Hot Articles

“December|2016”

Health Science

Title: Is a Pulse Absolutely Necessary During Cardiopulmonary Bypass?

Author: Gengo Sunagawa, Marijan Koprivanac, Jamshid H. Karimov, Nader Moazami & Kiyotaka Fukamachi

Journal: Expert Review of Medical Devices

Latest Articles: Accepted author version posted online: 28 Nov

Doi: 10.1080/17434440.2017.1265445

Abstract

Introduction: The benefits and disadvantages of pulsatility in mechanical circulatory support devices have been argued since before the first use of cardiopulmonary bypass (CPB) with a nonpulsatile pump. The debate over the superiority of either pulsatile or nonpulsatile perfusion during CPB persists, but recently, the evidence in favor of pulsatile perfusion during CPB is increasing. Complications associated with chronic nonpulsatile flow in patients implanted with left ventricular assist devices have renewed interest in generating pulsatility with these devices.

Area discussed: Here we review the definition of pulsatility, the outcomes of CPB using pulsatile and nonpulsatile pumps, and how best to produce and assess pulsatility. Those information were identified through online database and direct extraction of single studies cited in previously identified manuscripts.

Expert commentary: The newer generation of biocompatible pulsatile pumps that can generate physiologic pulsation may prove beneficial during temporary support for short use during CPB or intermediate support for cardiogenic shock.

Database

Taylor & Francis

Title: The development of an observational screening tool to assess safe, effective and appropriate walking aid use in people with multiple sclerosis

Author: Abby Eitzen, Marcia Finlayson, Leanne Carolan-Laing, Arthur Junn Nacionales, Christie Walker, Josephine O'Connor

Journal: Disability and Rehabilitation: Assistive Technology

Latest Articles: Accepted 21 Jul 2016, Published online: 20 Oct 2016

Doi: 10.1080/17483107.2016.1217085

Abstract

Purpose: The purpose of this study was to identify potential items for an observational screening tool to assess safe, effective and appropriate walking aid use among people with multiple sclerosis (MS). Such a tool is needed because of the association between fall risk and mobility aid use in this population.

Methods: Four individuals with MS were videotaped using a one or two straight canes, crutches or a rollator in different settings. Seventeen health care professionals from Canada, Ireland and the United States were recruited, and viewed the videos, and were then interviewed about the use of the devices by the individuals in the videos. Interview questions addressed safety, effectiveness and appropriateness of the device in the setting. Data were analyzed qualitatively. Coding consistency across raters was evaluated and confirmed.

Results: Nineteen codes were identified as possible items for the screening tool. The most frequent issues raised regardless of setting and device were "device used for duration/abandoned", "appropriate device", "balance and stability", "device technique", "environmental modification" and "hands free."

Conclusion: With the identification of a number of potential tool items, researchers can now move forward with the development of the tool. This will involve consultation with both healthcare professionals and people with MS.

Database

Taylor & Francis

[Health Science]

Title: Emerging drugs and drug targets against tuberculosis

Author: Nzungize Lambert, Abualgasim Elgaili Abdalla, Xiangke Duan & Jianping Xie

Journal: Journal of Drug Targeting

Published online: 02 Dec 2016

Doi: 10.1080/1061186X.2016.1258705

Abstract

Mycobacterium tuberculosis (M. tuberculosis), the causative agent of tuberculosis, uses various tactics to resist on antibiotics and evade host immunity. To control tuberculosis, antibiotics with novel mechanisms of action are urgently needed. Emerging new antibiotics and underlying novel drug targets are summarized in this paper.

Database

Taylor & Francis

[Health Science]

Title: Phase II Study of Dasatinib in Previously Treated Patients with Advanced Non-Small Cell Lung Cancer

Author: Michael J. Kelley, Gautam Jha, Debra Shoemaker, James E. Herndon II, Lin Gu, William T. Barry, Jeffrey Crawford & Neal Ready

Journal: Cancer Investigation

Published online: 02 Dec 2016

Doi: 10.1080/07357907.2016.1253710

Abstract

The Src pathway in activated in about one-third of non-small cell lung cancer (NSCLC) tumors. Dasatinib has Src-inhibitor activity. We examined the activity of dasatinib in 37 patients with advanced, previously treated NSCLC. Among the 29 patients who underwent pre-treatment biopsy for RNA biomarker analysis, 25 were treated with dasatinib 70 mg twice daily. There were no responses. Five patients discontinued treatment due to toxicity. Three patients had minor biopsy-related pneumothoraces. Given the lack of responses, no biomarkers were analyzed. Dasatinib 70 mg twice daily does not have activity nor is it well tolerated in unselected patients with advanced stage, previously treated NSCLC.

