บทความที่น่าสนใจประจำเดือน พฤศจิกายน 2557

สาขาวิทยาศาสตร์สุขภาพ

Title :	CHOPPI: A web tool for the analysis of immunogenicity risk from host cell proteins in CHO-based protein production
Author :	Bailey-Kellogg, C., Gutiérrez, A. H., Moise, L., Terry, F., Martin, W. D. and De Groot, A. S. (2014)
Journal :	Biotechnology and Bioengineering, Volume 111, Issue 11, pages 2170–2182, November 2014 (doi: 10.1002/bit.25286)
Abstract :	Despite high quality standards and continual process improvements in manufacturing, host cell protein (HCP) process impurities remain a substantial risk for biological products. Even at low levels, residual HCPs can induce a detrimental immune response compromising the safety and efficacy of a biologic. Consequently, advanced-stage clinical trials have been cancelled due to the identification of antibodies against HCPs. To enable earlier and rapid assessment of the risks in Chinese Hamster Ovary (CHO)-based protein production of residual CHO protein impurities (CHOPs), we have developed a web tool called CHOPPI, for CHO Protein Predicted Immunogenicity. CHOPPI integrates information regarding the possible presence of CHOPs (expression and secretion) with characterizations of their immunogenicity (T cell epitope count and density, and relative conservation with human counterparts). CHOPPI can generate a report for a specified CHO protein (e.g., identified from proteomics or immunoassays) or characterize an entire specified subset of the CHO genome (e.g., filtered based on confidence in transcription and similarity to human proteins). The ability to analyze potential CHOPs at a genomic scale provides a baseline to evaluate relative risk. We show here that CHOPPI can identify clear differences in immunogenicity risk among previously validated CHOPs, as well as identify additional "risky" CHO proteins that may be expressed during production and induce a detrimental immune response upon delivery. We conclude that CHOPPI is a powerful tool that provides a valuable computational complement to existing experimental approaches for CHOP risk assessment and can focus experimental efforts in the most important directions.
Database :	Wiley Online Library

Title :	[Association Between Interleukin-8 –251A/T Polymorphism and Risk of Lung Cancer: A Meta-Analysis.](#)
Author :	Ping Gao, Hong Zhao, Junhao You, Fangfang Jing, and Yi Hu
Journal :	Cancer Investigation: Posted online on October 14, 2014. (doi:10.3109/07357907.2014.964410)
Abstract :	This study is to evaluate the association between IL-8 –251A/T polymorphism and lung cancer risk in diverse populations. We performed a meta-analysis of six case-control studies that included 3,265 lung-cancer cases and 3,607 case-free controls. Overall, results showed that the IL-8 –251A/T polymorphism was not associated with a significantly increased risk of lung cancer in all genetic models. However, stratified by ethnicity, a significantly increased risk was found among Asians. In conclusion, IL-8 –251A/T polymorphism is associated with lung cancer susceptibility in Asians and the –251 A allele may increase risk of lung cancer in Asians.
Database :	Informa Healthcare

Title :	[Effects of cost-related medication nonadherence on financial health and retirement decisions among adults in late midlife](#)
Author :	Gail A. Jensen and Yong Li
Journal :	Journal of Pharmaceutical Health Services Research: Article first published online 7 NOV 2014	DOI: 10.1111/jphs.12076
Abstract :	Objectives Suboptimal adherence to prescribed medications due to cost is known to adversely affect physical health. In this study, we examine whether cost-related nonadherence (CRN) also affects 'financial health', e.g. an individual's personal finances or the timing of their retirement. Methods We examine this issue for 2927 adults in late midlife with chronic medical conditions who participated in the Health and Retirement Study and who reported regularly taking medication(s) for their condition over the period 1994 to 2004. We hypothesize CRN may indirectly influence financial health by contributing to the occurrence of negative health shocks. We estimate two sets of models, one to quantify the effects of CRN on the

occurrence of adverse health events, and another to quantify the effects of adverse health events on personal finances in 2004 and the timing of retirement. We then derive estimates of the indirect effects of CRN on financial health and on retirement decisions.

