one among the most important food legumes in terms of price and protein content. It grows alone and mixed with many cereal crops growing in north Ethiopia. This study was conducted with the objective of selecting tolerant and relatively high yielding *P. sativum* var. *abyssinicum* collections under different salt (NaCl) concentrations at laboratory conditions. The seeds of the six collections were obtained from four districts; two regional states of north Ethiopia with different attitudinal ranges 1868 m a.s.l. being the lowest and 2457 m a.s.l. the highest. The six on farm vigorously growing local collections, three from Ofla (T-001/08OF, T-002/08OF and, T-003/08OF), one from Sirinka (T-025/08Sr), one from Emba-Alaje (TA-026/15E/A) and one from Endamohoni (T-023/15MW) were studied for salt stress tolerances in controlled condition by priming in four salt treatment levels (5 dS/m, 7 dS/m, 9 dS/m and 15 dS/m). Distilled water (0 dS/m) was used as control. 50 surface sterilized seeds per petri dish were sown for the four salt treatments and the control. Collections T-001/08 from Ofla and T-023/08 from Endamohoni showed good growth performance at 5 dS/m. However, T-025/08Sr from Sirinka and TA-026/15E/A from Emba-Alaje responded positively up to 7 dS/m. At higher salinity level (9 dS/m) growth features decreased with increasing salinity stress. But, T-023/15MW, T-001/08OF, T-025/08Sr followed by TA-026/15E/A from lower to the higher resistances, respectively, could withstand lower (5 dS/m) to medium (7 dS/m) concentrations of salinity as compared to the other collections.

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Liquid biopsy: Innovative and non-invasive technique for the study of ALK gene rearrangements

Ana Martínez Rodríguez and Atocha Romero Alfonso

Hospital Universitario Puerta de Hierro, Spain

Statement of the Problem: Lung cancer is the one with the highest mortality rate in the world. There are two main types: Small-Cell Lung Carcinoma (SCLC) and Non-Small-Cell Lung Carcinoma (NSCLC). The discovery of Tyrosin Kinase Inhibitors (TKI) that target Anaplastic Lymphoma Kinase (ALK) gene rearrangements have achieved a huge success in the management of patients with ALK-positive NSCLC. Although a great advance in the treatment of these patients has been achieved, the initial diagnosis remains a challenge since it is confirmed by a tissue biopsy, which requires an invasive procedure. Liquid biopsy testing is a new, non-invasive technique, suitable to identify NSCLC patients that can benefit from ALK-targeted therapies. The objective of the study is to focus on liquid biopsy using a specific blood component, known as Tumor-Educated Blood Platelets (TEPs) and how they may assist in ALK gene rearrangements detection.

Methodology: Firstly, different methods for platelet RNA extraction were tested from blood of healthy donors. The chosen method was used to extract the mutated RNA from the TEPs of patients with NSCLC. The RNA profile of both populations was compared. Secondly, we determined the optimal digital PCR (dPCR) conditions to detect the presence of variant 3 of the EML4-ALK fusion gene in a positive control (cell line H2228). Finally, we used dPCR to analyze EML4-ALK rearrangements in TEPs from the blood of NSCLC patients.

Findings: Platelets are a valuable source for the non-invasive detection of EML4-ALK rearrangements. The type of RNA population present in platelets varies depending on the extraction method used. dPCR is a useful technique for the detection and quantification of EML4-ALK rearrangements.

Conclusion: In this study we present a standardized method to extract platelet RNA and detect EML4-ALK rearrangements using dPCR, for which there was no previous data on yields or optimization conditions. This will mean an improvement in the application of liquid biopsy as an alternative protocol in the search for biomarkers in patients with NSCLC.

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Use of an ionized salt nasal solution in asthmatics with high respiratory infection and its impact on inspiratory and expiratory flow

Eduardo Antonio Lara-Pérez¹, Felix Guillermo Márquez-Celedonio² and Cesar Virgen-Ortega³

¹Director of Clinasma, Mexico

²Director of Research in Medicine, Colombia

³President college of pediatrics of tabasco, Mexico

Background: Bronchial asthma is a condition that affects up to 13% of the school population, is associated with reduced inspiratory and expiratory flows, rhinitis and respiratory infections. Ionic nasal saline solution is an adjuvant option for treatment with bactericidal and virucidal effects.

Objective: To determine the effect of the use of ionized nasal saline in the Maximum Inspiratory Flow (MIF) and pPeak Expiratory Flow (PEF) and the frequency of respiratory infections in school children with bronchial asthma.

Material & Methods: Pre-experimental study with baseline demographic, anthropometric measurements, frequency of respiratory infections and inspiratory and expiratory flows. Follow-up for four months with monthly evaluations of mif, pef and presence of respiratory infections. Inferential analysis with: chi square, mann-whitney, wilcoxon and student's t.