Database

Taylor & Francis

Title:	IL-4Rα aptamer-liposome-CpG oligodeoxynucleotides suppress tumour growth by targeting the tumour microenvironment
Author:	Yu-Jie Liu, Xiao-Qian Dou, Fang Wang, Jing Zhang, Xiao-Lin Wang, Gui-Li Xu, Shen-Si Xiang, Xin Gao, Jie Fu & Hai-Feng Song
Journal:	Journal of Drug Targeting
Published online:	01 Dec 2016
Doi:	10.1080/1061186X.2016.1258569

Abstract

Tumour immunosuppressive microenvironments inhibit antigen-specific cellular responses and interfere with CpG-mediated immunotherapy. Overcoming tumour microenvironment (TME) immunosuppression is an important strategy for effective therapy. This study investigated the ability of a tumour-targeting IL-4Rα aptamer-liposome-CpG ODN delivery system to introduce CpG into tumours and overcome the immunosuppressive TME. The IL-4Rα-liposome-CpG delivery system was prepared. FAM-CpG visualisation was used to demonstrate tumour targeting in vitro and in vivo. Anti-tumour effects of this delivery system were evaluated in CT26 tumour-bearing mice. Mechanisms for conquering the TME were investigated. FAM-CpG was better distributed into the tumours upon treatment with IL-4Rα-liposome-FAM-CpG compared to distribution in the control group in vitro and in vivo. IL-4Rα-aptamer-liposome-CpG treatment inhibited distinct myeloid-derived suppressor cell populations in tumours and bone marrow. Similar profiles were observed for regulatory T cells in tumours. In CT26 tumour-bearing mice, IL-4Rα-liposome-CpG treatment exhibited enhanced anti-tumour activity. Increased mRNA levels of TNF-α, IL-2, and IL-12, and decreased mRNA levels of VEGF, IL-6, IL-10, MMP9, arginase-1, inducible NOS, CXCL9, p-Stat3, and NF-κB were observed in tumours upon IL-4R-liposome-CpG-treatment. The results suggested that pharmacologic targeting by the IL-4R aptamer-liposome-CpG system improves TME therapeutic benefit and provides a rationale for cancer immunotherapies.

Database

Taylor & Francis

Title: Clinical role of fluorescence imaging in colorectal surgery – a review

Author: Ido Mizrahi & Steven D. Wexner

Journal: Expert Review of Medical Devices

Published online: 05 Dec 2016

Doi: 10.1080/17434440.2017.1265444

Abstract

Introduction: Anastomotic leak (AL) after colorectal surgery is a devastating complication; decreased blood perfusion is an important risk factor. Surgeons rely on subjective measures to assess bowel perfusion. Fluorescence imaging (FI) with indocyanine green (ICG) provides a real-time objective assessment of intestinal perfusion.

Areas covered: A PubMed search using the terms 'fluorescence imaging', 'indocyanine green', 'colon and rectal surgery' was undertaken. Sixteen articles between 2010 to present were identified. Main outcomes were leak rate reduction, change in surgical plan, and technical feasibility. Change in surgical strategy due to FI was recorded in 11 studies. Two case control studies showed overall reduction of 4% and 12% in AL rate and one showed no change in AL rate between groups.

Expert commentary: According to the available literature, FI is technically feasible and alters surgical strategy in a non-negligible number of patients possibly effecting AL rates.

Database

Taylor & Francis

Title: Basis for molecular diagnostics and immunotherapy for esophageal cancer

Author: Joe Abdo, Devendra K. Agrawal & Sumeet K. Mittal

Journal: Expert Review of Anticancer Therapy

Published online: 23 Nov 2016

Doi: 10.1080/14737140.2017.1260449

Abstract

Introduction: Esophageal cancer (EC) is an extremely aggressive neoplasm, diagnosed in about 17,000 Americans every year with a mortality rate of more than 80% within five years and a median overall survival of just 13 months. For decades, the go-to regimen for esophageal cancer patients has been the use of taxane and platinum-based chemotherapy regimens, which has yielded the field's most dire survival statistics.

Areas covered: Combination immunotherapy and a more robust molecular diagnostic platform for esophageal tumors could improve patient management strategies and potentially extend lives beyond the current survival figures. Analyzing a panel of biomarkers including those affiliated with taxane and platinum resistance (ERCC1 and TUBB3) as well as immunotherapy effectiveness (PD-L1) would provide oncologists more information on how to optimize first-line therapy for EC.

Expert commentary: Of the 12 FDA-approved therapies in EC, zero target the genome. A majority of the approved drugs either target or are effected by proteomic expression. Therefore, a broader understanding of diagnostic biomarkers could give more clarity and direction in treating esophageal cancer in concert with a greater use of immunotherapy.

