Biomarkers and Ageing

Tuesday, 25 February 2014
Cineworld: The O2, London, SE10 0DX, UK
www.regonline.co.uk/biomarkage2014

Biomarkers of ageing could help to characterise biological age and be used, not only to identify individuals at high risk of developing age-associated diseases or disabilities, but also could lead to anti-ageing therapies. This event will discuss the current research to identify and characterise biomarkers for ageing in an informal atmosphere. Abstract submissions are encouraged for both oral and poster presentations and there will be plenty of opportunity of networking with experts in the field. Part of the 2014 Ageing Summit **www.AgeingSummit2014.com**. This event has **CPD accreditation.**

Meeting Chairs: *Professor David Melzer,* Epidemiology & Public Health Group, Medical School, University of Exeter, UK and *Dr Lorna Harries,* RNA-mediated disease mechanisms, Medical School, University of Exeter, UK

Abstracts for *poster presentation only* can be submitted up to two weeks before the event. **You can download the instructions for authors at : www.euroscicon.com/AbstractsForOralAndPosterPresentation.pdf**

Talk times include 5 – 10 minutes for questions

9:30 - 10:15 **Registration**

10:15 - 10:30 **Introduction by the Chairs**:*Professor David Melzer,* Epidemiology & Public Health Group, Medical School, University of Exeter, UK and *Dr Lorna Harries,* RNA-mediated disease mechanisms, Medical School, University of Exeter, UK

10:30 - 11:00 **Bone turnover markers and ageing-related loss of bone mass and strength**
Dr Pawel Szulc, INSERM UMR 1033, University of Lyon, France
In postmenopausal women and in older men, elevated BTM levels (which reflect higher bone turnover) are associated with lower BMD, poor bone microarchitecture (e.g. thinner cortex) and faster bone loss. Bone turnover rate is a major determinant of bone loss in older people. However, BTM measurement cannot be used for prediction of accelerated bone loss, because their correlation is not strong enough, especially in men. Higher BTM levels are associated with higher risk of fracture (i.e. lower bone strength). This association was found in postmenopausal and elderly women, but not older men. It was found mainly for major osteoporotic fractures (e.g. hip fracture), especially in short-term follow-ups (<5 years). This association was significant only for bone-specific BTM, mainly for bone resorption markers. The association between BTM levels and fracture risk remains significant after adjustment for BMD, which indicates that accelerated bone turnover is an independent determinant of bone fragility. However, currently, there are no official guidelines concerning the use of BTM for the fracture risk assessment in the clinical practice. In conclusion, measurement of BTM can improve our understanding of the mechanisms leading to the ageing-related loss of bone mass and strength.

11:00 - 11:30 **Maldi imaging mass spectrometry of ageing cartilage**
Dr. Mandy Peffers, Wellcome Veterinary Integrated Research fellow, University of Liverpool, Liverpool, UK

Matrix assisted laser desorption ionization (MALDI) imaging mass spectrometry (IMS) enables examination of proteins in-situ at a high spatial resolution. This study utilised this methodology to investigate the location and abundance of different cartilage proteins in ageing and osteoarthritic equine cartilage in order to determine changing molecular events distinct between aging and disease.

11:30 - 12:00 **Speakers' photo then mid-morning break and poster exhibition and trade show**
Please try to visit all the exhibition stands during your day at this event. Not only do our sponsors enable Euroscicon to keep the registration fees competitive, but they are also here specifically to talk to you.

12:00 - 12:30 **Interpretation and usefulness of current reference intervals for biochemical markers in frail elderly**
Mrs Maria Edvardsson, Reg Biomedical Laboratory Scientist, Laboratory, Finspång Health Care Centre, County Council of Östergötland, Sweden
Reference intervals provided by the laboratory are commonly established by measurements of samples from apparently healthy subjects in the ages 18-65 years. The aim was to compare values used to develop reference intervals for IgA, IgG, IgM, C3, C4 alanine aminotransferase, albumin, aspartate aminotransferase, creatinine, gamma-glutamyltransferase, lactate dehydrogenas, phosphate, sodium and urea, with values from nursing home residents (NHR), 80 years and older. Comparing laboratory results from elderly people with reference values for younger adults can be misleading or even dangerous, since normal conditions may appear pathological, or the contrary, and thus lead to unnecessary or even harmful treatment.