Results: We included 80 schoolchildren of 8.7 ± 2.1 years, height of 1.31 ± 2.1 m, 48 (60.0%) of male and 32 female (40%). The MIF evolved from 58.4 ± 19.3 l/sec initial and 104.7 ± 29.2 at four months ($p < 0.05$), PEF initiation 192.7 ± 58.7 to 222.3 ± 67.0 final ($p < 0.05$) respiratory infections 100% to 88.8% first month and 0.0% at the end ($p < 0.05$).

Conclusions: The administration of ionized nasal saline solution in asthmatic school children allows to recover values of MIF and PEF and to reduce the frequency of infectious airways, independently of the sex and category of acute or chronic infection.

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The use and efficacy of continuous glucose monitoring in type 1 diabetes treated with insulin pump therapy: A randomized controlled trial

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The aim of this multi-centre, randomized, controlled crossover study was to determine the efficacy of adding Continuous Glucose Monitoring (CGM) to insulin pump therapy (CSII) in type 1 diabetes. Children and adults (n=153) on CSII with hba1c 7.5–9.5% (58.5–80.3 mmol/mol) were randomized to (CGM) a Sensor On or Sensor Off arm for 6 months. After 4 months' washout, participants crossed over to the other arm for 6 months. Pediatric and adult participants were separately electronically randomized through the case report form according to a predefined randomization sequence in eight secondary and tertiary centres. The primary outcome was the difference in hba1c levels between arms after 6 months. 77 participants were randomized to the On/Off sequence and 76 to the Off/On sequence; all were included in the primary analysis. The mean difference in hba1c was -0.43% (-4.74 mmol/mol) in favor of the Sensor On arm (8.04% [64.34 mmol/mol] vs. 8.47% [69.08 mmol/mol]; 95% CI -0.32%, -0.55% [-3.50, -6.01 mmol/mol]; p<0.001). Following cessation of glucose sensing, hba1c reverted to baseline levels. Less time was spent with sensor glucose <3.9 mmol/l during the Sensor On arm than in the Sensor Off arm (19 vs 31 min/day; p=0.009). The mean number of daily boluses increased in the Sensor On arm (6.8±2.5 vs. 5.8±1.9, p<0.0001), together with the frequency of use of the temporary basal rate (0.75±1.11 vs. 0.26±0.47, p<0.0001) and manual insulin suspend (0.91±1.25 vs. 0.70±0.75, p<0.018) functions. Four vs. two events of severe hypo-glycaemia occurred in the Sensor On and Sensor Off arm, respectively. Continuous glucose monitoring was associated with decreased hba1c levels and time spent in hypo-glycaemia in individuals with type 1 diabetes using CSII. More frequent self-adjustments of insulin therapy may have contributed to these effects

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Errors in antibiotic therapy of acute otitis media in children

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Statement of the Problem: Acute Otitis Media (AOM) is one of the most common diseases in children. AOM is 25-40% in the structure of all pediatric ENT-pathology in Russia. Approximately 42% of prescriptions for oral antibiotics in children are prescribed for AOM. Mastoiditis is the most frequent and dramatic complication of AOM.

Methodology & Theoretical Orientation: We have analyzed the history of children with acute mastoiditis. For the period from 2009 to 2017 in our clinic made 161 antromastoidotomy. In the diagram obvious the increase in surgical activity, indicating an increase in the frequency of complicated AOM. In 46 cases, mastoiditis was accompanied by subperiosteal abscesses, 4 - perisinuous abscesses, 4 - thrombosis of the sigmoid sinus, 2 - abscess of the cerebellum, 1 - epidural abscess of the temporal lobe. Otogenic meningitis was diagnosed in 7 patients. None of the children were vaccinated against pneumococcal infection.

Findings: The high frequency of complications of acute otitis media in children is due to errors in antibiotic therapy. Analysis of failures of starting treatment revealed three main reasons: (1) The use of low doses (20-30 mg/kg/day) of amoxicillin, creating suboptimal concentrations of the antibiotic in the focus of inflammation; (2) the empirical appointment of oral cephalosporins of the 3rd generation (cefixime and, especially, ceftibutene), which have a reduced antipneumococcal activity; (3) use of macrolides as a first-line therapy (due to the progressive decrease of susceptibility of pneumococci to 14- and 15-member macrolides).

Conclusion & Significance: Despite vaccination against pneumococcus since 2014, Streptococcus pneumonia remains the main causative agent of AOM in Russia; this is due to the anti-vaccination approach among the population. At this stage, the treatment of AOM requires high anti-pneumococcal activity of starting antibiotics (amoxicillin in doses of 60-90 mg/kg/day or ceftriaxone in a dose of 75 mg/kg/day).