Database

Taylor & Francis

Title: Toll-like receptor 4 protects against stress-induced ulcers via regulation of glucocorticoid production in mice

Author: Liang Wang, Pengfei Luo, Fang Zhang, Yuelu Zhang, Xingtong Wang, Fei Chang, Yuechan Zhang, Hongtai Tang & Zhaofan Xia

Journal: Stress

Published online: 06 Dec 2016

Doi: 10.1080/10253890.2016.1224843

Abstract

Stress-induced gastric ulcer is an important life-threatening condition, while the molecular basis of its development is incompletely understood. Toll-like receptor 4 (TLR4), an innate immune pattern recognition receptor, can induce pro-inflammatory transcription, aggravating a stress ulcer. The present study found that TLR4 played a protective role in a mouse model of water immersion (23 °C) restraint stress. Wild-type (WT) and TLR4−/− male mice were respectively divided into five groups (5 per group), and exposed to the stressor for 0, 0.5, 1, 2, or 4 hours. Gastric ulcer index, determined post mortem, increased with time in both types of mice but was greater in TLR4−/− mice. Furthermore, increased serum cortisol and corticosterone concentrations were observed in WT mice only, and such increases were detected only in WT mice 4 h after lipopolysaccharide (LPS) treatment (2 mg/kg, intraperitoneal injection). Moreover, the administration of cortisol alleviated the gastric injury in TLR4−/− mice. Western blotting showed expression in the adrenal of P450scc (CYP11A1), the first rate-limiting enzyme in the synthesis of steroids, was increased 4 h after water immersion restraint stress or LPS treatment in WT mice, but was conversely decreased in TLR4−/− mice after either stressor. Furthermore, in adrenal glands of TLR4−/− mice, structural distortion of mitochondria (which contain CYP11A1) was found with electron microscopy, and lack of lipid-storing droplets was found using light microscopy on adrenal cryosections stained with Oil red O. These data indicate that TLR4 plays a protective role in stress-induced gastric ulcer that is exerted via impacting synthesis of glucocorticoid in the adrenal gland.

Database

Taylor & Francis

Title: Transient Treg depletion enhances therapeutic anti-cancer vaccination

Author: Scott A. Fisher, Wayne J. Aston, Jonathan Chee, Andrea Khong, Amanda L. Cleaver, et al.

Journal: Immunity, Inflammation and Disease

Early View: Version of Record online: 21 NOV 2016

Doi: 10.1002/iid3.136

Abstract

Introduction

Regulatory T cells (Treg) play an important role in suppressing anti- immunity and their depletion has been linked to improved outcomes. To better understand the role of Treg in limiting the efficacy of anti-cancer immunity, we used a Diphtheria toxin (DTX) transgenic mouse model to specifically target and deplete Treg.

Methods

Tumor bearing BALB/c FoxP3.dtr transgenic mice were subjected to different treatment protocols, with or without Treg depletion and tumor growth and survival monitored.

Results

DTX specifically depleted Treg in a transient, dose-dependent manner. Treg depletion correlated with delayed tumor growth, increased effector T cell (Teff) activation, and enhanced survival in a range of solid tumors. Tumor regression was dependent on Teffs as depletion of both CD4 and CD8 T cells completely abrogated any survival benefit. Severe morbidity following Treg depletion was only observed, when consecutive doses of DTX were given during peak CD8 T cell activation, demonstrating that Treg can be depleted on multiple occasions, but only when CD8 T cell activation has returned to base line levels. Finally, we show that even minimal Treg depletion is sufficient to significantly improve the efficacy of tumor-peptide vaccination.

Conclusions

BALB/c.FoxP3.dtr mice are an ideal model to investigate the full therapeutic potential of Treg depletion to boost anti-tumor immunity. DTX-mediated Treg depletion is transient, dose-dependent, and leads to strong anti-tumor immunity and complete tumor regression at high doses, while enhancing the efficacy of tumor-specific vaccination at low doses. Together this data highlight the importance of Treg manipulation as a useful strategy for enhancing current and future cancer immunotherapies.

Database

Wiley Online Library

Title: Germacrone inhibits adipogenesis and stimulates lipolysis via the AMP-activated protein kinase signalling pathway in 3T3-L1 preadipocytes

Author: Yuan-Ri Guo and Se-Young Choung

Journal: Journal of Pharmacy and Pharmacology

Early View: Version of Record online: 5 DEC 2016

Doi: 10.1111/jphp.12674

Abstract

Objectives

In a previous study, we reported that Aster spathulifolius Maxim extract (ASE) inhibited lipid accumulation and adipocyte differentiation in 3T3-L1 cells. Of the components in ASE, germacrone (GM) was identified as a potent bioactive constituent. GM is known for its anticancer and antiviral activity. However, the effects of GM and the molecular mechanism by which GM regulates adipogenesis and lipolysis were not reported. Therefore, we investigated the effect of GM on adipogenesis and lipolysis and to elucidate its underlying molecular mechanism.

Methods

We analysed the contents of intracellular triglyceride and carried out Western blotting and RT-qPCR to investigate the underlying mechanism.

Key findings

We demonstrate that GM suppresses adipogenic differentiation and the increase in lipolysis in 3T3-L1 cells. In particular, GM down-regulates the expression of early adipogenesis-related genes (e.g. KLF4, KLF5, C/EBP-β and C/EBP-δ) and major adipogenesis-related genes (C/EBP-α and PPAR-γ). Furthermore, GM increases the protein levels of phosphorylated AMP-activated protein kinase α (AMPKα), phosphorylated acetyl-coenzyme A carboxylase (ACC) and carnitine palmitoyltransferase (CPT1).

Conclusions

Our results suggest that GM may be a potent bioactive anti-adipogenic and lipolytic constituent via the regulation of adipogenesis, lipolysis and the AMPKα pathway.

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