Title: Evidence for the free radical/oxidative stress theory of ageing from the CHANCES consortium: a meta-analysis of individual participant data

Author: Ben Schöttker, Hermann Brenner, Eugène HJM Jansen, Julian Gardiner, Anne Peasey, Růžena Kubinová, Andrzej Pajsk, Roman Topor-Madry, Abdonas Tamosiunas, Kai-Uwe Saum, Bernd Holleczek, Hynek Pikhart and Martin Bobak


Abstract:
Background
The free radical/oxidative stress theory of ageing has received considerable attention, but the evidence on the association of oxidative stress markers with mortality is sparse.

Methods
We measured derivatives of reactive oxygen metabolite (D-ROM) levels as a proxy for the reactive oxygen species concentration and total thiol levels (TTL) as a proxy for the redox control status in 10,622 men and women (age range, 45–85 years), from population-based cohorts from Germany, Poland, Czech Republic, and Lithuania, of whom 1,702 died during follow-up.

Results
Both oxidative stress markers were significantly associated with all-cause mortality independently from established risk factors (including inflammation) and from each other in all cohorts. Regarding cause-specific mortality, compared to low D-ROM levels (≤340 Carr U), very high D-ROM levels (>500 Carr U) were strongly associated with both cardiovascular (relative risk (RR), 5.09; 95 % CI, 2.67–9.69) and cancer mortality (RR, 4.34; 95 % CI, 2.31–8.16). TTL was only associated with CVD mortality (RR, 1.30; 95 % CI, 1.15–1.48, for one-standard-deviation-decrease).
The strength of the association of TTL with CVD mortality increased with age of the participants (RR for one-standard-deviation-decrease in those aged 70–85 years was 1.65; 95 % CI, 1.22–2.24).

Conclusions
In these four population-based cohort studies from Central and Eastern Europe, the oxidative stress serum markers D-ROM and TTL were independently and strongly associated with all-cause and CVD mortality. In addition, D-ROM levels were also strongly associated with cancer mortality. This study provides epidemiological evidence supporting the free radical/oxidative stress theory of ageing and suggests that d-ROMs and TTL are useful oxidative stress markers associated with premature mortality.

Database: BMC Medicine

Title: Characterisation and novel analyses of acute stress response patterns in a population based cohort of young adults: influence of gender, smoking and BMI

Author: Carly E. Herbison, David Henley, Julie Marsh, Helen Atkinson, John P. Newnham, Stephen G. Matthews, Stephen J. Lye & Craig E. Pennell


This is the author accepted version which has not been proofed or edited

Abstract: Dysregulation of the biological stress-response system has been implicated in the development of psychological, metabolic and cardiovascular disease. Whilst changes in stress-response are often quantified as an increase or decrease in cortisol levels, three different patterns of stress response have been reported in the literature for the Trier Social Stress Test (TSST) (reactive-responder (RR), anticipatory-responder (AR) and non-responder (NR)). However, these have never been systematically analysed in a large population-based cohort. The aims of this study were to examine factors that contribute to TSST variation (gender, oral contraceptive use, menstrual cycle phase, smoking and BMI) using traditional methods and novel analyses of stress-response patterns. We analysed the acute stress-response of 798, 18-year-old participants from a community-based cohort.
using the TSST. Plasma adrenocorticotropic hormone (ACTH), plasma cortisol and salivary cortisol levels were quantified. RR, AR and NR patterns comprised 56.6%, 26.2% and 17.2% of the cohort respectively. Smokers were more likely to be NR than (RR or AR), (adjusted, p < 0.05). Overweight and obese subjects were less likely to be NR than the other patterns (adjusted, p < 0.05). Males were more likely to be RR than NR (adjusted, p=0.05). In addition we present a novel AUC measure (AUCR), for use when the TSST baseline concentration is higher than later timepoints. These results show that in a young adult cohort, stress-response patterns, in addition to other parameters vary with gender, smoking and BMI. The distribution of these patterns has the potential to vary with adult health and disease, and may represent a biomarker for future investigation.

Database: Taylor & Francis Online Journal

Title: Anti-tumor Effect of Ultrasound-induced Nordy-loaded Microbubbles Destruction

Author: Xing Hua MD, Jun Ding MD, Rui Li MD, Ying Zhang MM, Zejun Huang MM, Yanli Guo MD & Qinghai Chen MD


Abstract: Background Synthesized dl-Nordihydroguaiaretic acid (dl-NGDA or “Nordy”) can inhibit the growth of malignant human tumors, especially the tumor angiogenesis. However, its liposoluble nature limits its in vivo efficacy in the hydrosoluble circulation of human.

Purpose We tried to use the ultrasonic microbubble as the carrier and the ultrasound-induced destruction for the targeted release of Nordy and evaluate its in vitro and in vivo anti-tumor effect.