12:30 – 13:00 **Disrupted expression of splicing factors in human ageing**
Dr Lorna Harries, Senior Lecturer in Molecular Genetics, RNA-mediated disease mechanisms, University of Exeter Medical School, UK
Changes in splicing with age have been reported in man, potentially arising from age-related alterations in splicing factor (SF) expression. We examined differential expression of SFs with age, in blood from two human populations and in senescent primary cells in culture. 38% of SFs demonstrated age/senescence-related transcript expression changes both in vivo and in vitro. Ataxia Telangiectasia Mutated (ATM) emerged as a potential negative regulator of splicing factor expression, which was confirmed by siRNA against ATM in primary fibroblasts. These findings suggest that ATM, a core DNA damage protein, is a key regulator of the splicing machinery in man.

13:00 – 14:00 **Lunch, poster exhibition and trade show**
Please try to visit all the exhibition stands during your day at this event. Not only do our sponsors enable Euroscicon to keep the registration fees competitive, but they are also here specifically to talk to you.

14:00 – 15:00 **Discussion Panel**
This discussion session is an informal question and answer session. This is an ideal opportunity to get advice and opinion from experts in this area. This session is not for questions about specific talks, which can be asked after the speakers session, but for discussing either general topics or specific issues. There are three ways you can ask questions:
1. Before the session you can *submit your question to Euroscicon staff* at the registration desk,
2. Before and during the session you can *submit a question or comments, by email*, which will be provided on the day of the event
3. During the session you can *put your hand up* and join in

15:00 – 15:30 **Afternoon Tea, last poster session and trade show**

15:30 – 16:00 **Genomic biomarkers of human ageing**

Professor David Melzer, Epidemiology & Public Health Group, Medical School, University of Exeter, UK

Messenger RNA (mRNA) is an intermediate between DNA and proteins. Clinical tests based on gene expression / mRNA signatures are already in use, notably for sub-typing and prognosis in cancer. In the last five years there have been several key findings of gene expression and methylation biomarkers linked to ageing or related traits in humans. Larger scale human studies of in-vivo genome wide expression in blood (notably from our InCHIANTI aging genomics study) have identified age related changes in the ratio of splice variants (isoforms) with advancing age for several genes, perhaps explaining loss of function in specialized cells. Gene expression associations with age itself yielded a biomarker sets that is a powerful classifier of biological age. Gene expression markers associated with muscle strength and cognition showed striking concordance with certain mice models of muscle repair and beta-amyloid phagocytosis respectively. Several studies of methylation with age have confirmed associations with large numbers of markers, with marker sets having strong correlations with chronological age. The functional significance of these patterns is currently being explored. Major challenges for the future include accounting for cell and tissue heterogeneity and establishing the longer term predictive value of expression and methylation markers.

16:00 – 16:30 **Photoageing and the elastic fibre network**

Dr Rachel Watson, Senior Non-Clinical Lecturer, The University of Manchester, UK

In humans, ageing is a composite, combining intrinsic processes with those induced by interactions with our environment. Skin, more than any other organ, is subject to extreme environmental pressure, the major force being long term, chronic exposure to solar ultraviolet radiation (UVR). Skin is a specialised organ, composed of a cell-rich epidermis and a relatively cell-poor but extracellular matrix-rich dermis; this matrix has a complex composition, made up of many interacting proteins, which imbues skin with strength and elasticity. The effects of chronic UVR exposure to the dermal matrix will be discussed and we will explore why we see variation in the effects of UVR on specific dermal matrix components. Finally, we will look at strategies to partially repair the damage observed following long term sun exposure.

16:30 **Chairman's summing up**

Registration Website: www.regonline.co.uk/biomarkage2014

Meeting reports from this event will be published by *Biomarkers in Medicine* and by *HONNAO* publishing

Keywords: biochemical marker; reference value; aging; multi-disease; nursing home resident, Types of adaptive behavior, aging, hypothalamic-pituitary-adrenal axis, antioxidant enzymes, primates, Ageing, Splicing factors, Alternative Splicing, ATM, MALDI-IMS,cartilage, ageing, equine, ageing; frail; nursing home resident; biochemical marker; reference interval, ultraviolet radiation, reactive oxygen species, matrix metalloproteinases, elastin, fibrillin-rich microfibrils

About the Chairs

David Melzer is Professor of Epidemiology and Public Health at the Medical School, University of Exeter, UK. His research interests are in the causes and consequences of chronic disease in later life. David's group has analysed large genomics array datasets, leading and contributing to many genome-wide association studies of disease-associated and phenotypic ageing traits. Recent work (with Dr Lorna Harries, Molecular Genetics UEMS) has extended these approaches to gene expression and methylation array data. This work is part of a long-term collaboration with the Ferrucci research group at the US National Institute on Aging (at NIH). He has received research support from the US National Institutes of Health, the Wellcome Trust, British Heart Foundation, the Medical Research Council, Age UK, NIHR and other funders.