Key findings

Among adults in late midlife, CRN contributes significantly to reduced earnings and premature retirements. These effects happen because CRN raises the risk that serious health shocks occur over time, and such adverse events subsequently limit an individual's ability to continue working and accumulating wealth.

Conclusions

CRN can threaten more than just personal health. In late midlife, CRN can threaten an individual's ability to continue working and saving towards retirement.

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Title :	[Glucose concentration and streptomycin alter in vitro muscle function and metabolism](#)
Author :	Alastair Khodabukus and Keith Baar
Journal :	Journal of Cellular Physiology: Accepted manuscript online 30 OCT 2014 03:18PM EST | DOI: 10.1002/jcp.24857
Abstract :	Cell culture conditions can vary between laboratories and have been optimised for 2D cell culture. In this study, engineered muscle was cultured in 5.5 mM low glucose (LG) or 25 mM high glucose (HG) and in the absence or presence (+S) of streptomycin and the effect on C2C12 tissue-engineered muscle function and metabolism was determined. Following 2 weeks differentiation, streptomycin (3-fold) and LG (0.5-fold) significantly decreased force generation. LG and/or streptomycin resulted in upward and leftward shifts in the force-frequency curve and slowed time-to-peak tension and half-relaxation time. Despite changes in contractile dynamics, no change in myosin isoform was detected. Instead, changes in troponin isoform, calcium sequestering proteins (CSQ and parvalbumin) and the calcium uptake protein SERCA predicted the changes in contractile dynamics. Culturing in LG and/or streptomycin resulted in increased fatigue resistance despite no change in the mitochondrial enzymes SDH, ATPsynthase and cytochrome C. However, LG resulted in increases in the β-oxidation enzymes LCAD and

	VLCAD and the fatty acid transporter CPT-1, indicative of a greater capacity for fat oxidation. In contrast, HG resulted in increased GLUT4 content and the glycolytic enzyme PFK, indicative of a more glycolytic phenotype. These data suggest that streptomycin has negative effects on force generation and that glucose can be used to shift engineered muscle phenotype via changes in calcium-handling and metabolic proteins.
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Title :	[Liposomes Modified with Superhydrophilic Polymer Linked to a Nonphospholipid Anchor Exhibit Reduced Complement Activation and Enhanced Circulation](#)
Author :	Okhil K. Nag, Vivek R. Yadav, Brandon Croft, Andria Hedrick and Vibhudutta Awasthi
Journal :	Journal of Pharmaceutical Sciences: Article first published online, 12 NOV 2014 | DOI: 10.1002/jps.24254
Abstract :	We report the synthesis of an acyl-anchored superhydrophilic polymer (SHP) for external surface modification of liposome surface. N1-(2-aminoethyl)-N4-hexadecyl-2-tetradecylsuccinamide conjugated with SHP (HDAS–SHP) was synthesized and used for modifying the liposome surface. Unlike polyethylene glycol (PEG)–phospholipids, which are commonly used for manufacturing stealth liposomes, HDAS–SHP is devoid of both PEG and phosphoryl groups and possesses a zwitterionic polymeric chain. Circulation persistence of the 99mTc-labeled HDAS–SHP liposomes was documented by gamma camera imaging. After 24 h postinjection, approximately 30% of injected HDAS–SHP liposomes were present in blood as compared with only 4.5% of the plain liposomes. HDAS–SHP liposomes inhibited complement activation. They were found to be amenable to pH-gradient-based active loading of Adriamycin in a stable manner. At 37°C, HDAS–SHP liposomes provided better encapsulation efficiencies than the liposomes modified with DSPE-PEG2000. These results provide a strong basis for HDAS–SHP as a viable alternative to PEG–phospholipids for imparting stealth characteristics to drug delivery vehicles such as liposomes.
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Title :	[Unsaturated free fatty acids: a potential biomarker panel for early detection of gastric cancer](#)
Author :	Yaping Zhang, Ling Qiu, Yanmin Wang, Chengyan He, Xuzhen Qin, Yujie liu, Zhili Li
Journal :	Biomarkers: Posted online on October 30, 2014. (doi:10.3109/1354750X.2014.977951)
Abstract :	Changes in the levels of free fatty acids (FFAs) are closely associated with physiological status. Serum levels of C16:1, C18:3, C18:2, C18:1, C20:4, and C22:6 in 164 gastric cancer (GC) patients and 111 benign gastric disease (BGD) patients were significantly decreased compared with 252 healthy controls. Receiver operating characteristic analysis showed that the biomarker panel including C16:1, C18:3, C18:2, C20:4, and C22:6 presents a high diagnostic ability to differentiate early-stage GC patients from healthy controls plus BGD patients, with a sensitivity of 80.6% and a specificity of 72.7%.
Database :	Informa Healthcare