Methods Nordy-loaded lipid microbubbles were prepared by mechanical vibration. Effects of ultrasound-induced Nordy-loaded microbubbles destruction on proliferation of human umbilical vein endothelial cells (HUVECs), tumor derived endothelial cells (Td-ECs) and rabbit transplanted VX2 tumor models were evaluated.
Results The ultrasound-induced Nordy-loaded microbubbles destruction inhibited the proliferations of HUVECs and Td-ECs in vitro, and inhibited the tumor growth and the microvasculature in vivo. Its efficacy was higher than those of Nordy used only and Nordy with ultrasound exposure.

Conclusion Ultrasonic microbubbles can be used as the carrier of Nordy and achieve its targeted release with improved anti-tumor efficacy in the condition of ultrasound-induced microbubbles destruction.

Title: SmartSenior@home: Acceptance of an integrated ambient assisted living system. Results of a clinical field trial in 35 households

Author: M. Gövercin, S. Meyer, M. Schellenbach, E. Steinhagen-Thiessen, B. Weiss & M. Haesner


Abstract: Aims: The primary objective of the SmartSenior@home study was to examine the acceptance of the SmartSenior system by older adults. Methods: Twenty-eight partners from industry and research, including the health care sector, worked collaboratively to implement services aiming to maximize independence in old age. The prospective cohort study was conducted in Potsdam, Germany, with n = 35 older adults between 55 and 88 years of age in their apartments. All participants underwent extensive pre- and post-study visits with in-home interviews, functional assessments for cognition, fine motor skills, and mobility as well as responding to questionnaires on user acceptance and quality of life. Results: The results indicate moderate-to-high user acceptance for the SmartSenior system. In particular, the services for general assistance and health, such as audio/video communication, blood pressure monitoring, and communication with a health professional, were rated as very attractive. Less used and less accepted services were those promoting social interaction and reminder services. Conclusion: Besides reliable functioning of the SmartSenior system, the availability of a confidant seems to be the
most significant acceptance factor. As one conclusion of this trial, it is possible to develop, integrate, and test an infrastructure for ambient assisted living services in real life.

### Database
Taylor & Francis Online Journal

### Title
Emerging drugs for the treatment of perennial allergic rhinitis

### Author
Amelia Licari, Riccardo Castagnoli, Chiara Bottino, Alessia Marseglia, GianLuigi Marseglia & Giorgio Ciprandi

### Journal
Expert Opinion on Emerging Drugs, Pages: 1-11 | DOI: 10.1517/14728214.2016.1139082 -- Published online: 25 Jan 2016

### Abstract
Introduction: Allergic rhinitis is a worldwide health problem, currently affecting up to 40% of the general population, and characterized by the following symptoms in a variable degree of severity and duration: nasal congestion/obstruction, rhinorrhea, itchy nose and/or eyes, and/or sneezing. General symptoms like fatigue, reduced quality of sleep, impaired concentration and reduced productivity, if left untreated, may significantly affect quality of life. In addition, of being associated to various comorbidities, allergic rhinitis is also an independent risk factor for the development and worsening of asthma. Perennial allergic rhinitis is caused by allergens present around the year.

Areas covered: Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines currently recommend a stepwise therapeutic approach that combines patient education with specific allergen avoidance, symptomatic pharmacotherapy and allergen immunotherapy. The available treatment strategies provide suboptimal symptom relief in patients with moderate-to-severe disease who continue to experience symptoms while treated, even on multiple therapies.

Expert opinion: New insights into current therapy have been provided with the development of new symptomatic drugs with improved pharmacokinetics and safety. However, the ultimate research goal is beyond symptomatic treatment, and is mainly directed at modifying the immune response to allergens and prevent the progression of allergic rhinitis towards asthma. In this direction, promising advances are expected in the fields of allergen immunotherapy and biological drugs, such as omalizumab. Finally, significant research efforts are also focused on the growing...
number of new specific molecular targets involved in the Th2 pathway inflammation of allergic diseases.