Since gaining her PhD from University College London in 1994, **Lorna Harries** has worked at several institutions including the Biomedical Research Centre at the University of Dundee and the MRC Cell Mutation Unit at the University of Brighton. She established the RNA-mediated disease mechanisms group at the University of Exeter Medical School in 2006. The group has interests in -omics approaches to the study of human ageing and age-related disease processes in man, with a specific focus is on the impact of alternative messenger RNA processing, small RNA and epigenetic gene regulation.

About the Speakers

Pawel Szulc, M.D., Ph.D., graduated from the Medical Faculty in Warsaw, 1986. Researcher in the INSERM UMR 1033, Lyon, France. Member of the Committee of Scientific Advisors of the International Osteoporosis Foundation. Member of the Editorial Board of Osteoporosis International. Member of American Society for Bone and Mineral Research, International Bone and Mineral Society, International Society for Men's Health. Member of the Thematic Network on the Osteoporosis in Male (2001-06). Scientific interests: osteoporosis, sarcopenia, relationship between osteoporosis and cardiovascular diseases. Author of 60 papers and chapters concerning osteoporosis, mainly osteoporosis in men, bone turnover markers and vertebral fracture. Fellowships: French Government (1991) and European Community (1993).

Mandy Peffers graduated from the Royal Veterinary College in 1995 and following an internship at the University of Glasgow worked in bovine reproduction for 10 years before becoming a partner in a mixed veterinary proactice in Wales. In 2009 she undertook an MPhil and then PhD at the University of Liverpool as a Wellcome Veterinary Integrated Research Fellow. She is presently continuing her fellowship at Liverpool. Her interests include cartilage and tendon proteomics and transcriptomics in ageing and disaese.

Maria Edvardsson works as reg biomedical laboratory scientist at the laboratory in Finspång health care centre, county council of Östergötland, Sweden. In its work she takes blood samples and analyzes the analytes which are carried out on this laboratory. In addition she is working on reception for prescription of anticoagulant. Previously, she worked at blodcentral and for several years she has been responisble for chemical analytes. Interest in research has been found for a long time and Maria is since the spring 2013 adopted as a postgraduate at Linkoping University. Time is now divided between research work and work on the laboratory in Finspång.

Rachel Watson (BSc (hons), PhD) is a non-clinical senior lecturer in Aesthetic Dermatology within the Faculty of Medical & Human Sciences, University of Manchester. She received her BSc (Anatomy & Cell Biology) and PhD degrees from the University of Sheffield. Her research focuses on understanding human ageing, with particular reference to skin. This tissue ages by intrinsic and extrinsic mechanisms; the major environmental factor which impacts upon skin is long-term sun exposure (ultraviolet radiation, UVR), although other stimuli also exert effects

(sun-bed use, smoking, atmospheric pollutants etc).

POSTER PRESENTATIONS

MALDI IMAGING MASS SPECTROMETRY OF AGEING CARTILAGE

M.J. Peffers, B. Cillero-Pastor, P.D.Clegg
Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool, UK