Title :	[Applying micro-costing methods to estimate the costs of pharmacy interventions: an illustration using multi-professional clinical medication reviews in care homes for older people](#)
Author :	Tracey H. Sach, James Desborough, Julie Houghton, Richard Holland and on behalf of the CAREMED study team
Journal :	International Journal of Pharmacy Practice: Article first published online, 6 NOV 2014 | DOI: 10.1111/ijpp.12162
Abstract :	Objectives Economic methods are underutilised within pharmacy research resulting in a lack of quality evidence to support funding decisions for pharmacy interventions. The aim of this study is to illustrate the methods of micro-costing within the pharmacy context in order to raise awareness and use of this approach in pharmacy research. Methods Micro-costing methods are particularly useful where a new service or intervention is being evaluated and for which no previous estimates of the costs of providing the service exist. This paper describes the rationale for undertaking a micro-costing study before detailing and illustrating the process involved. The illustration relates to a recently completed trial of multi-professional medication reviews as an intervention provided in

	care homes. All costs are presented in UK£2012.
	Key findings
	In general, costing methods involve three broad steps (identification, measurement and valuation); when using micro-costing, closer attention to detail is required within all three stages of this process. The mean (standard deviation; 95% confidence interval (CI)) cost per resident of the multi-professional medication review intervention was £104.80 (50.91; 98.72 to 109.45), such that the overall cost of providing the intervention to all intervention home residents was £36,221.29 (95% CI, 32 810.81 to 39 631.77).
	Conclusions
	This study has demonstrated that micro-costing can be a useful method, not only for estimating the cost of a pharmacy intervention to feed into a pharmacy economic evaluation, but also as a source of information to help inform those designing pharmacy services about the potential time and costs involved in delivering such services.
Database :	Wiley Online Library

Title :	Optimisation of secondary prevention of stroke: a qualitative study of stroke patients' beliefs, concerns and difficulties with their medicines
Author :	Caroline Souter, Anne Kinnear, Moira Kinnear and Gillian Mead
Journal :	International Journal of Pharmacy Practice: Volume 22, Issue 6, pages 424–432, December 2014
Abstract :	**Objectives**
	The objectives of this study are to explore stroke patients' and carers' beliefs and concerns about medicines and identify the barriers to medication adherence for secondary stroke prevention.
	Methods
	Qualitative semistructured one-on-one interviews were conducted with 30 patients with diagnosis of stroke. Interviews were analysed using the framework approach.
	Key findings

| | The study suggests that stroke patients' and carers' perceptions of their medicines may influence medicine-taking behaviour. In some cases when beliefs outweighed concerns, practical barriers prevented participants taking their medicines. Negative beliefs about a medicine were strong enough to prevent some participants starting a new medicine. Participants' actions were influenced by the perceived consequences of not taking the medicine and the impact of the adverse effect on their quality of life. Concerns lessened with time with no adverse effects. The importance of the role of the carer and of a medicine-taking routine was evident. Participants reported the inadequacy of information provision and the desire to have more written and verbal information. Some reported total lack of contact with their general practitioner or community pharmacist after hospital discharge.

