บทความที่น่าสนใจประจำเดือน ตุลาคม 2559

สาขาวิทยาศาสตร์สุขภาพ

Title :	iRGD-mediated core-shell nanoparticles loading carmustine and O6-benzylguanine for glioma therapy
Author :	Chang Liu, Sen Yao, Xuqian Li, Feng Wang & Yanyan Jiang
Journal :	Journal of Drug Targeting: Published online: 06 Oct 2016, http://dx.doi.org/10.1080/1061186X.2016.1238091
Abstract :	iRGD (internalizing RGD) with high affinity to αv integrins was reported to enhance tumor penetrability by binding to neuropilin-1 (NRP-1). Based on our previous study, chitosan surface-modified poly (lactide-co-glycolides) nanoparticles (PLGA/CS NPs), loaded with carmustine (BCNU) and its sensitizer (O6-benzylguanine, BG) showed stronger anti-tumor effect than free drugs. In present study, PLGA/CS NPs (NPs) with core-shell structure were prepared and modified with iRGD or mPEG. F98, C6 or U87 cell lines with different receptors levels were selected for in vitro and in vivo studies. After administration of iRGD-mediated NPs, including iRGD-modified NPs (iRGD-NPs) and co-administration of iRGD and NPs (iRGD + NPs), their effects on glioma were compared with NPs. iRGD-NPs showed stronger cytotoxicity and cellular uptake than other groups. iRGD-NPs and iRGD + NPs displayed deeper tumor penetration and stronger anti-invasion effect on three dimensional (3D) glioma spheroids than NPs. On F98 glioma-bearing mice model, iRGD-mediated NPs showed enhanced crossing BBB ability and brain tumor accumulation levels. Correspondingly, the median survival time of iRGD + NPs, iRGD-NPs and NPs groups were 58, 49 and 34.5 days, respectively. Present studies supported the iRGD-mediated strategy to improve the efficacy of antitumor drug delivery system. Importantly, co-administration of iRGD may be a greater way over the conjugation of iRGD.
Database :	Taylor & Francis Online

Title :	[The future development of bacteria fighting medical devices: the role of graphene oxide](#)
Author :	Valentina Palmieri, Massimiliano Papi, Claudio Conti, Gabriele Ciasca, Giuseppe Maulucci & Marco De Spirito
Journal :	Expert Review of Medical Devices: Accepted author version posted online: 06 Oct 2016, http://dx.doi.org/10.1080/17434440.2016.1245612
Abstract :	The clinical challenge that research on antibacterial coatings faces nowadays is the need of reduction of resistant bacterial infections, major source of implant rejection and repeated surgery.

In order to avoid microorganisms attachment and biofilm formation, coating materials on medical devices have been developed with shortcomings represented by short-term durability and induction of new mechanisms of bacterial resistance. Graphene-based films and hydrogel could represent the next generation protective coatings due to their excellent mechanical, chemical and thermal properties, high nanoparticle adsorption and antibacterial action. In this short commentary, we will report the recent developments of graphene oxide based coatings. Graphene oxide is a water-soluble derivative of graphene that allows high drug loading and miscibility with polymers, making it mouldable in any desired shape. Recent applications in wound healing and tissue engineering will be discussed as well as critical issues prior to clinical use of graphene oxide coatings.

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| Database : | Taylor & Francis Online |

Title :	[Emerging drugs to reduce abnormal β-amyloid protein in Alzheimer's disease patients](#)
Author :	Francesco Panza, Davide Seripa, Vincenzo Solfrizzi, Bruno P. Imbimbo, Madia Lozupone, Antonio Leo, Rodolfo Sardone, Gaetano Gagliardi, Lucia Lofano, Bianca C. Creanza, Paola Bisceglia, Antonio Daniele, Antonello Bellomo, Antonio Greco & Giancarlo Logroscino
Journal :	Expert Opinion on Emerging Drugs: Published online: 06 Oct 2016, http://dx.doi.org/10.1080/14728214.2016.1241232
Abstract :	**Introduction**: Currently available drugs against Alzheimer's disease (AD) target cholinergic and glutamatergic neurotransmissions without affecting the underlying disease process. Putative disease-modifying drugs are in development and target β-amyloid (Aβ) peptide and tau protein, the principal neurophatological hallmarks of the disease. **Areas covered**: Phase III clinical studies of emerging anti-Aβ drugs for the treatment of AD were searched in US and EU clinical trial registries and in the medical literature until May 2016. **Expert opinion**: Drugs in Phase III clinical development for AD include one inhibitor of the β-secretase cleaving enzyme (BACE) (verubecestat), three anti-Aβ monoclonal antibodies (solanezumab, gantenerumab, and aducanumab), an inhibitor of receptor for advanced glycation end products (RAGE) (azeliragon) and the combination of cromolyn sodium and ibuprofen (ALZT-OP1). These drugs are mainly being tested in subjects during early phases of AD or in subjects at preclinical stage of familial AD or even in asymptomatic subjects at high risk of developing AD. The hope is to intervene in the disease process when it is not too late. However, previous clinical failures with anti-Aβ drugs and the lack of fully understanding of the pathophysiological role of Aβ in the development of AD, put the new drugs at substantial risk of failure.
Database :	Taylor & Francis Online