Introduction Osteoarthritis (OA) is an age related joint disease characterized by a loss of cartilage extracellular matrix (ECM). Age is the most common risk factor for its initiation and progression with symptomatic OA affecting 10–20% of people aged over 50 years. The explanation for this is an accumulation of 'wear and tear' injuries due to mechanical loading over many years. Although much work has been undertaken investigating the pathogenesis of OA the molecular mechanisms involved are not fully understood, with few validated markers for disease diagnosis and progression being available. Matrix assisted laser desorption ionization (MALDI) imaging mass spectrometry (IMS) enables examination of proteins *in-situ* at a high spatial resolution. This study utilised this methodology to investigate the location and abundance of different cartilage proteins in ageing and OA equine cartilage in order to determine changing molecular events distinct between aging and disease. **Methods** Full thickness equine cartilage slices from young (4 years old), old (greater than 15 years old) and OA old donors were removed from the mid condyle region of metacarpophalangeal joints. 12 μm thick sections were cut and following washing trypsin for digestion was applied by a high-accuracy position automatic chemical inkjet printer.
Alpha-Cyano-4-hydroxycinnamic acid matrix was deposited by a vibrational sprayer system. Synapt HDMS MALDI-Q-TOF was used to perform the imaging-mass spectrometry experiments with a raster size of 150 μm. Peptides were identified using MASCOT following profiling MS/MS experiments. Biomap software was used to generate ion images and quantify peptide intensity. The data analysis workflow used a number of AMOLF in-house build MATLAB software tools to undertake Principal Component Analysis (PCA) and Discriminant Analysis (DA) for data interpretation. **Results** Extracellular matrix proteins identified included cartilage oligomeric matrix protein, fibromodulin, biglycan and type II collagen. After combining all the spectra from the different conditions and following DA, the resulting discriminant functions (DF) classified the data in three groups according to their peptide profile: young, old and OA. Interestingly there was a large contribution of the old samples to the negative part of DF1 indicating that peptides within old samples were also present in OA samples. The spectra of young, old and OA samples after MALDI-IMS experiments were analyzed independently by PCA and DA to classify peptides specific to each group (young versus old and old versus OA), thus producing a catalogue of peptides distinct in ageing and disease. A number of OA and ageing markers were identified. Significant differences were evident for the peak intensity distribution of OA specific peptides including fibronectin peptides *m/z* 1349.6 and *m/z* 1401.7 ($p=0.018$, $p=0.02$) and the hypothetical marker with *m/z* 1366.5 ($p=0.001$) between ageing and OA samples. Age-related markers were also identified for COMP *m/z* 2256.1, the hypothetical marker *m/z* 2415.9 and fibromodulin peptide ELHLDHNQISR; *m/z* 1361.7 Furthermore there was a significant reduction in the intensity of this latter peptide and biglycan peptide NHLVEIPPNLPSSLVELR *m/z* 2027.2 ($p=0.001$, $p=0.02$) in OA compared to young and old cartilage indicating peptides potentially targeted for degradation in OA. **Conclusion** MALDI-IMS based molecular imaging provided a novel platform to study cartilage ageing and disease enabling age and disease specific markers in cartilage to be elucidated and spatially resolved. The *ex-vivo* imaging of aged and diseased cartilage provided 'label-free' and stain-free information regarding its biomolecular composition.

INTERPRETATION AND USEFULNESS OF CURRENT REFERENCE INTERVALS FOR BIOCHEMICAL MARKERS

IN MULTI-DISEASED ELDERLY.

M Edvardsson[a], M Sund-Levander[b], E Grodzinsky[c]

[a] Corresponding author: regBLS, Laboratory, Finspång Health Care Centre, County Council of Östergötland, Sweden. Phone + 46 101042412, Cell phone +46 70 2660551. E-mail: maria.edvardsson@lio.se [b]Division of Nursing Care, Department of Medicine, Faculty of Health Sciences, Linköping University, Linköping, Sweden. Phone + 46 13285627, Cell phone +46 702703874

E-mail: martha.sund-levander@liu.se [c] regBLS, Ass Professor Linköping University & The Research and Developing Unit in Local Health Care, County Council of Östergötland, University Hospital, SE 581 85 Linköping, Sweden. Phone: +46 10 1038505, Cell phone: +46 70 6205446. E-mail: ewa.grodzinsky@lio.se

Background: Reference intervals provided by the laboratory are commonly established by measurements of samples from apparently healthy subjects in the ages 18-65 years. Comparing laboratory results from elderly people with such reference intervals may be misleading or even dangerous, since they can falsely indicate disease in healthy elderly prompting unnecessary further diagnostic procedures and even unnecessary or even harmful treatment. The aim of the present study was to compare values used to develop reference intervals for IgA, IgG, IgM, C3 and C4 with values from nursing home residents (NHR), 80 years and older. The aim was also to compare values used to develop reference intervals established from the Nordic Reference Interval Project (NORIP), with results from NHR, 80 years and older, for alanine aminotransferase, albumin, aspartate aminotransferase, creatinine, *gamma**-glutamyltransferase*, lactate dehydrogenas, phosphate, sodium and urea. **Method**s: Blood samples were collected from 138 non-infected NHR age 80-98; mean age 86.8 ± 4.3. Only 10 individuals (7.2%) were diagnosed without dementia, diabetes mellitus type 2, chronic heart disease, stroke, liver or kidney disease, malnutrition and not treated by paracetamol. Plasma was analysed by routine laboratory assays. **Results:** Differences between values from NHR and values used to develop reference values occured for IgG ($p<0.01$), IgM, C3, C4, alanine aminotransferase, albumin, phosphate, sodium and urea ($p<0.001$). **Conclusion:** Comparing laboratory results from elderly people with reference values for younger adults can be misleading or even dangerous, since normal conditions may appear pathological, or the contrary, and thus lead to unnecessary or even harmful treatment.