Conclusions

Many of the difficulties stroke patients have adhering to secondary prevention strategies are potentially preventable with tailored information provision and appropriate monitoring and follow-up by primary healthcare professionals. We have designed an intervention addressing the identified barriers to medicine taking, the impact of which is currently being measured in a randomised controlled trial of a pharmacist-led home-based clinical medication review in stroke patients. |
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| Database : | Wiley Online Library |

Title :	Osteoarthritis disease progression model using six year follow-up data from the osteoarthritis initiative
Author :	Chaitali Passey, Holly Kimko, Partha Nandy and Leonid Kagan
Journal :	
Abstract :	The objective was to develop a quantitative model of disease progression of knee osteoarthritis over 6 years using the total WOMAC score from patients enrolled into the Osteoarthritis Initiative (OAI) study. The analysis was performed using data from the Osteoarthritis Initiative database. The time course of the total WOMAC score of patients enrolled into the progression cohort was characterized using non-linear mixed effect modeling in NONMEM. The effect of covariates on the status of the disease and the

	progression rate was investigated. The final model provided a good description of the experimental data using a linear progression model with a common baseline (19 units of the total WOMAC score). The WOMAC score decreased by 1.77 units/year in 89% of the population or increased by 1.74 units/year in 11% of the population. Multiple covariates were found to affect the baseline and the rate of progression, including BMI, sex, race, the use of pain medications, and the limitation in activity due to symptoms. A mathematical model to describe the disease progression of osteoarthritis in the studied population was developed. The model identified two sub-populations with increasing or decreasing total WOMAC score over time, and the effect of important covariates was quantified.
Database :	Wiley Online Library

Title :	Prevalence and determinants of fatty liver in normal-weight and overweight young adults. The Cardiovascular Risk in Young Finns Study.
Author :	Emmi Suomela, Mervi Oikonen, Johanna Virtanen, Riitta Parkkola, Eero Jokinen, Tomi Laitinen, Nina Hutri-Kähönen, Mika Kähönen, Terho Lehtimäki, Leena Taittonen, Päivi Tossavainen, Antti Jula, Britt-Marie Loo, Vera Mikkilä, Zobair Younossi, Jorma S. A. Viikari, Markus Juonala, Olli T. Raitakari
Journal :	Annals of Medicine: Posted online on October 21, 2014. (doi:10.3109/07853890.2014.966752)
Abstract :	Background and aims. Fatty liver may have different determinants in normal-weight and in obese individuals. We measured factors associated with fatty liver in 863 normal-weight (BMI < 25) and 1135 overweight/obese (BMI $\geq$ 25) young and middle-aged adults (45% male, age 34–49 years) in the population-based Cardiovascular Risk in Young Finns Study.

Methods and results. The prevalence of fatty liver detected with ultrasound was 29% in overweight/obese and 5% in normal-weight participants. In overweight/obese, the independent correlates were waist circumference (odds ratio for 1 standard deviation increase = 3.78), alanine transaminase (2.11), BMI (2.00), male sex (1.74), triglycerides (1.44), systolic blood pressure (1.31), fasting insulin (1.23), and physical activity (0.76). In normal weight, the |

independent correlates included alanine transaminase (3.05), smoking (2.56), systolic blood pressure (1.54), and alcohol intake (1.41). In normal-weight participants, the associations with fatty liver were stronger for alcohol intake and smoking, and weaker for triglycerides, than in overweight/obese participants (P for interaction < 0.05).

Conclusion.

Prevalence of fatty liver was 29% in overweight/obese and 5% in normal-weight adults. Differences in factors associated with fatty liver were seen between these two groups: alcohol intake and smoking were more strongly and triglycerides more weakly associated in normal-weight than in overweight/obese participants.

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