Title :	[Biomedical classification application and parameters optimization of mixed kernel SVM based on the information entropy particle swarm optimization](#)
Author :	Mi Li, Xiaofeng Lu, Xiaodong Wang, Shengfu Lu & Ning Zhong
Journal :	Computer Assisted Surgery: Accepted author version posted online: 04 Oct 2016,
Abstract :	The types of kernel function and relevant parameters' selection in support vector machine (SVM) have a major impact on the performance of the classifier. In order to improve the accuracy and generalization ability of the model, we used mixed kernel function SVM classification algorithm based on the information entropy particle swarm optimization (PSO): on the one hand, the generalization ability of classifier is effectively enhanced by constructing a mixed kernel function with global kernel function and local kernel function; on the other hand, the accuracy of classification is improved through optimization for related kernel parameters based on information entropy PSO. Compared with PSO-RBF kernel and PSO-mixed kernel, the improved PSO-mixed kernel SVM can effectively improve the classification accuracy through the classification experiment on biomedical datasets, which would not only prove the efficiency of this algorithm, but also show that the algorithm has good practical application value in biomedicine prediction.
Database :	Taylor & Francis Online

Title :	[Optimum treatment for mediastinal lymph node positive (N2) resectable non-small cell lung cancer: what is the role for surgery?](#)
Author :	Musaddiq Awan, Neelesh Sharma, Christopher W. Towe, Jimmy T. Efird, Mitchell Machtay & Tithi Biswas
Journal :	Expert Review of Anticancer Therapy: Published online: 06 Oct 2016, http://dx.doi.org/10.1080/14737140.2016.1240039
Abstract :	**Introduction**: A third of patients with Non-Small Cell Lung Cancer (NSCLC) present with Stage III disease with mediastinal (N2) nodal involvement representing an extremely heterogeneous population with a generally poor prognosis. **Areas covered**: This article describes the complexity of Stage III-N2 patients reviewing the outcomes of key clinical trials while highlighting the trial designs and subtleties that have created controversy in management. Both bimodality

approaches combining chemotherapy with either surgery or radiation and trimodality approaches combining chemotherapy with both local therapies are reviewed. Finally, prognostic factors and future directions are explored for the management of this population.

Expert commentary: Upfront surgery is not recommended for patients with Stage III-N2 NSCLC. Neoadjuvant approaches with both chemotherapy and chemoradiation are acceptable in a multidisciplinary setting if appropriate surgery is performed by a dedicated thoracic surgeon. Non-operative candidates should receive definitive concurrent chemoradiation. Innovative approaches are necessary to improve outcomes in this population.

Database :	Taylor & Francis Online

Title :	Bone Shaft Revascularization After Marrow Ablation is Dramatically Accelerated in BSP-/- Mice, Along With Faster Haematopoietic Recolonization
Author :	Wafa Bouleftour, Renata Neves Granito, Arnaud Vanden-Bossche, Odile Sabido, Bernard Roche, Mireille Thomas, Marie Thérèse Linossier, Jane E Aubin, Marie-Hélène Lafage-Proust, Laurence Vico and Luc Malaval
Journal :	Journal of Cellular Physiology: Accepted manuscript online: 5 OCT 2016 05:11AM EST | DOI: 10.1002/jcp.25630
Abstract :	The bone organ integrates the activity of bone tissue, bone marrow and blood vessels and the factors ensuring this coordination remain ill defined. Bone sialoprotein (BSP) is with osteopontin (OPN) a member of the Small Integrin Binding Ligand N-Linked Glycoprotein (SIBLING) family, involved in bone formation, hematopoiesis and angiogenesis. In rodents, bone marrow ablation induces a rapid formation of medullary bone which peaks by ～8 days (d8) and is blunted in BSP-/- mice. We investigated the coordinate hematopoietic and vascular recolonization of the bone shaft after marrow ablation of 2 month old BSP + /+ and BSP-/- mice. At d3, the ablated area in BSP-/- femurs showed higher vessel density (x4) and vascular volume (x7) than BSP + / +. Vessel numbers in the shaft of ablated BSP + /+ mice reached BSP-/- values only by d8, but with a vascular volume which was twice the value in BSP-/-, reflecting smaller vessel size in ablated mutants. At d6, a much higher number of Lin– (x3) as well as LSK (Lin- IL-7Rα- Sca-1hi c-Kithi,

