บทความที่น่าสนใจประจำเดือนธันวาคม 2558

สาขาวิทยาศาสตร์สุขภาพ

Title :	Uricosuric agents decrease the plasma urate level in rats by concomitant treatment with topiroxostat, a novel xanthine oxidoreductase inhibitor
Author :	Tetsuya Taniguchi, Naoki Ashizawa, Koji Matsumoto, Takashi Iwanaga and Kazuhiro Saitoh
Journal :	Journal of Pharmacy and Pharmacology: Article first published online 21 NOV 2015 | DOI: 10.1111/jphp.12490
Abstract :	**Objectives** The aim of this study was to establish the rat model for evaluating hypouricemic effects by some uricosuric agents. **Methods** Rats were made hyperuricemic by subcutaneous administration of potassium oxonate, a uricase inhibitor, or made hypouricemic by oral administration of topiroxostat, a xanthine oxidoreductase inhibitor. Furthermore, rats were co-treated with topiroxostat and inosine, a urate precursor. In each condition, hypouricemic effects by uricosuric agents were examined. **Key findings** In potassium oxonate-treated rats, treatment with uricosuric agents such as FYU-981, F12859 and probenecid showed no hypouricemic effect. On the other hand, in topiroxostat-treated rats, uricosuric agents remarkably lowered plasma urate level compared with topiroxostat treatment alone, with a dose dependency of 30 and 100 mg/kg for FYU-981 and F12859 each. The decrease in the plasma urate level observed in the topiroxostat-treated rats disappeared by further co-treatment with inosine. **Conclusions** Effects of uricosuric agents on the plasma urate level in rats were sensitive to the rate of urate formation. Induction of slower urate formation by topiroxostat provides valuable model for evaluation of hypouricemic effects by uricosuric agents in rats.
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Title :	Effect of starch-fortified turmeric bath on psoriasis: a parallel randomised controlled trial (pages 125–129)
Author :	Gunasekaran Shathirapathiy, Pradeep MK Nair and Salwa Hyndavi
Journal :	Focus on Alternative and Complementary Therapies: Article first published online - - 2 NOV 2015 | DOI: 10.1111/fct.12211
Abstract :	**Background** Naturopathic medicine uses starch-fortified turmeric baths (SFTBs) [i.e. a mixture of rice starch and turmeric (Curcuma longa)] to treat psoriasis. This study set out to understand the effects of SFTBs on psoriasis. **Methods** The study used a parallel-group RCT design. Seventy-seven patients were screened of which 60 psoriatic patients were recruited. The inclusion criteria were people with psoriasis, aged between 20 and 60 years, not taking any medications and without open lesions. Participants were randomly allocated to two groups of 30. The intervention arm (IA) received SFTBs along with naturopathy interventions whereas the control arm (CA) received naturopathy interventions only (e.g. massage, yoga, hydro, diet therapy). The Psoriasis Area and Severity Index was completed at baseline and post-intervention (day 10). **Results** A mixed-ANOVA was conducted to compare scores within and between groups. There was a significant main effect for time [Wilks's λ=0.27, F(1, 58)=153.94, P<0.001, partial η2=0.73], with both groups showing an improvement over time. The difference between groups post-intervention was also statistically significant [F(1, 58)=10.552, P<0.01, partial η2=0.154]. **Conclusion** Starch-fortified turmeric baths, as applied in this study, appears to improve psoriasis area and severity and can be used as a safe and inexpensive therapy in the management of psoriasis.
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Title :	Recent advances in squamous non-small cell lung cancer: evidence beyond predictive biomarkers
Author :	Carlo Genova, Erika Rijavec & Francesco Grossi
Journal :	Expert Review of Anticancer Therapy: Published online 02 Dec 2015, DOI:10.1586/14737140.2016.1121112
Abstract :	Squamous non-small cell lung cancer (NSCLC) has always been characterized by a limited number of therapeutic options and by the lack of actionable biomarkers compared to its non-squamous counterpart. Recent clinical trials have led to the approval of new anti-neoplastic drugs available to both non-squamous and squamous NSCLC, consisting in a vascular-disrupting agent and two immune check-point inhibitors; additionally, a monoclonal antibody targeting the epidermal growth factor receptor (EGFR) is currently under evaluation by the Food and Drug Administration (FDA). While predictive molecular biomarkers have not been identified with consistency and are still highly demanded, these agents proved themselves noteworthy and can be considered a powerful addition to the available treatments for squamous NSCLC.
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Title :	Infant adrenocortical reactivity and behavioral functioning: relation to early exposure to maternal intimate partner violence
Author :	Alytia A. Levendosky, G. Anne Bogat, Joseph S. Lonstein, Cecilia Martinez-Torteya, Maria Muzik, Douglas A. Granger & Alexander von Eye
Journal :	Stress: published online 02 Dec 2015, DOI: 10.3109/10253890.2015.1108303
Abstract :	Prenatal stress negatively affects fetal development, which in turn may affect infant hypothalamic–pituitary–adrenal (HPA) axis regulation and behavioral functioning. We examined effects of exposure to a traumatic stressor in families [intimate partner violence (IPV)] on both infants' HPA axis reactivity to stress and their internalizing and externalizing behaviors. Infants (n = 182, 50% girls, x age = 11.77 months) were exposed to a laboratory challenge task designed to induce frustration and