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Evaluation of the educational environment in the pediatric clinic residency in a provincial referral hospital

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Introduction: The Educational Environment (EE) is the scenario where the teaching-learning process takes place, focusing on clinical practice during medical residency. The Postgraduate Hospital Educational Environment Measure (PHEEM) survey allows making a valid and reliable quantitative evaluation of the EE of hospital post-graduate programs.

Objective: To evaluate the EE in the Pediatric Clinic Hospital of a Provincial Referral Hospital.

Method: Quantitative and descriptive study of cross-sectional design was performed using PHEEM questionnaire on residents of the Pediatric Hospital during 2015. The questionnaires, which were completed voluntarily and anonymously, contained 40 items with 5 response options. The possible maximum score was 160. Each item had a value between 0 and 4, with a score of 3.5 and above being identified as positive factor and between 2 and less indicating a problem to be solved. The scores for all the questions were aggregated for the overall score.

Results: A total of 19 residents (16 women and 3 men) completed the questionnaire, with a mean overall score of 112.83/160. The scores obtained corresponded to a more positive EE than a negative one with aspects to improve. The EE perceived by the residents was of acceptable autonomy, with well-oriented teaching and social support. Positive aspects were: No gender (3.10) or race (3.47) discrimination; Opportunities to work with other doctors at their level (3.47); Responsibilities according to their training (3.42); Training received gives them security (3.36); Top Residents with Teaching Skills (3.31); Clinical supervision at all times (3.21); Climate of respect (3.26); Motivation to achieve professional autonomy (3.26); Instructors with teaching skills (3.26). Conditions to improve were: difficulty in getting food during on-call.

Conclusions: The EE of the pediatrics residency of this hospital was more positive than negative, with some aspects to improve being identified.

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GATA2 directly represses cardiac fates to promote hematopoietic specification of human mesoderm

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In vertebrates, GATA2 is a master regulator of hematopoiesis, repeatedly used throughout embryo development and the adult life. Although it is well established that GATA2 is essential for the onset of mouse hematopoiesis, its role during early human hematopoietic development remains elusive. By combining time-controlled overexpression of GATA2 with genetic knockout experiments, we found that GATA2, at the mesoderm specification stage, promotes the generation of hemogenic progenitors and their further differentiation to hematopoietic progenitor cells, while negatively regulating cardiac differentiation. Surprisingly, genome-wide transcriptional and chromatin immune-precipitation analysis showed that GATA2 bound preferentially to regulatory regions, and repressed expression, of cardiac development-related genes. In contrast, genes important for hematopoietic differentiation were up-regulated by GATA2 in a mostly indirect manner. Collectively, our data reveal a previously unsuspected role of GATA2 as a direct repressor of cardiac fates, and highlight the importance of coordinating the specification and repression of alternative cell fates.

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RegenerAge System: Therapeutic effects of combinatorial biologics (mRNA and allogenic MSCs) with a spinal cord stimulation system on a patient with spinal cord section

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Bioquantine® a mRNA extract from *Xenopus laevis* frog oocytes (purified from intra- and extra-oocyte liquid phases of electroporated oocytes), showed potential as a treatment for a wide range of conditions in animal models, including Spinal Cord Injury (SCI) and Traumatic Brain Injuries (TBI) among others. The current study observed beneficial changes with Bioquantine® administration in a patient with severe SCI. Pluripotent stem cells have therapeutic and regenerative potential in clinical situations CNS disorders. One method of reprogramming somatic cells into pluripotent stem cells is to expose them to extracts prepared from *Xenopus laevis* oocytes. Due to ethical reasons and legal restrictions we selected a No Option patient, deciding to include in our protocol the RestoreSensor SureScan to complete it. Based on the electrical stimulation for rehabilitation and regeneration after spinal cord injury published by Hamid and MacEwan, we designed an improved delivery method for the *in-situ* application of MSCs and Bioquantine® in combination with the RestoreSensor® SureScan®. To the present day the patient who suffered a complete section of spinal cord at T12-L1 shows an improvement in sensitivity, strength in striated muscle and smooth muscle connection, 14 months after the first Bioquantine® and MSCs treatment and 9 months after the placement.