x2) and hematopoietic stem cells (HSC: Flt3- LSK, x2) were counted in BSP-/- marrow, indicating a faster recolonization. However, the proportion of LSK and HSC within the Lin- was lower in BSP-/- and more differentiated stages were more abundant, as also observed in unablated bone, suggesting that hematopoietic differentiation is favored in the absence of BSP. Interestingly, unablated BSP-/- femur marrow also contains more blood vessels than BSP+/+, and in both intact and ablated shafts expression of VEGF and OPN are higher, and DMP1 lower in the mutants.

In conclusion, bone marrow ablation in BSP-/- mice is followed by a faster vascular and hematopoietic recolonization, along with lower medullary bone formation. Thus, lack of BSP affects the interplay between hematopoiesis, angiogenesis and osteogenesis, maybe in part through higher expression of VEGF and the angiogenic SIBLING, OPN.

Database :	Wiley Online Library

Title :	Effects of testosterone treatment on body fat and lean mass in obese men on a hypocaloric diet: a randomised controlled trial
Author :	Mark Ng Tang Fui, Luke A. Prendergast, Philippe Dupuis, Manjri Raval, Boyd J. Strauss, Jeffrey D. Zajac and Mathis Grossmann
Journal :	BMC Medicine 2016 14:153 DOI: 10.1186/s12916-016-0700-9: Published on: 7 October 2016
Abstract :	**Background** Whether testosterone treatment has benefits on body composition over and above caloric restriction in men is unknown. We hypothesised that testosterone treatment augments diet-induced loss of fat mass and prevents loss of muscle mass. **Methods** We conducted a randomised double-blind, parallel, placebo controlled trial at a tertiary referral centre. A total of 100 obese men (body mass index $\geq$ 30 kg/m2) with a total testosterone level of or below 12 nmol/L and a median age of 53 years (interquartile range 47–60) receiving 10 weeks of a very low energy diet (VLED) followed by 46 weeks of weight maintenance were randomly assigned at baseline to 56 weeks of 10-weekly intramuscular testosterone undecanoate (n = 49, cases) or

matching placebo (n = 51, controls). The main outcome measures were the between-group difference in fat and lean mass by dual-energy X-ray absorptiometry, and visceral fat area (computed tomography).

Results

A total of 82 men completed the study. At study end, compared to controls, cases had greater reductions in fat mass, with a mean adjusted between-group difference (MAD) of –2.9 kg (–5.7 to –0.2; P = 0.04), and in visceral fat (MAD –2678 mm2; –5180 to –176; P = 0.04). Although both groups lost the same lean mass following VLED (cases –3.9 kg (–5.3 to –2.6); controls –4.8 kg (–6.2 to –3.5), P = 0.36), cases regained lean mass (3.3 kg (1.9 to 4.7), P < 0.001) during weight maintenance, in contrast to controls (0.8 kg (–0.7 to 2.3), P = 0.29) so that, at study end, cases had an attenuated reduction in lean mass compared to controls (MAD 3.4 kg (1.3 to 5.5), P = 0.002).

Conclusions

While dieting men receiving placebo lost both fat and lean mass, the weight loss with testosterone treatment was almost exclusively due to loss of body fat.

Database :	BioMed Central

Title :	PROTECTED-UK – Clinical pharmacist interventions in the UK critical care unit: exploration of relationship between intervention, service characteristics and experience level
Author :	Nicola Rudall, Catherine McKenzie, June Landa, Richard S. Bourne, Ian Bates and Rob Shulman
Journal :	International Journal of Pharmacy Practice: First published: 4 OCT 2016	DOI: 10.1111/ijpp.12304
Abstract :	Purpose Clinical pharmacist (CP) interventions from the PROTECTED-UK cohort, a multi-site critical care interventions study, were further analysed to assess effects of: time on critical care, number of interventions, CP expertise and days of week, on impact of intervention and ultimately contribution to patient care.

Methods

Intervention data were collected from 21 adult critical care units over 14 days. Interventions could be error, optimisation or consults, and were blind-coded to ensure consistency, prior to bivariate analysis. Pharmacy service demographics were further collated by investigator survey.