GENOMIC BIOMARKERS OF HUMAN AGEING

L Harries, L Pilling, A Holly, L Ferrucci, D Melzer

Professor David Melzer, Epidemiology & Public Health Group, Medical School, University of Exeter, Medical School Building, RD&E (Wonford), Barrack Road, Exeter, EX2 5DW, United Kingdom

Messenger RNA (mRNA) is an intermediate between DNA and proteins. Cells tightly regulate the abundance and format of new protein molecules in response to intra- and extra-cellular signals. The amount of mRNA produced at any point in time is a good proxy for the demand within cells for each protein. Clinical tests based on gene expression signatures are already in use, notably for sub-typing and prognosis in cancer. In the last five years there have been several key findings of gene expression and methylation biomarkers linked to ageing or related traits in humans. Larger scale human studies of in-vivo genome wide expression in blood (notably from our InCHIANTI aging genomics study) have identified age related changes in the ratio of splice variants (isoforms) for several genes with advancing age, perhaps explaining loss of function in specialized cells. The control of splicing in cells, especially in ageing is still poorly understood, but we have shown that ATM, an upstream responder to DNA damage, influences several key splicing proteins. Gene expression associations with age itself yielded a biomarker sets that is a powerful classifiers of biological age. Gene expression markers associated with muscle strength and cognition have shown striking concordance with certain mice models of muscle repair and beta-amyloid phagocytosis respectively. Several studies of methylation with age have confirmed associations with large numbers of markers, with marker sets having strong correlations with chronological age. The functional significance of these patterns is currently

being explored. Major challenges for the future include accounting for cell and tissue heterogeneity and establishing the longer term predictive value of expression and methylation markers. *Key papers from the group:* Holly et al, Towards a gene expression biomarker set for human biological age. Aging Cell. 2013 Apr;12(2):324-6. PMID: 23311345 Harries LW, et al. CCAAT-enhancer-binding protein-beta expression in vivo is associated with muscle strength. Aging Cell. 2011 Dec 8. PMID: 22152057

CARDIORESPIRATORY CAPACITY AND BIOMARKERS OF AGEING IN HUMANS: DNA DAMAGE, DNA REPAIR CAPACITY, LIPID PEROXIDATION AND ANTIOXIDANT CAPACITY.

J.P. Soares[1,2]; Z.A. dos Santos[1,3], A.F. Pereira[2,4], E.Veloso[1]; J. Benevides; M.M. Oliveira[1,5]; I.Gaivão[1,5]; M.P. Mota[1,2]
[1]University of Trás-os-Montes e Alto Douro, Vila Real, Portugal; [2]CIDESD; [3]Faculty Metodista Granbery, Minas Gerais, Brasil; [4]Polytechnique Institute of Setúbal;[5]CQ; [5]CECAV