	anger (i.e. arm restraint). Saliva samples were taken pre-task and 20 and 40 min post-task and then assayed for cortisol. Mothers reported on their pregnancy and postpartum IPV history, current mental health, substance use and their infants' behaviors. Structural equation modeling revealed that prenatal, but not postnatal, IPV was independently associated with infant cortisol reactivity and problem behavior. Maternal mental health predicted infant behavioral functioning but not infant HPA axis reactivity. These findings are consistent with the prenatal programing hypothesis; that is, early life stress affects later risk and vulnerability for altered physiological and behavioral regulation.
Database :	Taylor & Francis Online

Title :	Current views on inducing synthetic lethal RNAi responses in the treatment of cancer
Author :	Apollo D. Kacsinta & Steven F. Dowdy
Journal :	Expert Opinion on Biological Therapy: Published online 02 Dec 2015, DOI:10.1517/14712598.2016.1110141
Abstract :	**Introduction**: Cancer cells arise from normal cells that have incurred mutations in oncogenes and tumor suppressor genes. The mutations are often unique and not readily found in normal cells, giving rise to the opportunity of exploiting these mutations to induce synthetic lethality. Synthetic lethality occurs when inhibition or mutation in two or more separate genes leads to cell death while inhibition or mutations of either gene alone has no lethal effect on the cell. Using RNA interference (RNAi) to identify synthetic lethality has become a growingly popular screening approach. **Areas covered**: In this review, we cover the use of RNAi therapeutics to induce synthetic lethality in cancer. Additionally, we discuss several select small molecule inhibitors that were identified or verified by RNAi that induce synthetic lethality in specific cancers. We also discuss the identification of novel synthetic lethal combinations and the cancer model that the combination was validated in. Lastly, we discuss RNAi delivery vehicles.