Key findings

Of the 20 758 prescriptions reviewed, 3375 interventions were made (intervention rate 16.1%). CPs spent 3.5 h per day (mean, ±SD 1.7) on direct patient care, reviewed 10.3 patients per day (±SD 4.2) and required 22.5 min (±SD 9.5) per review. Intervention rate had a moderate inverse correlation with the time the pharmacist spent on critical care ($P = 0.05$; $r = 0.4$). Optimisation rate had a strong inverse association with total number of prescriptions reviewed per day ($P = 0.001$; $r = 0.7$). A consultant CP had a moderate inverse correlation with number of errors identified ($P = 0.008$; $r = 0.6$). No correlation existed between the presence of electronic prescribing in critical care and any intervention rate. Few centres provided weekend services, although the intervention rate was significantly higher on weekends than weekdays.

Conclusions

A CP is essential for safe and optimised patient medication therapy; an extended and developed pharmacy service is expected to reduce errors. CP services should be adequately staffed to enable adequate time for prescription review and maximal therapy optimisation.

Database :	Wiley Online Library

Title :	[Propolis modulates miRNAs involved in TLR-4 pathway, NF-**K**B activation, cytokine production and in the bactericidal activity of human dendritic cells](#)
Author :	Bruno J. Conti, Karina B. Santiago, Eliza O. Cardoso, Paula P. Freire, Robson F. Carvalho, Marjorie A. Golim and José M. Sforcin
Journal :	Journal of Pharmacy and Pharmacology: First published: 7 OCT 2016 | DOI: 10.1111/jphp.12628
Abstract :	Objectives

Dendritic cells (DCs) are antigen-presenting cells, essential for recognition and presentation of pathogens to T cells. Propolis, a resinous material produced by bees from various plants, exhibits numerous biological properties, highlighting its immunomodulatory action. Here, we assayed the effects of propolis on the maturation and function of human DCs.

Methods

DCs were generated from human monocytes and incubated with propolis and LPS. NF-ĸB and cytokines production were determined by ELISA. microRNA's expression was analysed by RT-qPCR and cell markers detection by flow cytometry. Colony-forming units were obtained to assess the bactericidal activity of propolis-treated DCs.

Key findings

Propolis activated DCs in the presence of LPS, inducing NF-kB, TNF-α, IL-6 and IL-10 production. The inhibition of hsa-miR-148a and hsa-miR-148b abolished the inhibitory effects on HLA-DR and pro-inflammatory cytokines. The increased expression of hsa-miR-155 may be correlated to the increase in TLR-4 and CD86 expression, maintaining LPS-induced expression of HLA-DR and CD40. Such parameters may be involved in the increased bactericidal activity of DCs against Streptococcus mutans.

Conclusion

Propolis modulated the maturation and function of DCs and may be useful in the initial steps of the immune response, providing a novel approach to the development of DC-based strategies and for the discovery of new immunomodulators.

Database :	Wiley Online Library

Title :	Recall and Cancer Detection Rates for Screening Mammography: Finding the Sweet Spot
Author :	Paula Grabler, et al.
Journal :	American Journal of Roentgenology | Sep 28, 2016 | Ahead of Print

| Abstract : | OBJECTIVE. The purpose of this study is to identify the optimal screening mammography recall rate range on the basis of cancer detection rates among breast imaging specialists at an academic institution.

MATERIALS AND METHODS. Medical outcome audit data collected in accordance with the Mammography Quality Standards Act from September 1, 2007, through August 31, 2012, were reviewed. Cancer detection rates were calculated from 984 screen-detected cancers identified in 188,959 total digital screening mammograms. The percentages of minimally invasive and early-stage cancers were also calculated. The 75 annual recall rates were analyzed two ways. First, they were separated into recall groups to assess cancer detection rate variation by the recall categories using rate ratios: less than 10%, 10% to less than 12%, 12% to less than 14%, and 14% or higher. Next, a linear regression with bootstrap bias correction was performed to assess changes in cancer detection rate with each unit increase in the recall rate up to 20%, with the recall category of less than 7% taken as reference. Annual cancer detection rates for a physician were grouped according to annual percentage recall rate.

RESULTS. Statistically significantly higher cancer detection rates were seen for recall rates 12% or higher, with rate ratios of 1.75 (95% CI, 1.40–2.19) and 2.06 (95% CI, 1.72–2.46) for the recall groups 12% to less than 14% and 14% and higher, respectively, compared with the less than 10% group. When taking the category 12% to less than 14% as the reference, there were no statistically significant differences between recall groups 12% to less than 14% and 14% or higher in cancer detection rate. A statistically significant increase in the cancer detection rate with each unit increase in the recall rate was seen only for recall rates 12% or higher.

CONCLUSION. These observations suggest that the sweet spot for optimal cancer detection is in the recall rate range 12% to less than 14% with the incremental benefit above this to be relatively small. A recall rate less than 10% may be too low. |
| Database : | American Roentgen Ray Society |