Introduction: Oxidative stress has been appointed as one of the main possible causes of ageing. These alterations may result in genetic instability, mutagenesis, disease, and cell death. However, lifestyle could attenuate these damage, probably increasing cell protection and repair mechanisms. An active lifestyle promotes cardiovascular capacity and possible stimulates cell signalling pathways that could result in functionality improvement. This study aimed to search for cardiovascular related benefits in some oxidative damaged markers of ageing (DNA strand breaks and lipid peroxidation), as well as, cell protection (antioxidant capacity) and DNA repair mechanisms. Methodology: Twenty healthy males between 42 and 73 years old (60.7± 10,7) were enrolled in this study. DNA damage (strand breaks) were evaluated by comet assay procedures[1], in peripheral blood mononuclear cells (PBMC), and Lipid peroxidation (estimated through TBARs test,[2]) and Total Antioxidant capacity[3] were analysed in plasma with the subjects in fasting conditions. Cardiovascular capacity was estimated through 6 minute walking test. The sample were divided into two groups of age, the older one >=65 years, and the middle one <65 years. Descriptive data analysis, coefficient correlations and independent-samples t-test were analysed in SPSS. Significant level was set at $p<0.05$. Results: The results indicated that DNA damage was positively related with TBARs ($r=0.463$) and inversely associated with cardiorespiratory capacity ($r= -0.428$). It was also found an inverse association between TBARs and antioxidant capacity ($r=-0.489$). The cardiorespiratory capacity was also inversely related with age ($r=-0.487$). When compared the two aged groups, it was found a lower DNA repair capacity compared to the middle aged group ($p=0,027$). Conclusion: Although our results have not shown any association between age and DNA damage however the repair capacity was lower in the older age group compared to the middle age group. It was found that the ones who have a higher cardiorespiratory capacity, have also a lower DNA damage and lipid peroxidation probably due to their higher antioxidant capacity. These results enhance the importance of an active lifestyle to improve cardiorespiratory capacity and cell protection against ROS.

[1]Collins, A.R. (2004). Molecular biotechnology 26, 249-261. [2]Willis, E.D. (1987). In K. Snell (Ed.) Lipid and biological membranes in biochemical toxicology: a pratical approach (127-152). IRL Press. [3]Miller, N.J. and C.A. Rice-Evans (1997). Free Radic Res. 26(3): p. 195-9. *Funding by FCT for the research grant* ***SFRH/BD/66438/2009,*** *and the project* ***PTDC/DES/121575/2010****.*

TO WHAT EXTENT CAN PHYSICAL EXERCISE ATTENUATE AGEING PROCESS?

Z.A. dos Santos[1,2], J.P. Soares[2,3], A.F. Pereira[3,4], H. Andrade[2], R. Paixão[2], I. Gaivão[2,6], M.M. Oliveira[2,5], M.P. Mota[2,3]
[1]Faculty Metodista Granbery, Minas Gerais, Brazil; [2]University of Trás-os-Montes e Alto Douro, Vila Real, Portugal; [3]CIDESD; [4]Polytechnique Institute of Setúbal;[5]CQ; [6]CECAV

Introduction: Ageing process has been associated with an increase in oxidative stress, either due to an increase e reactive oxygen species production (ROS) and/or a decrease in antioxidant capacity[(1,2)].This imbalance often results in an accumulation of macromolecule damage that leads to cell physiological attrition and dysfunction. To face this

problem the prescription of antioxidant supplements is widely use, particularly between older subjects. However, some studies revealed some conflicting results once the increase in antioxidants consumption may also result in ROS increase and promote carcinogenesis[3]. On the other hand, endogenous antioxidant production usually occurs due to cell injury by ROS increase. As physical exercise can stimulate antioxidant capacity, we hypothesize that oxidative stress cell damage markers could decrease as a consequence of exercise related antioxidant protection increase. **Methods:** Twenty two women over 40 years of age (from 40 to 82 yrs: 52.8 ± 9.9), not suffering from any motor incapacity, participated in this study. All the subjects were submitted to a controlled physical exercise program which intensity and volume was continuously adjusted during 16 weeks, 3 times per week. Cardiovascular capacity was estimated through 6 minute walking test, DNA damage (strand breaks and FPG'sensitive sites) was measured by comet assay procedures[4] in peripheral blood mononuclear cells (PBMC), and Lipid peroxidation (estimated through TBARs test[5]) and Total Antioxidant capacity[6] were analyzed in plasma with the subjects in fasting conditions. All the described variables were assessed before and at the end of the exercise program. Descriptive data analysis and paired samples t-test were done in SPSS. Significant level was set at $p<0.05$. **Results:** All the subjects improved significantly their cardiovascular capacity ($t=-4.331$, $p=.000$) which proved the efficacy and the control of the exercise program. This controlled exercise program resulted in significant decrease in oxidative damage parameters ($t=3.416$, $p=.002$ for DNA strand breaks; $t=3.903$, $p=.000$ for DNA FPG'sensitive sites and $t=2.816$, $p=.013$ for TBARs) and increase in total antioxidant capacity ($t=-10.396$, $p=.000$). **Conclusion:** These results clearly confirm the benefits of physical exercise in reducing cell damage and increasing endogenous antioxidant production. These results pointed out the benefits of regularly physical exercise in the protection of cell damage by ROS. **References:** [1]Ghosh, S., R. Lertwattanarak, et al. (2011). Diabetes **60**(8): 2051-2060. [2]Wang, C. H., S. B. Wu, et al. (2013). Exp Biol Med (Maywood) **238**(5): 450-460. [3]Block, K. I. (2004)." Integr Cancer Ther **3**(4): 342-348. [4]Collins, A.R. (2004). Molecular biotechnology 26, 249-261. [5]Willis, E.D. (1987). In K. Snell (Ed.) Lipid and biological membranes in biochemical toxicology: a pratical approach (127-152). IRL Press. [6]Miller, N.J. and C.A. Rice-Evans (1997). Free Radic Res. 26(3): p. 195-9.