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Design of 3D bio-printed scaffolds for cartilage regeneration

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Cartilage is a dense connective tissue with limited self-repair properties. Currently, the therapeutic use of autologous or allogenic chondrocytes makes up an alternative therapy to the pharmacological treatment. The design of a bio-printed 3D cartilage with chondrocytes and biodegradable biomaterials offers a new therapeutic alternative able of bridging the limitations of current therapies in the field. We have developed an enhanced printing processes-*Injection Volume Filling* (IVF) to increase the viability and survival of the cells when working with high temperature thermoplastics without the limitation of the scaffold geometry in contact with cells. We have demonstrated the viability of the printing process using chondrocytes for cartilage regeneration. This development will accelerate the clinical uptake of the technology and overcomes the current limitation when using thermoplastics as scaffolds. An alginate-based hydrogel combined with human chondrocytes (isolated from osteoarthritis patients) was formulated as bioink-A and the polylactic acid as bioink-B. The bioprinting process was carried out with the REGEMAT V1 bio-printer (Regemat 3D, Granada-Spain) through a IVF. The printing capacity of the bio-printing plus the viability and cell proliferation of bio-printed chondrocytes was evaluated after five weeks by confocal microscopy and Alamar Blue Assay (Biorad). Results showed that the IVF process does not decrease the cell viability of the chondrocytes during the printing process as the cells do not have contact with the thermoplastic at elevated temperatures. The viability and cellular proliferation of the bio-printed artificial 3D cartilage increased after 5 weeks. In conclusion, this study demonstrates the potential use of Regemat V1 for 3D bio-printing of cartilage and the viability of bio-printed chondrocytes in the scaffolds for application in regenerative medicine.

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The clash between modern medicine and alternative medicine "herbal" to treat infertility: The social aspect of the study

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The study focused on the negative effects of the infertility issue in the Palestinian society in the Gaza Strip and its impact on the psychological morale on men and women. The study aimed at the society's view in general and family members in particular on the behavior of the young man or girl. Modern medicine and alternative medicine, to treat infertility, modern medicine has customers and alternative medicine or Maismi according to customs and traditions herbal medicine, especially the treatment of "honey" also has customers. The study also focused on the negative effects of infertility in the Arab and Islamic worlds and Jaber. The study found that many cases of divorce were often caused by the encouragement of family members to the husband or other infertile or vice versa to seek divorce due to non-reproduction. One of the reasons for the divorce is also the shyness of going to the doctor and saying only, "This is God's command." There are many men who preferred to be treated. According to the herbal medicine and the reason for shyness without consulting the specialist doctor. The study concluded that the people who went to the doctor or the competent medical clinics for procreation obtained positive results through the cultivation of the tubes by the needle microscopy, insert sperm by needle and the children were happy now. The study also included Israeli measures that contributed to raising the rate of infertility in the Palestinian territories. The percentage has increased in recent years, especially in the southern West Bank, where there are areas that have been affected most because of the way the Israeli authorities bury the waste. The study also concluded that there are other environmental influences and their effect on stem cells. The study found that male infertility increased by more than 60% in men, 20% in women and 20% in unknown females. The study also showed the effect of asbestos tablets on male and female infertility.

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Understanding the motivations and side effects in healthy volunteers that donate bone marrow for mesenchymal stromal cell basic research

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Apart from being used for Hematopoietic Stem Cell (HSC) transplantation, the Mesenchymal Stromal Cell (MSC) populations in human Bone Marrow (BM) are being harnessed actively in clinical trials given their unique regenerative potential. Several studies have been published with regards to why Healthy Volunteers (HV) donates their BM for HSC transplantation. Predominant motives include: Altruism, normative considerations, empathetic feelings for the recipient/recipient's family, weighing of the risks and benefits associated with the procedure, and social obligation. Multiple sites are accessed to aspirate large volumes of BM (maximum 1500 ml) from donors for HSC transplantation and has been correlated with serious post-donation symptoms, which restrict donors for weeks: Excessive pain at the aspiration site, fatigue, severe post-spinal headache, fever, fainting, unexpected hospitalization and difficulty/pain while walking or sitting. A paucity of published data exists on the motivations of HV for donating their marrow for MSC basic research and the experienced side effects following the procedure.

Methodology: HV that previously donated their BM (30 ml) and provided informed consented (n=48) were administered a questionnaire to identify the order of their motivations for donating their marrow for basic research and the side effects they experienced following the procedure.

Results: The considered motivations resulted in the following descending order: To advance research for the benefit of future patients, compensation for participation, the research question was interesting, and lastly to avail of a free medical check-up. Of the 35 HV that experienced any side effect, pain, fatigue, nausea, and low blood pressure were reported - which all resolved within six days on average. No case of bleeding, fainting, vomiting, skin rash, infection or hospitalization was reported.

Conclusions: Donating BM for MSC basic research was primarily for future benefit of patients. The aspiration procedure can be deemed relatively safer compared to that for HSC transplantation – due to lower volumes of BM aspirated from a single collection site.

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