	Expert opinion: While RNAi therapeutics have great potential to treat cancer, due to the siRNA delivery problem, RNAi remains more commonly used as a tool, rather than a therapeutic. However, with emerging technological advances in the field of RNAi therapeutics, it is only a matter of time before RNAi-induced synthetic lethal clinical studies are initiated in cancer patients.
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Title :	Single nucleotide polymorphism in the SEPS1 gene may contribute to the risk of various human diseases: a meta-analysis
Author :	Hong-Yun Sun, Tai-Bin Liu, Qing-Chang Wang, Wei-Qiang Wu & Yu-Jing He
Journal :	Annals of Human Biology: Published online 18 Sep 2015, DOI:10.3109/03014460.2015.1070903
Abstract :	Background: Recently the G-105A promoter polymorphism in SEPS1 has been shown to increase pro-inflammatory cytokine expression and, thus, to be correlated with various types of human cancers and diseases. Aims: This study examined whether this functional polymorphism was related to the risks of several human diseases by performing a meta-analysis. Subjects and methods: This study identified all published studies in MEDLINE, Science Citation Index, the Cochrane Library, PubMed, Embase, Current Contents Index and three Chinese databases. Results and conclusions: Eleven case-control studies were incorporated into this meta-analysis. The results showed that carriers of the rs28665122 G > A polymorphism in the SEPS1 gene are at increased risk of developing diseases under five genetic models. According to the ethnicity-stratified sub-group analysis, SEPS1 rs28665122 polymorphism is significantly linked to increased risk of developing related diseases in Europeans under five genetic models; but not among Asians. This data indicates a statistical association between SEPS1 rs28665122 G > A variants and the development of various human diseases. Such findings suggest that SEPS1 may be a potential gene marker for disease diagnosis and prognosis.
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Title :	Plasma bilirubin values on admission and ventricular remodeling after a first anterior ST-segment elevation acute myocardial infarction
Author :	Berta Miranda, José A. Barrabés, Jaume Figueras, Victor Pineda, José Rodríguez-Palomares, Rosa-Maria Lidón, Antonia Sambola, Jordi Bañeras, Imanol Otaegui & David García-Dorado
Journal :	Annals of Medicine: Published online 02 Dec 2015, DOI:10.3109/07853890.2015.1112027
Abstract :	**Introduction**: Bilirubin may elicit cardiovascular protection and heme oxygenase-1 overexpression attenuated post-infarction ventricular remodeling in experimental animals, but the association between bilirubin levels and post-infarction remodeling is unknown. **Materials and methods**: In 145 patients with a first anterior ST-segment elevation acute myocardial infarction (STEMI), we assessed whether plasma bilirubin on admission predicted adverse remodeling (left ventricular end-diastolic volume [LVEDV] increase ≥20% between discharge and 6 months, estimated by magnetic resonance imaging). **Results**: Patients' baseline characteristics and management were comparable among bilirubin tertiles. LVEDV increased at 6 months ($P < 0.001$) with respect to the initial exam, but the magnitude of this increase was similar across increasing bilirubin tertiles (10.8 [30.2], 10.1 [22.9], and 12.7 [24.3]%, $P = 0.500$). Median (25–75 percentile) bilirubin values in patients with and without adverse remodeling were 0.75 (0.60–0.93) and 0.73 (0.60–0.92) mg/dL ($P = 0.693$). Absence of final TIMI flow grade 3 (odds ratio 3.92, 95% CI 1.12–13.66) and a history of hypertension (2.04, 0.93–4.50), but not admission bilirubin, were independently associated with adverse remodeling. Bilirubin also did not predict the increase in ejection fraction at 6 months. **Conclusions**: Admission bilirubin values are not related to LVEDV or ejection fraction progression after a first anterior STEMI and do not predict adverse ventricular remodeling.
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Title :	Advances in the treatment of idiopathic pulmonary fibrosis
Author :	Amen Sergew MD & Kevin K Brown MD
Journal :	Expert Opinion on Emerging Drugs: Published online 02 Dec 2015, DOI:10.1517/14728214.2015.1102886
Abstract :	**Introduction**: Idiopathic pulmonary fibrosis (IPF) is a lung limited, progressive fibrotic disease with a poor prognosis. The cause is unknown, and currently there is no treatment that reverses the disease or stops progression. This combination of a poor prognosis and the absence of curative therapy has prompted a sustained investigative effort to identify beneficial treatments. Recently released trial results suggest progress. **Areas covered**: Although the mechanism of disease is poorly understood, a number of compounds that influence pathways thought to play a mechanistic role have been studied for use in IPF. This article discusses a number of these landmark trials. **Expert opinion**: From these studies we conclude that the future treatment of IPF will include expanding pharmacological options. Recent studies have identified two agents that appear to slow disease progression and may offer a window into pathogenesis and future drug targets.
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Title :	Inequities in access to rehabilitation: exploring how acute stroke unit clinicians decide who to refer to rehabilitation
Author :	Elizabeth A. Lynch, Julie A. Luker, Dominique A. Cadilhac & Susan L. Hillier
Journal :	Disability and Rehabilitation: Published online 25 Nov 2015, DOI:10.3109/09638288.2015.1103791
Abstract :	**Purpose**: Less than half of the patients with stroke in Australian hospitals are assessed by rehabilitation specialists. We sought to explore how clinicians working in acute stroke units (ASUs) determine which patients to refer to rehabilitation services. Method: Qualitative descriptive study. Team meetings were observed and medical records were reviewed over four weeks at two ASUs. Focus groups were conducted with staff from eight ASUs in two states of Australia. Results:

	Rehabilitation was mentioned in team meetings for 50/64 patients (78%) during the observation period. Rehabilitation referrals were organised for 47 patients (94%) for whom rehabilitation was discussed (74% of the sample); and for no patients when rehabilitation was not discussed. Factors identified that influenced whether referrals were organised included the anticipated discharge destination; severity of stroke; staff expectations of the patient's recovery; and if there was advocacy by families about rehabilitation. Clinicians tended to refer the patients they considered would be accepted by the rehabilitation service. Staff at two ASUs expressed concern that referring all patients with stroke-related deficits to rehabilitation would be unfavourable with rehabilitation providers. Conclusions: Decisions made by ASU staff regarding who to refer to stroke rehabilitation are often not solely based on patients' rehabilitation requirements. **Implications for Rehabilitation** Not all patients on acute stroke units (ASUs) who may have benefited from rehabilitation were offered rehabilitation referrals. Criteria for rehabilitation referrals need to be made explicit and discussed openly with consumers, ASU clinicians and rehabilitation specialists. A change in rehabilitation assessment practices is required to provide data regarding the unmet rehabilitation needs of patients with stroke. New models of rehabilitation service delivery or increased rehabilitation services may be required to meet the rehabilitation needs of all patients with stroke.
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Title :	Melanoma cell surface-expressed phosphatidylserine as a therapeutic target for cationic anticancer peptide, temporin-1CEa
Author :	Che Wang, Yin-Wang Chen, Liang Zhang, Xian-Ge Gong, Yang Zhou & De-Jing Shang
Journal :	Journal of Drug Targeting: Published online 23 Nov 2015, DOI:10.3109/1061186X.2015.1113539
Abstract :	We have previously reported that temporin-1CEa, a cationic antimicrobial peptide, exerts preferential cytotoxicity toward cancer cells. However, the exact molecular

	mechanism for this cancer-selectivity is still largely unknown. Here, we found that the negatively charged phosphatidylserine (PS) expressed on cancer cell surface serves as a target for temporin-1CEa. Our results indicate that human A375 melanoma cells express 50-fold more PS than non-cancerous HaCaT cells. The expression of cell surface PS in various cancer cell lines closely correlated with their ability to be recognized, bound and killed by temporin-1CEa. Additionally, the cytotoxicity of temporin-1CEa against A375 cells can be ameliorated by annexin V, which binds to cell surface PS with high affinity. Moreover, the data of isothermal titration calorimetry assay further confirmed a direct binding of temporin-1CEa to PS, at a ratio of 1:5 (temporin-1CEa:PS). Interestingly, the circular dichroism spectra analysis using artificial biomembrane revealed that PS not only provides electrostatic attractive sites for temporin-1CEa but also confers the membrane-bound temporin-1CEa to form α-helical structure, therefore, enhances the affinity and membrane disrupting ability of temporin-1CEa. In summary, these findings suggested that the melanoma cells expressed PS may serve as a promising target for temporin-1CEa or other cationic anticancer peptides.
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