GENETIC VARIATION UNDERLYING COMMON HEREDITARY HYPERBILIRUBINAEMIA (GILBERT'S SYNDROME) AND RESPIRATORY HEALTH IN THE 1946 BRITISH BIRTH COHORT.

Laura J. Horsfall, Rebecca Hardy, Andrew Wong, Diana Kuh, Dallas M. Swallow

Research Department of Primary Care & Population Health, University College London Medical School, Royal Free Campus London NW3 2PF,.Tel: +44 (0) 207 794 0500, Fax: +44 (0) 207 794 1224 email: laura.horsfall@ucl.ac.uk

Background: Bilirubin has potent antioxidant properties and raised serum levels have been linked with lower rates of age-related diseases including respiratory disease. It is currently unknown whether the genetic variation underlying common hereditary hyperbilirubinemia (Gilbert's syndrome) is associated with differences in respiratory function. Objectives: To examine whether the genetic variation of uridine diphosphate glucuronosyltransferase (*UGT1A1*), which has a major influence on serum bilirubin levels, also influences respiratory function. Methods: Two functional variants of the *UGT1A1* regulatory region; rs8175347 (TA)n and rs4124874 c.-3279T>G were typed in 2,132 members of 1946 British birth cohort and regression models were fitted to examine the relationship with respiratory function. Results: The frequency of the low activity variants of rs8175347 and rs4124874 associated with raised bilirubin levels were 0.30 and 0.44 respectively. There was a statistically significant association between *UGT1A1* (TA)n genotypes and lung function at age 43, and an interaction with smoking status at age 53. Mean FEV1 and FVC at age 53 for heavy smokers (≥20 cigarettes per day) with *UGT1A1* (TA)n alleles underlying Gilbert's syndrome was 472 ml (95%CI: 228 to 715) and 580 ml (95%CI: 280 to 881) higher respectively compared with heavy smokers without these alleles. The odds of moderate to severe COPD by age 53 were less than half in those with the *UGT1A1* (TA)n alleles underlying Gilbert's syndrome (odds ratio 0.48 [95%CI: 0.26 to 0.88]). Conclusions: Alleles of *UGT1A1* that cause raised serum bilirubin are associated with increased lung function in adults suggesting raised bilirubin levels may

causally protect against age-related diseases.

Frequently asked questions about our events

- ***Is the delegate list available?***
  Yes this is available to everyone who attends the event and our sponsors.
  It is available in real time. To access the list please just log into your registration details or use the QR code on right of the agenda card which is provided on the day of the event.
  You will not be included in this list if you have opted out and you can do this by logging into your registration details. This list will not be sold or ever give out to third parties.
- ***Can I have the speakers slides?***
  We cannot give out the slides from our speaker's presentations as they are deleted immediately after each event. If you require a particular set of slides please approach the speaker. We will however have a meeting report and you will be emailed when this report is published.
- ***Can I have a notepad?***
  Notepads and pens are provided in the delegate bags and at the registration desk
- ***How can I keep up to date with Euroscicon Events?***
  To keep updated on our events and other Life Science News, please sign up for our newsletter at www.eurosciconnews.com
- ***I don't want my photograph on any Euroscicon promotional material***
  Please let our tech person know
- ***Is there WIFI?***
  Yes, please ask registration for log in details
- ***Can I have a CPD certificate?***
  Please leave your name with registration before the end of lunch a certificate will be created for you and available in the afternoon

Please remember that EuroSciCon is a small independent company with no subsidies from society memberships or academic rates for venues. We try to be as reasonably priced as possible and our delegate rates are substantially lower than comparable commercial meeting organisations.