**Database:** Taylor & Francis Online Journal

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<th><strong>Title</strong></th>
<th>Target-oriented therapy: Emerging drugs for atopic dermatitis</th>
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<tr>
<td><strong>Author</strong></td>
<td>Felix Lauffer MD &amp; Johannes Ring MD, PhD</td>
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<tr>
<td><strong>Abstract</strong></td>
<td>Introduction: Atopic dermatitis (AD) is a chronic inflammatory skin disease with a life-time prevalence of 10 – 20% in western countries. Patients suffer from stigmatizing eczematous skin lesions, persisting itch and sleep disorders. Starting usually in early childhood the course of AD is heterogeneous. While most frequently AD disappears before adolescence, about 30% of patients show a chronic persisting course. There is an urgent need for new therapeutic options as until now, specific drugs are missing. Areas covered: Over the last years research has made enormous progress in understanding mechanisms involved in AD pathogenesis. Th2 cells and their key cytokines IL-4 and IL-13 as well as TSLP, CRTH2 and IgE are targets for new compounds currently being tested in clinical trials. This review highlights new drugs for AD at all stages of development as well as current promising scientific approaches. Expert opinion: After decades of silence the market for AD drugs has recently become highly active. Amongst all new compounds, dupilumab - an antibody directed against IL-4 and IL-13 receptors - is the most advanced candidate showing convincing efficacy in several phase III studies. The availability of specific drugs for AD will open up a new era in dermatological therapy.</td>
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<td>Title :</td>
<td>Prospects for the use of ipilimumab in treating advanced prostate cancer</td>
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<td>Author :</td>
<td>Xiao X. Wei, Lawrence Fong &amp; Eric J. Small</td>
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<td>Journal :</td>
<td>Expert Opinion on Biological Therapy, Pages: 1-12</td>
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<td>Abstract :</td>
<td>Introduction: Ipilimumab is a fully human monoclonal antibody that blocks Cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) to potentiate antitumor T cell response. Ipilimumab is approved for the treatment of advanced melanoma based on improved overall survival. Clinical trials of ipilimumab in patients with metastatic castrate-resistant prostate cancer (mCRPC) have demonstrated some clinical activity, but have largely been disappointing to date. Areas covered: Results of key clinical studies of ipilimumab in the treatment of prostate cancer, including clinical efficacy and toxicities, are summarized. Expert opinion: There is likely a clinical benefit to ipilimumab in a subset of mCRPC patients. The development of biomarkers for enrichment treatment strategies that select for patients most likely to benefit from ipilimumab is a top priority. Similarly, an understanding of the factors predictive of toxicity will be important in the development of future treatment approaches.</td>
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| Title : | Ixekizumab: a new anti-IL-17A monoclonal antibody therapy for moderate-to-severe plaque psoriasis |
| Author : | Andrew Blauvelt |
| Journal : | Expert Opinion on Biological Therapy, Pages: 1-9 | DOI: 10.1517/14712598.2016.1132695 -- Published online: 25 Jan 2016 |
| Abstract : | Introduction: Psoriasis is a common, systemic, inflammatory disease with prominent skin and joint manifestations. Interleukin 17A (IL-17A) has been identified as a key effector cytokine that mediates immunopathogenesis of psoriasis. Ixekizumab, a humanized monoclonal antibody that targets IL-17A, has been found in clinical trials to dramatically reduce signs and symptoms of moderate-to-severe plaque psoriasis. Areas covered: The following areas are discussed: the basic structure and function of IL-17A, its role in the pathogenesis of psoriasis, the safety and efficacy of |
ixekizumab in clinical trials reported to date, and the possible impact of ixekizumab on the future therapeutic market for psoriasis.

Expert opinion: A large proportion of patients with psoriasis achieve clear or near clear skin during treatment with ixekizumab in a rapid and sustained manner. This supports the idea that IL-17A plays a central role in psoriasis immunopathogenesis.

While ixekizumab has been shown to be safe in trials up to 60 weeks, long-term safety data are not yet available. Because its efficacy is higher than all previously approved drugs for psoriasis thus far, approval and use of ixekizumab may lead to a treatment paradigm change for psoriasis, where clear or near clear skin becomes an acceptable and achievable treatment goal.

Database: Taylor & Francis Online Journal

Title: Applying computation biology and “big data” to develop multiplex diagnostics for complex chronic diseases such as osteoarthritis

Author: Guomin Ren & Roman Krawetz

Journal: Biomarkers, Pages: 1-7 | DOI: 10.3109/1354750X.2015.1105499, Published online: 26 Jan 2016

Abstract: The data explosion in the last decade is revolutionizing diagnostics research and the healthcare industry, offering both opportunities and challenges. These high-throughput “omics” techniques have generated more scientific data in the last few years than in the entire history of mankind. Here we present a brief summary of how “big data” have influenced early diagnosis of complex diseases. We will also review some of the most commonly used “omics” techniques and their applications in diagnostics. Finally, we will discuss the issues brought by these new techniques when translating laboratory discoveries to clinical practice.

Database: Taylor & Francis Online Journal

Title: MicroRNA Regulation of Acute Lung Injury and Acute Respiratory Distress Syndrome
The acute respiratory distress syndrome (ARDS), a severe form of acute lung injury (ALI), is a very common condition associated with critically ill patients, which causes substantial morbidity and mortality worldwide. Despite decades of research, effective therapeutic strategies for clinical ALI/ARDS are not available. In recent years, microRNAs (miRNAs), small non-coding molecules have emerged as a major area of biomedical research as they post-transcriptionally regulate gene expression in diverse biological and pathological processes, including ALI/ARDS. In this context, this present review summarizes a large body of evidence implicating miRNAs and their target molecules in ALI/ARDS originating largely from studies using animal and cell culture model systems of ALI/ARDS. We have also focused on the involvement of miRNAs in macrophage polarization, which play a critical role in regulating the pathogenesis of ALI/ARDS. Finally, the possible future directions that might lead to novel therapeutic strategies for the treatment of ALI/ARDS are also reviewed.